

104. The Enantioselective Synthesis of β -Amino Acids, Their α -Hydroxy Derivatives, and the *N*-Terminal Components of Bestatin and Microginin

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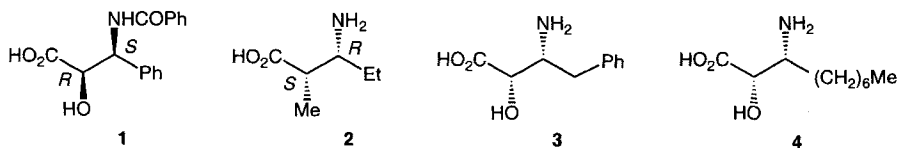
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L-Aspartic acid by tosylation, anhydride formation, and reduction with NaBH_4 was converted into (3*S*)-3-(tosylamino)butan-4-olide (**8**; Scheme 1). Treatment of **8** with ethanolic trimethylsilyl iodide gave the *N*-protected deoxy-iodo- β -homoserine ethyl ester **9**. The latter, on successive nucleophilic displacement with lithium dialkylcuprates ($\rightarrow$ **10a–e**), alkaline hydrolysis ($\rightarrow$ **11a–e**), and reductive removal of the tosyl group, produced the corresponding 4-substituted (3*R*)-3-aminobutanoic acids **12a–e** (ee > 99%). Electrophilic hydroxylation of **8** ($\rightarrow$ **19**; Scheme 3), subsequent iodo-esterification ($\rightarrow$ **21**; Scheme 4), and nucleophilic alkylation and phenylation afforded, after saponification and deprotection, a series of 4-substituted (2*S*,3*R*)-3-amino-2-hydroxybutanoic acids **24** including the *N*-terminal acids **24e** (= **3**) and **24f** (= **4**) of bestatin and microginin (de > 95%), respectively.

Introduction. – Although fairly rare, β -amino acids and their α -hydroxy derivatives are important because many of them occur in diverse natural products endowed with significant biological activity. Perhaps the most striking examples are provided by the potent anti-neoplastic agents, taxol [1] and the dolastatins [2], the activity of which depends on the constituent acids **1** and **2** having the ‘*syn*’ configuration. Also typical are bestatin, well-known as an immune-response modifier and inhibitor of aminopeptidase B [3], and microginin which inhibits angiotensin-converting enzyme [4]. The *N*-terminus of each molecule is composed of the ‘*syn*’ α -hydroxy- β -amino acids **3** and **4**, respectively. Apart from their intrinsic properties, β -amino acids are useful as intermediates for preparing β -lactams [5], piperidines [6], indolizidines [7], and modified peptides [8]. In view of their undeniable chemical and pharmaceutical potential, it is no surprise that much effort has been expended in devising enantioselective syntheses of β -amino acids in general [9] and of those specific to bestatin [10] and taxol [11] in particular.

Notwithstanding an apparent abundance of methods, we have discovered that (3*S*)-3-(*N*-tosylamino)butano-4-lactone (**8**), obtainable from L-aspartic acid (**5**), is a convenient template for constructing enantiomerically pure 2,4-disubstituted 3-aminobutanoic acids such as **2** [12]. We now describe fully how **8** and its (3*R*)-enantiomer **15** can be exploited

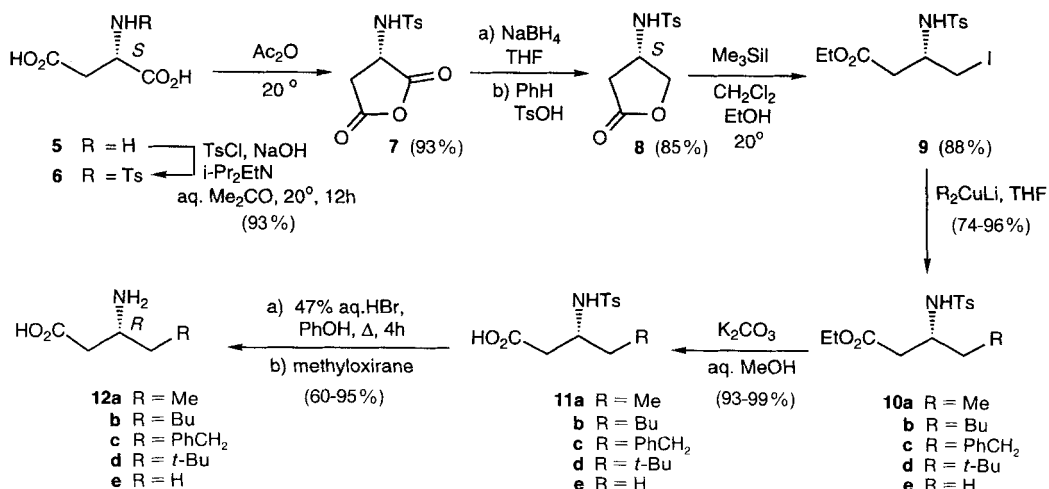


for preparing β -amino and α -hydroxy- β -amino acids of unquestionable configurational purity together with the components **3** and **4** of bestatin and microginin (for preliminary publications, see [13]).

Results and Discussion. – *β -Amino Acids.* First L-aspartic acid (**5**) was protected as its *N*-tolylsulfonyl (= tosyl; Ts) derivative **6**, converted to its anhydride **7** by lengthy exposure to Ac_2O , and then reduced with NaBH_4 to **8** in an overall yield of 74% (Scheme 1). Although care was taken to avoid heating, there was still a chance that some racemization might have occurred [14]. Consequently, the enantiomeric purity of **8** was verified by examining its ^1H -NMR spectrum at 200 MHz in the presence of the chiral shift reagent, $[\text{Eu}(\text{hfc})_3]$ (0.05M in CDCl_3). Only a single set of signals was observed in contrast to two for the corresponding lactone prepared from racemic aspartic acid.

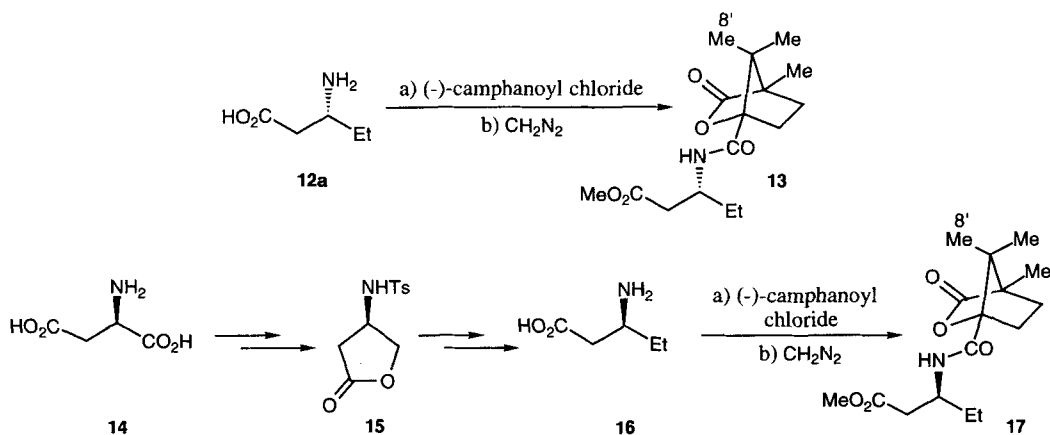
Next, submission of **8** to trimethylsilyl iodide in $\text{EtOH}/\text{CH}_2\text{Cl}_2$ under mild conditions [15] furnished the crucial deoxy-iodo- β -homoserine ester **9** in an overall yield of 65% from **5**. Nucleophilic substitution on **9** was carried out by adding it to a several-fold excess of the appropriate *Gilman* reagent or lithium organocuprate in THF at -40° . The Me, Bu, PhCH_2 , and even *t*-Bu groups were introduced in moderate to excellent yields to give the corresponding 4-substituted 3-(tosylamino)butanoates **10a–d**. The same procedure, when applied to lithium diphenylcuprate, was unsuccessful and caused β -elimination, presumably owing to the basicity of the reagent. Reductive de-iodination of **9** with tributyltin hydride proceeded normally to afford the parent ester **10e**. Alkaline hydrolysis of the esters **10a–e** to the (3*R*)-3-(tosylamino) acids **11a–e** was straightforward. Thereafter, the Ts group was removed reductively by heating in aqueous HBr solution and phenol, followed by treatment with methyloxirane [16], to furnish the target β -amino acids **12a–e** of (*R*)-configuration in overall yields of 35–42% and seven steps from L-aspartic acid (**5**; Scheme 1). All acids were characterized by negative optical rotations of similar magnitude, essentially proportional to molecular weight.

Scheme 1



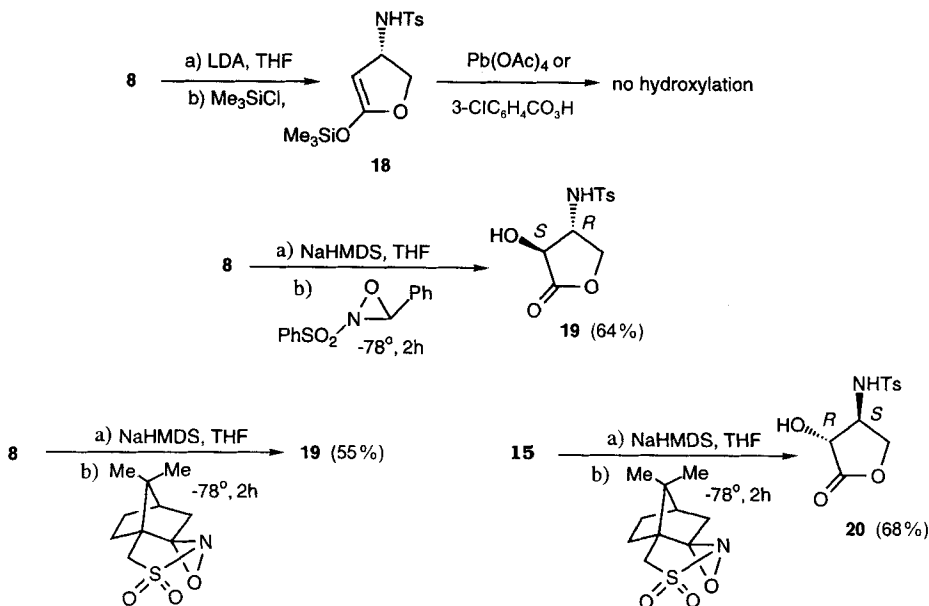
To ensure that the original chiral center had not been disturbed by exposure to base and acid, the enantiomeric purity of (3*R*)-3-aminopentanoic acid **12a** was compared with that of its (3*S*)-enantiomer **16** prepared by the same sequence of reactions from D-aspartic acid **14** via the (*R*)-lactone **15** (Scheme 2). It was reassuring to note that the optical rotations of the two acids were very nearly the same and of opposite sign. However, as a further check, the acids were converted to the *N*-camphanoyl methyl esters **13** and **17** by a standard procedure [17]. GC Analysis and examination of the ¹H-NMR spectra revealed that the diastereoisomers were clearly distinguishable, and that each was pure to greater than 99 %. It can, therefore, be concluded that the other acids in the series are also enantiomerically pure.

Scheme 2



α-Hydroxy-*β*-amino Acids. Apart from providing the 3-aminobutanoic structural element, the chiral template **8** lends itself ideally to diastereoselective functionalization at the C(2) position. Consequently, a logical approach to *α*-hydroxy-*β*-amino acids is to effect electrophilic hydroxylation. Disappointingly, several of the conventional reagents turned out to be unsatisfactory. *E.g.*, the trimethylsilyl-ether derivative **18** obtained from **8**, on treatment with 3-chloroperbenzoic acid [18] or lead tetracetate [19], led to recovery of **8** or the formation of complex mixtures (Scheme 3). Similarly, the successive treatment of **8** with 2 equiv. of sodium hexamethyldisilazide (NaHMDS) and bis(trimethylsilyl) peroxide in THF at -78° was equally ineffectual [20]. Fortunately, quenching of the dianion, derived from **8** under the same conditions, with racemic 3-phenyl-2-(phenylsulfonyl)oxaziridine [21] was largely successful. A single product, (2*S*,3*R*)-2-hydroxy-3-(tosylamino)butano-4-lactone (**19**), was formed in 64% yield (Scheme 3). The high diastereo-selectivity undoubtedly springs from the bulkiness of the amino substituent which forces the oxidant to attack the enolate in *trans* fashion, since no sign of any *cis* product was discerned. As the enolate is chiral, it was thought that a better yield might be achieved if the two reactants could be made to fit together more intimately. To this end, (+)-(camphorylsulfonyl)oxaziridine [22] was tried out on **8** and its (3*R*)-enantiomer **15**. The results were stereochemically identical. Only the *trans*-hydroxy lactones **19** and

Scheme 3

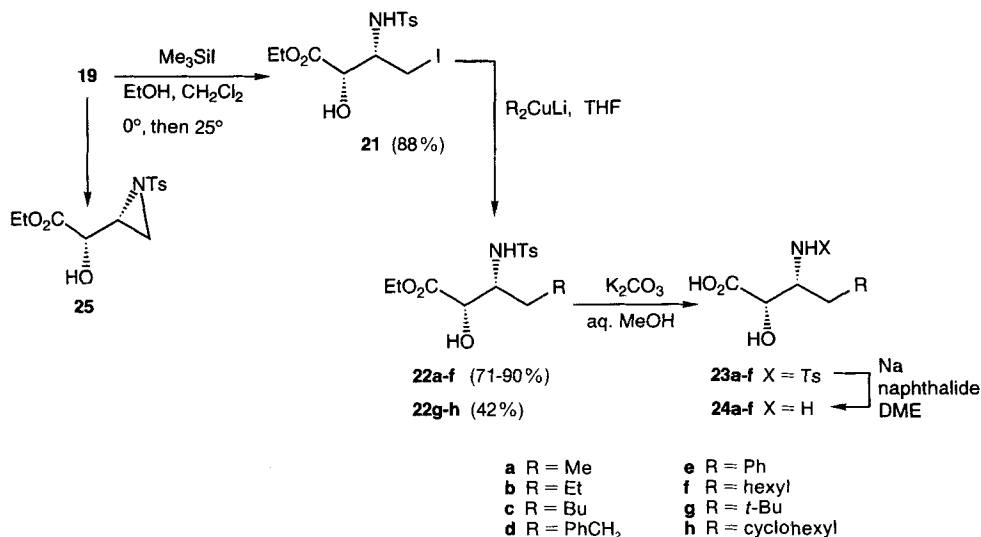


20 were formed in 55 and 68% yield, respectively. As expected, their optical rotations were perfectly complementary. Therefore, the matching or mismatching of the chiral partners was mechanistically insignificant.

Opening of **19** was brought about in the usual way by exposure to ethanolic trimethylsilyl iodide and gave the pivotal intermediate, ethyl (2*S*,3*S*)-2-hydroxy-4-iodo-3-(tosylamino)butanoate (**21**) in 88% yield (Scheme 4). It should be noted that the Ts group survives the preceding conditions, which would not have been the case for the usual carbamate protecting groups which are cleaved with trimethylsilyl chloride. Moreover, protection of the secondary OH group was not necessary. The tosylamino substituent has a further advantage, namely its lack of propensity to induce any competing *cis*-substitution through a proximity effect [23]. Such an effect is observed when carbamate-protected analogues of **8** are submitted to alkylation [24].

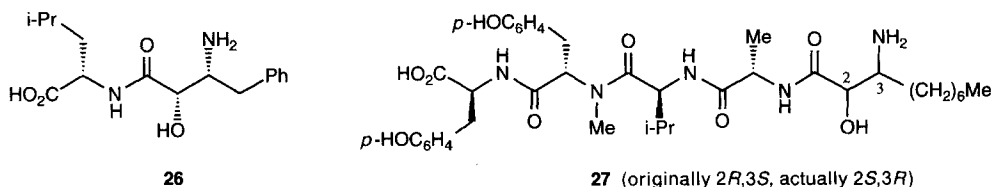
The butanoic chain was readily extended by adding **21** to various *Gilman* reagents in THF at low temperature. The introduction of Me, Et, Bu, and PhCH₂ groups proceeded smoothly to give **22a–d** in yields of 71–90%. Branched alkyl groups, *e.g.*, *t*-Bu and cyclohexyl, encountered some resistance as evidenced by yields of *ca.* 42% for **22g, h**. In contrast, the preparation and reaction of lithium diphenylcuprate under various conditions invariably led to β -elimination. However, by the simple expedient of allowing the reactants to stand for 1.5 h at 0° with stirring after initial mixing at -78°, phenylation to give **22e** was accomplished in 86% yield [25]. It appears that the first step entails the base-promoted formation of the aziridine **25**, which is only opened up by a second molecule of cuprate at the higher temperature. In fact, **25** was previously observed as a steady state during the reaction of **21** with morpholine [26]. The *N*-protected esters **22a–e** so obtained were then hydrolyzed with aqueous methanolic K₂CO₃ solution as before to

Scheme 4



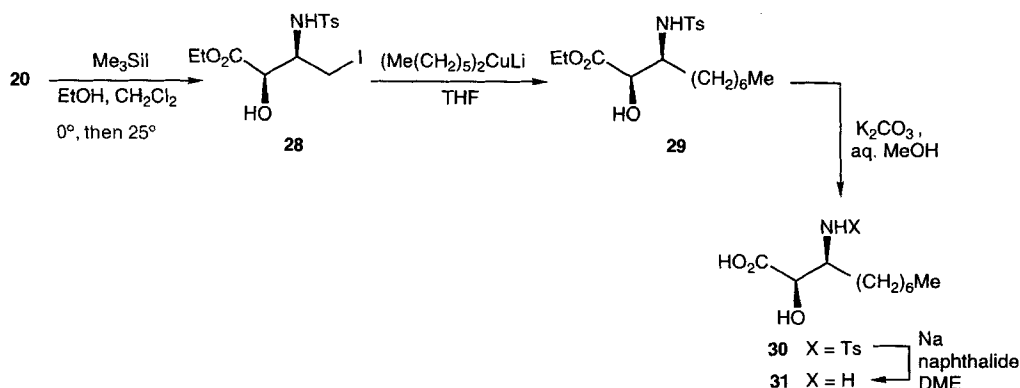
the α -hydroxy- β -tosylamino acids **23a–e**. Finally, in order to prevent elimination of the OH substituent, reductive deprotection was effected with sodium naphthalide in 1,2-dimethoxyethane (DME) [27] whereupon the desired (2*S*,3*R*)-3-amino-2-hydroxy-4-substituted butanoic acids **24a–e** were delivered in overall yields of 10–27% and some eight steps from L-aspartic acid (**5**). Inspection of the ¹H-NMR spectra revealed that they were single diastereoisomers. Their specific rotations were all negative, with the exception of that of phenylbutanoic acid **24e**.

Acid **24e** (= **3**) is the non-leucine part of bestatin (**26**) and has already been prepared by many different methods [10]. The spectral and physical data of the present sample were found to be identical to those previously reported. The procedure itself compares well with the others in being economical and highly diastereoselective.



It is obvious that **21** can be employed for making many other α -hydroxy- β -amino acids of 'syn' configuration. Furthermore, their enantiomeric counterparts will be just as accessible by performing the same reactions on the enantiomeric iodo ester **28** obtainable by opening the hydroxy lactone **20** (Scheme 5). The availability of a pair of products having opposite, but unequivocal configurations provides a means of verifying structures where uncertainty exists.

Scheme 5



Such a case is provided by the N-terminal acid of microginin (**27**). The latter is a linear pentapeptide, isolated from the fresh-water, blue-green alga, *Microcystis aeruginosa* [4]. Originally, the configuration at C(2) was proposed as (*R*) since the corresponding acid, obtained by hydrolysis, gave a CD spectrum in MeOH solution characterized by a negative Cotton effect at 215 nm. That of the NH₂-substituted C(3) was unassigned. We assumed it to be (*S*) on the basis of the generally observed 'syn' configuration of such acids, as exemplified by the C(13) side chain of taxol. Accordingly, in order to confirm the structure, we undertook the synthesis of both 'syn' diastereoisomers, the (2*S*,3*R*)- and (2*R*,3*S*)-3-amino-2-hydroxydecanoic acids (**4** and **31**, resp.). Treatment of **21** with lithium dihexylcuprate in the customary manner gave the ethyl decanoate **22f** in 93% yield (Scheme 4). Alkaline hydrolysis furnished **23f** and deprotection with sodium naphthalide in DME **24f** (= **4**) in 78% yield. The same procedure applied to **28** gave **31** in comparable yield *via* ester **29** and the tosylamino acid **30** (Scheme 5). Acids **4** and **31** were obtained in an overall yield of 30% from aspartic acid. They had similar melting points and their specific rotations were complementary and concordant with the configurations of other members of the aliphatic series, *viz.* **24a–e**. Comparison of their ¹H- and ¹³C-NMR spectra with those of the natural acid confirmed that it had the 'syn' configuration. The chemical shift and coupling constant of H–C(2), 3.56 ppm in (D₆)DMSO and 3.3 Hz, were characteristic of the 'syn' configuration of the C(2)–C(3) fragment.

The same 'syn' acids, together with the 'anti' diastereoisomers, have also been recently prepared in two different ways by the formal amination-hydroxylation of (*E*)-decanoate. In the first method [28], chirality was conferred by catalytic asymmetric dihydroxylation, whereas in the second [29], it was induced by *Michael* addition of a chiral amide with either tandem or sequential hydroxylation. The size and sign of the specific rotation exhibited by the 'syn' isomers **4** and **31** obtained by asymmetric dihydroxylation and our method are in excellent agreement (Table, Entries 4 and 5). However, there is a big discrepancy between the melting points (Entries 1 and 2). On the other hand, the melting points of the (2*S*,3*R*)-isomer **4** produced by *Michael* addition and our method are about the same (Entries 1 and 3). Unfortunately, the small positive rotations reported for both the (2*R*,3*R*)- and (2*S*,3*R*)-isomers prepared by *Michael* addition (Entry

Table. Melting Points and Specific Rotations of the Diastereoisomers of 3-Amino-2-hydroxydecanoic Acid Prepared by Different Methods

Entry ^{a)}	(2 <i>R</i> ,3 <i>R</i>)-Isomer	(2 <i>R</i> ,3 <i>S</i>)-Isomer 31	(2 <i>S</i> ,3 <i>S</i>)-Isomer	(2 <i>S</i> ,3 <i>R</i>)-Isomer 4
1	–	215–216°	–	211–214°
2	m.p. {	183–186°	152–156°	189–193°
3				
		225°	–	219–220°
4	[α] _D ^{23–25°} {	+34.7 (<i>c</i> = 0.46, <i>B</i>) ^{b)}	+6.0 (<i>c</i> = 0.25, <i>A</i>) ^{b)}	–5.5 (<i>c</i> = 0.37, <i>A</i>) ^{b)}
5				
6				
		+9.0 (<i>c</i> = 0.11, <i>B</i>) ^{b)}	–34.5 (<i>c</i> = 0.47, <i>B</i>) ^{b)}	–8.8 (<i>c</i> = 0.19, <i>B</i>) ^{b)}
		+3.4 (<i>c</i> = 0.7, <i>C</i>) ^{b)}	–	+5.4 (<i>c</i> = 0.59, <i>C</i>) ^{b)}

^{a)} Entries 1 and 4, this work; Entries 2 and 5, [28]; Entries 3 and 6, [29]. ^{b)} Solvents: *A* = 0.1*N* HCl/MeOH 1:2, *B* = MeOH, *C* = 1*N* HCl.

6) are not substantiated by the other data (Entries 4 and 5) and are incompatible with the designated structures. The size of the rotation for the (2*R*,3*R*)-isomer is too small, while the sign for the (2*S*,3*R*)-isomer should be negative (*cf.* Entries 4–6). The correct configuration of the N-terminal acid of microginin was unambiguously established by synthesis using asymmetric dihydroxylation and shown to be that of **4** [28], the opposite of that originally suggested.

Conclusion. – The preceding results demonstrate that L- and D-aspartic acids are easily convertible into the enantiomeric 3-(tosylamino)butano-4-lactones which serve as versatile templates for preparing β -amino acids and their α -hydroxy derivatives of ‘*syn*’ configuration in optically pure form. The key steps are the highly diastereoselective α -hydroxylation of the lactone and its subsequent opening to the reactive deoxy-iodo- β -homoserine ester thereby providing access, by appropriate nucleophilic substitution, to a wide range of molecules of biological significance. Although not performed, the ‘*syn*’ cyclohexylnorstatines which are important for synthesizing renin inhibitors [30], should be readily available from the esters **22h** and its enantiomer by saponification and deprotection.

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Experimental Part

General. See [12]. CC = Column chromatography; tosyl = tolylsulfonyl = (4-methylphenyl)sulfonyl. IR: in CHCl₃. NMR: in CDCl₃, except where noted. Solvents were either *puriss.* grade (*Fluka* or *Aldrich*) or distilled prior to use. Benzene, Et₂O, and THF were dried over Na-benzophenone and freshly distilled before use. Solns. of MeLi in Et₂O, BuLi in hexane, and *t*-BuLi in pentane were obtained from *Fluka*; solns. of PhLi in cyclohexane/Et₂O 70:30 (v/v), and cyclohexylmagnesium chloride in Et₂O from *Aldrich*. CuI and CuBr were purified before use according to a standard procedure [31].

(2*S*)-N-Tosylaspartic Acid (= (2*S*)-2-(Tosylamino)butanedioic Acid; **6**). To a soln. of L-aspartic acid (**5**; 2.0 g, 15.0 mmol) in aq. NaOH soln. (16 ml, 1.2 g, 30 mmol) at 0° was added toluene-4-sulfonyl chloride (3.16 g, 16.5 mmol), followed by (*i*-Pr)₂EtN (2.13 g, 16.5 mmol) and acetone (16 ml). After stirring for 10 min, a clear soln. formed which was stirred overnight at r.t. The soln. was washed (Et₂O, 2 × 10 ml), the combined Et₂O phase extracted with 5% aq. NaOH soln. (5 ml), and the combined basic aq. phase acidified at –10° with conc. aq. HCl

soln. to pH 1. The acidic aq. phase was extracted with Et₂O (4 × 10 ml) and the combined extract dried (MgSO₄) and evaporated: **6** (3.95 g, 92%). White solid. M.p. 114–116° (recryst., CHCl₃). $[\alpha]_D^{20} = +1.6$ ($c = 1.0$, AcOH). IR: 3247, 3032, 2933, 1730, 1406, 1340, 1161, 1094, 814. ¹H-NMR ((D₆)acetone): 7.76 (*d*, $J = 8.3$, 2 H); 7.35 (*d*, $J = 7.9$, 2 H); 4.24 (*t*, $J = 5.4$, 1 H); 3.64–3.50 (*m*, 1 H); 2.78 (*d*, $J = 5.7$, 2 H); 2.39 (*s*, 3 H). Anal. calc. for C₁₁H₁₃N₂O₆S: C 45.99, H 4.56, N 4.88; found: C 45.70, H 4.71, N 4.80.

(3*S*)-3-(*Tosylamino*)butano-4-lactone (= (3*S*)-4,5-dihydro-4-(*tosylamino*)furan-2(3*H*)-one; **8**). Acid **6** was converted to anhydride **7** and then to **8** according to our procedure described in [12].

(3*R*)-3-(*Tosylamino*)butano-4-lactone (**15**). D-Aspartic acid (**14**) was protected as the *N*-tosyl derivative and converted to **15** as described for **6** and **8**, resp.

(3*S*)-Ethyl 4-Iodo-3-(*tosylamino*)butanoate (**9**). To a soln. of **8** (13.1 g, 51.4 mmol) in dry CH₂Cl₂ (150 ml) containing abs. EtOH (15 ml) at 0° under N₂ was added Me₃SiI (21.3 ml, 156 mmol) by syringe [15]. The soln. was stirred at r.t. for 5.5 h. H₂O was added and stirring continued for 5 min. The org. layer was washed (5% aq. Na₂S₂O₃ soln. and H₂O), dried (MgSO₄), and evaporated and the crude product (21 g) recrystallized from Et₂O/hexane: **9** (18.28 g, 88%). Colorless crystals. M.p. 49–60°. $[\alpha]_D^{20} = -7.59$ ($c = 0.87$, CHCl₃). IR: 3360, 3033, 2988, 1725, 1413, 1340, 1159, 1091, 1024, 954, 813. ¹H-NMR: 7.77 (*d*, $J = 8.3$, 2 H); 7.32 (*d*, $J = 8.3$, 2 H); 5.43 (*d*, $J = 8.9$, 1 H); 4.06 (*qd*, $J = 7.1$, 2.4, 2 H); 3.56 (*m*, 1 H); 3.32 (*dd*, $J = 10.3$, 4.1, 1 H); 3.22 (*dd*, $J = 10.3$, 6.6, 1 H); 2.69 (*dd*, $J = 16.6$, 5.2, 1 H); 2.55 (*dd*, $J = 16.6$, 6.1, 1 H); 2.43 (*s*, 3 H); 1.23 (*t*, $J = 7.1$, 3 H). ¹³C-NMR: 170.31, 143.75, 137.40, 129.76, 127.04, 61.04, 50.47, 38.90, 21.50, 13.98, 10.53. MS: 412 (1, [*M* + I]⁺), 284 (14, [*M* – 128]⁺), 270 (17), 155 (43), 91 (100). Anal. calc. for C₁₃H₁₈INO₄S: C 37.97, H 4.41, N 3.41; found: C 38.00, H 4.36, N 3.49.

(3*R*)-Ethyl 3-(*Tosylamino*)pentanoate (**10a**). To a homogeneous soln. of Me₂CuLi (10.9 mmol; prepared from CuI and 1.6*M* MeLi in Et₂O) in dry THF (30 ml) at –40° was added **9** (1.0 g, 2.43 mmol) in dry THF (30 ml). The mixture was stirred for 6 h and then quenched with sat. aq. NH₄Cl soln. and extracted (Et₂O). The Et₂O extract was washed (brine), dried (MgSO₄), and evaporated. The resulting crude oil was subjected to flash chromatography (FC; SiO₂, hexane/AcOEt 3:2): **10a** (0.568 g, 77%). Colorless oil. $[\alpha]_D^{20} = +36.5$ ($c = 1.6$, CHCl₃). IR: 3300, 2996, 2893, 1740, 1606, 820. ¹H-NMR: 7.76 (*d*, $J = 8.0$, 2 H); 7.27 (*d*, $J = 8.0$, 2 H); 5.35 (*d*, $J = 8.8$, 1 H); 4.03 (*qd*, $J = 7.1$, 1.5, 2 H); 3.45 (*m*, 1 H); 2.40 (*s*, 3 H); 2.35 (*dd*, $J = 5.6$, 1.4, 2 H); 1.46 (*dt*, $J = 14.4$, 7.2, 2 H); 1.21 (*t*, $J = 7.1$, 3 H); 0.76 (*d*, $J = 7.5$, 3 H). ¹³C-NMR: 171.32, 143.22, 138.12, 129.59, 126.99, 60.64, 52.18, 38.35, 27.70, 21.46, 14.05, 10.22. MS: 299 (0.88, *M*⁺), 270 (100, [*M* – Et]⁺), 224 (13). Anal. calc. for C₁₄H₂₁NO₄S: C 56.17, H 7.07, N 4.68; found: C 55.98, H 7.14, N 4.52.

(3*R*)-Ethyl 3-(*Tosylamino*)octanoate (**10b**). As described for **10a**, with Bu₂CuLi (5 ml, 4 equiv.; prepared from CuBr and 1.6*M* BuLi in hexane) and **9** (0.200 g, 0.48 mmol): **10b** (0.178 g, 76%). Colorless oil. $[\alpha]_D^{20} = +23.5$ ($c = 1.3$, CHCl₃). IR: 3384, 2930, 2861, 1729, 1415, 1343, 1164, 1092, 1030, 964. ¹H-NMR: 7.73 (*d*, $J = 8.0$, 2 H); 7.25 (*d*, $J = 8.0$, 2 H); 5.28 (*d*, $J = 9.0$, 1 H); 4.03 (*q*, $J = 7.1$, 2 H); 3.49 (*m*, 1 H); 2.39 (*s*, 3 H); 2.36 (*dd*, $J = 5.8$, 3.2, 2 H); 1.48–1.08 (*m*, 8 H); 1.19 (*t*, $J = 7.1$, 3 H); 0.77 (*d*, $J = 6.4$, 3 H). ¹³C-NMR: 171.31, 138.05, 129.54, 126.99, 60.58, 50.62, 38.87, 34.57, 31.13, 25.28, 22.32, 21.42, 14.04, 13.80. MS: 341 (2, *M*⁺), 270 (100), 254 (27), 224 (13), 186 (26), 155 (44), 91 (76). Anal. calc. for C₁₇H₂₇NO₄S: C 59.80, H 7.97, N 4.10; found: C 59.40, H 7.71, N 4.04.

(3*R*)-Ethyl 5-Phenyl-3-(*tosylamino*)pentanoate (**10c**). As described for **10a**, with (PhCH₂)₂CuLi (20 ml, 4 equiv.; prepared from CuBr·Me₂S and PhCH₂Li (prepared from 0.87*M* PhCH₂OEt in Et₂O/THF 1:2)) and **9** (0.600 g, 1.44 mmol) in THF (15 ml): **10c** (0.693 g, 91%). Colorless oil. The product was used without purification in the next step.

(3*R*)-Ethyl 5,5-Dimethyl-3-(*tosylamino*)hexanoate (**10d**). As described for **10a**, with (*t*-Bu)₂CuLi (4 equiv.) and **9** (0.500 g, 1.2 mmol). The resulting crude oil was purified by FC (2×, silica gel, hexane/AcOEt 2:1): **10d** (0.307 g, 74%). Colorless oil. $[\alpha]_D^{20} = +33.6$ ($c = 1.1$, CHCl₃). IR: 3286, 2956, 1729, 1417, 1343, 1161, 1093, 1027, 951, 866. ¹H-NMR: 7.76 (*d*, $J = 8.0$, 2 H); 7.29 (*d*, $J = 8.0$, 2 H); 5.31 (*d*, $J = 8.0$, 1 H); 4.10 (*q*, $J = 7.2$, 2 H); 3.71 (*m*, 1 H); 2.42 (*s*, 3 H); 2.34 (*d*, $J = 4.6$, 2 H); 1.47 (*dd*, $J = 13.0$, 7.6, 1 H); 1.26 (*dd*, $J = 13.0$, 3.5, 1 H); 1.22 (*t*, $J = 7.2$, 3 H); 0.84 (*s*, 9 H). ¹³C-NMR: 171.48, 143.31, 138.34, 129.63, 127.05, 60.57, 48.56, 48.00, 40.28, 30.35, 29.63, 21.48, 14.10. MS: 341 (3, *M*⁺), 270 (100), 254 (26), 198 (20), 186 (33), 155 (82), 91 (99). Anal. calc. for C₁₇H₂₇NO₄S: C 59.80, H 7.97, N 4.10; found: C 59.79, H 7.95, N 4.07.

(3*R*)-Ethyl 3-(*Tosylamino*)butanoate (**10e**). Bu₃SnH (0.580 g, 1.95 mmol) was added by syringe under N₂ to a soln. of **8** (0.800 g, 1.95 mmol) and azobis[isobutyronitrile] (AIBN) (80 mg, 0.49 ml) in dry benzene (60 ml) which had been previously degassed with N₂ for 5 min. The soln. was then heated under reflux for 4 h, cooled to r.t., and evaporated. The resulting oily mixture was purified by FC (2×, silica gel, hexane/AcOEt 2:1): **10e** (0.368 g, 66%). Colorless oil. $[\alpha]_D^{20} = +28.1$ ($c = 1.0$, CHCl₃). IR: 3374, 3271, 2981, 1732, 1346, 1163, 1091, 813. ¹H-NMR: 7.75 (*d*, $J = 8.4$, 2 H); 7.28 (*d*, $J = 8.4$, 2 H); 5.28 (*d*, $J = 8.4$, 1 H); 4.05 (*qd*, $J = 7.1$, 1.4, 2 H); 3.67 (*m*, 1 H); 2.40 (*s*, 3 H); 2.39 (*dd*, $J = 5.10$, 0.89, 2 H); 1.20 (*t*, $J = 7.1$, 3 H); 1.12 (*d*, $J = 6.7$, 3 H). ¹³C-NMR: 171.12, 143.27, 137.91,

129.62, 126.96, 60.67, 46.55, 40.66, 21.45, 20.97, 14.05. MS: 270 (8, $[M - 15]^+$), 198 (6), 155 (77), 130 (91), 91 (100). Anal. calc. for $C_{13}H_{19}NO_4S$: C 54.72, H 6.71, N 4.91; found: C 54.54, H 6.64, N 4.90.

Hydrolysis of Esters 10a–e: General Procedure. To a soln. of the ester (2.0 mmol) in MeOH (10 ml) was added K_2CO_3 (0.550 g, 4.0 mmol) in H_2O (5 ml). The soln. was stirred at r.t. for 24 h, washed with Et_2O , and acidified with conc. aq. HCl soln. to pH 2. The mixture was extracted (Et_2O , 3 $\times$ 10 ml) and the extract washed (H_2O), dried ($MgSO_4$), and evaporated to give **11a–e**.

(3R)-3-(Tosylamino)pentanoic Acid (**11a**): Colorless solid (93%). M.p. 116–118°. $[\alpha]_D^{20} = +37.9$ ($c = 1.0$, $CHCl_3$). IR: 3376, 3029, 1718, 1414, 1333, 1234, 1201, 1158, 1092, 805. 1H -NMR: 7.75 (d , $J = 8.2$, 2 H); 7.28 (d , $J = 8.2$, 2 H); 5.50 (d , $J = 9.0$, 1 H); 3.50–3.36 (m , 1 H); 2.48 (d , $J = 0.79$, 1 H); 2.46 (d , $J = 1.4$, 1 H); 2.40 (s , 3 H); 1.51 (dt , $J = 14.4$, 7.3, 2 H); 0.77 (t , $J = 7.3$, 3 H). ^{13}C -NMR: 176.62, 143.49, 137.74, 129.70, 127.02, 51.92, 38.36, 27.57, 21.53, 10.30. MS: 271 (0.3, M^+), 242 (32), 212 (5), 155 (46), 91 (100). Anal. calc. for $C_{12}H_{17}NO_4S$: C 53.12, H 6.32, N 5.16; found: C 53.16, H 6.24, N 5.01.

(3R)-3-(Tosylamino)octanoic Acid (**11b**): Colorless solid (95%). M.p. 103–105°. $[\alpha]_D^{20} = +21.6$ ($c = 1.0$, $CHCl_3$). IR: 3378, 3031, 1720, 1418, 1207, 1158, 798. 1H -NMR: 7.75 (d , $J = 8.4$, 2 H); 7.27 (d , $J = 8.4$, 2 H); 5.41 (d , $J = 9.1$, 1 H); 3.49 (m , 1 H); 2.48 (d , $J = 5.1$, 2 H); 2.40 (s , 3 H); 1.46 (m , 2 H); 1.10 (m , 6 H); 0.78 (t , $J = 6.9$, 3 H). ^{13}C -NMR: 176.53, 143.45, 137.71, 129.63, 127.01, 50.32, 38.71, 34.42, 31.09, 25.37, 22.34, 21.45, 13.80. MS: 313 (0.3, M^+), 254 (6), 242 (43), 158 (12), 155 (53), 91 (100). Anal. calc. for $C_{15}H_{23}NO_4S$: C 57.49, H 7.40, N 4.47; found: C 57.24, H 7.40, N 4.50.

(3R)-5-Phenyl-3-(tosylamino)pentanoic Acid (**11c**): Colorless solid (86% from **8**). M.p. 116–118°. $[\alpha]_D^{20} = -2.5$ ($c = 1.0$, $CHCl_3$). IR: 3365, 3035, 1721, 1603, 1333, 1207, 1155, 792. 1H -NMR: 7.74 (d , $J = 8.2$, 2 H); 7.32–7.01 (m , 7 H); 5.64 (d , $J = 9.3$, 1 H); 3.55 (m , 1 H); 2.62–2.40 (m , 4 H); 2.41 (s , 3 H); 1.82 ($br. q$, 2 H). ^{13}C -NMR: 176.19, 143.63, 140.70, 137.72, 129.80, 128.43, 128.28, 127.07, 126.07, 50.01, 38.38, 36.10, 32.06, 21.55. MS: 347 (2, M^+), 288 (1), 242 (8), 176 (23), 155 (20), 117 (15), 91 (100), 88 (95). Anal. calc. for $C_{18}H_{21}NO_4S$: C 62.23, H 6.09, N 4.03; found: C 62.28, H 6.07, N 3.98.

(3R)-5,5-Dimethyl-3-(tosylamino)hexanoic Acid (**11d**): Colorless solid (94%). M.p. 108–110°. $[\alpha]_D^{20} = +39.2$ ($c = 1.1$, $CHCl_3$). IR: 3367, 3026, 2953, 1919, 1414, 1332, 1223, 1195, 1152, 1087, 1038, 804. 1H -NMR: 7.75 (d , $J = 8.4$, 2 H); 7.32 (d , $J = 8.4$, 2 H); 5.35 (d , $J = 9.2$, 1 H); 3.67 (m , 1 H); 2.45 (d , $J = 4.6$, 2 H); 2.42 (s , 3 H); 1.50 (dd , $J = 14.6$, 7.4, 1 H); 1.35 (dd , $J = 14.6$, 4.4, 1 H); 0.81 (s , 9 H). ^{13}C -NMR: 176.73, 143.59, 137.92, 129.75, 127.08, 48.48, 47.64, 40.30, 30.35, 29.60, 21.54. MS: 313 (1, M^+), 242 (100), 198 (14), 155 (77), 91 (84). Anal. calc. for $C_{15}H_{23}NO_4S$: C 57.48, H 7.40, N 4.47; found: C 57.48, H 7.47, N 4.55.

(3R)-3-(Tosylamino)butanoic Acid (**11e**): Colorless oil (100%). $[\alpha]_D^{20} = +25.8$ ($c = 1.1$, $CHCl_3$). IR: 3248, 3030, 2930, 1715, 1600, 1411, 1335, 1158, 1091. 1H -NMR: 7.75 (d , $J = 8.2$, 2 H); 7.28 (d , $J = 8.2$, 2 H); 5.60 (d , $J = 8.6$, 1 H); 3.68 (m , 1 H); 2.48 (d , $J = 5.4$, 2 H); 2.40 (s , 3 H); 1.12 (d , $J = 6.7$, 3 H). ^{13}C -NMR: 175.83, 143.55, 137.63, 129.76, 127.01, 46.33, 40.59, 21.25, 20.81. MS: 242 (18, $[M - 15]^+$), 198 (99), 155 (71), 102 (46), 91 (10). HR-MS: 242.0864 ($[C_{11}H_{15}NO_4S - Me]^+$; calc. 242.0869).

Deprotection of (3R)-3-Tosylamino Acids 11a–e: General Procedure. A mixture of the acid (0.82 mmol), phenol (0.245 g), and freshly distilled 47% aq. HBr soln. (3.0 ml) was heated under reflux for 4 h [16]. After cooling, the mixture was washed (AcOEt) and then the aq. phase evaporated. The crude hydrobromide so obtained (0.190 g) was then dissolved in dry EtOH (10 ml) and methyloxirane (2 ml). The resulting soln. was heated under reflux for 2 h. Evaporation gave the β -amino acids **12a–e**.

(3R)-3-Aminopentanoic Acid (**12a**): Colorless solid (92%). M.p. 181–183° ([32]: 180–182°). $[\alpha]_D^{20} = -38.6$ ($c = 1.1$, H_2O) ([32]: $[\alpha]_D = -37$ ($c = 0.7$, H_2O)). 1H -NMR (200 MHz, D_2O): 3.23 (m , 1 H); 2.38 (dd , $J = 16.6$, 5.1, 1 H); 2.22 (dd , $J = 16.6$, 8.1, 1 H); 1.48 (m , 2 H); 0.78 (t , $J = 7.4$, 3 H). Anal. calc. for $C_5H_{11}NO_2$: C 51.26, H 9.46, N 11.96; found: C 50.99, H 9.22, N 11.88.

(3R)-3-Aminooctanoic Acid (**12b**): Colorless solid (77%). M.p. 175–180° ([32]: 175–179°). $[\alpha]_D^{20} = -31.1$ ($c = 0.51$, H_2O) ([32]: $[\alpha]_D = -22$ ($c = 0.5$, $H_2O/MeOH$ 1:1)). 1H -NMR (D_2O): 3.36–3.27 (m , 1 H); 2.31 (dd , $J = 16.5$, 4.8, 1 H); 2.26 (dd , $J = 16.5$, 8.0, 1 H); 1.45 (dd , $J = 15.4$, 7.0, 2 H); 1.27–1.08 (m , 6 H); 0.69 (t , $J = 7.0$, 3 H). ^{13}C -NMR (100 MHz, D_2O): 179.15, 50.41, 39.44, 32.94, 31.46, 24.94, 22.51, 14.05. MS: 159 (4, M^+), 288 (1), 130 (3), 100 (13), 88 (100), 70 (32).

(3R)-3-Amino-5-phenylpentanoic Acid (**12c**): Colorless solid (95%). M.p. 215–217°. $[\alpha]_D^{20} = -28.4$ ($c = 0.56$, H_2O). 1H -NMR (200 MHz, D_2O): 7.38–7.15 (m , 5 H); 3.42 (m , 1 H); 2.72 (t , $J = 8.1$, 2 H); 2.60 (dd , $J = 16.8$, 4.1, 1 H); 2.40 (dd , $J = 16.8$, 8.9, 1 H); 1.92 (m , 2 H). Anal. calc. for $C_{11}H_{15}NO_2$: C 68.37, H 7.82, N 7.25; found: C 68.15, H 7.81, N 7.25.

(3R)-3-Amino-5,5-dimethylhexanoic Acid (**12d**): Colorless solid (60%). M.p. 200–202°. $[\alpha]_D^{20} = -32.5$ ($c = 1.2$, H_2O). 1H -NMR (200 MHz, D_2O): 3.38 (m , 1 H); 2.42 (dd , $J = 16.9$, 4.3, 1 H); 2.26 (dd , $J = 16.9$, 8.3, 1 H);

1.38 (*t*, *J* = 4.6, 2 H); 0.77 (*s*, 9 H). Anal. calc. for $C_8H_{17}NO_2$: C 60.35, H 10.76, N 8.80; found: C 60.08, H 10.3, N 8.75.

(3*R*)-3-Aminobutanoic Acid (**12e**): Colorless solid (89%). M.p. 200–202° ([33]: 212° for (*S*)-enantiomer). $[\alpha]_D^{20} = -39.6$ (*c* = 0.53, H_2O) ([34]: $[\alpha]_D = -39.8$ (*c* = 0.47, H_2O)). ¹H-NMR (200 MHz, D_2O): 3.37 (*m*, 1 H); 2.28 (*d*, *J* = 0.4, 1 H); 2.25 (*d*, *J* = 1.4, 1 H); 1.09 (*d*, *J* = 6.70, 3 H). Anal. calc. for $C_4H_9NO_2$: C 46.59, H 8.80, N 13.58; found: C 46.44, H 8.99, N 13.4.

Methyl (3*R*)-3-{[(1*S*,4*R*)-4,7,7-Trimethyl-3-oxo-2-oxabicyclo[2.2.1]hept-1-yl]carbonylamino}pentanoate (**13**). (–)-(1*S*,4*R*)-Camphanoyl chloride (= (1*S*,4*R*)-4,7,7-trimethyl-3-oxo-2-oxabicyclo[2.2.1]hept-1-ylcarbonyl chloride; 56 mg, 0.26 mmol) was added to **12a** (15 mg, 0.13 mmol) in 1*M* $NaHCO_3/Na_2CO_3$ buffer (pH 10; 3 ml) and toluene (0.5 ml) [17]. The mixture was vigorously stirred for 2 h and then acidified to pH 1 with 5% aq. HCl soln. Extraction (CH_2Cl_2 , 3 × 5 ml), drying of the combined org. extracts ($MgSO_4$), and evaporation gave a residue which was treated with excess CH_2H_2 in Et_2O for 15 min. Evaporation of the org. phase gave a crude product which was purified by FC (silica gel, hexane/AcOEt 1:1): **13** (22.5 mg, 51%). Colorless solid. M.p. 55–57°. $[\alpha]_D^{20} = +6.8$ (*c* = 0.69, $CHCl_3$). IR: 3694, 3418, 3026, 2957, 1785, 1734, 1672, 1528, 1231, 1175, 1014, 921. ¹H-NMR: 6.64 (*br. d*, 1 H); 3.66 (*s*, 3 H); 2.55–2.51 (*m*, 3 H); 1.92–1.69 (*m*, 2 H); 1.69–1.58 (*m*, 4 H); 1.11 (*s*, 3 H); 1.10 (*s*, 3 H); 0.94 (*t*, *J* = 7.0, 3 H); 0.90 (*s*, $Me(8'')$). MS: 311 (26, M^+), 282 (56), 264 (14), 238 (37), 198 (41), 172 (14), 153 (30), 130 (59), 109 (67), 83 (100). Anal. calc. for $C_{16}H_{25}NO_5$: C 61.72, H 8.09, N 4.50; found: C 61.31, H 8.16, N 4.14.

Methyl (3*S*)-3-{[(1*S*,4*R*)-4,7,7-Trimethyl-3-oxo-2-oxabicyclo[2.2.1]hept-1-yl]carbonylamino}pentanoate (**17**). A sample of (3*S*)-3-aminopentanoic acid (**16**) was prepared from lactone **15** and treated as described for **13**: **17** (50%). Colorless oil. $[\alpha]_D^{20} = -45.1$ (*c* = 0.77, $CHCl_3$). IR: 3411, 3022, 2964, 1785, 1734, 1670, 1528, 1234, 1196, 1054, 918. ¹H-NMR: 6.71 (*br. d*, 1 H); 3.68 (*s*, 3 H); 2.55–2.53 (*m*, 3 H); 1.95–1.73 (*m*, 2 H); 1.69–1.54 (*m*, 4 H); 1.11 (*s*, 6 H); 0.93 (*t*, *J* = 7.0, 3 H); 0.93 (*s*, $Me(8'')$). MS: 311 (14, M^+), 282 (30), 264 (12), 238 (29), 198 (31), 172 (10), 153 (27), 130 (49), 109 (67), 83 (100). HR-MS: 311.1740 ($C_{16}H_{25}NO_5^+$; calc. 311.1732).

Attempted Hydroxylation of *N*-{[(3*S*)-2,3-Dihydro-5-(trimethylsilyloxy)furan-3-yl]toluene-4-sulfonamide (**18**). To a stirred soln. of $LiN(i-Pr)_2$ (LDA; 0.86 mmol; prepared from (*i*-Pr)₂NH (133 μ l) and 1.6*M* BuLi (0.54 ml)) in THF (3 ml) was added **8** (0.100 g, 0.39 mmol) in THF (2 ml) at –78° under N_2 , and 15 min later, Me_3SiCl (100 μ l, 0.784 mmol). The stirred mixture was allowed to warm to r.t. over 3 h. Evaporation gave a residue to which dry pentane (15 ml) was added. Rapid filtration of the resulting soln. and evaporation afforded **18** as an oil. A soln. of 3-chloroperbenzoic acid (0.200 g, 50% in hexane) [18] was then added to a soln. of **18** in hexane (10 ml) at –0° with stirring (30 min) followed by $(Et_3NH)F$ (52 mg, 0.43 mmol). Filtration, dilution of the filtrate with Et_2O (15 ml), followed by successive washing (5% aq. HCl and 5% aq. Na_2CO_3 soln.), drying ($MgSO_4$), and evaporation, gave a residue, which proved to be **8** (by NMR).

A second sample of **18** was similarly prepared, dissolved in CH_2Cl_2 (2 ml), and added to a soln. of $Pb(OAc)_4$ (0.191 g, 0.43 mmol) [19] in CH_2Cl_2 (5 ml) at –15° under N_2 . After stirring for 30 min, workup as before gave **8**.

(2*S*,3*R*)-2-Hydroxy-3-(tosylamino)butano-4-lactone (= (3*S*,4*R*)-4,5-Dihydro-3-hydroxy-4-(tosylamino)furan-2(3*H*)-one; **19**). To a stirred soln. of $NaN(SiMe_3)_2$ ($NaHMDS$; 0.240 g, 1.25 mmol) in THF (10 ml), cooled to –78° under Ar, was added successively a soln. of **8** (0.128 g, 0.5 mmol) in THF (2 ml) and racemic 3-phenyl-2-(phenylsulfonyl)oxaziridine (0.261 g, 1.0 mmol) [21] in THF (5 ml) by syringe. After stirring for 2 h at –78°, the reaction was quenched with sat. aq. NH_4Cl soln. (5 ml). Evaporation of the org. phase gave a residue which was taken up in AcOEt (3 × 15 ml). The resulting soln. was washed with brine, dried ($MgSO_4$), and evaporated. Purification of the residue by CC (SiO_2 , CH_2Cl_2 /hexane/AcOEt 2:1:1) furnished **19**. Colorless oil (0.086 g, 64%). $[\alpha]_D^{25} = -23.4$ (*c* = 3.7, AcOEt). IR (KBr): 3400, 3213, 1764, 1598, 1455. ¹H-NMR: 7.67 (*d*, *J* = 8.0, 2 H); 7.20 (*d*, *J* = 8.0, 2 H); 6.41 (*d*, *J* = 4.0, 1 H); 4.50 (*d*, *J* = 8.8, 1 H); 4.15 (*s*, 1 H); 3.85 (*m*, *J* = 3.3, 2 H); 2.31 (*s*, 3 H). ¹H-NMR (D_6 acetone): 7.80 (*d*, *J* = 8.0, 2 H); 7.40 (*d*, *J* = 8.0, 2 H); 7.23 (*d*, *J* = 4.0, 1 H); 5.18 (*d*, *J* = 6.2, 1 H); 4.39 (*dd*, *J* = 8.8, 6.2, 1 H); 4.32 (*m*, 1 H); 3.93 (*m*, 2 H); 2.42 (*s*, 3 H). ¹³C-NMR: 174.86, 144.33, 136.14, 130.03, 127.12, 71.13, 68.07, 56.14, 21.53. MS: 271 (3, M^+), 214 (4), 197 (7), 155 (20), 116 (8), 91 (100). HR-MS: 271.0501 ($C_{11}H_{13}NO_5S^+$; calc. 271.0514).

Repetition of the above experiment with (+)-(2*R*,8*aS*)-(camphorsulfonyl)oxaziridine [22] as oxidant afforded **19** as a single product in 55% yield. $[\alpha]_D^{25} = -22.6$ (*c* = 0.52, AcOEt).

Repetition of the above experiment by employing bis(trimethylsilyl) peroxide [20] as oxidant was without effect on **8** regardless of the base used to generate the dianion (LDA or $KHMDS$).

(2*R*,3*S*)-2-Hydroxy-3-(tosylamino)butano-4-lactone (= (3*R*,4*S*)-4,5-Dihydro-3-hydroxy-4-(tosylamino)furan-2(3*H*)-one; **20**). As described for **19**, with **15** according to the above two procedures: **20** as single product in each case in 61 and 68% yield, resp. $[\alpha]_D^{25} = +21.6$ (*c* = 3.0, AcOEt) and $+22.4$ (*c* = 0.6, AcOEt).

(2*S*,3*S*)-Ethyl 2-Hydroxy-4-iodo-3-(tosylamino)butanoate (**21**). As described for **9**, with **19** (0.530 g, 1.96 mmol), CH_2Cl_2 (10 ml), EtOH (0.57 ml, 9.8 mmol), and Me_3SiI (0.8 ml, 5.9 mmol). The crude product was

purified by CC (silica gel, hexane/AcOEt 3:5): **21** (0.732 g, 88%). Colorless crystals after standing in the refrigerator overnight. M.p. 88.5–90°. $[\alpha]_D^{25} = +43.2$ ($c = 1.9$, AcOEt). IR (CH_2Cl_2): 3504, 3362, 1736. $^1\text{H-NMR}$: 7.66 (d , $J = 8.0$, 2 H); 7.25 (d , $J = 8.0$, 2 H); 5.14 (d , $J = 12.0$, 1 H); 4.57 (s , 1 H); 4.06 (qd , $J = 4.0$, 1 H); 3.84 (m , 1 H); 3.74 (qd , $J = 8.0$, 1 H); 3.23 (m , 1 H); 3.19 (m , 2 H); 2.36 (s , 3 H); 1.11 (t , $J = 8.0$, 3 H). $^{13}\text{C-NMR}$: 172.47, 143.79, 137.79, 129.76, 127.02, 69.99, 62.77, 56.50, 21.50, 13.83, 4.01. MS: 428 (3, $[M + 1]^+$), 354 (1), 324 (23), 155 (59), 91 (100). HR-MS: 426.9903 ($\text{C}_{13}\text{H}_{18}\text{INO}_5\text{S}^+$; calc. 426.9950).

(2*R*,3*R*)-Ethyl 2-Hydroxy-4-iodo-3-(tosylamino)butanoate (**28**). As described for **21**, with **20**: **28** (88%). Colorless crystals. M.p. 89–91°. $[\alpha]_D^{25} = -43.3$ ($c = 0.55$, AcOEt).

(2*S*,3*R*)-Ethyl 2-Hydroxy-3-(tosylamino)pentanoate (**22a**). As described for **10a**, with **21** and Me_2CuLi . Workup with AcOEt instead of Et_2O . CC (silica gel, hexane/AcOEt, 2:3) gave **22a** (71%). Colorless crystals. M.p. 75–76°. $[\alpha]_D^{25} = +35.2$ ($c = 8.25$, AcOEt). IR (CH_2Cl_2): 3510, 3374, 1733. $^1\text{H-NMR}$: 7.67 (d , $J = 8.0$, 2 H); 7.21 (d , $J = 8.0$, 2 H); 5.13 (d , $J = 9.6$, 1 H); 4.10 (m , 1 H); 4.07 (d , $J = 1.2$, 1 H); 3.94 (qd , $J = 7.2$, 1 H); 3.50 (q , $J = 7.6$, 1 H); 3.37 (d , $J = 5.2$, 1 H); 2.34 (s , 3 H); 1.55 (qd , $J = 7.0$, 1 H); 1.33 (qd , $J = 7.0$, 1 H); 1.19 (t , $J = 7.2$, 3 H); 0.71 (t , $J = 7.4$, 3 H). $^{13}\text{C-NMR}$: 173.10, 143.18, 138.44, 129.51, 126.91, 71.15, 62.36, 57.35, 25.56, 21.43, 14.13, 10.41. MS: 316 (1, $[M + 1]^+$), 298 (0.2), 286 (0.3), 242 (1), 212 (62), 184 (1), 155 (58), 91 (100). HR-MS: 212.0737 ($[\text{C}_{14}\text{H}_{21}\text{NO}_5\text{S} - \text{C}_4\text{H}_7\text{O}_3]^+$; calc. 212.0745).

(2*S*,3*R*)-Ethyl 2-Hydroxy-3-(tosylamino)hexanoate (**22b**). As described for **22a**, with **21** and Et_2CuLi : **22b** (93%). Colorless oil. $[\alpha]_D^{25} = +27.8$ ($c = 2.0$, AcOEt). $^1\text{H-NMR}$: 7.73 (d , $J = 8.4$, 2 H); 7.28 (d , $J = 8.4$, 2 H); 5.15 ($br. s$, 1 H); 4.21 (m , 1 H); 4.11 (s , 1 H); 4.00 (m , 1 H); 3.65 (q , $J = 8.0$, 1 H); 3.45 ($br. s$, 1 H); 2.41 (s , 3 H); 1.56 (m , 1 H); 1.28–1.19 (m , 6 H); 0.77 (t , $J = 7.2$, 3 H). $^{13}\text{C-NMR}$: 173.12, 143.21, 138.40, 129.52, 126.95, 71.45, 62.36, 55.66, 34.41, 21.47, 18.97, 14.00, 13.59. MS: 330 (3, $[M + 1]^+$), 226 (72), 155 (70), 91 (100). HR-MS: 330.1358 ($[\text{C}_{15}\text{H}_{23}\text{NO}_5\text{S} + \text{H}]^+$; calc. 330.1374).

(2*S*,3*R*)-Ethyl 2-Hydroxy-3-(tosylamino)octanoate (**22c**). As described for **22a**, with **21** and Bu_2CuLi : **22c** (85%). Colorless oil. $[\alpha]_D^{25} = +25.9$ ($c = 1.86$, AcOEt). $^1\text{H-NMR}$: 7.67 (d , $J = 8.4$, 2 H); 7.20 (d , $J = 8.4$, 2 H); 5.23 ($br. s$, 1 H); 4.14 (m , 1 H); 4.05 (m , 1 H); 4.01 (m , 1 H); 3.54 (m , $J = 7.6$, 1 H); 3.44 ($br. s$, 1 H); 2.34 (s , 3 H); 1.47 (m , 1 H); 1.20–0.7 ($br. m$, 13 H). $^{13}\text{C-NMR}$: 173.00, 143.20, 138.50, 129.50, 127.00, 71.60, 62.30, 56.00, 32.30, 31.20, 25.40, 22.20, 21.30, 14.10, 13.80. MS: 358 (15, $[M + 1]^+$), 340 (3), 284 (2), 254 (44), 155 (47), 91 (100). HR-MS: 358.1741 ($[\text{C}_{17}\text{H}_{27}\text{NO}_5\text{S} + \text{H}]^+$; calc. 358.1689).

(2*S*,3*R*)-Ethyl 2-Hydroxy-5-phenyl-3-(tosylamino)pentanoate (**22d**). As described for **22a**, with **21** and $(\text{PhCH}_2)_2\text{CuLi}$ (prepared from $\text{CuBr} \cdot \text{Me}_2\text{S}$ and PhCH_2Li [35]): **22d** (85%). Colorless oil which crystallized on standing in the refrigerator overnight. M.p. 110–111°. $[\alpha]_D^{25} = +18.5$ ($c = 7.5$, AcOEt). IR (CH_2Cl_2): 3475, 3280, 1734. $^1\text{H-NMR}$: 7.69 (d , $J = 8.4$, 2 H); 7.25 (m , 5 H); 7.03 (d , $J = 8.4$, 2 H); 4.95 (d , $J = 10.0$, 1 H); 4.20 (m , 2 H); 4.03 (m , 1 H); 3.72 (m , $J = 8.0$, 1 H); 3.22 (d , $J = 4.4$, 1 H); 2.54 (t , $J = 6.8$, 2 H); 2.43 (s , 3 H); 1.93 (m , 1 H); 1.62 (m , 1 H); 1.27 (t , $J = 6.8$, 3 H). $^{13}\text{C-NMR}$: 172.80, 143.40, 140.70, 138.20, 129.60, 128.40, 128.30, 127.00, 126.00, 71.20, 62.60, 55.30, 34.10, 32.00, 21.47, 13.97. MS: 392 (14, $[M + 1]^+$), 391 (1, M^+), 374 (1), 288 (11), 155 (15), 91 (100). HR-MS: 288.1080 ($[\text{C}_{20}\text{H}_{25}\text{NO}_5\text{S} - \text{C}_4\text{H}_7\text{O}_3]^+$; calc. 288.1058).

(2*S*,3*R*)-Ethyl 2-Hydroxy-4-phenyl-3-(tosylamino)butanoate (**22e**). To a suspension of CuBr (1.68 g, 11.7 mmol) in THF (20 ml) was added dropwise 1.5*M* PhLi in cyclohexane/ Et_2O 70:30 (v/v) (15.6 ml, 23.4 mmol) at 0° under Ar. After stirring for 10 min, the mixture was cooled to –78° and a soln. of **21** (0.500 g, 1.17 mmol) in THF (5 ml) added. Stirring at –78° was continued for 2 h and then for another 1.5 h at 0°. The mixture was quenched with aq. $\text{NH}_4\text{OH}/\text{NH}_4\text{Cl}$ soln. 1:8 (pH 9; 20 ml), stirred vigorously at r.t. for 30 min, and extracted with AcOEt (3 × 20 ml). The combined org. phase was washed successively with sat. aq. NH_4Cl soln., H_2O , and brine, dried (MgSO_4), and evaporated. The oil was purified by FC (SiO_2 , hexane/AcOEt, 4:1): **22e** (0.375 g, 86%). Pale yellow oil. $[\alpha]_D^{25} = +91.7$ ($c = 1.0$, AcOEt). IR (neat): 3478, 3280, 1732, 1598, 1495, 1449. $^1\text{H-NMR}$: 7.70 (d , $J = 8.0$, 2 H); 7.27–7.12 (m , 5 H); 7.10 (d , $J = 8.0$, 2 H); 5.36 (d , $J = 10.0$, 1 H); 4.17 (m , 1 H); 4.01 (m , 1 H); 3.96 (m , 1 H); 3.88 (m , 1 H); 3.51 (d , $J = 4.0$, 1 H); 2.87 (dd , $J = 13.2$, 10.0, 1 H); 2.66 (dd , $J = 13.2$, 5.6, 1 H); 2.41 (s , 3 H); 1.22 (t , $J = 7.2$, 3 H). $^{13}\text{C-NMR}$: 172.10, 143.80, 138.18, 136.97, 129.63, 128.62, 126.93, 126.71, 70.20, 62.50, 57.50, 38.50, 21.50, 13.90. MS: 304 (4, $[M - 73]^+$), 286 (1), 288 (28), 274 (29), 155 (49), 91 (100). HR-MS: 304.1042 ($[\text{C}_{19}\text{H}_{23}\text{NO}_5\text{S} - \text{CO}_2\text{C}_2\text{H}_5]^+$; calc. 304.1007).

(2*S*,3*R*)-Ethyl 2-Hydroxy-5,5-dimethyl-3-(tosylamino)hexanoate (**22g**). As described for **22a**, with **21** and $(t\text{-Bu})_2\text{CuLi}$ (prepared from $\text{CuBr} \cdot \text{Me}_2\text{S}$ and $t\text{-BuLi}$). After addition, the mixture was stirred for 6 h at –40° and for another 30 min at –20° and then worked up: **22g** (43%). Colorless oil. $^1\text{H-NMR}$: 7.67 (d , $J = 8.4$, 2 H); 7.23 (d , $J = 8.4$, 2 H); 4.75 (d , $J = 10.0$, 1 H); 4.15 (m , 1 H); 4.02 (m , 1 H); 3.97 (m , 1 H); 3.70 (m , 1 H); 3.00 (d , $J = 4.0$, 1 H); 2.36 (s , 3 H); 1.57 (m , 1 H); 1.22 (t , $J = 7.0$, 3 H); 1.06 (m , 1 H); 0.78 (s , 9 H). MS: 358 (25, $[M + 1]^+$), 341 (1), 284 (3), 254 (21), 198 (31), 155 (37), 91 (20), 57 (100). HR-MS: 284.1355 ($[\text{C}_{17}\text{H}_{27}\text{NO}_5\text{S} - \text{C}_3\text{H}_5\text{O}_2]^+$; calc. 284.1321).

(2*S*,3*R*)-Ethyl 2-Hydroxy-4-cyclohexyl-3-(tosylamino)butanoate (**22h**). As described for **22a**, with **21** and lithium dicyclohexylcuprate (prepared from CuBr·Me₂S and cyclohexylmagnesium chloride). After 30 h the mixture was worked up: **22h** (42%). Colorless solid. M.p. 114–115°. ¹H-NMR: 7.60 (*d*, *J* = 8.0, 2 H); 7.23 (*d*, *J* = 8.0, 2 H); 4.61 (*d*, *J* = 12.0, 1 H); 4.18 (*m*, 1 H); 4.01 (*m*, 2 H); 3.71 (*m*, 1 H); 3.06 (*d*, *J* = 4.4, 1 H); 2.36 (*s*, 3 H); 1.51–0.6 (br. *m*, 13 H); 1.22 (*t*, *J* = 7.2, 3 H). ¹³C-NMR: 172.07, 142.34, 138.33, 128.60, 125.41, 70.89, 62.02, 52.50, 38.84, 32.58, 32.37, 32.04, 25.82, 25.72, 21.99, 20.48, 13.04. MS: 384 (11, [*M* + 1]⁺), 310 (1), 280 (46), 198 (14), 155 (70), 91 (100). HR-MS: 384.1869 ([C₁₉H₂₉NO₅S + H]⁺; calc. 384.1844).

Acids 23a–e. The esters **22a–e** were hydrolyzed according to the *General Procedure* used for **10a–e** to give the acids **23a–d** as colorless solids and **23e** as oil in yields of 89, 90, 81, 89, and 84%, resp. M.p.'s 179–180°, 165–167°, 107–109°, and 166–168°, resp. [α]_D²⁵ = +32.9 (*c* = 4.3), +26.1 (*c* = 1.1), +22.0 (*c* = 6.5), +19.1 (*c* = 3.8), and +66.2 (*c* = 2.8), resp., all determined in acetone.

(2*S*,3*R*)-2-Hydroxy-3-(tosylamino)pentanoic Acid (**23a**): ¹H-NMR ((D₆)acetone): 7.75 (*d*, *J* = 8.4, 2 H); 7.34 (*d*, *J* = 8.4, 2 H); 6.18 (*d*, *J* = 7.0, 1 H); 4.16 (*d*, *J* = 2.4, 2 H); 3.53 (*m*, 1 H); 2.40 (*s*, 3 H); 1.61 (*m*, 1 H); 1.34 (*m*, 1 H); 0.75 (*t*, *J* = 7.2, 3 H). ¹³C-NMR ((D₆)acetone): 174.10, 143.60, 140.00, 130.20, 127.70, 71.85, 58.66, 25.35, 21.36, 10.81. MS: 258 (2, [*M* – 29]⁺), 212 (100), 155 (60), 91 (96). HR-MS: 212.0749 ([C₁₂H₁₇NO₅S – C₂H₃O₃]⁺; calc. 212.0745).

(2*S*,3*R*)-2-Hydroxy-3-(tosylamino)hexanoic Acid (**23b**): ¹H-NMR ((D₆)acetone): 7.74 (*d*, *J* = 8.0, 2 H); 7.35 (*d*, *J* = 8.0, 2 H); 6.04 (*d*, *J* = 9.0, 1 H); 4.12 (*s*, 1 H); 3.52 (*m*, 1 H); 2.40 (*s*, 3 H); 1.47 (*m*, 1 H); 1.23 (*m*, 3 H); 0.74 (*t*, *J* = 7.2, 3 H). ¹³C-NMR ((D₆)acetone): 173.95, 143.65, 140.54, 130.23, 127.79, 72.10, 56.76, 34.24, 21.37, 19.64, 13.92. MS: 302 (1, [*M* + 1]⁺), 256 (1), 226 (49), 155 (50), 91 (100). HR-MS: 226.0885 ([C₁₃H₁₉NO₅S – C₂H₃O₃]⁺; calc. 226.0902).

(2*S*,3*R*)-2-Hydroxy-3-(tosylamino)octanoic Acid (**23c**): ¹H-NMR ((D₆)acetone): 7.75 (*d*, *J* = 8.4, 2 H); 7.35 (*d*, *J* = 8.4, 2 H); 6.17 (*d*, *J* = 9.2, 1 H); 4.15 (*m*, 1 H); 3.59 (*q*, *J* = 7.2, 1 H); 2.40 (*s*, 3 H); 1.60 (*m*, 1 H); 1.28 (*m*, 1 H); 1.10 (*m*, 6 H); 0.78 (*t*, *J* = 7.2, 3 H). ¹³C-NMR ((D₆)acetone): 174.10, 143.70, 140.50, 130.20, 127.80, 72.30, 57.10, 32.10, 32.00, 26.20, 23.00, 21.40, 14.20. MS: 284 (1, [*M* – 45]⁺), 254 (60), 155 (50), 91 (100). HR-MS: 284.1257 ([C₁₅H₂₃NO₅S – CO₂H]⁺; calc. 284.1257).

(2*S*,3*R*)-2-Hydroxy-5-phenyl-3-(tosylamino)pentanoic Acid (**23d**): ¹H-NMR ((D₆)acetone): 7.73 (*d*, *J* = 6.6, 2 H); 7.35 (*d*, *J* = 8.0, 2 H); 7.23 (*m*, 2 H); 7.13 (*m*, 1 H); 7.02 (*d*, *J* = 8.0, 2 H); 6.33 (*d*, *J* = 12.0, 1 H); 4.25 (*s*, 1 H); 3.70 (*m*, 1 H); 2.45 (*m*, 2 H); 2.40 (*s*, 3 H); 1.94 (*m*, 1 H); 1.55 (*m*, 1 H). ¹³C-NMR ((D₆)acetone): 174.00, 143.70, 142.40, 140.40, 130.30, 129.10, 127.80, 126.80, 126.60, 72.10, 56.80, 34.00, 32.70, 21.40. MS: 288 (100, [*M* – 75]⁺), 255 (40), 155 (30), 91 (98). HR-MS: 363.1116 (C₁₈H₂₁NO₅S⁺; calc. 363.1140).

(2*S*,3*R*)-2-Hydroxy-4-phenyl-3-(tosylamino)butanoic Acid (**23e**): ¹H-NMR ((D₆)acetone): 7.73 (*d*, *J* = 8.0, 2 H); 7.32 (*d*, *J* = 8.0, 2 H); 7.24–7.10 (*m*, 5 H); 6.50 (*m*, 1 H); 3.96 (*s*, 1 H); 3.90 (*m*, 1 H); 2.88 (*t*, *J* = 13.0, 10.4, 1 H); 2.53 (*dd*, *J* = 13.0, 5.2, 1 H); 2.39 (*s*, 3 H). ¹³C-NMR ((D₆)acetone): 173.98, 143.69, 140.24, 138.72, 130.41, 130.16, 129.35, 127.76, 127.31, 70.55, 58.92, 38.47, 21.38. MS: 350 (32, [*M* + 1]⁺), 332 (1, [*M* – 17]⁺), 304 (7, [*M* – 45]⁺), 91 (100). HR-MS: 274.0902 ([C₁₇H₁₉NO₅S – C₂H₃O₃]⁺; calc. 274.0902).

Deprotection of (2*S*,3*R*)-2-Hydroxy-3-(tosylamino) Acids 23a–e: General Procedure. Na (96 mg, 4.17 mmol) was added to a soln. of naphthalene (0.65 g, 5.08 mmol) in freshly distilled MeOCH₂CH₂OMe (5 ml) under N₂ with stirring at r.t. until the soln. became dark green. A soln. of the acid (0.100 g) in MeOCH₂CH₂OMe (2 ml) was then added to the preceding soln. pre-cooled to –78°. After stirring for 30 min, the reaction was quenched with H₂O (10 ml) [27]. The aq. layer was extracted with Et₂O (5 × 2 ml) to remove naphthalene and then acidified with conc. aq. HCl soln. to pH 3. Evaporation of the aq. phase gave a crude product which was purified by CC (Amberlyst IR 120, H₂O, then 1*N* NH₃). The acids **24a–e** were formed as colorless solids in yields of 87, 80, 77, 79, and 82%, resp. M.p.'s 185–186°, > 230° (dec.), > 200°, 215–217°, and 236–237°, resp. [α]_D²⁵ = –13.4 (*c* = 1.2, H₂O), –9.8 (*c* = 1.1, H₂O/MeOH 1:1), –5.0 (*c* = 0.85, H₂O/MeOH 1:1), –3.5 (*c* = 0.66, H₂O/MeOH 2:1), and +29.2 (*c* = 0.25, 1*N*, HCl), resp.

(2*S*,3*R*)-3-Amino-2-hydroxypentanoic Acid (**24a**): ¹H-NMR (D₂O, dioxane as internal standard): 3.93 (*d*, *J* = 4.0, 1 H); 3.20 (*m*, 1 H); 1.59 (*m*, 1 H); 1.48 (*m*, 1 H); 0.83 (*t*, *J* = 7.2, 3 H). ¹³C-NMR (D₂O): 178.20, 71.50, 56.30, 23.30, 10.10. MS: 134 (1, [*M* + 1]⁺), 116 (2), 98 (2), 88 (4), 71 (3), 58 (100). HR-MS: 98.0598 ([C₅H₁₁NO₃ – H₃O₂]⁺; calc. 98.0605).

(2*S*,3*R*)-3-Amino-2-hydroxyhexanoic Acid (**24b**): ¹H-NMR (D₂O, dioxane as internal standard): 3.74 (*d*, *J* = 3.3, 1 H); 2.79 (*m*, 1 H); 2.21 (*d*, *J* = 3.7, 1 H); 1.30–1.10 (*m*, 4 H); 0.74 (*t*, *J* = 6.3, 3 H). ¹³C-NMR (D₂O): 180.87, 75.86, 53.59, 35.72, 19.80, 14.16. MS: 134 (1, [*M* + 1]⁺), 116 (2), 98 (2), 88 (4), 71 (3), 58 (100).

(2*S*,3*R*)-3-Amino-2-hydroxyoctanoic Acid (**24c**): ¹H-NMR (D₂O, dioxane as internal standard): 3.92 (*d*, *J* = 3.6, 1 H); 3.25 (*m*, 1 H); 1.55 (*m*, 1 H); 1.43 (*m*, 1 H); 1.26 (*m*, 2 H); 1.15 (*m*, 4 H); 0.71 (*t*, *J* = 7.2, 3 H).

^{13}C -NMR (D_2O): 178.80, 72.10, 54.90, 31.50, 30.20, 25.20, 22.50, 14.10. MS: 156 (14, $[M - 18]^+$), 130 (64), 100 (100). HR-MS: 130.1240 ($[\text{C}_8\text{H}_{17}\text{NO}_3 - \text{CO}_2\text{H}]^+$; calc. 130.1232).

(2*S*,3*R*)-3-Amino-2-hydroxy-5-phenylpentanoic Acid (**24d**): ^1H -NMR (D_2O , dioxane as internal standard): 7.18 (*m*, 5 H); 3.83 (*s*, 1 H); 2.90 (*m*, 1 H); 2.58 (*m*, 2 H); 1.69 (*m*, 1 H); 1.58 (*m*, 1 H). ^{13}C -NMR (D_2O): 180.10, 143.10, 129.60, 129.40, 127.00, 75.10, 53.90, 35.10, 32.70. MS: 134 (32), 132 (18), 117 (14), 91 (100). HR-MS: 210.1128 ($[\text{C}_{11}\text{H}_{15}\text{NO}_3 + \text{H}]^+$; calc. 210.1128).

(2*S*,3*R*)-3-Amino-2-hydroxy-4-phenylbutanoic Acid (**24e**): ^1H -NMR (D_2O , dioxane as internal standard): 7.24 (*m*, 5 H); 3.81 (*s*, 1 H); 3.42 (*m*, 1 H); 2.86 (*dd*, $J = 14.00$, 6.6, 1 H); 2.67 (*dd*, $J = 14.00$, 8.4, 1 H). MS: 194 (1, $[M - 1]^+$), 178 (1, $[M - 18]^+$), 150 (3), 120 (47), 91 (100). HR-MS: 120.0822 ($[\text{C}_{10}\text{H}_{13}\text{NO}_3 - \text{C}_2\text{H}_5\text{O}_2]^+$; calc. 120.0813).

(2*R*,3*R*)-Ethyl 2-Hydroxy-4-iodo-3-(tosylamino)butanoate (**28**). Treatment of **20** with EtOH and Me_3SiI as described for **19** $\rightarrow$ **21** gave **28** in similar yield. Pale yellow solid. M.p. 89–91°. $[\alpha]_{\text{D}}^{25} = -43.3$ ($c = 0.55$, AcOEt). IR (CH_2Cl_2): 3504, 3362, 1736. ^1H -NMR: 7.66 (*d*, $J = 8.0$, 2 H); 7.25 (*d*, $J = 8.0$, 2 H); 5.14 (*d*, $J = 12.0$, 1 H); 4.57 (*s*, 1 H); 4.06 (*qd*, $J = 4.0$, 1 H); 3.84 (*m*, 1 H); 3.74 (*qd*, $J = 8.0$, 1 H); 3.23 (*m*, 1 H); 3.19 (*m*, 2 H); 2.36 (*s*, 3 H); 1.11 (*t*, $J = 8.0$, 3 H). ^{13}C -NMR: 172.48, 143.82, 137.78, 129.77, 127.03, 69.96, 62.80, 56.46, 21.52, 13.84, 4.04. MS: 428 (10, $[M + 1]^+$), 410 (1), 354 (1), 324 (34), 155 (65), 91 (100). HR-MS: 353.9648 ($[\text{C}_{13}\text{H}_{18}\text{INO}_2\text{S} - \text{C}_3\text{H}_5\text{O}_2]^+$; calc. 353.9660).

(2*S*,3*R*)-Ethyl 2-Hydroxy-3-(tosylamino)decanoate (**22f**). To a suspension of CuI (0.469 g, 0.35 mmol) in THF (8 ml) was added 1.3M $\text{Me}(\text{CH}_2)_5\text{Li}$ in Et_2O (3.4 ml, 4.43 mmol) at -40° under Ar with stirring. Addition of **21** (0.150 g, 0.35 mmol) in THF (2 ml) was followed by stirring at -30° for 18 h. The mixture was worked up as described for **22a**: **22f** (0.130 g, 96%). Yellow oil. $[\alpha]_{\text{D}}^{25} = +31.3$ ($c = 4.53$, AcOEt). IR (neat): 3500, 3280, 1736, 1446, 1330. ^1H -NMR: 7.34 (*d*, $J = 8.4$, 2 H); 7.29 (*d*, $J = 8.4$, 2 H); 4.78 (*d*, $J = 10.0$, 1 H); 4.21 (*m*, 1 H); 4.11 (*dd*, $J = 4.4$, 1.8, 1 H); 4.02 (*m*, 1 H); 3.64 (*q*, $J = 8.1$, 1 H); 3.17 (*d*, $J = 8.1$, 1 H); 2.43 (*s*, 3 H); 1.60 (*m*, 2 H); 1.34–1.14 (*m*, 13 H); 0.87 (*t*, $J = 7.2$, 3 H). ^{13}C -NMR: 173.03, 143.31, 138.39, 129.57, 127.02, 71.41, 62.51, 55.80, 32.53, 31.64, 29.07, 25.79, 22.60, 21.48, 14.04. MS: 386 (18, $[M + 1]^+$), 368 (3), 312 (2), 282 (38), 155 (49), 91 (100). HR-MS: 386.2012 ($[\text{C}_{19}\text{H}_{31}\text{NO}_2\text{S} + \text{H}]^+$; calc. 386.2001).

(2*S*,3*R*)-2-Hydroxy-3-(tosylamino)decanoic Acid (**23f**). Hydrolysis of **22f** by the General Procedure gave **23f** (80%). Colorless solid. M.p. 118–119°. $[\alpha]_{\text{D}}^{25} = +30.3$ ($c = 2.3$, acetone). IR (KBr): 3450, 3252, 1747, 1599, 1495. ^1H -NMR ($(\text{D}_6)\text{acetone}$): 7.54 (*d*, $J = 8.0$, 2 H); 7.36 (*d*, $J = 8.0$, 2 H); 6.20 (*d*, $J = 9.2$, 1 H); 4.14 (*d*, $J = 2.8$, 1 H); 3.60 (*m*, 1 H); 2.40 (*s*, 3 H); 1.30–1.00 (*m*, 12 H); 0.85 (*t*, $J = 7.2$, 3 H). ^{13}C -NMR ($(\text{D}_6)\text{acetone}$): 206.20, 143.60, 140.53, 130.23, 127.81, 72.27, 57.00, 32.38, 32.01, 32.00, 29.80, 26.50, 23.30, 21.40, 14.30. MS: 358 (1, $[M + 1]^+$), 312 (1, $[M - 45]^+$), 282 (37), 155 (49), 91 (100). HR-MS: 282.1529 ($[\text{C}_{17}\text{H}_{27}\text{NO}_4\text{S} - \text{C}_2\text{H}_3\text{O}_3]^+$; calc. 282.1528).

(2*S*,3*R*)-3-Amino-2-hydroxydecanoic Acid (**24f** = **4**). Deprotection of **23f** by the General Procedure (Na naphthalide) gave **4** (68%). Colorless solid. M.p. 211–214°. $[\alpha]_{\text{D}}^{25} = -5.5$ ($c = 0.37$, 0.1N HCl/MeOH 1:2). IR (KBr): 3333, 3200, 3090, 1722. ^1H -NMR (D_2O , dioxane as internal standard): 3.92 (*d*, $J = 3.7$, 1 H); 3.29 (*m*, 1 H); 1.57 (*m*, 1 H); 1.45 (*m*, 1 H); 1.26–1.10 (*m*, 10 H); 0.69 (*t*, $J = 7.0$, 3 H). ^{13}C -NMR (D_2O): 161.12, 72.10, 54.88, 31.87, 30.22, 29.23, 29.00, 25.60, 22.85, 14.26. MS: 171 (2, $[M - 32]^+$), 158 (6, $[M - 45]^+$), 128 (100). HR-MS: 128.1464 ($[\text{C}_{10}\text{H}_{21}\text{NO}_3 - \text{C}_2\text{H}_3\text{O}_3]^+$; calc. 128.1488).

(2*R*,3*S*)-Ethyl 2-Hydroxy-3-(tosylamino)decanoate (**29**). As described for **22f**, with **28**: **29** (93%). Yellow oil. $[\alpha]_{\text{D}}^{25} = -32.0$ ($c = 1.8$, AcOEt). IR, ^1H -NMR, ^{13}C -NMR, and MS: identical to those of **22f**.

(2*R*,3*S*)-2-Hydroxy-3-(tosylamino)decanoic Acid (**30**). Hydrolysis of **29** by the General Procedure gave **30** (95%). Colorless solid. M.p. 215–216°. $[\alpha]_{\text{D}}^{25} = -29.8$ ($c = 0.62$, acetone). IR, ^1H -NMR, ^{13}C -NMR, and MS: identical to those of **23f**.

(2*R*,3*S*)-3-Amino-2-hydroxydecanoic Acid (**31**). Deprotection of **30** by the General Procedure (Na naphthalide) gave **31** (82%). Colorless solid. M.p. 211–214°. $[\alpha]_{\text{D}}^{25} = +6.0$ ($c = 0.25$, 0.1N HCl/MeOH 1:2). IR, ^1H -NMR, ^{13}C -NMR, and MS: identical to those of **4**.

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