

Synthesis of Highly Enantio-Enriched α -Amino Acids by Carboxylation of *N*-(α -Lithioalkyl)oxazolidinones

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N-(α -Stannylalkyl)oxazolidinones can be obtained as a mixture of diastereomers in three steps from aldehydes with yields dependent on the R group of R-CHO. They can be transformed by a tin-lithium exchange to *N*-(α -lithioalkyl)oxazolidinones which equilibrate rapidly to one diastereomer. These compounds give rise, after carboxylation, to the diastereopure *N*-(α -carboxyalkyl)oxazolidinones. Transforma-

tion of the oxazolidinone moiety to a free amino group is accomplished by a Birch-type reduction. Using this method, L-methionine, L-alanine, L-leucine and L-homocysteine were obtained in good yields and ee = 92% to 95%. The short time required for the whole sequence makes this method ideal for synthesising 1-[¹¹C]amino acids.

Introduction

There is a continued interest in the synthesis of enantiopure α -amino acids and many approaches have been devoted to this problem.^[1] If the four possible bond disconnections **a–d** (Figure 1) are considered, the majority of studies are concerned either with the formation of the carbon–R bond **a** (mainly by enantioselective alkylation of a glycine derivative) or with that of the carbon–hydrogen bond **b** (more often by catalytic hydrogenation of an α -keto acid enamine). Comparatively, the methods involving the formation of the carbon–nitrogen bond **c** (electrophilic amination of an ester enolate equivalent) are far less frequent and only a few reports have described the formation of the carbon–CO₂H bond **d**.

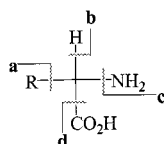


Figure 1

In this last category, the Strecker reaction^[2] is probably the one most widely used; the key step relies on the nucleophilic addition of a cyanide to the C=N bond of an imine, the nitrile functionality being converted into the carboxylic acid, generally by acid hydrolysis. Some asymmetric versions of this reaction have been described giving α -amino acids with enantiomeric excesses of up to 99%.^[3] However, in this context, the simplest method would appear to be the direct carboxylation of an α -amino organometallic species. Surprisingly, the few studies which have been performed us-

ing this approach are concerned mainly with the synthesis of *N*-alkylated α -amino acids: (*R*)-Boc-proline from *N*-Boc-pyrrolidine (ee 88%),^[4] (*R*)-Boc-phenylsarcosine from *N*-Boc-methylbenzylamine (ee 81%).^[5] To our knowledge, the only enantioselective carboxylation of an α -amino lithium reagent giving access to α -amino esters with a primary amino group was described by Duhamel et al. These authors formed the organometallic species by deprotonation of a benzylimine using a chiral lithium amide to obtain esters of phenylglycine with an ee of up to 40%.^[6]

This paper describes the synthesis of several enantiopure α -amino acids by carboxylation of *N*-(α -lithioalkyl)oxazolidinone reagents obtained by the tin-lithium exchange of the corresponding *N*-(α -stannylalkyl)oxazolidinones **1** (Figure 2). This method, originally designed, carried out and optimised for the preparation of L-methionine,^[7] was extended to other amino acids. When this preparative sequence was used as such, it was found that yields were very dependent on the R group of the target amino acid.

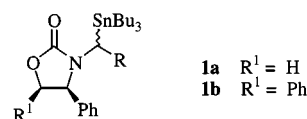


Figure 2

Results and Discussion

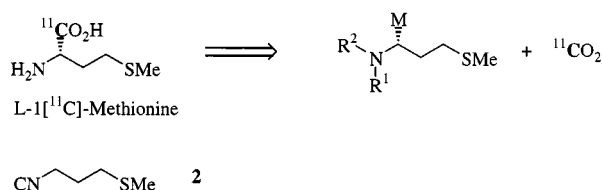
Synthesis of L-Methionine

The aim of this work was the development of a synthetic method for L-methionine which would be able to produce this amino acid labelled with ¹¹C on the carboxyl group (L-1-[¹¹C]methionine) for utilisation in Positron Emission Tomography (PET).^[8] Since this amino acid is inter alia involved in protein synthesis, particularly in the human brain, PET imaging using the labelled compound is a tool for localising a tumour and monitoring its development. Pres-

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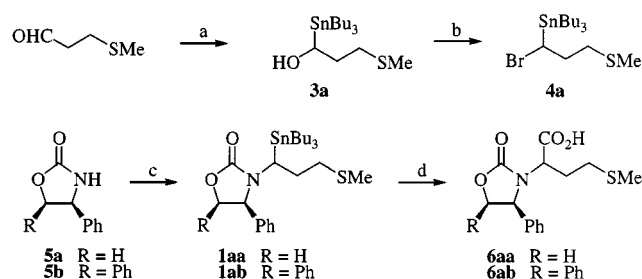
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ently, L-[^{11}C] CH_3 methionine is used routinely for this purpose but, as a part of the metabolism of L-methionine involves the transfer of the methyl group to nucleic acids and lipids,^[9] there is some imprecision in the amounts actually going into protein and this subsequently perturbs the interpretation of PET results. It was therefore evident that [^{11}C]methionine labelled on a carbon atom other than the methyl group was needed. In addition, as $^{11}\text{CO}_2$ is directly produced by the cyclotron, it appeared then that the most useful tool for PET could be L-1-[^{11}C]methionine formed by the carboxylation of an α -amino organometallic reagent (Scheme 1). This project therefore had two criteria to fulfil: (i) high enantioselective synthesis in good yields of L-1-[^{11}C]methionine, and (ii) short synthesis times (less than 40 min) because the half life of [^{11}C] is 20.4 min.



Scheme 1

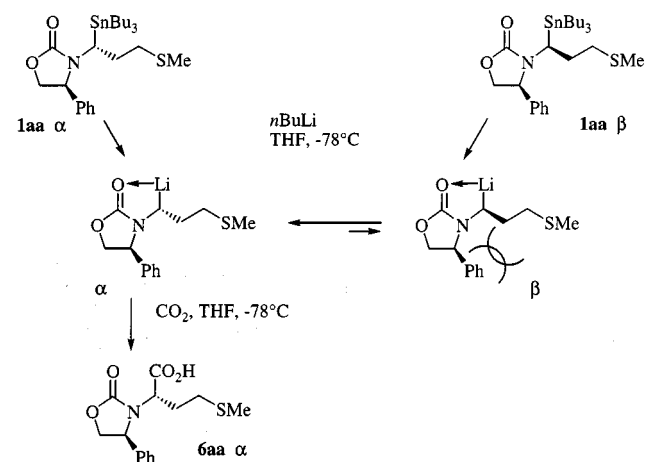
As previously reported,^[7] the α -amino lithio derivative was selected since it can be obtained either by direct deprotonation of nitrogen precursors of the amino group (for example isocyanide **2**)^[10] or by heteroatom to lithium exchange using principally α -aminostannanes. The enantioselective deprotonation of **2** by $n\text{BuLi}$ /sparteine^[11] being completely unsuccessful, the tin–lithium exchange was used, taking advantage of the results of Pearson et al.^[12] who obtained diverse amino derivatives with good diastereoselectivity using organolithium species obtained from enantiopure oxazolidinones **1**.^[13] The required compounds **1aa** and **1ab** (1:1 mixture of diastereomers) were prepared as depicted in Scheme 2 from 3-methylthiopropanal.



Scheme 2. Reagents and conditions: (a) Bu_3SnLi , THF -78°C (85%); (b) $\text{CBr}_4/\text{PPh}_3$, CH_2Cl_2 -70°C to room temp. (94%); (c) NaH , DMF room temp. then **4a** (**1aa**: 90%; **1ab**: 87%); (d) $n\text{BuLi}$, THF -78°C then CO_2 bubbling

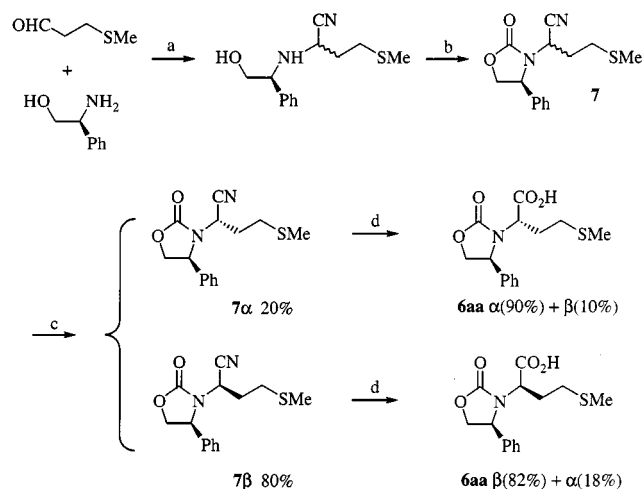
The treatment of **1aa** with one equivalent of $n\text{BuLi}$ in THF at -78°C followed by carboxylation by gaseous CO_2 and acid work up led, in less than 15 min, to the oxazolidino acid **6aa** as a single diastereomer with a yield of 85%.

The same reaction performed with **1ab** also gave **6ab** with complete diastereoselectivity (yield 78%). It is noteworthy that this diastereoselectivity can be obtained using as starting product the diastereomeric mixture of **1aa** and a transmetallation step lasting only 5 min. This contrasts with the results obtained in a preliminary study where the pure diastereomers of **1aa** isolated by silica gel chromatography were first transmetallated by $n\text{BuLi}$ at -78°C and then treated with tributyltin chloride. Under these conditions, and regardless of the transmetallation time, one diastereomer, anticipated to be **1aaa** was recovered in pure form and was identical to the starting material, while the other diastereomer **1aab** needed 30 min before the introduction of the electrophile Bu_3SnCl in order to be completely transformed to **1aaa**. It should be noted, though, that when the transmetallation of **1aab** was carried out in 5 min a mixture of **1aab** (40%) and **1aaa** (60%) is obtained (Scheme 3). These results verified the hypothesis of Pearson et al.,^[12] showing that the two diastereomeric α -aminolithio derivatives are in an equilibrium which is displaced towards the α -isomer because there is less steric interaction between the phenyl group and the methylthioethyl substituent. The fast displacement of this equilibrium in the presence of CO_2 showed also that the carboxylation of the α -isomer of the lithio species proceeded faster than of the β one. Finally, as the pure acid **6aa** was transformed into L-methionine (see below), the α configuration was also attributed to this intermediate with the implication that the carboxylation occurs with retention of configuration (Scheme 3).



Scheme 3

For comparison, the diastereomers **6aaa** and **6aab** were prepared as shown in Scheme 4 by a Strecker-type sequence where the carboxy functionality was obtained by acid hydrolysis of a nitrile. Fortunately, the two diastereomers of the nitrile **7** were separable by silica gel chromatography and hydrolysed with an important retention of configuration giving the acids **6aaa** and **6aab**. The configuration of these acids was verified after their conversion into enantiomers of methionine. The comparison of their ^1H and ^{13}C NMR spectra showed unambiguously the total diastereoselectivity of the carboxylation process depicted in Scheme 3.



Scheme 4. Reagents and conditions: (a) NaCN, MeOH reflux (67%); (b) triphosgene®, Et₃N, CH₂Cl₂ room temp. (89%); (c) SiO₂ chrom. separation; (d) HCl 12 N, 55° C. (90%)

Finally, the chiral auxiliary of **6aa** and **6ab** had to be removed in a short time and by a mild procedure which permitted the conservation of the configurational integrity of the stereogenic carbon previously formed. The first method used for transforming the oxazolidinone group to the corresponding primary amine was the palladium-ammonium formate hydrogenolysis.^[14] As could be anticipated, this reaction was unsuccessful with **6aa**, but **6ab** was deprotected in less than 15 min by running the reaction in refluxing methanol. Unfortunately, the separation of methionine from excess formate proved to be difficult and took too long for our purpose. On the contrary, a Birch–Evans protocol^[14] using lithium in liq. NH₃ in the presence of *t*BuOH/THF at –78 °C, followed by a fast ion exchange chromatography transformed **6aa** in 15 min to L-methionine with an 85% yield. The analysis of this α -amino acid by chiral HPLC [column: chirobiotic T astec®, elution with EtOH/H₂O (60:40) at 1 mL/min] showed its enantiopurity and permitted its identification with L-methionine by its retention time of 5.2 min (under the same conditions, D-methionine has a t_R of 8.06 min).

These results show that the totally enantioselective preparation of L-methionine can be done by carboxylation of an enantiopure *N*-(α -lithioalkyl)oxazolidinone; the entire process requires 35–40 min and is consequently suitable for the preparation of L-1-[¹¹C]methionine. The preparation of the labelled compound has already been done with a radio-

chemical yield of 15–25%.^[16] Once the optimisation for the routine preparation of labelled compound been accomplished, full details will be published elsewhere.^[17]

Extension of the Method to the Synthesis of Other α -Amino Acids

In view of the good results (high yield, and stereoselectivity) observed in the preparation of pure L-methionine by direct carboxylation of a *N*-(α -lithioalkyl)oxazolidinone we tried to determine whether a similar approach could be used for the synthesis of some other α -amino acids such as L-leucine, L-alanine, L-homocysteine, L-phenylalanine, L-valine and L-serine (Figure 3).

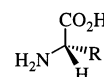
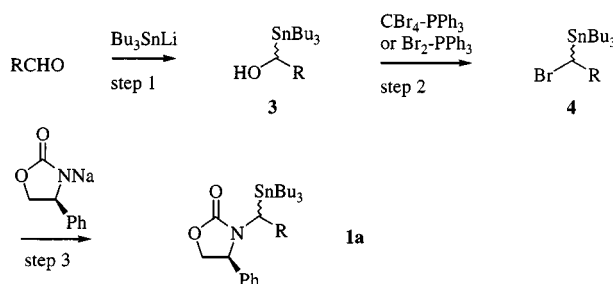


Figure 3. R = CH₂CHMe₂ (leucine), Me (alanine), *i*Pr (valine), CH₂CH₂SH (homocysteine), Bzl (phenylalanine), CH₂OH (serine)

The *N*-(α -stannylalkyl)oxazolidinones **1a** were prepared by the sequence depicted for L-methionine (Scheme 2) starting from the corresponding commercially available aldehydes RCHO (Scheme 5), with the exception of 3-benzylthiopropional which was prepared by the reaction of benzyl thiol with acrolein.^[18] For each step, the experimental conditions of the methionine sequence were used, with the exception of the bromination (step 2) where, for reasons of easier purification, Ph₃P–Br₂ was used instead of PPh₃–CBr₄ in the case of entries 1,2 and 4 of Table 1. As can be seen in this table, the yields of each step depend on the nature of R and are generally lower than those observed for the methionine sequence.



Scheme 5

Again, the transformation of the *N*-(α -stannylalkyl)oxazolidinones was accomplished using the same conditions

Table 1

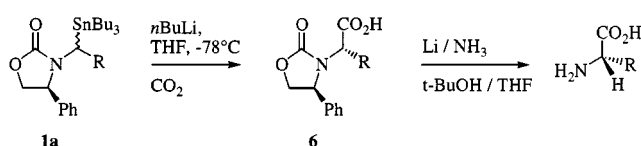
R	Target L-amino acid	Step 1 [%]	Step 2 [%]	Step 3 [%]	Overall yield [%]
<i>i</i> Bu	leucine	3b [64]	4b [57]	1b [84]	30.5
Me	alanine	3c [44]	4c [42]	1c [71]	13
BzlS(CH ₂) ₂	homocysteine	3d [52]	4d [70]	1d [90]	33
Bzl	phenyl alanine	3e [45]	4e [80]	1e [10]	3.6
<i>n</i> Pr	valine	3f [64]	4f [31]	1f [< 5]	≈ 1
BzlOCH ₂	serine	3g [35]	4g [53]	1g [55]	10

as those which were successful for the transformation of **1aa** to L-methionine. As yields of the synthesis of the α -stannyloxazolidinones **1** varied with the R substituent, attempts at enantioselective preparation of the corresponding α -amino acids were made only on **1b**, **1c**, **1d**, and **1g**. The results are listed in Table 2.

Table 2

starting material	6 [%]	amino acid	ee [%]
1b	6b [85]	L-leucine	95
1c	6c [72]	L-alanine	95
1d	6d [80]	L-homocysteine	92
1g	6g [0]	—	—

In the first three cases, the yields are good and the expected α -amino acid is obtained with a high enantiomeric excess (Scheme 6). Unfortunately the oxazolidino acid **6g** could not be obtained. In this last case, we observed loss of the starting stannane (TLC) only when three equivalents of butyllithium were used; this excess of butyllithium, however, resulted in the formation after carboxylation of a complex mixture from which it was impossible to isolate the expected **6g**.



Scheme 6

The amino acids were purified on an ion-exchange resin (Dowex 50 W-X8) and identified by ^1H NMR spectroscopy in $\text{D}_2\text{O}/\text{DCI}$ by comparison with commercial samples. Their optical purity was determined from the ^{19}F NMR spectra of their Mosher amides prepared in a conventional manner from the methyl esters;^[19] the nature of the isolated enantiomer and the enantiomeric excess were determined by comparison with the spectra of nonracemic mixtures of the corresponding Mosher amides prepared from commercially available D- and L-amino acids – the racemic homocysteine was used. In the case of leucine, only the L-isomer was detected while for alanine and homocysteine, both enantiomers were present with a large predominance of the L isomer.

As for methionine, the entire process giving the amino acid from **1** can be run in 35–40 min, which should allow the implementation of this method for the preparation of enantiopure 1- ^{11}C natural or unnatural α -amino acids.

Conclusion

In conclusion, the results presented here show that the carboxylation of *N*-(α -lithioalkyl)oxazolidinones provides a new method for obtaining enantiopure α -amino acids with the possibility of labelling the carboxyl group not only by

^{11}C (the main purpose of this study) but also with ^{13}C and ^{14}C .

Experimental Section

General Remarks: All procedures were conducted in oven dried glassware under positive nitrogen pressure and using syringe-needle transfer techniques. DMF and $i\text{Pr}_2\text{NH}$ were distilled from CaH_2 , THF from sodium/benzophenone. – ^1H (200 MHz or 300 MHz) and ^{13}C NMR (50 MHz or 75 MHz) spectra were recorded on a Bruker AC 200 or AM 300. Chemical shifts are reported as δ values relative to the solvent peak of CHCl_3 set to 7.26 for ^1H and 77.16 for ^{13}C . ^{19}F NMR spectra were recorded at 188 MHz on a Bruker AC 200 with CFCl_3 as internal standard. – IR spectra were carried out on a Perkin–Elmer 298 spectrophotometer. – Melting points were determined in open capillaries and are uncorrected. – Optical rotation values were determined using a Perkin–Elmer 241 polarimeter. – Flash chromatography (FC) were performed using Merck 60 (40–63 μm) silica. – Mass spectra were recorded on a Nermag R-10-10S (70 eV). – Elemental analyses were performed at the SCA Solaize (France). – Oxazolidinones **5a** and **5b** were prepared from their corresponding amino alcohols by using triphosgene.^[20]

Preparation of α -Hydroxyorganostannanes

1-Tributylstannyl-3-methylthio Propan-1-ol (3a): To $i\text{Pr}_2\text{NH}$ (0.93 mL, 6.6 mmol) in THF (7 mL) was added dropwise *n*-butyllithium (2.5 M hexane solution, 6.6 mmol) at 0 °C. The solution was stirred for 15 min and Bu_3SnH (1.77 mL, 6.6 mmol) was added during 5 min. After 30 min, the reaction mixture was chilled to -78°C and a solution of 3-methylthiopropional (0.66 mL, 6.6 mmol) in THF (3 mL) was added dropwise. After stirring for an additional 30 min the mixture was warmed to room temp., quenched with saturated ammonium chloride (30 mL) and extracted with Et_2O (3 $\times$ 15 mL). The combined organic phases were washed with brine (3 $\times$ 40 mL), dried (Na_2SO_4) and concentrated. Purification of the crude product by FC (petroleum ether then petroleum ether/AcOEt = 90:10) gave pure **3a** (2.21 g, 85%) as an oil. – IR (film): $\tilde{\nu}$ = 3320, 2840, 1470 cm^{-1} . – ^1H NMR (CDCl_3 , 200 MHz): δ = 0.85–0.95 (m, 15 H), 1.25–1.60 (m, 12 H), 1.95–2.10 (m, 2 H), 2.10 (s, 3 H), 2.65 (t, J = 7 Hz, 2 H), 4.20–4.25 (m, 1 H). – ^{13}C NMR (50 MHz): δ = 8.6 (CH_2 , Bu_3Sn), 13.7 (CH_3 , Bu_3Sn), 15.5 (CH_3), 27.5 (CH_2 , Bu_3Sn), 29.2 (CH_2 , Bu_3Sn), 32.6 (CH_2), 36.8 (CH_2), 67.4 (CH). – EI MS; m/z (%): 313 (6), 279 (8), 269 (6), 177 (7), 64 (100), 63 (20), 57 (18), 55 (14), 47 (31), 45 (19), 41 (12).

3-Methyl-1-(tributylstannyl)butan-1-ol (3b): Prepared as described for **3a** from isovaleraldehyde (18 mmol). Purification by FC (petroleum ether then petroleum ether/AcOEt 90:10), colourless oil, yield 64%. – IR (film): $\tilde{\nu}$ = 3400, 1460, 1375 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.95–1.05 (m, 21 H), 1.22–1.38 (m, 7 H), 1.45–1.58 (m, 6 H), 1.75–1.88 (m, 2 H), 4.19 (m, 1 H). – ^{13}C NMR (CDCl_3 , 75 MHz): δ = 8.4 (CH_2 , Bu_3Sn), 13.7 (CH_3 , Bu_3Sn), 21.7 (CH_3), 23.5 (CH_3), 25.0 (CH), 27.5 (CH_2 , Bu_3Sn), 29.3 (CH_2 , Bu_3Sn), 47.5 (CH_2), 66.4 (CH).

1-(Tributylstannyl)ethan-1-ol (3c): Prepared as described for **3a** from acetaldehyde (18 mmol). Purification by FC (petroleum ether then petroleum ether/AcOEt = 90:10), colourless oil, yield 44%. – IR (film): $\tilde{\nu}$ = 3320, 1455 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.87–0.95 (m, 15 H), 1.23–1.53 (m, 12 H), 1.58–1.67 (m, 3 H), 2.20 (d, J = 2.6 Hz, 1 H), 4.16 (q, J = 7.5 Hz, 1 H). – ^{13}C NMR (CDCl_3 , 300 MHz): δ = 8.3 (CH_2 , Bu_3Sn), 13.7 (CH_3 , Bu_3Sn), 24.5 (CH_3), 27.5 (CH_2 , Bu_3Sn), 29.4 (CH_2 , Bu_3Sn), 63.6 (CH).

3-(Benzylthio)-1-(tributylstannyl)propan-1-ol (3d): Prepared as described for **3a** from 3-(benzylthio) propanal^[17] (9.5 mmol). Purification by FC (petroleum ether then petroleum ether/AcOEt 90:10), colourless oil, yield 52% – IR (film): $\tilde{\nu}$ = 3400, 3080, 3060, 3020 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.88–1.02 (m, 15 H), 1.27–1.52 (m, 12 H), 2.01–2.12 (m, 2 H), 2.40–2.60 (m, 2 H) 3.70 (s, 2 H), 4.20 (dd, J = 3.9 Hz, J = 9.6 Hz, 1 H), 7.26–7.42 (m, 5 H). – ^{13}C NMR (CDCl_3 , 50 MHz): δ = 8.7 (CH_2 , Bu_3Sn), 13.8 (CH_3 , Bu_3Sn), 27.6 (CH_2 , Bu_3Sn), 26.7 (CH_2), 29.3 (CH_2 , Bu_3Sn), 36.5 (CH_2), 37.2 (CH_2), 67.3 (CH), 127.1 (CH), 128.6 (CH), 128.9 (CH), 138.5 (C).

2-Phenyl-1-(tributylstannyl)ethanol (3e): Prepared as described for **3a** from phenylacetaldehyde (18 mmol). Purification by FC (petroleum ether, then petroleum ether/AcOEt 90:10), colourless oil, yield 45%. – IR (film): $\tilde{\nu}$ = 3400, 3080, 3040, 3020, 1455, 750, 700 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.87–0.97 (m, 15 H), 1.27–1.57 (m, 12 H), 3.04 (m, 2 H), 3.7 (d, J = 2.2 Hz, 1 H), 4.21 (dd, J = 6.1 Hz, J = 9 Hz, 1 H), 7.21–7.37 (m, 5 H). – ^{13}C NMR (CDCl_3 , 50 MHz): δ = 8.7 (CH_2 , Bu_3Sn), 13.8 (CH_3 , Bu_3Sn), 27.5 (CH_2 , Bu_3Sn), 29.3 (CH_2 , Bu_3Sn), 44.5 (CH_2), 68.7 (CH), 126.5 (CH), 128.6 (CH), 129.1 (CH), 139.9 (C).

2-Methyl-1-(tributylstannyl)propan-1-ol (3f): Prepared as described for **3a** starting from 2-methyl propanal (18 mmol). Purification by FC (petroleum ether then petroleum ether/AcOEt 90:10), colourless oil, yield 64%. – IR (film): $\tilde{\nu}$ = 3300, 1475, 1390 cm^{-1} . – ^{13}C NMR (CDCl_3 , 50 MHz): δ = 9.3 (CH_2 , Bu_3Sn), 13.6 (CH_3 , Bu_3Sn), 17.3 (CH_3), 19.8 (CH_3), 27.5 (CH_2 , Bu_3Sn), 29.3 (CH_2 , Bu_3Sn), 35.5 (CH), 76.4 (CH).

2-Benzyloxy-1-(tributylstannyl)ethan-1-ol (3g): Prepared as described for **3a** from 2-benzyloxy ethanal (5.9 mmol). Purification by FC (petroleum ether then petroleum ether/AcOEt 90:10), colourless oil, yield 35%. – IR (film): $\tilde{\nu}$ = 3350, 3070, 3030 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.78–0.90 (m, 15 H), 1.22–1.58 (m, 12 H), 2.16 (d, J = 4.8 Hz, 1 H, OH), 3.76 (d, J = 5.15 Hz, 2 H), 4.23 (dd, J = 4.8, 5.15 Hz, 1 H), 4.52 (d, J_{AB} = 11.52 Hz, 1 H), 4.58 (d, J_{AB} = 11.52 Hz, 1 H) 7.25–7.36 (m, 5 H). – ^{13}C NMR (CDCl_3 , 75 MHz): δ = 8.8 (CH_2 , Bu_3Sn), 13.7 (CH_3 , Bu_3Sn), 27.5 (CH_2 , Bu_3Sn), 29.2 (CH_2 , Bu_3Sn), 67.7 (CH), 72.9 (CH_2), 76.2 (CH_2), 127.7 (CH), 127.8 (CH), 128.4 (CH), 138.3 (C).

Preparation of α -Bromo Organostannanes

1-Bromo-3-(methylthio)-1-(tributylstannyl)propane (4a): A solution of triphenylphosphane (1.3 g, 4.96 mmol) in CH_2Cl_2 (7 mL) was added at -78°C to the alkoxystannane **3a** (1.037 g, 2.62 mmol) in CH_2Cl_2 (8 mL), then a solution of tetrabromomethane (2.33 g, 7.03 mmol) in CH_2Cl_2 (7 mL) was introduced dropwise. The reaction mixture was stirred for 1 h at -78°C and warmed slowly to room temp within ca. 2 h. The solvent was removed by evaporation and the residue was filtered on a short column of silica gel eluting with CH_2Cl_2 . Solvent was removed and the crude product was purified by FC (petroleum ether) to give pure **4a** (1.13 g, 94%) as a colourless oil. – IR (film): $\tilde{\nu}$ = 1470, 1380 cm^{-1} . – ^1H NMR (CDCl_3 , 200 MHz): δ = 0.90–0.97 (m, 15 H), 1.30–1.6 (m, 12 H), 2.10 (s, 3 H), 2.10–2.25 (m, 2 H), 2.55–2.85 (m, 2 H), 3.75 (dd, J = 5.45 Hz, J = 9.1 Hz, 1 H). – ^{13}C NMR (CDCl_3 , 50 MHz): δ = 10.2 (CH_2 , Bu_3Sn), 13.8 (CH_3 , Bu_3Sn), 15.7 (CH_3), 27.5 (CH_2 , Bu_3Sn), 29.1 (CH_2 , Bu_3Sn), 34.3 (CH_2), 36.9 (CH_2), 37.6 (CH). – EI-MS; m/z (%): 403 (15), 401 (24), 399 (20), 323 (21), 321 (18), 313 (31), 311 (18), 289 (7), 257 (11), 235 (15), 127 (29), 119 (10), 61 (100), 57 (72), 41 (81). – $\text{C}_{16}\text{H}_{35}\text{BrNSSn}$ (458.13): calcd. C 41.95, H 7.70; found C 41.96, H 7.89.

1-Bromo-3-methyl-1-(tributylstannyl)butane (4b): To triphenylphosphane (0.695 g, 2.65 mmol) in CH_2Cl_2 was added at 0°C 2.75 mL of a 0.97 M bromine solution in CH_2Cl_2 . To the white suspension of the $\text{PPh}_3\cdot\text{Br}_2$ complex was added dropwise a solution of the hydroxystannane **3b** in CH_2Cl_2 (2.7 mL). The reaction mixture was warmed to room temp. and stirred for 4 h. Solvent was removed under reduced pressure and the residue was purified by FC (petroleum ether). Pure **4b** (0.67 g, 57%) was obtained as a colourless oil. – IR (film): $\tilde{\nu}$ = 1470, 1380 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.85–1.05 (m, 21 H), 1.28–1.38 (m, 6 H), 1.48–1.64 (m, 7 H), 1.89–2.10 (m, 2 H), 3.72 (dd, J = 4.25 Hz, J = 11.95 Hz, 1 H). – ^{13}C NMR (CDCl_3 , 50 MHz): δ = 9.8 (CH_2 , Bu_3Sn), 13.7 (CH_3 , Bu_3Sn), 20.6 (CH_3), 23.1 (CH_3), 26.9 (CH), 27.5 (CH_2 , Bu_3Sn), 29.0 (CH_2 , Bu_3Sn), 37.3 (CH), 46.7 (CH_2).

1-Bromo-1-(tributylstannyl)ethane (4c): Prepared as described for **4b** starting from **3c** (12.6 mmol). Purification by FC (petroleum ether), colourless oil, yield 42%. – IR (film): $\tilde{\nu}$ = 1470, 1380, 1120, 1000 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.85–1.00 (m, 15 H), 1.27–1.40 (m, 6 H), 1.48–1.57 (m, 6 H), 1.92 (d, J = 7.7 Hz, 3 H), 3.69 (q, J = 7.7 Hz, 1 H). – ^{13}C NMR (CDCl_3 , 50 MHz): δ = 9.7 (CH_2 , Bu_3Sn), 13.8 (CH_3 , Bu_3Sn), 25.0 (CH_3), 27.5 (CH_2 , Bu_3Sn), 29.0 (CH_2 , Bu_3Sn), 32.4 (CH).

3-(Benzylthio)-1-bromo-1-(tributylstannyl)propane (4d): Prepared as described for **4a** starting from **3d** (6 mmol). Purification by FC (petroleum ether), colourless oil, yield 70%. – IR (film): $\tilde{\nu}$ = 3080, 3040, 1610, 1590, 1380, 970, 720 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.82–0.97 (m, 15 H) 1.22–1.57 (m, 12 H), 2.10–2.32 (m, 2 H), 2.52–2.75 (m, 2 H), 3.70 (dd, J = 3.9 Hz, J = 9.6 Hz, 1 H), 3.72 (s, 2 H), 7.26–7.32 (s, 5 H). – ^{13}C NMR (CDCl_3 , 75 MHz): δ = 10.0 (CH_2 , Bu_3Sn), 13.8 (CH_3 , Bu_3Sn), 27.5 (CH_2 , Bu_3Sn), 29.0 (CH_2 , Bu_3Sn), 31.5 (CH_2), 36.6 (CH_2), 37.0 (CH), 37.5 (CH_2), 127.1 (CH), 128.6 (CH), 128.9 (CH) 138.6 (C).

1-Bromo-2-phenyl-1-(tributylstannyl)ethane (4e): Prepared as described for **4a** starting from **3e** (18 mmol). Purification by FC (petroleum ether), colourless oil, yield 45%. – IR (film): $\tilde{\nu}$ = 3060, 3020 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.80–0.97 (m, 15 H), 1.22–1.50 (m, 12 H), 3.30 (dd, J = 7.73, J_{AB} = 13.98 Hz, 1 H), 3.37 (dd, J = 8.82 Hz, J_{AB} = 13.98 Hz, 1 H), 3.80 (dd, J = 7.73 Hz, J = 8.82 Hz, 1 H), 7.22–7.37 (m, 5 H). – ^{13}C NMR (CDCl_3 , 75 MHz): δ = 10.2 (CH_2 , Bu_3Sn), 13.8 (CH_3 , Bu_3Sn), 27.5 (CH_2 , Bu_3Sn), 29.0 (CH_2 , Bu_3Sn), 38.2 (CH), 44.3 (CH_2), 126.9 (CH), 128.5 (CH), 128.9 (CH), 140.6 (C).

1-Bromo-2-methyl-1-(tributylstannyl)propane (4f): Prepared as described for **4b** starting from **3f** (6.8 mmol). Purification by FC (petroleum ether), colourless oil, yield 31%. – IR (film): $\tilde{\nu}$ = 1470 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.85–1.10 (m, 21 H), 1.25–1.60 (m, 12 H), 2.05–2.15 (m, 1 H), 3.68 (d, J = 4.78 Hz, 1 H). – ^{13}C NMR (CDCl_3 , 50 MHz): δ = 10.8 (CH_2 , Bu_3Sn), 13.7 (CH_3 , Bu_3Sn), 22.2 (CH_3), 23.0 (CH_3), 27.5 (CH_2 , Bu_3Sn), 29.0 (CH_2 , Bu_3Sn), 34.8 (CH), 50.4 (CH).

2-Benzyloxy-1-bromo-1-(tributylstannyl)ethane (4g): Prepared as described for **4a** starting from **3g** (3.7 mmol). Purification by FC (petroleum ether), colourless oil, yield 53%. – IR (film): $\tilde{\nu}$ = 3060, 3020 cm^{-1} . – ^1H NMR (CDCl_3 , 300 MHz): δ = 0.85–1.10 (m, 15 H), 1.25–1.54 (m, 12 H), 3.73 (t, J = 5.88 Hz, 1 H), 3.94 (d, J = 5.88 Hz, 2 H), 4.55 (d, J_{AB} = 11.55 Hz, 1 H), 4.60 (d, J_{AB} = 11.55 Hz, 1 H), 7.27–7.36 (m, 5 H). – ^{13}C NMR (CDCl_3 , 75 MHz): δ = 10.3 (CH, Bu_3Sn), 13.7 (CH_3 , Bu_3Sn), 27.4 (CH_2 , Bu_3Sn), 28.9 (CH_2 , Bu_3Sn), 35.7 (CH), 72.8 (CH_2), 74.9 (CH_2), 127.7 (CH), 127.8 (CH), 128.4 (CH), 138.1 (C).

Preparation of *N*-(α -Stannylalkyl)oxazolidinones

(4*S*,1'*R*)-3-[3-(Methylthio)-1-(tributylstannyl)propyl]-4-phenyloxazolidin-2-one (1*aa*) and (4*S*,1'*S*)-3-[3-(Methylthio)-1-(tributylstannyl)propyl]-4-phenyloxazolidin-2-one (1*ab*): Sodium hydride (72 mg, 60% dispersion in oil, 1.8 mmol) was added at room temp. to a solution of (*S*)-4-phenyloxazolidin-2-one (0.24 g, 1.47 mmol) in DMF (6 mL). The mixture was stirred for 30 min before adding a solution of bromostannane **4a** (0.825 g, 1.8 mmol) in DMF (1.2 mL). After 4 h, water was carefully added to the mixture and the solution was extracted with AcOEt (3 $\times$ 25 mL). The combined organic phases were washed with brine (3 $\times$ 30 mL), dried over Na₂SO₄ and concentrated under reduced pressure. The residue was purified by FC (petroleum ether/AcOEt = 90:10 then 80:20), a 1:1 mixture of diastereomers **1aa**/**1ab** was obtained as a colourless oil (0.715 g, 90%). The two diastereomers were separated by FC (petroleum ether/AcOEt = 95:5).

1aa: [α]_D = +22.9 (*c* = 2.2, CHCl₃). – IR (film): $\tilde{\nu}$ = 3080, 3060, 3040, 1740, 1605, 1590, 760, 700 cm⁻¹. – ¹H NMR (CDCl₃, 300 MHz): δ = 0.75–0.95 (m, 15 H), 1.15–1.50 (m, 12 H) 2.10 (s, 3 H), 1.85–2.15 (m, 2 H), 2.45 (t, *J* = 7.0 Hz, 2 H) 2.75 (dd, *J* = 5.99 Hz, *J* = 6.61 Hz, 1 H), 4.15 (dd, *J* = 7.35 Hz, *J* = 8.82 Hz, 1 H), 4.60 (t, *J* = 8.82 Hz, 1 H), 4.86 (dd, *J* = 7.35 Hz, *J* = 8.82 Hz, 1 H), 7.30–7.45 (m, 5 H). – ¹³C NMR (CDCl₃, 50 MHz): δ = 10.9 (CH₂, Bu₃Sn), 13.7 (CH₃, Bu₃Sn), 27.4 (CH₂, Bu₃Sn), 29.0 (CH₂, Bu₃Sn), 30.9 (CH₂), 32.7 (CH₂), 40.1 (CH), 61.5 (CH), 69.3 (CH₂), 127.4 (CH₂), 129.1 (CH₂), 138.0 (C), 158.7 (C). – C₂₅H₄₃NO₂SSn (540.4): calcd. C 55.57, H 8.02; found C 55.96, H 8.16.

1ab: Eluting first. – [α]_D = +21.5 (*c* = 2.3, CHCl₃). – IR (film): $\tilde{\nu}$ = 3080, 3060, 3040, 1740, 1605, 1590, 760, 700 cm⁻¹. – ¹H NMR (CDCl₃, 300 MHz): δ = 0.80–0.95 (m, 15 H) 1.20–1.55 (m, 12 H), 1.79 (s, 3 H), 1.85–1.95 (m, 2 H), 2.10–2.20 (m, 2 H), 2.92 (apparent t, *J* = 7.6 Hz, 1 H), 4.24 (dd, *J* = 5.52 Hz, *J* = 6.61 Hz, 1 H), 4.48–4.62 (m, 2 H), 7.41 (m, 5 H). – ¹³C NMR (CDCl₃, 50 MHz): δ = 10.4 (CH₂, Bu₃Sn), 13.6 (CH₃, Bu₃Sn), 14.8 (CH₃), 27.4 (CH₂, Bu₃Sn), 29.1 (CH₂, Bu₃Sn), 31.4 (CH₂), 32.4 (CH₂), 43.7 (CH) 63.4 (CH), 69.5 (CH₂), 127.9 (CH), 129.1 (CH), 129.3 (CH), 138.4 (C), 158.6 (C). – C₂₅H₄₃NO₂SSn (540.4): calcd. C 55.57, H 8.02; found C 55.62, H 8.05.

(4*S*,5*R*,1'*R*)-3-[3-(Methylthio)-1-(tributylstannyl)propyl]-4,5-diphenyloxazolidin-2-one (1*ba*) and (4*S*,5*R*,1'*S*)-3-[3-(Methylthio)-1-(tributylstannyl)propyl]-4,5-diphenyloxazolidin-2-one (1*bb*): Prepared as described for **1aa** by alkylation of the sodium salt of (4*S*,5*R*)-4,5-diphenyloxazolidin-2-one with the bromostannane **4a** (2.8 mmol). FC purification (petroleum ether/AcOEt 90:10) gave a 1:1 mixture of diastereomers **1ba** and **1bb** as a viscous oil, yield 87%. – IR (α + β , film): $\tilde{\nu}$ = 3060, 3020, 1735 cm⁻¹. The two diastereomers were separated by FC (petroleum ether/AcOEt = 95:5).

1ba: [α]_D = +18.3 (*c* = 1.2, CHCl₃). – ¹H NMR (CDCl₃, 200 MHz): δ = 0.75–1.00 (m, 15 H), 1.20–1.60 (m, 12 H), 1.95–2.10 (m, 2 H), 2.10 (s, 3 H), 2.45–2.60 (m, 2 H), 2.79 (t, *J* = 6.25 Hz, 1 H), 5.22 (d, *J* = 8.6 Hz, 1 H), 5.81 (d, *J* = 8.6 Hz, 1 H), 6.81–7.12 (m, 10 H). – ¹³C NMR (CDCl₃, 50 MHz): δ = 11.3 (CH₂, Bu₃Sn), 13.7 (CH₃, Bu₃Sn), 15.6 (CH₃), 27.5 (CH₂, Bu₃Sn), 29.1 (CH₂, Bu₃Sn), 31.3 (CH₂), 32.8 (CH₂), 41.1 (CH₂), 66.3 (CH), 78.8 (CH), 125.9 (CH), 127.7 (CH), 127.8 (CH), 128.2 (CH, $\times$ 2), 128.3 (CH), 134.1 (C), 135.1 (C), 159.2 (C).

1bb: Eluting first. – [α]_D = +18.3 (*c* = 1.2, CHCl₃). – ¹H NMR (CDCl₃, 200 MHz): δ = 0.80–1.00 (m, 15 H), 1.15–1.60 (m, 12 H), 1.75 (s, 3 H), 1.90–2.25 (m, 4 H), 3.1 (dd, *J* = 6.8, 7.6 Hz, 1 H),

4.86 (d, *J* = 8.4 Hz, 1 H), 5.77 (d, *J* = 8.4 Hz, 1 H), 6.9–7.03 (m, 10 H). – ¹³C NMR (CDCl₃, 50 MHz): δ = 10.3 (CH₂, Bu₃Sn), 13.4 (CH₂, Bu₃Sn), 14.6 (CH₃), 27.2 (CH₂, Bu₃Sn), 28.8 (CH₂, Bu₃Sn), 31.2 (CH₂), 32.2 (CH₂), 44.3 (CH), 67.9 (CH), 78.9 (CH), 125.5 (CH), 127.3 (CH), 127.5 (CH), 127.8 (CH), 128.2 (CH), 128.3 (CH), 134.8 (C), 135.0 (C), 158.2 (C), 170.6 (C).

(4*S*,1'*R*)-3-[3-Methyl-1-(tributylstannyl)butan-1-yl]-4-phenyloxazolidin-2-one (1*ba*) and (4*S*,1'*S*)-3-[3-methyl-1-(tributylstannyl)butan-1-yl]-4-phenyloxazolidin-2-one (1*bb*): Prepared as described for **1aa** by alkylation of the sodium salt of (*S*)-4-phenyloxazolidin-2-one with the bromostannane **4b** (7.4 mmol). FC purification (petroleum ether/AcOEt 90:10) gave a 1:1 mixture of diastereomers **4ba** and **4bb** as a viscous oil, yield 84%. The two diastereomers are separated by FC (petroleum ether = 95/5).

1ba: [α]_D = +23.05 (*c* = 1.2, CHCl₃). – IR (α + β , film): $\tilde{\nu}$ = 3080, 3060, 3020, 1745 cm⁻¹. – ¹H NMR (CDCl₃, 300 MHz): δ = 0.78 (d, *J* = 6.25 Hz, 3 H), 0.82–0.92 (m, 15 H), 1.22–1.50 (m, 16 H), 1.64–1.72 (m, 2 H), 2.71 (t, *J* = 7.5 Hz, 1 H), 4.10 (dd, *J* = 7.72, *J*_{AB} = 8.8 Hz, 1 H), 4.59 (apparent t, *J* = 9 Hz, 1 H), 4.83 (apparent t, *J* = 8.3 Hz, 1 H), 7.26–7.42 (m, 5 H). – ¹³C NMR (CDCl₃, 75 MHz): δ = 10.6 (CH₂, Bu₃Sn), 13.7 (CH₃, Bu₃Sn), 22.5 (CH₃), 22.7 (CH₃), 26.6 (CH), 27.5 (CH₂, Bu₃Sn) 29.1 (CH₂, Bu₃Sn), 39.4 (CH), 40.8 (CH), 62.2 (CH), 69.4 (CH₂), 127.4 (CH), 129.1 (CH), 129.2 (CH), 138.3 (C), 158.6 (C). – C₂₆H₄₅NO₂Sn (522.35): calcd. C 59.79, H 8.68; found C 60.00, H 8.93.

1bb: Eluting first. – [α]_D = +23.9 (*c* = 2.4, CHCl₃). – ¹H NMR (CDCl₃, 300 MHz): δ = 0.54 (d, *J* = 6.6 Hz, 3 H), 0.58 (d, *J* = 6.6 Hz, 1 H), 0.83–0.93 (m, 15 H), 1.24–1.50 (m, 13 H), 1.62–1.78 (m, 2 H), 2.84 (dd, *J* = 6.98 Hz, *J* = 9.19 Hz, 1 H), 4.21 (m, 1 H), 4.48–4.60 (m, 2 H), 7.34–7.40 (m, 5 H). – ¹³C NMR (CDCl₃, 75 MHz): δ = 10.2 (CH₂, Bu₃Sn), 13.7 (CH₃, Bu₃Sn), 21.9 (CH₃), 22.6 (CH₃), 25.8 (CH), 27.5 (CH₂, Bu₃Sn), 29.2 (CH₂, Bu₃Sn), 41.6 (CH₂), 42.6 (CH), 63.2 (CH), 69.5 (CH₂), 128.1 (CH), 129.1 (CH), 129.3 (CH), 138.4 (C), 158.4 (C). – C₂₆H₄₅NO₂Sn (522.35): calcd. C 59.79, H 8.68; found C 59.61, H 8.53.

(4*S*,1'*R*)-3-[1-(Tributylstannyl)ethyl]-4-phenyloxazolidin-2-one (1*ca*) and (4*S*,1'*S*)-3-[1-(Tributylstannyl)ethyl]-4-phenyloxazolidin-2-one (1*cb*): Prepared as described for **1aa** by alkylation of the sodium salt of (*S*)-4-phenyloxazolidin-2-one with the bromostannane **4c**. – Scale 5.2 mmol. – A FC purification (petroleum ether/AcOEt = 90/10) gave a 1/1 mixture of diastereomers **1ca** and **1cb** as a viscous oil, yield 71%. The two diastereomers were separated by FC (petroleum ether/AcOEt = 95/5).

1ca: [α]_D = +39.7 (*c* = 1.35, CHCl₃). – IR (α + β , film): $\tilde{\nu}$ = 3065, 3025, 1740 cm⁻¹. – ¹H NMR (CDCl₃, 300 MHz): δ = 0.84–0.92 (m, 15 H), 1.18–1.31 (m, 9 H), 1.40–1.50 (m, 6 H), 2.58 (q, *J* = 7.3 Hz, 1 H), 4.05 (apparent t, *J*_{AB} = 8.1 Hz, 1 H), 4.57 (t, *J* = 8.8 Hz, 1 H), 4.93 (apparent t, *J*_{AB} = 8.1 Hz, 1 H), 7.26–7.44 (m, 5 H). – ¹³C NMR (CDCl₃, 75 MHz): δ = 10.7 (CH₂, Bu₃Sn), 13.8 (CH₃, Bu₃Sn), 15.9 (CH₃), 27.5 (CH₂, Bu₃Sn), 29.2 (CH₂, Bu₃Sn), 35.2 (CH), 59.8 (CH), 69.4 (CH₂), 127.2 (CH), 129.0 (CH), 129.2 (CH), 138.1 (C), 158.9 (C). – C₂₃H₃₉NO₂Sn (480.27): calcd. C 55.2 H 8.18; found C 57.54, H 8.38.

1cb: Eluting first – [α]_D = +24 (*c* = 1.9, CHCl₃). – ¹H NMR (CDCl₃, 300 MHz): δ = 0.84–0.94 (m, 15 H) 1.16 (d, *J* = 7.4 Hz, 3 H), 1.26–1.55 (m, 12 H), 2.78 (m, 1 H), 4.14 (dd, *J* = 5.9 Hz, *J* = 7.35 Hz, 1 H), 4.51–4.62 (m, 2 H), 7.31–7.47 (m, 5 H). – ¹³C NMR (CDCl₃, 75 MHz): δ = 10.2 (CH₂, Bu₃Sn), 13.7 (CH₃, Bu₃Sn), 18.8 (CH₃), 27.5 (CH₂, Bu₃Sn), 29.2 (CH₂, Bu₃Sn), 39.2

(CH), 63.6 (CH), 69.7 (CH₂), 127.6 (CH), 129.1 (CH), 129.2 (CH), 139.3 (C), 158.5 (C).

(4*S*,1'*R*)-3-[3-(Benzylthio)-1-(tributylstannyl)propyl]-4-phenyloxazolidin-2-one (1d α) and (4*S*,1'*S*)-3-[3-(Benzylthio)-1-(tributylstannyl)propyl]-4-phenyloxazolidin-2-one (1d β): Prepared as described for **1aa** by alkylation of the sodium salt of (*S*)-4-phenyloxazolidin-2-one with the bromostannane **4d** (2.6 mmol). FC purification (petroleum ether/AcOEt 90:10) gave a 1:1 mixture of diastereomers **4d α** and **4d β** , yield 90%. The two diastereomers were separated by FC (petroleum ether/AcOEt 95:5).

1d α : [α]_D = +25.5 (*c* = 1.5, CHCl₃) – IR (α + β , film): $\tilde{\nu}$ = 3080, 3060, 3020, 1740, 1600, 760, 700 cm⁻¹. – ¹H NMR (CDCl₃, 300 MHz): δ = 0.78–0.92 (m, 15 H), 1.18–1.38 (m, 12 H) 1.83 (m, 1 H), 2.04 (m, 1 H), 2.37 (dd, *J* = 6.6, 8.5 Hz, 2 H), 2.67 (dd, *J* = 5.9, 7.4 Hz, 1 H), 3.70 (s, 2 H), 4.08 (dd, *J* = 7.0 Hz, *J*_{AB} = 8.8 Hz, 1 H), 4.45 (t, *J* = 8.8 Hz, 1 H), 4.62 (dd, *J* = 6.6 Hz, *J*_{AB} = 8.8 Hz, 1 H), 7.20–7.40 (m, 10 H). – ¹³C NMR (CDCl₃, 75 MHz): δ = 10.9 (CH₂, Bu₃Sn), 13.8 (CH₃, Bu₃Sn), 27.5 (CH₂, Bu₃Sn), 29.0 (CH₂, Bu₃Sn), 29.8 (CH₂), 31.1 (CH₂), 36.4 (CH), 40.1 (CH₂), 61.5 (CH), 69.3 (CH₂), 127.1 (CH), 128.6 (CH), 128.9 (CH), 129.1 (CH), 129.2 (CH), 138.1 (C), 138.3 (C), 158.6 (C). – C₃₁H₄₇NO₂SSn (616.49): calcd. C 60.40, H 7.68; found C 60.47, H 7.76.

1d β : Eluting first. – [α]_D = +27.2 (*c* = 1.5, CHCl₃). – ¹H NMR (CDCl₃, 300 MHz): δ = 0.82–0.93 (m, 15 H), 1.27–1.49 (m, 12 H), 1.80–2.09 (m, 4 H), 2.86 (t, *J* = 6.7 Hz, 1 H), 3.35 (d, *J*_{AB} = 13.6 Hz, 1 H), 3.44 (d, *J*_{AB} = 13.6 Hz, 1 H), 4.2 (dd, *J* = 5.9 Hz, *J* = 7.3 Hz, 1 H), 4.47–4.58 (m, 2 H), 7.15–7.39 (m, 10 H). – ¹³C NMR (CDCl₃, 75 MHz): δ = 10.4 (CH₂, Bu₃Sn), 13.8 (CH₃, Bu₃Sn), 27.5 (CH₂, Bu₃Sn), 29.1 (CH₂, Bu₃Sn), 31.6 (CH₂), 35.5 (CH₂), 43.9 (CH), 63.4 (CH), 69.6 (CH₂), 126.9 (CH), 128.0 (CH), 128.5 (CH), 128.9 (CH), 129.2 (CH), 129.4 (CH), 138.3 (C), 158.7 (C).

(4*S*,1'*R*)-4-Phenyl-3-[2-phenyl-1-(tributylstannyl)ethyl]oxazolidinon-2-one (1e α) and (4*S*,1'*S*)-4-Phenyl-3-[2-phenyl-1-(tributylstannyl)ethyl]oxazolidinon-2-one (1e β): Prepared as described for **1aa** by alkylation of the sodium salt of (*S*)-4-phenyloxazolidin-2-one with the bromostannane **4e** (2.5 mmol). FC purification (petroleum ether/AcOEt 90:10) gave a 1:1 mixture of diastereomers **1e α** and **1e β** , yield 10%. An attempt to separate the two diastereomers by FC (petroleum ether/AcOEt 95:5) was unsuccessful. Nevertheless when the reaction of the 1:1 mixture was conducted with one equivalent of *n*BuLi (THF, –70 °C), **1e α** was found not to have reacted and was recovered as such after work up and purification.

1e α : IR (α + β , film): $\tilde{\nu}$ = 3080, 3060, 3020, 1745, 1600, 1495, 700 cm⁻¹. – ¹H NMR (CDCl₃, 300 MHz): δ = 0.78–0.90 (m, 15 H), 1.18–1.45 (m, 12 H), 2.77 (dd, *J* = 4.8 Hz, *J* = 14.3 Hz, 1 H), 2.78 (dd, *J* = 4.8 Hz, *J* = 12.1 Hz, 1 H), 3.12 (dd, *J* = 12.1 Hz, *J* = 14.3 Hz, 1 H), 3.76 (dd, *J*_{AB} = 7.3 Hz, *J* = 8.8 Hz, 1 H), 3.96 (dd, *J*_{AB} = 5.3 Hz, *J*_{AB} = 8.5 Hz, 1 H), 4.31 (apparent t, *J* = 8.8 Hz, 1 H), 6.96–7.35 (m, 10 H). – ¹³C NMR (CDCl₃, 75 MHz): δ = 10.5 (CH₂, Bu₃Sn), 13.8 (CH₃, Bu₃Sn), 27.5 (CH₂, Bu₃Sn), 29.0 (CH₂, Bu₃Sn), 38.3 (CH₂), 43.2 (CH), 62.3 (CH), 69.3 (CH₂), 126.6 (CH), 127.5 (CH), 128.7 (CH), 128.96 (CH), 129.02 (CH), 138.0 (C), 141.6 (C) 158.4 (C).

1e β : ¹³C NMR (CDCl₃, 50 MHz, selected data deduced from a spectra of an α/β mixture): δ = 38.3 (CH₂, C^{2'}), 46.1 (CH, C^{1'}), 63.6 (CH, C⁴) 69.7 (CH₂, C⁵), 158.4 (C, C²).

(4*S*,1'*R*)-3-[2-Methyl-1-(tributylstannyl)propyl]-4-phenyloxazolidin-2-one (1fa) and (4*S*,1'*S*)-3-[2-Methyl-1-(tributylstannyl)propyl]-4-

phenyloxazolidin-2-one (1f β): Prepared as described for **1aa** by alkylation of the sodium salt of (*S*)-4-phenyloxazolidin-2-one with the bromostannane **4f** (2 mmol). FC purification (petroleum ether/AcOEt 90:10) gave a 1:1 mixture of diastereomers **1fa** and **1f β** , yield 5%. The two diastereomers were separated by FC (petroleum ether/AcOEt 95:5).

1fa: [α]_D = +10.5 (*c* = 1.2, CHCl₃). – IR (α + β , film): $\tilde{\nu}$ = 3070, 3030, 1740 cm⁻¹. – ¹H NMR (CDCl₃, 300 MHz): δ = 0.82–0.88 (m, 18 H), 0.92 (d, *J* = 6.6 Hz, 3 H), 1.19–1.44 (m, 12 H), 2.20–2.35 (m, 1 H), 2.43 (d, *J* = 7.4 Hz, 1 H), 4.15 (dd, *J* = 7.7 Hz, *J* = 8.8 Hz, 1 H), 4.62 (apparent t, *J* = 8.8 Hz, 1 H), 4.88 (dd, *J* = 7.7 Hz, *J* = 8.8 Hz, 1 H), 7.26–7.42 (m, 5 H). – ¹³C NMR (CDCl₃, 75 MHz): δ = 11.7 (CH₂, Bu₃Sn), 13.7 (CH₃, Bu₃Sn), 21.6 (CH₃), 21.8 (CH₃), 27.5 (CH₂, Bu₃Sn), 29.1 (CH₂, Bu₃Sn), 31.05 (CH), 49.4 (CH), 62.7 (CH), 69.4 (CH₂), 127.7 (CH), 129.1 (CH), 129.2 (CH), 137.9 (C), 158.9 (C).

1f β : Eluting first – [α]_D = +30.55 (*c* = 1.2, CHCl₃) – ¹H NMR (CDCl₃, 300 MHz): δ = 0.60 (d, *J* = 6.6 Hz, 3 H), 0.73 (d, *J* = 6.6 Hz, 3 H), 0.86–0.93 (m, 15 H), 1.23–1.57 (m, 12 H), 2.10–2.22 (m, 1 H), 2.44 (d, *J* = 9.2 Hz, 1 H), 4.27 (apparent t, *J* = 7.7 Hz, 1 H), 4.50 (dd, *J* = 7.3, *J*_{AB} = 8.8 Hz, 1 H), 4.57 (dd, *J* = 8.1 Hz, *J*_{AB} = 8.8 Hz, 1 H) 7.34–7.42 (m, 5 H). – ¹³C NMR (CDCl₃, 75 MHz): δ = 11.2 (CH₂, Bu₃Sn), 13.7 (CH₃, Bu₃Sn), 21.6 (CH₃), 21.8 (CH₃), 27.6 (CH₂, Bu₃Sn), 29.2 (CH₂, Bu₃Sn), 30.4 (CH), 53.7 (CH), 63.9 (CH), 69.4 (CH₂), 128.5 (CH), 129.0 (CH), 129.3 (CH), 138.0 (C), 159.0 (C).

(4*S*,1'*R*)-3-[Benzyloxy-1-(tributylstannyl)ethyl]-4-phenyloxazolidin-2-one (1g α) and (4*S*,1'*S*)-3-[Benzyloxy-1-(tributylstannyl)ethyl]-4-phenyloxazolidin-2-one (1g β): Prepared as described for **1aa** by alkylation of the sodium salt of the bromostannane **4g** (1 mmol). FC purification (petroleum ether/AcOEt 90:10) gave a 1:1 mixture of diastereomers **1g α** and **1g β** , yield 55%. An attempt to separate the two diastereomers by FC was unsuccessful. – IR (α + β , film): $\tilde{\nu}$ = 3080, 3060, 3030, 1745, 1605, 1590, 1495 cm⁻¹. – ¹³C NMR (CDCl₃, 75 MHz): δ = 10.7–11.1 (CH₂, Bu₃Sn), 13.7–13.8 (CH₃, Bu₃Sn), 27.5–27.8 (CH₂, Bu₃Sn), 29.08, 29.11 (CH₂, Bu₃Sn), 41.9, 45.2 (CH), 63.1, 63.2 (CH), 69.60, 70.0 (CH₂) 70.4, 72.53 (CH₂), 72.62, 73.1 (CH₂), 127.50–129.14 (CH, Ar), 138.20, 138.46, 138.51, 138.95 (C) 158.85, 158.89 (C).

Transmetalation of the *N*-(α -Stannylalkyl)oxazolidinones **1a–d** and Carboxylation

(2*S*,4'*S*)-4-Methylthio-2-(2'-oxo-4'-phenyloxazolidin-3'-yl)butanoic Acid (6aaa): To the 1:1 mixture of diastereomers **1aaa** and **1a β** (0.92 g, 1.7 mmol) in THF (17 mL) was added dropwise *n*BuLi (0.68 mL, 1.7 mmol, 2.5 M solution in hexanes) at –78 °C. The yellow mixture was stirred for 5 min and CO₂ was bubbled through the solution. The mixture was poured into water (40 mL) and extracted with petroleum ether (2 $\times$ 30 mL). The aqueous phase was acidified to pH 1 with HCl 6 N and extracted with CH₂Cl₂ (3 $\times$ 50 mL). The combined organic phases were dried over Na₂SO₄ and evaporated under reduced pressure to afford **6aaa** as a viscous oil (0.427 g, 85%). – *Note 1:* the yield could be increased by using a slight excess of *n*BuLi (ca 90% with 1.2 equiv.) but it was not applicable to our procedure due to probable loss of radioactivity by formation of 1-[¹⁴C] pentanoic acid. – *Note 2:* the total time of the process was drastically reduced to 15–20 min when small scale (range: 35–150 μ mol) manipulations using conical microvial glassware were adopted. In this case, CO₂ bubbling needed 30 sec to 1 min and the number of extractions were reduced to 1 or 2; yields: 60 to 85%.

6aaa: $[\alpha]_D = +16.4$ ($c = 1.05$, CHCl_3). – IR (film): $\tilde{\nu} = 3500, 3100, 3030, 1760, 1480, 1460, 1410 \text{ cm}^{-1}$. – ^1H NMR (CDCl_3 , 200 MHz): $\delta = 1.95$ (s, 3 H), 2.05 (m, 2 H), 2.41 (t, $J = 7.5 \text{ Hz}$, 2 H), 4.27 (dd, $J = 6.9 \text{ Hz}$, $J = 8.6 \text{ Hz}$, 1 H), 4.44 (dd, $J = 5.2 \text{ Hz}$, $J = 9.4 \text{ Hz}$, 1 H), 4.72 (apparent t, $J = 8.8 \text{ Hz}$, 1 H), 5.00 (dd, $J = 6.9 \text{ Hz}$, $J = 8.9 \text{ Hz}$, 1 H), 7.40 (m, 5 H), 9.30 (broad s, 1 H). – ^{13}C NMR (CDCl_3 , 50 MHz): 15.0 (CH_3), 28.4 (CH_2), 30.6 (CH_2), 55.3 (CH), 60.1 (CH), 71.0 (CH_2), 127.7 (CH), 129.3 (CH), 129.4 (CH), 138.4 (C), 158.9 (C), 174.8 (C). – EI MS; m/z (%): 221 (20), 203 (18), 104 (100), 103 (28), 91 (32), 77 (21), 61 (43), 51 (12), 45 (20). – CI HRMS: calcd. for $\text{C}_{14}\text{H}_{18}\text{NO}_4\text{S}$ (MH^+): 296.0956; found 296.0956.

(2*S*,4'*S*,5'*R*)-4-(Methylthio)-2-(2'-oxo-4',5'-diphenyloxazolidin-3'-yl)butanoic Acid (6ab): Prepared as described for **6aaa** starting from **1ab** (1:1 mixture of diastereomers α and β , 2 mmol). Viscous oil, yield 78%. – $[\alpha]_D = +22.6$ ($c = 1.05$, CHCl_3). – ^1H NMR (CDCl_3 , 200 MHz): $\delta = 1.84$ (s, 3 H), 2.05 (m, 2 H), 2.38 (t, $J = 7.5 \text{ Hz}$, 2 H), 4.65 (dd, $J = 5.7 \text{ Hz}$, $J = 8.9 \text{ Hz}$, 1 H), 5.25 (d, $J = 8.3 \text{ Hz}$, 1 H), 6.10 (d, $J = 8.3 \text{ Hz}$, 1 H), 7.05 (m, 10 H), 10.10 (broad s, 1 H). – ^{13}C NMR (CDCl_3 , 50 MHz): $\delta = 14.7$ (CH_3), 28.9 (CH_2), 30.7 (CH_2), 57.0 (CH), 63.9 (CH), 81.3 (CH), 126.0 (CH), 127.8 (CH), 128.0 (CH), 128.2 (CH), 134.2 (C), 135.8 (C), 159.7 (C), 175.6 (C). – EI MS; m/z (%): 180 (42), 179 (34), 165 (22), 105 (33), 91 (43), 77 (53), 61 (34), 51 (71), 50 (40), 47 (62), 45 (73), 44 (100).

(2*S*,4'*S*)-4-Methyl-2-(2'-oxo-4'-phenyloxazolidin-3'-yl)pentanoic Acid (6b): Prepared as described for **6aaa** from **1b** (0.8 mmol). Viscous oil, yield 85%. – $[\alpha]_D = +49.5$ ($c = 0.5$, CHCl_3). – ^1H NMR (CDCl_3 , 300 MHz): $\delta = 0.49$ (d, $J = 6.2 \text{ Hz}$, 3 H), 0.85 (d, $J = 6.2 \text{ Hz}$, 3 H), 1.21–1.48 (m, 3 H), 4.25 (dd, $J = 6.6 \text{ Hz}$, $J = 8.8 \text{ Hz}$, 1 H), 4.48 (dd, $J = 4.0 \text{ Hz}$, $J = 10.3 \text{ Hz}$, 1 H), 4.71 (apparent t, $J = 8.8 \text{ Hz}$, 1 H), 5.04 (dd, $J = 6.6 \text{ Hz}$, $J = 8.8 \text{ Hz}$, 1 H), 7.39 (m, 5 H), 10.18 (broad s, 1 H). – ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 21.1$ (CH_3), 22.5 (CH_3), 24.4 (CH), 37.9 (CH_2), 55.6 (CH), 59.4 (CH), 71.1 (CH_2), 127.6 (CH), 129.18 (CH), 129.19 (CH), 139.3 (C), 159.6 (C), 175.3 (C).

(2*S*,4'*S*)-4-Methyl-2-(2'-oxo-4'-phenyloxazolidin-3'-yl)propanoic Acid (6c): Prepared as described for **6aaa** starting from **1c** (1 mmol). Viscous oil, yield 72%. – $[\alpha] = +98$ ($c = 0.6$, MeOH). – ^1H NMR (CD_3OD , 300 MHz): $\delta = 1.10$ (d, $J = 7.4 \text{ Hz}$, 6 H), 4.09 (dd, $J = 6.6 \text{ Hz}$, $J = 8.5 \text{ Hz}$, 1 H), 4.32 (q, $J = 7.4 \text{ Hz}$, 1 H), 4.70 (apparent t, $J = 8.8 \text{ Hz}$, 1 H), 5.10 (dd, $J = 6.6 \text{ Hz}$, $J = 8.8 \text{ Hz}$, 1 H), 7.28–7.44 (m, 5 H). – ^{13}C NMR (CD_3OD , 75 MHz): $\delta = 18.5$ (CH_3), 56.2 (CH), 63.0 (C), 75.0 (CH_2), 130.8 (CH), 132.5 (CH), 132.8 (CH), 143.9 (C), 163.6 (C), 176.7 (C).

(2*S*,4'*S*)-4-(Benzylthio)-2-(2'-oxo-4'-phenyloxazolidin-3'-yl)butanoic Acid (6d): Prepared as described for **6aaa** starting from **1d** (1 mmol). Viscous oil, yield 80%. – $[\alpha] = +14$ ($c = 3.1$, CHCl_3). – ^1H NMR (CDCl_3 , 300 MHz): $\delta = 1.75$ – 2.12 (m, 2 H), 2.32 (m, 2 H), 3.58 (broad s, 2 H), 4.19 (dd, $J = 6.98 \text{ Hz}$, $J = 8.83 \text{ Hz}$, 1 H), 4.34 (dd, $J = 5.15 \text{ Hz}$, $J = 9.56 \text{ Hz}$, 1 H), 4.60 (t, $J = 8.83 \text{ Hz}$, 1 H), 4.84 (dd, $J = 6.98 \text{ Hz}$, $J = 8.82 \text{ Hz}$, 1 H), 7.18 – 7.40 (m, 10 H), 9.0 (broad s, 1 H). – ^{13}C NMR (CDCl_3 , 75 MHz): $\delta = 27.9$ (CH_2), 28.6 (CH_2), 35.9 (CH_2), 55.4 (CH), 60.1 (CH), 71.0 (CH_2), 127.1 (CH), 127.7 (CH), 128.6 (CH), 128.9 (CH), 129.26 (CH), 129.32 (CH), 138.1 (C), 138.3 (C), 158.9 (C), 174.9 (C).

Preparation of 6aa β . – **(2*R*,4'*S*)-4-Methylthio-2-(2'-oxo-4'-phenyloxazolidin-3'-yl)butanenitrile (7a)** and **(2*R*,4'*S*)-4-Methylthio-2-(2'-oxo-4'-phenyloxazolidin-3'-yl)butanenitrile (7b)**: To a mixture of (*S*)-4-phenylglycinol (1.4 g, 10.2 mmol) and potassium cyanide (0.548 g, 11.2 mmol) in CH_2Cl_2 (10 mL) was added 3-methylthio-propanal (1.02 mL, 10.2 mmol). Acetic acid (0.93 mL, 16.25 mmol) was added dropwise at room temp. and the resulting solution was

stirred for 2 h at 60° C then overnight at room temp. The mixture was evaporated under reduced pressure, dissolved with water (50 mL) and extracted with CH_2Cl_2 ($4 \times 50 \text{ mL}$). The combined organic phases were dried over Na_2SO_4 and the solvent was removed by rotary evaporation. The crude product was then briefly purified on silica gel (petroleum ether/AcOEt, 60:40) to give a diastereomeric mixture of amino alcohols (1.7 g, 6.8 mmol) which was redissolved in CH_2Cl_2 (9 mL) and pyridine (1.15 mL, 14.2 mmol). A solution of triphosgene® (0.706 g, 2.38 mmol) in CH_2Cl_2 (8 mL) was then added dropwise at 0 °C and stirred for 3 h. After one night the mixture was diluted with diethyl ether (200 mL), washed with HCl (0.6 N, 30 mL) and brine (20 mL). The organic phase was dried over Na_2SO_4 and the solvent was removed. The ^1H NMR spectrum showed the crude product to be an 80:20 diastereomeric ratio of **7a**/**7b**. After FC purification and collection of the pure fractions (petroleum ether/AcOEt, 70:30 then 60:40) pure **7a** (1.56 g, 83%; 55% from phenylglycinol) and **7b** (0.11 g, 6%; 4% from phenylglycinol) were obtained.

7a: white solid, m.p. 74 °C. – $[\alpha]_D = +96$ ($c = 1$, CHCl_3). – IR (KBr): $\tilde{\nu} = 3060, 3005, 2240, 1765, 780, 760, 700 \text{ cm}^{-1}$. – ^1H NMR (CDCl_3 , 200 MHz): $\delta = 1.98$ (s, 3 H), 2.10–2.45 (m, 2 H), 2.47–2.60 (m, 2 H), 4.26 (dd, $J = 7.8 \text{ Hz}$, $J = 8.6 \text{ Hz}$, 1 H), 4.59 (dd, $J = 7.7 \text{ Hz}$, $J = 7.9 \text{ Hz}$, 1 H), 4.79 (apparent t, $J = 8.7 \text{ Hz}$, 1 H), 4.86 (dd, $J = 7.9 \text{ Hz}$, $J = 8.5 \text{ Hz}$, 1 H), 7.35–7.50 (m, 5 H). – EI MS; m/z (%): 276 (12), 217 (13), 171 (8), 158 (5), 130 (5), 116 (6), 104 (100), 91 (17), 77 (18), 61 (21), 51 (16), 47 (15). – $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_2\text{S}$ (276.36): calcd. C 60.85, H 5.84; found C 60.68, H 5.65.

7b: Eluting first, viscous oil. – $[\alpha]_D = +58$ ($c = 1$, CHCl_3). – IR (film): $\tilde{\nu} = 3060, 3015, 2220, 1750, 1605, 1590, 790, 765, 700 \text{ cm}^{-1}$. – ^1H NMR (CDCl_3 , 200 MHz): $\delta = 1.53$ –1.72 (m, 2 H), 1.97 (m, 3 H), 2.35–2.50 (m, 2 H), 4.32 (dd, $J = 7.3$, 8.9 Hz, 1 H), 4.73 (apparent t, $J = 8.9 \text{ Hz}$, 1 H), 4.98 (dd, $J = 7.3 \text{ Hz}$, $J = 8.5 \text{ Hz}$, 1 H), 7.49 (m, 5 H). – EI MS; m/z (%): 276 (7), 130 (5), 116 (7), 105 (8), 104 (100), 91 (22), 77 (20), 61 (22), 51 (22), 45 (19). – $\text{C}_{14}\text{H}_{16}\text{N}_2\text{O}_2\text{S}$ (276.36): calcd. C 60.85, H 5.84; found C 60.56, H 5.90.

(2*R*,4'*S*)-4-Methylthio-2-(2'-oxo-4'-phenyloxazolidin-3'-yl)butanoic Acid (6aa β): The nitrile **7b** (1.56 g, 5.64 mmol) finely suspended in HCl (12 N, 16 mL) was stirred for 5 h at 55° C. The mixture was cooled to room temp. and poured into water (40 mL) and CH_2Cl_2 (100 mL). The aqueous phase was extracted with CH_2Cl_2 ($2 \times 100 \text{ mL}$) and the combined organic phases were dried over Na_2SO_4 . The solvent was removed under reduced pressure to give 1.5 g (yield 90%) of a viscous oil. ^1H NMR spectroscopy showed this crude product to be a 10:90 diastereomeric mixture of **6aaa**/**6aa β** .

6aa β : ^1H NMR (CDCl_3 , 200 MHz): $\delta = 1.92$ (s, 3 H), 2.20–2.42 (m, 2 H), 2.50–2.65 (m, 2 H), 3.84 (dd, $J = 4.9 \text{ Hz}$, $J = 9.0 \text{ Hz}$,), 4.24 (apparent t, $J = 9.0 \text{ Hz}$, 1 H), 4.69 (apparent t, $J = 8.7 \text{ Hz}$, 1 H), 4.94 (apparent t, $J = 9.0 \text{ Hz}$, 1 H), 7.42 (m, 5 H). – ^{13}C NMR (CDCl_3 , 50 MHz): $\delta = 14.7$ (CH_3), 27.6 (CH_2), 30.8 (CH_2), 54.8 (CH), 62.5 (CH), 70.2 (CH_2), 127.3 (CH), 128.1 (CH), 129.6 (CH), 136.1 (C), 158.8 (C), 174.9 (C).

Preparation of Amino Acids

L-Methionine: To a solution of lithium (0.048 g, 6.8 mmol) dissolved in ammonia (ca. 30 mL) were added compound **6aaa** (0.25 g, 0.85 mmol) in THF (5 mL) and *t*BuOH (0.65 mL) at –70° C. After 5 min, the deep blue mixture was decolourised by adding NH_4Cl (0.5 g) and the solvents were quickly removed under reduced pressure with gentle warming. The white residue was taken

up in water (30 mL), acidified to pH 1 and extracted with Et₂O (2 × 10 mL). NaOH was added until pH 9 was reached and the solution was filtered through a DOWEX 50W×8 (H⁺ form, 28–35 mesh, 20 g) ion exchange column. An elution with water (100 mL, pH acid to neutral), was followed by aqueous 2% NH₄OH. Positive ninhydrin fractions were collected and evaporated, yielding pure methionine (0.107 g, 85%). The structure was confirmed by comparison of ¹H NMR spectroscopic data (DCI 1 N or NaOD 1 N) with authentic samples. CSP-HPLC analysed on a Chirobiotic T (Astec®) column [4.6 × 250 mm, 5 µm, eluent: EtOH/H₂O 60:40 at 1 mL min⁻¹, det. UV 200 nm] showed only one peak (*ee* 95%) at *t*_R = 5.19 min (D-isomer: *t*_R = 8.06 min).

L-Leucine: Prepared as described for L-methionine starting from compound **6b** (0.88 mmol), yield 74%. The structure was confirmed by comparison of ¹H NMR spectroscopic data (DCI, 1 N) with an authentic sample. *ee* 95% determined by ¹⁹F NMR spectroscopic analysis of the Mosher amide derivative,^[18] only one peak was detected at δ = -69.30 [D-isomer δ = -69.6].

L-Alanine: Prepared as described for L-methionine starting from compound **6c** (0.76 mmol), yield 84%. The structure was confirmed by comparison of ¹H NMR spectroscopic data (DCI 1 N) with an authentic sample. *ee* 95% determined by ¹⁹F NMR spectroscopic analysis of the Mosher amide derivative.^[18] A 98:2 ratio in favour of the L-isomer (δ = -69.28) was found (D-isomer δ = -69.68).

L-Homocysteine: Prepared as described for L-methionine starting from compound **6d** (0.45 mmol), yield 74%. The structure was confirmed by comparison of ¹H NMR spectroscopic data (DCI 1 N) with an authentic sample. *ee* = 92% established by ¹⁹F NMR spectroscopic analysis of the Mosher amide derivative.^[18] A 96:4 ratio in favour of the L-isomer was found. [δ = -69.26, -69.34 and -69.72 (*S*-acyl)]; D-isomer [δ = -69.56, -69.60 and -69.69 (*S*-acyl)]. Because of degradation on the analytical support, CSP-HPLC analysis was not suitable in this case.

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