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Enzymatic synthesis of enantiomerically enriched D- and L-3-silylated alanines by deracemization of DL-5-silylmethylated hydantoins

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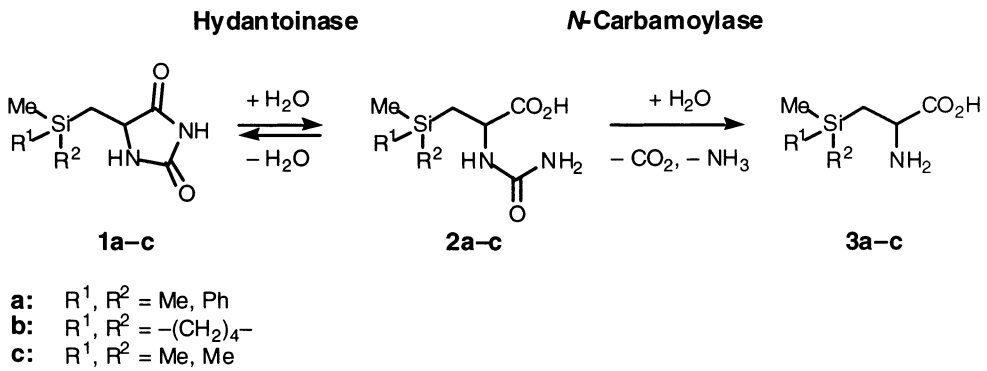
Abstract—The hydantoinase process was shown to be extendable to the production of highly lipophilic, silicon-containing amino acids. Two hydantoinases of different origin and stereoselectivities and one L-*N*-carbamoylase were used for the highly stereoselective bioconversion of (dimethyl)phenylsilyl- and 1-methyl-1-silacyclopentyl substituted alanine derivatives. The enantiomeric purities and absolute configuration of the products were determined with reference compounds that were synthesized with the aid of the Evans oxazolidinone auxiliary.

1. Introduction

Non-proteinogenic amino acids are important building blocks for peptide chemistry.[1–5] They mainly serve as surrogates for natural counterparts, resulting in interesting modified properties of the altered parent structures. Among the non-natural amino acids, silicon-containing compounds are of increasing interest. With their large hydrophobic groups they are expected to offer several advantages when incorporated into peptides, such as the prevention of hydrophobic pocket collapse, higher lipophilicity, and enhanced stability towards proteolytic enzymatic degradation.[6] The latter feature was in fact observed with a renin inhibitor, where replacement of an L-phenylalanine residue by L-3-(trimethylsilyl)alanine resulted in enhanced stability of the peptide towards digestive proteolytic cleavage. The inhibitory power of the compound was only marginally affected.[7] The synthesis, and in particular the stereoselective synthesis, of silicon-containing amino acids is thus a field of growing activity.

Several approaches towards optically active silicon-containing amino acids have been published. Apart from resolution of racemates,[8,9] several stereoselective syntheses have been reported. The Schöllkopf, Seebach, or



Scheme 1.

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Myers methods of asymmetric α-alkylation of glycine enolate equivalents,[6,7,10,11] the Evans procedure of asymmetric α-bromination of carboxylic acid derivatives followed by substitution of the bromine atom,[12] and Sibi's method of β-substitution of serine derivatives[6] gave (in principle) access to either antipode of the desired amino acid in high enantiomeric excesses (e.e.). The overall yields attained with these methods, however, were low, and (except for Sibi's method, which is, however, restricted to phenyl substituted silanes) stoichiometric chiral auxiliaries had to be employed.

We have recently shown that D- or L-3-(trimethylsilyl)alanine (D-**3c** or L-**3c**) are accessible by deracemization using the hydantoinase process.[13] The hydantoinase process consists of a cascade of two hydrolytic enzymes, a hydantoinase and an *N*-carbamoylase (Scheme 1).[14] The hydantoinase is responsible for the partial hydrolysis of hydantoins **1** to the respective *N*-carbamoyl amino acids **2** and the *N*-carbamoylase for the subsequent deaminocarbonylation to the corresponding amino acids **3**. The deaminocarbonylation can also be effected by chemical means. Because 5-monosubstituted hydantoins **1** often racemize spontaneously under slightly alkaline conditions (for racemization constants see Ref. 14), the enzymatically accepted enantiomeric form of the hydantoin is constantly resupplied from the racemate. Alternatively, a hydantoin racemase can be involved in this conversion.[14] A theoretical yield of 100% is thus possible for the formation of enantiomerically pure amino acids by the dynamic kinetic resolution of racemic hydantoins. In particular, amino acid D-**3c** was obtained from hydantoin DL-**1c** in 88% yield and with an enantiomeric excess of 96% by this process.[13]

We show in the following that two further silicon-containing amino acids (**3a** and **3b**) with more bulky silicon groups are also accessible in virtually enantiomerically pure form by the hydantoinase process, that enzymes of the hydantoinase process are thus not limited to the conversion of only the simplest and most uncritical silicon-containing hydantoin **1c** and *N*-carbamoyl amino acid **2c**.

2. Results and discussion

2.1. Biotransformations

For the extension of our foregoing study,[13] the previously successfully applied hydantoinase from *Arthrobacter aurescens* DSM 3745[15] in immobilized form,[16] which was reported to be L-selective for the conversion of DL-5-indolylmethylhydantoin and DL-5-benzylhydantoin,[14] the commercially available immobilized D-hydantoinase from *Bacillus thermoglucosidasius* and the immobilized L-*N*-carbamoylase from *A. aurescens* DSM 3747[17] were investigated with the new substrates. The racemic hydantoins DL-**1a** and DL-**1b**[18] were thus treated in H_2O at pH 8.5 with the two hydantoinases, and the racemic *N*-carbamoyl amino acids DL-**2a** and DL-**2b**[18] with the L-*N*-carbamoylase to yield the respective hydrolysis products (Scheme 1).

Both hydantoin substrates were accepted by the two hydantoinases: however, DL-**1a** was converted at a much higher rate than DL-**1b**. After 2 hours, **1a** was converted already to 50% while 80% of **1b** was still present. The difference in rate for the transformations of the two compounds is not clear. It might be a consequence of the different solubility of the two substrates. Whereas DL-**1a** is readily soluble in the reaction medium, DL-**1b** does not completely dissolve at 23°C.

The curve in Fig. 1 represents the kinetics of the transformation of DL-**1a** with hydantoinase of *B. thermoglucosidasius* over 4 days. A bend in the curve is seen after 50% conversion (ca. 2 hours). Evidently, the enzyme-catalyzed hydrolysis of the accepted enantiomeric form of **1a** is faster than the racemization of its antipode under the slightly basic reaction conditions. After >50% conversion of the racemic samples and complete consumption of one of the enantiomers, it was in fact found that the hydantoins of type **1** were basically enantiomerically pure. The overall rate of the transformation of DL-**1a** could possibly be slightly enhanced by departing from the pH maximum of the biotransformation and performing the reaction under more basic conditions.

All bioconversions with both hydantoinases and both hydantoins delivered the D-configured *N*-carbamoyl amino acids of type **2** as the major products. The enantioselectivities were virtually absolute for the hydantoinase of *B. thermoglucosidasius* (e.e.s of >98% for both substrates). For the hydantoinase of *A. aurescens* DSM 3745, which is known to change its enantiomer selectivity depending on the substrate,[14] the extent of selectivity was substrate dependent: DL-**1a** delivered the *N*-carbamoyl product D-**2a** without a detectable amount of the L-enantiomer (e.e. of >98%) while D-**2b** was produced from DL-**1b** together with its

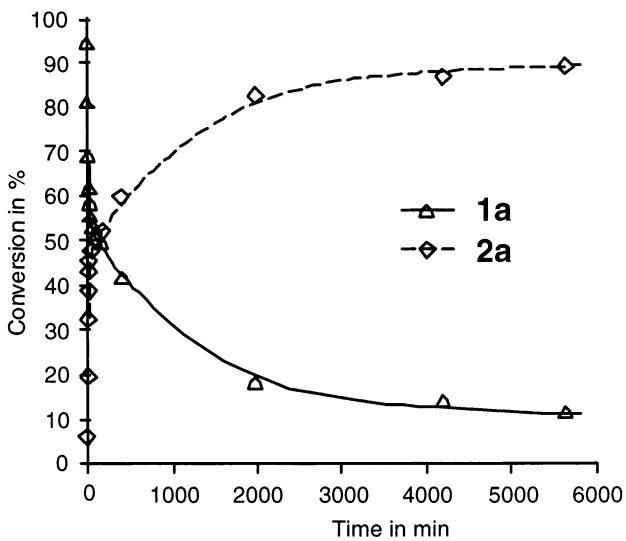


Figure 1. Kinetics of the transformation of DL-**1a** with hydantoinase of *B. thermoglucosidasius* over a period of 4 days.

antipode with an e.e. of 84%. The hydantoinase of *A. aurescens* DSM 3745 preferred the D-enantiomeric forms of the hydantoins **1a** and **1b**, as was found for the trimethylsilyl substituted hydantoin **1c**. The transformations thus parallel the reactions towards methionine[15] and contrast the conversions towards tryptophan[15] and phenylalanine.[19]

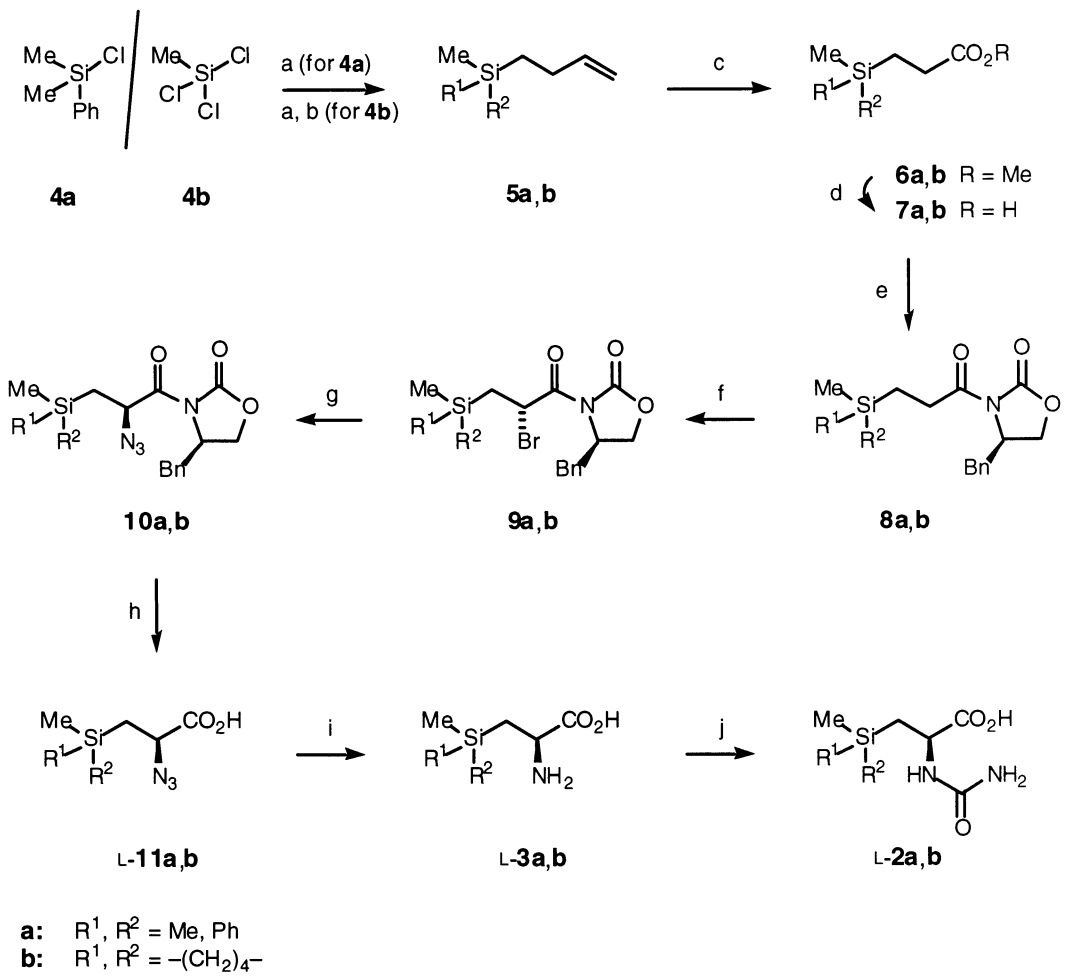
Deaminocarbonylation of racemic *N*-carbamoyl amino acids DL-**2a** and DL-**2b** was effected by treatment of the two compounds with immobilized L-*N*-carbamoylase from *A. aurescens* DSM 3747 in the presence of H_2O. The reactions stopped for both substrates at 50% conversion. Again, the rate of conversion of the (dimethyl)phenylsilyl-containing substrate **2a** was markedly faster than that of the less soluble silacyclopentyl derivative **2b**. As in the case of 3-(trimethylsilyl)alanine, **3c**, the reaction was completely L-selective: solely one enantiomeric substrate was consumed, and the remaining *N*-carbamoyl amino acids **2a** and **2b** were found to be of virtually pure D-configuration (e.e. >98%), with no trace of their corresponding enantiomers detectable by HPLC analysis.

2.2. Analytical methods

Compounds of type **1**, **2**, and **3** were quantified by reversed phase HPLC on a Gromasil ODS 1 PE column according to May.[15] E.e.s of compounds of type **1** and **2** were measured by HPLC on a chiral stationary phase. In contrast to the amino acids D-/L-**3a** and D-/L-**3b**, the hydantoins D-/L-**1a** and D-/L-**1b** as well as the *N*-carbamoyl amino acids D-/L-**2a** and D-/L-**2b** could be separated on the Nucleodex β-PM column. Therefore, the amino acids were transformed into the respective *N*-carbamoyl amino acids to be analyzed. Enantioselectivities were subsequently determined by comparison of the *N*-carbamoyl amino acids deriving from biotransformations with *N*-carbamoyl amino acids of known absolute configuration deriving from classical synthesis (see below).

2.3. Synthesis of the enantiomerically enriched amino acids and *N*-carbamoyl amino acids

The enantiomerically enriched reference compounds L-**2a**, L-**2b**, L-**3a**, and L-**3b** were synthesized in analogy to



Scheme 2. (a) 1-Butenylmagnesium bromide, Et_2O; (b) (butane-1,4-diyl)dimagnesium dibromide, Et_2O; (c) O_3, 2.5N NaOH in MeOH, CH_2Cl_2, −60°C; (d) LiOH, H_2O/THF 1:1, 0°C; (e) (1) NaH, THF, 23°C, (2) Me_3COCl, 0°C, (3) (*R*)-4-benzyl-2-oxazolidinone, BuLi, −78°C; (f) (1) Bu_2BOTf, iPr_2NEt, CH_2Cl_2, −78→0°C, (2) NBS, CH_2Cl_2, −78°C; (g) *N*,*N*,*N*′,*N*′-tetramethylguanidinium azide, MeCN, 0°C; (h) LiOH, THF/H_2O 3:1, 0°C; (i) PtO_2, H_2 (1 atm), EtOH/H_2O 1:1; (j) (1) KOCN, H_2O, 70°C, (2) HOAc, 10°C.

a procedure of Walkup et al.[12] (Scheme 2). The required base structures, acids **7a** and **7b**, were prepared as follows: treatment of chlorosilane **4a** with homoallylmagnesium bromide afforded homoallylic silane **5a**; the respective silacyclopentyl substituted analogue **5b** was obtained from trichloro(methyl)silane **4b** with 1 equivalent of homoallyl Grignard reagent, followed by 1 equivalent of (butane-1,4-diyl)dimagnesium dibromide. Ozonolysis of **5a** and **5b** in the presence of NaOH and MeOH afforded esters **6a** and **6b**, which were readily hydrolyzed to the respective acids **7a** and **7b**. (Ozonolysis under neutral conditions and oxidative workup directly afforded the two acids **7a** and **7b**, but in much lower yield.) Acids **7a** and **7b** were then converted using the Walkup procedure via the Evans amides **8a** and **8b** and the bromo compounds **9a** and **9b** to the azido products **10a** and **10b**.[12] In contrast to Walkup's description, hydrolysis of compounds **10a** and **10b** to the acids L-**11a** and L-**11b** could not be performed by treatment with aqueous H_2O_2 and LiOH because almost complete decomposition of the silicon-containing substrates occurred under these conditions. Hydrolysis with LiOH alone, however, afforded the desired acids L-**11a** and L-**11b** in good yields. Reduction of the azido groups of compounds L-**11a** and L-**11b** to form the desired amino acids L-**3a** and L-**3b** was effected by catalytic hydrogenation in aqueous EtOH over a PtO_2 catalyst. Catalytic hydrogenation was far superior to the alternative Staudinger reduction with Ph_3P[12,20] as it afforded the products in almost quantitative yields and in virtually pure form. Amino acids L-**3a** and L-**3b** were finally transferred into the *N*-carbamoyl derivatives L-**2a** and L-**2b** using a slightly modified procedure as described earlier for the racemic compounds.[18]

3. Conclusion

These investigations show that both hydantoinases and L-*N*-carbamoylase accept sterically demanding silicon-containing amino acid derivatives of type **1** and **2**. The hydantoins as well as the *N*-carbamoyl amino acids were transformed with high enantioselectivity into the respective enantiomerically enriched hydrolysis products. Thus, the hydantoinase process is applicable for the conversion of rather unusual, very lipophilic substrates. For further investigations it would be of interest to test D-*N*-carbamoylases as well as hydantoin racemases described in the literature[14] for their acceptance of these substrates.

4. Experimental

4.1. General

Unless otherwise stated, all chemicals were of reagent grade and purchased from Fluka Chemie AG or Merck AG. Aq. solns were prepared with ultrapure H_2O (NANOpure II, Fa. Barnstedt, Newton, MA, USA). DL-5-{[(Dimethyl)phenylsilyl]methyl}oxazolidin-2,4-dione (DL-5-{(dimethyl)phenylsilyl]methyl}hydantoin, DL-**1a**), DL-5-[(1-methyl-1-silacyclopentyl)methyl]oxazolidin-2,4-dione (DL-5-[(1-methyl-1-silacyclopentyl)-methyl]hydantoin, DL-**1b**), DL-2-carbamoylamino-3-[(dimethyl)phenylsilyl]propionic acid (DL-*N*-carbamoyl-3-[(dimethyl)phenylsilyl]alanine, DL-**2a**), and DL-2-carbamoylamino-3-(1-methyl-1-silacyclopentyl)propionic acid (DL-*N*-carbamoyl-3-(1-methyl-1-silacyclopentyl)alanine, DL-**2b**) were synthesized as described previously.[18] Chemical manipulations were carried out under argon in oven-dried glass equipment. For reactions, Et_2O and THF were freshly distilled from Na with benzophenone ketyl as indicator; dry CH_2Cl_2 was purchased from Merck AG and stored over molecular sieves. Extracts were washed with satd aq. NH_4Cl soln and brine and were dried over $MgSO_4$. Chromatography: Merck silica gel 60 (40–63 μm). Optical rotation: Perkin–Elmer polarimeter 241. Mp: Mettler FP5/FP52. IR spectra: neat liquid films between NaCl plates for liquids and as KBr presslings for solids; Perkin–Elmer 297 or 781; in cm^{-1}. ^1H NMR spectra in $CDCl_3$; Bruker AC-300 (300 MHz), ARX-300 (300 MHz), or AMX-600 (600 MHz); δ in ppm rel. to $CHCl_3$ (δ 7.26), J in Hz. ^{13}C NMR spectra in $CDCl_3$; Bruker ARX-300 (75.5 MHz); δ in ppm rel. to $CDCl_3$ (δ 77.0); multiplicities from DEPT-135 and DEPT-90 experiments; the interpretation of the NMR spectra is based on cross-correlation with a number of reference samples. Mass spectrometry (MS): Finnigan MAT 90 or Finnigan SSQ 700; electron-impact MS (EI MS) at 70 eV; chemical-ionization MS (CI MS) with NH_3 as the reactant gas; molecular ions, quasi-molecular ions, and characteristic fragments either with interpretation or $\geq$20 rel.%; in m/z (rel.%).

4.2. Enzymes

Enriched hydantoinase from *B. thermoglucosidasius* (Hyd 1, carrier-fixed) was a gift from Roche Diagnostics (Penzberg, Germany). Hydantoinase from *A. aurescens* DSM 3745 was purified from recombinant *Escherichia coli* and immobilized on Eupergit C250L.[16] L-*N*-Carbamoylase from *A. aurescens* DSM 3747 was purified from recombinant *E. coli*[17] and immobilized on EAH-Sepharose.[16]

4.3. Analytical methods

The concentrations of compounds of type **1**, **2**, and **3** were determined with reversed-phase HPLC (RP-HPLC) on a Gromsil ODS 1 PE column (5 μm, 250× 4.6 mm, Grom, Herrenberg, Germany) according to a literature procedure[15] with UV detection at 210 nm. Eluent: aq. H_3PO_4 (85%, 7 mL) in H_2O (2000 mL) and MeOH (500 mL); flow rate: 1.0 mL min^{-1}; retention times: 66.1 min (DL-**1a**); 47.6 min (DL-**1b**); 59.5 min (DL-**2a**); 41.3 min (DL-**2b**); 37.7 min (DL-**3a**); 22.7 min (DL-**3b**).

The separation of the enantiomers of DL-**1** and DL-**2** was accomplished by chiral HPLC on an ET 200/4 Nucleodex β-PM column (Macherey–Nagel, Düren, Germany) with UV detection at 210 nm. Eluent A: aq.

H_3PO_4 (85%, 3 mL) in H_2O (842 mL) and MeOH (211 mL), pH adjusted to 3.7 with concd aq. NaOH soln; flow rate: 0.7 mL min^{-1}; retention times: 168.4 min (D-**1a**); 176.2 min (L-**1a**). Eluent B: aq. H_3PO_4 (85%, 3 mL) in H_2O (842 mL) and MeOH (563 mL), pH adjusted to 3.7 with concd aq. NaOH soln; flow rate: 0.6 mL min^{-1}; retention times: 96.1 min (D-**1b**); 77.8 min (L-**1b**); 16.9 min (D-**2a**); 22.3 min (L-**2a**); 19.4 min (D-**2b**); 24.6 min (L-**2b**).

4.4. Biotransformations with hydantoinases

4.4.1. Biotransformation of DL-1a. Immobilized hydantoinase from *A. aurescens* DSM 3745 (232 mg) was added to 0.5 mM soln of DL-**1a** (1 mL) in tris/HCl buffer (0.1 M, pH 8.5, tris = tris(hydroxymethyl)aminomethane), and the mixture was incubated with shaking at 37°C for the bioconversion. At different intervals, mixing was interrupted and samples (100 μL) were drawn from the clear supernatant, diluted with HPLC eluant (900 μL), centrifuged, and analyzed by RP and chiral HPLC. Chiral HPLC revealed the formation of D-**2a** and L-**2a** with an enantiomeric excess >98% (no L-**2a** was detected). 50% conversion was reached after 125 min.

Analogously to above, DL-**1a** (1 mL of 0.5 mM soln in tris/HCl buffer (0.1 M, pH 8.5)) was treated with hydantoinase from *B. thermoglucosidasius* (35 mg) to yield D-**2a** and L-**2a** in a ratio of 99:1. 50% conversion was reached after 122 min.

4.4.2. Biotransformation of DL-1b. Analogously to Section 4.4.1, DL-**1b** (1 mL of 0.5 mM soln in tris/HCl buffer (0.1 M, pH 8.5)) was treated with hydantoinase from *A. aurescens* DSM 3745 (217 mg) and D-hydantoinase from *B. thermoglucosidasius* (35 mg) to yield D-**2b** and L-**2b** in ratios of 92:8 and 99:1, respectively. 50% conversions were reached after 8 and 6 h, respectively.

4.5. Biotransformations with *N*-carbamoylase

4.5.1. Biotransformation of DL-2a. Analogously to Section 4.4.1, DL-**2a** (1 mL of 0.5 mM soln in tris/HCl buffer (0.1 M, pH 8.5)) was treated with immobilized L-*N*-carbamoylase from *A. aurescens* DSM 3747 (94 mg) to yield (presumably highly enriched) L-**3a**. The reaction stopped after consumption of 50% of the starting material, leaving D-**2a** and L-**2a** in a ratio of <1:99. 50% conversion was reached after 130 min; sample preparation for HPLC analysis as described above.

4.5.2. Biotransformation of DL-2b. Analogously to Section 4.4.1, DL-**2b** (1 mL of 0.5 mM soln in tris/HCl buffer (0.1 M, pH 8.5)) was treated with immobilized L-*N*-carbamoylase from *A. aurescens* DSM 3747 (67 mg) to yield (presumably highly enriched) L-**3b** and leaving D-**2b** and L-**2b** in a ratio of <1:99 after complete transformation (50% conversion). 50% conversion after 195 min; sample preparation for HPLC analysis as described above.

4.6. Synthesis of the enantiomerically enriched reference compounds

4.6.1. 4-[(Dimethyl)phenylsilyl]but-1-ene 5a. Neat 4-bromobut-1-ene (6.82 g, 50.5 mmol) was added dropwise to a suspension of Mg (1.24 g, 51.0 mmol) in Et_2O (250 mL) at 23°C. After the exothermic reaction ceased, it was stirred at 23°C for another 30 min. Neat chloro(dimethyl)phenylsilane (**4a**, 8.5 g, 50.0 mmol) was added dropwise, it was warmed to 40°C for 3 days, and quenched with excess H_2O. Extraction with Et_2O and distillation (50°C, 2 torr) via a Vigreux column afforded **5a** as a colorless liquid (7.9 g, 41.8 mmol, 84%). IR: 3075m, 3050w, 3000w, 2960m, 2905m, 2890w, 2840w, 1640w, 1430m, 1410w, 1255s, 1120s, 1055m, 1025m, 1000w, 905m, 895m, 835s, 790s, 780m, 730m, 700s, 605s. ^{1}H NMR: 7.54–7.51 (m, 2 arom. H); 7.38–7.35 (m, 3 arom. H); 5.89 (ddt, J = 16.8, 10.3, 6.5, CH=); 4.99 (d, J = 17.1, 1H, CH_2=); 4.90 (d, J = 10.4, 1H, CH_2=); 2.13–2.05 (m, CH_2CH=); 0.90–0.85 (m, CH_2Si); 0.30 (s, 2 MeSi). ^{13}C NMR: 141.5 (d, CH=); 139.2 (s, arom. C); 133.6 (d, 2 arom. C); 128.3 (d, arom. C); 127.7 (d, 2 arom. C); 112.8 (t, H_2C=); 27.9 (t, CH_2CH=); 14.8 (t, CH_2Si); −3.0 (q, 2 MeSi). EI MS: 175 (13, $[M-Me]^+$), 135 (100, $[M-C_4H_7]^+$), 121 (30), 105 (23). The spectral data of **5a** are in agreement with published data.[21]

4.6.2. 4-(1-Methyl-1-silacyclopentyl)but-1-ene 5b. Neat 4-bromobut-1-ene (20.65 g, 153.0 mmol) was added dropwise to a suspension of Mg (3.79 g, 156.0 mmol) in Et_2O (150 mL) at 23°C. After the exothermic reaction ceased, the mixture was stirred at 23°C for a further 30 min. The mixture was slowly transferred via a cannula to a flask containing trichloro(methyl)silane **4b** (22.4 g, 150.0 mmol) in Et_2O (150 mL), and it was stirred for 15 h (soln A) at 23°C. In a separate flask, 1,4-dibromobutane (33.7 g, 156.0 mmol) was added dropwise to a suspension of Mg (7.61 g, 313.0 mmol) in Et_2O (300 mL) at 23°C. After the exothermic reaction ceased, the mixture was stirred for an additional 15 h at 23°C (soln B). Solns A and B were simultaneously transferred via cannulae to a flask that was kept at 23°C. The resultant mixture was stirred for 24 h at 23°C (GC control) and quenched by addition of a satd aq. NH_4Cl soln (200 mL). Extraction with Et_2O/pentane (1:1) and distillation (70°C, 26 torr) via a Vigreux column afforded **5b** as a colorless liquid (5.7 g, 36.8 mmol, 25%). IR: 3075w, 2935s, 2920s, 2895m, 2855m, 1640w, 1440w, 1405w, 1250m, 1070s, 1050m, 1030m, 1020m, 990w, 905m, 895m, 855w, 830m, 790m, 780m, 765m, 705m, 650m, 610m. ^{1}H NMR: 5.89 (ddt, J = 16.8, 10.3, 6.3, CH=); 5.00 (ddt, J = 17.1, 2.0, 1.7, 1H, CH_2=); 4.90 (ddt, J = 10.1, 2.0, 1.3, 1H, CH_2=); 2.15–2.05 (m, CH_2CH=); 1.64–1.50 (m, 2 C$H_2$$CH_2$Si); 0.73–0.68 (m, CH_2Si); 0.65–0.42 (m, 2 CH_2CH_2Si); 0.08 (s, MeSi). ^{13}C NMR: 141.6 (d, CH=); 112.8 (t, H_2C=); 28.4 (t, CH_2CH=); 27.3 (t, 2 $CH_2$$CH_2$Si); 14.3 (t, CH_2Si); 11.8 (t, 2 $CH_2$$CH_2$Si); −3.2 (q, MeSi). EI MS: 154 (1, $M^{+\bullet}$), 139 (7, $[M-Me]^+$), 99 (100, $[M-C_4H_7]^+$), 98 (29), 97 (79), 83 (22), 71 (45), 55 (29), 45 (25), 43 (39). Due to high volatility, no microanalysis could be performed.

4.6.3. Methyl 3-[(dimethyl)phenylsilyl]propionate 6a. A stream of ozone was passed through a soln of **5a** (0.16 g, 0.82 mmol) in a mixture of CH_2Cl_2 (50 mL) and NaOH/MeOH (2.5 M, 1.6 mL) at −60°C until the blue color of O_3 persisted. Excess ozone was removed with a stream of N_2, and the mixture was allowed to warm to 23°C. H_2O (3 mL) was added, and the mixture extracted with Et_2O. The solvent was carefully evaporated (35°C, 200 mbar) and the residue chromatographed (Et_2O/pentane 1:10) to give **6a** as a colorless liquid (0.15 g, 0.67 mmol, 82%). IR: 3070m, 3050m, 3000m, 2950s, 2920m, 2900m, 2880m, 2870m, 1780s, 1435s, 1425s, 1350m, 1290m, 1250s, 1210s, 1160s, 1115s, 1050m, 1025m, 1000w, 980w, 915w, 880w, 840s, 830s, 780s, 730s, 700s. ^{1}H NMR: 7.54–7.48 (m, 2 arom. H); 7.40–7.34 (m, 3 arom. H); 3.63 (s, MeO); 2.34–2.28 (m, CH_2CO); 1.15–1.09 (m, CH_2Si); 0.31 (s, 2 MeSi). ^{13}C NMR: 175.2 (s, CO); 138.1 (s, arom. C); 133.5 (d, 2 arom. C); 129.1 (d, arom. C); 127.8 (d, 2 arom. C); 51.5 (q, MeO); 28.6 (t, *C*H_2CO); 10.9 (t, CH_2Si); −3.4 (q, 2 MeSi). EI MS: 207 (64, $[M-Me]^+$), 151 (33), 145 (59, $[M-C_6H_5]^+$), 135 (100, $[M-C_4H_7O_2]^+$), 121 (27), 117 (33), 105 (34), 91 (26), 89 (25), 59 (52), 57 (8), 43 (26). The spectral data of **6a** are in agreement with published data.[22]

4.6.4. Methyl 3-(1-methyl-1-silacyclopentyl)propionate 6b. Analogously to Section 4.6.3, **5b** (5.68 g, 36.8 mmol) was treated with O_3 in CH_2Cl_2 (250 mL) and NaOH/MeOH (2.5 M, 15.2 mL) to give, after chromatography (Et_2O/pentane 1:10), **6b** as a colorless liquid (4.32 g, 23.2 mmol, 63%). IR: 2935m, 2920m, 2895m, 2855m, 1745s, 1450w, 1435w, 1405w, 1355w, 1250m, 1210m, 1160w, 1125w, 1075m, 1045w, 1030m, 1020w, 860w, 830m, 785m, 770m, 710w, 655m, 605s. ^{1}H NMR: 3.68 (s, MeO); 2.36–2.30 (m, CH_2CO); 1.61–1.51 (m, 2 C*H*$_2$CH$_2$Si); 0.97–0.92 (m, CH_2Si); 0.61–0.48 (m, 2 CH$_2$C*H*$_2$Si); 0.10 (s, MeSi). ^{13}C NMR: 175.5 (s, CO); 51.6 (q, MeO); 29.0 (t, *C*H_2CO); 27.2 (t, 2 *C*H$_2$CH$_2$Si); 11.5 (t, 2 CH$_2$*C*H$_2$Si); 10.3 (t, CH_2Si); −3.5 (q, MeSi). EI MS: 157 (17), 130 (38), 99 (9, $[M-C_4H_7O_2]^+$), 59 (25), 57 (30), 56 (21), 45 (29), 43 (99), 41 (100). Due to high volatility, no microanalysis could be performed.

4.6.5. 3-[(Dimethyl)phenylsilyl]propionic acid 7a. A mixture of **6a** (3.15 g, 14.2 mmol) in THF (28.6 mL) and aq. LiOH soln (0.5 m, 28.6 mL, 14.3 mmol) was stirred at 23°C for 15 h. The solvent was evaporated, and the residue carefully acidified with aq. HCl soln (1N) to pH 1. Extraction with Et_2O and filtration through a plug of SiO_2 (Et_2O) afforded **7a** as a slightly yellow oil (2.96 g, 12.9 mmol, 91%). IR: 3070m, 3050m, 3020m, 3000m, 2950s, 2895m, 2880m, 1710s, 1490w, 1425s, 1405m, 1295m, 1260s, 1250s, 1220m, 1190m, 1165s, 1110s, 1090s, 910m, 835s, 820s, 780s, 730s, 700s. ^{1}H NMR: 7.52–7.47 (m, 2 arom. H); 7.37–7.34 (m, 3 arom. H); 2.35–2.29 (m, CH_2CO); 1.13–1.07 (m, CH_2Si); 0.31 (s, 2 MeSi). ^{13}C NMR: 180.8 (s, CO); 137.9 (s, arom. C); 133.5 (d, 2 arom. C); 129.2 (d, arom. C); 127. 9 (d, 2 arom. C); 28.6 (t, *C*H_2CO); 10.7 (t, CH_2Si); −3.4 (q, 2 MeSi). CI MS: 226 (35, $[M+NH_4]^+$), 148 (100), 131 (22). The spectral data are in agreement with published data.[12]

4.6.6. 3-(1-Methyl-1-silacylclopentyl)propionic acid 7b. Analogously to Section 4.6.5, **6b** (4.30 g, 23.1 mmol) was treated with LiOH (23.1 mmol) for 15 h to give **7b** as a slightly yellow oil (3.11 g, 18.0 mmol, 78%). IR: 2935m, 2920m, 2895m, 2855m, 1710s, 1450w, 1425w, 1410w, 1285w, 1245m, 1075m, 1030w, 910w, 855w, 830m, 790w, 770m, 710w, 605s. ^{1}H NMR: 2.39–2.33 (m, CH_2CO); 1.60–1.50 (m, 2 C*H*$_2$CH$_2$Si); 0.97–0.91 (m, CH_2Si); 0.61–0.47 (m, 2 CH$_2$C*H*$_2$Si); 0.10 (s, MeSi). ^{13}C NMR: 180.6 (s, CO); 29.0 (t, *C*H_2CO); 27.2 (t, 2 *C*H$_2$CH$_2$Si); 11.5 (t, 2 CH$_2$*C*H$_2$Si); 10.0 (t, CH_2Si); −3.5 (q, MeSi). EI MS: 143 (44), 130 (33), 129 (22), 115 (100), 101 (31), 99 (30, $[M-C_3H_5O_2]^+$), 89 (29), 87 (29), 75 (20), 70 (32), 61 (26), 59 (47), 55 (24). Anal. calcd for $C_8H_{16}O_2Si$ (172.092): C, 55.77; H, 9.36. Found: C, 55.84; H, 9.28%.

4.6.7. (*R*)-4-Benzyl-3-{3-[(dimethyl)phenylsilyl]propionyl}oxazolidin-2-one 8a. A dispersion of NaH (60% in oil, 0.15 g, 3.74 mmol) was added at 23°C to a soln of **7a** (0.71 g, 3.40 mmol) in THF (17 mL) and the resultant suspension cooled to 0°C, trimethylacetyl chloride (0.43 g, 3.53 mmol) was added, and the mixture was stirred for 2 h (soln A, this was then cooled to −78 °C prior to the addition of soln B). In a separate flask, BuLi (2 M in hexane, 1.9 mL, 3.8 mmol) was added slowly at −78°C to a soln of (*R*)-4-benzyloxazolidin-2-one (0.60 g, 3.36 mmol) in THF (17 mL), and the mixture stirred for 30 min (soln B).

Soln B was transferred by syringe into soln A, cooled to −78°C. After stirring at −78°C for 1.5 h and at 23°C for 2 h, it was quenched with H_2O, extracted with Et_2O, and chromatographed (AcOEt/hexane 1:9) to give **8a** as colorless crystals (1.04 g, 2.82 mmol, 84%). Mp 74.1–75.0°C (hexane) (lit.[12] 62–64°C); $[\alpha]_D=-37.9$ (*c* 1.16, $CHCl_3$), lit.[12] $[\alpha]_D=-34.0$ (*c* 2.0, $CHCl_3$). IR: 3070s, 3025s, 2975s, 2950s, 2905s, 1950m, 1795s, 1700s, 1605m, 1530m, 1500s, 1475s, 1455s, 1425s, 1385s, 1295s, 1250s, 1200s, 1160s, 1110s, 1075s, 1050s, 1015s, 975s, 920s, 905s, 840s, 800s, 775s, 755s, 740s, 700s, 620s. ^{1}H NMR (600 MHz): 7.56–7.53 (m, 2 arom. H); 7.38–7.35 (m, 3 arom. H); 7.34–7.31 (m, 2 arom. H); 7.29–7.27 (m, 1 arom. H); 7.21–7.18 (m, 2 arom. H); 4.62–4.57 (symm. m, eight lines, HCN); 4.17–4.11 (m, H_2CO); 3.26 (dd, $J=13.4$, 3.4, 1 benzyl H); 2.95, 2.90 (*AB* of *ABXY*, $J_{AB}=16.8$, $J_{AX}=J_{BY}=9.8$, $J_{AY}=J_{BX}=6.4$, H_2CC=O); 2.71 (dd, $J=13.4$, 9.8, 1 benzyl H); 1.16, 1.13 (*XY* of *ABXY*, $J_{XY}=16.8$, $J_{XA}=J_{YB}=9.8$, $J_{YA}=J_{XB}=6.4$, CH_2Si); 0.34 (s, 2 MeSi). ^{13}C NMR: 174.5 (s, CON); 153.3 (s, COO); 138.2, 135.4 (2s, 2 arom. C); 133.6, 129.4 (2d, 2×2 arom. C); 129.1 (d, arom. C); 128.9, 127.8 (2d, 2×2 arom. C); 127.3 (d, arom. C); 66.1 (t, CH_2O); 55.2 (d, CHN); 37.9 (t, *C*H_2Ph); 30.3 (t, *C*H_2CO); 10.2 (t, CH_2Si); −3.2 (q, 2 MeSi). CI MS: 384 (16, $[M+NH_4+NH_3-H_2O]^+$), 367 (6, $[M+NH_4-H_2O]^+$), 351 (10, $[M+NH_3-H_2O-Me]^+$), 289 (100, $[M+NH_3-H_2O-Ph]^+$). The spectral data of **8a** are in agreement with published data.[12]

4.6.8. (*R*)-4-Benzyl-3-[3-(1-methyl-1-silacylopentyl)propionyl]oxazolidin-2-one 8b. Analogously to Section 4.6.7, **7b** (0.20 g, 1.15 mmol) was deprotonated with NaH (1.27 mmol), activated with trimethylacetyl chloride (0.14 g, 1.20 mmol), and treated with lithiated (*R*)-4-benzyloxazolidin-2-one (1.14 mmol) to give, after chromatography (AcOEt/hexane 1:9), **8b** as a colorless oil, which crystallized upon cooling to 4°C (0.31 g, 0.95 mmol, 83%). Mp 50.8–51.8°C (hexane); $[\alpha]_D = -42.3$ (*c* 2.47, $CHCl_3$). IR (film): 3025w, 2935s, 2920m, 2895m, 2850m, 1785s, 1700s, 1605w, 1495w, 1480w, 1450m, 1435w, 1385s, 1365m, 1350m, 1325w, 1290w, 1250s, 1215s, 1195m, 1180m, 1160m, 1100m, 1075m, 1050m, 1030m, 1020m, 975w, 915w, 855w, 835m, 780m, 765m, 750m, 735m, 705m, 660m, 600s. ^{1}H NMR (600 MHz): 7.35–7.20 (m, 5 arom. H); 4.69–4.61 (m, HCN); 4.19 (dd, $J = 9.0$, 7.6, 1 H, H_2CO); 4.16 (dd, $J = 9.1$, 3.0, 1 H, H_2CO); 3.30 (dd, $J = 13.4$, 3.3, 1 benzyl H); 2.96, 2.91 (*AB* of *ABXY*, $J_{AB} = 16.7$, $J_{AX} = J_{BY} = 10.8$, $J_{AY} = J_{BX} = 5.7$, $H_2CC{=}O$); 2.76 (dd, $J = 13.4$, 9.6, 1 benzyl H); 1.60–1.56 (quint.-like m, 2 CH_2CH_2Si); 1.00, 0.95 (*XY* of *ABXY*, $J_{XY} = 14.6$, $J_{XA} = J_{YB} = 10.8$, $J_{YA} = J_{XB} = 5.7$, CH_2Si); 0.66–0.51 (m, 2 CH_2CH_2Si); 0.12 (s, MeSi). ^{13}C NMR: 174.6 (s, CON); 153.4 (s, COO); 135.4 (s, arom. C); 129.4, 128.9 (2d, 2×2 arom. C); 127.3 (d, arom. C); 66.1 (t, CH_2O); 55.2 (d, CHN); 37.9 (t, CH_2Ph); 30.7 (t, CH_2CO); 27.2 (t, 2 CH_2CH_2Si); 11.6 (t, 2 CH_2CH_2Si); 9.6 (t, CH_2Si); −3.4 (q, MeSi). CI MS: 349 (17, $[M+NH_4]^+$), 333 (22), 332 (100, $[M+H]^+$), 262 (57). Anal. calcd for $C_{18}H_{25}NO_3Si$ (331.482): C, 65.22; H, 7.60; N, 4.23. Found: C, 65.33; H, 7.49; N, 4.05%.

4.6.9. (4*R*,2′*S*)-4-Benzyl-3-{2-bromo-3-[(dimethyl)phenylsilyl]propionyl}oxazolidin-2-one 9a. Ethyldiisopropylamine (0.49 g, 3.85 mmol) and a soln of dibutylboryl trifluoromethanesulfonate (1 M in CH_2Cl_2, 3.8 mL, 3.8 mmol) were added subsequently to a soln of **8a** (1.01 g, 2.75 mmol) in CH_2Cl_2 (10 mL) at −78°C. The mixture was allowed to warm to 0°C, kept at this temperature for 4 h, and re-cooled to −78°C before the mixture was transferred with a syringe to a soln of *N*-bromosuccinimide (0.61 g, 3.43 mmol, freshly recrystallized from H_2O) in CH_2Cl_2 (60 mL) at −78°C. After 2 h, satd aq. $NaHCO_3$ soln (10 mL) was added to the reddish soln, and the mixture was allowed to warm to 23°C. Extraction with CH_2Cl_2, evaporation and chromatography (AcOEt/hexane 5:95) afforded **9a** as a colorless oil (0.91 g, 2.04 mmol, 75%). $[\alpha]_D = -60.6$ (*c* 0.85, $CHCl_3$), lit.[12] $[\alpha]_D = -48.0$ (*c* 0.8, $CHCl_3$). IR: 3090w, 3065w, 3030w, 3000w, 2955w, 2920w, 2860w, 1780s, 1705s, 1605w, 1575w, 1495w, 1475w, 1455w, 1425m, 1385s, 1350m, 1290w, 1260s, 1210m, 1200s, 1170m, 1110m, 1105m, 1075w, 1050w, 1030w, 1015w, 1000w, 975w, 920w, 870w, 835s, 780w, 760m, 735m, 705s, 640m, 600s. ^{1}H NMR: 7.51–7.14 (m, 10 arom. H); 5.90 (dd, $J = 12.6$, 4.2, HCBr); 4.16–4.08 (m, HCN); 4.04–3.83 (m, H_2CO); 3.12 (dd, $J = 13.7$, 3.4, 1 benzyl H); 2.67 (dd, $J = 13.7$, 9.5, 1 benzyl H); 2.22 (dd, $J = 13.7$, 12.6, 1 H, CH_2Si); 1.65 (dd, $J = 14.1$, 4.2, 1 H, CH_2Si); 0.39 (s, 2 MeSi). ^{13}C NMR: 169.1 (s, CON); 151.9 (s, COO); 136.4, 134.8 (2s, 2 arom. C); 134.2, 129.4 (2d, 2×2 arom. C); 129.3 (d, arom. C); 128.9, 127.7 (2d, 2×2 arom. C); 127.3 (d, arom. C); 65.7 (t, CH_2O); 54.7 (d, CHN); 42.0 (d, CHBr); 36.9 (t, CH_2Ph); 23.5 (t, CH_2Si); −2.5, −2.6 (2q, 2 MeSi). CI MS: 465/463 (88/84, $[M+NH_4]^+$), 448/446 (7/7, $[M+H]^+$), 432/430 (16/15, $[M-Me]^+$), 370/368 (100/99, $[M-Ph]^+$), 366 (30, $[M-Br]^+$), 290 (20), 249 (30), 232 (22). The spectral data for **9a** are in agreement with published data.[12]

4.6.10. (4*R*,2′*S*)-4-Benzyl-3-[2-bromo-3-(1-methyl-1-silacyclopentyl)propionyl]-oxazolidin-2-one 9b. Analogously to Section 4.6.9, **8b** (1.19 g, 3.61 mmol) was treated with ethyldiisopropylamine (0.70 g, 5.39 mmol) and dibutylboryl trifluoromethanesulfonate (5.32 mmol), and the resulting boron enolate was brominated with *N*-bromosuccinimide (0.86 g, 4.8 mmol) to give **9b** as a colorless oil (1.12 g, 2.73 mmol, 76%). $[\alpha]_D = -37.5$ (*c* 4.37, $CHCl_3$). IR: 3085w, 3060w, 3025m, 2930s, 2855s, 2800w, 1780s, 1705s, 1605w, 1585w, 1495m, 1480m, 1450m, 1385s, 1345m, 1290m, 1260s, 1215s, 1195s, 1170m, 1105s, 1075m, 1050m, 1030m, 1020m, 975m, 920w, 865w, 835m, 775m, 760m, 735m, 705s, 650s, 600s. ^{1}H NMR: 7.34–7.17 (m, 5 arom. H); 5.93 (dd, $J = 10.1$, 6.0, HCBr); 4.72–4.59 (m, HCN); 4.22–4.12 (m, H_2CO); 3.29 (dd, $J = 13.5$, 3.4, 1 benzyl H); 2.76 (dd, $J = 13.5$, 9.6, 1 benzyl H); 1.91 (dd, $J = 14.1$, 10.1, 1 H, CH_2Si); 1.58 (dd, $J = 14.1$, 6.1, 1 H, CH_2Si); 1.58–1.48 (m, 2 CH_2CH_2Si); 0.65–0.45 (m, 2 CH_2CH_2Si); 0.12 (s, MeSi). ^{13}C NMR: 169.6 (s, CON); 152.4 (s, COO); 134.8 (s, arom. C); 129.4, 128.9 (2d, 2×2 arom. C); 127.4 (d, arom. C); 66.1 (t, CH_2O); 55.2 (d, CHN); 42.6 (d, CHBr); 36.9 (t, CH_2Ph); 27.0 (t, 2 CH_2CH_2Si); 22.3 (t, CH_2Si); 12.3, 12.0 (2t, 2 CH_2CH_2Si); −2.8 (q, MeSi). CI MS: 429/427 (100/97, $[M+NH_4]^+$), 412/410 (12/11, $[M+NH_4-Me]^+$), 349 (77), 332 (53), 330 (25), 279 (66), 249 (99), 195 (21). Anal. calcd for $C_{18}H_{24}BrNO_3Si$ (410.378): C, 52.68; H, 5.89; N, 3.41. Found: C, 52.84; H, 6.07; N, 3.27%.

4.6.11. (4*R*,2′*R*)-3-{2-Azido-3-[(dimethyl)phenylsilyl]propionyl}-4-benzyloxazolidin-2-one 10a. A soln of tetramethylguanidinium azide (3.80 g, 24.0 mmol) in MeCN (100 mL) was added dropwise to a soln of **9a** (2.30 g, 5.15 mmol) in MeCN (50 mL) at 0°C. After 4 h, satd aq. $NaHCO_3$ soln (5 mL) was added, the mixture was extracted with Et_2O, evaporated and the residue chromatographed (AcOEt/hexane 1:9) to give **10a** as colorless crystals (1.41 g, 3.46 mmol, 67%). Mp 123.0–124.0°C ($CHCl_3$) (lit.[12] 118–120°C); $[\alpha]_D = -9.2$ (*c* 3.38, $CHCl_3$), lit.[12] $[\alpha]_D = +3.1$ (*c* 5.0, benzene). IR: 3070w, 3025w, 2970w, 2110s, 1800s, 1695s, 1500w, 1455m, 1425m, 1385s, 1370s, 1295m, 1240s, 1210s, 1200s, 1115s, 1050m, 1020m, 990m, 895m, 880m, 860m, 840s, 805m, 760m, 735s, 705s, 670w, 645w, 615w. ^{1}H NMR: 7.62–7.56 (m, 2 arom. H); 7.42–7.16 (m, 8 arom. H); 4.83 (dd, $J = 11.1$, 4.2, HCN_3); 4.73–4.63 (m, HCN); 4.28–4.16 (m, H_2CO); 3.22 (dd, $J = 13.4$, 3.4, 1 benzyl H); 2.70 (dd, $J = 13.4$, 9.5, 1 benzyl H); 1.61–1.26 (m, CH_2Si); 0.47, 0.46 (2s, 2 MeSi). ^{13}C NMR: 172.4 (s, CON); 152.7 (s, COO); 137.4, 134.8 (2s, 2 arom. C); 133.7, 129.4, 129.0, 127.9, 127.5 (5d, 10 arom. C); 66.7 (t, CH_2O); 57.4 (d, CHN_3); 55.1 (d, CHN); 37.6 (t, CH_2Ph); 18.8 (t, CH_2Si); −2.9, −3.3 (2q, 2 MeSi). CI MS: 426 (100, $[M+NH_4]^+$), 366 (100, $[M-N_3]^+$), 331 (72, $[M-Ph]^+$), 249 (26), 195 (30). The spectral data are in agreement with published data.[12]

4.6.12. (4*R*,2′*R*)-3-[2-Azido-3-(1-methyl-1-silacyclopentyl)propionyl]-4-benzyl-oxazolidin-2-one 10b. Analogously to Section 4.6.11, **9b** (0.75 g, 1.82 mmol) was treated with tetramethylguanidinium azide (1.44 g, 9.07 mmol) to give **10b** as a colorless oil (0.51 g, 1.36 mmol, 75%). $[\alpha]_D=-8.8$ (*c* 7.75, $CHCl_3$). IR: 3085w, 3060w, 3025w, 2930s, 2855s, 2800w, 2110s, 1785s, 1705s, 1605w, 1585w, 1495w, 1480w, 1455m, 1385s, 1375s, 1350m, 1305w, 1290w, 1245s, 1215s, 1195s, 1155w, 1115m, 1075m, 1055w, 1030m, 1020m, 995w, 895m, 880m, 855w, 835m, 805w, 780m, 765m, 740m, 705m, 655m, 630m, 600m. ^{1}H NMR: 7.41–7.16 (m, 5 arom. H); 4.86 (dd, $J=11.1$, 4.2, HCN_3); 4.76–4.68 (m, HCN); 4.31–4.20 (m, H_2CO); 3.31 (dd, $J=13.3$, 3.0, 1 benzyl H); 2.78 (dd, $J=13.3$, 9.6, 1 benzyl H); 1.66–1.57 (m, 2 CH_2CH_2Si); 1.42–1.18 (m, CH_2Si); 0.81–0.53 (m, 2 CH_2CH_2Si); 0.24 (s, MeSi). ^{13}C NMR: 172.6 (s, CON); 152.8 (s, COO); 134.8 (s, arom. C); 129.4, 129.0 (2d, 2×2 arom. C); 127.5 (d, arom. C); 66.7 (t, CH_2O); 57.6 (d, CHN_3); 55.2 (d, CHN); 37.7 (t, CH_2Ph); 27.1, 27.0 (2t, 2 CH_2CH_2Si); 18.0 (t, CH_2Si); 12.1, 11.8 (2t, 2 CH_2CH_2Si); −3.2 (q, MeSi). CI MS: 390 (85, $[M+NH_4]^+$), 345 (42), 331 (22), 330 (100, $[M-N_3]^+$), 279 (28), 195 (21), 116 (38), 73 (20), 61 (63). Anal. calcd for $C_{18}H_{24}N_4O_3Si$ (372.494): C, 58.04; H, 6.49; N, 15.04. Found: C, 58.19; H, 6.62; N, 14.95%.

4.6.13. (*R*)-2-Azido-3-[(dimethyl)phenylsilyl]propionic acid L-11a. A mixture of **10a** (1.40 g, 3.42 mmol) and $LiOH\cdot H_2O$ (0.29 g, 6.90 mmol) in THF/H_2O (94 mL, 3:1) was stirred for 1 h at 0°C. Satd aq. $NaHCO_3$ soln (20 mL) was added and the THF evaporated at 15 torr. Extraction of the aq. residue with CH_2Cl_2 to remove the auxiliary, acidification with aq. HCl soln (1N) to pH 1, extraction with AcOEt, and filtration through a plug of SiO_2 afforded L-**11a** as a colorless oil (0.84 g, 3.38 mmol, 99%). $[\alpha]_D=-13.3$ (*c* 2.95, $CHCl_3$), lit.[12] $[\alpha]_D=-9.2$ (*c* 2.94, $CHCl_3$). IR: 3070m, 3045m, 3020m, 2955s, 2895m, 2110s, 1720s, 1430s, 1420m, 1335m, 1300m, 1260s, 1250s, 1230s, 1190m, 1155w, 1115s, 1030w, 1020w, 1000w, 940m, 885s, 840m, 825s, 800m, 735s, 700s, 595m. ^{1}H NMR: 10.86 (s, HOOC); 7.57–7.51 (m, 2 arom. H); 7.42–7.36 (m, 3 arom. H); 3.77 (dd, $J=9.5$, 6.1, HCN_3); 1.45 (dd, $J=14.9$, 6.5, CH_2Si, 1 H); 1.37 (dd, $J=14.9$, 9.5, CH_2Si, 1 H); 0.43, 0.41 (2s, 2 MeSi). ^{13}C NMR: 177.8 (s, CO); 136.9 (s, arom. C); 133.5 (d, 2 arom. C); 129.5 (d, 1 arom. C); 128.0 (d, 2 arom. C); 59.0 (d, CHN_3); 18.8 (t, CH_2Si); −2.7, −3.1 (2q, 2 MeSi). CI MS: 267 (18, $[M+NH_4]^+$), 178 (98), 152 (100). The spectral data of **11a** are in agreement with published data.[12]

4.6.14. (*R*)-2-Azido-3-(1-methyl-1-silacyclopentyl)propionic acid L-11b. Analogously to Section 4.6.13, **10b** (0.27 g, 0.74 mmol) was treated with $LiOH\cdot H_2O$ (0.062 g, 1.47 mmol) to yield L-**11b** as a colorless oil (0.148 g, 0.69 mmol, 94%). $[\alpha]_D=-7.7$ (*c* 4.05, $CHCl_3$). IR: 2930s, 2895m, 2855m, 2800w, 2110s, 1720s, 1460w, 1450w, 1420m, 1405m, 1335w, 1305w, 1255s, 1245s, 1200m, 1190m, 1155w, 1075s, 1030m, 1020m, 945w, 925w, 885m, 860m, 835s, 805m, 780m, 715w, 655m, 595m. ^{1}H NMR: 11.52 (s, HOOC); 3.88 (dd, $J=8.8$, 6.6, HCN_3); 1.61–1.56 (m, 2 CH_2CH_2Si); 1.31 (d, $J=4.2$, CH_2Si, 1 H); 1.28 (d, $J=2.7$, CH_2Si, 1 H); 0.71–0.57 (m, 2 CH_2CH_2Si); 0.19 (s, MeSi). ^{13}C NMR: 178.0 (s, CO); 59.3 (d, CHN_3); 27.0 (t, 2 CH_2CH_2Si); 18.1 (t, CH_2Si); 12.0, 11.9 (2t, 2 CH_2CH_2Si); −3.2 (q, MeSi). EI MS: 114 (25), 101 (33), 99 (45), 98 (20), 97 (33), 88 (22), 87 (27), 86 (36), 85 (51), 74 (74), 71 (53), 70 (41), 61 (40), 60 (31), 59 (62), 55 (45), 45 (100), 44 (25), 43 (79), 42 (28), 41 (28), 31 (36), 29 (28), 28 (25). Anal. calcd for $C_8H_{15}N_3O_2Si$ (213.093): C, 45.05; H, 7.09; N, 19.70. Found: C, 45.23; H, 6.87; N, 19.47%.

4.6.15. (*R*)-2-Amino-3-[(dimethyl)phenylsilyl]propionic acid (=L-3-[(dimethyl)phenylsilyl]alanine) L-3a. A soln of **11a** (0.363 g, 1.45 mmol) in $EtOH/H_2O$ (20 mL, 1:1) was treated with PtO_2 (0.049 g, 0.21 mmol) and kept under H_2 (760 torr) for 3 h. The catalyst was removed by filtering the mixture through cotton, and evaporation of the solvent afforded pure L-**3a** as a colorless solid (0.323 g, 1.45 mmol, 100%). Mp 207.8–209.2°C (H_2O, decomposition); $[\alpha]_D=+36.2$ (*c* 0.13, 1N aq. HCl soln), lit.[12] $[\alpha]_D=+28.8$ (*c* 0.5, HCl salt in H_2O). The spectral data of L-**3a** are identical with those of DL-**3a** reported earlier.[18]

4.6.16. (*R*)-2-Amino-3-(1-methyl-1-silacyclopentyl)propionic acid (=L-3-(1-methyl-1-silacyclopentyl)alanine) L-3b. Analogously to Section 4.6.15, **11b** (0.062 g, 0.29 mmol) was hydrogenated with PtO_2 catalyst (0.050 g, 0.22 mmol) to yield L-**3b** as a colorless solid (0.049 g, 0.26 mmol, 90%). Mp 241°C (H_2O, start of decomposition); $[\alpha]_D=+26.4$ (*c* 1.00, 1N aq. HCl soln). The spectral data of L-**3b** are identical with those of DL-**3b** reported earlier.[18]

4.6.17. (*R*)-2-Carbamoylamino-3-[(dimethyl)phenylsilyl]-propionic acid (=L-*N*-carbamoyl-3-[(dimethyl)phenylsilyl]alanine) L-2a. A mixture of L-**3a** (0.110 g, 0.49 mmol) and KOCN (0.040 g, 0.50 mmol) in H_2O (4 mL) was stirred at 70°C for 3 h. The mixture was cooled to 10°C and AcOH (2 mL) was added. The precipitated product was collected by filtration and dried at 10^{-2} torr to yield L-**2a** as a colorless solid (0.110 g, 0.41 mmol, 84%). The enantiomeric purity of L-**2a** was determined by chiral HPLC to exceed 99%. Mp 148.2–148.9°C (H_2O); $[\alpha]_D=+11.2$ (*c* 0.74, MeOH). The spectral data of L-**2a** are identical with those of DL-**2a** reported earlier.[18]

4.6.18. (*R*)-2-Carbamoylamino-3-(1-methyl-1-silacyclopentyl)propionic acid (=L-*N*-carbamoyl-3-(1-methyl-1-silacyclopentyl)alanine) L-2b. Analogously to Section 4.6.17, L-**3b** (0.88 g, 0.47 mmol) was treated with KOCN (0.040 g, 0.50 mmol) to yield L-**2b** as a colorless solid (0.062 g, 0.27 mmol, 57%). The enantiomeric purity of L-**2b** was determined by chiral HPLC to exceed 99%. Mp 142.8–143.4°C (H_2O); $[\alpha]_D=+5.5$ (*c* 0.51, MeOH). The spectral data of L-**2b** are identical in all respects with those of DL-**2b** reported earlier.[18]

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