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ORIGINAL PAPER

Dipeptides with 3-(trimethylstannyl)alanine building blocks: synthesis, characterization, and reactivity

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Abstract 3-(Trimethylstannyl)alanine esters containing a free amino group react with different *N*-benzoyloxycarbonyl amino acids in the presence of *N*,*N*′-dicyclohexylcarbodiimide to yield new dipeptides with *β*-(trimethylstannyl)alanine building blocks. Reactions at the stannyl group were studied in more detail in two glycyl alaninates. Their reaction with Me_3SnCl without solvent yields the chlorostannyl-substituted compounds. The glycyl alaninates react with two equivalents of bromine to give the dibromostannylated compounds.

Keywords Tin compounds · Bioinorganic chemistry · Amino acids · Peptides · NMR spectroscopy

Introduction

Organotin compounds of dipeptides have been well known for some years [1]. The most thoroughly investigated examples are the di- and triorganotin derivatives of glycylglycine and of alanylglycine [2–6]. In the last 20 years numerous tri- and diorganotin dipeptides were synthesized and their biological properties tested [7–11]. The stannylated dipeptides mostly have been screened for antitumor, anti-inflammatory, and cardiovascular activities [12]. A review of the antimicrobial activity of organotin(IV) compounds including numerous dipeptides [13] was recently published as was a review on the toxicity and cardiovascular activity [14]. The tin atom in all the compounds described in the aforementioned reports and in nearly all stannylated dipeptides known so far is coordinated with nitrogen and/or oxygen atoms of functional groups. Diorganotin(IV) derivatives of different dipeptides have been synthesized by the reaction of diorganotin dichloride with the sodium salt of various dipeptides [15, 16]. In these diorganotin(IV) dipeptides the tin atom is coordinated with the dipeptide through the COO^-, NH_2, and $N_{peptide}$ groups. In triorganotin(IV) dipeptides synthesized by reaction of bis(triorganotin)oxide and the appropriate *N*-acetylpeptide using dehydrating agents [17] or by reaction of triorganotin(IV) chlorides with the sodium salt of N-protected dipeptides [18], the tin atom is coordinated by the carboxylic group and by the oxygen atom of the amidocarbonyl group. Only very few tin-containing dipeptides are known, prior to the current article, in which the tin atom is directly bound to carbon. One example is the product of palladium-catalyzed stanna-allylation of the α-CH_2 group of different dipeptides [19]. These stannylated dipeptides possess a large synthetic potential regarding side-chain modifications or conversion into the iodo derivatives by metal–halogen exchange. A second example is the synthesis of *N*-Boc-*p*-(tri-*n*-butylstannyl)-L-phenylalanine tetrafluorophenyl ester [20] starting from *N*-Boc-*p*-iodo-L-phenylalanine and bis(tributyltin).

Our research into C-stannylated amino acid derivatives [21, 22] was extended to C-stannylated dipeptides, which can be synthesized from 3-(trimethylstannyl)alanine esters which have a free amino group [23]. This C-stannylated alanine could be obtained by reaction of *N*-(diphenylmethylene)glycine ester with iodomethyl triorganostannanes. The resulting 3-(triorganostannyl)-*N*-(diphenylmethylene)alanine ester could be transformed by mild two-phase hydrolysis to 3-(triorganostannyl)alanine ester hydrochloride. The corresponding alanine ester was obtained after treatment with NH_3 in chloroform, but these compounds were of limited stability. With the alanine esters in hand we next investigated whether the stability of the 3-(trimethylstannyl)alanine esters was

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nevertheless sufficient for further reactions. This issue should be answered by these studies.

In our research we were encouraged by two points: first, the reported anticancer activity of stannylated dipeptides with Sn–O/N coordination [24] and second it should be interesting to compare these known compounds with C-stannylated ones in the light of the hypothesis that the antileukemic activity of organotin compounds is due to the formation of $R_3Sn(IV)$ species as a result of hydrolytic processes [25].

We describe here our first results on the synthesis and reactivity of C-stannylated dipeptides with 3-(trimethylstannyl)alanine building blocks.

Results and discussion

There are numerous methods to synthesize dipeptides starting from amino acids containing a free amino group. For the synthesis of stannylated dipeptides it seemed useful to adopt the carbodiimide method based on Shehan and Hess's work [26]. The synthesis of 3-(trimethylstannyl)alanine derivatives of glycine ($R^1 = H$, **3a**–**3d**), L-alanine ($R^1 = CH_3$, **3e**, **3f**), D,L-valine ($R^1 = CH(CH_3)_2$, **3g**, **3h**), and L-phenylalanine ($R^1 = CH_2Ph$, **3i**, **3j**) succeeded in good yields (Scheme 1).

The stannylated dipeptides **3** are colorless, low melting solids which are very soluble in halogenated hydrocarbons and diethyl ether, but less soluble in hydrocarbons. The dipeptides **3** were characterized by elemental analysis, ^1H and ^{119}Sn NMR spectroscopy, and IR spectroscopy.

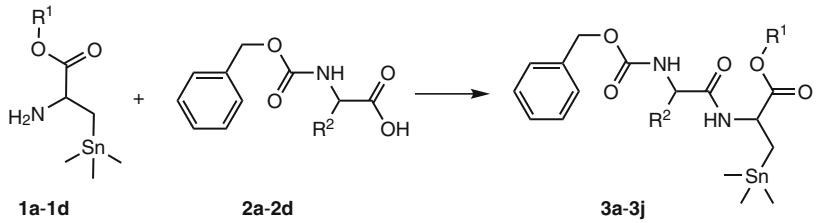
The starting β-(trimethylstannyl)alanine esters were used as a racemic mixture. The product of reaction of this racemic mixture with derivatives of achiral glycine yield **3a**–**3d** as a racemic mixture also. Their ^{119}Sn NMR spectra show only one single signal and the proton NMR spectra show sharp signals without any splitting.

In the case of synthesis of **3e**–**3j** the results are more complicated. Since these new molecules contain two stereocenters the products should be mixtures of diastereoisomers. This can be seen in the ^{119}Sn NMR spectra which are well separated into two signals ($\Delta\delta = 0.26$–0.37 ppm) of nearly equal intensity. Also, the ^1H NMR signals are split. After column chromatography and fractional crystallization the isomers could be isolated. These isolated isomers were characterized by NMR data given in the "Experimental". Their stereochemistry is not yet finally determined.

The assignments of ^1H resonances are in accordance with literature values for the dipeptides without tin substituents [27] and the integration areas are equivalent to the number of protons.

The ^{119}Sn NMR shift of these dipeptides is situated in the region for tetramethyltin compounds [28] indicating a tetra-coordination at the tin atom. There are no interactions between tin and the functional groups of the rest of the molecule. The spectroscopic data are given in the "Experimental".

Scheme 1



1a-1d **2a-2d** **3a-3j**

a: R^1 = Me
b: R^1 = Et
c: R^1 = Bz
d: R^1 = *t*-Bu

a: R^2 = H (gly)
b: R^2 = CH_3 (L-ala)
c: R^2 = $CH(CH_3)_2$ (D,L-val)
d: R^2 = CH_2Ph (L-phe)

a: R^1 = Me, R^2 = H (gly)
b: R^1 = Et, R^2 = H (gly)
c: R^1 = Bz, R^2 = H (gly)
d: R^1 = *t*-Bu, R^2 = H (gly)
e: R^1 = Me, R^2 = CH_3 (L-ala)
f: R^1 = Et, R^2 = CH_3 (L-ala)
g: R^1 = Me, R^2 = $CH(CH_3)_2$ (D,L-val)
h: R^1 = Et, R^2 = $CH(CH_3)_2$ (D,L-val)
i: R^1 = Me, R^2 = CH_2Ph (L-phe)
j: R^1 = Et, R^2 = CH_2Ph (L-phe)

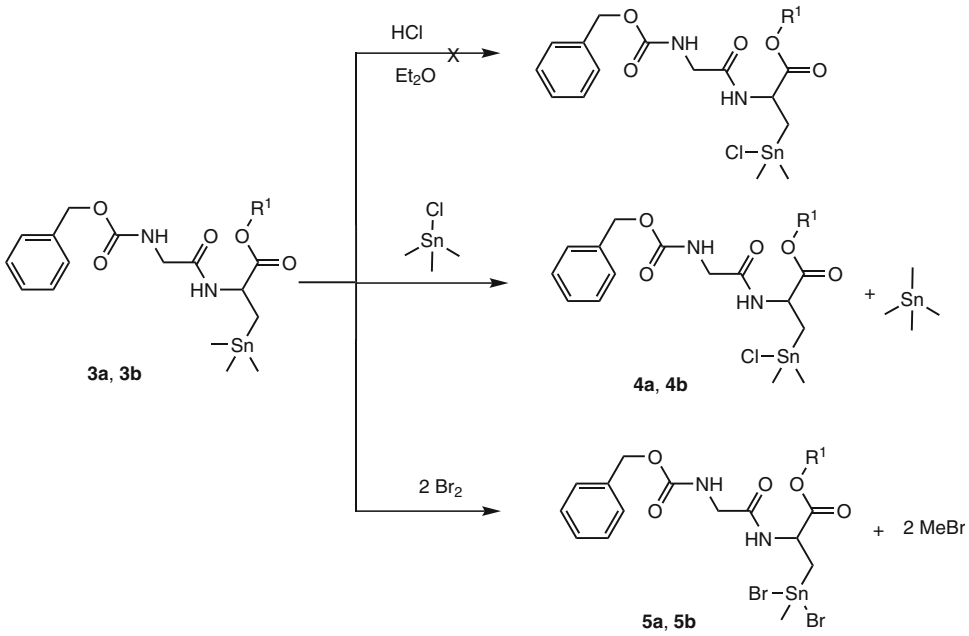
The stannylated dipeptides **3** show the chemical behavior typical for compounds with this substitution pattern. The dipeptides **3a** and **3b** were studied in more detail. The alkyl groups at tin atom can be substituted by halogen atoms by reaction either with Me_3SnCl without a solvent at 60 °C to give **4** or with bromine resulting in **5** (Scheme 2). No reaction occurred when **3a** was treated with HCl in diethyl ether at room temperature—the starting material was recovered.

In all tin compounds containing electronegative substituents at the metal atom—like **4** and **5**—the tin has a strong tendency to coordinate with donor groups. Which interactions can be expected between the Lewis acid tin atom in **4** and **5** and the functional groups existing in the dipeptides? The three C=O groups of these molecules should be of different donor ability and on the other hand there would be a five-membered ring in case of coordination to the ester C=O group and a six-membered ring in case of coordination to the amide C=O group. The also imaginable intramolecular coordination between the tin atom and the carbamide C=O would give an instable nine-membered ring—a coordination that is rather improbable.

The association behavior of tin atom with functional groups may be readily observed by ^{119}Sn NMR because the coordination number of the tin atom increases on association. The spectroscopic data are summarized in the "Experimental". Both the high field shift of ^{119}Sn signal and the increase of $^{2}J(^{119}SnC^{1}H_3)$ coupling constant of **4** compared with Me_3SnCl (in CCl_4: δ ^{119}Sn = +164.2 ppm, $^{2}J(^{119}SnC^{1}H_3)$ = 58.1 Hz) [28, 29] refer to pentacoordinated tin as result of intramolecular interactions of this atom with one donor group of the dipeptide. If one donor group is intramolecularly coordinated in **4a** (and **4b**) as a consequence of the asymmetry of the molecule the protons of the tin-bonded methyl groups should absorb at different frequencies in the ^{1}H spectra. Indeed, in the ^{1}H spectrum of **4a** (and **4b**) in $CDCl_3$ two sharp signals appear for the methyl groups at the tin atom, which are flanked by tin satellites. This splitting of Sn-methyl signal refers to coordination-induced configuration stability of the tin atom. Such configuration stabilization is very well documented [30, 31] (and references cited in the latter) and was observed by us for similar compounds [22, 23, 32]. The Sn···C=O coordination was also reflected in the IR spectra. One of the three C=O signals of **4a** (and **4b**) is bathochromically shifted by nearly 20 cm^{-1} compared with corresponding signals in **3a** (and **3b**). On the basis of our research of Sn···O=C coordination in comparable systems [21–23], this shift could be allocated to a relation between the Lewis acid tin atom and intramolecularly coordinated amide C=O, while the ester C=O and the carbamide C=O rest unchanged. The preferred interaction of a monohalogenated tin atom with the C=O function of an amide group was clearly demonstrated by us by crystal structure analysis of 3-(diphenylchlorostannyl)-*N*-acetylalanine ethyl ester [21].

The reaction of **3a** and **3b** with bromine yields the dibromostannanes **5a** and **5b** which are very soluble in halogenated hydrocarbons. The ^{119}Sn signal of **5** is shifted to higher field compared with that in Me_2SnBr_2 (in CCl_4: δ ^{119}Sn = +70 ppm, $^{2}J(^{119}SnC^{1}H_3)$ = 66.3 Hz) [28, 29]. This is a clear illustration of increase of the coordination number at the tin atom of **5**. The bathochromic shift of

Scheme 2



amide C=O of **5** in comparison with **3** demonstrates the coordination of amide C=O with the tin atom. Likewise the ester C=O signal is shifted to higher wavelengths and overlaps with the signal for the N(H)–C(O)=O group. Also in the light of earlier results [21–23], IR and NMR data reveal that tin in **5** is hexacoordinated by intramolecular coordination of the amide C=O and ester C=O group.

Conclusions

3-(Trimethylstannyl)alanine esters **1a**–**1d** which have a free amino group react with *N*-benzoyloxycarbonyl derivatives of glycine (R^2 = H, **2a**), L-alanine (R^2 = CH_3, **2b**), D,L-valine (R^2 = $CH(CH_3)_2$, **2c**), and L-phenylalanine (R^2 = CH_2Ph, **2d**) to give C-stannylated dipeptides **3a**–**3j** in good yields. The dipeptides **3** were characterized by elemental analysis, ^1H and ^{119}Sn NMR spectroscopy, and IR spectroscopy.

The product of reaction of the racemic *β*-(trimethylstannyl)alanine esters with derivatives of achiral glycine yield **3a**–**3d** as a racemic mixture also. In the case of dipeptides with L-alanine (R^1 = CH_3, **3e**, **3f**), D,L-valine (R^1 = $CH(CH_3)_2$, **3g**, **3h**), and L-phenylalanine (R^1 = CH_2Ph, **3i**, **3j**) the products contain two stereocenters and are mixtures of diastereoisomers. After column chromatography and fractional crystallization the isomers could be isolated and were characterized by spectroscopy, but their stereochemistry is not yet finally determined.

The stannylated dipeptides **3** show the chemical behavior typical for compounds with this substitution pattern. The dipeptides **3a** and **3b** were studied in more detail. The alkyl groups at tin atom can be substituted by halogen atoms by reaction either with Me_3SnCl without a solvent at 60 °C to give **4** or with bromine resulting in **5**.

Experimental

The amino acids were purchased from Sigma and transformed into their *N*-benzoyloxycarbonyl derivatives according to standard Schotten–Baumann procedures [33]. The 3-(triorganostannyl)alanine esters [23] were prepared from iodomethyl triorganostannane [34] and *N*-(diphenylmethylene)glycine esters. All operations with tin-containing compounds were carried out under dry argon. The elemental microanalyses were determined using an Elemental Analyzer from Carlo Erba. Melting points were detected with a Kofler heating table microscope. The IR spectra were recorded with a Zeiss specord or Mattson 5000 FT-IR spectrometer. All the NMR spectra were recorded in $CDCl_3$ solution by means of Bruker AC 80, WP 200, or Varian unity 500 spectrometer. Chemical shifts (δ) are reported in ppm and the coupling constants (J) are in Hz.

*General procedure for 3-(trimethylstannyl)dipeptides **3***

To a stirred mixture of 3-(trimethylstannyl)alanine ester (3.1 mmol) in 20 cm^3 $CHCl_3$ at 0 °C were added the corresponding amount of *N*-benzoyloxycarbonyl amino acid dissolved in chloroform and then *N*,*N*′-dicyclohexylcarbodiimide (DCC, 3.1 mmol) also dissolved in chloroform. The mixture was stirred for 1 h at 0 °C and then 24 h at room temperature. The precipitate was filtered off. The filtrate was extracted with a saturated aqueous solution of $NaHCO_3$ and then with water. The organic layer was dried over Na_2SO_4. The solvent was removed under vacuum and the product was crystallized by addition of ether and low boiling hydrocarbon and by cooling. The products given in the "Experimental" were obtained by fractional crystallization.

N-(Benzoyloxycarbonyl)glycyl-(3-trimethylstannyl)alanine methyl ester (**3a**, $C_{17}H_{26}N_2O_5Sn$)
Yield: 76.3 %; m.p.: 101–104 °C; ^1H NMR (500 MHz, $CDCl_3$, 30 °C): δ = 0.09 (s, 9H, $SnMe_3$, $^2J(^{119}SnC^1H)$ = 54.7 Hz), 1.19 (m, 2H, $SnCH_2$), 3.70 (s, 3H, COOMe), 3.86 (m, 2H, CCH_2N), 4.59–4.71 (m, 1H, CH, $^3J(^{119}Sn^1H)$ = 41.4 Hz), 5.12 (s, 2H, OCH_2), 5.30 (br s, 1H, NH), 6.37 (d, 1H, NH), 7.28–7.36 (m, 5H, C_6H_5) ppm; ^{119}Sn NMR ($CDCl_3$): δ = −0.9 ppm; IR (Nujol): $\bar{\nu}$ (CO) = 1,641, 1,673, 1,733 cm^{-1}.

N-(Benzoyloxycarbonyl)glycyl-(3-trimethylstannyl)alanine ethyl ester (**3b**, $C_{18}H_{28}N_2O_5Sn$)
Yield: 77.7 %; m.p.: 86–87.5 °C; ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.10 (s, 9H, $SnMe_3$, $^2J(^{119}SnC^1H)$ = 54.7 Hz), 1.26 (m + t, 5H, $SnCH_2$ + OCH_2CH_3), 3.86 (m, 2H, CCH_2N), 4.15 (m, 2H, $COOCH_2$), 4.64 (m, 1H, CH, $^3J(^{119}Sn^1H)$ = 40.7 Hz), 5.12 (s, 2H, OCH_2), 5.30 (br s, 1H, NH), 6.38 (d, 1H, NH), 7.33-7.36 (m, 5H, C_6H_5) ppm; ^{119}Sn NMR ($CDCl_3$): δ = −1.14 ppm; IR (KBr): $\bar{\nu}$ (CO) = 1,652, 1,689, 1,731 cm^{-1}.

N-(Benzoyloxycarbonyl)glycyl-(3-trimethylstannyl)alanine benzyl ester (**3c**, $C_{23}H_{30}N_2O_5Sn$)
Yield: 84.8 %; oil; ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.05 (s, 9H, $SnMe_3$, $^2J(^{119}SnC^1H)$ = 54.7 Hz), 1.24 (m, 2H, $SnCH_2$), 3.85 (m, 2H, CCH_2N), 4.69 (m, 1H, CH, $^3J(^{119}Sn^1H)$ = 41.6 Hz), 5.12 (s + m, 4H, 2 x OCH_2), 5.44 (m, 1H, NH), 6.56 (d, 1H, NH), 7.32 (m, 10H, C_6H_5) ppm; ^{119}Sn NMR ($CDCl_3$): δ = −0.7 ppm.

N-(Benzoyloxycarbonyl)glycyl-(3-trimethylstannyl)alanine t-butyl ester (**3d**, $C_{20}H_{32}N_2O_5Sn$)
Yield: 78.8 %; m.p.: 87–91 °C; ^1H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.10 (s, 9H, $SnMe_3$, $^2J(^{119}SnC^1H)$ = 54.6 Hz), 1.24 (m, 2H, $SnCH_2$), 1.44 (s, 9H, COO-*t*-Bu), 3.86 (m, 2H, CCH_2N), 4.54 (m, 1H, CH, $^3J(^{119}Sn^1H)$ = 46.5 Hz), 5.11 (s, 2H, OCH_2), 5.37 (m, 1H, NH), 6.41 (d, 1H, NH), 7.33 (m, 5H, C_6H_5) ppm; ^{119}Sn NMR ($CDCl_3$): δ = −1.5 ppm.

N-(Benzoyloxycarbonyl)-L-alanyl-(3-trimethylstannyl)alanine methyl ester (**3e**, $C_{18}H_{28}N_2O_5Sn$)
Yield: 57.2 %; m.p.: 88–91 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 0.10$ (s, 9H, $SnMe_3$, $^2J(^{119}SnC^1H) = 54.7$ Hz), 1.18 (m, 2H, $SnCH_2$), 1.36 (d, 3H, CCH_3), 3.68 (s, 3H, COOMe), 4.23 (m, 1H, C*H*Me), 4.60 (m, 1H, CH, $^3J(^{119}Sn^1H) = 40.6$ Hz), 5.10 (s, 2H, OCH_2), 5.21 (d, 1H, NH), 6.50 (d, 1H, NH), 7.33 (m, 5H, C_6H_5) ppm; ^{119}Sn NMR ($CDCl_3$): $\delta = -1.39$ ppm.

N-(Benzoyloxycarbonyl)-L-alanyl-(3-trimethylstannyl)alanine ethyl ester (**3f**, $C_{19}H_{30}N_2O_5Sn$)
Yield: 56.5 %; oil; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): $\delta = 0.08$ (s, 9H, $SnMe_3$, $^2J(^{119}SnC^1H) = 54.7$ Hz), 1.22 (m + t, 5H, $SnCH_2$ + $COOCCH_3$), 1.34 (d, 3H, CCH_3), 4.13 (qu, 2H, $COOCH_2$), 4.26 (m, 1H, C*H*Me), 4.60 (m, 1H, CH), 5.07 (s, 2H, OCH_2), 5.55 (m, 1H, NH), 6.75 (d, 1H, NH), 7.29 (m, 5H, C_6H_5) ppm; ^{119}Sn NMR ($CDCl_3$): $\delta = -1.67$ ppm.

N-(Benzoyloxycarbonyl)-D,L-valyl-(3-trimethylstannyl)alanine methyl ester (**3g**, $C_{20}H_{32}N_2O_5Sn$)
Yield: 57.6 %; m.p.: 98–102 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): $\delta = 0.10$ (s, 9H, $SnMe_3$, $^2J(^{119}SnC^1H) = 54.6$ Hz), 0.88 (d, $J = 6.8$ Hz, 3H, CMe), 0.95 (d, $J = 6.8$ Hz, 3H, CMe), 1.18 (m, 2H, $SnCH_2$), 2.13–2.29 (m, 1H, C*H*Me_2), 3.68 (s, 3H, COOMe), 4.02 (m, 1H, CH), 4.60 (m, 1H, CH), 5.10 (s, 2H, OCH_2), 5.22 (m, 1H, NH), 6.37 (d, 1H, NH), 7.33 (m, 5H, C_6H_5) ppm; ^{119}Sn NMR ($CDCl_3$): $\delta = -1.57$ ppm.

N-(Benzoyloxycarbonyl)-D,L-valyl-(3-trimethylstannyl)alanine ethyl ester (**3h**, $C_{21}H_{34}N_2O_5Sn$)
Yield: 58.3 %; m.p.: 84–88 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): $\delta = 0.10$ (s, 9H, $SnMe_3$, $^2J(^{119}SnC^1H) = 54.7$ Hz), 0.92 (d, $J = 6.8$ Hz, 3H, CMe), 0.95 (d, $J = 6.8$ Hz, 3H, CMe), 1.18 (m, 2H, $SnCH_2$), 1.25 (t, 3H, COOCMe), 2.07–2.14 (m, 1H, C*H*Me_2), 3.94 (m, 1H, CH), 4.08–4.21 (qu, 2H, $COOCH_2$), 4.62 (m, 1H, CH, $^3J(^{119}Sn^1H) = 40.9$ Hz), 5.09 (s, 2H, OCH_2), 5.28 (m, 1H, NH), 6.13 (d, 1H, NH), 7.30 (m, 5H, C_6H_5) ppm; ^{119}Sn NMR ($CDCl_3$): $\delta = -2.26$ ppm.

N-(Benzoyloxycarbonyl)-L-phenylalanyl-(3-trimethylstannyl)alanine methyl ester (**3i**, $C_{24}H_{32}N_2O_5Sn$)
Yield: 67.8 %; m.p.: 104–108 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): $\delta = 0.06$ (s, 9H, $SnMe_3$, $^2J(^{119}SnC^1H) = 54.7$ Hz), 1.01 (m, 2H, $SnCH_2$), 3.06 (d, 2H, CCH_2), 3.66 (s, 3H, COOMe), 4.40 (m, 1H, CCHN), 4.55 (m, 1H, SnCCH), 5.06 (s, 2H, OCH_2), 5.20 (m, 1H, NH), 6.20 (d, 1H, NH), 7.23 (m, 10H, C_6H_5) ppm; ^{119}Sn NMR ($CDCl_3$): $\delta = -1.96$ ppm.

N-(Benzoyloxycarbonyl)-L-phenylalanyl-(3-trimethylstannyl)alanine ethyl ester (**3j**, $C_{25}H_{34}N_2O_5Sn$)
Yield: 64.5 %; m.p.: 63–68 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): $\delta = 0.07$ (s, 9H, $SnMe_3$, $^2J(^{119}SnC^1H) = 54.7$ Hz), 1.02 (m, 2H, $SnCH_2$), 1.23 (t, 3H, $COOCCH_3$), 3.06 (d, 2H, CCH_2), 4.07 (m, 2H, $COOCH_2C$), 4.39 (m, 1H, CCH_2Ph), 4.53 (m, 1H, SnCCH), 5.07 (s, 2H, OCH_2), 5.20 (m, 1H, NH), 6.15 (d, 1H, NH), 7.23 (m, 10H, C_6H_5) ppm; ^{119}Sn NMR ($CDCl_3$): $\delta = -2.15$ ppm.

General procedure for 3-(chlorodimethylstannyl)dipeptides ***4***

Compound **3** (1.5 mmol) and 1.7 mmol Me_3SnCl were well mixed and heated to 60 °C for 2 days. Volatile products were then removed under vacuum. The residue was treated with ether, the mixture filtered from undissolved particles, and crystallized by addition of hydrocarbons. Recrystallization occurs from diethyl ether/petroleum benzene (b.p. 60–80 °C, Merck).

N-(Benzoyloxycarbonyl)glycyl-(3-chlorodimethylstannyl)alanine methyl ester (**4a**, $C_{16}H_{23}ClN_2O_5Sn$)
Yield: 81 %; m.p.: 93–99 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 30 °C): $\delta = 0.62$ (s, 3H, SnMe, $^2J(^{119}SnC^1H) = 67.4$ Hz), 0.75 (s, 3H, SnMe, $^2J(^{119}SnC^1H) = 66.9$ Hz), 1.79 (d, $J = 12.5$ Hz, 2H, $SnCH_2$, $^2J(^{119}SnC^1H) = 76.5$ Hz), 3.81 (s, 3H, COOMe + m, 2H, CCH_2N), 4.34 (m, 1H, CCHN), 5.14 (s, 2H, OCH_2), 5.16 (d, 1H, NH), 7.35 (m, 5H, C_6H_5), 7.43 (m, 1H, NH) ppm; ^{119}Sn NMR ($CDCl_3$): $\delta = 0.67$ ppm; IR (KBr): $\bar{\nu}$ (CO) = 1,628, 1,710, 1,736 cm^{-1}.

N-(Benzoyloxycarbonyl)glycyl-(3-chlorodimethylstannyl)alanine ethyl ester (**4b**, $C_{17}H_{25}ClN_2O_5Sn$)
Yield: 78 %; m.p.: 87–93 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 30 °C): $\delta = 0.62$ (s, 3H, SnMe, $^2J(^{119}SnC^1H) = 69.8$ Hz), 0.77 (s, 3H, SnMe, $^2J(^{119}SnC^1H) = 68.4$ Hz), 1.32 (t, 3H, $COOCCH_3$), 1.70 (d, 2H, $SnCH_2$), 3.84 (m, 2H, CCH_2N), 4.19–4.30 (m, 1H, CCHN + qu, 2H, $COOCH_2C$), 5.12 (s, 2H, OCH_2), 5.26 (d, 1H, NH), 7.38 (m, 5H, C_6H_5), 7.53 (m, 1H, NH) ppm; ^{119}Sn NMR ($CDCl_3$): $\delta = 0.3$ ppm; IR (KBr): $\bar{\nu}$ (CO) = 1,627, 1,711, 1,732 cm^{-1}.

General procedure for 3-(dibromomethylstannyl)dipeptides ***5***

To a stirred solution of **3** (2 mmol) in 15 cm^3 chloroform at −30 °C was added dropwise a solution of 0.64 g bromine (4 mmol) in chloroform. After 1 h stirring at room temperature the solvent was removed under vacuum. The residue was crystallized from diethyl ether/petroleum benzene (b.p. 60–80 °C, Merck).

N-(Benzoyloxycarbonyl)glycyl-(3-dibromomethylstannyl)alanine methyl ester
(**5a**, $C_{15}H_{20}Br_2N_2O_5Sn$)
Yield: 58 %; m.p.: 38–41 °C; ^{1}H NMR (500 MHz, $CDCl_3$, 30 °C): $\delta = 1.47$ (s, 3H, MeSn, $^2J(^{119}SnC^1H) = 97.1$ Hz), 2.02 (m, 2H, $SnCH_2$), 3.82 (s, 3H, COOMe), 3.87 (m, 2H, CCH_2), 4.49 (m, 1H, CCHN), 5.14 (s, 2H, OCH_2), 5.24 (m,

1H, NH), 7.26 (m, 5H, C_6H_5), 7.59 (m, 1H, NH) ppm; ^{119}Sn NMR ($CDCl_3$): $\delta = -139.6$ ppm; IR (KBr): $\bar{\nu}$ (CO) = 1,620, 1,706 cm^{-1}.

N-(Benzoyloxycarbonyl)glycyl-(3-dibromomethylstannyl)alanine ethyl ester (**5b**, $C_{16}H_{22}Br_2N_2O_5Sn$)
Yield: 53 %; ^{1}H NMR (500 MHz, $CDCl_3$, 30 °C): $\delta = 1.31$ (t, 3H, COOCMe), 1.47 (s, 3H, MeSn, $^2J(^{119}SnC^1H) = 96.4$ Hz), 1.92 (m, 2H, $SnCH_2$), 3.87 (m, 2H, CCH_2), 4.27 (qu, 2H, $COOCH_2C$), 4.48 (m, 1H, CCHN), 5.14 (s, 2H, OCH_2), 5.20 (m, 1H, NH), 7.18 (m, 5H, C_6H_5), 7.44 (m, 1H, NH) ppm; ^{119}Sn NMR ($CDCl_3$): $\delta = -141.7$ ppm; IR (KBr): $\bar{\nu}$ (CO) = 1,621, 1,708 cm^{-1}.

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