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Synthesis of Silicon-Containing α-Amino Acids and Hydantoins

Richard J. Smith,[1] Svetoslav Bratovanov, and Stefan Bienz*

Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich

Abstract: Three new silicon-containing α-amino acids **6a–c** and their respective hydantoin derivatives **8a–c** have been prepared in racemic form. Alkylation of an α-amino cyanoacetate derivative with iodomethyl-substituted silanes, followed by hydrolysis gave the amino acids, and the subsequent reactions with KOCN and with HCl gave the hydantoins. The hydantoins are planned to be subjected to a biotechnological deracemization process.
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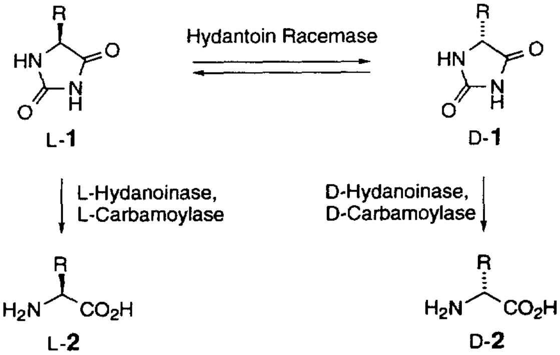
INTRODUCTION

There is a worldwide increase of interest in the synthesis and the use of optically pure natural and unnatural α-amino acids.[2] Such compounds are principally available by three processes: by enantioselective synthesis, by resolution, or by deracemization. The last of the three processes is of particular interest since it would allow to use the chemically most simple synthetic pathways towards racemic compounds and would still permit to obtain the desired enantiomerically pure substrates in theoretically quantitative yields. Syldatk *et al.* have developed such a deracemization process based on a combination of biotransformations:[3] they transferred racemic hydantoins **1** efficiently into either of the two antipodes of the respective α-amino acids **2** by use of three synergetically acting enzymes: a hydantoin racemase — providing rapid interconversion of the enantiomeric hydantoins L-**1** and D-**1** into each other — and a combination of L- or D-selective hydantoinases

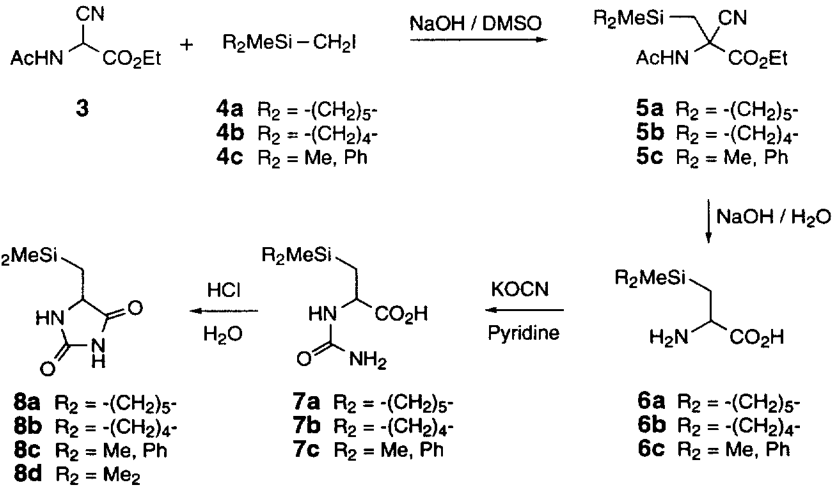


Scheme 1

and carbamoylases — responsible for the enantiomer-selective degradation of either the L- or the D-hydantoins **1** to the respective enantiomerically pure α-amino acids (Scheme 1). A number of optically pure unusual and unnatural α-amino acids have been prepared by this "hydantoinase" process so far. The method has also been applied to the synthesis of D-3-(trimethylsilyl)alanine (D-TMS-Ala),[4] a compound that was successfully used as a bioisoster for phenylalanine in renin inhibitors.[5] Since silylated amino acids others than TMS-Ala could be of substantial interest as substitutes for natural lipophilic amino acids, too, we planned to use the "hydantoinase" process for the preparation of the optically active amino acids D-**6a–c** and L-**6a–c**. In the following we describe the synthesis of the racemic precursor compounds **6a–c** and their respective hydantoin derivatives **8a–c**.

RESULTS AND DISCUSSION

For the synthesis of the compounds **8a–c**, we followed a reaction sequence that was earlier used for the preparation of TMS-substituted hydantoin **8d** (Scheme 2).[6] Treatment of cyanoacetate derivative **3** with the iodomethyl-substituted silanes **4a–c**[11,12] in the presence of base provided the respective alkylated derivatives **5a–c** in moderate yields. These compounds were hydrolyzed with aqueous NaOH and gave rise to the amino acids **6a–c** after decarboxylation of the intermediary malonic acid derivatives. It is crucial for the hydrolysis step to use at least three equivalents of base and to heat the reaction mixture for a prolonged period of time (usually 12–48 h). The use of less NaOH or shorter reaction times gave incomplete transformations. As a result, considerable amounts of *N*-acetyl amino acids were isolated. Conversion of the amino acids **6a–c** to the corresponding hydantoins **8a–c** was attained by their treatment with KOCN in pyridine/H_2O and the subsequent cyclization of the crude *N*-carbamoylamino acids **7a–c** with HCl.[13] The overall yields of the hydantoins **8a–c** summed up to approximately 20–23% (10% for the phenyl-substituted compound **8c**) when the reaction



Scheme 2

sequences were performed stepwise with isolation and purification of the intermediary amino acids **6a–c**. When purification of these intermediates was omitted, the yields increased to 40–48% (20% for **8c**). The significantly lower amounts that were obtained in the preparation of the (dimethyl)phenylsilyl-substituted compound **8c** was attributed to the fairly labile Ph–Si bond. Particularly in the hydrolysis step, under the prolonged action of hydroxide base, an ample amount of insoluble material was formed, and the yield of the desired product decreased drastically.

The synthetic pathway towards silicon-containing α-amino acids and hydantoins presented in this paper is straightforward and leads to the desired products — except for **6c**/**8c** — in reasonable overall yields. Problematic in the reaction sequence are two steps: the initial alkylation reaction (formation of **5a–c** from **3** and **4a–c**) and in the preparation of the phenyl-substituted silicon compound **6c**, as already mentioned above, the hydrolysis step. The alkylation reaction seems to be difficult mostly for steric reasons: with smaller and more reactive electrophiles, like, *e.g.*, MeI but also with Me_3SiCH_2I, the yields were considerably higher (up to 90% as compared to approximately 45%). We have also tested alternative glycine enolate equivalents (enolates of *N*-benzylidene glycine or of phthalimido-protected glycine) that thus gave inferior results.

EXPERIMENTAL

General Remarks. Unless otherwise stated: all org. solvents were distilled prior to use. All moisture-sensitive reactions were carried out under a blanket of Ar. Extracts were dried ($MgSO_4$) and evaporated *in vacuo*. Column chromatography (SiO_2): silica gel *Merck 60* (40–63 µm). M.p.: *Mettler FP-5/FP-52*; d = decomposition. IR: *Perkin-Elmer 781*; as KBr pellets; data in $\tilde{\nu}$ (cm^{-1}) with *s* (strong), *m* (middle), and *w* (weak) with respect to the most intense absorption. ^1H NMR: at 300 MHz in $CDCl_3$; *Bruker AC-300* or *Bruker ARX-300*; δ in ppm relative to $CHCl_3$ ($\delta = 7.26$) or DMSO ($\delta = 2.49$); *J* in Hz; multiplicities denoted as *s* = singlet, *d* = doublet, *t* = triplet, *q* = quadruplet, *quint.* = quintuplet, and *m* = multiplet. ^{13}C NMR: at 75.6 MHz in $CDCl_3$; *Bruker ARX-300*; δ in ppm relative to $CDCl_3$ ($\delta = 77.0$) or DMSO ($\delta = 39.7$); multiplicities from DEPT90 and DEPT135 experiments. CI-MS (chemical ionization mass spectrometry) with NH_3 as the reactant gas: *Finnigan SSQ 700* or *Finnigan MAT 90*; ESI-MS (electrospray ionization mass spectrometry): *Finnigan TSQ 700*; signals at *m/z* > 50 and >10% rel. abundance, for ESI-MS: base peak and quasi-molecular ions only; data in *m/z* (relative abundance of major isotope in percent, where appropriate). Elemental analyses: *Elementar Vario EL.*

Ethyl 2-Acetamido-2-cyano-3-(1-methyl-1-silacyclohex-1-yl)propionate (5a): A soln. of ethyl *N*-acetamidocyanoacetate (**3**, 1.17 g, 6.88 mmol) in DMSO (10 ml) was added at 23°C to a soln. of NaOEt (0.47 g, 6.86 mmol) in DMSO (10 ml). After 4 h, 1-(iodomethyl)-1-methylsilacyclohexane[11] (**4a**, 1.47 g, 5.80 mmol) was added dropwise and the resultant mixture was stirred at 23°C for 48 h. It was quenched with H_2O, extracted with Et_2O, and chromatographed (AcOEt/hexane 1:1) to give **5a** (0.85 g, 2.87 mmol, 49%) as colorless crystals. M.p.: 97.8–98.6°C (AcOEt/hexane). IR: 3270*s*, 3190*m*, 3020*m*, 2990*m*, 2910*s*, 2850*m*, 2790*w*, 1760*s*, 1710*w*, 1695*m*, 1660*s*, 1535*s*, 1480*w*, 1460*w*, 1445*m*, 1405*m*, 1390*m*, 1375*m*, 1360*m*, 1340*w*, 1300*s*, 1265*s*, 1205*s*, 1180*s*, 1160*w*, 1125*w*, 1115*w*, 1095*w*, 1020*s*, 995*m*, 970*w*, 910*s*, 870*w*, 845*s*, 820*s*, 795*s*, 780*m*, 760*w*, 705*w*, 685*m*, 645*w*. ^{1}H NMR: 6.21 (*s*, HN); 4.36, 4.26 (2*dq*, *J* = 10.7, 7.1, $MeCH_2$); 2.05 (*s*, MeCO); 1.77, 1.49 (*AB*, *J* = 14.6, $SiCH_2$); 1.75–1.40 (*m*, $CH_2CH_2CH_2$); 1.37 (*t*, *J* = 7.1, $MeCH_2$); 0.67 (*q*-like *m*, '*J*' = 7.1, 2 $SiCH_2$); 0.18 (*s*, MeSi). ^{13}C NMR: 169.3 (*s*, MeCO); 167.3 (*s*, CO_2Et); 117.3 (*s*, C≡N); 63.7 (*t*, OCH_2); 54.5 (*s*, CC≡N); 29.6 (*t*, $Si(CH_2)_2CH_2$); 24.0 (*t*, 2 $SiCH_2CH_2$); 23.8 (*t*, $SiCH_2$); 22.6 (*q*, *Me*CO); 13.8 (*q*, $MeCH_2$); 13.1 (*t*, 2 $SiCH_2$); –4.3 (*q*, MeSi). CI-MS: 314 (100, $[M + NH_4]^+$), 297 (12, $[M + H]^+$), 270 (5), 256 (15), 225 (17). Anal. Calcd. for $C_{14}H_{24}N_2O_3Si$ (296.45): C ,56.72 H 8.16, N .9.45 Found: C 55.85, H 7.93, N 9.65.

Ethyl 2-Acetamido-2-cyano-3-(1-methyl-1-silacyclopent-1-yl)propionate (5b): Analogously to the preparation of **5a**, **3** (3.13 g, 18.4 mmol) was deprotonated with NaOEt (1.25 g, 18.4 mmol) and alkylated with 1-(iodomethyl)-1-methylsilacyclopentane[11] (**4b**, 3.72 g, 15.5 mmol). The solid obtained after work-up was recrystallized (AcOEt) and gave **5b** (2.00 g, 7.08 mmol, 46%) as colorless crystals. M.p.: 129.8–131.5°C (AcOEt). IR: 3260*s*, 3030*m*, 3000*m*, 2930*s*, 2850*m*, 2800*w*, 1760*s*, 1710*m*, 1660*s*, 1650*s*, 1550*m*, 1540*s*, 1505*m*, 1480*m*, 1450*m*, 1405*m*, 1390*m*, 1375*s*, 1360*m*, 1300*s*, 1270*s*, 1200*s*, 1155*m*, 1115*m*, 1090*m*, 1075*s*, 1020*s*, 960*w*, 925*w*, 865*s*, 835*s*, 805*s*, 785*s*, 775*s*, 710*m*, 670*m*, 655*m*. ^{1}H NMR: 6.21 (*s*, HN); 4.36, 4.26 (2*dq*, *J* = 10.7, 7.1, $MeCH_2$); 2.05 (*s*, MeCO); 1.78, 1.58 (*AB*, *J* = 14.6, $SiCH_2$); 1.61–1.54 (*m*, 2 $SiCH_2CH_2$); 1.37 (*t*, *J* = 7.1, $MeCH_2$); 0.70–0.56 (*m*, 2 $SiCH_2$); 0.26 (*s*, MeSi). ^{13}C NMR: 169.3 (*s*, MeCO); 167.1 (*s*, CO_2Et); 117.3 (*s*, C≡N); 63.8 (*t*, OCH_2); 54.6 (*s*, CC≡N); 26.9, 26.8 (2*t*, 2 $SiCH_2CH_2$); 24.5 (*t*, $SiCH_2$); 22.6 (*q*, *Me*CO); 13.8 (*q*, $MeCH_2$); 12.4, 12.3 (2*t*, 2 $SiCH_2$); –2.5 (*q*, MeSi). CI-MS: 300 (100, $[M + NH_4]^+$), 283 (20, $[M + H]^+$), 256 (7), 242 (13). Anal. Calcd. for $C_{13}H_{22}N_2O_3Si$ (282.42): C 55.29, H 7.85, N 9.92. Found: C 54.76, H 7.77, N 10.03.

Ethyl 2-Acetamido-2-cyano-3-[(dimethyl)phenylsilyl]propionate (5c): Analogously to the preparation of **5a**, **3** (1.17 g, 6.88 mmol) was deprotonated with NaOEt (0.47 g, 6.86 mmol) and alkylated with (iodomethyl)dimethylphenylsilane[12] (**4c**, 1.58 g, 5.70 mmol). The solid obtained after work-up was chromatographed (AcOEt/hexane 1:1) and gave **5c** (0.80 g, 2.51 mmol, 44%) as colorless crystals. The analogous reaction performed with KO*t*-Bu instead of NaOEt as the base delivered the same product in 33% yield. M.p.: 89.9–92.1°C (AcOEt/hexane). IR: 3240*s*, 3190*m*, 3065*m*, 3040*m*, 3020*m*, 2980*m*, 2930*m*, 2890*m*, 2840*w*, 2220*w*, 1765*s*, 1750*s*, 1700*m*, 1660*s*, 1650*s*, 1605*m*, 1565*w*, 1535*s*, 1485*w*, 1470*w*, 1445*m*, 1425*m*, 1415*m*, 1395*m*, 1370*m*, 1360*m*, 1300*s*, 1270*s*, 1245*s*, 1210*s*, 1160*w*, 1115*s*, 1095*w*, 1040*w*, 1020*s*, 1000*m*, 970*w*, 955*w*, 870*w*, 845*s*, 820*s*, 790*s*, 775*m*, 725*s*, 700*s*, 630*w*. ^{1}H NMR: 7.59–7.56 (*m*, 2 arom. H); 7.45–7.43 (*m*, 3 arom. H); 5.76 (*s*, HN); 4.11 (*q*, *J* = 7.1, $MeCH_2$); 2.04 (*s*, MeCO); 1.90, 1.62 (*AB*, *J* = 14.8, $SiCH_2$); 1.25 (*t*, *J* = 7.1, $MeCH_2$); 0.53, 0.40 (2*s*, Me_2Si). ^{13}C NMR: 169.3 (*s*, MeCO); 167.0 (*s*, CO_2Et); 136.4 (*s*, arom. C); 133.8 (*d*, 2 arom. C); 130.1 (*d*, arom. C); 128.4 (*d*, 2 arom. C); 117.4 (*s*, C≡N); 63.4 (*t*, OCH_2); 54.4 (*s*, CC≡N); 24.9 (*t*, $SiCH_2$); 22.0 (*q*, *Me*CO); 13.7 (*q*, $MeCH_2$); –2.8, –3.0 (2*q*, Me_2Si). CI-MS: 336 (6, $[M + NH_4]^+$), 319 (4, $[M + H]^+$), 303 (9), 292 (10), 278 (9), 241 (100). Anal. Calcd. for $C_{16}H_{22}N_2O_3Si$ (318.45): C 60.35, H 6.96, N 8.80. Found: C 59.97, H 6.86, N 8.93.

3-(1-Methyl-1-silacyclohex-1-yl)alanine (6a): A soln. of **5a** (0.77 g, 2.60 mmol) and NaOH (2.0 g, 50.0 mmol) in H_2O (20 ml) was refluxed for 12 h. It was cooled to 0°C and acidified with conc. aq. HCl soln. to pH = 6. The thus formed precipitate was filtered off and chromatographed (CH_2Cl_2/EtOH/AcOH 14:4:1) to give **6a** (0.45 g, 2.23 mmol, 86%) as colorless crystals. M.p.: 239.8–241.3(d)°C (H_2O). IR: 3400*m*, 3000*s*, 2910*s*, 2850*s*, 2610*m*, 2520*m*, 1745*s*, 1590*m*, 1500*m*, 1445*m*, 1400*w*, 1345*w*, 1250*s*, 1205*m*, 1180*s*, 1160*s*, 1075*w*, 1025*w*, 990*m*, 910*m*, 860*m*, 810*s*, 800*s*, 755*m*, 720*m*, 705*w*, 675*w*. ^1H NMR (DMSO/DCl): 3.69 (*dd*, J = 12.1, 4.1, CH); 1.68–1.40 (*m*, 2 $SiCH_2CH_2$); 1.41–1.22 (*m*, $Si(CH_2)_2CH_2$); 1.17, 1.01 (*AB* of *ABX*, J_{AB} = 14.3, J_{AX} = 4.2, J_{BX} = 12.2, $SiCH_2$); 0.65–0.45 (*m*, 2 $SiCH_2$); 0.01 (*s*, MeSi). ^{13}C NMR (DMSO/DCl): 171.7 (*s*, CO_2H); 50.2 (*d*, CH); 29.5 (*t*, $Si(CH_2)_2CH_2$); 24.0, 23.9 (2*t*, 2 $SiCH_2CH_2$); 16.8, 13.1, 12.7 (3*t*, 3 $SiCH_2$); –4.4 (*q*, MeSi). CI-MS: 202 ([*M* + H]$^+$). Anal. Calcd. for $C_9H_{19}NO_2Si$ (201.34): C 53.69, H 9.51, N 6.96. Found: C 53.22, H 9.22, N 6.83.

3-(1-Methyl-1-silacyclopent-1-yl)alanine (6b): Analogously to the preparation of **6a**, **5b** (1.9 g, 6.73 mmol) was hydrolyzed with NaOH (2.0 g, 50.0 mmol) and gave, after recrystallization of the crude product (H_2O), **6b** (0.92 g, 4.89 mmol, 73%) as colorless crystals. M.p.: 252(d)°C (H_2O). IR: 3420*m*, 3040*s*, 2920*s*, 2850*s*, 1675*s*, 1600*s*, 1550*s*, 1430*s*, 1395*s*, 1345*m*, 1320*m*, 1245*s*, 1170*s*, 1130*s*, 1075*s*, 1025*s*, 885*w*, 860*m*, 830*s*, 775*s*, 740*m*, 705*m*, 650*m*, 635*w*. ^1H NMR (DMSO/DCl): 3.66 (*dd*, J = 12.4, 4.2, CH); 1.24 (*s*, 2 $SiCH_2CH_2$); 1.11, 0.91 (*AB* of *ABX*, J_{AB} = 14.1, J_{AX} = 4.2, J_{BX} = 13.3, $SiCH_2$); 0.33–0.20 (*m*, 2 $SiCH_2$); –0.08 (*s*, MeSi). ^{13}C NMR (DMSO/DCl,): 172.7 (*s*, CO_2H); 52.3 (*d*, CH); 28.2, 28.1 (2*t*, 2 $SiCH_2CH_2$); 19.5, 14.2, 13.5 (3*t*, 3 $SiCH_2$); –1.4 (*q*, MeSi). CI-MS: 188 ([*M* + H]$^+$). Anal. Calcd. for $C_8H_{17}NO_2Si$ (187.32): C 51.30, H 9.15, N 7.48. Found: C 51.08, H 9.11, N 7.32.

3-[(Dimethyl)phenylsilyl]alanine (6c): Analogously to the preparation of **6a**, **5c** (0.62 g, 1.93 mmol) was hydrolyzed with NaOH (2.0 g, 50.0 mmol) and gave, after recrystallization of the crude product (H_2O), **6c** (0.30 g, 1.35 mmol, 70%, contaminated with inorganic impurities) as a colorless amorphous solid. M.p.: 213.7–215.3(d)°C (H_2O). IR: 3420*m*, 3060*s*, 1610*s*, 1515*m*, 1505*m*, 1485*m*, 1470*w*, 1455*w*, 1425*s*, 1415*m*, 1390*s*, 1345*m*, 1315*m*, 1245*s*, 1180*m*, 1140*w*, 1115*m*, 1020*w*, 995*w*, 885*w*, 835*s*, 810*m*, 780*s*, 740*m*, 725*s*, 700*s*, 665*w*, 635*w*, 620*w*. ^1H NMR (DMSO/DCl): 7.48–7.45 (*m*, 2 arom. H); 7.33–7.30 (*m*, 3 arom. H); 3.73 (*dd*, J = 12.0, 4.1, CH); 1.40, 1.26 (*AB* of *ABX*, J_{AB} = 14.4, J_{AX} = 4.2, J_{BX} = 12.3, $SiCH_2$); 0.27, 0.24 (2*s*, Me_2Si). ^{13}C NMR (DMSO/DCl): 172.3 (*s*, CO_2H); 139.0 (*s*, arom. C); 134.9 (*d*, 2 arom. C); 130.8 (*d*, arom. C); 129.5 (*d*, 2 arom. C); 51.7 (*d*, CH); 19.6 (*t*, $SiCH_2$); –1.1, –1.5 (2*q*, Me_2Si). ESI-MS (MeOH): 246 ([*M* + Na]$^+$), 224 ([*M* + H]$^+$).

***N*-Carbamoyl-3-(1-methyl-1-silacyclohex-1-yl)alanine (7a) and 5-[(1-Methyl-1-silacyclohex-1-yl)methyl]imidazolidine-2,4-dione (8a):** *From 6a:* A suspension of **6a** (0.20 g, 1.0 mmol) and KOCN (0.10 g, 1.2 mmol) in H_2O/pyridine (1:1, 4 ml) was heated to 60°C for 2 h (the reactants were dissolved completely). It was cooled to 23°C, pyridine was extracted with AcOEt, and the aq. layer acidified with aq. HCl soln. (6N, 1 ml) and AcOH (1 ml) (formation of a precipitate). The mixture was heated to reflux for 1 h, cooled to 4°C and stored at this temperature for 15 h to complete crystallization of the desired product. The precipitate was filtered off and dried to give **8a** (0.12 g, 0.55 mmol, 55%). The *N*-carbamoyl intermediate **7a** was obtained, when the intermediary formed precipitate (after treatment of **6a** with KOCN and acidification) was filtered off, washed with H_2O, and dried. *From 3:* Analogously to the preparation of **5a**, **3** (14.36 g, 84.4 mmol) was deprotonated with NaOEt (6.7 g, 92.8 mmol) and alkylated with **4a** (18.64 g, 73.3 mmol). Analogously to the preparation of **6a**, the crude **5a** was directly hydrolyzed with NaOH (20 g, 0.50 mol, in 200 ml of H_2O, reflux for 48 h), and the thus obtained crude amino acid was subsequently treated as above with KOCN (7.3 g, 90 mmol) in H_2O/pyridine (1:1, 200 ml) and then with aq. HCl soln. (6N, 40 ml) and AcOH (40 ml) at reflux. Recrystallization (H_2O) of the crude product afforded **8a** (8.0 g, 35.3 mmol, 48%) as colorless crystals.

Data of **7a**: M.p.: 123(d)°C (H_2O). IR: no reasonable spectrum was obtained. ^1H NMR (DMSO): 5.92 (*d*, *J* = 6.7, HN); 5.39 (*s*, H_2N); 3.72 (*q*, *J* = 6.8, CH); 1.68–1.42 (*m*, 2 $SiCH_2CH_2$); 1.39–1.20 (*m*, $Si(CH_2)_2CH_2$); 1.01, 0.89 (*AB* of *ABX*, J_{AB} = 14.3, J_{AX} = 6.9, J_{BX} = 6.8, $SiCH_2$); 0.67–0.42 (*m*, 2 $SiCH_2$); 0.00 (*s*, MeSi). ^{13}C NMR (DMSO): 176.5, 158.3 (2*s*, 2 C=O); 51.9 (*d*, CH); 30.0 (*t*, $Si(CH_2)_2CH_2$); 24.4 (*t*, 2 $SiCH_2CH_2$); 20.3, 13.8, 13.7 (3*t*, 3 $SiCH_2$); –3.8 (*q*, MeSi). CI-MS (compound decomposes): 30°C: 263 (100); 60°C: 279 (25), 263 (100); 150°C: 528 (19), 391 (20), 365 (35), 295 (8), 279 (100), 263 (13), 223 (4); 250°C: 536 (7), 462 (4), 367 (10), 314 (29), 279 (8), 255 (13), 227 (48), 202 (33), 184 (50), 158 (90), 145 (40), 132 (46), 130 (100), 114 (73). ESI-MS (MeOH): 479 (19), 463 (19), 369 (20), 338 (35), 327 (44), 311 (18), 283 (36), 245 (100, $[M + H]^+$), 228 (34), 190 (75), 175 (68), 139 (48).

Data of **8a**: M.p.: 174.8–175.9°C (H_2O). IR: 3280*m*, 3180*m*, 3060*m*, 2910*s*, 2845*m*, 2790*w*, 2750*w*, 1775*s*, 1730*s*, 1695*m*, 1680*w*, 1645*w*, 1555*w*, 1535*w*, 1440*m*, 1415*s*, 1380*m*, 1335*m*, 1295*m*, 1255*m*, 1205*m*, 1185*m*, 1095*m*, 1040*w*, 1005*w*, 990*m*, 910*m*, 895*m*, 870*m*, 825*s*, 800*s*, 740*m*, 710*w*, 695*w*, 675*w*, 645*m*, 630*w*. ^1H NMR (DMSO): 10.53, 7.78 (2*s*, br., 2 HN); 4.08 (*t*, *J* = 6.3, CH); 1.62–1.23 (*m*, $CH_2CH_2CH_2$); 1.03, 0.94 (*AB* of *ABX*, J_{AB} = 14.8, J_{AX} = 7.1, J_{BX} = 6.2, $SiCH_2$); 0.62–0.51 (*m*, 2 $SiCH_2$); 0.05 (*s*, MeSi). ^{13}C NMR (DMSO): 177.3, 157.3 (2*s*, 2 C=O); 55.1 (*d*, CH); 29.6 (*t*, $Si(CH_2)_2CH_2$); 24.0 (*t*, 2 $SiCH_2CH_2$); 17.3, 13.2, 13.1 (3*t*, 3 $SiCH_2$); –3.9 (*q*, MeSi). CI-MS: 244 (100, $[M + NH_4]^+$), 227 (4, $[M + H]^+$). Anal. Calcd. for $C_{10}H_{18}N_2O_2Si$ (226.35): C 53.06, H 8.02, N 12.38. Found: C 52.88, H 7.94, N 12.11.

***N*-Carbamoyl-3-(1-methyl-1-silacyclopent-1-yl)alanine (7b) and 5-[(1-Methyl-1-silacyclopent-1-yl)methyl]imidazolidine-2,4-dione (8b):** *From 6b*: Analogously to the preparation of **7a** and **8a**, **6b** (0.75 g, 4.0 mmol) was reacted with KOCN (0.39 g, 4.8 mmol) in H_2O/pyridine (1:1, 16 ml) then with aq. HCl soln. (6N, 4 ml) and AcOH (4 ml) to form **8b** (0.50 g, 2.35 mmol, 58%). *N*-Carbamoyl amino acid **7b** was collected, as described above, after acid treatment before heating to reflux. *From 3*: Analogously to the preparation of **8a**, **3** (11.41 g, 67.1 mmol) was deprotonated with NaOEt (4.56 g, 67.1 mmol) and alkylated with **4b** (13.60 g, 56.5 mmol). It was hydrolyzed with NaOH (80 g, 2.0 mol, in 400 ml of H_2O, reflux 48 h), treated with KOCN (5.2 g, 64.0 mmol) in H_2O/pyridine (1:1, 200 ml), then with aq. HCl soln. (54 ml) and AcOH (54 ml). Recrystallization (H_2O) of the crude product afforded **8b** (4.8 g, 22.5 mmol, 40%) as colorless crystals.

Data of **7b**: M.p.: 146(d)°C (H_2O). IR: 3410*s*, 3380*s*, 3230*s*, 2935*s*, 2835*m*, 2480*w*, 1880*w*, 1690*s*, 1680*s*, 1660*s*, 1640*s*, 1560*s*, 1550*s*, 1540*s*, 1470*m*, 1450*w*, 1415*m*, 1405*m*, 1315*m*, 1295*m*, 1240*s*, 1200*m*, 1175*m*, 1150*m*, 1075*s*, 1050*s*, 1030*s*, 910*w*, 860*m*, 830*m*, 810*s*, 775*m*, 725*w*, 710*w*, 685*w*, 650*w*, 620*w*. ^1H

NMR (DMSO): 6.10 (*d*, *J* = 8.5, HN); 5.53 (*s*, H_2N); 4.08 (*dt*, *J* = 9.6, 6.0, CH); 1.49 (*quint.*, *J* = 3.7, 2 $SiCH_2\mathit{CH}_2$); 1.06, 0.94 (*AB* of *ABX*, J_{AB} = 14.5, J_{AX} = 5.9, J_{BX} = 9.8, $SiCH_2$); 0.64–0.37 (*m*, 2 $SiCH_2$); 0.09 (*s*, MeSi). ^{13}C NMR (DMSO): 176.0, 158.1 (2*s*, 2 C=O); 49.6 (*d*, CH); 26.8, 26.7 (2*t*, 2 $SiCH_2\mathit{CH}_2$); 19.4, 12.0, 11.9 (3*t*, 3 $SiCH_2$); –2.7 (*q*, MeSi). CI-MS: 248 (25, $[M + NH_4]^+$), 231 (100, $[M + H]^+$), 213 (10, $[M + H - H_2O]^+$ ≙ **[8b** + H]$^+$), 188 (86, $[M + H - CONH]^+$ ≙ **[6b** + H]$^+$).

Data of **8b**: M.p.: 163.5–164.2°C (H_2O). IR: 3220*s*, 3060*s*, 2920*s*, 2850*m*, 2745*w*, 1770*s*, 1735*s*, 1695*w*, 1685*w*, 1555*w*, 1485*w*, 1450*m*, 1415*s*, 1380*m*, 1320*m*, 1305*m*, 1245*m*, 1205*s*, 1140*s*, 1070*s*, 1040*s*, 1005*m*, 945*w*, 890*m*, 860*m*, 835*s*, 805*s*, 785*m*, 760*m*, 740*m*, 715*w*, 700*w*, 650*m*, 635*m*. ^1H NMR (DMSO): 10.55, 7.81 (2*s*, br. 2 HN); 4.15–4.10 (*m*, CH); 1.49 (*quint.*-like *m*, '*J*' = 3.7, 2 $SiCH_2\mathit{CH}_2$); 1.09, 1.03 (*AB* of *ABX*, J_{AB} = 14.8, J_{AX} = 6.4, J_{BX} = 6.0, $SiCH_2$); 0.62–0.43 (*m*, 2 $SiCH_2$); 0.10 (*s*, MeSi). ^{13}C NMR (DMSO): 177.1, 157.3 (2*s*, 2 C=O); 55.3 (*d*, CH); 26.7 (*t*, 2 $SiCH_2\mathit{CH}_2$); 18.3, 12.4, 12.3 (3*t*, 3 $SiCH_2$); –2.3 (*q*, MeSi). CI-MS: 230 (100, $[M + NH_4]^+$), 213 (17, $[M + H]^+$). Anal. Calcd. for $C_9H_{16}N_2O_2Si$ (212.33): C 50.91, H 7.60, N 13.19. Found: C 50.72, H 7.33, N 12.98.

***N*-Carbamoyl-3-[(dimethyl)phenylsilyl]alanine (7c) and 5-{[(Dimethyl)phenylsilyl]methyl}imidazolidine-2,4-dione (8c):** *From 6c*: Analogously to the preparation of **7a** and **8a**, **6c** (0.22 g, 1.0 mmol) was reacted with KOCN (0.10 g, 1.2 mmol) in H_2O/pyridine (1:1, 4 ml) then with aq. HCl soln. (6N, 1 ml) and AcOH (1 ml) to form **8c** (0.12 g, 0.49 mmol, 49%). *N*-Carbamoyl amino acid **7c** was collected, as described above, after acid treatment before heating to reflux. *From 3*: Analogously to the preparation of **8a**, **3** (5.71 g, 33.6 mmol) was deprotonated with NaOEt (2.65 g, 36.9 mmol) and alkylated with **4c** (8.34 g, 30.2 mmol). It was hydrolyzed with NaOH (80 g, 2.0 mol, in 400 ml of H_2O, reflux 48 h), treated with KOCN (1.65 g, 20.5 mmol) in H_2O/pyridine (1:1, 90 ml), then with aq. HCl soln. (6N, 11 ml) and AcOH (11 ml). Recrystallization (H_2O) of the crude product afforded **8c** (1.50 g, 6.04 mmol, 20%) as colorless crystals.

Data of **7c**: M.p.: 150.0–150.4°C (H_2O). IR: 3520*s*, 3460*s*, 3360*s*, 3280*s*, 3110*m*, 3060*m*, 2960*m*, 2890*m*, 2710*m*, 2520*m*, 1715*s*, 1660*m*, 1645*m*, 1615*s*, 1565*s*, 1555*s*, 1505*m*, 1485*m*, 1470*w*, 1455*w*, 1430*m*, 1415*m*, 1390*m*, 1340*w*, 1250*s*, 1210*s*, 1170*s*, 1140*m*, 1110*s*, 1070*m*, 1020*w*, 1000*w*, 950*w*, 920*w*, 835*s*, 800*m*, 775*m*, 730*m*, 700*s*, 675*w*, 665*w*. ^1H NMR (DMSO): 7.51–7.48 (*m*, 2 arom. H); 7.35–7.33 (*m*, 3 arom. H); 6.14 (*d*, *J* = 8.5, HN); 5.54 (*s*, H_2N); 4.08 (*dt*, *J* = 9.6, 5.5, CH); 1.21, 1.04 (*AB* of *ABX*, J_{AB} = 14.6, J_{AX} = 5.3, J_{BX} = 10.1, $SiCH_2$); 0.25, 0.23 (2*s*, Me_2Si). ^{13}C NMR (DMSO): 176.1, 158.2 (2*s*, 2 C=O); 138.8 (*s*, arom. C); 133.5 (*d*, 2 arom. C); 129.1 (*d*, arom. C); 127.9 (*d*, 2 arom. C); 49.4 (*d*, CH); 19.9 (*t*, $SiCH_2$); –2.1, –2.6 (2*q*, Me_2Si). CI-MS (100°): 284 (5, $[M + NH_4]^+$), 280 (18), 267 (47, $[M + H]^+$), 266 (100, $[M + NH_4 - H_2O]^+$), 249 (9, $[M + H - H_2O]^+$ ≙ **[8c** + H]$^+$), 233 (20), 224 (82, $[M + H - CONH]^+$ ≙ **[6c**+ H]$^+$), 189 (67), 185 (30), 171 (58).

Data of **8c**: M.p.: 160.3–161.2°C (H_2O). IR: 3220*s*, 3180*s*, 3120*s*, 3060*s*, 2960*m*, 2900*m*, 2740*w*, 1770*s*, 1730*s*, 1695*m*, 1680*w*, 1645*w*, 1635*w*, 1485*w*, 1425*s*, 1415*s*, 1375*m*, 1325*w*, 1305*m*, 1245*m*, 1205*m*, 1195*m*, 1145*w*, 1110*m*, 1090*m*, 1040*m*, 1000*w*, 890*w*, 835*s*, 795*m*, 765*m*, 740*m*, 725*m*, 695*m*, 630*m*. ^1H NMR (DMSO): 10.54, 7.74 (2*s*, br., 2 HN); 7.52–7.49 (*m*, 2 arom. H); 7.37–7.33 (*m*, 3 arom. H); 4.03 (*dt*, *J* = 6.9, 1.5, CH); 1.23, 1.09 (*AB* of *ABX*, J_{AB} = 14.9, J_{AX} = 6.8, J_{BX} = 7.0, $SiCH_2$); 0.31 (*s*, Me_2Si). ^{13}C NMR (DMSO): 177.2, 157.4 (2*s*, 2 C=O); 138.6 (*s*, arom. C); 133.5 (*d*, 2 arom. C); 129.2 (*d*, arom. C); 127.9 (*d*, 2 arom. C); 55.1 (*d*, CH); 19.1 (*t*, $SiCH_2$); –2.1, –2.2 (2*q*, Me_2Si). CI-MS: 266 (100, $[M + NH_4]^+$), 249 (12, $[M + H]^+$), 233 (5), 171 (55). Anal. Calcd. for $C_{12}H_{16}N_2O_2Si$ (248.36): C 58.03, H 6.49, N 11.28. Found: C 57.88, H 6.33, N 11.13.

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