Towards Functionalized Silicon-Containing α-Amino Acids: Asymmetric Syntheses of Sila Analogs of Homoserine and Homomethionine

by **Richard J. Smith**[1]) and **Stefan Bienz***

Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057 Zürich
(phone: +41 1 635 4245; fax. +41 1 635 6812; e-mail: sbienz@oci.unizh.ch)

Dedicated to Dr. *Günther Ohloff* on the occasion of his 80th birthday

The homoserine and homomethionine sila analogs, (*R*)-$HOSi(Me_2)CH_2CH(NH_2)CO_2H$ ((*R*)-**21**) and (*R*)-$MeSCH_2Si(Me_2)CH_2CH(NH_2)CO_2H$ ((*R*)-**24**), respectively, were each synthesized in nine steps and in 30 and 23% overall yield, respectively, from commercially available $ClSiMe_2CH_2Cl$. The key step of both syntheses was the asymmetric α-bromination of an *Evans* amide to introduce the stereogenic center of the amino acids with defined absolute configuration. While the preparation of the homomethionine analog (*R*)-**24** followed the expected pathway, the sila analog of homoserine, (*R*)-**21,** was unexpectedly formed during the catalytic hydrogenation of an N_3CH_2-substituted silane derivative.

Introduction. – Nonproteinogenic and unnatural amino acids are important building blocks for peptide chemistry [1–3], and, among such compounds, sila amino acids are of increasing interest [3–13]. With their large hydrophobic groups, they are expected and have been shown to offer several advantages over classical amino acids when incorporated into peptides, such as prevention of hydrophobic-pocket collapse, higher lipophilicity, and enhanced stability towards proteolytic enzymatic degradation [2][9].

Several approaches towards enantiomerically pure sila amino acids have been reported. Apart from resolution or dynamic resolution of racemic mixtures [3][5–7], several stereoselective syntheses have been performed. In these syntheses, either the Si-containing side chains were introduced by diastereoselective alkylation of chiral glycine anion synthons [3][8–10] or by β-substitution of serine derivatives [11]. Alternatively, the amino acids were prepared by stereoselective α-amination of β-silylated carboxylic acids [7][12]. While most of the previous studies targeted rather simple trialkyl- or trialkyl/triarylsilanes, *Tacke et al.* reported the first enantioselective synthesis of Si-containing amino acids that are hetero-functionalized at a Si-containing side chain [10]. However, the hetero group, an amino function, was introduced early in the synthetic scheme, limiting the versatility of the method. In continuation of our investigations [6][7][13], we were looking for a more flexible route to functionalized sila amino acids, considering halogenomethyl-substituted silanes such as **4** as precursors.

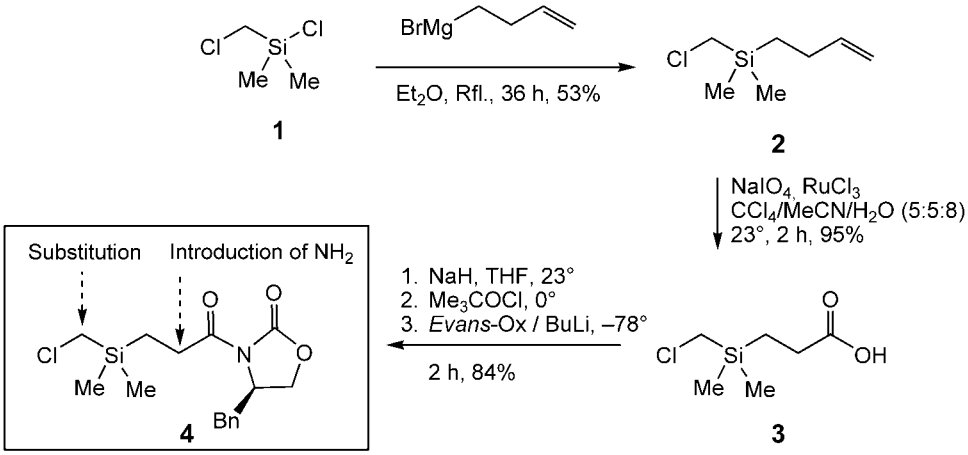
Results and Discussion. – According to the reaction sequence already described for the preparation of other sila amino acids [7], we prepared β-silylated *Evans* amide **4** to

[1]) Part of the Ph.D. thesis of *R. J. S.*, University of Zurich.

be converted to differently functionalized amino acids by appropriate substitution at the $ClCH_2$ group and stereoselective α-amination of the amide.

Chloro(chloromethyl)dimethylsilane (**1**) was thus treated with but-3-enyl magnesium bromide to afford (but-3-enyl)silane **2** in 53% yield (*Scheme 1*). This compound was converted in a single step, in 95% yield, to carboxylic acid **3** by reaction with $NaIO_4$ in the presence of $RuCl_3$ [14]. The alternative route through ozonolysis of **2** in MeOH/NaOH, followed by hydrolysis of the intermediary ester with aqueous LiOH [7], was less satisfactory: this reaction sequence yielded merely 27% of compound **3**. Synthesis of *Evans* amide **4** was completed in 84% yield by successive treatment of acid **3** with NaH (formation of the sodium carboxylate), 2,2-dimethylpropanoyl chloride (formation of a mixed anhydride), and the lithium salt of (*R*)-4-benzyloxazolidin-2-one (= *Evans*-Ox).

Scheme 1

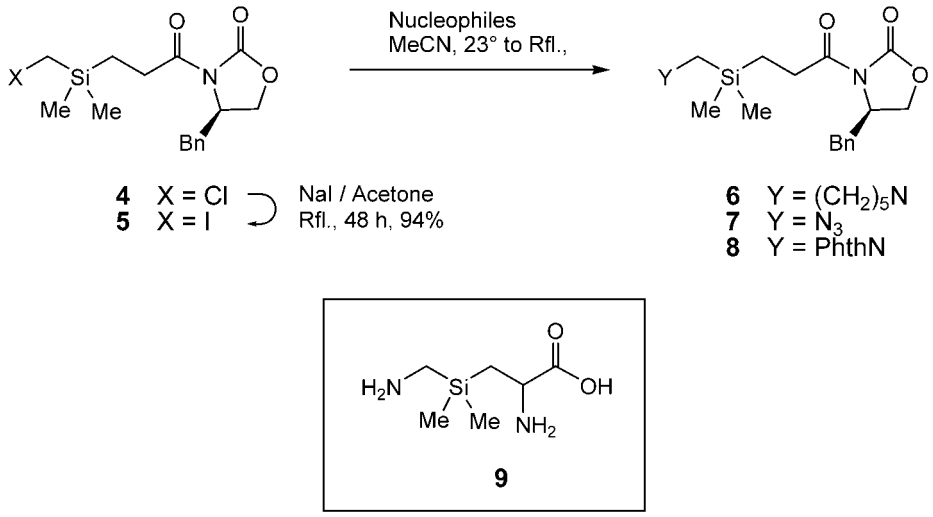


From compound **4**, two possible paths were open to form functionalized α-amino acids. The $ClCH_2$ group at the Si-atom could be manipulated in a first stage by replacement of the Cl-atom with an appropriate nucleophile before the required α-amino group would be introduced (path *A*; *cf. Scheme 2*) or *vice versa* (path *B*; *cf. Scheme 5*).

We first studied path *A* with the initial replacement of the Cl-atom in compound **4** with N-nucleophiles. Treatment of **4** with amines such as 3-phenylpropanamine, $PhCH_2NH_2$, Et_2NH, $(i\text{-}Pr)_2NH$, and piperidine, however, revealed immediately that the $ClCH_2$ group in **4** is not sufficiently reactive for the attempted transformations[2]) (*Scheme 2*). Even when the Cl-atom was exchanged by an I-atom, substitution at the halogenomethyl group was ineffective: ICH_2-substituted silane **5**, obtained by *Finkelstein* reaction from **4**, remained unchanged when treated with most of the amines mentioned above. Only when piperidine was used, the expected substitution

[2]) *Sieburth et al.* reported a successful transformation of (chloromethyl)(trimethyl)silane into (benzyl)-[(trimethylsilyl)methyl]amine in DMSO at 80° [15]. These reaction conditions led, in our case, to decomposition of the starting material **4**.

Scheme 2



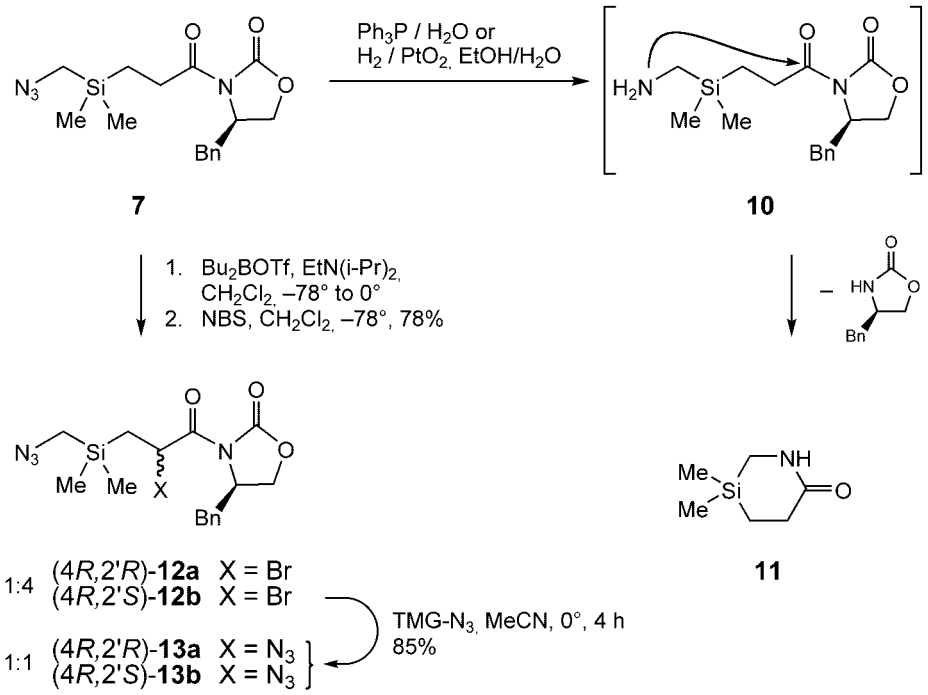
product **6** was formed in 73% yield. Successful were also the substitution reactions performed with the *N*,*N*,*N*′,*N*′-tetramethylguanidinium azide (TMG-N_3) and with potassium phthalimide (PhthNK; at 60° for 14 d). Reaction with these nucleophiles delivered azide **7** and phthalimide **8** in excellent 94 and 99% yields, respectively. Interestingly, while the azide anion reacted quite efficiently with **5**, the equally small cyanide ion was ineffective for substitution.

Unfortunately, neither of the two compounds **7** or **8** could be converted stereoselectively to the amino acid **9** possessing the NH_2CH_2 group at the Si-atom. Reduction of **7** with Ph_3P in the presence of H_2O or by catalytic hydrogenation led to the six-membered silalactam **11** in 99% yield – a compound that was not amenable to stereoselective amination – rather than to the desired amino compound **10** (*Scheme 3*). The lactam **11** was most probably formed *via* compound **10**, which cyclized with substitutive expulsion of the *Evans* auxiliary.

Without prior release of the protected amino groups, the two compounds **7** and **8** were also treated with dibutylboron triflate/EtN(i-Pr)$_2$, followed by *N*-bromosuccinimide (NBS) to effect stereoselective α-bromination of the *Evans* amides. While compound **7** led to the desired bromides **12a**/**12b** (78% yield, ratio 4 : 1; *Scheme 3*), the corresponding bromides **14a**/**14b** from **8** were not obtained (*Scheme 4*). Instead, propenoyl-oxazolidinone **15** was produced quantitatively. Apparently, the initially formed bromides **14a**/**14b** rapidly underwent elimination, possibly supported by the neighboring phthalimido groups as indicated in *Scheme 4*. We observed the same elimination with compound **16**, which possesses, like the phthalimides **14a**/**14b**, a carboxylic O-atom in position 5 with respect to the Si-atom, and which delivered **15** as the sole product upon bromination, too. We have, however, no further evidence for the proposed mechanism.

In an attempt to complete the enantioselective synthesis of amino acid **9**, the two isomers (4*R*,2′*R*)-**12a** and (4*R*,2′*S*)-**12b** were separated by chromatography, and the

Scheme 3

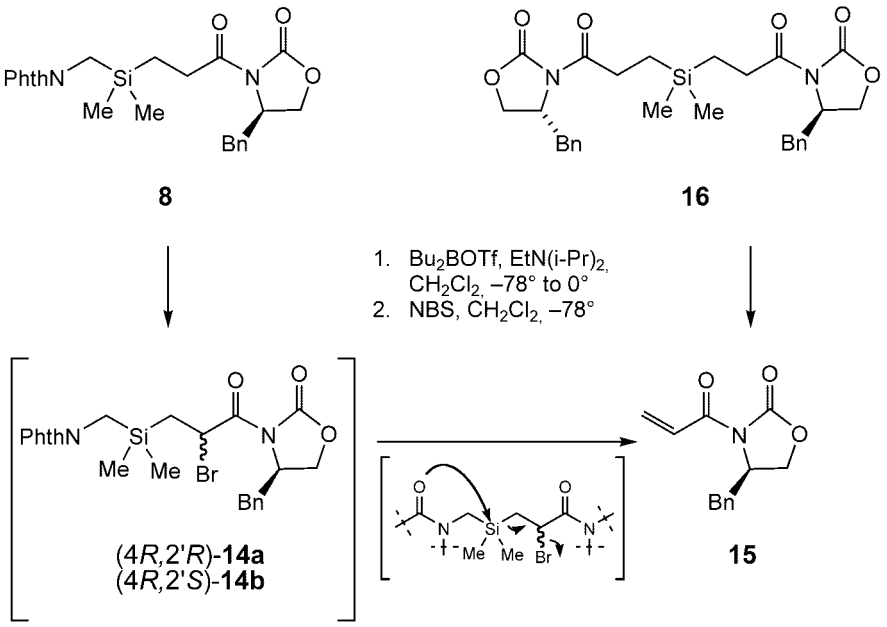


major diastereoisomer, (4*R*,2′*S*)-**12b**, was reacted with TMG-N_3 to replace the Br-atom. The substitution reaction proceeded smoothly (85% yield), however, not stereospecifically: the diastereoisomeric diazides **13a**/**13b**, which were not separable by chromatography, were formed in virtually equal amounts. The reason for this unspecific formation of the diazides **13a**/**13b** is not clear. Until now, a similar nonspecific reaction course has not been observed with analogous compounds, which possess groups other than N_3CH_2 attached to the Si-atom (see also below).

Since functionalized sila amino acids were not accessible in enantiomerically enriched form through path *A*, the alternative route *B*, in which the order of functionalization at the $ClCH_2$ group and at the α-position to the *Evans* amide were reversed, was tested.

Starting with compound **4**, we easily prepared bromo compounds **17a**/**17b** (80% yield, ration 4 : 1) by bromination of the *Evans* amide *via* its boron enolate as described above (*Scheme 5*). The two diastereoisomers (4*R*,2′*R*)-**17a** and (4*R*,2′*S*)-**17b**, were readily separated by chromatography, and the isomer (4*R*,2′*S*)-**17b**, the structure of which was established by a single-crystal X-ray-analysis (*cf. Fig.* in *Exper. Part*), was converted to the azide (4*R*,2′*R*)-**18a** (99% yield) by treatment with TMG-N_3. In contrast to the analogous reaction with (4*R*,2′*S*)-**12b**, no epimerization was observed this time. Subsequent *Finkelstein* reaction exchanged the Cl-atom of the $ClCH_2$ group by an I-atom to afford the iodinated compound (4*R*,2′*R*)-**19a** (96% yield). This compound was treated with a number of N-nucleophiles. Again, most of the

Scheme 4



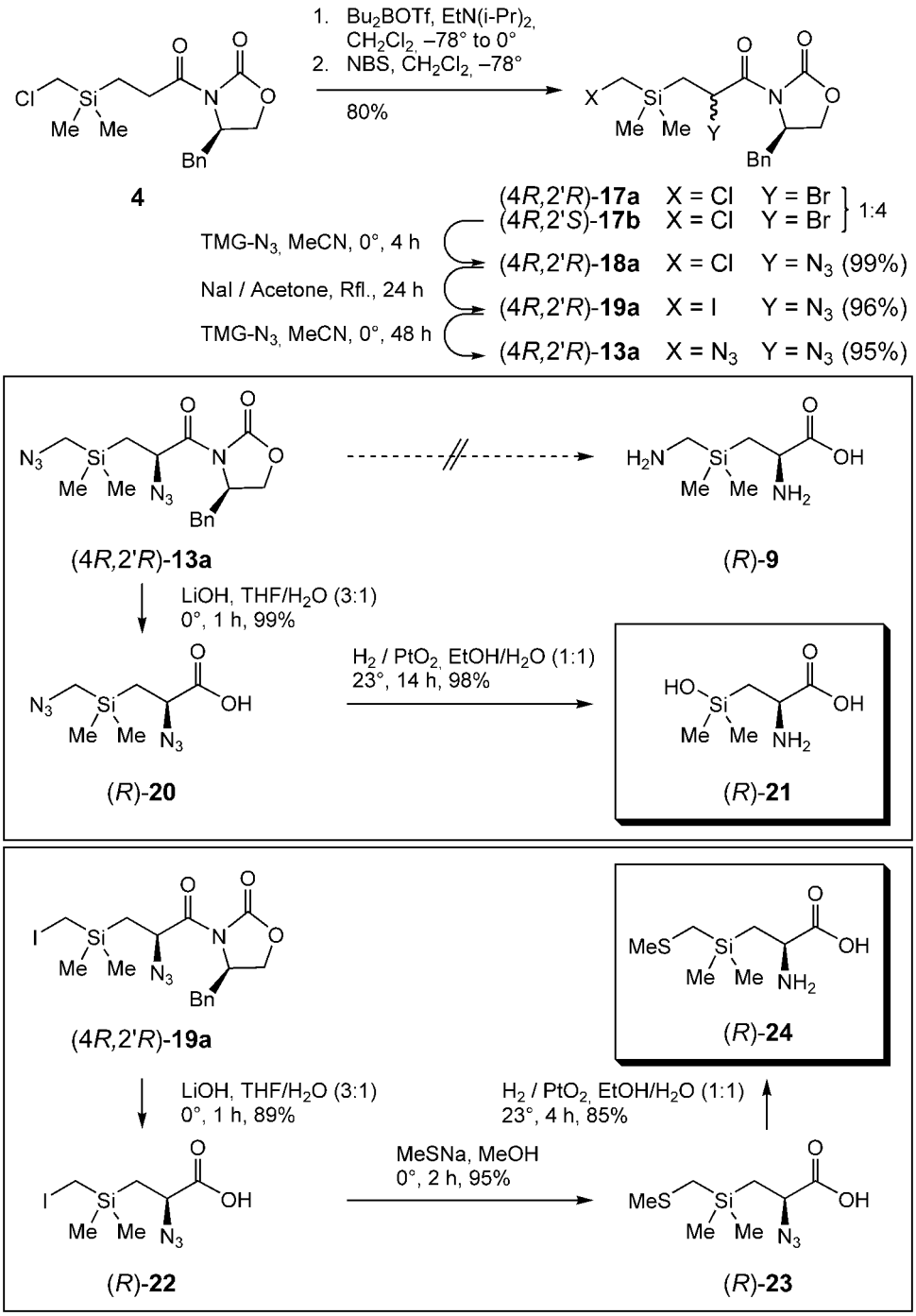
nucleophiles did not give the desired substitution products. Neither the cyanide and phthalimide anions nor 3-phenylpropanamine, $PhCH_2NH_2$, Et_2NH, $(i\text{-}Pr)_2NH$, or piperidine provided the desired substitution products. Either no reaction occurred or, under forcing conditions, (4*R*,2′*R*)-**19a** decomposed. Only the azide anion was able to introduce an N-functionality into the compound. Treatment of (4*R*,2′*R*)-**19a** with TMG-N_3 produced the diazide (4*R*,2′*R*)-**13a** in 95% yield.

With compound (4*R*,2′*R*)-**13a** at hand, the synthesis of the desired sila analog of ornithine, (*R*)-**9**, was planned to be completed by hydrolytic removal of the *Evans* auxiliary and reductive conversion of the two N_3 into NH_2 groups.

According to the procedure described in [7], hydrolysis of the *Evans* auxiliary with aqueous LiOH produced readily and in the excellent yield of 99% the carboxylic acid (*R*)-**20**. The subsequent catalytic hydrogenation of (*R*)-**20**, however, did not give the desired sila-ornithine (*R*)-**9**. To our astonishment, the homoserine analog (*R*)-**21** was formed instead. We have not been able to determine the enantiomeric purity of this compound yet, but the sample of (*R*)-**21** arose at least in optically active and, thus, enantiomerically enriched form ($[\alpha]_D^{20} = +7.8$ ($c = 1.90$, H_2O)). The mechanism for the conversion of the N_3CH_2 to the $HOSi(Me)_2$ group is not clear. It is possible that an intermediate hydrosilane is formed by hydrogenolysis, which would deliver the corresponding silanol in the presence of transition-metal catalysts and H_2O, as is well-known in the literature [16].

With compound (4*R*,2′*R*)-**19a** at hand, we were also able to synthesize the enantiomerically pure homomethionine analog (*R*)-**24** (*Scheme 5*). Hydrolytic removal of the *Evans* auxiliary from diastereoisomerically pure (2*R*)-**19a** by treatment with

Scheme 5


1. Bu2BOTf, EtN(i-Pr)2, CH2Cl2, –78° to 0°
2. NBS, CH2Cl2, –78°
80%
4
(4R,2'R)-17a X = Cl Y = Br
(4R,2'S)-17b X = Cl Y = Br
1:4
TMG-N3, MeCN, 0°, 4 h
(4R,2'R)-18a X = Cl Y = N3 (99%)
NaI / Acetone, Rfl., 24 h
(4R,2'R)-19a X = I Y = N3 (96%)
TMG-N3, MeCN, 0°, 48 h
(4R,2'R)-13a X = N3 Y = N3 (95%)
(4R,2'R)-13a
(R)-9
LiOH, THF/H2O (3:1)
0°, 1 h, 99%
H2 / PtO2, EtOH/H2O (1:1)
23°, 14 h, 98%
(R)-20
(R)-21
(4R,2'R)-19a
(R)-24
LiOH, THF/H2O (3:1)
0°, 1 h, 89%
H2 / PtO2, EtOH/H2O (1:1)
23°, 4 h, 85%
MeSNa, MeOH
0°, 2 h, 95%
(R)-22
(R)-23

aqueous LiOH in THF afforded acid (*R*)-**22** in 89% yield. The ICH_2 group remained unaffected during this basic hydrolysis. Reaction with MeSNa, on the other side, converted compound (*R*)-**22** efficiently (even at low temperatures) to methylsulfanyl derivative (*R*)-**23** (95% yield). The reduction of the N_3 group to obtain the desired amino acid (*R*)-**24** was performed by hydrogenation of (*R*)-**23** in aqueous EtOH in the presence of PtO_2 as catalyst (85% yield). The enantiomer purity (ee > 99%) of the amino acid (*R*)-**24** obtained was determined with its *N*-carbamoyl derivative by means of HPLC analysis on a chiral column by the method described in [7].

Conclusions. – We have shown with the preparation of the sila analogs of homoserine and homomethionine, (*R*)-**21** and (*R*)-**24**, respectively, that functionalized silicon-containing amino acids can be prepared divergently starting from chloro(chloromethyl)dimethylsilane (**1**). Two major problems arose: *1*) the substitution of the halogen atom at the halogenomethyl group attached to the Si-atom was inefficient, even when the Cl-atom was exchanged by an I-atom, and *2*) β-elimination occurred too readily with α-brominated, β-silylated carboxylic acid derivatives during our attempts to synthesize sila analogs of ornithine and glutamic acid, possibly due to neighboring-group participation.

Experimental Part

1. *General*. Unless otherwise stated, all chemicals were of reagent grade and purchased from *Fluka Chemie AG* or *Merck AG*. Chemical manipulations were carried out under Ar 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 sat. aq. NH_4Cl soln. and brine, and were dried ($MgSO_4$). Chromatography: *Merck* silica gel *60* (40–63 μm). Optical Rotation: *Perkin-Elmer Polarimeter 241*. M.p.: *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}. ^{1}H-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 95*, *Finnigan SSQ 700*, or *Finnigan TSQ 700*; electron impact (EI) at 70 eV; chemical ionization (CI) with NH_3 as the reactant gas; electrospray-ionization (ESI) with MeOH as the solvent; molecular ions, quasi-molecular ions, and characteristic fragments either with interpretation or ≥ 20 rel.%; in *m/z* (rel.%). Elemental Analysis: *Elementar Vario EL*.

2. *(But-3-enyl)(chloromethyl)dimethylsilane* (**2**). 4-Bromobut-1-ene (22.13 g, 163.9 mmol) in Et_2O (50 ml) was added dropwise at 23° to a suspension of Mg (3.94 g, 161.9 mmol) in Et_2O (250 ml). After the exothermic reaction ceased, it was stirred for another 3 h at 23°. *Chloro(chloromethyl)dimethylsilane* (**1**; 23.04 g, 161.0 mmol) in Et_2O (50 ml) was added dropwise, the mixture was warmed to reflux for 36 h, and the reaction was quenched with an excess of H_2O. Extraction with Et_2O and distillation (80°, 45 Torr) *via* a *Vigreux* column afforded **2** (13.98 g, 53%). Colorless liquid. IR: 3075*w*, 2995*w*, 2970*m*, 2960*m*, 2920*m*, 2840*w*, 1640*m*, 1445*w*, 1415*w*, 1395*m*, 1250*s*, 1175*w*, 995*m*, 910*s*, 900*s*, 845*s*, 835*s*, 810*s*, 790*s*, 650*m*, 605*s*. ^{1}H-NMR: 5.87 (*ddt*, *J* = 16.5, 10.1, 6.3, CH=); 5.01 (*ddd*, *J* = 17.0, 3.5, 1.7, 1 H, CH_2=); 4.92 (*ddd*, *J* = 10.1, 3.2, 1.4, 1 H, CH_2=); 2.79 (*s*, $ClCH_2$); 2.15–2.06 (*m*, CH_2CH=); 0.79–0.73 (*m*, CH_2Si); 0.12 (*s*, Me_2Si). ^{13}C-NMR: 143.0 (*d*, CH=); 115.2 (*t*, CH_2=); 32.3 (*t*, CH_2Cl); 29.6 (*t*, CH_2CH=); 14.8 (*t*, $SiCH_2$); −2.5 (*q*, Me_2Si). EI-MS: 113 (100, $[M - CH_2Cl]^+$), 107 (15, $[M - C_4H_7]^+$), 93 (14), 85 (48), 81 (26), 79 (71), 63 (18), 59 (77).

3. *3-[(Chloromethyl)(dimethyl)silyl]propanoic Acid* (**3**). A mixture of **2** (2.07 g, 12.77 mmol) and $NaIO_4$ (11.25 g, 52.6 mol) in CCl_4 (25 ml), MeCN (25 ml), and H_2O (39 ml) was stirred at 23° for 2 min. $RuCl_3 \cdot H_2O$ (70 mg, 0.30 mmol) was added, and the resultant biphasic mixture was stirred vigorously for 2 h at 23°. After the exothermic reaction ceased, CH_2Cl_2 (100 ml) was added, the phases were separated, and the aq. phase was extracted three times with CH_2Cl_2 (50 ml). Chromatography (Et_2O/hexan 1:2) afforded **3** (2.20 g, 95%). Yellowish liquid. IR: 3030*m*, 2955*s*, 2920*s*, 2895*m*, 2660*m*, 1710*s*, 1425*m*, 1410*m*, 1330*w*, 1295*m*, 1250*s*, 1180*m*,

1130*w*, 1105*w*, 1040*w*, 920*m*, 845*s*, 815*m*, 795*m*, 700*w*, 640*m*. ^{1}H-NMR: 2.80 (*s*, $ClCH_2$); 2.44–2.38 (*m*, CH_2CO); 1.03–0.97 (*m*, $SiCH_2$); 0.14 (*s*, Me_2Si). ^{13}C-NMR: 180.7 (*s*, CO); 29.8 (*t*, $ClCH_2$); 28.3 (*t*, CH_2CO); 8.6 (*t*, $SiCH_2$); −4.8 (*q*, Me_2Si). CI-MS: 163 (11), 162 (100 $[M-Cl+NH_4]^+$), 145 (5). Anal. calc. for $C_6H_{13}ClO_2Si$ (180.70): C 39.88, H 7.25; found: C 40.13, H 7.04.

4. *(*R*)-4-Benzyl-3-{3-[(chloromethyl)(dimethyl)silyl]propanoyl}-1,3-oxazolidin-2-one* (**4**). A dispersion of NaH (60% in oil, 1.28 g, 32.0 mmol) was added at 23° to a soln. of **3** (5.63 g, 31.13 mmol) in THF (200 ml), and the resulting suspension was cooled to 0°. Pivaloyl chloride (3.80 g, 31.50 mmol) was added, and the mixture was stirred for 2 h and then cooled to −78° (soln. *A*). In a separate flask, BuLi (1.6M in hexane, 19.9 ml, 31.80 mmol) was added slowly at −78° to a soln. of (*R*)-4-benzyloxazolidin-2-one (5.56 g, 31.40 mmol) in THF (80 ml), and the mixture was stirred for 30 min (soln. *B*). Soln. *B* was then transferred by syringe into soln. *A* at −78°. After stirring at −78° for 2 h and at 23° for 2 h, the reaction was quenched with H_2O, and the mixture was extracted with Et_2O and chromatographed (AcOEt/hexane 1:9) to give **4** (8.92 g, 84%). Colorless oil. $[\alpha]_D^{20} = -40.3$ (c = 1.49, $CHCl_3$). IR: 3060*w*, 3030*w*, 2955*m*, 2920*m*, 1780*s*, 1700*s*, 1605*w*, 1495*m*, 1480*m*, 1455*m*, 1385*s*, 1355*s*, 1290*m*, 1250*s*, 1210*s*, 1200*s*, 1180*m*, 1160*m*, 1100*s*, 1075*m*, 1050*m*, 1030*m*, 1015*m*, 975*m*, 920*w*, 845*s*, 815*m*, 785*m*, 760*m*, 750*m*, 740*m*, 705*s*, 635*m*. ^{1}H-NMR: 7.37–7.18 (*m*, 5 arom. H); 4.71–4.62 (sym. *m*, 8 lines, HCN); 4.24–4.13 (*m*, H_2CO); 3.31 (*dd*, J = 13.6, 3.3, 1 H, $PhCH_2$); 3.06–2.88 (*m*, $CH_2C{=}O$); 2.84 (*s*, CH_2Cl); 2.77 (*dd*, J = 13.4, 9.6, 1 H, $PhCH_2$); 1.07–0.99 (*m*, CH_2Si); 0.18 (*s*, Me_2Si). ^{13}C-NMR: 174.1 (*s*, CON); 153.4 (*s*, COO); 135.3 (*s*, arom. C); 129.4, 128.9 (2*d*, 4 arom. C); 127.3 (*d*, arom. C); 66.2 (*t*, CH_2O); 55.2 (*d*, HCN); 37.9 (*t*, $PhCH_2$); 30.1 (*t*, CH_2CO); 30.0 (*t*, $ClCH_2$); 8.2 (*t*, $SiCH_2$); −4.7 (*q*, Me_2Si). CI-MS: 360 (8), 359 (39), 358 (18), 357 (100, $[M+NH_4]^+$), 340 (11, $[M+H]^+$). Anal. calc. for $C_{16}H_{22}ClNO_3Si$ (339.89): C 56.54, H 6.52, N 4.12; found: C 56.84, H 6.67, N 3.97.

5. *(*R*)-4-Benzyl-3-{3-[(iodomethyl)(dimethyl)silyl]propanoyl}-1,3-oxazolidin-2-one* (**5**). A soln. of **4** (1.14 g, 3.34 mmol) in acetone (20 ml) was added to a suspension of NaI (0.53 g, 3.54 mmol) in acetone (80 ml), and the resulting mixture was stirred at 65° for 48 h. Evaporation of the solvent and chromatography (AcOEt/hexane 1:9) afforded **5** (1.40 g, 97%). Colorless oil. $[\alpha]_D^{20} = -29.4$ (c = 3.17, $CHCl_3$). IR: 3085*w*, 3060*w*, 3025*w*, 2955*m*, 2925*w*, 2900*w*, 2860*w*, 1780*s*, 1695*s*, 1605*w*, 1585*w*, 1495*w*, 1480*w*, 1455*m*, 1440*w*, 1385*s*, 1350*s*, 1330*m*, 1290*m*, 1250*s*, 1215*s*, 1195*s*, 1180*m*, 1160*m*, 1105*m*, 1075*m*, 1050*m*, 1030*w*, 1010*m*, 975*m*, 920*w*, 905*w*, 840*s*, 805*m*, 785*m*, 760*m*, 750*m*, 735*m*, 705*s*, 610*m*. ^{1}H-NMR: 7.37–7.18 (*m*, 5 arom. H); 4.71–4.62 (sym. *m*, 8 lines, HCN); 4.24–4.16 (*m*, CH_2O); 3.30 (*dd*, J = 13.3, 3.0, 1 H, $PhCH_2$); 2.99–2.91 (*AB* of *ABX*, $CH_2C{=}O$); 2.77 (*dd*, J = 13.4, 9.6, 1 H, $PhCH_2$); 2.06 (*s*, ICH_2); 1.09–1.01 (*m*, CH_2Si); 0.20 (*s*, Me_2Si). ^{13}C-NMR: 174.1 (*s*, CON); 153.4 (*s*, COO); 135.2 (*s*, arom. C); 129.4, 128.9 (2*d*, 4 arom. C); 127.3 (*d*, arom. C); 66.2 (*t*, CH_2O); 55.2 (*d*, HCN); 37.9 (*t*, $PhCH_2$); 30.1 (*t*, CH_2CO); 9.3 (*t*, $SiCH_2$); −3.2 (*q*, Me_2Si); −14.2 (*t*, ICH_2). CI-MS: 450 (24), 449 (100, $[M+NH_4]^+$), 432 (16, $[M+H]^+$), 382 (9), 381 (51), 359 (8), 357 (21), 324 (8), 323 (37), 301 (20), 300 (27), 284 (10), 267 (11), 210 (12), 195 (18), 73 (11). Anal. calc. for $C_{16}H_{22}INO_3Si$ (431.34): C 44.55, H 5.14, N 3.25; found: C 44.32, H 5.27, N 3.05.

6. *(*R*)-4-Benzyl-3-(3-{dimethyl[(piperidin-1-yl)methyl]silyl}propanoyl)-1,3-oxazolidin-2-one* (**6**). EtN(i-Pr)$_2$ (39 mg, 0.30 mmol) and piperidine (26 mg, 0.30 mmol) were added at 23° to a soln. of **5** (98 mg, 0.21 mmol) in MeCN (10 ml). The mixture was stirred for 66 h at 23°, concentrated *in vacuo*, and chromatographed (NH_3/EtOH/$CHCl_3$, 1:2:97) to afford **6** (51 mg, 73%). Pale-brownish oil. $[\alpha]_D^{20} = -30.4$ (c = 2.29, $CHCl_3$). IR: 3085*w*, 3060*w*, 3025*m*, 2930*s*, 2850*m*, 2775*m*, 2740*m*, 2700*m*, 2670*w*, 1765*s*, 1700*s*, 1605*w*, 1570*w*, 1495*w*, 1480*w*, 1455*m*, 1440*m*, 1385*s*, 1365*s*, 1325*m*, 1295*m*, 1250*s*, 1225*s* 1215*s*, 1200*m*, 1180*m*, 1160*m*, 1105*s*, 1075*w*, 1050*m*, 1040*m*, 1030*w*, 1015*w*, 995*w*, 975*w*, 915*w*, 860*m*, 840*s*, 780*m*, 760*m*, 750*m*, 735*m*, 705*s*. ^{1}H-NMR: 7.36–7.17 (*m*, 5 arom. H); 4.71–4.61 (sym. *m*, 8 lines, HCN); 4.23–4.12 (*m*, CH_2O); 3.29 (*dd*, J = 13.4, 3.3, 1 H, $PhCH_2$); 3.04–2.85 (*m*, $CH_2C{=}O$); 2.76 (*dd*, J = 13.4, 9.6, 1 H, $PhCH_2$); 2.40–2.30 (*m*, 2 NCH_2); 1.96 (*s*, NCH_2Si); 1.62–1.53 (*m*, $(CH_2CH_2)_2N$); 1.42–1.33 (*m*, $CH_2(CH_2CH_2)_2N$); 1.03–0.86 (*m*, $SiCH_2$); 0.11 (*s*, Me_2Si). ^{13}C-NMR: 174.7 (*s*, CON); 153.4 (*s*, COO); 135.3 (*s*, arom. C); 129.4, 128.9 (2*d*, 4 arom. C); 127.3 (*d*, arom. C); 66.1 (*t*, CH_2O); 58.4 (*t*, 2 NCH_2); 55.2 (*d*, CHN); 50.0 (*t*, NCH_2Si); 37.9 (*t*, $PhCH_2$); 30.3 (*t*, CH_2CO); 26.0 (*t*, 2 CH_2CH_2N); 23.6 (*t*, $CH_2(CH_2CH_2)_2N$); 10.0 (*t*, $SiCH_2$); −2.9 (*q*, Me_2Si). CI-MS: 391 (8), 390 (22), 389 (100, $[M+H]^+$), 338 (6), 290 (7, $[M-C_6H_{12}N]^+$); 258 (24). Anal. calc. for $C_{21}H_{32}N_2O_3Si$ (388.58): C 64.91, H 8.30, N 7.21; found: C 64.91, H 8.29, N 7.17.

7. *(*R*)-3-{3-[(Azidomethyl)(dimethyl)silyl]propanoyl}-4-benzyl-1,3-oxazolidin-2-one* (**7**). A soln. of *N*,*N*,*N*′,*N*′-tetramethylguanidinium azide (TMG-N_3; 0.52 g, 3.28 mmol) in MeCN (10 ml) was added at 23° to stirred soln. of **5** (0.35 g, 0.82 mmol) in MeCN (10.0 ml), and the mixture was stirred for 48 h at 23°. It was concentrated *in vacuo*, and the residue was dissolved in AcOEt. The mixture was washed with H_2O, dil. aq. $Na_2S_2O_3$ soln., and brine. Chromatography (AcOEt/hexane 1:9) afforded **7** (0.28 g, 94%). Pale-yellowish oil. $[\alpha]_D^{20} = -42.8$ (c = 1.68, $CHCl_3$). IR: 3085*w*, 3060*w*, 3030*w*, 2960*m*, 2920*m*, 2895*m*, 2180*m*, 2090*s*, 1780*s*, 1700*s*,

1605*w*, 1495*m*, 1480*m*, 1455*m*, 1440*m*, 1385*s*, 1350*s*, 1330*m*, 1290*s*, 1250*s*, 1215*s*, 1195*s*, 1180*s*, 1160*m*, 1100*s*, 1075*m*, 1050*m*, 1030*m*, 1010*m*, 975*m*, 910*m*, 850*s*, 795*m*, 760*s*, 750*m*, 735*s*, 705*s*. ^{1}H-NMR: 7.37–7.19 (*m*, 5 arom. H); 4.71–4.62 (sym. *m*, 8 lines, HCN); 4.26–4.13 (*m*, CH_2O); 3.30 (*dd*, *J* = 13.3, 3.3, 1 H, PhCH_2); 3.00–2.92 (*AB* of *ABX*, $CH_2C{=}O$); 2.86 (*s*, N_3CH_2); 2.77 (*dd*, *J* = 13.4, 9.6, 1 H, PhCH_2); 1.04–0.96 (*m*, $SiCH_2$); 0.16 (*s*, Me_2Si). ^{13}C-NMR: 174.0 (*s*, CON); 153.4 (*s*, COO); 135.2 (*s*, arom. C); 129.4, 128.9 (2*d*, 4 arom. C); 127.3 (*d*, arom. C); 66.2 (*t*, CH_2O); 55.2 (*d*, HCN); 41.0 (*t*, N_3CH_2); 37.9 (*t*, PhCH_2); 30.0 (*t*, CH_2CO); 8.5 (*t*, $SiCH_2$); −4.4 (*q*, Me_2Si). CI-MS: 292 (7), 291 (25), 290 (100, $[M-CH_2N_3]^+$), 239 (24), 211 (10), 167 (6), 108 (12). Anal. calc. for $C_{16}H_{22}N_4O_3Si$ (346.46): C 55.47, H 6.40, N 16.17; found: C 55.40, H 6.47, N 16.17.

8. *2-[({3-[(4*R*)-4-Benzyl-2-oxo-1,3-oxazolidin-3-yl]-3-oxopropyl}(dimethyl)silyl)methyl]-1*H*-isoindole-1,3(2*H*)-dione* (**8**). A soln. of potassium phthalimide (0.44 g, 2.37 mmol) in MeCN (20 ml) was added at 23° to a stirred soln. of **5** (0.68 g, 1.58 mmol) in MeCN (50.0 ml), and the mixture was stirred for 48 h at 23°. The mixture was warmed to 60° and stirred for an additional 14 d. The solvent was removed, and the residue was chromatographed (AcOEt/hexane 1:4) to give **8** (0.71 g, 99%). Colorless oil. $[\alpha]_D^{20} = -31.3$ (*c* = 1.77, $CHCl_3$). IR: 3085*w*, 3060*w*, 3030*w*, 2950*m*, 2910*m*, 2250*w*, 1780*s*, 1730*m*, 1710*s*, 1700*s*, 1610*w*, 1495*w*, 1480*w*, 1465*m*, 1455*m*, 1410*s*, 1385*s*, 1305*m*, 1285*m*, 1250*s*, 1225*s*, 1215*s*, 1195*m*, 1185*s*, 1155*m*, 1100*m*, 1060*s*, 1040*w*, 1010*m*, 970*m*, 910*m*, 885*s*, 845*s*, 810*m*, 790*m*, 760*m*, 730*s*, 720*s*, 700*s*. ^{1}H-NMR: 7.83–7.77 (*m*, 2 arom. H (Phth)); 7.70–7.64 (*m*, 2 arom. H (Phth)); 7.36–7.17 (*m*, 5 arom. H); 4.69–4.60 (sym. *m*, 10 lines, HCN); 4.23–4.13 (*m*, CH_2O); 3.28 (*dd*, *J* = 13.4, 3.3, 1 H, PhCH_2); 3.25 (*s*, PhthNCH_2); 3.03–2.97 (sym. *m*, 6 lines, $CH_2C{=}O$); 2.75 (*dd*, *J* = 13.3, 9.7, 1 H, PhCH_2); 1.07–0.96 (*m*, $SiCH_2$); 0.15, 0.14 (2*s*, Me_2Si). ^{13}C-NMR: 174.2 (*s*, CON); 168.5 (*s*, CO (Phth)); 153.4 (*s*, COO); 135.3 (*s*, arom. C); 133.6 (*d*, 2 arom. C (Phth)); 132.2 (*s*, 2 arom. C (Phth)); 129.4, 128.9 (2*d*, 4 arom. C); 127.3 (*d*, arom. C); 122.9 (*d*, 2 arom. C (Phth)); 66.1 (*t*, CH_2O); 55.2 (*d*, HCN); 37.8 (*t*, PhCH_2); 30.0 (*t*, CH_2CO); 27.8 (*t*, PhthNCH_2); 9.0 (*t*, $SiCH_2$); −3.68, −3.72 (2*q*, Me_2Si). CI-MS: 470 (10), 469 (35), 468 (100, $[M+NH_4]^+$), 451 (21), 449 (24), 323 (17), 291 (13), 290 (12, $[M-CH_2NPhth]^+$), 251 (11), 249 (8), 235 (15), 218 (11), 195 (37), 175 (61). Anal. calc. for $C_{24}H_{26}N_2O_5Si$ (450.56): C 63.98, H 5.82, N 6.22; found: C 63.87, H 5.87, N 6.13.

9. *3,3-Dimethyl-1-aza-3-silacyclohexan-6-one* (**11**). A soln. of **7** (0.27 g, 0.79 mmol) in THF (10 ml) was treated at 23° for 24 h with Ph_3P (0.21 g, 0.80 mmol) and H_2O (0.02 g, 1.1 mmol). The solvent was removed, and the residue was chromatographed (MeOH/CH_2Cl_2, 1:12) to afford **11** (0.11 g, 99%). Colorless crystals. M.p. 44.8–54.3° (CH_2Cl_2). IR: 3200*m*, 3060*w*, 2955*m*, 2930*m*, 2900*m*, 2860*m*, 1750*w*, 1660*s*, 1470*m*, 1435*m*, 1415*m*, 1385*m*, 1245*m*, 1225*m*, 1210*m*, 1190*w*, 1135*s*, 1120*m*, 1080*w*, 930*w*, 845*s*, 810*s*, 760*m*, 720*m*, 700*m*. ^{1}H-NMR: 6.87 (br. *s*, NH); 2.27 (*d*, *J* = 3.8, NCH_2Si); 2.10–2.02 (*m*, $COCH_2$); 0.55–0.48 (*m*, $SiCH_2$); −0.21 (*s*, Me_2Si). ^{13}C-NMR: 176.8 (*s*, CON); 30.5 (*t*, CH_2CO); 29.9 (*t*, CH_2N); 7.5 (*t*, $SiCH_2$); −3.6 (*q*, Me_2Si). CI-MS: 289 (9), 288 (24), 287 (100), 145 (8), 144.2 (60, $[M+H]^+$). Anal. calc. for $C_6H_{13}NOSi$ (143.26): C 50.30, H 9.15, N 9.78; found: C 50.21, H 9.33, N 9.65.

10. *(4*R*)-3-{(2*R*)-3-[(Azidomethyl)(dimethyl)silyl]-2-bromopropanoyl}-4-benzyl-1,3-oxazolidin-2-one and (4*R*)-3-{(2*S*)-3-[(Azidomethyl)(dimethyl)silyl]-2-bromopropanoyl}-4-benzyl-1,3-oxazolidin-2-one* ((4*R*,2′*R*)-**12a** and (4*R*,2′*S*)-**12b**, resp.). $EtN(i\text{-}Pr)_2$ (0.16 g, 1.24 mmol) and a soln. of dibutylboryl trifluoromethanesulfonate (Bu_2BOTf; 1M in CH_2Cl_2, 1.2 ml, 1.2 mmol) were added subsequently at −78° to a soln. of **7** (0.304 g, 0.88 mmol) in CH_2Cl_2 (4.0 ml). The mixture was allowed to warm to 0°, kept at this temp. for 4 h, and was recooled to −78°, before the mixture was transferred with a double-tipped needle (insulated to maintain the temp.) to a soln. of *N*-bromosuccinimide (NBS; 0.21 g, 1.17 mmol, freshly recrystallized from H_2O) in CH_2Cl_2 (10 ml) at −78°. After 1 h, sat. aq. $NaHCO_3$ soln. (3.2 ml) was added to the dark red soln., and the mixture was allowed to warm to 23°. Extraction with CH_2Cl_2 and chromatography (AcOEt/hexane, 5:95) afforded (4*R*,2′*R*)-**12a** (58 mg, 16%) and (4*R*,2′*S*)-**12b** (232 mg, 62%) as yellowish oils.

Data of (4*R*,2′*R*)-**12a**: $[\alpha]_D^{20} = -40.72$ (*c* = 1.01, $CHCl_3$). IR: 3085*w*, 3060*m*, 3030*m*, 3000*m*, 2960*m*, 2920*m*, 2180*m*, 2090*s*, 1780*s*, 1705*s*, 1605*w*, 1585*w*, 1495*m*, 1480*m*, 1455*m*, 1380*s*, 1350*s*, 1290*s*, 1260*s*, 1210*s*, 1200*s*, 1175*s*, 1105*s*, 1075*m*, 1045*m*, 1030*m*, 1015*m*, 1000*w*, 970*m*, 910*w*, 850*s*, 800*m*, 760*s*, 750*s*, 735*m*, 705*m*. ^{1}H-NMR: 7.39–7.21 (*m*, 5 arom. H); 5.95 (*dd*, *J* = 9.7, 6.2, BrHC); 4.71–4.62 (*m*, HCN); 4.28–4.16 (*m*, CH_2O); 3.41 (*dd*, *J* = 13.2, 3.4, 1 H, PhCH_2); 2.90 (*s*, N_3CH_2); 2.70 (*dd*, *J* = 13.2, 10.4, 1 H, PhCH_2); 1.95 (*dd*, *J* = 14.4, 9.7, 1 H, $SiCH_2$); 1.60 (*dd*, *J* = 14.4, 6.2, 1 H, $SiCH_2$); 0.21, 0.20 (2*s*, 2 MeSi). ^{13}C-NMR: 169.6 (*s*, CON); 152.5 (*s*, COO); 135.0 (*s*, arom. C); 129.4, 129.1 (2*d*, 4 arom. C); 127.5 (*d*, arom. C); 66.4 (*t*, CH_2O); 56.1 (*d*, HCN) 41.4 (*d*, BrCH); 41.2 (*t*, N_3CH_2); 37.9 (*t*, PhCH_2); 21.4 (*t*, $SiCH_2$); −3.6, −3.8 (2*q*, 2 MeSi). CI-MS: 444 (30, $[M+NH_4]^+$), 442 (28, $[M+NH_4]^+$), 371 (21), 370 (100, $[M-CH_2N_3]^+$), 369 (21), 368 (97, $[M-CH_2N_3]^+$), 291 (17), 290 (78), 279 (36), 250 (9), 249 (64), 195 (38).

*Data of (4*R*,2′*S*)-**12b**: $[\alpha]_D^{20} = -39.87$ (*c* = 1.63, $CHCl_3$). IR: 3085*w*, 3060*w*, 3030*w*, 3000*w*, 2960*m*, 2920*m*, 2870*w*, 1780*s*, 1705*s*, 1605*w*, 1585*w*, 1495*w*, 1480*w*, 1455*m*, 1445*w*, 1385*s*, 1350*m*, 1290*m*, 1260*s*, 1210*s*, 1200*s*,

1175*m*, 1105*m*, 1075*m*, 1045*m*, 1030*w*, 1015*m*, 1000*w*, 975*m*, 920*w*, 875*m*, 845*s*, 800*w*, 760*m*, 750*m*, 735*m*, 705*m*, 645*m*, 600*m*. ^{1}H-NMR: 7.38–7.16 (*m*, 5 arom. H); 5.96 (*dd*, *J* = 10.1, 5.8, BrHC); 4.79–4.64 (*m*, HCN); 4.27–4.18 (*m*, CH_2O); 3.32 (*dd*, *J* = 13.6, 3.7, 1 H, PhCH_2); 2.88 (*s*, N_3CH_2); 2.79 (*dd*, *J* = 13.7, 9.6, 1 H, PhCH_2); 1.95 (*dd*, *J* = 14.4, 10.1, 1 H, SiCH_2); 1.61 (*dd*, *J* = 14.4, 5.8, 1 H, $SiCH_2$); 0.18, 0.17 (2*s*, 2 MeSi). ^{13}C-NMR: 169.4 (*s*, CON); 152.4 (*s*, COO); 134.8 (*s*, arom. C); 129.4, 129.0 (2*d*, 4 arom. C); 127.4 (*d*, arom. C); 66.2 (*t*, CH_2O); 55.1 (*d*, HCN) 41.6 (*d*, BrCH); 41.1 (*t*, N_3CH_2); 37.0 (*t*, PhCH_2); 21.5 (*t*, $SiCH_2$); −3.7, −4.0 (2*q*, 2 MeSi). CI-MS: 444 (32, $[M+NH_4]^+$), 442 (29, $[M+NH_4]^+$), 371 (19), 370 (100, $[M-CH_2N_3]^+$), 369 (23), 368 (98, $[M-CH_2N_3]^+$), 291 (12), 290 (83), 279 (29), 250 (11), 249 (66), 195 (42). Anal. calc. for $C_{16}H_{21}BrN_4O_3Si$ (425.35): C 45.18, H 4.98, N 13.17; found: C 45.04, H 4.92, N 12.93.

11. *(4*R*)-3-{(2*R*)-2-Azido-3-[(azidomethyl)(dimethyl)silyl]propanoyl}-4-benzyl-1,3-oxazolidin-2-one and (4*R*)-3-{(2*S*)-2-Azido-3-[(azidomethyl)(dimethyl)silyl]propanoyl}-4-benzyl-1,3-oxazolidin-2-one* ((4*R*,2′*R*)-**13a** and (4*R*,2′*S*)-**13b**, resp.). A soln. of TMG-N_3 (0.66 g, 4.2 mmol) in MeCN (30 ml) was added at 0° to a stirred soln. of (4*R*,2′*S*)-**12b** (0.38 g, 0.89 mmol) in MeCN (20.0 ml). The mixture was stirred for 4 h at 0°, and sat. aq. $NaHCO_3$ soln. (2 ml) was added. The mixture was extracted with Et_2O and chromatographed (AcOEt/hexane, 1:4) to afford an inseparable mixture (4*R*,2′*R*)-**13a**/(4*R*,2′*S*)-**13b** (ratio 1:1, 0.29 g, 85%). Colorless oil.

*Data of (4*R*,2′*R*)-**13a**/(4*R*,2′*S*)-**13b***: IR: 3085*w*, 3060*w*, 3025*m*, 2960*w*, 2920*w*, 2180*w*, 2095*s*, 1780*s*, 1705*s*, 1605*w*, 1495*w*, 1480*w*, 1455*w*, 1385*s*, 1370*m*, 1350*m*, 1290*m*, 1245*s*, 1210*s*, 1195*m*, 1110*m*, 1070*w*, 1045*w*, 1030*w*, 1015*w*, 990*w*, 895*w*, 880*w*, 850*w*, 810*w*, 760*m*, 735*w*, 705*m*. ^{1}H-NMR: 7.38–7.28 (*m*, 6 arom. H); 7.24–7.19 (*m*, 4 arom. H); 4.98 (*dd*, *J* = 8.1, 6.9, N_3CH (**13a**)); 4.87 (*dd*, *J* = 10.9, 4.1, N_3CH (**13b**)); 4.77–4.64 (*m*, 2 HCN); 4.31–4.21 (*m*, 2 CH_2O); 3.38–3.26 (*m*, $PhCH_2$); 2.95, 2.93 (2*s*, 2 N_3CH_2); 2.84 (*dd*, *J* = 13.5, 9.4, 1 H, PhCH_2); 2.81 (*dd*, *J* = 13.4, 9.6, 1 H, PhCH_2); 1.30–1.24 (*m*, 2 $SiCH_2$); 0.26, 0.25 (2*s*, 2 Me_2Si). ^{13}C-NMR: 172.05, 171.95 (2*s*, 2 CON); 152.8 (*s*, 2 COO); 134.70, 134.65 (2*s*, 2 arom. C); 129.41, 129.38, 129.05, 129.02 (4*d*, 8 arom. C); 127.57, 127.53 (2*d*, 2 arom. C); 66.9, 66.6 (2*t*, 2 CH_2O); 57.16, 57.14 (2*d*, 2 N_3CH); 55.4, 55.1 (2*d*, 2 HCN) 41.0 (*t*, 2 N_3CH_2); 37.67, 37.64 (2*t*, 2 PhCH_2); 17.0, 16.9 (2*t*, 2 $SiCH_2$); −4.0, −4.3 (2*q*, 2 Me_2Si). ESI-MS 410 (100, $[M+Na]^+$), 397 (31), 331 (9).

12. *(*R*)-4-Benzyl-3-(prop-2-enoyl)-1,3-oxazolidin-2-one* (**15**). *From* **8** ($EtN(i\text{-}Pr)_2$ (0.29 g, 2.25 mmol) and a soln. of Bu_2BOTf (1M in CH_2Cl_2, 2.2 ml, 2.2 mmol) were added subsequently at −78° to a soln. of **8** (0.72 g, 1.60 mmol) in CH_2Cl_2 (20 ml). The mixture was allowed to warm to 0°, kept at this temp. for 4 h, and was re-cooled to −78°, before the mixture was transferred with a double-tipped needle (insulated to maintain the temp.) to a soln. of NBS (0.35 g, 1.95 mmol, freshly recrystallized from H_2O) in CH_2Cl_2 (20 ml) at −78°. After 1 h, sat. aq. $NaHCO_3$ soln. (3.2 ml) was added, and the mixture was allowed to warm to 23°. Extraction with CH_2Cl_2 and chromatography (AcOEt/hexane, 5:95) afforded **15** (0.34 g, 99%). Colorless crystals.

From **16**. The same reaction performed with *(4*R*,4′*R*)-3,3′-[(dimethylsilanediyl)bis(1-oxopropane-3,1-diyl)]bis(4-benzyl-1,3-oxazolidin-2-one)* (**16**; 1.13 g, 2.16 mmol [17]) delivered quantitatively **15**. Spectroscopic data of **15** are in agreement with those given in [18].

13. *(4*R*)-4-Benzyl-3-{(2*R*)-2-bromo-3-[(chloromethyl)(dimethyl)silyl]propanoyl}-1,3-oxazolidin-2-one and (4*R*)-4-Benzyl-3-{(2*S*)-2-bromo-3-[(chloromethyl)(dimethyl)silyl]propanoyl}-1,3-oxazolidin-2-one* ((4*R*,2′*R*)-**17a** and (4*R*,2′*S*)-**17b**, resp.). $EtN(i\text{-}Pr)_2$ (0.50 g, 3.83 mmol) and a soln. of Bu_2BOTf (1M in CH_2Cl_2, 3.8 ml, 3.80 mmol) were added subsequently at −78° to a soln. of **4** (0.93 g, 2.74 mmol) in CH_2Cl_2 (10 ml). The mixture was allowed to warm to 0°, kept at this temp. for 4 h, and was re-cooled to −78°, before the mixture was transferred with a double-tipped needle (insulated to maintain the temp.) to a soln. of NBS (0.65 g, 3.64 mmol, freshly recrystallized from H_2O) in CH_2Cl_2 (20 ml) at −78°. After 1 h, sat. aq. $NaHCO_3$ soln. (10 ml) was added to the reddish soln., and the mixture was allowed to warm to 23°. Extraction with CH_2Cl_2 and chromatography (AcOEt/hexane 5:95) afforded a mixture of (4*R*,2′*R*)-**17a** (0.18 g, 0.43 mmol, 16%) and (4*R*,2′*S*)-**17b** (0.74 g, 64%) as a colorless oil and as colorless crystals, respectively.

*Data of (4*R*,2′*R*)-**17a***: $[\alpha]_D^{20} = -36.73$ (*c* = 2.86, $CHCl_3$). IR: 3085*w*, 3060*w*, 3030*w*, 3000*w*, 2960*m*, 2920*m*, 2870*w*, 1780*s*, 1705*s*, 1605*w*, 1585*w*, 1495*m*, 1480*w*, 1455*m*, 1445*w*, 1385*s*, 1350*s*, 1290*m*, 1260*s*, 1210*s*, 1200*s*, 1175*m*, 1105*m*, 1075*m*, 1045*m*, 1030*m*, 1015*m*, 1000*w*, 970*m*, 920*w*, 875*m*, 845*s*, 800*w*, 760*m*, 750*m*, 735*m*, 705*m*, 645*m*, 625*m*, 600*m*. ^{1}H-NMR: 7.39–7.20 (*m*, 5 arom. H); 5.94 (*dd*, *J* = 9.6, 6.3, BrHC); 4.71–4.62 (*m*, HCN); 4.28–4.16 (*m*, CH_2O); 3.41 (*dd*, *J* = 13.3, 3.4, 1 H, PhCH_2); 2.83 (*AB* of *AB*, J_{AB} = 5.4, $ClCH_2$); 2.71 (*dd*, *J* = 13.3, 10.3, 1 H, PhCH_2); 1.98 (*dd*, *J* = 14.5, 9.6, 1 H, SiCH_2); 1.66 (*dd*, *J* = 14.5, 6.3, 1 H, SiCH_2); 0.23, 0.22 (2*s*, 2 MeSi). ^{13}C-NMR: 169.6 (*s*, CON); 152.5 (*s*, COO); 135.0 (*s*, arom. C); 129.4, 129.1 (2*d*, 4 arom. C); 127.5 (*d*, arom. C); 66.4 (*t*, CH_2O); 56.1 (*d*, HCN); 41.5 (*d*, BrHC); 37.9 (*t*, $PhCH_2$); 30.0 (*t*, $ClCH_2$); 21.3 (*t*, $SiCH_2$); −3.9, −4.1 (2*q*, 2 MeSi). CI-MS: 439 (30), 438 (24), 437 (100, $[M+NH_4]^+$), 436 (18), 435 (73, $[M+NH_4]^+$), 357 (9), 338 (6, $[M-Br]^+$), 249 (30), 195 (9), 164 (28), 147 (34), 115 (9). Anal. calc. for $C_{16}H_{21}BrClNO_3Si$ (418.79): C 45.89, H 5.05, N 3.34; found: C 46.11, H 4.93, N 3.33.

*Data of (4*R*,2′*S*)-***17b***: Crystals suitable for X-ray crystal-structure determination were obtained from hexane. M.p. 99.2–100.0° (hexane). $[\alpha]_D^{20} = -39.48$ ($c = 1.35$, $CHCl_3$). IR: 3085*w*, 3060*w*, 3030*w*, 3000*w*, 2960*m*, 2920*m*, 2870*w*, 1780*s*, 1705*s*, 1605*w*, 1585*w*, 1495*w*, 1480*w,* 1455*m*, 1445*w*, 1385*s*, 1350*m*, 1290*m*, 1260*s*, 1210*s*, 1200*s*, 1175*m*, 1105*m*, 1075*m*, 1045*m*, 1030*w*, 1015*m*, 1000*w*, 975*m*, 920*w*, 875*m*, 845*s*, 800*w*, 760*m*, 750*m*, 735*m*, 705*m*, 645*m*, 600*m*. ^{1}H-NMR: 7.37–7.22 (*m*, 5 arom. H); 5.90 (*dd*, $J = 9.8$, 6.1, BrHC); 4.76–4.67 (*m*, HCN); 4.27–4.18 (*m*, CH_2O); 3.32 (*dd*, $J = 13.5$, 3.4, 1 H, PhCH_2); 2.83 (*s*, $ClCH_2$); 2.79 (*dd*, $J = 13.5$, 9.6, 1 H, PhCH_2); 1.97 (*dd*, $J = 14.5$, 9.9, 1 H, SiCH_2); 1.67 (*dd*, $J = 14.4$, 6.0, 1 H, SiCH_2); 0.21, 0.20 (2*s*, 2 MeSi). ^{13}C-NMR: 169.5 (*s*, CON); 152.4 (*s*, COO); 134.8 (*s*, arom. C); 129.4, 129.0 (2*d*, 4 arom. C); 127.4 (*d*, arom. C); 66.2 (*t*, CH_2O); 55.2 (*d*, HCN); 41.6 (*d*, BrCH); 37.0 (*t*, PhCH_2); 30.1 (*t*, $ClCH_2$); 21.3 (*t*, $SiCH_2$); −3.9, −4.2 (2*q*, 2 MeSi). CI-MS: 440 (7), 439 (29), 438 (25), 437 (100, $[M + NH_4]^+$), 436 (19), 435 (73, $[M + NH_4]^+$), 359 (6), 357 (17), 338 (9, $[M - Br]^+$), 250 (9), 249 (55), 195 (12). Anal. calc. for $C_{16}H_{21}BrClNO_3Si$ (418.79): C 45.89, H 5.05, N 3.34; found: C 45.97, H 5.13, N 3.31. For X-ray crystal-structure determination, see *Sect. 23*.

14. *(4*R*)-3-{(2*R*)-2-Azido-3-[(chloromethyl)(dimethyl)silyl]propanoyl}-4-benzyl-1,3-oxazolidin-2-one* ((4*R*,2′*R*)-**18a**). A soln. of TMG-N_3 (4.49 g, 28.4 mmol) in MeCN (300 ml) was added dropwise at 0° to a soln. of (4*R*,2′*S*)-**17b** (3.21 g, 7.67 mmol) in MeCN (50.0 ml). After 4 h, the mixture was concentrated, and H_2O (50 ml) was added. The mixture was extracted with Et_2O and chromatographed (AcOEt/hexane 1:9) to afford (4*R*,2′*R*)-**18a** (2.89 g, 99%). Pale-yellowish oil. $[\alpha]_D^{20} = -19.5$ ($c = 2.35$, $CHCl_3$). IR: 3085*w*, 3060*w*, 3025*m*, 2960*m*, 2925*m*, 2855*w*, 2105*s*, 1780*s*, 1705*s*, 1605*w*, 1500*m*, 1480*m*, 1455*m*, 1390*s*, 1365*s*, 1350*s*, 1290*m*, 1245*s*, 1210*s*, 1195*s*, 1110*s*, 1075*m*, 1050*m*, 1020*m*, 995*m*, 895*s*, 880*s*, 845*s*, 810*m*, 760*s*, 735*s*, 705*s*, 665*m*, 630*m*. ^{1}H-NMR: 7.37–7.29 (*m*, 3 arom. H); 7.23–7.20 (*m*, 2 arom. H); 4.87 (*dd*, $J = 10.3$, 4.2, N_3CH); 4.77–4.68 (*m*, HCN); 4.32–4.22 (*m*, CH_2O); 3.29 (*dd*, $J = 13.4$, 3.1, 1 H, PhCH_2); 2.90 (*s*, $ClCH_2$); 2.82 (*dd*, $J = 13.7$, 9.5, 1 H, PhCH_2); 1.38–1.18 (*m*, $SiCH_2$); 0.29, 0.27 (2*s*, 2 MeSi). ^{13}C-NMR: 172.1 (*s*, CON); 152.8 (*s*, COO); 134.6 (*s*, arom. C); 129.4, 129.0 (2*d*, 4 arom. C); 127.5 (*d*, arom. C); 66.8 (*t*, CH_2O); 57.1 (*d*, N_3CH); 55.1 (*d*, HCN); 37.6 (*t*, PhCH_2); 30.0 (*t*, $ClCH_2$); 16.8 (*t*, $SiCH_2$); −4.4, −4.7 (2*q*, 2 MeSi). CI-MS: 401 (9), 400 (39), 399 (25), 398 (100, $[M + NH_4]^+$), 357 (6), 355 (11), 354 (6), 353 (28), 340 (6), 338 (13, $[M - N_3]^+$), 331 (10, $[M - CH_2Cl]^+$), 284 (7), 249 (7), 247 (5), 195 (11), 176 (9). Anal. calc. for $C_{16}H_{21}ClN_4O_3Si$ (380.90): C 50.45, H 5.56, N 14.71; found: C 50.35, H 5.57, N 14.68.

15. *(4*R*)-3-{(2*R*)-2-Azido-3-[(iodomethyl)(dimethyl)silyl]propanoyl}-4-benzyl-1,3-oxazolidin-2-one* ((4*R*,2′*R*)-**19a**). A soln. of (4*R*,2′*R*)-**18a** (1.77 g, 4.6 mmol) in acetone (50 ml) was added to a suspension of NaI (0.72 g, 4.8 mmol) in acetone (100 ml). The mixture was stirred for 2 h at 23° and for another 24 h at 64°. Evaporation of the solvent and chromatography (AcOEt/hexane 1:9) afforded (4*R*,2′*R*)-**19a** (2.07 g, 96%). Yellow oil. $[\alpha]_D^{20} = -15.1$ ($c = 2.11$, $CHCl_3$). IR: 3090*w*, 3060*w*, 3030*w*, 2960*m*, 2925*m*, 2860*w*, 2110*s*, 1785*s*, 1705*s*, 1605*w*, 1500*w*, 1480*w*, 1455*m*, 1390*s*, 1375*s*, 1350*m*, 1290*m*, 1245*s*, 1215*s*, 1195*s*, 1110*s*, 1075*m*, 1050*m*, 1030*m*, 1015*m*, 995*m*, 895*m*, 880*m*, 840*s*, 800*m*, 760*m*, 740*m*, 705*m*, 665*m*, 630*m*. ^{1}H-NMR: 7.38–7.28 (*m*, 3 arom. H); 7.23–7.19 (*m*, 2 arom. H); 4.85 (*dd*, $J = 9.9$, 5.1, N_3CH); 4.77–4.68 (*m*, HCN); 4.33–4.21 (*m*, CH_2O); 3.29 (*dd*, $J = 13.7$, 3.3, 1 H, PhCH_2); 2.82 (*dd*, $J = 13.4$, 9.5, 1 H, PhCH_2); 2.13 (*s*, ICH_2); 1.38–1.25 (*m*, $SiCH_2$); 0.31, 0.30 (2*s*, 2 MeSi). ^{13}C-NMR: 172.2 (*s*, CON); 152.8 (*s*, COO); 134.6 (*s*, arom. C); 129.4, 129.0 (2*d*, 4 arom. C); 127.6 (*d*, arom. C); 66.8 (*t*, CH_2O); 57.2 (*d*, N_3CH); 55.1 (*d*, HCN); 37.7 (*t*, PhCH_2); 17.9 (*t*, $SiCH_2$); −2.8, −2.9 (2*q*, 2 SiMe); −14.4 (*t*, ICH_2). CI-MS: 492 (6), 491 (24), 490 (100, $[M + NH_4]^+$), 445 (12), 400 (8), 398 (21), 331 (14, $[M - CH_2I]^+$), 319 (20), 317 (16), 302 (8), 290 (10), 249 (6), 247 (8), 195 (23). Anal. calc. for $C_{16}H_{21}IN_4O_3Si$ (472.35): C 40.68, H 4.48, N 11.86; found: C 40.83, H 4.55, N 11.90.

16. *(4*R*)-3-{(2*R*)-2-Azido-3-[(azidomethyl)(dimethyl)silyl]propanoyl}-4-benzyl-1,3-oxazolidin-2-one* ((4*R*,2′*R*)-**13a**). A soln. of TMG-N_3 (1.67 g, 10.6 mmol) in MeCN (20 ml) was added at 23° to a stirred soln. of (4*R*,2′*R*)-**19a** (1.25 g, 2.65 mmol) in MeCN (20.0 ml). The soln. was stirred for 48 h at 23°, sat. aq. $NaHCO_3$ soln. (2 ml) was added, and the mixture was extracted with Et_2O. The org. phase was concentrated *in vacuo*, and chromatography of the residue (AcOEt/hexane, 1:4) afforded (4*R*,2′*R*)-**13a** (0.97 g, 95%). Colorless oil. $[\alpha]_D^{20} = -15.7$ ($c = 2.95$, $CHCl_3$). IR: 3085*w*, 3060*w*, 3025*m*, 2960*w*, 2920*w*, 2180*w*, 2095*s*, 1780*s*, 1705*s*, 1605*w*, 1495*w*, 1480*w*, 1455*w*, 1385*s*, 1370*m*, 1350*m*, 1290*m*, 1245*s*, 1210*s*, 1195*m*, 1110*m*, 1070*w*, 1045*w*, 1030*w*, 1015*w*, 990*w*, 895*w*, 880*w*, 850*w*, 810*w*, 760*m*, 735*w*, 705*m*. ^{1}H-NMR: 7.38–7.27 (*m*, 3 arom. H); 7.24–7.19 (*m*, 2 arom. H); 4.86 (*dd*, $J = 10.9$, 4.1, N_3CH); 4.77–4.64 (*m*, HCN); 4.32–4.21 (*m*, CH_2O); 3.29 (*dd*, $J = 13.4$, 3.3, 1 H, PhCH_2); 2.94 (*s*, N_3CH_2); 2.81 (*dd*, $J = 13.4$, 9.6, 1 H, PhCH_2); 1.34–1.24 (*m*, 2 $SiCH_2$); 0.26 (*s*, Me_2Si). ^{13}C-NMR: 172.0 (*s*, CON); 152.8 (*s*, COO); 134.6 (*s*, arom. C); 129.4, 129.0 (2*d*, 4 arom. C); 127.5 (*d*, 1 arom. C); 66.8 (*t*, CH_2O); 57.1 (*d*, N_3CH); 55.1 (*d*, HCN); 41.0 (*t*, N_3CH_2); 37.6 (*t*, PhCH_2); 17.0 (*t*, $SiCH_2$); −4.1, −4.3 (2*q*, Me_2Si). ESI-MS: 410 (100, $[M + Na]^+$), 397 (31), 331 (9). Anal. calc. for $C_{16}H_{21}N_7O_3Si$ (387.47): C 49.60, H 5.46, N 25.30; found: C 49.40, H 5.51, N 25.20.

17. *(*R*)-2-Azido-3-[(azidomethyl)(dimethyl)silyl]propanoic Acid* ((*R*)-**20**). A mixture of (4*R*,2′*R*)-**13a** (890 mg, 2.29 mmol) and LiOH · H_2O (0.20 g, 4.75 mmol) in THF/H_2O (48 ml, 3:1) was stirred at 0° for 1 h. Sat. aq. $NaHCO_3$ soln. (10 ml) was added, and the THF was evaporated. Extraction of the aq. residue with CH_2Cl_2 to remove the auxiliary, acidification with aq. HCl soln. (1M) to pH 2, extraction with AcOEt, and filtration through a plug of SiO_2 afforded (*R*)-**20** (518 mg, 99%). Colorless oil. $[\alpha]_D^{20} = -22.2$ ($c = 2.09$, $CHCl_3$). IR: 2960*s*, 2900*s*, 2640*m*, 2180*s*, 2100*s*, 1720*s*, 1410*s*, 1335*m*, 1290*s*, 1255*s*, 1230*s*, 1200*s*, 1150*m*, 1060*m*, 1040*m*, 945*m*, 890*s*, 850*s*, 810*s*, 705*m*. ^{1}H-NMR: 10.90 (br. *s*, COOH); 3.97 (*X* of *ABX*, $J_{AX} = 6.3$, $J_{BX} = 9.1$, N_3CH); 2.91 (*s*, N_3CH_2); 1.32, 1.25 (*AB* of *ABX*, $J_{AB} = 14.9$, $J_{AX} = 6.3$, $J_{BX} = 9.1$, $SiCH_2$); 0.21 (*s*, Me_2Si). ^{13}C-NMR: 177.2 (*s*, COOH); 58.8 (*d*, N_3CH); 41.1 (*t*, N_3CH_2); 17.0 (*t*, $SiCH_2$); −4.0, −4.1 (*q*, Me_2Si). CI-MS: 190 (11), 189 (93, $[M + NH_4 - CH_2N_3 - H]^+$), 149 (11), 148 (100, $[M + NH_4 - CH_2N_3 - N_3]^+$), 144 (11), 131 (11), 92 (10), 91 (8). Anal. calc. for $C_6H_{12}N_6O_2Si$ (228.28): C 31.57, H 5.30, N 36.81; found: C 31.43, H 5.47, N 36.73.

18. *(*R*)-2-Amino-3-[hydroxy(dimethyl)silyl]propanoic Acid* ((*R*)-**21**). A soln. of (*R*)-**20** (0.46 g, 2.01 mmol) in EtOH/H_2O (30 ml, 1:1) was treated at 23° for 14 h with $PtO_2 \cdot H_2O$ (0.079 g, 0.32 mmol) under H_2 (1 atm). The catalyst was removed by filtration through a plug of cotton, and evaporation of the solvent afforded pure (*R*)-**21** (0.323 g, 98%). Colorless solid. $[\alpha]_D^{20} = +7.8$ ($c = 1.90$, H_2O). M.p. 194.0° (start of dec.). IR: 3420*m*, 3040*s*, 1605*s*, 1585*s*, 1510*s*, 1420*s*, 1390*s*, 1345*m*, 1310*m*, 1255*s*, 1185*w*, 1135*m*, 1040*s*, 845*s*, 825*s*, 795*s*, 720*w*. ^{1}H-NMR (D_2O): 3.80 (*X* von *ABX*, $J_{AX} = 6.0$, $J_{BX} = 9.5$, NCH); 1.22, 1.13 (*AB* von *ABX*, $J_{AB} = 14.7$, $J_{AX} = 6.0$, $J_{BX} = 9.5$, $SiCH_2$); 0.19, 0.18 (2*s*, 2 MeSi). ^{13}C-NMR (D_2O): 174.7 (*s*, COOH); 51.7 (*d*, NCH); 19.2 (*t*, $SiCH_2$); −1.7, −2.2 (2*q*, 2 MeSi). ESI-MS: 331 (18), 309 (25 $[2M + H - H_2O]^+$, Siloxan), 186 (21), 164 (96 $[M + H]^+$), 146 (28 $[M + H - H_2O]^+$), 129 (100 $[M + H - H_2O - NH_3]^+$), 92 (12), 75 (28).

19. *(*R*)-2-Azido-3-[(iodomethyl)(dimethyl)silyl]propanoic Acid* ((*R*)-**22**). A mixture of (4*R*,2′*R*)-**19a** (0.90 g, 1.90 mmol) and LiOH · H_2O (0.24 g, 5.72 mmol) in THF/H_2O (32 ml, 3:1) was stirred for 1 h at 0°. Sat. aq. $NaHCO_3$ soln. (10 ml) was added, and the THF was evaporated. Extraction of the aq. residue with CH_2Cl_2 to remove the auxiliary, acidification with aq. HCl soln. (1M) to pH 2, extraction with AcOEt, and filtration through a plug of SiO_2 afforded (*R*)-**22** (0.53 g, 89%). Yellow oil. $[\alpha]_D^{20} = -12.3$ ($c = 2.14$, $CHCl_3$). IR: 2965*m*, 2950*m*, 2910*m*, 2630*w*, 2120*s*, 1730*s*, 1420*m*, 1405*m*, 1400*m*, 1380*m*, 1300*m*, 1260*s*, 1235*s*, 1210*m*, 1090*w*, 1030*w*, 950*m*, 890*m*, 845*s*, 815*s*, 735*w*, 710*m*. ^{1}H-NMR: 10.46 (*s*, COOH); 3.99–3.87 (*m*, N_3CH); 2.07 (*s*, ICH_2); 1.44–1.30 (*m*, $SiCH_2$); 0.25 (*s*, Me_2Si). ^{13}C-NMR: 177.4 (*s*, COOH); 58.8 (*d*, N_3CH); 17.8 (*t*, $SiCH_2$); −2.8 (*q*, Me_2Si); −14.7 (*t*, ICH_2). CI-MS: 216 (6), 204 (14), 203 (100, $[M - I + NH_3]^+$), 195 (21), 189 (30), 162 (8), 158 (14), 148 (32), 131 (9). Anal. calc. for $C_6H_{12}IN_3O_2Si$ (313.17): C 23.01, H 3.86, N 13.42; found: C 23.22, H 3.92, N 13.32.

20. *(*R*)-2-Azido-3-{dimethyl[(methylsulfanyl)methyl]silyl}propanoic Acid* ((R)-**23**). NaSMe (0.30 g, 4.28 mmol) was added at 0° to a soln. of (*R*)-**22** (0.58 g, 1.85 mmol) in MeOH (10 ml), and the mixture was stirred for 2 h. The solvent was evaporated, and the residue was dissolved in H_2O, acidified with aq. HCl soln. (1M) to pH 2, and extracted with AcOEt. Chromatography (MeOH/CH_2Cl_2 1:20) afforded (*R*)-**23** (0.41 g, 95%). Pale-yellowish oil. $[\alpha]_D^{20} = -19.4$ ($c = 3.44$, $CHCl_3$). IR: 2970*s*, 2925*s*, 2900*s*, 2120*s*, 1720*s*, 1430*s*, 1420*s*, 1320*m*, 1255*s*, 1235*s*, 1205*s*, 1150*m*, 1070*w*, 1050*w*, 965*m*, 890*s*, 845*s*, 810*s*, 800*m*, 700*m*. ^{1}H-NMR: 9.78 (*s*, COOH); 3.95 (*X* of *ABX*, $J_{AX} = 6.3$, $J_{BX} = 9.5$, HCN_3); 2.16 (*s*, MeS); 1.87 (*s*, CH_2S); 1.32, 1.25 (*AB* of *ABX*, $J_{AB} = 14.8$, $J_{AX} = 6.3$, $J_{BX} = 9.5$, $SiCH_2$); 0.19 (*s*, Me_2Si). ^{13}C-NMR: 177.4 (*s*, COOH); 59.9 (*d*, N_3CH); 20.3 (*q*, MeS); 20.0 (*t*, CH_2S); 17.7 (*t*, $SiCH_2$); −3.0, −3.1 (2*q*, Me_2Si). CI-MS: 251 (30, $[M + H + NH_3]^+$), 235 (7), 234 (47, $[M + H]^+$), 208 (8), 206 (15), 203 (11), 193 (11), 191 (23), 190 (12), 189 (100), 177 (9), 164 (6), 163 (8), 162 (63), 157 (7), 146 (9), 144 (5), 136 (37), 117 (6), 116 (8). Anal. calc. for $C_7H_{15}N_3O_2SSi$ (233.36): C 23.01, H 3.86, N 13.42; found: C 23.22, H 3.92, N 13.32.

21. *(*R*)-2-Amino-3-{dimethyl[(methylsulfanyl)methyl]silyl}propanoic Acid* ((*R*)-**24**). A soln. of (*R*)-**23** (0.07 g, 0.32 mmol) in EtOH/H_2O (20 ml, 1:1) was treated with $PtO_2 \cdot H_2O$ (0.05 g, 0.22 mmol) and H_2 (1 atm) for 5 h. The catalyst was removed by filtration through a plug of cotton, and evaporation of the solvent afforded pure (*R*)-**24** (0.06 g, 85%). Colorless solid. $[\alpha]_D^{20} = +9.9$ ($c = 1.55$, H_2O). M.p. 186° (start of dec.). IR: 3440*m*, 3060*m*, 2960*m*, 2920*m*, 1630*s*, 1610*s*, 1530*m*, 1515*s*, 1430*s*, 1395*s*, 1355*m*, 1325*m*, 1260*s*, 1190*w*, 1140*w*, 1065*s*, 970*w*, 850*s*, 830*s*, 795*s*, 700*w*. ^{1}H-NMR (DMSO/DCl): 3.80 (*X* of *ABX*, $J_{AX} = 4.6$, $J_{BX} = 11.6$, HCN); 2.07 (*s*, MeS); 1.82 (*s*, CH_2S); 1.20, 1.11 (*AB* of *ABX*, $J_{AB} = 14.4$, $J_{AX} = 4.6$, $J_{BX} = 11.6$, CH_2Si); 0.11, 0.09 (2*s*, Me_2Si). ^{13}C-NMR (DMSO/DCl): 171.3 (*s*, COOH); 50.0 (*d*, NCH); 19.6 (*q*, MeS); 19.4 (*t*, CH_2S); 17.3 (*t*, $SiCH_2$); −2.7, −3.0 (2*q*, Me_2Si). ESI-MS: 236 (12), 230 (24 $[M + Na]^+$), 209 (8), 208 (50 $[M + H]^+$), 191 (25), 151 (24), 147 (14), 137 (100), 119 (19).

22. *Determination of the Enantiomeric Purity of (*R*)-**24**.* A mixture of (*R*)-**24** (70 mg, 0.36 mmol) and KOCN (0.03 g, 0.38 mmol) in H_2O (5 ml) was stirred for 3 h at 70°. The mixture was cooled to 10°, and AcOH (2 ml) was added. The precipitated product was collected by filtration and dried at 10^{-2} Torr to yield (*R*)-2-[(aminocarbonyl)amino]-3-{dimethyl[(methylsulfanyl)methyl]silyl}propanoic acid (60 mg, 0.23 mmol, 63%) as

a colorless solid. $[\alpha]_D^{20} = +4.0$ ($c = 1.21$, MeOH). M.p. 133.6–143.4°. IR: 3400*s*, 3260*m*, 2935*s*, 2360*w*, 2480*w*, 1690*s*, 1630*s*, 1560*s*, 1540*s*, 1470*m*, 1420*m*, 1310*m*, 1220*m*, 1185*m*, 1135*m*, 1025*s*, 910*w*, 860*m*, 820*m*, 750*w*, 725*w*, 710*w*, 695*w*. ^{1}H-NMR (MeOH): 4.12 (*dd*, $J = 9.4$, 5.6, HCN); 2.07 (*s*, MeS); 1.80 (*s*, CH_2S); 1.25–0.94 (*m*, $SiCH_2$); 0.082, 0.078 (2*s*, Me_2Si). ^{13}C-NMR (MeOH): 176.0 (*s*, COOH); 158.1 (*s*, CON); 52.8 (*d*, NCH); 21.3 (*t*, CH_2S); 20.9 (*t*, $SiCH_2$); 20.4 (*q*, MeS); −2.6, −2.7 (2*q*, Me_2Si). CI-MS: 268 (27, $[M + NH_4]^+$), 251 (100, $[M + H]^+$), 233 (11, $[M + H - H_2O]^+$), 208 (83, $[M + H - CONH]^+$). The enantiomeric purity of this material was established as >99% by chiral RP-HPLC with *ET 200/4 Nucleodex β-PM* (5 μm, 200 × 4 mm, *Macherey-Nagel*, CH-Oensingen), mobile phase: 3 g of H_3PO_4 (85%), 842 ml of H_2O, 400 ml of MeOH, flow: 0.6 ml min^{-1}; t_R ((*R*)-isomer) 12.4 min, t_R ((*S*)-isomer) 10.4 min; UV detection at 215 nm.

23. *X-Ray Crystal-Structure Determination for Compound (4*R,*2′*R*)*-**17b**[3]). The data collection and refinement parameters are summarized in the *Table*, and a view of the molecule is shown in *Figure*. All measurements were performed on a *Nonius KappaCCD* diffractometer [19] with graphite-monochromated

Table. *Crystallographic Data of Compound (4*R,*2′*S*)*-**17b**

Crystallized from	hexane
Empirical formula	$C_{16}H_{21}BrClNO_3Si$
Formula weight [g mol^{-1}]	418.78
Crystal color, habit	colorless, prism
Crystal dimensions [mm]	0.20 × 0.25 × 0.25
Crystal temp. [K]	160 (1)
Radiation, wavelength [Å]	MoK_α, 0.71073
Crystal system	orthorhombic
Space group	$P2_12_12_1$ (#19)
Z	4
Reflections for cell determination	25249
2θ Range for cell determination [°]	4–50
Unit-cell parameters a [Å]	8.5646 (1)
b [Å]	10.3502 (1)
c [Å]	21.1820 (2)
α [°]	90
β [°]	90
γ [°]	90
V [Å^3]	1877.69 (3)
D_x [g cm^{-3}]	1.481
μ [mm^{-1}]	2.414
Absorbtion corrections (min; max)	0.547; 0.673
$2\theta_{(max)}$ [°]	50
Total reflections measured	35012
Symmetry-independent reflections	3298
Reflections used [$I > 2\theta(I)$]	3162
Parameters refined	219
Reflection/parameter ratio	14.4
R	0.0286
wR	0.0303
Weights: p in $w = [\sigma^2(F_o) + (pF_o)^2]^{-1}$	0.005
Goodness-of-fit s	2.484
Secondary extinction coefficient	1.46 (8) × 10^{-6}
Final Δ_{max}/σ	0.0009
$\Delta\rho$(max; min) [e Å^{-3}]	0.28; −0.26

[3]) Crystallographic data (excluding structure factors) for **17b** has been deposited with the *Cambridge Crystallographic Data Center* as supplementary publication No. CCDC-189270. Copies of the data can be obtained free of charge on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44-(0)-1223-336033; email: deposit@ccdc.cam.ac.uk).

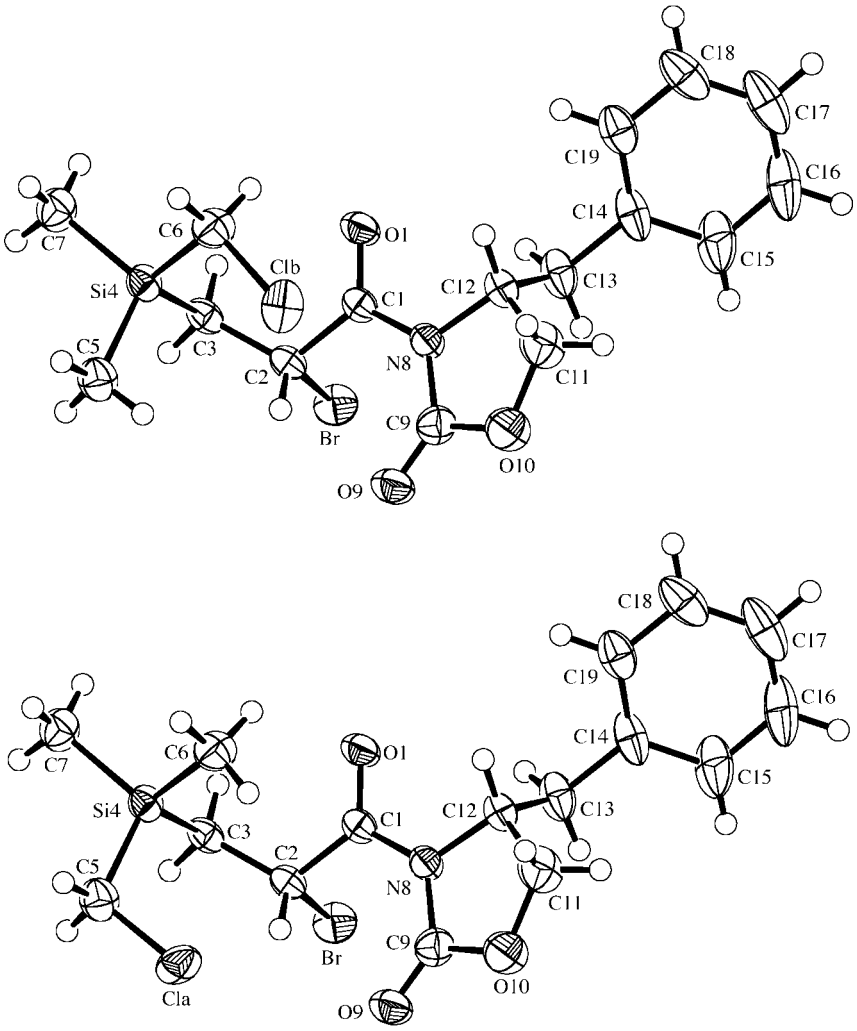


Figure. *ORTEP Plots* [30] *of the two disordered conformations of the structure (4*R,*2′*S*)*-**17b** (50% probability ellipsoids; H-atoms given arbitrary displacement parameters for clarity)

MoK_α radiation (λ 0.71073 Å) and an *Oxford Cryosystems Cryostream 700* cooler. The unit-cell constants and an orientation matrix for data collection were obtained from a least-squares refinement of the setting angles of 25249 reflections in the range $4° < 2\theta < 50°$. The mosaicity was 0.453 (1)°. A total of 356 frames were collected by using ω scans with $\varkappa$ offsets, 18-s exposure time, and a rotation angle of 1.8° per frame, and a crystal-detector distance of 33.0 mm.

Data reduction was performed with *HKL Denzo* and *Scalepack* [20]. The intensities were corrected for *Lorentz* and polarization effects, and a numerical absorption correction [21] was applied. Standard reflection intensities were not monitored. The space group was uniquely determined by the systematic absences. Equivalent reflections, other than *Friedel* pairs, were merged.

The structure was solved by direct methods using *SIR92* [22], which revealed the positions of all non-H-atoms. The $ClCH_2$ group and one of the other Me substituents on the Si-atom group are disordered over two

conformations such that these groups appear to have switched positions in the alternate conformation. The major conformation occurs in 56% of the molecules. The non-H-atoms were refined anisotropically. All of the H-atoms were fixed in geometrically calculated positions (d(C–H) = 0.95 Å), and each was assigned a fixed isotropic displacement parameter with a value equal to 1.2 U_{eq} of its parent atom. Refinement of the structure was carried out on F using full-matrix least-squares procedures, which minimized the function $\Sigma w(|F_o| - |F_c|)^2$. The weighting scheme was based on counting statistics and included a factor to downweight the intense reflections. Plots of $\Sigma w(|F_o| - |F_c|)^2$ *vs.* $|F_o|$, reflection order in data collection, $\sin\theta/\lambda$, and various classes of indices showed no unusual trends. A correction for secondary extinction was applied. The refinement of the absolute structure parameter [23] yielded a value of $-0.007(5)$, which confidently confirms that the refined coordinates.

Neutral-atom scattering factors for non-H-atoms were taken from [24], and the scattering factors for H-atoms were taken from [25]. Anomalous dispersion effects were included in F_c [26]; the values for f' and f'' were those of [27]. The values of the mass attenuation coefficients are those of [28]. All calculations were performed using the *teXsan* crystallographic software package [29].

We thank *A. Guggisberg* for helpful discussions and the analytical laboratories of our institute for spectra and analyses, especially Dr. *G. Hopp-Rentsch*, *N. Walch*, and *S. Jurt* for NMR spectra, *N. Bild* and *M. Tzouros* for mass spectra, *A. Deambrosi* for elemental analyses, and Dr. *A. Linden* for the X-ray crystal-structure analysis. Financial support from the *Swiss National Science Foundation* and *the Novartis Stipendienfonds* are also gratefully acknowledged.

REFERENCES

[1] G. C. Barrett, 'Chemistry and Biochemistry of the Amino Acids', Chapman and Hall, London, 1985; R. M. Williams, 'Synthesis of Optically Active α-Amino Acids', Pergamon, New York, 1989; I. Wagner, H. Musso, *Angew. Chem., Int. Ed.* **1983**, *22*, 816; Y. Ohfune, *Acc. Chem. Res.* **1992**, *25*, 360; R. O. Duthaler, *Tetrahedron* **1994**, *50*, 1539; J. M. Padrón, G. Kokotos, T. Martín, T. Markidis, W. A. Gibbons, V. S. Martín, *Tetrahedron: Asymmetry* **1998**, *9*, 3381; T. Kawamoto, H. Yamanaka, A. Tanaka, *Appl. Biochem. Biotechnol.* **2000**, *88*, 17; B. Vivet, F. Cavelier, J. Martinez, C. Didierjean, M. Marraud, A. Aubry, *Acta Crystallogr., Sect. C* **2000**, *56*, 1452; N. Wehofsky, J.-D. Wissmann, M. Alisch, F. Bordusa, *Biochim. Biophys. Acta* **2000**, *1479*, 114; D. J. Ager, T. Li, D. P. Pantaleone, R. F. Senkpeil, P. P. Taylor, I. G. Fotheringham, *J. Mol. Catal. B-Enzym.* **2001**, *11*, 199; M. d. C. Terán Moldes, G. Costantino, M. Marinozzi, R. Pellicciari, *Farmaco* **2001**, *56*, 609; A. Boto, R. Hernández, A. Montoya, E. Suárez, *Tetrahedron Lett.* **2002**, *43*, 8269; P. CaliCalí, M. Begtrup, *Tetrahedron* **2002**, *58*, 1595; S. Chandrasekhar, A. Raza, M. Takhi, *Tetrahedron: Asymmetry* **2002**, *13*, 423; K.-H. Park, M. J. Kurth, *Tetrahedron* **2002**, *58*, 8629; M. J. O'Donnell, J. Alsina, W. L. Scott, *Tetrahedron Lett.* **2003**, *44*, 8403; H. H. Wasserman, Y. O. Long, J. Parr, *Tetrahedron Lett.* **2003**, *44*, 361.

[2] H. Ishikawa, H. Yamanaka, T. Kawamoto, A. Tanaka, *Appl. Microbiol. Biotechnol.* **1999**, *51*, 470; H. Ishikawa, H. Yamanaka, T. Kawamoto, A. Tanaka, *Appl. Microbiol. Biotechnol.* **1999**, *53*, 19.

[3] M. Merget, K. Gunther, M. Bernd, E. Gunther, R. Tacke, *J. Organomet. Chem.* **2001**, *628*, 183.

[4] L. Birkhofer, A. Ritter, *Liebigs Ann. Chem.* **1958**, *612*, 22; T. H. Porter, W. Shive, *J. Med. Chem.* **1968**, *11*, 402; R. Fitzi, D. Seebach, *Tetrahedron* **1988**, *44*, 5277.

[5] H. Yamanaka, T. Fukui, T. Kawamoto, A. Tanaka, *Appl. Microbiol. Biotechnol.* **1996**, *45*, 51; A. Tanaka, H. Yamanaka, T. Kawamoto, *Ann. N. Y. Acad. Sci.* **1996**, *799*, 762; Y. Tsuji, H. Yamanaka, T. Fukui, T. Kawamoto, A. Tanaka, *Appl. Microbiol. Biotechnol.* **1997**, *47*, 114.

[6] M. Pietzsch, T. Waniek, R. J. Smith, S. Bratovanov, S. Bienz, C. Syldatk, *Monatsh. Chem.* **2000**, *131*, 645.

[7] R. J. Smith, M. Pietzsch, T. Waniek, C. Syldatk, S. Bienz, *Tetrahedron: Asymmetry* **2001**, *12*, 157.

[8] U. Schöllkopf, *Angew. Chem., Int. Ed.* **1981**, *20*, 798; D. Seebach, A. Fadel, *Helv. Chim. Acta* **1985**, *68*, 1243; D. Seebach, E. Juaristi, D. D. Miller, C. Schickli, T. Weber, *Helv. Chim. Acta* **1987**, *70*, 827; A. G. Myers, J. L. Gleason, T. Yoon, D. W. Kung, *J. Am. Chem. Soc.* **1997**, *119*, 656; V. I. Handmann, M. Merget, R. Tacke, *Z. Naturforsch., B* **2000**, *55*, 133; B. Vivet, F. Cavelier, J. Martinez, *Eur. J. Org. Chem.* **2000**, 807; R. Tacke, M. Merget, R. Bertermann, M. Bernd, T. Beckers, T. Reissmann, *Organometallics* **2000**, *19*, 3486.

[9] B. Weidmann, *Chimia* **1992**, *46*, 312.

[10] R. Tacke, V. I. Handmann, *Organometallics* **2002**, *21*, 2619.

[11] M. P. Sibi, B. J. Harris, J. J. Shay, S. Hajra, *Tetrahedron* **1998**, *54*, 7221.

[12] R. D. Walkup, D. C. Cole, B. R. Whittlesey, *J. Org. Chem.* **1995**, *60*, 2630.

[13] R. J. Smith, S. Bratovanov, S. Bienz, *Tetrahedron* **1997**, *53*, 13695.
[14] P. H. J. Carlsen, T. Katsuki, V. S. Martin, K. B. Sharpless, *J. Org. Chem.* **1981**, *46*, 3936.
[15] S. M. Sieburth, J. J. Somers, H. K. O'Hare, *Tetrahedron* **1996**, *52*, 5669.
[16] G. H. Barnes Jr., N. E. Daughenbaugh, *J. Org. Chem.* **1966**, *31*, 885; M. Lee, S. Ko, S. Chang, *J. Am. Chem. Soc.* **2000**, *122*, 12011; M. Shi, K. M. Nicholas, *J. Chem. Res., Synop.* **1997**, *11*, 400.
[17] R. J. Smith, Ph.D. Thesis, University of Zurich, 2002.
[18] D. A. Evans, K. T. Chapman, J. Bisaha, *J. Am. Chem. Soc.* **1988**, *110*, 1238; D. A. Evans, S. J. Miller, T. Lectka, *J. Am. Chem. Soc.* **1993**, *115*, 6460; D. A. Evans, D. M. Barnes, J. S. Johnson, T. Lectka, P. von Matt, S. J. Miller, J. A. Murry, R. D. Norcross, E. A. Shaughnessy, K. R. Campos, *J. Am. Chem. Soc.* **1999**, *121*, 7582; F. M. Hauser, R. A. Tommasi, *J. Org. Chem.* **1991**, *56*, 5758; O. Kitagawa, A. Hashimoto, Y. Kobayashi, T. Taguchi, *Chem. Lett.* **1990**, *8*, 1307; C. Thom, P. Kocienski, *Synthesis* **1992**, *6*, 582.
[19] R. Hooft, KappaCCD Collect Software. Nonius BV, Delft, The Netherlands, 1999.
[20] Z. Otwinowski, W. Minor, *Methods Enzymol.* **1997**, *276*, 307.
[21] P. Coppens, L. Leiserowitz, D. Rabinovich, *Acta Crystallogr.* **1965**, *18*, 1035.
[22] A. Altomare, G. Cascarano, C. Giacovazzo, A. Guagliardi, M. C. Burla, G. Polidori, M. Camalli, *J. Appl. Crystallogr.* **1994**, *27*, 435.
[23] H. D. Flack, *Acta Crystallogr., Sect. A* **1983**, *39*, 876; G. Bernardinelli, H. D. Flack, *Acta Crystallogr., Sect. A* **1985**, *41*, 500.
[24] E. N. Maslen, A. G. Fox, M. A. O'Keefe, in 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 6.1.1.1, p. 477.
[25] R. F. Stewart, E. R. Davidson, W. T. Simpson, *J. Chem. Phys.* **1965**, *42*, 3175.
[26] J. A. Ibers, W. C. Hamilton, *Acta Crystallogr.* **1964**, *17*, 781.
[27] D. C. Creagh, W. J. McAuley, in 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 4.2.6.8, p. 219.
[28] D. C. Creagh, J. H. Hubbell, in 'International Tables for Crystallography', Ed. A. J. C. Wilson, Kluwer Academic Publishers, Dordrecht, 1992, Vol. C, Table 4.2.4.3, p. 200.
[29] teXsan: Single Crystal Structure Analysis Software. Version 1.10, Molecular Structure Corporation, The Woodlands, Texas, 1999.
[30] C. K. Johnson, ORTEPII, Report ORNL-5138, Oak Ridge National Laboratory 1976.

Received March 17, 2004