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Synthesis of Silicon Containing Alanines†

Mukund P. Sibi,* Brant J. Harris, John J. Shay, and Saumen Hajra

Center for Main Group Chemistry, Department of Chemistry, North Dakota State University
Fargo, ND 58105-5516

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Abstract: The synthesis of silicon containing alanines in optically pure form from an electrophilic alaninol synthon is described. The overall chemical yields for the synthesis of the novel amino acids range from 19-39%.

Keywords: Silicon Amino Acids; Oxazolidinone; Silyl Copper Reagents

New methods for the synthesis of non-protenogenic amino acids in optically pure form are an area of continued interest since these compounds serve as useful surrogates for their natural counterparts.[1] We have been evaluating new methodologies for the preparation of amino acids which contain large hydrophobic moieties.[2] Peptides derived from these unnatural amino acids may offer such advantages as prevention of hydrophobic pocket collapse, higher lipophilicity, and stability toward proteolytic enzymatic degradation. We surmised that triaryl or alkylaryl silicon containing functional groups at the β-position of alanine could function as such a hydrophobic unit due to their bulk and inertness.[3] In this letter we report the successful application of an electrophilic alanine synthon, readily available from serine, in the synthesis of silicon containing alanines (equation 1).

Electrophilic Alanine Synthon — **1** X = OTS, I — Silicon Modified Alanine (1)

We have been exploring the utility of nucleophilic and electrophilic alaninol (alanine) synthons derived from serine as starting materials for the preparation of unnatural amino alcohols and amino acids.[4] In previous work from this laboratory, the reaction of **1** with copper reagents to furnish substituted oxazolidinones was reported.[5] The present work involves the extension of this methodology to silicon nucleophiles to form

e-mail: Sibi@plains.nodak.edu; Fax: 701-231-8831

† Dedicated to our colleague and friend Professor Madeleine M. Joullie in celebration of forty years of distinguished teaching and research at the University of Pennsylvania.

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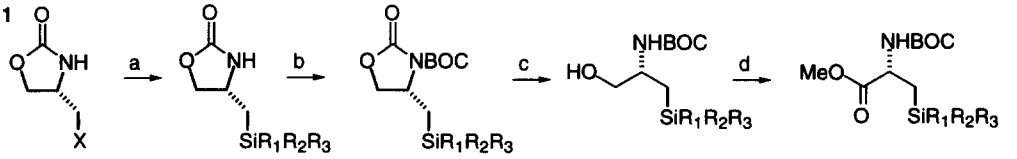
substituted oxazolidinones which on further modification provide the desired amino acids. An efficient synthesis of the alaninol precursor **1** (X = OTS and I) has been achieved starting from L-serine methylester hydrochloride in high overall yields without any chromatographic purification.[6] Nucleophilic displacements using **1** (X = OTs) and several different copper species[7] derived from silyl lithiums were examined (Scheme 1). These reactions indicated the formation of compounds **2** with moderate efficiency. The next set of reactions used **1** (X = I) as the starting material. Treatment of **1** with an excess of silyl copper species ($2SiR_3Li$[8] + CuCN) indicated the formation of **2** cleanly in higher yields than those obtained from the tosylate.[9] The convenient method of Seebach's[10] for *in situ* generation of silyl coppers (n-$Bu_2CuCNLi$ + SiR_3Cl) and further treatment with **1** (X = I) gave none of the desired silyl oxazolidinone **2**. Thus, all the nucleophilic displacement reactions (see Table) were carried out using the higher order copper reagents ($2SiR_3Li$ + CuCN) by addition of 2-3 equivalents of the copper species to the iodide (tosylate) at -78 °C followed by slowly warming to 0 °C (~4-7 hours) and quenching with 10% NH_4OH/saturated ammonium chloride. The purified yields in the displacement reactions were moderate to good (40-78%). Additionally, products from elimination reactions were observed in small amounts when the iodo starting material was used.[11] The silyl oxazolidinones **2** have the potential to function as a new bulky chiral auxiliary similar to the versatile Evans auxiliary, oxazolidinone derived from phenylalaninol.[12]

Scheme 1



1 X = OTs, I **2** **3** **4** **5**

key: [a] $SiR_1R_2R_3Li$, CuCN; [b] BOC_2O, NEt_3, cat. DMAP; [c] Cs_2CO_3, MeOH; [d] (1) Jones Reagent, Acetone, (2) TMS diazomethane

The next step in the sequence involved the conversion of **2** to **3** using standard conditions. Thus, treatment of **2** with di-tert-butyl dicarbonate and triethylamine in dichloromethane at room temperature for 2 hours furnished **3** in high yields (97-99%). With the protected oxazolidinones in hand, selective hydrolysis of the endo carbonyl was carried out using the procedure developed by Kunieda.[13] Treatment of **3a-e** with catalytic Cs_2CO_3 in methanol at room temperature for 12-24 h furnished the *N*-BOC alcohols in very good yields (68-87%). There are several methods in the literature for the conversion of *N*-protected amino alcohols to the corresponding amino acids.[14] Jones reagent proved to be ideal for the oxidation of **4**. Treatment of an acetone solution of **4** with an equivalent amount of the freshly prepared Jones reagent furnished the product amino acids which were subsequently converted to their methyl esters **5** using TMS diazomethane.[15] The deprotection of the *N*-BOC protecting group was not observed during the oxidation reaction. Several aspects of the synthetic sequence in the preparation of **5** are noteworthy. The overall yield for the amino esters starting from the iodo oxazolidinone is **5a**, 39%; **5b**, 19%; **5c**, 30%; and **5d**, 20%. The optical purity of **5a-5d** was established to be >98% by chiral HPLC and comparison with racemic materials. The method is amenable to scale up. The nature of the substituents on the silicon is limited only by the ease of the generation of the silyl

lithium reagents. One key point of the methodology is the formation of the (*S*)-enantiomeric series of the final amino acids starting from the natural L-serine methylester.

Table. Synthesis of Silicon Containing Alanines

	Silicon Substituent						
Compound	R_1	R_2	R_3	Yield%, **2**[a,b,c]	Yield%, **3**	Yield%, **4**	Yield%, **5**
a	Ph	Ph	Ph	78	99	87	58
b	Ph	CH_3	CH_3	42 (33)	99	68	68
c	Ph	Ph	CH_3	63	97	78	63
d	Ph	Ph	t-Bu	40 (43)	98	84	62

[a] Yields are for isolated material after column purification. [b] 2-3 equivalents of the silyl copper was used. [c] The yields in parenthesis are from reactions when the tosylate was used as the substrate.

In conclusion, we have developed a general methodology for the efficient synthesis of novel silicon containing alanines. The extension of the methodology to other silicon containing amino acids as well as chain extended alanines are underway. Additionally, silicon substituted oxazolidinones **2** hold promise as new bulky chiral auxiliaries.

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Experimental Procedures. Methylene chloride and triethylamine were distilled from calcium hydride. Tetrahydrofuran and benzene were distilled from benzophenone/ketyl prior to use. Methanol was distilled from magnesium. Thin layer chromatographic analyses were performed on silica gel Whatmann-60F glass plates and components were visualized by illumination with UV light or by staining with phosphomolybdic acid. Flash chromatography were performed using E. Merck silica gel 60 (230-400 mesh). Melting points were determined using a Thomas Hoover capillary melting point apparatus or Fisher-Johns melting point apparatus. All glassware was oven/and or flame dried, assembled hot, and cooled under a stream of dry nitrogen or argon before use. Reactions with air sensitive materials were carried out by standard syringe techniques.

^{1}H NMR were recorded on a JEOL GSX-400 (400 MHz), JEOL GSX-270 (270 MHz) spectrometers. Chemical shifts are reported in parts per million (ppm) down field from TMS, using residual $CHCl_3$ (7.27 ppm) as an internal standard. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublets of doublets, m = multiplet, br = broad), integration and coupling constant(s). ^{13}C NMR were recorded on a JEOL-GSX-400 (100 MHz) and JEOL GSX-270 (65 MHz) spectrometers using broad band proton decoupling. Chemical shifts are reported in parts per million (ppm) down field from TMS, using the middle resonance of $CDCl_3$ (77.0 ppm) as an internal standard. HPLC analyses were carried out on either an ISCO system comprising of a 2360 pump, 2350 gradient programmer and a V^4 variable wavelength

UV detector connected to a Hewlett-Packard 3396 II integrator or a Waters M-45 pump connected to an ISCO 228 Absorbance Detector with a type 6 optical unit and a Hewlett-Packard 3396-II integrator. HPLC columns were purchased from Daicel Chemical Ind., Ltd. Rotations were recorded on a JASCO-DIP-370 instrument. Elemental analyses were performed in house on a Perkin Elmer Series II CHNS/O Analyzer 2400.

Typical procedure for Nucleophilic Displacements: To a slurry of CuCN (0.45 g, 5 mmol) in 10 mL THF at 0 °C was added dropwise Ph_3SiLi (prepared from 2.95 g, 10 mmol of Ph_3SiCl and lithium wire, 0.21 g, 30 mmol). This was stirred for 30 minutes at 0° C and then cooled to -78° C. A solution of **1** (X = I) (0.377g, 1.6 mmol) in 3 mL THF was added dropwise. The green reaction mixture was allowed to warm to ambient temperature over 4 h and quenched with 10% NH_4OH in sat. NH_4Cl Solution. Normal workup followed by silica gel column purification gave **2a** as a white solid (0.47g, 78%).

4-(*S*)-Triphenylsilylmethyl oxazolidin-2-one (2a): mp 149-150 °C; Rf 0.29 (1:1 EtOAc:Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55-7.49 (m, 15H), 5.24 (s, 1H), 4.19-4.12 (m, 2H), 3.79 (m, 1H), 1.89-1.84 (m, 1H), 1.77-1.71 (m, 1H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 159.2,135.6, 133.3, 130.3, 128.5, 72.5, 50.2, 20.9; $[\alpha]_D^{25}$ +18.50 ° (c=1.00, CH_2Cl_2); Analysis Calc'd for $C_{22}H_{21}N_1O_2Si_1$: C, 73.50, H, 5.89; N, 3.90; found: C, 73.78; H, 6.01; N, 3.86.

4-(*S*)-Dimethylphenylsilylmethyl oxazolidin-2-one (2b): mp 71-72 °C; Rf 0.11 (40% EtOAc:60% Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.52-7.39 (m, 5H), 4.74 (s, 1H), 4.32 (t, 1H, *J*=8.1 Hz), 3.97 (m, 1H), 3.83-3.77 (m, 2H), 1.22 (dd, 1H, *J*=7.0 and 14.7 Hz), 1.12 (dd, 1H, *J*=7.3 and 14.7 Hz), 0.36 (s, 6H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 159.2, 137.0, 133.3, 129.7, 128.3, 72.3, 50.2, 23.6, -2.7; $[\alpha]_D^{25}$ -5.70 ° (c=1.00, CH_2Cl_2); Analysis Calc'd for $C_{12}H_{17}N_1O_2Si_1$: C, 61.24 H, 7.28; N, 5.95 found: C, 60.92; H, 7.12; N, 5.93.

4-(*S*)-Diphenylmethylsilylmethyl oxazolidin-2-one (2c): mp 123-124 °C; Rf 0.11 (50% EtOAc:50% Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.52-7.39 (m, 10H), 4.87 (s, 1H), 4.27 (t, 1H, *J*=8.1 Hz), 4.04 (m, 1H), 3.81 (dd, 1H, *J*=7.3 and 8.1), 1.55 (dd, 1H, *J*=7.3 and 14.7 Hz), 1.44 (dd, 1H, *J*=7.0 and 14.7 Hz), 0.63 (s, 3H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 159.3, 135.14, 135.08, 134.3, 129.9, 128.3, 128.2, 72.2, 50.1, 22.0, -3.8; $[\alpha]_D^{25}$ +4.10 ° (c=1.00, CH_2Cl_2); Analysis Calc'd for $C_{17}H_{19}N_1O_2Si_1$: C, 68.65 H, 6.44; N, 4.71 found: C, 68.70; H, 6.32; N, 4.53.

4-(*S*)-*tert*-Butyldiphenylsilylmethyl oxazolidin-2-one (2d): mp 139-140 °C; Rf 0.17 (40% EtOAc:60% Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.63-7.41 (m, 10H), 4.45(s, 1H), 4.11 (t, 1H, *J*=8.1 Hz), 3.97-3.87 (m, 1H), 3.75 (dd, 1H, *J*=7.0 and 8.4 Hz), 1.56 (dd, 1H, *J*=7.7 and 15.0 Hz), 1.48 (dd, 1H, *J*=6.2 and 15.0 Hz), 1.05 (s, 9H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 158.9, 135.9, 135.8, 133.02, 132.96, 130.0, 129.9, 128.3, 128.2, 72.5, 50.2, 27.6, 18.0, 17.6; $[\alpha]_D^{25}$ +26.90 ° (c=1.00, CH_2Cl_2); Analysis Calc'd for $C_{20}H_{25}N_1O_2Si_1$: C, 70.76 H, 7.42; N, 4.13 found: C, 70.43; H, 7.31; N, 4.10.

Typical Procedure for BOC Protection: To a solution of 0.4228 g (1.18 mmol) of **2a**, 0.30 g (1.4 mmol) BOC_2O, and 0.18 mL (1.3 mmol) Et_3N in 12 mL CH_2Cl_2 was added ~5 mg DMAP and stirred at RT for 2 h.

The reaction was quenched with 10% citric acid solution and extracted with CH_2Cl_2. The combined organic extracts were washed H_2O, and brine, dried over anhydrous $MgSO_4$ and the solvent was evaporated. The crude product was purified by silica gel chromatography.

3-*N*-(*tert*-Butoxycarbonyl)-4-(*S*)-dimethylphenylsilylmethyl oxazolidin-2-one (3a): mp 126-127 °C; Rf 0.24 (20% EtOAc:80% Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.59-7.40 (m, 15H), 4.56-4.47 (m, 1H), 3.76 (t, 1H, *J*=8.4 Hz), 3.47 (dd, 1H, *J*=3.5 and 9.0 Hz), 2.36 (dd, 1H, *J*=1.1 and 14.3 Hz), 1.75 (dd, 1H, *J*=12.5 and 14.3 Hz), 1.53 (s, 9H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 152.0, 149.5, 135.5, 133.3, 130.1, 128.3, 83.8, 67.4, 53.4, 28.0, 18.9; $[\alpha]_D^{25}$ -31.70 ° (c=1.00, CH_2Cl_2); Analysis Calc'd for $C_{27}H_{29}N_1O_4Si_1$: C, 70.56 H, 6.36; N, 3.05; found: C, 70.52; H, 6.23; N, 2.96.

3-*N*-(*tert*-Butoxycarbonyl)-4-(*S*)-dimethylphenylsilylmethyl oxazolidin-2-one (3b): mp 61-62 °C; Rf 0.47 (40% EtOAc:60% Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.51-7.38 (m, 5H), 4.37-4.28 (m, 1H), 4.03 (t, 1H, *J*=8.4 Hz), 3.59 (dd, 1H, *J*=3.7 and 8.8 Hz), 1.53 (m, 10H), 1.22 (dd, 1H, *J*=11.9 and 14.1 Hz), 0.38 (s, 3H), 0.37 (s, 3H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 152.2, 149.4, 137.0, 133.5, 129.8, 128.4, 83.7, 67.8, 53.4, 28.1, 22.2, -2.4, -2.8; $[\alpha]_D^{25}$ -45.30° (c=1.00, CH_2Cl_2); Analysis Calc'd for $C_{17}H_{25}N_1O_4Si_1$: C, 60.87 H, 7.51; N, 4.18; found: C, 60.49; H, 7.17; N, 4.15.

3-*N*-(*tert*-Butoxycarbonyl)-4-(*S*)-diphenylmethylsilylmethyl oxazolidin-2-one (3c): mp 96-97 °C; Rf 0.59 (50% EtOAc:50% Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55-7.39 (m, 10H), 4.46-4.37 (m, 1H), 3.90 (t, 1H, *J*=8.6 Hz), 3.53 (dd, 1H, *J*=3.7 and 8.8 Hz), 1.96 (dd, 1H, *J*=2.0 and 14.2 Hz), 1.53 (m, 10H), 0.65 (s, 3H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 152.1, 149.4 135.2, 135.0, 134.5, 134.4, 130.1, 130.0, 128.40, 128.36, 83.9, 67.6, 53.4, 28.2, 20.4, -3.5; $[\alpha]_D^{25}$ -36.00° (c=1.00, CH_2Cl_2); Analysis Calc'd for $C_{22}H_{27}N_1O_4Si_1$: C, 66.47; H, 6.85; N, 3.52; found: C, 66.52; H, 6.63; N, 3.52.

3-*N*-(*tert*-Butoxycarbonyl)-4-(*S*)-*tert*-butyldiphenylsilylmethyl oxazolidin-2-one (3d): mp 123-124 °C; Rf 0.60 (40% EtOAc:60% Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.71-7.59 (m, 4H), 7.44-7.39 (m, 6H), 4.41-4.28 (m, 1H), 3.54 (t, 1H, *J*=8.3 Hz), 3.28 (dd, 1H, *J*=3.5 and 9.0 Hz), 2.10 (dd, 1H, *J*=1.5 and 14.3 Hz), 1.59-1.41 (m, 10H), 1.06 (s, 9H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 152.1, 149.5, 136.0, 135.8, 133.6, 132.5, 129.9, 128.2, 128.1, 83.8, 67.1, 53.7, 28.2, 27.6, 18.2, 15.7; $[\alpha]_D^{25}$ -16.80° (c=1.00, CH_2Cl_2); Analysis Calc'd for $C_{25}H_{33}N_1O_4Si_1$: C, 68.30; H, 7.57; N, 3.19; found: C, 68.17; H, 7.40 N, 3.08.

Typical Procedure for Oxazolidinone Cleavage: To a solution of 0.5448 g (1.18 mmol) of **3a** in 12 mL MeOH was added 0.155 g (0.48 mmol) of Cs_2CO_3 and stirred at RT while monitoring the reaction by TLC. When the reaction was judged complete, 0.18 g (0.94 mmol) of citric acid was added. The solvent was removed, H_2O was added and extracted with CH_2Cl_2. The combined organic extracts were washed with brine and dried over anhydrous $MgSO_4$. Purification was accomplished by silica gel chromatography or recrystallization.

2-(*S*)-*N*-(*tert*-Butoxycarbamoyl)-3-triphenylsilyl-1-propanol (4a): mp 127-128 °C; Rf 0.30 (40% EtOAc:60% Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.35 (m, 15H), 4.45 (m, 1H), 3.95 (m, 1H), 3.59 (m, 1H), 3.46 (m, 1H), 2.46 (m, 1H), 1.73-1.54 (m, 2H), 1.33 (s, 9H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 155.9, 135.5, 134.2, 129.7, 128.1, 79.4, 68.5, 50.1, 28.2, 16.5; $[\alpha]_D^{25}$ -3.60° (c=1.00, CH_2Cl_2); Analysis Calc'd for $C_{26}H_{31}N_1O_3Si_1$: C, 72.02; H, 7.21; N, 3.23; found: C, 72.01; H, 7.14; N, 3.20.

2-(*S*)-*N*-(*tert*-Butoxycarbamoyl)-3-dimethylphenylsilyl-1-propanol (4b): mp 96-97 °C; Rf 0.22 (30% EtOAc:70% Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51-7.49 (m, 2H), 7.36-7.34 (m, 3H), 4.50 (d, 1H, *J*=8.0 Hz), 3.78 (s, 1H), 3.53 (m, 1H), 3.39 (m, 1H), 2.64 (s, 1H), 1.40 (s, 9H), 1.04-0.93 (m, 2H), 0.33 (s, 6H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 156.0, 138.6, 133.4, 129.1, 127.9, 79.5, 68.5, 50.1, 28.3, 19.0, -2.7; $[\alpha]_D^{25}$ -3.90° (c=1.00, CH_2Cl_2); Analysis Calc'd for $C_{16}H_{27}N_1O_3Si_1$: C, 62.10; H, 8.79; N, 4.53; found: C, 61.71; H, 8.46; N, 4.56.

2-(*S*)-*N*-(*tert*-Butoxycarbamoyl)-3-diphenylmethylsilyl-1-propanol (4c): mp 68-70 °C; Rf 0.48 (50% EtOAc:50% Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52-7.50 (m, 4H), 7.40-7.33 (m, 6H), 4.41 (m, 1H), 3.86 (bs, 1H), 3.57 (bs, 1H), 3.41 (m, 1H), 2.28 (bs, 1H), 1.55-1.29 (m, 11H), 0.63 (s, 3H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 155.9, 136.5, 134.3, 129.5, 128.0, 79.5, 68.4, 50.1, 28.3, 17.4, -4.3; $[\alpha]_D^{25}$ -12.92° (c=1.05, CH_2Cl_2); Analysis Calc'd for $C_{21}H_{29}N_1O_3Si_1$: C, 67.89; H, 7.87; N, 3.77; found: C, 67.70; H, 7.79; N, 3.79.

2-(*S*)-*N*-(*tert*-Butoxycarbamoyl)-3-*tert*-butyldiphenylsilyl-1-propanol (4d): mp 93-95 °C; Rf 0.50 (40% EtOAc:60% Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65-7.37 (m, 10H), 4.37 (d, 1H, *J*=7.0 Hz), 3.74 (bs, 1H), 3.47 (bs, 1H), 3.35 (bs, 1H), 2.49 (bs, 1H), 1.50-1.36 (m, 11H), 1.04 (s, 9H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 155.9, 135.8, 134.2, 133.9, 129.4, 129.3, 127.8, 79.2, 68.3, 50.3, 28.2, 27.7, 18.1, 13.3; $[\alpha]_D^{25}$ -1.05° (c=1.24, CH_2Cl_2); Analysis Calc'd for $C_{24}H_{35}N_1O_3Si_1$: C, 69.69; H, 8.53; N, 3.39; found: C, 69.32; H, 8.40; N, 3.39.

Typical Procedure for Oxidation Followed by Esterification: To a solution of 88.1 mg (0.20 mmol) of **4a** in 1 mL of acetone cooled to 0 °C was added freshly prepared Jones reagent dropwise every 20- 30 minutes. The reaction was monitored by TLC and judged complete after 3 h. The solvent was removed, quenched with H_2O, extracted with EtOAc. The combined organic extracts were washed with sat. $NaHCO_3$, H_2O, and brine, and dried over $MgSO_4$. The resultant acid was used in the next step without purification.

To a solution of acid (0.20 mmol) in 1.5 mL benzene and 0.5 mL MeOH was added 0.13 mL (0.26 mmol) of a 2 M solution of $TMSCHN_2$ in hexanes. Evolution of gas was observed and the reaction was complete almost immediately. The reaction was quenched with H_2O and solvent was evaporated. The aqueous solution was extracted with CH_2Cl_2 and the combined organic layers were washed with brine and dried over anhydrous $MgSO_4$. Purification was accomplished by silica gel chromatography or recrystallization.

2-(*S*)-*N*-(*tert*-Butoxycarbamoyl)-3-triphenylsilyl methylpropionate (5a): mp 142-144 °C; Rf 0.18 (20% EtOAc:80% Hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54-7.31 (m, 15H), 4.77 (d, 1H, *J*=7.5 Hz), 4.45 (appt q,

1H), 3.36 (s, 3H), 1.97 (dd, 1H, *J*=6.7 and 14.8 Hz), 1.81 (dd, 1H, *J*=8.8 and 14.8 Hz), 1.34 (s, 9H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 174.1, 154.8, 137.7, 133.8, 129.9, 128.2, 79.7, 51.9, 50.6, 28.3, 18.1; $[\alpha]_D^{25}$ -30.00° (c=0.66, CH_2Cl_2); Analysis Calc'd for $C_{27}H_{31}N_1O_4Si_1$: C, 70.25 H, 6.77; N, 3.03; found: C, 70.04; H, 6.80; N, 2.85. The enantiomeric purity was checked with chiral HPLC [Column: Chiralcel OD (0.46 cm x 25 cm); λ: 254 nm; Solvent: hexane: i-PrOH=99:1, flow rate=1.0 mL/min. R_t 17 min (*S*-isomer); R_t 24 min. (*R*-isomer)]

2-(*S*)-*N*-(*tert*-Butoxycarbamoyl)-3-triphenylsilyl methylpropionate (5b): oil; Rf 0.38 (30% EtOAc:70% Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.50 (m, 2H), 7.35 (m, 3H), 4.82 (d, 1H, *J*=7.8 Hz), 4.32 (dd, 1H, *J*=8.5 and 14.9 Hz), 3.54 (s, 1H), 1.40-1.33 (m, 10H), 1.18 (dd, 1H, *J*=9.3 and 14.7 Hz), 0.35 (s, 3H), 0.32 (s, 3H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 174.4, 155.0, 138.2, 133.5, 129.3, 128.0, 79.8, 52.1, 50.6, 28.4, 20.6, -2.7, -2.9; $[\alpha]_D^{25}$ -22.56 (c=1.25, CH_2Cl_2); Analysis Calc'd for $C_{17}H_{27}N_1O_4Si_1$: C, 60.50 H, 8.06; N, 4.15; found: C, 60.29; H, 7.67; N, 4.12. The enantiomeric purity was checked with chiral HPLC [Column: Chiralcel AD (0.46 cm x 25 cm); λ: 254 nm; Solvent: hexane: i-PrOH=93:7, flow rate=0.7 mL/min. R_t 11 min (*S*-isomer); R_t 13.7 min. (*R*-isomer)]

2-(*S*)-*N*-(*tert*-Butoxycarbamoyl)-3-diphenylmethylsilyl methylpropionate (5c): mp 44-46 °C; Rf 0.70 (40% EtOAc:60% Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.53-7.48 (m, 4H), 7.38-7.25 (m, 6H), 4.84 (d, 1H, *J*=7.8 Hz), 4.41 (appt. q, 1H), 3.42 (s, 3H), 1.73-1.67 (m, 1H), 1.56-1.50 (m, 1H), 1.38 (s, 9H), 0.67 (s, 3H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 174.1, 154.9, 136.4, 135.9, 134.4, 129.7, 129.6, 128.1, 79.8, 52.0, 50.6, 28.4, 19.1, -4.4; $[\alpha]_D^{25}$ -35.76 (c=1.18, CH_2Cl_2); Analysis Calc'd for $C_{22}H_{29}N_1O_4Si_1$: C, 66.13 H, 7.32; N, 3.51; found: C, 66.49; H, 6.36; N, 3.44. The enantiomeric purity was checked with chiral HPLC [Column: Chiralcel AD (0.46 cm x 25 cm); λ: 254 nm; Solvent: hexane: i-PrOH=93:7, flow rate=0.7 mL/min. R_t 13 min (*S*-isomer); R_t 21 min. (*R*-isomer)]

2-(*S*)-*N*-(*tert*-Butoxycarbamoyl)-3-*tert*-butyldiphenylsilyl methylpropionate (5d): oil; Rf 0.61 (40% EtOAc:60% Hexanes); ^1H NMR (400 MHz, $CDCl_3$) δ 7.65-7.59 (m, 4H), 7.42-7.35(m, 6H), 4.61 (d, 1H, *J*=7.2 Hz), 4.25 (appt. q, 1H), 3.36 (s, 3H), 1.75 (dd, 1H, *J*=6.2 and 15.0 Hz), 1.57 (dd, 1H, *J*=8.9 and 15.0 Hz), 1.30 (s, 9H), 1.02 (s, 9H). ^{13}C NMR (200 MHz, $CDCl_3$) δ 174.2, 154.7, 136.0, 135.9, 133.8, 133.2, 129.5, 127.92, 127.87, 79.5, 51.9, 50.7, 28.3, 27.8, 18.3, 14.7; $[\alpha]_D^{25}$ -29.01 (c=1.72, CH_2Cl_2); Analysis Calc'd for $C_{25}H_{35}N_1O_4Si_1$: C, 67.99 H, 7.99; N, 3.17; found: C, 68.05; H, 7.12; N, 2.86. The enantiomeric purity was checked with chiral HPLC [Column: Chiralcel AD (0.46 cm x 25 cm); λ: 254 nm; Solvent: hexane: i-PrOH=98:2, flow rate=1.0 mL/min. R_t 11 min (*S*-isomer); R_t 17.5 min. (*R*-isomer)]

References and Footnotes

1. (a) Duthaler, R. O. *Tetrahedron* **1994**, *50*, 1539 and references cited therein. (b) Williams, R. M. *Synthesis of Optically Active α-Amino Acids*; Pergamon: New York, 1989. (c) *Chemistry and Biochemistry of the Amino Acids*; Barrett, G. C., Ed.; Chapman and Hall: London, 1985. (d) Wagner, I.; Musso, H. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 816. (e) Ohfune, Y. *Acc. Chem. Res.* **1992**, *25*, 360.

2. A variety of diphenyl alanines have been synthesized by a novel methodology. Sibi, M. P.; Deshpande, P. K.; La Loggia, A. J. US Patent 5623087.
3. There are few reports on the synthesis of silicon containing amino acids: Walkup, R. D.; Cole, D. C.; Whittlesey, B. R. *J. Org. Chem.* **1995**, *60*, 2630 and references cited therein. Fitzi, R.; Seebach, D. *Tetrahedron* **1988**, *44*, 5277. Smith, R. J.; Bratovanov, S.; Bienz, S. *Tetrahedron* **1997**, *53*, 13695.
4. (a) Sibi, M. P.; Renhowe, P. *Tetrahedron Lett.* **1990**, *31*, 7407. (b) Sibi, M. P.; Li, B. *Tetrahedron Lett.* **1992**, *33*, 4115. (c) Sibi, M. P.; Christensen, J. W.; Li, B.; Renhowe, P. *J. Org. Chem.* **1992**, *57*, 4329.
5. Sibi, M. P.; Rutherford, D.; Sharma, R. *J. Chem. Soc., Perkin Trans 1*, **1994**, 1675.
6. Procedure for the synthesis (R)-4-hydroxymethyl-2-oxazolidinone, precursor for **1**, has been communicated. Sibi, M. P.; Harris, B.; Renhowe, P. A.; Christensen, J. W.; Rutherford, D.; Li, B.; Lu, J. *Org. Synth.* submitted for publication. Also see ref. 4 for some details.
7. For general information on organocopper reagents see: *Organocopper Reagents*, Taylor, R. J. K. Ed.: Oxford University Press, Oxford, 1994; Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon: Oxford, 1992. For recent reviews on organocopper reagents see: Krause, N.; Gerold, A. *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 186; Lipshutz, B.; Sengupta, S. *Org. React.* **1992**, *41*, 135; Lipshutz, B. in *Organometallics in Synthesis*, Schlosser, M. Ed.: Wiley, Chichester, 1994.
8. The silyl lithiums were generated form the corresponding chlorosilanes and lithium metal under sonication conditions: Sharma, S.; Oehlschlager, A. C. *Tetrahedron* **1989**, *45*, 557. For the preparation and use of silyl copper reagents see Crump, R. A. N. C.; Fleming, I.; Hill, J. H. M.; Parker, D.; Reddy, L.; Waterson, D. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3277 and references cited therein; Cuadrado, P.; González, A. M.; González, B.; Pulido, F. J. *Synth. Commun.* **1989**, *19*, 275; Buynak, J. D.; Strickland, J. B.; Lamb, G. W.; Khasnis, D.; Modi, S.; Williams, D.; Zhang, H. *J. Org. Chem.* **1991**, *56*, 7076.
9. The molarity of the silyl lithiums were determined by titration. Fleming, I.; Roberts, R. S.; Smith, S. C. *Tetrahedron Lett.* **1996**, *37*, 9395.
10. Amberg, W.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 1718.
11. Typically, 1-7% of an allyl carbamate was formed by cleavage of the oxazolidinone in reactions where the displacements were not efficient.
12. The utility of silyl oxazolidinones **2** in conjugate additions, aldol condensations and Diels-Alder reactions are currently being explored.
13. Ishizuka, T.; Kunieda, T. Tetrahedron *Lett.* **1987**, *28*, 4185.
14. Conversion of amino alcohols to amino acids: (a) Sasaki, N. A.; Hashimoto, C.; Pauly, R. *Tetrahedron Lett.* **1989**, *30*, 1943. (b) Beaulieu, P. L.; Duceppe, J.-S.; Johnson, C. *J. Org. Chem.* **1991**, *56*, 4196. (c) Beaulieu, P. L.; Schiller, P. W. Tetrahedron *Lett.* **1988**, *29*, 2019. (d) Burgess, K.; Liu, L. T.; Pal, B. *J. Org. Chem.* **1993**, *58*, 4758. (e) Bertozzi, C. R.; Hoeprich, Jr. P. D.; Bednarski, M. D. *J. Org. Chem.* **1992**, *57*, 6092. (f) Sibi, M. P.; Deshpande, P. K.; La Loggia, A. J.; Christensen, J. W. *Tetrahedron Lett.* **1995**, *36*, 8961.
15. Hashimoto, N.; Aoyama, T.; Shioiri, T. *Chem. Pharm. Bull. Jpn.* **1981**, *29*, 1475.