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SELECTIVE TRIISOPROPYLSILYLATION OF α -AMINO ACIDS: PROTECTION WITHOUT RACEMIZATION[‡]

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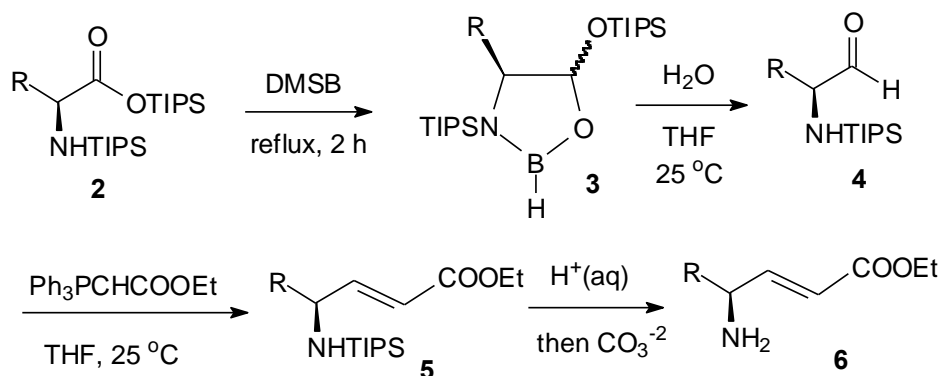
[‡] This work is dedicated to our good friend and, hopefully, future Nobel laureate, Professor Akira Suzuki on the occasion of his 80th birthday.

Abstract – The mono-, di- and trisilylation of α -amino acids with TIPSOTf is described. Treatment of the α -amino acids, proline and tryptophan with TIPSOTf in MeCN provides a quantitative yield of the corresponding ammonium salts of the *O*-TIPS esters (**4**). Employing two (2) equivalents of TIPSOTf/EDIPA produces *N,O*-bis-TIPS amino acid derivatives (**2**) without racemization as stable compounds (73–87%, 13 examples). Three (3) equivalents of this silylation mixture produces the corresponding tris-TIPS derivatives **6** (62–88%, 6 examples) from amino acids which contain protic functionality in their side chain. While this trisilylation procedure is ineffective for tryptophan, the *N,O*-bis-TIPS derivative **2m** is easily prepared through this method, and the third silylation is achieved without racemization employing *t*-BuLi/R₃SiX producing *N*₁-SiR₃-*N,O*-bis-TIPS tryptophans (51–97%, 4 examples).

INTRODUCTION

Essential building blocks for the proteins of life, α -amino acids are of great interest in biochemistry, food science and medicinal chemistry.¹ For applications to synthetic chemistry, their use can be limited by low solubility in organic solvents, a consequence of their zwitterionic nature.² This issue can be resolved by derivatization of either the amine or carboxylate group. The amine functionality is usually converted to an *N*-alkoxycarbonyl derivative³ and the carboxylate moiety to an alkyl ester.⁴ In principle, silylation of these groups would be an ideal way to both solubilize amino acids and protect these functionalities by eliminating both the zwitterionic structure as well as intermolecular hydrogen bonding at the same time.

Racemization should also be dramatically reduced compared to their carbamate counterparts. Trimethylsilyl (TMS) esters have been used as temporary protection for the carboxyl group because they are easily cleaved but their hydrolytic instability make them unsuitable for storage, and they are only prepared *in situ*.^{4,5} Persilylation of α -amino acids has been similarly used to enhance their volatility for their analysis by GC,⁶ to study their fragmentation behavior in the mass spectrometer,⁷ and in inverse solid-phase peptide synthesis.⁸



Scheme 1. Conversion of TIPS silylated amino acids (**2**) to **6** through **4**.

We became interested in the use of the triisopropylsilyl (TIPS) group as a protecting group in α -amino acid chemistry because it was known to not only retard reactions at the silicon center, but also, at adjacent centers.⁹ We developed an efficient protocol for the synthesis of representatives examples of stable and optically pure *N,O*-bis-TIPS- α -amino acid esters (**2**) from their amino acid precursors. Their borane-mediated reduction to enantiomerically pure *N*-TIPS- amino aldehydes (**4**) was accomplished through the hydrolysis of the intermediate oxazaborolidines **3**.¹⁰ These silylated derivatives proved to be remarkably stable and easy to handle making them particularly well-suited for further conversions. Thus, through Wittig chemistry, we demonstrated their conversion to α,β -unsaturated- γ -amino esters **6** (Scheme 1). The derived Mosher amides were rigorously analyzed by NMR comparing these products to the diastereomeric mixtures obtained from racemic amino acids determining that $\leq 1\%$ racemization had occurred in this overall process for the eight (8) representative examples chosen.¹⁰ *Therefore, during the silylation, reduction, hydrolysis, olefination, desilylation and acylation procedures, no detectable racemization occurs!* Herein, we present an extension of the TIPS silylation chemistry to more functionalized amino acids as well as to mono- and tri-TIPS derivatives.

RESULTS AND DISCUSSION

In this and our previous studies, our first challenge was to develop a workable procedure for solubilizing the amino acids (**1**) sufficiently to permit silylation to occur. We investigated known TIPS silylation

procedures for carboxylic acids finding them to be ineffective for **1**.^{9a} Requiring the extremely reactive TIPSOTf to observe any silylation, we found non-polar solvents and most polar solvents to be unsatisfactory. We were encouraged by our initial findings with THF at reflux temperature, but faced the challenge of avoiding its polymerization.¹¹ Fortunately, this could be achieved through the dropwise addition of TIPSOTf to the mixture of **1** and amine base. Our initial studies utilized DBU which was quite effective for the preparation of **2**, but this procedure resulted in extensive racemization in some cases (*e.g.*, L-serine and L-phenylglycine). As noted above, these problems were eliminated employing the highly hindered ethyldiisopropylamine (EDIPA, Hünig's base) which produced the desired *N,O*-bis-TIPS amino acids (**2**) in high yields as pure, stable compounds without significant racemization ($\leq 1\%$) (eqn. 1). This procedure has now been applied to thirteen (13) examples which are given in Table 1. In the case of proline, we also demonstrated that the corresponding *N,O*-bis-TBDMS derivative (**2k'**) was readily prepared in 76% yield employing TBDMSOTf instead of TIPSOTf in this protocol.

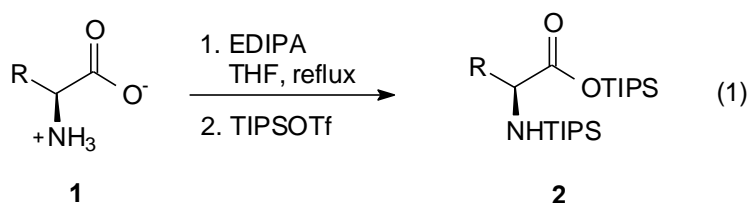


Table 1. Disilylation of α -amino acids

entry	R	1	2 (%) ^a
a	Me	<i>S</i>	74
b	Pr	<i>S</i>	72
c	Pr	<i>R</i>	83
d	(CH ₂) ₂ SMe	<i>S</i>	72
e	CH ₂ CHMe ₂	<i>S</i>	82
f	Bn	<i>S</i>	87
g	CH ₂ OBn	<i>S</i>	82
h	Ph	<i>S</i>	85
i	<i>i</i> -Pr	<i>S</i>	85
j	<i>s</i> -Bu	2 <i>S</i> ,3 <i>S</i>	87
k	(CH ₂) ₃ ^b	<i>S</i>	86
l	H	—	81
m	(3-indolyl)methyl	<i>S</i>	85

^a Isolated yields of pure material. ^b Proline.

The silylation procedure was particularly effective; producing **2** as liquid compounds except in the case of the indolyl derivative **2m** which was obtained as a crystalline solid from dry hexane through a slow

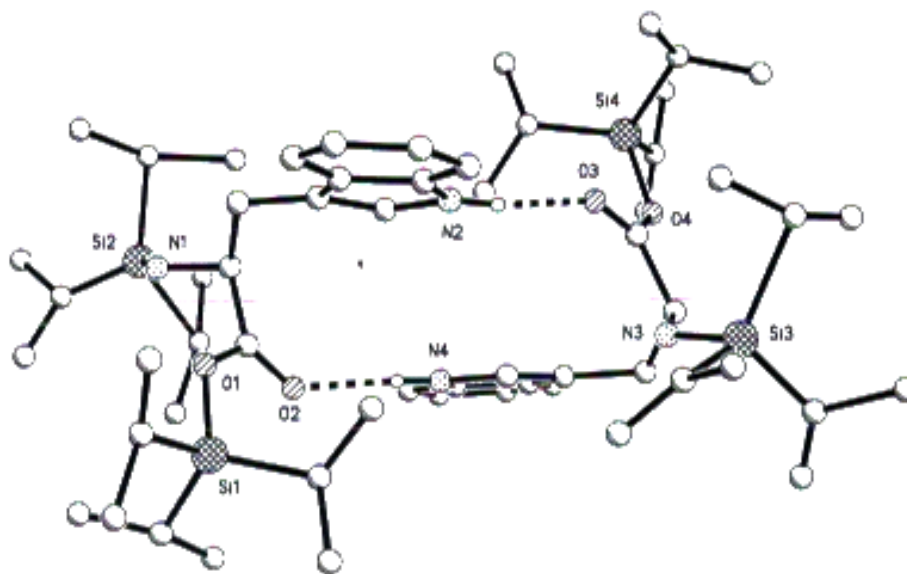
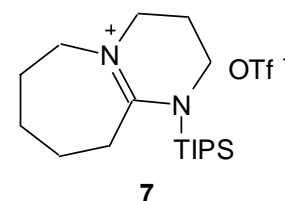


Figure 1. Crystal structure of (+)-*N,O*-bis-triisopropylsilyl-(*L*)-tryptophan **2m** dimer obtained by X-ray diffraction methods.

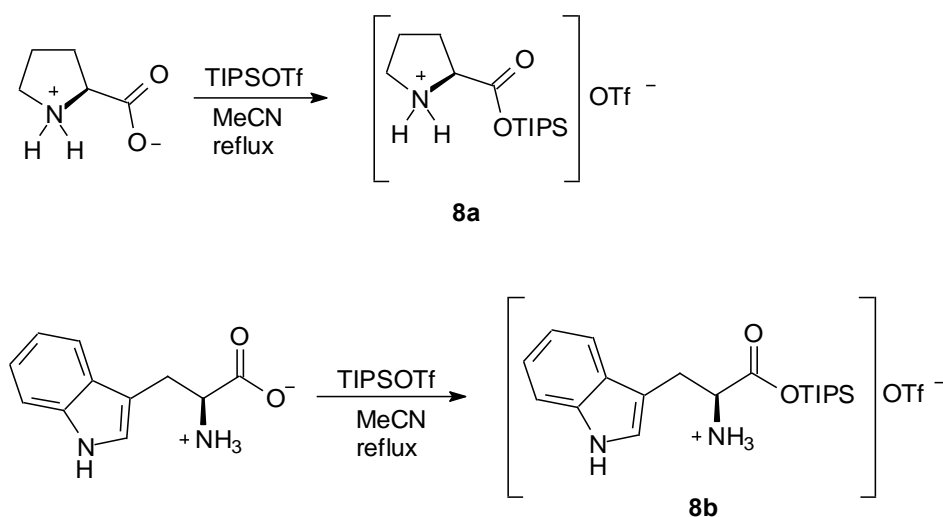
evaporation technique. We were curious as to the reason this compound was crystalline. Fortunately, the crystals proved to be of sufficient quality for X-ray analysis and the solid state structure of **2m** was determined and is depicted in Figure 1. The molecule forms a dimer through H-bonding between the indole's NH and the TIPS ester carbonyl oxygen. These interactions are possible due to the planarity of the indolyl groups which fit between the TIPS groups on each monomeric component. Large Si-N-C ($\sim 129^\circ$) and Si-O-C ($126, 129^\circ$) are also observed due to the influence of the steric bulk of the TIPS groups.

We also examined the solution (CCl_4) and solid state (KBr pellet) IR spectra of **2m** to note differences which may be attributable to the presence of this H-bonding. Historically, this technique has played a major role in related phenomena in amino acid chemistry.^{13–15} Thus, the solution N–H stretching bands ($3488, 3390\text{ cm}^{-1}$) coalesce to a single broadened absorbance at 3370 cm^{-1} in the solid state. Also, the solution $\nu_{\text{C=O}}$ (1716 cm^{-1}) is lowered to 1701 cm^{-1} in the solid state. These changes are in agreement with the dimeric structure of **2m** in the solid state compared to its being monomeric in solution.

It was of interest to better understand the nature of the silylation process which ultimately produces **2**. Toward this end, we returned to an examination of the TIPSOTf/DBU system in CDCl_3 by ^{13}C NMR. We observed an exothermic reaction between TIPSOTf and DBU forming the corresponding *N*-TIPS amidinium triflate (**7**) as evidenced by a downfield shift of C-7 from $\delta 160.5$ in DBU itself, to $\delta 171.8$ in the salt ($\delta 166.0$ in DBU-HOTf).¹² Moreover, the signals observed for the TIPS



group in this DBU salt (δ 13.7, 20.9) are significantly shifted downfield from those in TIPSOTf (δ 11.9, 18.0). We isolated **3** in quantitative yield from a similar reaction in THF (3 h, 25 °C) as an air-sensitive solid. However, no comparable reaction is observed between EDIPA and TIPSOTf in refluxing THF even after 24 h. This suggested that with the EDIPA process, the amino acids were reacting directly with TIPSOTf at the solid-liquid interface. Thus, we added one equivalent of TIPSOTf to a suspension of phenylalanine in hot THF and found that the triflic acid salt of its *O*-TIPS ester is produced along with a large amount of *poly*-THF. This process appeared promising if the use of THF could be avoided. Fortunately, the reaction proceeds cleanly in dry acetonitrile at reflux temperature and two of these monotriisopropylsilyl esters **8** were prepared as their triflic acid salts in quantitative yields in 4 h (Scheme 2). While very sensitive to atmospheric moisture, these salts are stable for several weeks when stored under N₂ at -20 °C. It is significant that the extent of silylation with TIPSOTf apparently could be so conveniently controlled through the proper choice of stoichiometry and reaction conditions.



Scheme 2. Monosilylation of proline and tryptophan with TIPSOTf.

We chose to extend the triisopropylsilylation methodology to α -amino acids which contain additional protic functionality in the side chain. Trisilylation was accomplished to provide **10** in excellent yields for a variety of amino acids (eqn. 2, Table 2). These silylated derivatives **10** proved to be very stable, further illustrating the versatility and value of this new TIPS silylation methodology.

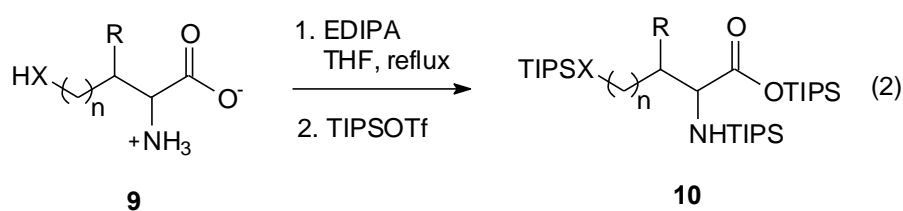
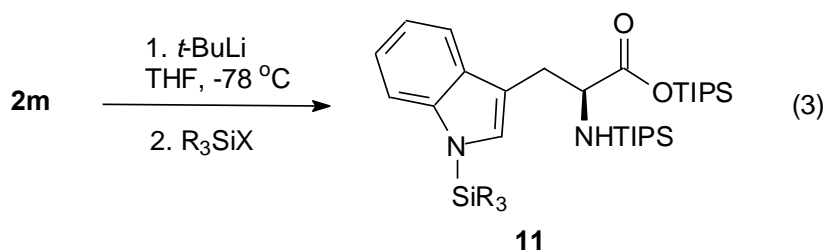


Table 2. Synthesis of *tris*-TIPS α -amino acid esters **10**.

entry	R	5	n	X	yield of 10 (%) ^a
a	H	<i>S</i>	0	O	88
b	H	<i>S</i>	0	S	85
c	H	<i>S</i>	0	OC ₆ H ₄	86
d	Me	2 <i>S</i> ,3 <i>R</i>	0	O	78
e	H	<i>S</i>	3	NH	62
f	H	<i>S</i>	0	CO ₂	77

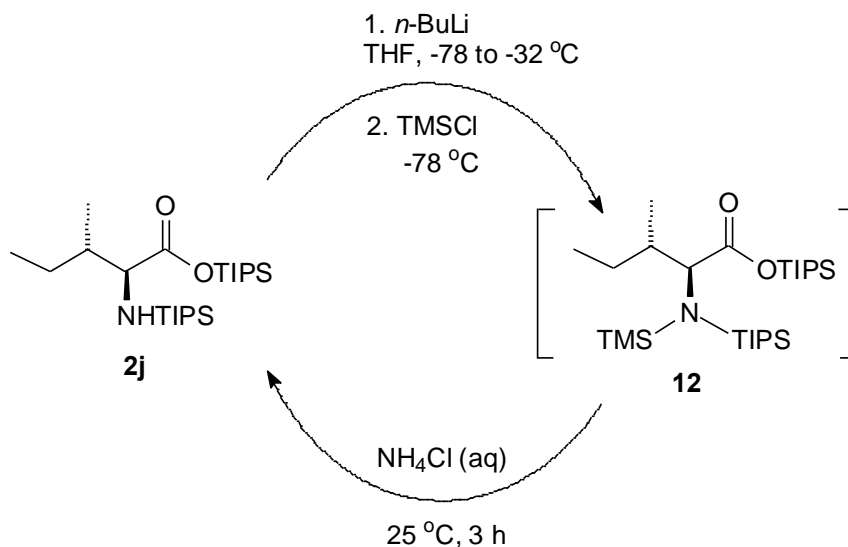
^a Isolated yields of pure material.

The trisilylation of tryptophan proved to be more challenging. Fortunately, this was achieved through the further silylation of **2m** with its deprotonation employing *t*-BuLi (THF, -78 °C) followed by treatment with R₃SiX. This operation produces an intermediate reddish solution of the indolyl lithium amide which is smoothly silylated (eqn. 3). Thus, by varying the silylating agent, *N*₁-SiR₃ derivatives **11** can be prepared including the *tris*-TIPS derivative **7c** (Table 3). As expected, the trisilylated derivatives **11** are liquids, a consequence of the removal of the hydrogen-bonding which led to the dimeric form of **2m**. It should also be noted that the TIPS-protected ester and amine functionalities did not undergo a discernable reaction with *t*-BuLi suggesting that the TIPS group offers wide-ranging protection for amino acids. *Thus, when 2m is deprotonated with t-BuLi as above and MeOH (1 equiv) added followed by TMSCl (1 equiv), re-isolation of 2m (94%) reveals that the optical rotation of 2m is unchanged, demonstrating that neither the alkyl lithium nor the intermediate indolyl lithium racemizes the TIPS-protected amino ester 2m!*

**Table 3.** *N*-Indolic silylation of **2m**.

entry	SiR ₃	X	yield of 11 (%) ^a
a	TMS	Cl	97
b	TES	Cl	93
c	TIPS	OTf	66
d	TBDMS	OTf	51

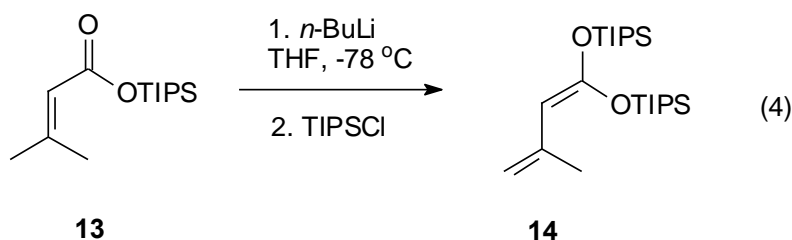
^a Isolated yields of pure material.



Scheme 3. Deprotonation, silylation and desilylation of **2j**.

We chose to examine this reactivity further. Thus, isoleucine **2j** was treated with *n*-BuLi at -78 °C, and the mixture was allowed to slowly warm to -32 °C to lithiate **2j** (Scheme 3). Silylation with TMSCl at -78 °C results in 92% conversion (GC) of **2j** to a new compound **12** whose MS and IR are consistent with *N*-trimethylsilylation (MS *m/z* (relative intensity) 517 (M^+ , 15), 502 ($M-Me^+$, 15), 474 ($M-(i-Pr)^+$, 100); IR (KCl) 1734 cm^{-1}). Treatment of the reaction mixture with aqueous NH₄Cl (3 h, 25 °C) gave after workup, an 80% isolated yield of recovered **2j** (99% GC purity) which was found to have identical spectroscopic properties to the original **2j** as well as *the same optical rotation!* Again, the TIPS groups in **2** evidently prevent addition to the ester or deprotonation of the α -carbon to form the corresponding enolates.

We also chose to examine the reaction of an *O*-TIPS ester which lacked the NHTIPS substitution with alkyllithium reagents to see whether or not they would add to the ester. Toward this end, we prepared triisopropylsilyl β -methylcrotonate (**13**) and treated it at -78 °C in THF with *n*-BuLi. After three hours, silylation of the dienolate with TIPSCl gave the corresponding disilylketene acetal **14** in 73% yield (eqn. 4).



This experiment clearly demonstrates that, if any ester enolates were formed from **2**, they would be silylated to produce observable side products. Moreover, one TIPS group is enough to prevent the addition of unhindered organolithiums (*i.e.*, *n*-BuLi) from adding to the carboxy group to ultimately produce the 3°-carbinols which are observed from standard esters. The two TIPS groups in **2** prevent their addition to

the carboxy group as well as enolate formation which would lead to racemization. These organolithiums can be used with impunity to deprotonate other positions for additional silylations.

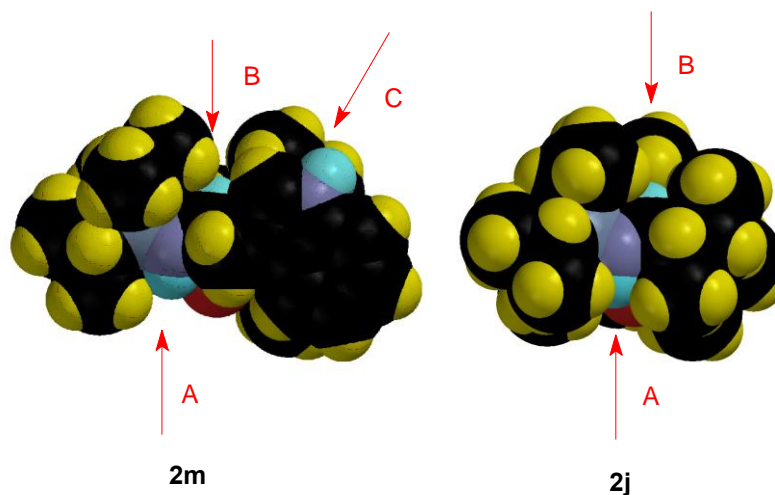


Figure 2. Spartan 06-generated structures for **2m** and **2j** showing in aquamarine color, the possible protons which can be removed by alkyllithiums (A ($N-H$), B ($\alpha-H$), C (N_I-H)).

This unusual reactivity of **2** with organolithiums led us to generate MM structures for both **2m** and **2j** (Spartan 06) to better understand the role of the TIPS groups in limiting access to the α -proton in these derivatives. These structures are illustrated in Figure 2. In **2m**, the indolic H is clearly accessible (**C**) with both **A** and **B** hydrogens being far less available for reaction with *t*-BuLi. From a pKa standpoint, **B** is far more acidic than either **A** or **C**, but it is deeply buried in an ionophobic region which sterically blocks access to the base. With the less hindered $N-H$ site (**C**) found in **2m** not present in **2j**, the base has no choice but to react with the NHTIPS moiety (proton **A**) which has both a carboxy oxygen and amino nitrogen to help coordinate the base during deprotonation. Once again, access to the **B** proton is denied by the TIPS groups and the optical purity of **2** is preserved.

CONCLUSIONS

In this study, a procedure for the mono-, di-, and trisilylation of α -amino acids was reported. Because of the large steric bulk of the triisopropylsilyl (TIPS) group, these silyl derivatives are stable and can be handled under a dry atmosphere. The monosilylation of proline and tryptophan is achieved with 1 equiv of TIPSOTf in MeCN to produce the corresponding *O*-TIPS esters (**8**) quantitatively. The *N,O*-bis-TIPS amino acids **2** are produced (72–87%, 13 examples) using the TIPSOTf/EDIPA combination in refluxing THF. With protic side-chain functionality, this methodology can be used to produce the tri-TIPS derivatives **10** (62–88%, 6 examples). In the case of tryptophan, disilylation occurs under the normal

TIPSOTf/EDIPA conditions to provide **2m** which forms a crystalline dimer whose X-ray structure was determined. Further silylation occurs through *t*-BuLi deprotonation of **2m** followed by silylation with TMSCl, TESCl, TIPSOTf or TBDMSOTf to provide the corresponding *N*₁-SiR₃-*N*,*O*-bis-TIPS-tryptophans **11** (51–97%) without significant racemization. The TIPS groups in **2** offer protection from organolithiums against either their addition to the carboxy group or α -deprotonation leading to enolate formation

EXPERIMENTAL

General information.

All experiments were carried out in pre-dried glassware (12 h, 150 °C) under nitrogen atmosphere. Standard handling techniques for air-sensitive compounds were also employed for all the operations. Nuclear magnetic resonance (NMR) spectra were obtained using General Electric DPX-300 and DRX-500 spectrometers. ¹H (300 MHz), ¹³C (75 MHz) and ¹¹B (96.5 MHz) NMR were recorded in CDCl₃ (δ 7.26 and 77.0 respectively) and of C₆D₆ (δ 7.15 AND 128.0) as the internal standard. Infrared spectra were recorded on a Nicolet 740 GC FT-IR, a Perkin-Elmer 282 or a Nicolet series 6000 FT-IR spectrophotometer. Mass spectral data were obtained with a Hewlett-Packard 5995 A GC/MS spectrometer (70 eV), Fisons VG Autospect. High-resolution mass spectral data were obtained with a Micromass VG AutoSpec magnetic sector mass spectrometer (70 eV). Optical rotations were measured employing a Perkin-Elmer 243B polarimeter.

General procedure for the silylation of α -amino acids **1**.

To a refluxing suspension of the amino acid (20.0 mmol) in dry THF (80 mL) under N₂ atmosphere, EDIPA (40.0 mmol, 6.97 mL) was added. TIPSOTf (40.0 mmol, 10.75 mL) was added dropwise by syringe pump (3.00 mL/h, d = 20 mm), avoiding overheating. The solid amino acid gradually entered into solution. After the addition was complete, heating was maintained for 4 h. The reaction was cooled to room temperature under positive N₂ pressure and THF was removed under vacuum. The remaining oil was diluted in dry hexane (100 mL) and stirred for a few minutes. The phases were allowed to partition and the upper phase was filtered *via cannula* through neutral alumina (Brockmann, activity [I]) into another flask. The ethyldiisopropylammonium salt phase was washed with hexane (2 x 50 mL) and filtered. The organic extracts were combined and concentrated. TIPSOH was slowly distilled (bp 40–42 °C, 0.4 torr) leaving the pure **2** which are air and moisture sensitive oils. However, they can be stored in dry hexane at -20 °C under an inert atmosphere for several weeks. Compounds **2a-h** were already published.¹⁰

(+)-*N,O*-bis-(Triisopropylsilyl)-(L)-valine (2i). 85% (12.8 g, 29.75 mmol) from (*S*)-valine (35.0 mmol, 4.1 g). ^1H NMR (300 MHz, CDCl_3) δ 0.93 (d, $J = 7.0$ Hz, 3H), 0.97 (d, $J = 6.8$ Hz, 3H), 1.03 (bs, 21H), 1.08 (bs, 18H), 1.22-1.35 (m, 4H), 1.90-1.97 (m, 1H), 3.40 (dd, $J = 4.2, 12.7$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 12.0, 12.1, 12.5, 17.8, 18.0, 18.3, 18.4, 18.6, 34.3, 61.7, 175.3. IR (neat, NaCl) 3380, 2960, 2868, 1721, 886 cm^{-1} . HRMS (EI) Exact mass calc. for $\text{C}_{23}\text{H}_{51}\text{NO}_2\text{Si}_2$ 429.3458; Found (M-H) 428.3454. Anal. Calcd for $\text{C}_{23}\text{H}_{51}\text{NO}_2\text{Si}_2$: C 64.27%; H 11.96%. Found C 64.24%; H 12.04%. $[\alpha]_{\text{D}}^{25} + 6.8$ (c 25.5, CCl_4).

(+)-*N, O*-bis-(Triisopropylsilyl)-(L)-isoleucine (2j). 87% (12.9 g, 29.2 mmol) from (L)-isoleucine (33.5 mmol, 4.4 g). ^1H NMR (300 MHz, CDCl_3) δ 0.93 (t, $J = 6.9$ Hz, 3H), 1.05 (d, $J = 6.7$ Hz, 18H), 1.25 (d, $J = 7.6$ Hz, 3H), 1.29 (septet, $J = 7.5$, 3H), 1.48 (broad m, 3H), 1.57 (broad m, 2H), 1.60 (broad m, 1H), 3.39 (d, $J = 4.2$ Hz, 1H), 3.52 (dd, $J = 12.3, 3.9$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 12.0, 12.3, 14.9, 17.7, 17.8, 17.9, 25.7, 42.2, 60.2, 175.1. IR (neat, NaCl) 3390, 2960, 2868, 1710, 1465 cm^{-1} . HRMS (EI) Exact mass calc. for $\text{C}_{21}\text{H}_{46}\text{NO}_2\text{Si}_2$ 400.3067; Found (M- C_3H_7) 400.3055. Anal. Calcd for $\text{C}_{23}\text{H}_{51}\text{NO}_2\text{Si}_2$: C 64.92%; H 12.05%. Found C 65.14%; H 12.10%. $[\alpha]_{\text{D}}^{25} + 18.1$ (c 23.3, CCl_4).

(-)-*N,O*-bis-(Triisopropylsilyl)-(L)-proline (2k). 86% (4.1 g, 9.6 mmol) from (*S*)-proline (11.2 mmol, 1.3 g). ^1H NMR (300 MHz, C_6D_6) δ 1.05 (m, 39H), 1.29 (m, 3H), 1.42 – 1.99 (m, 4H), 3.07 (ddd, $J = 9.4, 8.1, 4.9$ Hz, 1H), 3.31 (ddd, $J = 9.4, 8.1, 6.3$ Hz, 1H), 4.11 (dd, $J = 8.2, 2.5$ Hz, 1H). ^{13}C NMR (75 MHz, C_6D_6) δ 12.4, 12.9, 18.1, 18.8, 25.1, 32.1, 48.2, 62.5, 175.9. IR (neat, NaCl) 2960, 2868, 1731, 1460, 881 cm^{-1} . Anal. Calcd for $\text{C}_{23}\text{H}_{49}\text{NO}_2\text{Si}_2$: C 64.56%; H 11.57%. Found C 64.63%; H 11.58%. $[\alpha]_{\text{D}}^{25} -13.9$ (c 11.1, CHCl_3).

***N,O*-bis-(Triisopropylsilyl)-glycine (2l).** 81% (6.61 g, 17.0 mmol) from glycine (21.0 mmol, 1.58 g). ^1H NMR (300 MHz, C_6D_6) δ 1.07-1.12 (m, 4H), 1.16 (d, $J = 6.0$ Hz, 18H), 1.21 (d, $J = 6.0$ Hz, 18H), 1.34-1.46 (m, 3H), 3.75 (d, $J = 6.7$ Hz, 2H). ^{13}C NMR (75 MHz, C_6D_6) δ 11.9, 12.3, 17.9, 18.4, 46.1, 173.7. IR (neat, NaCl) 3396, 2945, 2868, 1721, 1547, 1460, 1204, 1148, 881 cm^{-1} . GC-MS (70 eV) m/z 344 ($\text{M}^+-(i\text{-Pr})$).

(+)-*N,O*-bis-(Triisopropylsilyl)-(L)-tryptophan (2m). 85% (10.98 g, 21.3 mmol) from 5.11 g of (L)-tryptophan (25.0 mmol). ^1H NMR (500 MHz, C_6D_6) δ 1.05 (m, 39H), 1.31 (septet, $J=7.5$ Hz, 3H), 3.14 (dd, $J = 14.3, 5.9$ Hz, 1H), 3.34 (dd, $J = 14.3, 7.0$ Hz, 1H), 4.09 (ddd, $J = 12.4, 7.0, 5.9$ Hz, 1H), 6.72 (s, 2H), 7.03 (m, 1H), 7.17 (m, 2H), 7.83 (m, 1H). ^{13}C NMR (125 MHz, C_6D_6) δ 12.3, 12.3, 18.0, 18.0,

18.4, 18.6, 34.6, 57.9, 111.3, 112.0, 119.2, 119.6, 122.2, 122.7, 128.4, 136.6, 175.6. ^{29}Si NMR (99 MHz, C_6D_6) δ 4.9, 20.9. IR (neat, NaCl) 3487, 3396, 2853, 2919, 1706, 1624, 1470, 892 cm^{-1} . HRMS (EI) Exact mass calc. for $\text{C}_{29}\text{H}_{53}\text{N}_2\text{O}_2\text{Si}_2$ 517.3346; found 517.3647 ($\text{M}^+ + \text{H}$). Anal. Calcd for $\text{C}_{29}\text{H}_{52}\text{N}_2\text{O}_2\text{Si}_2$: C 67.38%; H 10.14%. Found C 67.35%; H 10.13%. Melting point, 47–48 $^\circ\text{C}$. $[\alpha]_{\text{D}}^{25} + 19.6$ (c 12.1, CHCl_3).

Table 4. Crystal and structure refinement data for (+)-*N,O*-bis-triisopropylsilyl-(L)-tryptophan (**2m**).

Parameter	Data
Empirical formula	$\text{C}_{29}\text{H}_{52}\text{N}_2\text{O}_2\text{Si}_2$
Formula weight	516.905
Crystal system	Triclinic
Space group	<i>P</i> 1
Unit cell dimensions	
<i>a</i> (Å)	9.877(3)
<i>b</i> (Å)	12.867 (4)
<i>c</i> (Å)	14.762 (4)
α (°)	113.546 (6)
β (°)	90.540 (6)
γ (°)	103.079 (5)
Volume (Å ³)	1664.7 (8)
<i>Z</i>	2
Density (Calcd) (Mg m^{-3})	1.031
Absorption coefficient (mm^{-1})	0.131
θ range for data collection (°)	1.51 to 27.71
Reflections collected	11503
Independent reflections	9545 [<i>R</i> (int) = 0.0299]
Data/ restraints/ parameters	9545/ 11/ 659
Goodness-of-fit on F^2	0.970
Final <i>R</i> indices [$I > 2\sigma(I)$]	<i>R</i> 1 = 0.0890, <i>wR</i> 2 = 0.2368
<i>R</i> indices (all data)	<i>R</i> 1 = 0.1822, <i>wR</i> 2 = 0.2806

(-)-*N,O*-bis-(*tert*-Butyldimethylsilyl)-(S)-proline (**2k'**). 76% (2.71 g, 7.89 mmol) from (S)-proline(10.34 mmol, 1.19 g). ^1H NMR (300 MHz, CDCl_3) δ 0.00 (s, 3H), 0.09 (s, 6H), 0.86 (s, s, 9H), 1.24-1.34 (m, 1H),

1.68-1.73 (m, 1H), 1.9-1.83 (m, 1H), 2.11-1.98 (m, 1H), 3.1-3.22 (m, 2H), 3.94 (dd, $J = 2.6, 8.6$ Hz, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ -5.67, -5.56, -5.02, -4.96, 17.6, 20.2, 25.5, 25.7, 26.7, 31.8, 48.3, 62.6, 177.6. IR (neat, NaCl) 3160, 2940, 2843, 1711, 1470, 1363, 1076, 999, 666 cm^{-1} . GC-MS (70 eV) m/z 286 (M^+ -*tert*-Bu). Anal. Calcd for $\text{C}_{13}\text{H}_{28}\text{N}_2\text{O}_2\text{Si}_2$: C 59.44%; H 10.89%. Found C 59.43%; H 11.05%. $[\alpha]_{\text{D}}^{25}$ - 12.0 (c 9.0, hexanes).

***N*-(Triisopropylsilyl)-1,8-diazammoniumbicyclo[5.4.0]undec-7-ene triflate (7).** To a solution of DBU (1.38 g, 9.06 mmol) in dry THF (36 mL) under N_2 atmosphere, 1.15 equiv of TIPSOTf (10.42 mmol, 2.8 mL) was added dropwise by syringe pump (2.80 mL/h, $d = 13$ mm) at room temperature. After the addition was complete, stirring was maintained for 2 h. THF was removed under vacuum. The remaining solid was washed with dry hexane (100 mL). The phases were allowed to partition and the liquid phase was removed *via cannula* affording **7** in quantitative yield. This substance is an air and moisture sensitive solid and must be used immediately.. ^1H NMR (300 MHz, CDCl_3) δ 1.06 (bs, 9H), 1.08 (bs, 9H), 1.30 (sept. $J = 9.0$ Hz, 3H), 1.63-1.74 (bs, 6H), 2.71-2.75 (m, 2H), 3.38 (t, $J = 3.0$ Hz, 2H), 3.56 (d, $J = 6.0$ Hz, 2H), 3.64-3.67 (m, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 13.7, 16.6, 18.0, 20.9, 23.9, 24.9, 28.0, 33.0, 43.6, 49.6, 55.5, 171.8. HRMS (EI) Exact mass calc. for $\text{C}_{18}\text{H}_{37}\text{N}_2\text{Si}$ 309.2726; found 309.2727 (M^+ - CF_3SO_3).

General procedure for the monosilylation of 1. To a refluxing suspension of the amino acid **1** (20.0 mmol) in dry acetonitrile (80 mL) under N_2 atmosphere, TIPSOTf (20.0 mmol, 5.4 mL) was fast added. After the addition was complete, heating was maintained for 4 h. The reaction was cooled to room temperature under positive N_2 pressure and the solvent was removed under vacuum. The remaining solid was washed with dry hexane (2 x 50 mL) and filtered leaving the pure **4** in quantitative yield. These substances are air and moisture sensitive solids. However, they can be stored neat at -20 °C under an inert atmosphere for several weeks.

(+)-(S)-Proline triisopropylsilyl ester hydrotrifluoromethanesulfonate (8a). ^{13}C NMR (75 MHz, CDCl_3) δ 11.3, 11.7, 12.2, 17.4, 23.3, 28.7, 46.8, 60.6, 113.7, 117.9, 122.1, 126.3, 168.5. IR (neat, NaCl) 3498, 2884, 2679, 1721, 1598, 1460, 1358, 1296, 1240, 1163, 902, 728, 641, 569 cm^{-1} . HRMS (EI) Exact mass calc. for $\text{C}_{14}\text{H}_{30}\text{NO}_2\text{Si}$ 272.2046; found 272.2040 (M^+ - CF_3SO_3). $[\alpha]_{\text{D}}^{25}$ + 15.6 (c 12.2, CHCl_3).

(+)-(S)-Tryptophan triisopropylsilyl ester hydrotrifluoromethanesulfonate (8b). ^1H NMR (300 MHz, CDCl_3) δ 1.10-1.15 (m, 18H), 1.32-1.40 (m, 3H), 3.1-3.3 (m, 1H), 3.5-3.6 (m, 1H), 4.0-4.2 (bs, 1H), 6.88 (bs, 3H), 7.0-7.1 (m, 2H), 7.29 (s, 1H), 7.32-7.37 (m, 1H), 7.43-7.45 (m, 1H), 9.0 (bs, 1H). ^{13}C NMR (75

MHz, CDCl₃) δ 11.8, 17.5, 26.3, 54.3, 105.6, 112, 117.7, 119.5, 122.0, 126.0, 136.6, 168.1. HRMS (EI) Exact mass calc. for C₂₀H₃₃N₂O₂Si 361.2311; found 361.2310 (M⁺-CF₃SO₃). $[\alpha]_D^{25}$ - 12.0 (c 5.0, THF).

General procedure for the trisilylation of α -amino acids **1** with reactive side chains.

To a refluxing suspension of the amino acid (20.0 mmol) in dry THF (120 mL) under N₂ atmosphere, EDIPA (40.0 mmol, 6.97 mL) was added. TIPSOTf (60 mmol, 16.1 mL) was added dropwise by syringe pump (1.5 mL/h, d = 20 mm), avoiding overheating. The solid amino acid gradually entered into solution. After the addition was complete, heating was maintained for 6 h. The reaction was cooled to room temperature under positive N₂ pressure and THF was removed under vacuum. The remaining oil was diluted in dry hexane (100 mL) and stirred for a few minutes. The phases were allowed to partition and the upper phase was filtered *via cannula* through neutral alumina (Brockmann, activity [I]) into another flask. The ethyldiisopropylammonium salt phase was washed with hexane (2 x 50 mL) and filtered. The organic extracts were combined and concentrated. TIPSOH was slowly distilled (bp 40-42 °C, 0.4 torr) leaving the pure material **10**. These substances are air and moisture sensitive oils. However, they can be stored in dry hexane at -20 °C under an inert atmosphere for several weeks.

(+)-N,O,O-tris-(Triisopropylsilyl)-(S)-serine (10a): 88% (7.57 g, 13.20 mmol) from 1.58 g of (S)-serine (15.0 mmol). ¹H NMR (300 MHz, CDCl₃) δ 1.06 (m, 58H), 1.30 (m, 6H), 3.52 (ddd, *J* = 12.9, 5.6, 3.4 Hz, 1H), 3.75 (dd, *J* = 9.1, 5.7, 3.8 Hz, 1H), 4.00 (dd, *J* = 9.1, 3.4 Hz, 1H). ¹³C NMR (75 MHz, CDCl₃) δ 11.8, 12.0, 12.0, 17.9, 18.0, 18.3, 58.7, 68.6, 174.2. IR (neat, NaCl) 3400, 2945, 2868, 1726, 1465, 881, 784 cm⁻¹. HREIMS (DIP) Exact mass calc. for C₃₀H₆₇NO₃Si₃ 530.3881; found 530.3870 (M⁺-C₃H₇). $[\alpha]_D^{20}$ +4.1 (c 6.5, hexanes).

(+)-N,O,S-tris-(Triisopropylsilyl)-(S)-cysteine (10b): 85% (10.03 g, 17.02 mmol) from 2.42 g of (S)-cysteine (19.97 mmol). ¹H NMR (300 MHz, C₆D₆) δ 0.97 to 1.54 (m, 63H), 2.93 (dd, *J* = 11.0, 7.1 Hz, 1H), 3.06 (dd, *J* = 11.0, 4.3 Hz, 1H), 3.88 (ddd, *J* = 12.8, 7.1, 4.3 Hz, 1H). ¹³C NMR (75 MHz, C₆D₆) δ 12.2, 12.4, 13.0, 18.2, 18.5, 18.7, 33.8, 58.6, 173.9. ²⁹Si NMR (59.6 MHz, C₆D₆) 5.1, 22.2, 23.2. IR (neat, NaCl) 3395, 2950, 2863, 1721, 1460, 881 cm⁻¹; HRMS (EI) Exact mass calc. for C₃₀H₆₇NO₂SSi₃ 588.4122; found 588.4132 (M⁺-1); Anal. Calcd for C₃₀H₆₆NO₂SSi₃: C 61.05%; H 11.44%. Found C 61.11%; H 11.56%. $[\alpha]_D^{20}$ +6.8 (c 23.7, CCl₄).

(+)-N,O,O-tris-(Triisopropylsilyl)-(S)-tyrosine (10c): 86% (11.18 g, 17.21 mmol) from 3.62 g of (S)-tyrosine (20.0 mmol). ¹H NMR (300 MHz, CDCl₃) δ 0.97 (m, 18H), 1.06 (m, 36H), 1.23 (m, 9H), 1.56 (broad s, 1H), 2.81 (dd, *J* = 13.5, 6.2 Hz, 1H), 2.91 (dd, *J* = 13.5, 6.7 Hz, 1H), 3.70 (broad m, 1H),

6.75 (dd, $J = 6.5, 2.0$ Hz, 2H), 7.04 (dd, $J = 6.5, 2.0$ Hz, 2H). ^{13}C NMR (75 MHz, CDCl_3) δ 11.9, 12.0, 12.7, 17.8, 17.9, 18.2, 18.3, 43.5, 58.4, 119.4, 130.0, 130.4, 154.7, 175.3. IR (neat, NaCl) 3380, 2934, 2852, 1721, 1608, 1501, 1460 cm^{-1} . HRMS (EI) Exact mass calc. for $\text{C}_{33}\text{H}_{64}\text{NO}_3\text{Si}_3$ 606.4194; found ($\text{M}^+ - \text{C}_3\text{H}_7$) 606.4203. Anal. Calcd for $\text{C}_{36}\text{H}_{71}\text{NO}_3\text{Si}_3$: C 66.50%; H 11.01%. Found C 66.72%; H 11.08%. $[\alpha]_{\text{D}}^{20} +7.58$ (c 13.6, hexanes).

(+)-*N,O,O*-tris-(Triisopropylsilyl)-(2*S*,3*R*)-threonine (10d): 78% (3.20 g, 5.44 mmol) from 0.83 g of (2*S*,3*R*)-threonine (6.98 mmol). ^1H NMR (300 MHz, CDCl_3) δ 4.08 (m, 1H), 3.63 (dd, $J = 12.86, 4.15$ Hz, 1H), 1.40-1.25 (m, $J = 6.3$ Hz, 9H), 1.10-1.03 (m, 58H), ^{13}C NMR (75 MHz, CDCl_3) δ 173.6, 72.2, 61.7, 18.31, 18.30, 18.13, 18.11, 17.93, 12.5, 12.06, 11.98. GC-MS (EI) m/z : 544 ($\text{M}^+ - \text{C}_3\text{H}_7$). Anal. Cal. for $\text{C}_{31}\text{H}_{69}\text{NO}_3\text{Si}_3$: C 63.31%; H 11.82%. Found C 63.12%; H 11.92. $[\alpha]_{\text{D}}^{25} +18.97$ (c 10.7, hexanes).

(+)-*N,O,N'*-tris-(Triisopropylsilyl)-(S)-lysine (10e): 62% (1.60 g, 2.60 mmol) from 0.61 g of (S)-lysine (4.17 mmol). ^1H NMR (300 MHz, CDCl_3) δ 0.20 (bs, 1H), 1.00-1.08 (m, 58H), 1.15-1.41 (m, 10H), 1.60-1.64 (m, 2H), 2.74 (bs, 2H), 3.46-3.54 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ 11.7, 11.8, 12.0, 17.8, 18.2, 18.3, 22.4, 35.1, 38.0, 42.7, 56.5, 175.9. IR (neat, NaCl) 3392, 2942, 2892, 2866, 1721, 1463, 1249, 1191, 995, 883, 671 cm^{-1} . HRMS (EI) Exact mass calc. for $\text{C}_{33}\text{H}_{75}\text{N}_2\text{O}_2\text{Si}_3$ 615.5136; found ($\text{M}^+ + \text{H}$) 615.5136. $[\alpha]_{\text{D}}^{25} +12.4$ (c 2.1, hexanes).

Bis-Triisopropylsilyl (-)-(S)-(N)-triisopropylsilylaspartate (10f): 77% (1.88 g, 3.13 mmol) from 0.54 g of (S)-aspartic acid (4.06 mmol). ^1H NMR (300 MHz, C_6D_6) δ 0.98-1.12 (m, 54H), 1.16-1.35 (m, 9H), 1.51 (d, $J = 12.2$ Hz, 1H), 2.74 (dd, $J = 6.1, 17.0$ Hz, 1H), 2.96 (dd, $J = 3.3, 17.0$ Hz, 1H), 3.69-3.74 (m, 1H). ^{13}C NMR (75 MHz, C_6D_6) δ 12.17, 12.25, 12.4, 18.0, 18.1, 18.5, 43.6, 53.3, 171.1, 174.1. HRMS (EI) Exact mass calc. for $\text{C}_{31}\text{H}_{68}\text{NO}_4\text{Si}_3$ 602.4456; found ($\text{M}^+ + \text{H}$) 602.4453. $[\alpha]_{\text{D}}^{25} -2.1$ (c 8.9, hexanes).

General Procedure to prepare trisilylated tryptophans (11). To a solution of **2m** in THF (0.2 M) at -78°C , 1 equiv of *tert*-butyllithium (1.7 M solution in hexanes) was added dropwise. The solution turned dark yellow to orange. After 15 min, 1 equiv of R_3SiX was slowly added. The solution became colorless to pale yellow. The reaction was quenched with 1 mL of dry MeOH and allowed to reach room temperature. The reaction mixture was concentrated under vacuum. The remaining oil was diluted in dry hexanes (20 mL/equiv of substance) and filtered *via canula* through neutral alumina. To explore the possibility of the organolithium process resulting in partial racemization, after the above deprotonation was complete, 1 equiv. of MeOH was slowly added and the solution became colorless to pale yellow. The reaction mixture was neutralized with 1 equiv. of TMSCl and allowed to reach room temperature.

Concentration under vacuum gave an oil which was diluted in pentane (10 mL/equiv. of substance) and filtered under nitrogen through neutral alumina. After vacuuming off the pentane, the concentrated organic layer was distilled under high vacuum to recover **2m** (94%) whose specific rotation remained unchanged from its original value (see above).

(+)-*N,O*-bis-Triisopropylsilyl-*N*_I-trimethylsilyl-(*S*)-tryptophan (11a). 97% (2.91 g, 4.95 mmol) from 2.64 g of **2m** (5.11 mmol). ¹H NMR (300 MHz, CDCl₃) δ 0.54 (s, 9H), 1.00-1.06 (m, 39H), 1.12-1.30 (m, 4H), 3.01 (dd, *J* = 6.4, 14.2 Hz, 1H), 3.22 (dd, *J* = 6.6, 14.2 Hz, 1H), 3.93 (ddd, *J* = 6.4, 6.6, 13.0 Hz, 1H), 7.02 (s, 1H), 7.12-7.21 (m, 2H), 7.43-7.46 (m, 1H), 7.64-7.67 (m, 1H). ¹³C NMR (75 MHz, C₆D₆) δ -0.60, -0.2, 0.18, 11.49, 11.87, 11.93, 12.25, 12.33, 17.72, 17.74, 18.14, 18.26, 34.4, 57.4, 112.8, 113.8, 119.1, 119.4, 121.3, 128.2, 131.5, 140.5, 175.9. IR (neat, NaCl) 3396, 2945, 2858, 1721, 1608, 1552, 1455, 1255, 1178 cm⁻¹. HRMS (EI) Exact mass calc. for C₂₉H₅₃N₂O₂Si₃ 545.3415; found 545.3395 (M⁺-C₃H₇). [α]³¹_D +17.2 (c 4.6, pentane).

(+)-*N,O*-bis-Triisopropylsilyl-*N*_I-triethylsilyl-(*S*)-tryptophan (11b). 93% (2.96 g, 4.69 mmol) from 2.60 g of **2m** (5.03 mmol). ¹H NMR (300 MHz, CDCl₃) δ 0.28-1.25 (m, 58H), 3.14 (dd, *J* = 6.4, 14 Hz, 1H), 3.42 (dd, *J* = 6.1, 14 Hz, 1H), (ddd, *J* = 6.1, 6.4, 12.6 Hz, 1H), 7.19-7.29 (m, 3H), 7.42-7.52 (m, 1H), 7.80-7.95 (m, 1H). ¹³C NMR (75 MHz, C₆D₆) δ 4.6, 6.9, 12.3, 12.4, 17.7, 18.1, 18.5, 18.6, 34.3, 57.4, 113.1, 114.5, 119.4, 120.0, 121.9, 128.7, 132.2, 141.3, 175.6. IR (neat, NaCl) 3391, 2934, 2868, 1716, 1608, 1445, 1301, 1173, 1142, 1009 cm⁻¹. HRMS (EI) Exact mass calc. for C₃₂H₅₉N₂O₂Si₃ 587.3884, found 587.3722. [α]²⁵_D +12.9 (c 26.7, CCl₄).

(+)-*N,O,N*_I-tris-Triisopropylsilyl-(*S*)-tryptophan (11c). 66% (2.15 g, 3.2 mmol) from 2.5 g of **2m** (4.83 mmol). ¹H NMR (300 MHz, CDCl₃) δ 0.99 (m, 21H), 1.08 (d, *J* = 7.3 Hz, 18H), 1.18 (d, *J* = 7.5 Hz, 9H), 1.18 (d, *J* = 7.5 Hz, 9H), 1.31 (m, 3H), 1.72 (septet, *J* = 7.5 Hz, 3H), 3.05 (dd, *J* = 14.5, 6.3 Hz, 1H), 3.30 (dd, *J* = 14.5, 6.0 Hz, 1H), 3.99 (m, 1H), 7.14 (m, 4H), 7.48 (m, 1H), 7.64 (m, 1H). ¹³C NMR (75 MHz, C₆D₆) δ 12.3, 12.4, 13.2, 18.1, 18.3, 18.5, 18.6, 34.2, 57.5, 114.1, 114.4, 119.3, 120.0, 122.0, 129.4, 132.3, 141.7, 175.5. ²⁹Si NMR (99 MHz, C₆D₆) 4.7, 12.2, 20.9. IR (neat, NaCl) 3396, 3078, 3042, 2945, 2889, 2863, 1721, 1460 cm⁻¹. HRMS (EI) Exact mass calc. for C₃₈H₇₂N₂O₂Si₃ 672.4902; Found 672.4874 (M⁺). Anal. Calcd for C₃₈H₇₂N₂O₂Si₃: C 67.79%; H 10.78%. Found C 67.94%; H 10.91%. [α]²⁰_D +10.2 (c 16.0, CCl₄).

(+)-*N,O*-bis-Triisopropylsilyl-*N*_I-*tert*-butyldimethylsilyl-(*S*)-tryptophan (11d). 51% (2.28 g, 3.62 mmol) from 3.67 g of **2m** (7.10 mmol). ¹H NMR (300 MHz, CDCl₃) δ 0.52-0.60 (m, 6H), 0.92-0.99 (m,

27H), 1.00 (d, $J = 1.3$ Hz, 9H), (bs, 9H), 1.18-1.34 (m, 7H), 2.97 (dd, $J = 6.4, 14.3$ Hz, 1H), 3.18 (dd, $J = 6.5, 14.3$ Hz, 1H), 3.85-3.95 (m, 1H), 7.01 (s, 1H), 7.06-7.17 (m, 3H), 7.41-7.44 (m, 1H), 7.55-7.64 (m, 1H). ^{13}C NMR (75 MHz, CDCl_3) δ -4.0, 11.9, 12.0, 17.7, 18.1, 18.3, 19.4, 26.3, 34.4, 57.6, 114.1, 114.5, 119.4, 120.0, 121.9, 129.4, 132.2, 141.9, 175.5. IR (neat, NaCl) 3386, 3085, 3052, 2940, 2860, 1720, 1611, 1500, 1447, 1255, 1134 cm^{-1} . HRMS (EI) Exact mass calc. for $\text{C}_{32}\text{H}_{59}\text{N}_2\text{O}_2\text{Si}_3$ 587.3884. Found 587.3873. $[\alpha]_{\text{D}}^{25} +14.6$ (c 10.6, hexanes).

Deprotonation of 2j with *n*-BuLi, silylation and disilylation. To **2j** (0.132 g, 1.00 mmol) and tetradecane (0.170 g, 1.00 mmol) in THF (10 mL) at -78 °C, *n*-BuLi (0.5 mL of 2.1 M in hexanes, 1.1 mmol) was added slowly with vigorous stirring. After 30 min, the solution was allowed to reach -32 °C, whereupon it was recooled to -78 °C. TMSCl (0.212 g, 1.1 mmol) was added dropwise via syringe. After 1 h, the mixture was allowed to warm to 25 °C. GC analysis revealed a 92% conversion to a new compound whose MS and IR were consistent with *N*-trimethylsilylation to give **12** (MS m/z (relative intensity) 517 (M^+ , 15), 502 ($\text{M}-\text{Me}^+$, 15), 474 ($\text{M}-(i\text{-Pr})^+$, 100); IR (KCl) 1734 cm^{-1}). An aqueous solution of NH_4Cl (5 mL, 10 w/v) was added to the reaction mixture which was stirred vigorously for 3 h. The mixture was extracted with hexane (25 mL), and this solution was washed with water (6 X 25 mL) dried (K_2CO_3) and concentrated (0.05 Torr, 2 h) to remove the solvents and tetradecane. The recovered **2j** (80%, 99% GC purity) was found to have identical spectroscopic properties to the original material as well as the same optical rotation.

Triisopropylsilyl 3-methylcrotonate (13). To a well stirred solution of imidazole (4.09 g, 60 mmol), 3-methylcrotonic acid (3.02 g, 30 mmol) in dry DMF (15 mL) at 25 °C, TIPSCl (5.78 g, 30 mmol) was added dropwise. The resulting reaction mixture was allowed to stir for 5 h. Extraction with hexane (3 x 10 mL) and careful concentration using vacuum produced 6.11 g (80 %) of **13**. Anal. Calcd for $\text{C}_{14}\text{H}_{28}\text{O}_2\text{Si}$: C, 65.57; H, 11.00. Found: C, 65.83; H, 11.08. ^1H NMR (CDCl_3) δ 1.09 (d, $J = 7.3$ Hz, 18H), 1.28 (sept, $J = 7.4$ Hz, 3H), 1.88 (d, $J = 1.0$ Hz, 3H), 2.14 (d, $J = 1.0$ Hz, 3H), 5.71 (m, 1H). ^{13}C NMR (CDCl_3) δ 11.8, 17.7, 19.8, 27.1, 117.7, 155.9, 166.1. IR 1690, 1640, 1220, 870 cm^{-1} . MS (relative intensity) m/z 213 (100), 99 (6), 83 (56), 75 (78), 73 (8).

1,1-bis-(Triisopropylsiloxy)-3-methyl-1,3-butadiene (14). To a well-stirred solution of *n*-BuLi (3.24 mL, 1.7 M, 5.5 mmol) in dry THF (25 mL) at -78 °C, **13** (1.28 g, 5.0 mmol) was added dropwise over 20 min. After 3 h, TIPSCl (0.97 g, 5.0 mmol) was added and the mixture was allowed to warm to 25 °C. Hexane (25 mL) was added and the resulting mixture was extracted with brine (3 X 15 mL). The organic layer was dried (Na_2SO_4), concentrated and distilled to give 1.5 g (73%) of **14** (bp 127 °C, 0.025 Torr). Upon

standing, **14** solidifies (mp 44–45 °C). ¹H NMR (500 MHz, CDCl₃) δ 1.12 (d, *J* = 7.4 Hz, 18H), 1.13 (d, *J* = 7.4 Hz, 18H), 1.25 (m, 6H), 1.92 (d, *J* = 0.6 Hz, 3H), 4.27 (s, 1H), 4.38 (dd, *J* = 2.8, 1.4 Hz, 1H), 4.70 (dq, *J* = 2.8, 0.6 Hz, 1H). ¹³C NMR (CDCl₃) δ 13.0, 13.6, 18.0, 23.7, 86.7, 106.6, 140.8, 152.2. IR (CCl₄) 3090, 1640, 1190, 600 cm⁻¹. MS (relative intensity) *m/z* 412 (20), 397 (35), 75 (23), 50 (100). HRMS (EI) Exact mass calc. for C₂₃H₄₈O₂Si₂ 412.3192; found 412.3181.

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