JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

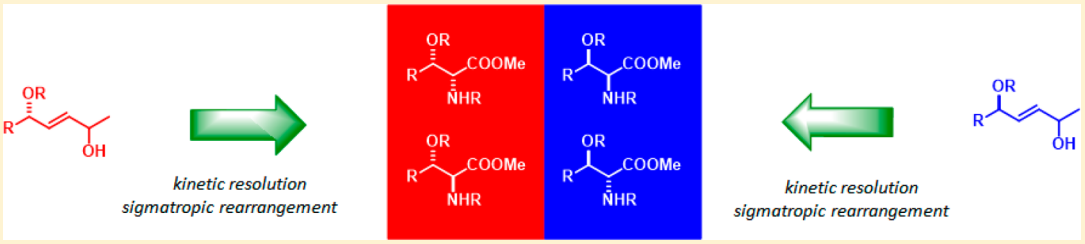
Synthesis of β- and γ-Hydroxy α-Amino Acids via Enzymatic Kinetic Resolution and Cyanate-to-Isocyanate Rearrangement

Piotr Szcześniak,[†] Agnieszka Październiok-Holewa,[‡] Urszula Klimczak,[†] and Sebastian Stecko*[,†]

[†]Institute of Organic Chemistry, Polish Academy of Sciences, Kasprzaka 44/52, 01-224 Warsaw, Poland

[‡]Department of Organic Chemistry, Bioorganic Chemistry and Biotechnology, Silesian University of Technology, Krzywoustego 4, 44-100 Gliwice, Poland

Supporting Information



ABSTRACT: A new strategy for stereoselective preparation of all four isomers of β- and γ-hydroxy α-amino acids is presented. The developed procedure is based on enzymatic kinetic resolution and cyanate-to-isocyanate rearrangement as key steps. Stereocontrol is achieved by proper choice of the starting hydroxyacid, the course of kinetic resolution, and the stereospecific sigmatropic rearrangement step, which proceeds with full chirality transfer.

INTRODUCTION

β- and γ-hydroxy α-amino acids are important structural motifs of numerous naturally occurring molecules exhibiting interesting pharmacological properties.[1−8] An excellent example of this class of compounds is threonine and its three isomers. L-Threonine can be found in several polypeptide drugs such as sermoreline, used for the treatment of dwarfism,[9] ceruletide, a smooth muscle and digestive secretions stimulator,[10] exenatide, which is a GLP-1 antagonist for treatment of diabetes mellitus type 2,[11] or enfuvirtide, an HIV fusion inhibitor.[12] D-Threonine is also a structural motif in various natural products.[4−6] The diastereomers of threonines, *allo*-threonines, are also widespread in nature, as representatives of nonproteinogenic amino acids. L- and D-*allo*-threonine motifs were found in bioactive peptides, for instance antiviral viscosin,[13] antibiotic hormaomycin,[14] antitumor astins[15] and phytotoxic syringopeptins.[16] Also other hydroxy amino acids, such as β-phenyl serines, β-hydroxyleucines, or β-hydroxytyrosines, are found in the structure of a number of cyclic polypeptides active against HIV (e.g., callipeltines,[17] neamphamide,[18] papuamides,[19] mirabamides,[20] and celebesides[21]). Another non-natural amino acid, (2*R*,3*R*)-β-cyclohexyl-serine, constitutes a part of aplaviroc (GSK-873140), a CCR5 antagonist used in the treatment of HIV infection.[22] Finally, β-phenylserine and β-hydroxytyrosine are present in antibiotics such as vancomycin,[23] bouvardin,[24] chloramphenicol,[25] hypeptin[26] and katanosins.[27]

Functionalized β- and γ-hydroxy α-amino acids are not only attractive building blocks for the synthesis of complex organic molecules[28] but also used as chiral catalysts and ligands[29] for enantioselective transformations.[30]

The importance of hydroxylated α-amino acids, either as a structural element of bioactive peptides or as intermediates in the synthesis of complex molecules and catalysts, resulted in the development of a multitude of methods for their asymmetric synthesis. Typical approaches for the preparation of hydroxylated amino acids are based on Sharpless asymmetric dihydroxylation or epoxidation of allyl alcohols,[31] catalytic hydrogenation of α-amino-β-keto esters,[32] aldol reaction,[33] biocatalyzed transformations,[34] and others.[35−37]

Since all isomeric (enantiomeric and diasteromeric) forms of hydroxy amino acids are interesting from a biological as well as a synthetic point of view, synthetic protocols that enable the preparation of all four isomers are desirable. Herein, we report an efficient method for the selective preparation of diastereomeric hydroxy amino acids from simple precursors, hydroxy carboxylic acids, via an enzymatic kinetic resolution and enantiospecific cyanate-to-isocyanate sigmatropic rearrangement reaction sequence.

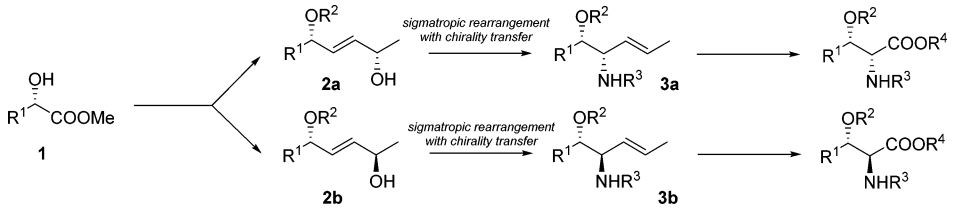
RESULTS AND DISCUSSION

The key feature of our proposal is the stereoselective formation of allyl alcohols **2a**,**b** from the corresponding chiral hydroxyacid with a general structure represented by **1** and the transformation of **2a**,**b** into allylamines **3a**,**b** by a sigmatropic rearrangement, as outlined in Scheme 1.

Received: October 19, 2014
Published: November 11, 2014

   dx.doi.org/10.1021/jo502026a | J. Org. Chem. 2014, 79, 11700−11713

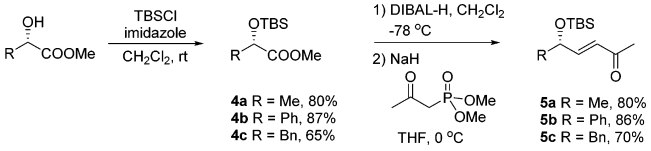
Scheme 1



The concerted nature of the rearrangement step should transpose the stereogenic center with full chirality transfer to provide the corresponding allylamine regardless of the configuration of the other stereocenter, originating from the starting hydroxyacid. Thus, varying the configuration of the initial hydroxyacid and employing independent stereoselective generation of a second allylic stereogenic center should enable the furnishing of isomeric hydroxy allylamines after the sigmatropic rearrangement. Simple transformations of the double bond in hydroxy allylamines (**3**) will allow access to the corresponding hydroxy amino acids and their derivatives.

Our first efforts were directed toward the synthesis of L-threonine and its isomers starting from methyl L- and D-lactate. Thus, methyl L-lactate was *O*-silylated with TBSCl to afford ester **4a**, which was converted into enone **5a** via a one-pot reduction and Horner–Wadsworth–Emmons olefination[38] sequence in 80% after 2 steps (Scheme 2).

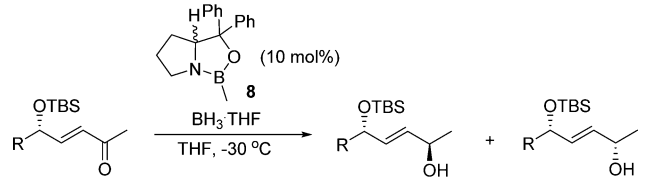
Scheme 2



Next, we focused on the stereoselective transformation of enone **5** into alcohols **6** and **7**. Disappointingly, Corey–Bakshi–Shibata reduction[39] of enone **5a** with $BH_3{\cdot}Me_2S$ in the presence of chiral oxazaborolidine (***S*)-8** yielded a hardly separable mixture of alcohols **6a** and **7a** in a 4:1 ratio (Scheme 3). Lowering the reaction temperature from −30 to −78 °C did not increase the reaction selectivity. Therefore, due to lack of synthetic attractiveness, this approach to the synthesis of diastereomeric alcohols **6** and **7** was rejected.

Searching for an effective method of stereoselective synthesis of alcohols of type **6** and **7**, we turned to enzymatic kinetic resolution[40] of diastereomeric alcohols **9**. For this purpose,

Scheme 3



enone	catalyst	6:7 ratio	yield
5a	(*S*)-Me-CBS	4:1	78%
5a	(*R*)-Me-CBS	1:4	80%
5b	(*S*)-Me-CBS	81:19	92%
5b	(*R*)-Me-CBS	13:87	74%

enone **5a** was subjected to Luche reduction[41] to afford a mixture of alcohols **9a** (Scheme 4). Enzymatic kinetic resolution of **9a** with vinyl acetate in the presence of lipase Novozyme 435 provided alcohol **7a** (*dr* > 95%, NMR) along with acetate **10a** (Scheme 4). Basic hydrolysis of the latter gave alcohol **6a** in 88% yield (*dr* > 95%, NMR, Scheme 4).

Subsequently, the transformation of allyl alcohol **6a** and **7a** into the corresponding allylamines was carried out. In the preliminary report,[42] we demonstrated that such a transformation can be efficiently performed through a cyanate-to-isocyanate rearrangement reaction.[43] We also demonstrated that this procedure has several significant advantages over other known processes, for example, Overman rearrangement (vide infra).[44]

Thus, allylic alcohols **6a** and **7a** were transformed into carbamates **11a** and **12a** by treatment with trichloroacetyl isocyanate (TCA-NCO) (Scheme 5). The resulting carbamates are stable and easier to handle than the corresponding trichloroacetimidates used in the Overman reaction.

Dehydration of **11a** by treatment with trifluoroacetyl anhydride (TFAA) in the presence of Et_3N at 0 °C for 1 h provided allyl cyanate **13**, which spontaneously rearranged to allyl isocyanate **14** (Scheme 6). This compound was not isolated, but directly trapped with MeOLi to provide stereospecifically carbamate **15** in 75% overall yield after 3 steps. Following the same one-pot, three-step protocol, carbamate **12a** was transformed into cyanate **16**, which rearranged to isocyanate **17**. Direct treatment of **17** with MeOLi gave carbamate **18** in 60% yield after 3 steps. Mild and transition-metal-free reaction conditions, in contrast to Overman rearrangement, are additional advantages of the employed process. Moreover, treatment of the resulting allyl isocyanate (e.g., **14** or **17**) with various nucleophiles opens a direct route to variously *N*-functionalized allylamines and, in consequence, differently protected amino acids (Table 1).

Finally, ozonolysis of **15** and **18** in the presence of 2.5 M methanolic NaOH (Marshall's procedure[45]) gave methyl L-*allo*-threonate **29** and methyl D-threonate **30**, respectively (Scheme 7). Similarly, allylamines **19**–**21** and **22**–**24** were converted into the corresponding amino esters **31**–**33** and **34**–**36** (Scheme 7).

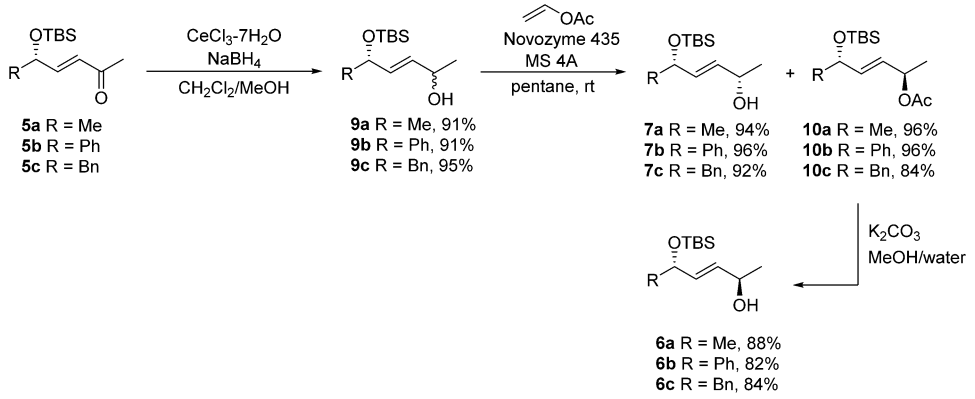
Next, we prepared another two isomers of threonine, methyl L-threonate ***ent*-34** and methyl D-*allo*-threonate ***ent*-31**, starting from methyl D-lactate and following the reaction sequence presented in Scheme 8.

The same approach was used to prepare *β*-phenyl-serines **38**, **40** and *γ*-phenyl-threonines **39** and **41**, starting from methyl L-mandelate and methyl L-phenyllactate, respectively (see Schemes 4, 5, and 7).

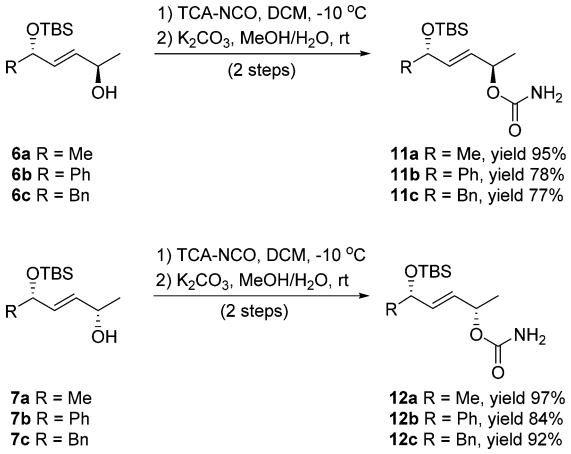
The above strategy is also applicable to the preparation of *γ*-hydroxy *α*-amino acids. This was exemplified by the synthesis of the corresponding amino acids **43a**/**45a** and **43b**/**45b** starting from commercially available methyl (*S*)-3-hydroxy-2-

dx.doi.org/10.1021/jo502026a | J. Org. Chem. 2014, 79, 11700–11713

Scheme 4



Scheme 5

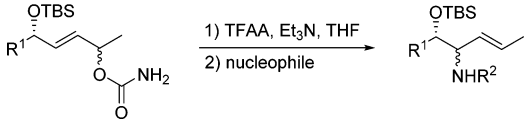


methylpropanoate (Roche methyl ester) and methyl (*R*)-3-hydroxybutanoate, as shown in Scheme 9.

CONCLUSIONS

In conclusion, we described a new strategy for stereoselective preparation of all isomers of *β*-hydroxy *α*-amino acids. The developed procedure is based on enzymatic kinetic resolution and cyanate-to-isocyanate rearrangement as key steps. Proper choice of the starting hydroxyacid and the course of kinetic resolution enables the synthesis of all isomeric allyl diols. These, in turn, allow the stereoselective synthesis of all isomeric *β*-hydroxy *α*-amino acids, such as threonines, after rearrangement and further oxidation of the double bond. We have also presented an extension of this strategy that enables preparation

Table 1. Synthesis of *N*-Protected Allylamines via Dehydration/Cyanate-to-Isocyanate Rearrangement[a]

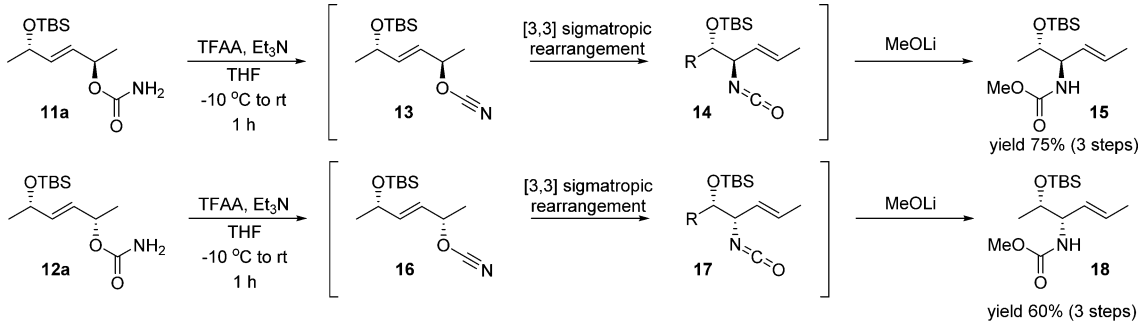


entry	carbamate	nucleophile	R^2	yield [%][b]
1	**11a**	MeOLi	Moc (**15**)	75
2	**11a**	BnOLi	Cbz (**19**)	76
3	**11a**	*t*-BuOLi	Boc (**20**)	84
4	**11a**	MeMgBr	Ac (**21**)	83
5	**12a**	MeOLi	Moc (**18**)	86
6	**12a**	BnOLi	Cbz (**22**)	70
7	**12a**	*t*-BuOLi	Boc (**23**)	76
8	**12a**	MeMgBr	Ac (**24**)	86
9	**11b**	BnOLi	Cbz (**25**)	77
10	**12b**	BnOLi	Cbz (**26**)	67
11	**11c**	BnOLi	Cbz (**27**)	82
12	**12c**	BnOLi	Cbz (**28**)	60

[a]Reaction conditions: A cooled solution of carbamate (1 equiv) and Et_3N (6 equiv) in dry THF was treated with TFAA (2 equiv). After 1 h, a solution of nucleophile (ROLi or RMgBr) was added; [b]Isolated yield after 3 steps. TFAA = trifluoroacetyl anhydride

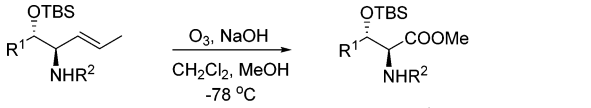
of *γ*-hydroxy *α*-amino acids. The incorporation of the amino functionality in the cyanate-to-isocyanate rearrangement step has several advantages. The reaction proceeds under mild conditions and does not require any transition-metal catalyst. The allyl carbamates, precursors of allyl isocyanates, are easily prepared and handled. As shown, the stereochemical course of sigmatropic rearrangement does not depend on the other

Scheme 6

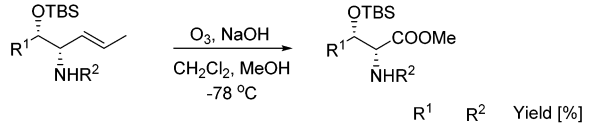


dx.doi.org/10.1021/jo502026a | J. Org. Chem. 2014, 79, 11700−11713

Scheme 7



		R1	R2	Yield [%]
15 R1 = Me, R2 = Moc	**29**	Me	Moc	85
19 R1 = Me, R2 = Cbz	**31**	Me	Cbz	71
20 R1 = Me, R2 = Boc	**32**	Me	Boc	92
21 R1 = Me, R2 = Ac	**33**	Me	Ac	82
25 R1 = Ph, R2 = Cbz	**38**	Ph	Cbz	86
26 R1 = Bn, R2 = Cbz	**39**	Bn	Cbz	89



		R1	R2	Yield [%]
18 R1 = Me, R2 = Moc	**30**	Me	Moc	88
22 R1 = Me, R2 = Cbz	**34**	Me	Cbz	82
23 R1 = Me, R2 = Boc	**35**	Me	Boc	80
24 R1 = Me, R2 = Ac	**36**	Me	Ac	86
27 R1 = Ph, R2 = Cbz	**40**	Ph	Cbz	77
28 R1 = Bn, R2 = Cbz	**41**	Bn	Cbz	82

stereogenic center present in the initial allyl carbamate. Thus, the effective chirality transfer allows for stereospecific preparation of either *erythro* or *threo* hydroxy allylamines. In addition, the allyl isocyanates, formed during the sigmatropic rearrangement, can be easily and directly functionalized by treatment with a nucleophile, which enables the preparation of differently protected allylamines.

EXPERIMENTAL SECTION

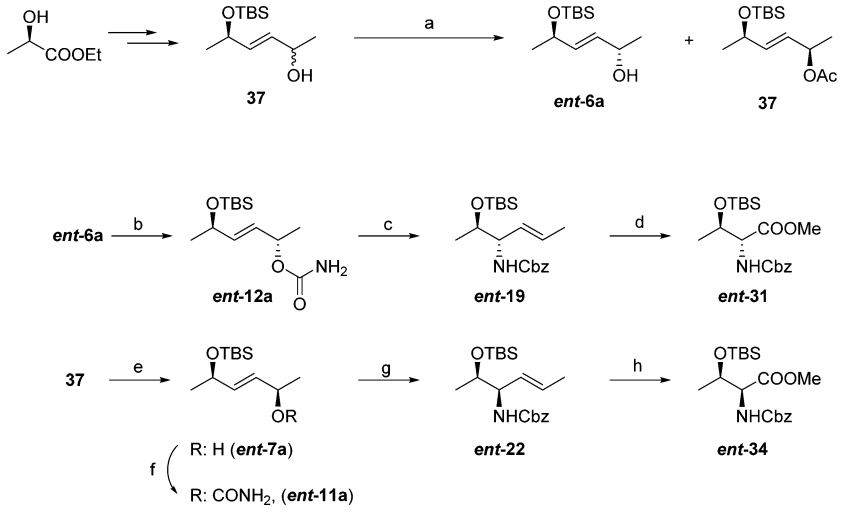
Methyl (*S*)-O-(*t*-Butyldimethylsilyl)-lactate (4a). Methyl L-lactate (20 g, 19.4 mL, 169 mmol) and imidazole (22 g, 320 mmol) were dissolved in dry CH_2Cl_2 (350 mL). The solution was cooled to −15 °C and a solution of TBSCl (23 g, 155 mmol) in dry CH_2Cl_2 was added. The reaction mixture was stirred for 3 h at room temperature. After that time, water (200 mL) was added and the organic phase was separated and dried over anhydr. Na_2SO_4. After removal of the solvent, the residue was chromatographed on silica gel (5% AcOEt in cyclohexane) to afford 31.3 g (80%) of product **4a** as a colorless oil. $[\alpha]_D^{22}$ −31.5 (*c* 1.4, CH_2Cl_2) [lit. −31.7 (*c* 0.66, $CHCl_3$)[46]]; *Spectral data:*[47] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.33 (m, 3H, CH_3O), 4.24−4.10 (m, 1H, CH_3CH), 1.39 (d, *J* 6.8 Hz, 3H, CH_3CH), 0.90 (s, 9H, *t*-BuSi), 0.10 (s, 3H, CH_3Si), 0.07 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 174.6, 68.4, 51.8, 25.7, 21.4, 18.3, −5.1, −5.3; HRMS (ESI-TOF) *m*/*z* calcd for $C_{11}H_{24}O_3SiNa$ [M + Na^+] 255.1392. Found 255.1390.

Ethyl (*R*)-O-(*t*-Butyldimethylsilyl)-lactate (*ent*-4a). Prepared in the same manner as compound **4a**. $[\alpha]_D^{22}$ +30.1 (*c* 1.0, CH2Cl2); HRMS (ESI-TOF) *m*/*z* calcd for $C_{11}H_{24}O_3SiNa$ [M + Na^+] 255.1392. Found 255.1392.

Methyl (*S*)-2-(*t*-Butyldimethylsilyloxy)-2-phenylacetate (4b). To a solution of methyl (*S*)-(+)-mandelate (5 g, 30 mmol) and imidazole (4.1 g, 60 mmol) in dry CH_2Cl_2 (100 mL), a solution of TBSCl (4.3 g, 28.5 mmol) in CH_2Cl_2 (20 mL) was added. The reaction mixture was stirred overnight. Water (50 mL) was added, and the resulting mixture was stirred for 15 min. The organic layer was separated, and the aqueous layer was washed with CH_2Cl_2 (2 × 50 mL). The combined organic extracts were washed with brine (25 mL) and dried over anhydr. $MgSO_4$, and solvent was removed under diminished pressure. The residue was chromatographed on silica gel (5% AcOEt in hexanes) to afford 7.3 g of product **4b** (87%) as a colorless oil. $[\alpha]_D^{23}$ +52.8 (*c* 1.95, CH_2Cl_2) [lit.[48] +51.3 (*c* 1.03, $CHCl_3$)]; *Spectral data:*[48] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.51−7.27 (m, 5H, Ph), 5.25 (s, 1H, PhC*H*), 3.69 (s, 3H, CH_3O), 0.92 (s, 9H, *t*-BuSi), 0.12 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 172.7, 139.3, 128.5, 128.2, 126.5, 74.6, 52.3, 25.8, 18.5, −4.9, −5.0; IR (ATR) *v*: 1761 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{15}H_{24}O_3SiNa$ [M + Na^+] 303.1392. Found 303.1394.

Methyl (*S*)-2-((*t*-Butyldimethylsilyl)oxy)-3-phenylpropanoate (4c). Methyl L-phenyllactate (5.5 g, 30.5 mmol) and imidazole (2.7 g, 40 mmol) were dissolved in dry CH_2Cl_2 (150 mL). The solution was cooled to −15 °C, and a solution of TBSCl (4.5 g, 30 mmol) in dry CH_2Cl_2 (15 mL) was added. The reaction mixture was stirred for 3 h at room temperature. After that time, water (10 mL) was added, and the organic phase was separated and dried over anhydr. Na_2SO_4. After removal of solvent, the residue was chromatographed on silica gel (5% AcOEt in cyclohexane) to afford 5.7 g (65%) of product **4c** as a colorless oil. $[\alpha]_D^{24}$ −32.8 (*c* 2.05, CH_2Cl_2); ^{1}H

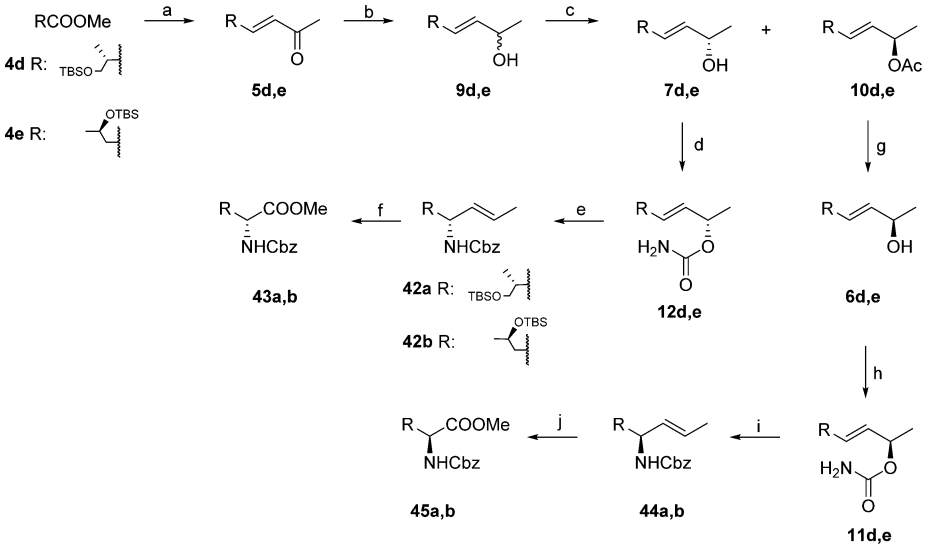
Scheme 8[a]



[a]Reagents and conditions: (a) vinyl acetate, Novozyme 435, MS 4 Å, pentane, rt (92% of ***ent*-6a** and 94% of **37**); (b) i. TCA-NCO, CH_2Cl_2, 0 °C; ii. aq. K_2CO_3, MeOH, rt (91%); (c) i. TFAA, Et_3N, THF, −10 °C; ii. BnOH, LiHMDS, THF (80%); (d) O_3, NaOH, CH_2Cl_2/MeOH, −78 °C (73%); (e) aq. K_2CO_3, MeOH, rt (84%); (f) i. TCA-NCO, CH_2Cl_2, 0 °C; ii. aq. K_2CO_3, MeOH, rt (90%); (g) i. TFAA, Et_3N, THF, −10 °C; ii. BnOH, LiHMDS, THF (75%); (h) O_3, NaOH, CH_2Cl_2/MeOH, −78 °C (83%). TCA-NCO = trichloroacetyl isocyanate, TFAA = trifluoroacetyl anhydride.

dx.doi.org/10.1021/jo502026a | *J. Org. Chem.* 2014, 79, 11700−11713

Scheme 9[a]



[a]Reagents and conditions: (a) i. DIBAL-H, CH_2Cl_2, −78 °C; ii. dimethyl(2-oxopropyl)phosphonate, NaH, THF, (77% for **4d**, 75% for **4e**); (b) $CeCl_3{\cdot}7H_2O$, $NaBH_4$, CH_2Cl_2/MeOH, rt (90% for **9d**, 86% for **9e**); (c) vinyl acetate, Novozyme 435, MS 4 Å, pentane (94% for **10d**, 94% for **7d**, 92% for **10e**, and 96% for **7e**); (d) i. TCA-NCO, CH_2Cl_2, 0 °C; ii. aq. K_2CO_3, MeOH, rt (79% for **12d**, 84% for **12e**); (e) i. TFAA, Et_3N, THF, −10 °C; ii. BnOH, LiHMDS, THF (87% for **42a**, 78% for **42b**); (f) O_3, NaOH, CH_2Cl_2/MeOH, −78 °C (87% for **43a**, 60% for **43b**); (g) aq. K_2CO_3, MeOH, rt (85% for **6d**, 65% for **6e**); (h) i. TCA-NCO, CH_2Cl_2, 0 °C; ii. aq. K_2CO_3, MeOH, rt (97% for **11d**, 74% for **11e**); (i) i. TFAA, Et_3N, THF, −10 °C; ii. BnOH, LiHMDS, THF (88% for **44a**, 87% for **44b**); (j) O_3, NaOH, CH_2Cl_2/MeOH, −78 °C (87% for **45a**, 93% for **45b**); TCA-NCO = trichloroacetyl isocyanate, TFAA = trifluoroacetyl anhydride.

NMR (500 MHz, $CDCl_3$) δ: 7.35−7.12 (m, 5H, Ph), 4.34 (dd, *J* 9.0, 3.9 Hz, 1H, C*H*COOMe), 3.72 (s, 3H, CH_3O), 3.07 (dd, *J* 13.4, 3.9 Hz, 1H, PhCH*H*), 2.88 (dd, *J* 13.4, 9.0 Hz, 1H, PhC*H*H), 0.79 (s, 9H, *t*-*Bu*Si), −0.12 (s, 3H, CH_3Si), −0.21 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 173.7, 137.6, 129.9, 128.3, 126.7, 74.0, 41.8, 27.1, 25.7, 18.4, −5.4, −5.5; IR (film) v: 1762 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{16}H_{26}O_3SiLi$ [M + Li$^+$] 301.1811. Found 301.1804.

Methyl (*S*)-3-((*t*-Butyldimethylsilyl)oxy)-2-methylpropanoate (4d). Methyl (S)-(+)-3-hydroxy-2-methylpropionate (5.0 g, 42.3 mmol) and imidazole (3.4 g, 50.0 mmol) were dissolved in dry CH_2Cl_2 (150 mL). The solution was cooled to −15 °C, and a solution of TBSCl (6.45 g, 43.0 mmol) in dry CH_2Cl_2 (20 mL) was added. The reaction mixture was stirred for 3 h at room temperature. After that time, water (100 mL) was added, and the organic phase was separated and dried over anhydr. Na_2SO_4. After removal of solvent, the residue was chromatographed on silica gel (10% AcOEt in cyclohexane) to afford 8.6 g (88%) of product **4d** as a colorless oil. $[\alpha]_D^{24}$ +20.3 (*c* 1.3 CH_2Cl_2) [lit.[49] +18.8 (*c* 1, $CHCl_3$)]; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 3.77 (dd, *J* 9.7, 6.9 Hz, 1H, TBSOC*H*H), 3.67 (s, 3H, CH_3O), 3.65 (dd, *J* 9.7, 6.1 Hz, 1H, TBSOCH*H*), 2.70−2.59 (m, 1H, CH_3CH), 1.14 (d, *J* 7.0 Hz, 3H, CH_3CH), 0.87 (s, 9H, *t*-BuSi), 0.07−0.01 (m, 6H, 2× CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 175.4, 65.2, 51.5, 42.5, 25.7, 18.2, 13.4, −5.5; IR (film) *v*: 1743, 1256, 1099, 838, 777 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{11}H_{24}O_3SiNa$ [M + Na$^+$] 255.1392. Found 255.1388.

Methyl (*R*)-3-((*t*-Butyldimethylsilyl)oxy)butanoate (4e). Methyl (*R*)-(−)-3-hydroxybutyrate (6.0 g, 50.79 mmol) and imidazole (5.2 g, 76.38 mmol) were dissolved in dry CH_2Cl_2 (200 mL). The solution was cooled to −15 °C, and a solution of TBSCl (7.6 g, 50.79 mmol) in dry CH_2Cl_2 (25 mL) was added. The reaction mixture was stirred for 3 h at room temperature. After that time, water (100 mL) was added, and the organic phase was separated and dried over anhydr. Na_2SO_4. After removal of the solvent, the residue was chromatographed on silica gel (10% AcOEt in cyclohexane) to afford 4.27 g (63%) of product as a colorless oil. $[\alpha]_D^{24}$ −32.5 (*c* 1.34, CH_2Cl_2) [lit.[50] −32 (*c* 1.3, $CHCl_3$)]; *Spectral data:*[47] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 4.37−4.19 (m, 1H, CH_3CH), 3.66 (s, 3H, CH_3O), 2.48 (dd, *J* 14.5, 7.7 Hz, 1H, CH*H*COOMe), 2.37 (dd, *J* 14.5, 5.3 Hz, 1H, C*H*HCOOMe), 1.19 (d, *J* 6.1 Hz, 3H, CH_3CH), 0.86 (s, 9H, *t*-*Bu*Si), 0.06 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ 172.2, 66.0, 51.5, 44.9, 25.8, 24.1, 18.1, −4.4, −4.9; IR (film) *v*: 2955, 2930, 1743, 1256, 1085, 837, 776 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{11}H_{24}O_3SiNa$ [M + Na$^+$] 255.1392. Found 255.1392.

(*S*,*E*)-5-((*t*-Butyldimethylsilyl)oxy)hex-3-en-2-one (5a). To a solution of ester **4a** (10 g, 43 mmol) in dry CH_2Cl_2 (200 mL) at −78 °C, a 1 M solution of DIBAL-H in hexanes (43 mL, 43 mmol) was added over 1 h (syringe pump). In a second flask, to a suspension of NaH (2.24 g, 60% disp. in mineral oil, 56 mmol) in dry THF (200 mL), dimethyl (2-oxopropyl)phosphonate (9.3 g, 7.7 mL, 56 mmol) was slowly added, and the mixture was stirred at room temperature for 1 h to produce the HWE reagent solution. When reduction was completed (TLC control, 20% AcOEt in hexanes), a solution of HWE reagent was cannulated into the aldehyde solution at −78 °C. The resulting mixture was allowed to warm up slowly to room temperature and was stirred for 3 h. Sat. aq. Rochelle salt (100 mL) was carefully added to the mixture, and stirring was continued for 30 min. The mixture was diluted with Et_2O (300 mL). The organic layer was separated, and the aqueous solution was extracted with Et_2O (4 × 50 mL). The combined organic extracts were dried over Na_2SO_4, and solvents were removed under reduced pressure. The residue was purified by chromatography on silica gel (10% AcOEt/hexanes) to give 7.95 g of **5a** (80%) as a colorless oil. $[\alpha]_D^{22}$ +8.8 (*c* 2.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.73 (dd, *J* 15.8, 3.9 Hz, 1H, C*H*═CHCOMe), 6.22 (d, *J* 15.8 Hz, 1H, CH═C*H*COMe), 4.52−4.41 (m, 1H, C*H*Me), 2.26 (m, 3H, CH_3CO), 1.27 (d, *J* 6.4 Hz, 3H, CH_3CH), 0.91 (s, 9H, *t*-*Bu*Si), 0.07 (s, 3H, CH_3Si), 0.06 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 198.9, 150.8, 128.3, 67.9, 27.4, 25.9, 23.8, 18.4, −4.7; IR (film) *v*: 1681 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{12}H_{24}O_2SiNa$ [M + Na$^+$] 251.1443. Found 251.1438.

(*R*,*E*)-5-((*t*-Butyldimethylsilyl)oxy)hex-3-en-2-one (*ent*-5a). Prepared in the same manner as compound **5a**. $[\alpha]_D^{22}$ −9.1 (*c* 1.5, $CHCl_3$); HRMS (ESI-TOF) *m*/*z* calcd for $C_{12}H_{24}O_2SiNa$ [M + Na$^+$] 251.1443. Found 251.1441.

(*R*,*E*)-5-((*t*-Butyldimethylsilyl)oxy)-5-phenylpent-3-en-2-one (5b). Compound **5b** was prepared in the same manner as compound **5a**. Yield 86%; colorless oil; $[\alpha]_D^{25}$ +46.2 (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.40−7.23 (m, 5H, Ph), 6.77 (dd, *J* 15.8, 4.8 Hz, 1H, C*H*═CHCOMe), 6.34 (dd, *J* 15.8, 1.5 Hz, 1H, CH═C*H*COMe),

dx.doi.org/10.1021/jo502026a | J. Org. Chem. 2014, 79, 11700−11713

5.39−5.29 (m, 1H, C*H*Ph), 2.23 (s, 3H, CH_3CO), 0.91 (s, 9H, *t*-*Bu*Si), 0.07 (s, 3H, CH_3Si), −0.04 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 198.9, 149.3, 141.8, 128.7, 128.2, 127.9, 126.3, 74.5, 27.2, 25.9, 18.4, −4.72, −4.74; IR (film) ν: 1678, 1254, 838 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{27}O_2Si$ [M + H$^+$] 291.1780. Found 291.1777.

(*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)-6-phenylhex-3-en-2-one (5c). Compound **5c** was prepared in the same manner as compound **5a**. Purification by chromatography on silica gel (10% AcOEt/hexanes). Yield 3.29 g (70%) starting from 4.53 g (15.38 mmol) of ester **4c**; colorless oil; $[\alpha]_D^{23}$ +4.2 (*c* 2.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.36−7.10 (m, 5H), 6.75 (dd, *J* 15.9, 4.9 Hz, 1H, CH═C*H*-COMe), 6.20 (dd, *J* 15.9, 1.5 Hz, 1H, C*H*═CH−COMe), 4.55−4.39 (m, 1H, CH_3CO), 2.89−2.76 (m, 2H, PhCH_2), 2.23 (s, 3H, CH_3CO), 0.86 (s, 9H, *t*-*Bu*Si), −0.08 (s, 3H, CH_3Si), −0.20 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 198.6, 149.2, 137.6, 129.9, 129.3, 128.4, 126.7, 73.4, 44.6, 27.4, 25.9, 18.3, −4.7, −5.2; IR (film) ν: 1680, 1254, 1118 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{28}O_2SiNa$ [M + Na$^+$] 327.1756. Found 327.1753.

(*R*,*E*)-6-(*t*-Butyldimethylsilyloxy)-5-methylhex-3-en-2-one (5d). Compound **5d** was prepared in the same manner as compound **5a**. Purification by chromatography on silica gel (10% AcOEt/hexanes). Yield 4.1 g (77%) starting from 5 g (21.6 mmol) of ester **4d**; colorless oil; $[\alpha]_D^{23}$ +25.3 (*c* 2.05, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.78 (dd, *J* 16.2, 7.1 Hz, 1H, C*H*═CHCOMe), 6.08 (dd, *J* 16.2, 1.2 Hz, 1H, CH═C*H*COMe), 3.57−3.53 (m, 2H, CH_2OTBS), 2.56−2.47 (m, 1H, −C*H*CH$_3$), 2.24 (s, 3H, CH_3CO), 1.06 (d, *J* 6.8 Hz, 3H, CH_3CH), 0.89 (s, 9H, *t*-BuSi), 0.03 (s, 6H, 2 × CH$_3$Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 198.7, 150.6, 130.7, 66.9, 39.3, 26.7, 25.8, 25.7, 15.5, −5.4; IR (film) ν: 1679, 1254, 1098 cm^{-1}; HRMS (ESI-TOF): m/z calcd for $C_{13}H_{26}O_2SiNa$ [M + Na$^+$] 265.1600. Found 265.1599.

(*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)hept-3-en-2-one (5e). Compound **5e** was prepared in the same manner as compound **5a**. Purification by chromatography on silica gel (10% AcOEt/hexanes). Yield 3.02 g (75%) starting from 3.8 g (16.35 mmol) of ester **4e**; colorless oil. $[\alpha]_D^{22}$ −14.9 (*c* 1.15, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.80 (dt, *J* 16.0, 7.4 Hz, 1H, C*H*═CHCO), 6.07 (d, *J* 16.0 Hz, 1H, CH═C*H*CO), 3.94 (hept, *J* 6.0 Hz, 1H, CH_3CH), 2.38−2.28 (m, 2H, CH_2CH═CH), 2.23 (s, 3H, CH_3CO), 1.16 (d, *J* 6.1 Hz, 3H, CH_3CH), 0.87 (s, 9H, *t*-BuSI), 0.05 (s, 3H, CH_3Si), 0.03 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 198.4, 145.2, 133.2, 67.6, 42.6, 26.6, 25.7, 23.8, 18.0, −4.5, −4.8; IR (film) ν: 1742, 1677, 1254, 836, 775 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{26}O_2SiNa$ [M + Na$^+$] 265.1600. Found 265.1591.

(5*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-ol (9a). To a suspension of enone **5a** (5 g, 21.9 mmol) and $CeCl_3{\cdot}7H_2O$ (9.86 g, 26 mmol) in CH_2Cl_2-MeOH (3:1 v/v, 100 mL), $NaBH_4$ (910 mg, 24.1 mmol) was added portionwise. After stirring at ambient temperature for 3 h, the reaction mixture was partitioned between CH_2Cl_2 (120 mL) and sat. aq. sodium potassium tartrate (50 mL). The organic layer was separated, and the aqueous layer was washed with CH_2Cl_2 (4 × 50 mL). The combined organic solutions were dried over anhydr. Na_2SO_4, and the solvent was removed under reduced pressure. The residue was chromatographed on silica gel (20% AcOEt/hexanes) to afford 4.59 g (91%) of a mixture of alcohols **9a**. HRMS (ESI-TOF) m/z calcd for $C_{12}H_{26}O_2SiNa$ [M + Na$^+$] 253.1600. Found 253.1596.

(5*R*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-ol (5-*epi*-9a). Prepared in the same manner as compound **9a**. Yield 89% (NMR); HRMS (ESI-TOF) m/z calcd for $C_{12}H_{26}O_2SiNa$ [M + Na$^+$] 253.1600. Found 253.1598.

(5*R*,*E*)-5-((*t*-Butyldimethylsilyl)oxy)-5-phenylpent-3-en-2-ol (9b). Prepared in the same manner as compound **9a** and was used directly in the next step. Yield 91%; HPLC: Chiralpak IB, 5% *i*-PrOH/hexanes, flow 1 mL/min, R_t 7.1 min (2*R*,5*R*) and 8.7 min (2*S*,5*R*).

(*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)-6-phenylhex-3-en-2-ol (9c). Prepared in the same manner as compound **9a**. Purification by chromatography on silica gel (10% AcOEt/hexanes). Yield 95%.

(5*R*,*E*)-6-(*t*-Butyldimethylsilyloxy)-5-methylhex-3-en-2-ol (9d). Prepared in the same manner as compound **9a**. Purification by chromatography on silica gel (10% AcOEt/hexanes); Yield 90%.

(6*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)hept-3-en-2-ol (9e). Prepared in the same manner as compound **9a** and used without further purification. Yield 86%.

Enzymatic Kinetic Resolution of Alcohols 9a. A suspension of alcohols **9a** (4.06 g, 17.2 mmol), Novozyme 435 (100 mg), 4 Å molecular sieves (500 mg), and vinyl acetate (25 mL) in pentane (30 mL) was stirred overnight. The progress of the reaction was followed by ^{1}H NMR. The reaction mixture was filtered through Celite, and the solvent was removed under diminished pressure. The residue was chromatographed on silica gel (15% AcOEt/hexanes) to afford 2.28 g of acetate **10a** (96%) and 1.93 g of alcohol **7a** (94%).

(2*R*,5*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-yl Acetate (10a). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.69 (dd, *J* 15.5, 5.1 Hz, 1H, C*H*═CH), 5.59 (ddd, *J* 15.5, 6.2, 1.1 Hz, 1H, CH═C*H*), 5.38−5.28 (m, 1H, C*H*OAc), 4.34−4.23 (m, 1H, C*H*OTBS), 2.02 (s, 3H, CH_3CO), 1.29 (d, *J* 6.5 Hz, 3H, CH_3), 1.19 (d, *J* 6.4 Hz, 3H, CH_3), 0.88 (s, 9H, *t*-BuSi), 0.04 (s, 3H, CH_3Si), 0.03 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.4, 136.7, 128.1, 70.6, 68.6, 26.0, 24.4, 21.5, 20.4, 18.4, −4.5, −4.6; IR (film) ν: 1739, 1241, 1101, 836 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{28}O_3SiNa$ [M + Na$^+$] 295.1705. Found 295.1703.

(2*S*,5*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-ol (7a). *dr* > 95:5 (NMR); $[\alpha]_D^{23}$ −3.5 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.70−5.60 (m, 2H, C*H*═C*H*), 4.34−4.25 (m, 2H, 2 × C*H*), 1.25 (d, *J* 6.4 Hz, 3H, CH_3), 1.20 (d, *J* 6.4 Hz, 3H, CH_3), 0.89 (s, 9H, *t*-BuSi), 0.05 (s, 3H, CH_3Si), 0.05 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ; 134.7, 132.6, 68.7, 68.4, 26.0, 24.5, 23.5, 18.4, −4.4, −4.6; IR (film) ν: 3348, 1254, 1084, 1058, 835 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{12}H_{26}O_2SiNa$ [M + Na$^+$] 253.1600. Found 253.1593.

(2*S*,5*R*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-ol (*ent*-6a). Yield 1.1 g (47%); $[\alpha]_D^{23}$ −31.6 (*c* 0.9, CH_2Cl_2); HRMS (ESI-TOF) m/z calcd for $C_{12}H_{26}O_2SiNa$ [M + Na$^+$]253.1600. Found 253.1597.

Enzymatic Kinetic Resolution of Alcohols 9b. A suspension of alcohols **9b** (1.96 g, 6.7 mmol), Novozyme 435 (100 mg), 4 Å molecular sieves (500 mg), and vinyl acetate (25 mL) in pentane (30 mL) was stirred overnight. The progress of the reaction was followed by ^{1}H NMR. The reaction mixture was filtered through a Celite pad, and solvents were removed under diminished pressure. The residue was chromatographed on silica gel (10% AcOEt/hexanes) to afford 1.07 g of acetate **10b** (96%) and 0.98 g of alcohol **7b** (96%).

(2*R*,5*R*,*E*)-5-((*t*-Butyldimethylsilyl)oxy)-5-phenylpent-3-en-2-yl Acetate (10b). Colorless oil; $[\alpha]_D^{22}$ +64.9 (*c* 1.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.30−7.16 (m, 5H, Ph), 5.77−5.66 (m, 2H, CH═CH), 5.34−5.28 (m, 1H, CH$_3$C*H*), 5.13 (d, *J* 4.5 Hz, 1H, PhC*H*), 1.97 (s, 3H, CH_3CO), 1.25 (d, *J* 6.5 Hz, 3H, CH_3CH), 0.87 (s, 9H, *t*-BuSi), 0.02 (s, 3H, CH_3Si), −0.05 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.4, 143.6, 135.3, 128.9, 128.4, 127.3, 126.2, 74.9, 70.4, 26.0, 21.5, 20.3, 18.5, −4.4, −4.7; IR (film) ν: 1740, 1241, 837 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{30}O_3SiNa$ [M + Na$^+$] 357.1862. Found 357.1863.

(2*S*,5*R*,*E*)-5-((*t*-Butyldimethylsilyl)oxy)-5-phenylpent-3-en-2-ol (7b). Colorless oil; $[\alpha]_D^{22}$ +21.7 (*c* 1.49, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.26−7.14 (m, 5H, Ph), 5.78−5.64 (m, 2H, CH═CH), 5.12 (d, *J* 4.8 Hz, 1H, PhC*H*), 4.31−4.20 (m, 1H, CH$_3$C*H*), 1.20 (d, *J* 6.4 Hz, 3H, CH_3CH), 0.86 (s, 9H, *t*-BuSi), 0.01 (s, 3H, CH_3Si), −0.06 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 143.9, 133.6, 133.5, 128.35, 127.2, 126.1, 75.0, 68.3, 26.0, 23.3, 18.5, −4.4, −4.6; IR (film) ν: 3348, 1255, 836 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{28}O_2SiNa$ [M + Na$^+$] 315.1756. Found 315.1760.

Enzymatic Kinetic Resolution of Alcohols 9c. A suspension of alcohols **9c** (2.8, 9.14 mmol), Novozyme 435 (135 mg), 4 Å molecular sieves (680 mg), and vinyl acetate (14 mL) in pentane (40 mL) was stirred overnight. The progress of the reaction was followed by ^{1}H NMR. The reaction mixture was filtered through a Celite pad, and solvents were removed under diminished pressure. The residue was

dx.doi.org/10.1021/jo502026a | *J. Org. Chem.* 2014, 79, 11700−11713

chromatographed on silica gel (10% → 20% AcOEt/hexanes) to afford 1.33 g of acetate **10c** (84%) and 1.28 g of alcohol **7c** (92%).

(2*R*,5*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)-6-phenylhex-3-en-2-yl Acetate (10c). Colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.30−7.09 (m, 5H, Ph), 5.71 (dd, *J* 15.4, 5.7 Hz, 1H, CH=C*H*), 5.56 (ddd, *J* 15.5, 6.3, 0.8 Hz, 1H, C*H*=CH), 5.36−5.29 (m, 1H, C*H*O−), 4.26 (q, *J* 6.1 Hz, 1H, C*H*O−), 2.74 (d, *J* 6.5 Hz, 2H, CH_2Ph), 2.02 (s, 3H, CH_3CO), 1.27 (d, *J* 6.5 Hz, 3H, C*H*CH_3), 0.84 (d, *J* 9.4 Hz, 9H, *t*-BuSi), −0.12 (s, 3H, CH_3Si), −0.21 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.6, 138.6, 134.9, 130.1, 129.4, 128.2, 126.3, 74.2, 70.5, 45.2, 25.9, 21.5, 20.4, 18.34, −4.6, −5.1; HRMS (ESI-TOF) *m*/*z* calcd for $C_{20}H_{32}O_3SiNa$ [M + Na^+] 371.2018. Found 371.2012.

(2*S*,5*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)-6-phenylhex-3-en-2-ol (7c). Colorless oil; $[\alpha]_D^{23}$ −9.7 (*c* 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.34−7.04 (m, 5H, Ph), 5.73−5.56 (m, 2H, C*H*=C*H*), 4.34−4.20 (m, 2H, 2× C*H*O−), 2.76 (d, *J* 6.5 Hz, 2H, CH_2Ph), 1.22 (d, *J* 6.4 Hz, 3H, CH_3CH), 0.84 (s, 9H, *t*-BuSi), −0.09 (s, 3H, CH_3Si), −0.20 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.6, 133.8, 132.8, 129.9, 128.0, 126.1, 74.1, 68.3, 45.2, 25.8, 23.3, 18.2, −4.6, −5.2; IR (film) *v*: 3353, 1254, 1078, 835 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{18}H_{30}O_2SiNa$ [M + Na^+] 329.1913. Found 329.1908.

Enzymatic Kinetic Resolution of Alcohols 9d. A suspension of alcohols **9d** (2.45 g, 10 mmol), Novozyme 435 (150 mg), 4 Å molecular sieves (750 mg), and vinyl acetate (11 mL) in pentane (50 mL) was stirred overnight. The progress of the reaction was followed by ^{1}H NMR. The reaction mixture was filtered through a Celite pad, and solvents were removed under diminished pressure. The residue was chromatographed on silica gel (10% → 20% AcOEt/hexanes) to afford 1.36 g of acetate **10d** (94%) and 1.15 g of alcohol **7d** (94%, *dr* 95:5, NMR).

(2*R*,5*R*,*E*)-6-(*tert*-Butyldimethylsilyloxy)-5-methylhex-3-en-2-yl Acetate (10d). $[\alpha]_D^{23}$ +56.2 (*c* 1.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.64 (dd, *J* 15.6, 6.9 Hz, 1H, CH=C*H*), 5.49 (dd, *J* 15.6, 6.5 Hz, 1H, C*H*=CH), 5.32 (p, *J* 6.4 Hz, 1H, C*H*OAc), 3.47 (dd, *J* 9.7, 6.4 Hz, 1H, CH*H*OTBS), 3.41 (dd, *J* 9.7, 6.7 Hz, 1H, C*H*HOTBS), 2.37−2.25 (m, 1H, C*H*CH_3), 2.03 (s, 3H, CH_3CO), 1.29 (d, *J* 6.4 Hz, 3H, CH_3CHOAc), 0.98 (d, *J* 6.8 Hz, 3H, CH_3CH), 0.89 (s, 9H, *t*-BuSi), 0.03 (s, 6H, 2 × CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ 170.5, 135.6, 129.3, 71.2, 67.9, 39.0, 26.1, 21.5, 20.5, 18.5, 16.3, −5.2, −5.2; HRMS (ESI-TOF) *m*/*z* calcd for $C_{15}H_{30}O_3SiNa$ [M + Na^+] 309.1862. Found 309.1858.

(2*S*,5*R*,*E*)-6-(*t*-Butyldimethylsilyloxy)-5-methylhex-3-en-2-ol (7d). Colorless oil; $[\alpha]_D^{25}$ +4.5 (*c* 2.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.64−5.47 (m, 2H, C*H*=C*H*), 4.32−4.22 (m, 1H, C*H*OH), 3.48 (dd, *J* 9.7, 6.3 Hz, 1H, CH*H*OTBS), 3.40 (dd, *J* 9.7, 6.8 Hz, 1H, C*H*HOTBS), 2.37−2.21 (m, 1H, C*H*CH$_3$), 1.26 (d, *J* 6.3 Hz, 3H, CH_3CHOH), 0.99 (d, *J* 6.8 Hz, 3H, CH_3CH), 0.89 (s, 9H, *t*-BuSi), 0.04 (s, 6H, 2 × CH_3Si); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 134.1, 133.6, 69.2, 68.1, 39.0, 26.1, 23.6, 18.5, 16.6, −5.17, −5.19; IR (film) *v*: 3350, 1255, 1120, 1091, 837 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{13}H_{28}O_2SiNa$ [M + Na^+] 267.1756. Found 267.1756.

Enzymatic Kinetic Resolution of Alcohols 9e. A suspension of alcohols **9e** (2.4 g,), Novozyme 435 (146 mg), 4 Å molecular sieves (730 mg), and vinyl acetate (23 mL) in pentane (45 mL) was stirred overnight. The progress of the reaction was followed by ^{1}H NMR. The reaction mixture was filtered through a Celite pad, and solvents were removed under diminished pressure. The residue was chromatographed on silica gel (10% to 20% AcOEt/hexanes) to afford 1.28 g of acetate **10e** (92%) and 1.16 g of alcohol **7e** (96%, *dr* 94:6, NMR).

(2*R*,6*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)hept-3-en-2-yl Acetate (10e). Colorless oil; $[\alpha]_D^{22}$ +21.7 (*c* 2.2, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.74−5.62 (m, 1H, C*H*=CH), 5.47 (ddt, *J* 15.4, 6.6, 1.2 Hz, 1H, CH=C*H*), 5.35−5.26 (m, 1H, C*H*), 3.86−3.76 (m, 1H, C*H*), 2.20−2.06 (m, 2H, CH_2), 2.02 (s, 3H, CH_3CO), 1.28 (d, *J* 6.5 Hz, 3H, CH_3), 1.10 (d, *J* 6.1 Hz, 3H, CH_3), 0.87 (s, 9H, *t*-BuSi), 0.03 (s, 3H, CH_3Si), 0.03 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.3, 131.5, 129.9, 70.9, 68.3, 42.5, 25.8, 25.7, 23.6, 21.4, 20.2, 18.1, −4.5, −4.8; HRMS (ESI-TOF) *m*/*z* calcd for $C_{15}H_{30}O_3SiNa$ [M + Na^+] 309.1862. Found 309.1862.

(2*S*,6*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)hept-3-en-2-ol (7e). Colorless oil; $[\alpha]_D^{22}$ −13.7 (*c* 2.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.68−5.59 (m, 1H, C*H*=CH), 5.54 (dd, *J* 15.4, 6.4 Hz, 1H, CH=C*H*), 4.32−4.21 (m, 1H, C*H*), 3.86−3.77 (m, 1H, C*H*), 2.22−2.07 (m, 2H, CH_2), 1.25 (d, *J* 6.4 Hz, 3H, CH_3), 1.12 (d, *J* 6.1 Hz, 3H), 0.88 (s, 9H, *t*-BuSi), 0.045 (s, 3H, CH_3Si), 0.042 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ 136.3, 127.6, 68.9, 68.5, 42.4, 25.8, 23.5, 23.3, 18.1, −4.5, −4.7; IR (film) *v*: 3345, 1256, 1077, 1060, 833 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{13}H_{28}O_2SiNa$ [M + Na^+] 267.1756. Found 267.1754.

(2*R*,5*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-ol (6a). To a solution of acetate **10a** (2.15 g, 7.89 mmol) in MeOH (12 mL), a solution of K_2CO_3 (2.18 g, 15.77 mmol) in H_2O (5 mL) was added, and the resulting mixture was kept at ambient temperature. The progress of hydrolysis was followed by TLC (20% AcOEt/hexanes). After stirring overnight, MeOH was removed under diminished pressure and the aqueous solution was extracted with CH_2Cl_2 (3 × 50 mL). The combined organic extracts were dried over anhydr. Na_2SO_4, and the solvent was removed under diminished pressure. The residue was chromatographed on silica gel (10% → 20% AcOEt/hexanes) to afford 1.61 g of alcohol **6a** (88%) as a colorless oil. $[\alpha]_D^{23}$ +32 (*c* 1.1, CH_2Cl_2); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.74−5.57 (m, 2H, C*H*=C*H*), 4.40−4.22 (m, 2H, CH_3C*H*OTBS, CH_3C*H*OH), 1.27 (d, *J* 6.4 Hz, 3H, CH_3CH), 1.21 (d, *J* 6.4 Hz, 3H, CH_3CH), 0.90 (s, 9H, *t*-*Bu*Si), 0.06 (s, 3H, CH_3Si), 0.05 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.8, 132.6, 68.7, 68.6, 26.1, 24.5, 23.5, 18.4, −4.4, −4.6; IR (film) *v*: 3342, 1255, 1080, 1062, 834 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{12}H_{26}O_2SiNa$ [M + Na^+] 253.1600. Found 253.1591.

(2*R*,5*R*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-ol (*ent*-7a). Yield 752 mg (84%); colorless oil; $[\alpha]_D^{23}$ +3.7 (*c* 1.2, $CHCl_3$); HRMS (ESI-TOF) *m*/*z* calcd for $C_{12}H_{26}O_2SiNa$ [M + Na^+] 253.1600. Found 253.1598.

(2*R*,5*R*,*E*)-5-((*t*-Butyldimethylsilyl)oxy)-5-phenylpent-3-en-2-ol (6b). Prepared in the same manner as compound **6a**. Purification by chromatography on silica gel (15% AcOEt/hexanes). Yield 0.76 g (82%) starting from 1.07 g (3.21 mmol) of acetate **10b**; colorless oil; *dr* 95:5 (NMR); $[\alpha]_D^{23}$ +21.6 (*c* 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.27−7.14 (m, 5H, Ph), 5.75−5.62 (m, 2H, CH=CH), 5.12 (d, *J* 5.0 Hz, 1H, PhC*H*), 4.28−4.20 (m, 1H, CH_3C*H*), 1.21 (d, *J* 6.4 Hz, 3H, CH_3CH), 0.85 (s, 9H, *t*-BuSi), 0.00 (s, 3H, CH_3Si), −0.06 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 143.9, 133.7, 133.5, 128.4, 127.2, 126.1, 75.1, 68.4, 26.0, 23.3, 18.5, −4.4, −4.6; IR (film) *v*: 3348, 1255, 836 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{17}H_{28}O_2SiNa$ [M + Na^+] 315.1756. Found 315.1751.

(2*R*,5*S*,*E*)-5-((*t*-Butyldimethylsilyl)oxy)-6-phenylhex-3-en-2-ol (6c). Prepared in the same manner as compound **6a**. Purification by chromatography on silica gel (10% AcOEt/hexanes). Yield 0.98 g (84%) starting from 1.33 g (3.82 mmol) of acetate **10c**; as colorless oil; $[\alpha]_D^{23}$ +0.6 (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.29−7.14 (m, 5H, Ph), 5.67 (dd, *J* 15.8, 5.4 Hz, 1H, CH=C*H*), 5.61 (dd, *J* 15.8, 5.6 Hz, 1H, C*H*=CH), 4.34−4.22 (m, 2H, CH_3C*H*, BnC*H*), 2.76 (d, *J* 6.5 Hz, 2H, PhCH_2CH), 1.23 (d, *J* 6.4 Hz, 3H, CH_3C*H*), 0.83 (s, 9H, *t*-*Bu*Si), −0.10 (s, 3H, CH_3Si), −0.21 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 138.7, 134.0, 132.9, 130.1, 128.2, 126.3, 74.3, 68.5, 45.3, 26.0, 23.4, 18.3, −4.5, −5.1; IR (film) *v*: 3349, 1254, 1077, 855 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{18}H_{30}O_2SiNa$ [M + Na^+] 329.1913. Found 329.1910.

(2*R*,5*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)-5-methylhex-3-en-2-ol (6d). Prepared in the same manner as compound **6a**. Purification by chromatography on silica gel (10% AcOEt/hexanes). Yield 1.08 g (85%) starting from 1.4 g (4.88 mmol) of acetate **10d**; colorless oil; *dr* 94:6 (NMR); $[\alpha]_D^{23}$ +18 (*c* 1.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.59 (dd, *J* 15.6, 6.0 Hz, 1H, CH=C*H*), 5.54 (dd, *J* 15.6, 5.6 Hz, 1H, C*H*=CH), 4.30−4.22 (m, 1H, CH=CHC*H*OH), 3.49 (dd, *J* 9.7, 6.2 Hz, 1H, TBSOCH*H*), 3.40 (dd, *J* 9.7, 6.9 Hz, 1H, TBSOC*H*H), 2.36−2.27 (m, 1H, C*H*CH$_3$), 1.26 (d, *J* 6.3 Hz, 3H, CH_3), 0.99 (d, *J* 6.8 Hz, 3H, CH), 0.89 (s, 9H, *t*-Bu) 0.04 (s, 6H, 2 × CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ 134.0, 133.5, 69.1, 68.1, 38.9, 26.1, 23.5, 18.5, 16.6, −5.2; IR (film) *v*: 3348, 1471, 1255, 1089, 838, 775 cm^{-1};

HRMS (TOF-ESI) m/z calcd for $C_{13}H_{28}O_2SiNa$ [M + Na^+] 267.1756. Found 267.1748.

(2*R*,6*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)hept-3-en-2-ol (6e). Prepared in the same manner as compound **6a**. Purification by chromatography on silica gel (10% AcOEt/hexanes). Yield 808 mg (65%) starting from 1.45 g (5.1 mmol) of acetate **10e** ; colorless oil; *dr* 95:5 (NMR); $[\alpha]_D^{22}$ +1.4 (*c* 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.67−5.58 (m, 1H, C*H*═CH), 5.53 (dd, *J* 15.4, 6.4 Hz, 1H, CH═C*H*), 4.30−4.19 (m, 1H, C*H*), 3.81 (h, *J* 6.1 Hz, 1H, Ci), 2.20−2.06 (m, 2H, CH_2), 1.24 (d, *J* 6.3 Hz, 3H, CH_3), 1.10 (d, *J* 6.1 Hz, 3H, CH_3), 0.86 (s, 9H, *t*-BuSi), 0.03 (s, 3H, CH_3Si), 0.02 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 136.3, 127.6, 68.9, 68.4, 42.5, 25.8, 23.5, 23.3, 18.1, −4.5, −4.7; IR (film) ν: 3358, 1256, 836, 774 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{28}O_2SiNa$ [M + Na^+] 267.1756. Found 267.1751.

(2*R*,5*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-yl Carbamate (11a). To a solution of alcohol **6a** (1.89 g, 8.2 mmol) in dry CH_2Cl_2 (30 mL) cooled to −10 °C, neat TCA-NCO (1.88 g, 1.2 mL, 10.0 mmol) was added. The progress of the reaction was followed by TLC (20% AcOEt/hexanes). After 1 h, the solvent was removed under diminished pressure. The residue was dissolved in MeOH (40 mL) and water (10 mL), and K_2CO_3 (4.2 g, 30.0 mmol) was added. The progress of the reaction was followed by TLC (20% AcOEt/hexanes). After 2 h, MeOH was removed under diminished pressure and the aqueous solution was extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2SO_4, and the solvent was removed under diminished pressure. The residue was chromatographed on silica gel (20% AcOEt/hexanes) to afford 2.13 g of carbamate **11a** (95%) as a colorless oil. $[\alpha]_D^{24}$ +20.3 (*c* 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.70 (ddd, *J* 15.5, 5.0, 0.8 Hz, 1H, CH═C*H*), 5.61 (ddd, *J* 15.5, 6.1, 1.1 Hz, 1H, C*H*═CH), 5.24 (p, *J* 6.4 Hz, 1H, CH_3CH), 4.60 (s, 2H, NH_2), 4.30 (p, *J* 6.0 Hz, 1H, CH_3CH), 1.31 (d, *J* 6.5 Hz, 3H, CH_3CH), 1.20 (d, *J* 6.4 Hz, 3H, CH_3CH), 0.89 (s, 9H, *t*-BuSi), 0.05 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.2, 136.4, 128.1, 71.2, 68.5, 25.8, 24.3, 20.4, 18.3, −4.6, −4.8; IR (film) ν: 3509, 3248, 3276, 1717 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{27}NO_3SiNa$ [M + Na^+] 296.1658. Found 296.1657.

(2*S*,5*R*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-yl Carbamate (*ent*-11a). Prepared as compound **11a**. Yield 872 mg (90%); colorless oil; $[\alpha]_D^{21}$ −19.3 (*c* 2.0, $CHCl_3$); HRMS (ESI-TOF) m/z calcd for $C_{13}H_{27}NO_3SiNa$ [M + Na^+] 296.1658; Found 296.1655.

(2*R*,5*R*,*E*)-5-((*t*-Butyldimethylsilyl)oxy)-5-phenylpent-3-en-2-yl Carbamate (11b). Prepared as compound **11a**. Purification by chromatography on silica gel (15% AcOEt/hexanes). Yield 724 mg (90%) starting from 681 mg (2.33 mmol) of alcohol **6b**; colorless oil; $[\alpha]_D^{22}$ +40.5 (*c* 1.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.29−7.16 (m, 5H, Ph), 5.80−5.66 (m, 2H, CH═CH), 5.25−5.17 (m, 1H, CH_3CH), 5.13 (d, *J* 4.7 Hz, 1H, PhC*H*), 4.64 (s, 2H, NH_2), 1.26 (d, *J* 6.5 Hz, 3H, CH_3CH), 0.86 (s, 9H, *t*-BuSi), 0.02 (s, 3H, CH_3Si), −0.06 (s, 3H, CH_3Si); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 156.4, 143.6, 135.0, 129.1, 128.3, 127.2, 126.1, 74.8, 71.1, 26.0, 20.5, 18.5, −4.4, −4.7; IR (film) ν: 3503, 3352, 1718, 1047, 837 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{29}NO_3SiNa$ [M + Na^+] 358.1814. Found 358.1811.

(2*R*,5*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)-6-phenylhex-3-en-2-yl Carbamate (11c). Prepared in the same manner as compound **11a**. Purification by chromatography on silica gel (20% AcOEt/hexanes). Yield 783 mg (77%) starting from 890 mg (2.9 mmol) of alcohol **6c**; colorless oil; $[\alpha]_D^{22}$ +30 (*c* 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.32−7.10 (m, 5H, Ph), 5.73 (ddd, *J* 15.5, 5.7, 1.0 Hz, 1H, C*H*═CH), 5.58 (ddd, *J* 15.5, 6.2, 1.2 Hz, 1H, CH═C*H*), 5.23 (p, *J* 6.4 Hz, 1H, BnC*H*OTBS), 4.59 (s, 2H, NH_2), 4.26 (q, *J* 6.0 Hz, 1H, CH_3CH), 2.83−2.66 (m, 2H, PhCH_2CH), 1.28 (d, *J* 6.5 Hz, 3H, CH_3CH), 0.83 (s, 9H, *t*-BuSi), −0.11 (s, 3H, CH_3Si), −0.21 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.2, 138.5, 134.6, 129.9, 129.4, 127.9, 126.1, 74.0, 71.1, 45.1, 25.8, 20.4, 18.2, −4.7, −5.3; IR (film) ν: 3499, 3345, 3273, 3204, 1717, 1388, 1255, 1051, 836, 777 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{31}NO_3SiNa$ [M + Na^+] 372.1971. Found 372.1974.

(2*R*,5*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)-5-methylhex-3-en-2-yl Carbamate (11d). Prepared in the same manner as compound **11a**. Purification by chromatography on silica gel (15% AcOEt/hexanes). Yield 1.16 g (97%) starting from 1 g (4.09 mmol) of alcohol **6d**; yellowish oil; $[\alpha]_D^{21}$ +20.1 (*c* 1.09, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 5.65 (ddd, *J* 15.6, 6.8, 0.8 Hz, 1H, C*H*═CH), 5.50 (ddd, *J* 15.6, 6.3, 1.1 Hz, 1H, CH═C*H*), 5.26−5.18 (m, 1H, CH_3CHO), 4.67−4.52 (br s, 2H, NH2), 3.48 (dd, *J* 9.7, 6.3 Hz, 1H, C*H*HOTBS), 3.40 (dd, *J* 9.7, 7.0 Hz, 1H, CH*H*OTBS), 2.37−2.27 (m, 1H, CH_3CHCH_2OTBS), 1.62 (d, *J* 6.4 Hz, 3H, CH_3CHCH_2OTBS), 0.98 (d, *J* 6.8 Hz, 3H, CH_3CHO), 0.88 (s, 9H, 3 × CH_3C), 0.03 (s, 6H, 2 × CH_3Si); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 156.3, 135.1, 129.4, 71.8, 67.78, 38.8, 26.9, 25.9, 20.5, 18.3, 16.2, −5.36, −5.39; IR (film) ν: 3501, 3442, 3341, 3205, 1717, 1379, 1050, 833 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{29}NO_3SiNa$ [M + Na^+] 310.1814. Found 310.1813.

(2*R*,6*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)hept-3-en-2-yl Carbamate (11e). Prepared in the same manner as compound **11a**. Purification by chromatography on silica gel (10% AcOEt/hexanes). Yield 870 mg (74%) starting from 770 mg (4.1 mmol) of alcohol **6e**; colorless oil; $[\alpha]_D^{22}$ +9.9 (*c* 2.0, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 5.73−5.65 (m, 1H, C*H*═CH), 5.48 (ddt, *J* 15.5, 6.4, 1.2 Hz, 1H, CH═C*H*), 5.24−5.15 (m, 1H, C*H*), 4.55 (s, 2H, NH_2), 3.86−3.71 (m, 1H, C*H*), 2.21−2.07 (m, 2H, CH_2), 1.29 (d, *J* 6.5 Hz, 3H, CH_3), 1.10 (d, *J* 6.1 Hz, 3H, CH_3), 0.87 (s, 9H, *t*-BuSi), 0.03 (s, 3H, CH_3Si), 0.03 (s, 3H, CH_3Si); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 156.2, 131.7, 129.7, 71.7, 68.3, 42.6, 25.8, 23.5, 20.4, 18.1, −4.5, −4.8; IR (film) ν: 3509, 3447, 3347, 3203, 1714, 1377, 1049, 835 cm^{-1}; HRMS (ESI-TOF) m/z $C_{14}H_{29}NO_3SiNa$ [M + Na^+] 310.1814. Found 310.1811.

(2*S*,5*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-yl Carbamate (12a). Prepared in the same manner as compound **11a**. Purification by chromatography on silica gel (20% AcOEt/hexanes). Yield 1.85 g (97%) starting from 1.61 g (7 mmol) of alcohol **7a**; colorless oil. $[\alpha]_D^{24.5}$ −23.5 (*c* 1.41, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.70 (dd, *J* 15.5, 5.0 Hz, 1H, C*H*═CH), 5.61 (ddd, *J* 15.5, 5.9, 1.1 Hz, 1H, CH═C*H*), 5.24 (m, 1H, CH), 4.72 (s, 2H, NH_2), 4.28 (m, 1H, C*H*), 1.30 (d, *J* 6.5 Hz, 3H, CH_3), 1.20 (d, *J* 6.4 Hz, 3H, CH_3), 0.89 (s, 9H, *t*-BuSi), 0.08−0.02 (m, 6H, 2 × CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.4, 136.2, 128.1, 71.0, 68.5, 25.8, 24.2, 20.4, 18.2, −4.6, −4.8; IR (film) ν: 3507, 3349, 1716 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{27}NO_3SiNa$ [M + Na^+] 296.1658; Found 296.1656.

(2*R*,5*R*,*E*)-5-(*t*-Butyldimethylsilyloxy)hex-3-en-2-yl Carbamate (*ent*-12a). Prepared as compound **11a**. Yield 660 mg (91%); colorless oil. $[\alpha]_D^{22}$ +23.0 (*c* 1.2 $CHCl_3$); HRMS (ESI-TOF) m/z calcd for $C_{13}H_{27}NO_3SiNa$ [M + Na^+] 296.1658. Found 296.1656.

(2*S*,5*R*,*E*)-5-((*t*-Butyldimethylsilyl)oxy)-5-phenylpent-3-en-2-yl Carbamate (12b). Prepared in the same manner as compound **11a**. Purification by chromatography on silica gel (15% AcOEt/hexanes). Yield 737 mg (92%) starting from 700 mg (2.4 mmol) of alcohol **7b**; colorless oil; $[\alpha]_D^{24}$ −2.8 (*c* 1.1, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.27−7.16 (m, 5H, Ph), 5.78−5.65 (m, 2H, CH═CH), 5.25−5.18 (m, 1H, CH_3CH), 5.12 (d, *J* 5.0 Hz, 1H, PhC*H*), 4.58 (br s, 2H, NH_2), 1.26 (d, *J* 6.5 Hz, 3H, CH_3CH), 0.86 (s, 9H, *t*-BuSi), 0.02 (s, 3H, CH_3Si), −0.06 (s, 3H, CH_3Si); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 156.4, 143.7, 134.8, 129.2, 128.3, 127.2, 126.2, 74.9, 70.9, 26.0, 20.5, 18.5, −4.4, −4.7; IR (film) ν: 3492, 3347, 3273, 1717, 1052 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{18}H_{29}NO_3SiNa$ [M + Na^+] 358.1814. Found 358.1812.

(2*S*,5*S*,*E*)-5-(*t*-Butyldimethylsilyloxy)-6-phenylhex-3-en-2-yl Carbamate (12c). Prepared in the same manner as compound **11a**. Purification by chromatography on silica gel (20% AcOEt/hexanes). Yield 1.3 g (95%) starting from 1.2 g (3.92 mmol) of alcohol **7c**; as colorless oil; $[\alpha]_D^{25}$ −27.3 (*c* 3.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.31−7.12 (m, 5H, Ph), 5.73 (ddd, *J* 15.5, 5.8, 1.1 Hz, 1H, C*H*═CH), 5.59 (ddd, *J* 15.5, 6.2, 1.2 Hz, 1H, CH═C*H*), 5.23 (p, *J* 6.2 Hz, 1H, C*H*OTBS), 4.61 (br s, 2H, NH_2), 4.25 (q, *J* 6.0 Hz, 1H, C*H*OCONH$_2$), 2.81−2.68 (m, 2H, PhCH_2CH), 1.27 (d, *J* 6.5 Hz, 3H, CHCH_3), 0.83 (s, 9H, *t*-BuSi), −0.11 (s, 3H, CH_3Si), −0.22 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.4, 138.6, 134.7, 130.1, 129.6, 128.1, 126.3, 74.2, 71.2, 45.2, 25.9, 20.6, 18.3, −4.6, −5.1; IR (film) ν: 3504, 3342, 3273, 1718, 1387, 1053, 836, 778 cm^{-1}; HRMS

dx.doi.org/10.1021/jo502026a | *J. Org. Chem.* 2014, 79, 11700−11713

(ESI-TOF) m/z calcd for $C_{19}H_{31}NO_3SiNa$ [M + Na^+] 372.1971. Found 372.1977.

(2*R*,5*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)-5-methylhex-3-en-2-yl Carbamate (12d). Prepared in the same manner as compound **11a**. Purification by chromatography on silica gel (20% AcOEt/hexanes). Yield 933 mg (79%) starting from 1 g (4.09 mmol) of compound **7d**; yellowish oil; $[\alpha]_D^{23}$ −11.3 (c 1.25, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.63 (dd, J 15.7, 7.1 Hz, 1H, CH=C*H*), 5.49 (dd, J 15.7, 6.4 Hz, 1H, C*H*=CH), 5.25−5.18 (m, 1H, $CH_3CHOCONH_2$), 4.60 (s, 2H, NH_2), 3.47 (dd, J 9.7, 6.3 Hz, 1H, TBSOCH*H*), 3.40 (dd, J 9.7, 6.8 Hz, 1H, TBSOC*H*H), 2.36−2.26 (m, 1H, C*H*CH$_3$), 1.30 (d, J 6.4 Hz, 3H, $CH_3CHOCONH_2$), 0.99 (d, J 6.8 Hz, 3H, C*H*$_3$CH), 0.89 (s, 9H, t-BuSi), 0.03 (s, 6H, 2 × C*H*$_3$Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.5, 135.4, 129.6, 72.0, 67.9, 39.1, 26.1, 20.7, 18.5, 16.5, −5.19, −5.22; IR (film) ν: 3344, 1715, 1372, 1040, 832, 777 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{29}NO_3SiNa$ [M + Na^+] 310.1814. Found 310.1806.

(2*S*,6*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)hept-3-en-2-yl Carbamate (12e). Prepared in the same manner as compound **11a**. Purification by chromatography on silica gel (15% AcOEt/hexanes). Yield 1.09 g (84%) starting from 1.1 g (4.5 mmol) of alcohol **7e**; colorless oil; $[\alpha]_D^{23}$ −25.7 (c 0.64, $CHCl_3$); ^{1}H NMR (500 MHz, CDCl3) δ: 5.68 (dtd, J 15.6, 7.3, 1.1 Hz, 1H, C*H*=CH), 5.49 (dd, J 15.5, 6.4 Hz, 1H, CH=C*H*), 5.20 (qt, J 6.7, 3.3 Hz, 1H, C*H*), 4.55 (s, 2H, NH_2), 3.84−3.82 (m, 1H, CH), 2.22−2.14 (m, 1H, C*H*H), 2.14−2.05 (m, 1H, CH*H*), 1.29 (d, J 6.5 Hz, 3H, C*H*$_3$), 1.10 (d, J 6.1 Hz, 3H, C*H*$_3$), 0.86 (s, 9H, t-BuSi), 0.02 (s, 3H, C*H*$_3$Si), 0.02 (s, 3H, C*H*$_3$Si); ^{13}C NMR (126 MHz, cdcl$_3$) δ 156.3, 131.7, 129.5, 71.7, 68.4, 42.6, 25.8, 23.5, 20.4, 18.1, −4.5, −4.7; IR (film) ν: 3349, 1717, 1377, 1049, 836, 775 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{29}NO_3SiNa$ [M + Na^+] 310.1814. Found 310.1809.

Methyl ((2*S*,3*R*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)hex-4-en-3-yl)carbamate (15). To a solution of carbamate **11a** (100 mg, 0.366 mmol) and Et_3N (222 mg, 305 μL, 2.196 mmol) in dry THF (5 mL) cooled to −20 °C, TFAA (153 mg, 111 μL, 0.732 mmol) was added, and the resulting mixture was slowly warmed to room temperature. The progress of the reaction was followed by TLC (20% AcOEt in hexanes). In a separate flask, a 1 M soln. of LiHMDS in THF (2.2 mL, 2.2 mmol) was added to anhydr. MeOH (2 mL) in dry THF (5 mL). When the rearrangement reaction was completed (ca. 1 h), the solution of MeOLi was cannulated, and reaction mixture was stirred overnight at room temperature. The progress of the reaction was followed by TLC (20% AcOEt in hexanes). After removal of solvents, the crude product was absorbed on silica gel and chromatographed (10% AcOEt in hexanes) to give 100 mg of carbamate **15** (95%) as a colorless oil. $[\alpha]_D^{23}$ −7.6 (c 0.64, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.66 (dd, J 15.4, 6.4 Hz, 1H, CH=C*H*CH$_3$), 5.42 (ddd, J 15.4, 7.7, 1.4 Hz, 1H, C*H*=CHCH$_3$), 4.89 (s, 1H, NH), 4.04−3.82 (m, 2H, 2 × CH), 3.66 (s, 3H, C*H*$_3$O), 1.70 (dd, J 6.4, 1.4 Hz, 3H, CH=CHC*H*$_3$), 1.06 (d, J 6.2 Hz, 3H, C*H*$_3$CH), 0.89 (s, 9H, t-BuSi), 0.05 (s, 6H, 2 × C*H*$_3$Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 158.9, 131.8, 129.3, 72.9, 61.4, 54.6, 28.4, 23.0, 20.7, 20.5, −1.7, −2.3; IR (film) ν: 3334, 1714, 1254, 835 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{29}NO_3SiNa$ [M + Na^+] 310.1814. Found 310.1820.

Methyl ((2*S*,3*S*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)hex-4-en-3-yl)carbamate (18). Prepared in the same manner as compound **15**. Purification by chromatography on silica gel (10% AcOEt in hexanes). Yield 103 mg (86%) starting from 100 mg (0.366 mmol) of compound **12a**; colorless oil; $[\alpha]_D^{22}$ +0.5 (c 0.9, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.65−5.55 (m, 1H, CH=C*H*CH$_3$), 5.41 (ddd, J 15.3, 6.1, 1.6 Hz, 1H, C*H*=CHCH$_3$), 4.99 (s, 1H, NH), 4.03−3.91 (m, 1H, CH), 3.89−3.81 (m, 1H, CH), 3.68 (s, 3H, C*H*$_3$O), 1.70−1.67 (m, 3H, CH=CHC*H*$_3$), 1.14 (d, J 6.2 Hz, 3H, C*H*$_3$CH), 0.88 (s, 9H, t-BuSi), 0.04 (s, 3H, C*H*$_3$Si), 0.02 (s, 3H, C*H*$_3$Si); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 156.9, 130.6, 126.1, 70.5, 58.0, 52.0, 25.7, 20.9, 18.0, 17.6, −4.5, −4.9; IR (film) ν: 3449, 3341, 1733, 1718, 1504, 1254, 1070, 835, 776 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{14}H_{29}NO_3SiNa$ [M + Na^+] 310.1814; Found 310.1814.

Benzyl ((2*S*,3*R*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)hex-4-en-3-yl)carbamate (19). To a cooled to −20 °C solution of carbamate **11a** (150 mg, 0.55 mmol) and Et_3N (333 mg, 460 μL, 3.29 mmol) in dry THF (10 mL), TFAA (230 mg, 150 μL, 1.1 mmol) was added, and the resulting mixture was slowly warmed to room temperature. The progress of the reaction was followed by TLC (20% AcOEt in hexanes). In a separate flask, a 1 M soln. of LiHMDS in THF (3.3 mL, 3.29 mmol) was added to anhydr. BnOH (350 μL) in 10 mL of THF. When rearrangement was completed (ca. 1 h), the solution of BnOLi was cannulated, and the reaction mixture was stirred overnight at room temperature. The progress of the reaction was followed by TLC (10% AcOEt in hexanes). After removal of solvents, the crude product was supported on silica gel and chromatographed (5% AcOEt in hexanes) to give 138 mg of carbamate **19** (76%) as a colorless oil; $[\alpha]_D^{22}$ −3.3 (c 0.87, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6) δ: 7.34−7.23 (m, 5H, Ph), 7.09 (d, J 8.1 Hz, 1H, NH), 5.47 (dd, J 16.0, 6.4 Hz, 1H, CH=C*H*), 5.36 (dd, J 16.0, 6.6 Hz, 1H, C*H*=CH), 5.01−4.93 (m, 2H, PhC*H*$_2$O), 3.80−3.65 (m, 2H, C*H*OTBS, C*H*NHCbz), 1.59 (d, J 6.2 Hz, 3H, C*H*$_3$), 0.98 (d, J 6.1 Hz, 3H, C*H*$_3$), 0.80 (s, 9H, t-BuSi), −0.03 (s, 3H, C*H*$_3$Si), −0.05 (s, 3H, C*H*$_3$Si); ^{13}C NMR (126 MHz, DMSO-d_6) δ: 155.5, 137.3, 129.2, 128.3, 127.7, 127.6, 126.43, 69.9, 65.1, 59.0, 25.7, 20.2, 17.7, 17.6, −4.6, −4.9; IR (film) ν: 3450, 3334, 1723, 1255, 835, 776 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{33}NO_3SiNa$ [M + Na^+] 386.2127. Found 386.2126.

Benzyl ((2*R*,3*S*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)hex-4-en-3-yl)-carbamate (*ent*-19). Prepared in the same manner as compound **19**. Yield 163 mg (80%); colorless oil; $[\alpha]_D^{22}$ +3.5 (c 0.95, $CHCl_3$); HRMS (ESI-TOF) m/z calcd for $C_{20}H_{33}NO_3SiNa$ [M + Na^+] 386.2127. Found 386.2125.

Benzyl ((1*S*,2*R*,*E*)-1-((*t*-Butyldimethylsilyl)oxy)-1-phenylpent-3-en-2-yl)carbamate (25). Prepared in the same manner as compound **19**; Purification by chromatography on silica gel (5% AcOEt in hexanes); Yield 183 mg (77%) starting from 200 mg (0.56 mmol) of carbamate **11b**; colorless oil; $[\alpha]_D^{22}$ +61.8 (c 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, C_6D_6) δ: 7.40−6.97 (m, 10H, 2 × Ph), 5.42 (dd, J 15.3, 6.8 Hz, 1H, C*H*=CH), 5.33−5.22 (m, 1H, CH=C*H*), 5.14 (d, J 12.3 Hz, 1H, OC*H*HPh), 5.09 (d, J 12.3 Hz, 1H, OCH*H*Ph), 4.99 (br s, 1H, NH), 4.84 (d, J 8.0 Hz, 1H, CH), 4.58−4.47 (m, 1H, CH), 1.38 (br d, J 6.3 Hz, 3H, C*H*$_3$CH=CH), 0.93 (s, 9H, t-BuSi), 0.03 (s, 3H, C*H*$_3$Si), −0.14 (s, 3H, C*H*$_3$Si); ^{13}C NMR (126 MHz, C_6D_6, signals at range 129.5−127.7 ppm were omitted due to overlapping with solvent residual peaks) δ: 155.6, 142.0, 137.5, 127.5, 126.8, 77.1, 66.7, 60.2, 26.0, 25.9, 18.4, 17.7, −4.6, −5.0; IR (film) ν: 3451, 3332, 1724, 1495, 1255, 834, 697 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{25}H_{35}NO_3SiNa$ [M + Na^+] 448.2284. Found 448.2285.

Benzyl ((2*S*,3*R*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)-1-phenylhex-4-en-3-yl)carbamate (27). Prepared in the same manner as compound **19**. Purification by chromatography on silica gel (5% AcOEt in hexanes). Yield 215 mg (82%) starting from 200 mg (0.572 mmol) of compound **11c**; colorless oil; $[\alpha]_D^{23}$ −4.3 (c 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.53−6.97 (m, 10H, 2 × Ph), 5.75−5.61 (m, 1H, C*H*=CH), 5.58−5.45 (m, 1H, CH=C*H*), 5.14−5.02 (m, 2H, OC*H*$_2$Ph), 4.94 (s, 1H, NH), 4.12−3.94 (m, 2H, 2 × C*H*), 2.82−2.58 (m, 2H, C*H*$_2$Ph), 1.75 (d, J 5.5 Hz, 3H, C*H*$_3$CH=CH), 0.86 (s, 9H, t-BuSi), 0.00 (s, 3H, C*H*$_3$Si), −0.26 (s, 3H, C*H*$_3$Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.4, 138.0, 136.7, 130.0, 129.5, 128.4, 128.4, 128.3, 127.9, 126.4, 126.3, 75.5, 66.5, 57.0, 40.7, 25.9, 18.1, 18.0, −4.7, −4.9; IR (film) ν: 3453, 3335, 1720, 1497, 1254, 835, 698 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{26}H_{38}NO_3Si$ [M + H^+] 440.2621. Found 440.2618.

Benzyl ((2*R*,3*R*,*E*)-1-((*t*-Butyldimethylsilyl)oxy)-2-methylhex-4-en-3-yl)carbamate (44a). Prepared in the same manner as compound **19**. Purification by chromatography (4% AcOEt in hexanes). Yield 176 mg (88%) starting from 150 mg (0.522 mmol) of compound **11d**; yellowish oil; $[\alpha]_D^{22}$ +7.2 (c 1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.37−7.27 (m, 5H, Ph), 5.84 (s, 1H, NH), 5.66−5.56 (m, 1H, CH$_3$C*H*=CH), 5.39 (dd, J 15.0, 5.6 Hz, 1H, CH$_3$CH=C*H*), 5.16−5.04 (m, 2H, C*H*$_2$OPh), 4.17−4.09 (m, 1H, C*H*NHCbz), 3.80−3.71 (m, 1H, TBSOC*H*HCH), 3.48 (dd, J 10.0, 4.3 Hz, 1H, TBSOCH*H*CH), 1.78−1.71 (m, 1H, CH$_3$C*H*), 1.69 (d, J 6.4 Hz, 3H, C*H*$_3$CH=CH), 0.99 (d, J 6.9 Hz, 3H, C*H*$_3$CH), 0.89 (s, 9H, (CH$_3$)$_3$CSi), 0.04 (s, 6H, 2 × C*H*$_3$Si); ^{13}C NMR (126 MHz,

$CDCl_3$) δ: 156.1, 137.0, 130.5, 128.3, 127.75, 127.72, 126.1, 66.2, 65.1, 56.6, 38.4, 25.8, 18.1, 17.7, 14.4, −5.71, −5.73; IR (film) ν: 3409, 3334, 1726, 1712, 1086 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{21}H_{35}NO_3SiNa$ [M + Na^+] 400.2284. Found 400.2288.

Benzyl ((4*S*,6*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)hept-2-en-4-yl)carbamate (44b). Prepared in the same manner as compound **19**. Purification by chromatography on silica gel (6% AcOEt in hexanes). Yield 230 mg (87%) starting from 200 mg (0.697 mmol) of compound **11e**; colorless oil; $[\alpha]_D^{22}$ −16.5 (*c* 3.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.36−7.28 (m, 5H, Ph), 5.66−5.54 (m, 1H, C*H*=CH), 5.49−5.34 (m, 1H, CH=C*H*), 5.16−5.02 (m, 2H, 2 × CH), 4.26−4.17 (m, 1H), 4.05−3.91 (m, 1H), 1.68 (d, *J* 6.3 Hz, 3H, CH_3), 1.15 (d, *J* 6.1 Hz, 3H, CH_3), 0.89 (s, 9H, *t*-BuSi), 0.06 (s, 6H, 2 × CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.7, 136.9, 131.5, 128.3, 127.9, 127.8, 125.6, 66.3, 66.1, 50.7, 44.1, 25.9, 23.9, 17.9, 17.6, −4.1, −4.8; IR (film) ν: 3330, 1709, 1528, 1255, 836, 775 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{21}H_{35}NO_3SiNa$ [M + Na^+] 400.2284. Found 400.2282.

Benzyl ((2*S*,3*S*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)hex-4-en-3-yl)carbamate (22). Prepared in the same manner as compound **19**. Purification by chromatography on silica gel (10% AcOEt in hexanes); Yield 140 mg (70%) starting from 150 mg (0.549 mmol) of compound **12a**; colorless oil; $[\alpha]_D^{23}$ −12.1 (*c* 1.21, $CHCl_3$); ^{1}H NMR (500 MHz, PhMe-d_7, 70 °C) δ: 7.26−6.94 (m, 5H, Ph), 5.56−5.45 (m, 1H, CH=C*H*), 5.36 (dd, *J* 15.4, 4.6 Hz, 1H, C*H*=CH), 5.12−4.99 (m, 2H, PhCH_2O), 4.86−4.75 (m, 1H, NH), 4.20−4.07 (m, 1H, C*H*), 3.79−3.67 (m, 1H, C*H*), 1.53 (d, *J* 6.4 Hz, 3H, CH_3CH), 1.03 (d, *J* 6.0 Hz, 3H, CH_3CH), 0.86 (s, 9H, *t*-BuSi), −0.03 (s, 6H, 2 × CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 156.3, 136.7, 130.5, 128.5, 128.4, 128.1, 128.0, 128.0, 126.3, 70.6, 66.7, 58.2, 25.8, 20.9, 18.0, 17.6, −4.5, −4.9; IR (film) ν: 3445, 3331, 1727, 1494, 1097 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{33}NO_3SiNa$ [M + Na^+] 386.2127. Found 386.2123.

Benzyl ((2*R*,3*R*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)hex-4-en-3-yl)carbamate (*ent*-22). Prepared in the same manner as compound **19**. Yield 155 mg (75%); colorless oil; $[\alpha]_D^{24}$ +11.8 (*c* 1.1, $CHCl_3$); HRMS (ESI-TOF) m/z calcd for $C_{20}H_{33}NO_3SiNa$ [M + Na^+] 386.2127. Found 386.2123.

Benzyl ((1*S*,2*S*,*E*)-1-((*t*-Butyldimethylsilyl)oxy)-1-phenylpent-3-en-2-yl)carbamate (26). Prepared in the same manner as compound **19**. Purification by chromatography on silica gel. Yield 127 mg (67%) starting from 150 mg (0.448 mmol) of compound **12b**; colorless oil; $[\alpha]_D^{21}$ +20.1 (*c* 1.09, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.39−7.24 (m, 10H, 2 × Ph), 5.67−5.55 (m, 1H, C*H*=CH), 5.49 (ddd, *J* 15.3, 5.9, 1.6 Hz, 1H, CH=C*H*), 5.06−4.95 (m, 3H, C*H*, OCH_2Ph), 4.75 (s, 1H, NH), 4.35−4.20 (m, 1H, C*H*), 1.69 (d, *J* 6.4 Hz, 3H, CH_3CH=CH), 0.89 (s, 9H, *t*-BuSi), 0.02 (s, 3H, CH_3Si), −0.13 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.8, 141.5, 136.6, 129.4, 128.4, 128.3, 128.0(x2), 127.9, 127.4, 126.9, 126.3(x2), 66.5, 59.1, 25.8, 18.2, 17.7, −4.7, −5.1; IR (film) ν: 3447, 3336, 1724, 1499, 1096 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{25}H_{35}NO_3SiNa$ [M + Na^+] 448.2284. Found 448.2284.

Benzyl ((2*S*,3*S*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)-1-phenylhex-4-en-3-yl)carbamate (28). Prepared in the same manner as compound **19**. Purification by chromatography (10% AcOEt in hexanes). Yield 153 mg (60%) starting from 200 mg (0.573 mmol) of compound **12c**; colorless oil; $[\alpha]_D^{25}$ −6.3 (*c* 0.65, $CHCl_3$); ^{1}H NMR (500 MHz, DMSO-d_6/CD_3OD 4:1) δ: 7.44−7.00 (m, 10H, 2 × Ph), 5.68−5.43 (m, 2H, CH=CH), 5.11−5.02 (m, 2H, OCH_2Ph), 4.14−4.04 (m, 1H, CH), 3.82−3.71 (m, 3H), 2.83 (dd, *J* 13.4, 2.8 Hz, 1H, C*H*HPh), 2.37 (dd, *J* 13.4, 9.0 Hz, 1H, CH*H*Ph), 1.66 (d, *J* 5.7 Hz, 3H, CH_3CH=CH), 0.75 (s, 9H, *t*-BuSi), −0.11 (s, 3H, CH_3Si), −0.50 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, DMSO-d_6) δ: 155.6, 139.1, 137.1, 129.4, 128.3, 127.9, 127.8, 127.7, 127.7, 126.3, 125.9, 75.8, 65.3, 56.7, 38.7, 25.6, 17.7, 17.6, −5.0, −5.6; IR (film) ν: 3444, 3340. 1724, 1497, 1086 cm-^{1}; HRMS (TOF-ESI) m/z calcd for $C_{26}H_{37}NO_3SiNa$ [M + Na^+] 462.2440. Found 462.2434.

Benzyl ((2*R*,3*S*,*E*)-1-((*t*-Butyldimethylsilyl)oxy)-2-methylhex-4-en-3-yl)carbamate (42a). Prepared in the same manner as compound **19**. Purification by chromatography (4% AcOEt in hexanes). Yield 173 mg (87%) starting from 150 mg (0.522 mmol) of compound **12d**; colorless oil; $[\alpha]_D^{22}$ +4.3 (*c* 1.8, $CHCl_3$)^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.38−7.26 (m, 5H, Ph), 5.97 (d, *J* 6.8 Hz, 1H, NH), 5.63 (m, 1H, CH_3C*H*=CH), 5.38 (ddd, *J* 15.3, 6.6, 1.3 Hz, 1H, CH_3CH=C*H*), 5.16−4.98 (m, 2H, OCH_2Ph), 4.14 (m, 1H, C*H*NHCbz), 3.53 (ps t, *J* 10.1, 9.1 Hz, 1H, C*H*HOTBS), 3.47 (dd, *J* 10.1, 4.9 Hz, 1H, CH*H*OTBS), 2.04−1.91 (m, 1H, CH_3C*H*), 1.71 (d, *J* 6.3 Hz, 3H, CH_3CH=CH), 0.90 (s, 9H, (CH_3)$_3$CSi), 0.81 (d, *J* 7.1 Hz, 3H, CH_3CH), 0.05 (s, 6H, 2 × CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.6, 137.0, 128.3, 127.8, 127.7, 127.5, 66.2, 65.8, 56.4, 39.0, 25.8, 18.1, 17.8, 13.6, −5.7; IR (film) ν: 3415, 3334, 1726, 1712, 1504, 1252, 1094, 837, 776 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{21}H_{35}NO_3SiNa$ [M + Na^+] 400.2284. Found 400.2284.

Benzyl ((4*R*,6*R*,*E*)-6-((*t*-Butyldimethylsilyl)oxy)hept-2-en-4-yl)carbamate (42b). Prepared in the same manner as compound **19**. Purification by chromatography on silica gel (10% AcOEt in hexanes). Yield 206 mg (78%) starting from 200 mg (0.697 mmol) of compound **12e**; colorless oil; $[\alpha]_D^{21}$ −9.3 (*c* 0.81, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) δ: 7.35−7.27 (m, 5H, Ph), 5.70−5.52 (m, 1H, C*H*=CH), 5.44−5.29 (m, 1H, CH=C*H*), 5.18−4.98 (m, 2H, OCH_2Ph), 4.80 (s, 1H, NH), 4.23−4.08 (m, 1H, C*H*), 3.92−3.76 (m, 1H, C*H*), 1.72−1.60 (m, 5H, CH_2, CH_3CH=CH), 1.14 (d, *J* 5.6 Hz, 3H, CH_3), 0.85 (s, 9H, *t*-BuSi), 0.02 (s, 3H, CH_3Si), 0.00 (s, 3H, CH_3Si); ^{13}C NMR (151 MHz, $CDCl_3$) δ: 136.6, 131.7, 128.4, 128.0, 126.2, 126.0, 66.5, 58.1, 50.9, 45.4, 25.9, 24.1, 18.0, 17.7, −4.1, −4.7; IR (film) ν: 3330, 1708, 1530, 1254, 836, 774 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{21}H_{35}NO_3SiNa$ [M + Na^+] 400.2284. Found 400.2285.

***t*-Butyl ((2*S*,3*R*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)hex-4-en-3-yl)carbamate (20).** To a cooled to −20 °C solution of carbamate **11a** (150 mg, 0.55 mmol) and Et_3N (333 mg, 460 μL, 3.29 mmol) in dry THF (10 mL), TFAA (230 mg, 150 μL, 1.1 mmol) was added, and the resulting mixture was warmed to room temperature slowly. The progress of the reaction was followed by TLC (20% AcOEt in hexanes). In a separate flask, a 1 M soln. of LiHMDS in THF (3.3 mL, 3.29 mmol) was added to anhydr. *t*-BuOH (0.5 mL) in dry THF (10 mL). When rearrangement was completed (ca. 1 h), the solution of *t*-BuOLi was cannulated, and the reaction mixture was stirred overnight at room temperature. The progress of the reaction was followed by TLC (20% AcOEt in hexanes). After removal of solvents, the crude product was supported on silica gel and chromatographed (10% AcOEt in hexanes) to give 151 mg of carbamate **20** (84%) as a colorless oil. $[\alpha]_D^{22}$ +4.8 (*c* 1.4, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.72−5.54 (m, 1H, CH_3C*H*=CH), 5.41 (ddd, *J* 15.3, 7.7, 1.3 Hz, 2H, CH_3CH=C*H*), 4.73 (s, 1H, NH), 4.03−3.73 (m, 2H, C*H*OTBS, C*H*NHBoc), 1.70 (dd, *J* 6.5, 1.3 Hz, 3H, CH_3CH=CH), 1.43 (s, 9H, (CH_3)$_3$CO), 1.05 (d, *J* 6.3 Hz, 3H, CH_3CH), 0.90 (s, 9H, (CH_3)$_3$CSi), 0.06 (s, 3H, CH_3Si), 0.05 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 158.1, 130.1, 126.7, 70.3, 28.4, 25.8, 20.4, 18.0, 17.9, −4.4, −4.9; IR (film) ν: 3458, 3349, 1716, 1494, 1175, 835, 776 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{35}NO_3SiNa$ [M + Na^+] 352.2284. Found 352.2275.

***t*-Butyl ((2*S*,3*S*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)hex-4-en-3-yl)carbamate (23).** Prepared in the same manner as compound **20**. Purification by chromatography on a short pad of silica gel (20% AcOEt in hexanes). Yield 138 mg (76%) starting from 150 mg (0.549 mmol) of compound **12a**; yellowish oil; $[\alpha]_D^{22}$ −13.0 (*c* 0.48, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.62−5.52 (m, 1H, C*H*=CH), 5.40 (ddd, *J* 15.4, 5.8, 1.3 Hz, 1H, CH=C*H*), 4.89−4.71 (m, 1H, C*H*), 4.01−3.88 (m, 1H, NH), 3.89−3.79 (m, 1H, C*H*), 1.68 (d, *J* 6.4 Hz, 3H, CH_3), 1.45 (s, 9H, *t*-BuO), 1.13 (d, *J* 6.2 Hz, 3H, CH_3), 0.88 (s, 9H, *t*-BuSi), 0.04 (s, 3H, CH_3Si), 0.02 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 155.9, 130.9, 125.7, 100.0, 70.7, 28.4, 25.8, 20.8, 18.0, 17.6, −4.4, −4.8; IR (film) ν: 3453, 1721, 1494, 1173, 835, 776 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{17}H_{35}NO_3SiNa$ [M + Na^+] 352.2284. Found 352.2283.

***N*-((2*S*,3*R*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)hex-4-en-3-yl)-acetamide (21).** To a cooled to −20 °C solution of carbamate **11a** (300 mg, 1.1 mmol) and Et_3N (668 mg, 920 μL, 6.6 mmol) in dry THF (10 mL), TFAA (462 mg, 305 μL, 2.2 mmol) was added, and the resulting mixture was warmed to room temperature slowly. The

progress of the reaction was followed by TLC (20% AcOEt in hexanes). After 1 h, a solution was cooled to −10 °C and a 3 M soln. of MeMgBr (6.6 mmol, 2.2 mL) was added. After 4 h, the reaction was quenched by addition of sat. aq. NH_4Cl. The organic layer was separated, and the aqueous one was extracted with CH_2Cl_2. After removal of solvents, the crude product was supported on silica gel and chromatographed (25% AcOEt in hexanes) to give 250 mg of carbamate **21** (83%) as a colorless oil. $[\alpha]_D^{23}$ −21.2 (*c* 0.86, $CHCl_3$); ^{1}H NMR (500 MHz, C_6D_6) *δ*: 5.59−5.49 (m, 1H, C*H*=CH), 5.43 (ddd, *J* 15.4, 8.0, 1.5 Hz, 1H, CH=C*H*), 5.21 (br d, *J* 7.0 Hz, 1H, NH), 4.42 (td, *J* 8.3, 3.2 Hz, 1H, C*H*CH=CH), 3.84 (qd, *J* 6.3, 3.4 Hz, 1H, CH_3CH), 1.60 (s, 3H, CH_3CO), 1.49 (dd, *J* 6.3, 1.1 Hz, 3H, CH_3CH=CH), 0.93 (d, *J* 6.3 Hz, 3H, CH_3), 0.89 (s, 9H, *t*-BuSi), −0.05 (s, 6H, 2 × CH_3Si); ^{13}C NMR (126 MHz, C_6D_6) *δ*: 167.2, 129.1, 126.8, 70.2, 56.9, 25.6, 22.8, 20.3, 17.8, 17.6, −4.7, −5.2; IR (film) *ν*: 3282, 1649, 1550, 835, 775 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{14}H_{29}NO_2SiNa$ [M + Na$^+$] 294.1865. Found 294.1864.

***N*-((2*S*,3*S*,*E*)-2-((*t*-Butyldimethylsilyl)oxy)hex-4-en-3-yl)-acetamide (24).** Prepared in the same manner as compound **21**. Purification by chromatography on silica gel (25% AcOEt in hexanes). Yield 184 mg (92%) starting from 200 mg (0.731 mmol) of compound **12a**; colorless oil; $[\alpha]_D^{22}$ −2.1 (*c* 2.0, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 5.76 (d, *J* 7.2 Hz, 1H, NH), 5.62−5.53 (m, 1H, C*H*=CH), 5.43−5.35 (m, 1H, CH=C*H*), 4.33−4.25 (m, 1H, C*H*CH=CH), 3.92−3.82 (m, 1H, C*H*CH_3), 2.03 (s, 3H, CH_3CO), 1.67 (d, *J* 6.4 Hz, 3H, CH_3CH=CH), 1.11 (d, *J* 6.2 Hz, 3H, CH_3CH), 0.88 (s, 9H, *t*-BuSi), 0.05 (s, 3H, CH_3Si), 0.03 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 169.6, 130.3, 126.2, 70.5, 56.0, 25.8, 23.5, 21.0, 18.0, 17.6, −4.4, −4.9; IR (film) *ν*: 3289, 1651, 1094, 835 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{14}H_{30}NO_2Si$ [M + H$^+$] 272.2046. Found 272.2044.

Methyl *O*-(*t*-Butyldimethylsilyl)-*N*-(methoxycarbonyl)-L-*allo*-threoninate (29). Ozone was passed through a stirred solution of carbamate **15** (50 mg, 0.185 mmol) in 10 mL of CH_2Cl_2 and 0.64 mL of 2.5 M methanolic NaOH at −70 °C. The progress of the reaction was followed by TLC (AcOEt/hexane 1:4). After 1 h, yellow precipitation occurred and reaction mixture became blue. At this point, oxygen was bubbled through the reaction mixture for 20 min. It was than diluted with water (15 mL) and CH_2Cl_2 (15 mL), and the resulting mixture was warmed slowly to room temperature. The organic layer was separated, and the aqueous one was extracted with CH_2Cl_2 (3 × 15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, and the solvent was removed under diminished pressure. The residue was chromatographed on silica gel to (20% AcOEt in hexanes) to afford 47 mg of product **29** (85%) as a pale-yellow oil. $[\alpha]_D^{22}$ +25.4 (*c* 1.3, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 5.41 (d, *J* 7.3 Hz, 1H, NH), 4.29−4.21 (m, 1H, C*H*NH), 4.10−4.00 (m, 1H, C*H*OTBS), 3.71 (s, 3H, CH_3O), 3.65 (s, 3H, CH_3O), 1.21 (d, *J* 6.4 Hz, 3H, CH_3CH), 0.83 (s, 9H, *t*-BuSi), 0.02 (s, 3H, CH_3Si), 0.01 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 170.5, 156.3, 69.8, 60.0, 52.3, 52.0, 25.6, 20.4, 17.8, −4.6, −5.2; IR (film) *ν*: 3443, 3345, 1732, 1512, 1254, 835, 777 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{13}H_{28}NO_5Si$ [M + H$^+$] 306.1737. Found 306.1732.

Methyl *N*-((Benzyloxy)carbonyl)-*O*-(*t*-butyldimethylsilyl)-L-*allo*-threoninate (31). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel to (20% AcOEt in hexanes). Yield 75 mg (71%) starting from 100 mg (0.275 mmol) of compound **19**; colorless oil; $[\alpha]_D^{25}$ +22 (*c* 3.65, $CHCl_3$) [lit.[51] +27.3 (*c* 0.55, CH_2Cl_2)]; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.40−7.29 (m, 5H, Ph), 5.50 (d, *J* 7.2 Hz, 1H, NH), 5.20−5.06 (m, 2H, OCH_2Ph), 4.35−4.26 (m, 1H, C*H*), 4.16−4.05 (m, 1H, C*H*), 3.74 (s, 3H, $COOCH_3$), 1.24 (d, *J* 6.3 Hz, 3H, CH_3CH), 0.86 (m, 9H, *t*-Bu), 0.04 (s, 3H, CH_3), 0.03 (s, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 170.5, 155.8, 136.5, 128.6, 128.3, 128.2, 70.01, 67.1, 60.2, 52.2 25.7, 20.6, 18.0, −4.4, −5.0; IR (film) *ν*: 3441, 3354, 1730, 1507 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{19}H_{31}NO_5SiNa$ [M + Na$^+$] 404.1869. Found 404.1870.

Methyl *N*-((Benzyloxy)carbonyl)-*O*-(*t*-butyldimethylsilyl)-D-*allo*-threoninate (*ent*-31). Prepared in the same manner as compound **25**. Yield 53 mg (73%); colorless oil; $[\alpha]_D^{22}$ −21 (*c* 1.5, $CHCl_3$); HRMS (ESI-TOF) *m*/*z* calcd for $C_{19}H_{31}NO_5SiNa$ [M + Na$^+$] 404.1869. Found 404.1861.

Methyl *N*-(*tert*-Butoxycarbonyl)-*O*-(*t*-butyldimethylsilyl)-L-*allo*-threoninate (32). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (20% AcOEt in hexanes). Yield 58 mg (92%) starting from 60 mg (0.182 mmol) of compound **20**; colorless oil; $[\alpha]_D^{23}$ +33.8 (*c* 0.7, $CHCl_3$); ^{1}H NMR (600 MHz, $CDCl_3$) *δ*: 5.25 (d, *J* 7.5 Hz, 1H, NH), 4.26−4.17 (m, 1H, C*H*NH), 4.10−4.01 (m, 1H, C*H*OTBS), 3.73 (s, 3H, CH_3O), 1.43 (s, 9H, *t*-BuO), 1.22 (d, *J* 6.4 Hz, 3H, CH_3CH), 0.85 (s, 9H, *t*-BuSi), 0.03 (s, 6H, 2 × CH_3Si); ^{13}C NMR (151 MHz, $CDCl_3$) *δ*: 170.7, 155.1, 79.8, 69.9, 59.6, 52.0, 28.3, 25.6, 20.5, 17.9, −5.1; IR (film) *ν*: 3447, 3365, 1747, 1719, 1499, 1167, 836, 777 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{16}H_{33}NO_5SiNa$ [M + Na$^+$] 370.2026. Found 370.2018.

Methyl *N*-Acetyl-*O*-(*t*-butyldimethylsilyl)-L-*allo*-threonate (33). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel to (20% AcOEt in hexanes). Yield 130 mg (82%) starting from 150 mg (0.55 mmol) of compound **21**; colorless oil; $[\alpha]_D^{25}$ +52.8 (*c* 1.16, $CHCl_3$) [lit.[52] +47 (*c* 0.32, $CHCl_3$)]; ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 6.20 (d, *J* 8.0 Hz, 1H, NH), 4.53 (dd, *J* 8.1, 3.4 Hz, 1H, C*H*NHCbz), 4.08 (qd, *J* 6.4, 3.4 Hz, 1H, CH_3CH), 3.75 (s, 3H, CH_3O), 2.02 (s, 3H, CH_3CO), 1.26 (d, *J* 6.4 Hz, 3H, CH_3CH), 0.87 (s, 9H, *t*-*Bu*Si), 0.04 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 170.6, 169.5, 70.1, 58.5, 52.2, 25.8, 23.4, 20.9, 18.0, −4.4, −4.9; IR (film) *ν*: 3289, 1747, 1660, 1546, 1256, 835 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{13}H_{27}NO_4SiNa$ [M + Na$^+$] 312.1607. Found 312.1611.

Methyl (2*S*,3*S*)-2-(((Benzyloxy)carbonyl)amino)-3-((*t*-butyldimethylsilyl)oxy)-3-phenylpropanoate (38). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (20% AcOEt in hexanes); Yield 40 mg (86%) starting from 37 mg (0.106 mmol) of compound **25**; colorless oil; $[\alpha]_D^{23}$ +75.9 (*c* 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.36−7.27 (m, 10H, 2 × Ph), 5.30 (br d, *J* 7.6 Hz, 1H, NH), 5.06 (br d, *J* 4.2 Hz, 1H, PhC*H*OTBS), 4.59 (br dd, *J* 8.5, 4.3 Hz, 1H, C*H*NH), 3.66 (s, 3H, CH_3O), 3.64−3.60 (m, 2H, OCH_2Ph), 0.89 (s, 9H, *t*-BuSi), 0.06 (s, 3H, CH_3Si), −0.14 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 170.2, 156.2, 140.1, 139.4, 128.1(x3), 127.9, 126.2(x2), 75.3, 61.1, 52.3, 51.9, 25.6, 18.1, −4.9, −5.4; IR (film) *ν*: 3442, 3335, 1733, 1513, 1257, 838, 779 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{24}H_{33}NO_5SiNa$ [M + Na$^+$] 466.2026. Found 466.2029.

Methyl (2*S*,3*S*)-2-(((Benzyloxy)carbonyl)amino)-3-((*t*-butyldimethylsilyl)oxy)-4-phenylbutanoate (39). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (20% AcOEt in hexanes). Yield 74 mg (89%) starting from 80 mg (0.182 mmol) of compound **26**; colorless oil; $[\alpha]_D^{23}$ +24.1 (*c* 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.40−7.19 (m, 10H, 2 × Ph), 5.53 (d, *J* 6.9 Hz, 1H, NH), 5.09 (br s, 2H, OCH_2Ph), 4.46−4.37 (m, 1H, C*H*NH), 4.30−4.18 (m, 1H, C*H*OTBS), 3.79 (s, 3H, CH_3O), 2.93 (dd, *J* 13.6, 6.3 Hz, 1H, C*H*HPh), 2.82 (dd, *J* 13.6, 7.9 Hz, 1H, CH*H*Ph), 0.81 (s, 9H, *t*-BuSi), −0.02 (s, 3H, CH_3Si), −0.33 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 169.4, 160.3, 137.7, 129.7, 128.5, 128.4, 128.1, 128.0, 126.6, 75.2, 66.9, 58.5, 52.2, 40.7, 25.7, 17.9, −4.9, −5.2; IR (film) *ν*: 3439, 3362, 1727, 1256, 1101, 837, 777, 699 cm^{-1}; HRMS (ESI-TOF) *m*/*z* calcd for $C_{25}H_{36}NO_5Si$ [M + H$^+$] 458.2363. Found 458.2363.

Methyl (2*S*,3*R*)-2-(((Benzyloxy)carbonyl)amino)-4-((*t*-butyldimethylsilyl)oxy)-3-methylbutanoate (45a). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (10% AcOEt in hexanes). Yield 52 mg (87%) starting from 60 mg (0.159 mmol) of compound **44a**; colorless oil; $[\alpha]_D^{22}$ −1.1 (*c* 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) *δ*: 7.44−7.27 (m, 5H, Ph), 6.03 (d, *J* 8.3 Hz, 1H, NH), 5.21−4.97 (m, 2H, OCH_2Ph), 4.35 (dd, *J* 8.6, 4.3 Hz, 1H, C*H*NH), 3.73 (s, 3H, CH_3O), 3.63 (dd, *J* 10.4, 3.8 Hz, 1H, C*H*HOTBS), 3.50 (dd, *J* 10.4, 5.5 Hz, 1H, CH*H*OTBS), 2.24−2.28 (m, 1H, C*H*CH_3), 1.03 (d, *J* 7.1 Hz, 3H, CH_3CH), 0.89 (s, 9H, *t*-BuSi), 0.04 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) *δ*: 172.5, 156.6, 136.5, 128.4, 127.9, 127.7, 66.7, 65.2, 57.8, 52.1, 36.6, 25.8, 18.1, 14.4, −5.7; IR (film) *ν*: 3400, 1729, 838 cm^{-1};

dx.doi.org/10.1021/jo502026a | *J. Org. Chem.* 2014, 79, 11700−11713

HRMS (ESI-TOF) m/z calcd for $C_{20}H_{34}NO_5Si$ [M + H^+] 396.2206. Found 396.2205.

Methyl (2*S*,4*R*)-2-(((Benzyloxy)carbonyl)amino)-4-((*t*-butyldimethylsilyl)oxy)pentanoate (45b). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (20% AcOEt in hexanes). Yield 58 mg (93%) starting from 60 mg (0.159 mmol) of compound **44b**; colorless oil; $[\alpha]_D^{22}$ −26.2 (c 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.40−7.28 (m, 5H, Ph), 5.83 (d, J 6.7 Hz, 1H, NH), 5.14 (d, J 12.5 Hz, 1H, OC*H*HPh), 5.08 (d, J 12.5 Hz, 1H, OCH*H*Ph), 4.46−4.39 (m, 1H, C*H*NH), 4.01−3.93 (m, 1H, C*H*OTBS), 3.73 (s, 3H, CH_3O), 1.96−1.86 (m, 1H, C*H*H), 1.85−1.77 (m, 1H, CH*H*), 1.17 (d, J 6.1 Hz, 3H, CH_3CH), 0.88 (s, 9H, *t*-BuSi), 0.06 (s, 6H, 2 × CH_3Si); ^{13}C NMR (126 MHz, cdcl$_3$) δ 173.0, 156.0, 136.5, 128.4, 127.9, 127.8, 66.7, 66.2, 52.2, 52.1, 40.3, 25.8, 23.8, 17.9, −4.2, −5.0; IR (film) ν: 3343, 1725, 1255, 1217, 836, 776 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{33}NO_5SiNa$ [M + Na^+] 418.2026. Found 418.2026.

Methyl *O*-(*t*-Butyldimethylsilyl)-*N*-(methoxycarbonyl)-D-threoninate (30). Prepared in the same manner as compound **25**; Purification by chromatography on silica gel (15% AcOEt in hexanes). Yield 44 mg (88%) starting from 54 mg (0.164 mmol) of compound **18**; colorless oil; $[\alpha]_D^{23}$ +14.3 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 5.35 (d, J 9.3 Hz, 1H, NH), 4.47−4.39 (m, 1H, C*H*OTBS), 4.24 (dd, J 9.3, 1.5 Hz, 1H, C*H*NH), 3.72 (s, 3H, CH_3O), 3.71 (s, 3H, CH_3O), 1.20 (d, J 6.3 Hz, 3H, CH_3CH), 0.84 (s, 9H, *t*-BuSi), 0.04 (s, 3H, CH_3Si), −0.02 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.4, 157.3, 68.8, 59.9, 52.4, 52.2, 25.6, 20.8, 17.8, −4.4, −5.4; IR (film) ν: 3440, 3346, 1729, 1510, 1255, 836, 777 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{27}NO_5SiNa$ [M + Na^+] 328.1556. Found 328.1556.

Methyl *N*-((Benzyloxy)carbonyl)-*O*-(*t*-butyldimethylsilyl)-D-threoninate (34). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (20% AcOEt in hexanes). Yield 85 mg (82%) starting from 100 mg (0.275 mmol) of compound **22**; a colorless oil; $[\alpha]_D^{25}$ +8.6 (c 0.7, $CHCl_3$) [lit.[51] +9 (c 1, $CHCl_3$)]; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.44−7.29 (m, 5H, Ph), 5.43 (d, J 9.5 Hz, 1H, NH), 5.14 (br s, 2H, OCH_2Ph), 4.50−4.40 (m, 1H, CH$_3$C*H*OTBS), 4.28 (dd, J 9.6, 1.6 Hz, 1H, C*H*NHCbz), 3.73 (s, 3H, OCH_3), 1.21 (d, J 6.3 Hz, 3H, CH_3CH), 0.84 (s, 9H, (CH_3)$_3$C), 0.04 (s, 3H, CH_3), −0.01 (s, 3H, CH_3); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.3, 156.7, 136.3, 128.5, 128.1, 128.1, 68.8, 67.1, 59.9, 52.2, 25.6, 20.8, 17.8, −4.4, −5.4; IR (film) ν: 3448, 3356, 1730, 1507 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{19}H_{31}NO_5SiNa$ [M + Na^+] 404.1869. Found 404.1866.

Methyl *N*-((Benzyloxy)carbonyl)-*O*-(*t*-butyldimethylsilyl)-L-threoninate (*ent*-34). Prepared in the same manner as compound **25**. Yield 50 mg (83%); colorless oil; $[\alpha]_D^{22}$ −8.2 (c 1.1, $CHCl_3$); HRMS (ESI-TOF) m/z calcd for $C_{19}H_{31}NO_5SiNa$ [M + Na^+] 404.1869. Found 404.1865.

Methyl *N*-(*t*-Butoxycarbonyl)-*O*-(*t*-butyldimethylsilyl)-D-threoninate (35). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (20% AcOEt in hexanes). Yield 90 mg (80%) starting from 107 mg (0.325 mmol) of compound **23**; colorless oil; $[\alpha]_D^{22}$ +3.3 (c 0.6, CHCl3) [lit.[53] for ***ent*-35**: −1.1 (c 2.4, $CHCl_3$)]; ^{1}H NMR (600 MHz, C_6D_6) δ: 5.54 (d, J 9.7 Hz, 1H, NH), 4.59 (dd, J 9.9, 1.9 Hz, 1H, C*H*NH), 4.37 (qd, J 6.2, 1.9 Hz, 1H, CH$_3$C*H*OTBS), 3.40 (s, 3H, CH_3O), 1.52 (s, 9H, *t*-BuO), 1.17 (d, J 6.3 Hz, 3H, CH_3CH), 0.92 (s, 9H, *t*-BuSi), 0.00 (s, 3H, CH_3Si), −0.02 (s, 3H, CH_3Si); ^{13}C NMR (151 MHz, C_6D_6) δ: 171.1, 156.0, 79.1, 69.0, 59.5, 51.2, 28.0, 25.4, 20.4, 17.6, −4.8, −5.7; IR (film) ν: 3457, 1755, 1721, 15000, 1168 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{16}H_{33}NO_5SiNa$ [M + Na^+] 370.2026. Found 370.2020.

Methyl *N*-Acetyl-*O*-(*t*-butyldimethylsilyl)-D-threoninate (36). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (25% AcOEt in hexanes). Yield 65 mg (86%) starting from 70 mg (0.260 mmol) of compound **24**; colorless oil; $[\alpha]_D^{23}$ −5.3 (c 0.8, $CHCl_3$) [lit.[52] for ***ent*-36**: +6.5 (c 0.02, CH_2Cl_2)]; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 6.08 (d, J 9.0 Hz, 1H, NH), 4.54 (dd, J 9.4, 1.8 Hz, 1H, C*H*NH), 4.41 (qd, J 6.3, 1.8 Hz, 1H, CH$_3$C*H*OTBS), 3.69 (s, 3H, CH_3O), 2.06 (s, 3H, CH_3CO), 1.14 (d, J 6.3 Hz, 3H, CH_3CH), 0.82 (s, 9H, *t*-BuSi), 0.02 (s, 3H, CH_3Si), −0.03 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.1, 170.4, 68.8, 57.7, 52.2, 25.6, 23.2, 20.8, 17.8, −4.5, −5.4; IR (film) ν: 3302, 1749, 1662, 1531, 1254, 1096, 838, 777 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{13}H_{28}NO_4Si$ [M + H^+] 290.1788. Found 290.1787.

Methyl (2*R*,3*S*)-2-(((Benzyloxy)carbonyl)amino)-3-((*t*-butyldimethylsilyl)oxy)-3-phenylpropanoate (40). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (20% AcOEt in hexanes). Yield 48 mg (77%) starting from 60 mg (0.141 mmol) of compound **27**; colorless oil; $[\alpha]_D^{22}$ +46.8 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.41−7.22 (m, 10H, 2 × Ph), 5.51 (d, J 9.6 Hz, 1H, NH), 5.32 (s, 1H, PhC*H*), 5.02−4.91 (m, 2H, OCH_2Ph), 4.49 (dd, J 9.8, 1.8 Hz, 1H, C*H*NH), 3.77 (s, 3H, CH_3O), 0.87 (s, 9H, *t*-BuSi), −0.02 (s, 3H, CH_3Si), −0.15 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 170.8, 156.1, 140.4, 136.3, 128.5, 128.1, 128.1, 128.0, 127.8, 126.1, 74.6, 66.9, 61.1, 52.4, 29.7, 25.6, 18.1, −4.7, −5.6; IR (film) ν: 3308, 1745, 1667, 1536, 1252, 1101, 836, 777 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{24}H_{33}NO_5SiNa$ [M + Na^+] 466.2026. Found 466.2029.

Methyl (2*R*,3*S*)-2-(((Benzyloxy)carbonyl)amino)-3-((*t*-butyldimethylsilyl)oxy)-4-phenylbutanoate (41). Prepared in the same manner as compound **25a**. Purification by chromatography on silica gel (10% AcOEt in hexanes). Yield 76 mg (82%) starting from 90 mg (0.205 mmol) of compound **28**; colorless oil; $[\alpha]_D^{23}$ +18.4 (c 1.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.47−7.13 (m, 10H, 2 × Ph), 5.47 (d, J 9.8 Hz, 1H, NH), 5.22 (d, J 12.2 Hz, 1H, OC*H*HPh), 5.16 (d, J 12.2 Hz, 1H, OCH*H*Ph), 4.48−4.36 (m, 1H, BnC*H*OSi), 4.27 (br d, J 9.8 Hz, 1H, C*H*NH), 3.68 (s, 3H, CH_3O), 2.90−2.74 (m, 2H, CH_2Ph), 0.86 (s, 9H, *t*-BuSi), −0.00 (s, 3H, CH_3Si), −0.04 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 171.6, 156.6, 136.8, 136.4, 129.5, 128.7, 128.5, 128.4, 128.2, 127.6, 126.9, 126.8, 74.3, 67.1, 56.7, 52.2, 41.2, 25.7, 17.9, −4.7, −5.2; IR (film) ν: 3372, 1723, 834 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{25}H_{35}NO_5SiNa$ [M + Na^+] 480.2182. Found 480.2180.

Methyl (2*R*,3*R*)-2-(((Benzyloxy)carbonyl)amino)-4-((*t*-butyldimethylsilyl)oxy)-3-methylbutanoate (43a). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (25% AcOEt in hexanes). Yield 64 mg (87%) starting from 60 mg (0.159 mmol) of compound **41a**; colorless oil; $[\alpha]_D^{23}$ +9.8 (c 0.7, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.39−7.27 (m, 5H, Ph), 5.70 (d, J 8.5 Hz, 1H, NH), 5.16−5.03 (m, 2H, OCH_2Ph), 4.50 (dd, J 8.8, 3.4 Hz, 1H, C*H*NH), 3.73 (s, 3H, CH_3O), 3.57−3.45 (m, 2H, CH_2OTBS), 0.89 (s, 9H, *t*-BuSi), 0.03 (s, 6H, 2 × CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 172.4, 156.1, 136.4, 128.4, 128.0, 127.9, 66.8, 65.2, 56.2, 52.1, 37.9, 25.8, 18.1, 12.3, −5.6; IR (film) ν: 3375, 1725, 837 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{34}NO_5Si$ [M + H^+] 396.2206. Found 396.2198.

Methyl (2*R*,4*R*)-2-(((Benzyloxy)carbonyl)amino)-4-((*t*-butyldimethylsilyl)oxy)pentanoate (43b). Prepared in the same manner as compound **25**. Purification by chromatography on silica gel (10% AcOEt in hexanes). Yield 62 mg (60%) starting from 100 mg (0.265 mmol) of compound **42b**; colorless oil; $[\alpha]_D^{22}$ −4.8 (c 0.5, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.42−7.27 (m, 5H, Ph), 5.57 (d, J 5.8 Hz, 1H, NH), 5.15−5.10 (m, 2H, OCH_2Ph), 4.43−4.26 (m, 1H, C*H*NH), 4.10−3.94 (m, 1H, C*H*OTBS), 3.73 (s, 3H, CH_3O), 2.00−1.80 (m, 2H, CH_2), 1.20−1.16 (m, 4H, CH_3C*H*), 0.87 (s, 9H, *t*-BuSi), 0.05 (s, 3H, CH_3Si), 0.04 (s, 3H, CH_3Si); ^{13}C NMR (126 MHz, $CDCl_3$) δ: 173.0, 155.8, 136.3, 128.4, 128.0, 128.0, 66.9, 66.4, 52.2, 41.3, 29.7, 25.8, 23.6, 17.9, −4.4, −4.8; IR (film) ν: 3370, 1721, 836 cm^{-1}; HRMS (ESI-TOF) m/z calcd for $C_{20}H_{33}NO_5SiNa$ [M + Na^+] 418.2026. Found 418.2019.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H and ^{13}C NMR spectra for selected compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

dx.doi.org/10.1021/jo502026a | J. Org. Chem. 2014, 79, 11700−11713

AUTHOR INFORMATION

Corresponding Author

*E-mail: sebastian.stecko@icho.edu.pl (S.S.).

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENTS

Author is grateful to Polish Ministry of Science and Higher Education for financial support of research (*Iuventus Plus Grant* No. IP2011 051871 and IP2010 039070). The authors are grateful to The Regional Council of Mazovia and European Union within European Regional Development Fund for a Ph.D. student scholarship (P.S.). The authors are also grateful to The European Union within the Structural Funds No. POKL.04.01.01-00-114/09-01 for a postdoctoral fellowship (A.P.-H.)

REFERENCES

(1) Hughes, A. B., Ed. *Amino Acids, Peptides and Proteins in Organic Chemistry: Protection Reactions, Medicinal Chemistry, Combinatorial Synthesis*; Wiley: Weinheim, 2011; Vol 4.

(2) Pollegioni, L., Servi, S., Eds. *Unnatural Amino Acids*; Springer: New York, 2012.

(3) Williams, R. M. *Synthesis of Optically Active α-Amino Acids*; Pergamon Press: Oxford, U.K., 1989.

(4) Baltz, R. H.; Miao, V.; Wrigley, S. K. *Nat. Prod. Rep.* **2005**, *22*, 717−741.

(5) Castanho, M., Santos, N., Eds. *Peptide Drug Discovery and Development: Translational Research in Academia and Industry*; Wiley: Weinheim, 2011.

(6) Phoenix, D. A.; Dennison, S. R.; Harris, F. *Antimicrobial Peptides*; Wiley: Weinheim, 2012.

(7) Molinski, V. L. *Handbook of Marine Natural Products: Isolation, Structure, Medicine and Synthesis*; Wiley & Sons, Inc.: New York, 2012.

(8) Groner, B. *Peptides as Drugs: Discovery and Development*; Wiley: Weinheim, 2009.

(9) (a) Prakash, A.; Goa, K. *BioDrugs* **1999**, *12*, 139−157. (b) Esposito, P.; Barbero, L.; Caccia, P.; Caliceti, P.; D'Antonio, M.; Piquet, G.; Veronese, F. M. *Adv. Drug Delivery Rev.* **2003**, *55*, 1279−1291.

(10) (a) Zaninovic, V.; Gukovskaya, A. S.; Gukovsky, I.; Mouria, M.; Pandol, S. J. *Am. J. Physiol. Gastrointest. Liver Physiol.* **2000**, *279*, G666−G6676. (b) Ibii, N.; Ikeda, M.; Takahara, Y.; Eigyo, M.; Akiyoshi, T.; Matsushita, A. *Peptides* **1989**, *10*, 779−783.

(11) (a) Briones, M.; Bajaj, M. *Expert Opin. Pharmacother.* **2006**, *7*, 1055−1064. (b) Mann, R. J.; Nasr, N. E.; Sinfield, J. K.; Paci, E.; Donnelly, D. *Br. J. Pharmacol.* **2010**, *160*, 1973−1984.

(12) (a) Lalezari, J. P.; Eron, J. J.; Carlson, M.; Cohen, C.; DeJesus, E.; Arduino, R. C.; Gallant, J. E.; Volberding, P.; Murphy, R. L.; Valentine, F.; Nelson, E. L.; Sista, P. R.; Dusek, A.; Kilby, J. M. *AIDS (London, U.K.)* **2003**, *17*, 691−698. (b) Greenberg, M. L.; Cammack, N. J. *Antimicro. Chemother.* **2004**, *54*, 333−340. (c) Fung, H. B.; Guo, Y. *Clin. Ther.* **2004**, *26*, 352−378.

(13) (a) Burke, T. R., Jr; Knight, M.; Chandrasekhar, B.; Ferretti, J. A. *Tetrahedron Lett.* **1989**, *30*, 519−522. (b) Laycock, M. V.; Hildebrand, P. D.; Thibault, P.; Walter, J. A.; Wright, J. L. C. *J. Agric. Food Chem.* **1991**, *39*, 483−489. (c) Saini, H. S.; Barragán-Huerta, B. E.; Lebrón-Paler, A.; Pemberton, J. E.; Vázquez, R. R.; Burns, A. M.; Marron, M. T.; Seliga, C. J.; Gunatilaka, A. A. L.; Maier, R. M. *J. Nat. Prod.* **2008**, *71*, 1011−1015.

(14) (a) Zindel, J.; de Meijere, A. *J. Org. Chem.* **1995**, *60*, 2968−2973. (b) Andres, N.; Wolf, H.; Zähner, H.; Rössner, E.; Zeeck, A.; König, W. A.; Sinnwell, V. *Helv. Chim. Acta* **1989**, *72*, 426−437. (c) Rössner, E.; Zeeck, A.; König, W. A. *Angew. Chem., Int. Ed.* **1990**, *29*, 64−65. (d) Hofer, I.; Crusemann, M.; Radzom, M.; Geers, B.; Flachshaar, D.; Cai, X.; Zeeck, A.; Piel, J. *Chem. Biol.* **2011**, *18*, 381−91.

(15) (a) Morita, H.; Nagashima, S.; Takeya, K.; Itokawa, H. *J. Chem. Soc., Perkin Trans. 1* **1995**, 2327−2331. (b) Rossi, F.; Zanotti, G.; Saviano, M.; Iacovino, R.; Palladino, P.; Saviano, G.; Amodeo, P.; Tancredi, T.; Laccetti, P.; Corbier, C.; Benedetti, E. *J. Pept. Sci.* **2004**, *10*, 92−102.

(16) Ballio, A.; Barra, D.; Bossa, F.; Collina, A.; Grgurina, I.; Marino, G.; Moneti, G.; Paci, M.; Segre, A.; Simmaco, M. *FEBS Lett.* **1991**, *291*, 109−112.

(17) Zampella, A.; D'Auria, M. V.; Paloma, L. G.; Casapullo, A.; Minale, L.; Debitus, C.; Henin, Y. *J. Am. Chem. Soc.* **1996**, *118*, 6202−6209.

(18) Oku, N.; Gustafson, K. R.; Cartner, L. K.; Wilson, J. A.; Shigematsu, N.; Hess, S.; Pannell, L. K.; Boyd, M. R.; McMahon, J. B. *J. Nat. Prod.* **2004**, *67*, 1407−1411.

(19) Ford, P. W.; Gustafson, K. R.; McKee, T. C.; Shigematsu, N.; Maurizi, L. K.; Pannell, L. K.; Williams, D. E.; Dilip de Silva, E.; Lassota, P.; Allen, T. M.; Van Soest, R.; Andersen, R. J.; Boyd, M. R. *J. Am. Chem. Soc.* **1999**, *121*, 5899−5909.

(20) Plaza, A.; Gustchina, E.; Baker, H. L.; Kelly, M.; Bewley, C. A. *J. Nat. Prod.* **2007**, *70*, 1753−1760.

(21) Plaza, A.; Bifulco, G.; Keffer, J. L.; Lloyd, J. R.; Baker, H. L.; Bewley, C. A. *J. Org. Chem.* **2008**, *74*, 504−512.

(22) (a) Nakata, H.; Maeda, K.; Miyakawa, T.; Shibayama, S.; Matsuo, M.; Takaoka, Y.; Ito, M.; Koyanagi, Y.; Mitsuya, H. *J. Virol.* **2005**, *79*, 2087−2096. (b) Nishizawa, R.; Nishiyama, T.; Hisaichi, K.; Matsunaga, N.; Minamoto, C.; Habashita, H.; Takaoka, Y.; Toda, M.; Shibayama, S.; Tada, H.; Sagawa, K.; Fukushima, D.; Maeda, K.; Mitsuya, H. *Bioorg. Med. Chem. Lett.* **2007**, *17*, 727−731.

(23) Williams, D. H. *Acc. Chem. Res.* **1984**, *17*, 364−369.

(24) Jolad, S. D.; Hoffman, J. J.; Torrance, S. J.; Wiedhopf, R. M.; Cole, J. R.; Arora, S. K.; Bates, R. B.; Gargiulo, R. L.; Kriek, G. R. *J. Am. Chem. Soc.* **1977**, *99*, 8040−8044.

(25) Chênevert, R.; Thiboutot, S. *Synthesis* **1989**, 444−446.

(26) Shoji, J.; Hinoo, H.; Hattori, T.; Hirooka, K.; Kimura, Y.; Yoshida, T. *J. Antibiot.* **1989**, *42*, 1460−1464.

(27) Kato, T.; Hinoo, H.; Terui, Y.; Kikuchi, J.; Shoji, J. *J. Antibiot.* **1988**, *41*, 719−725.

(28) Hanessian, S.; Vakiti, R. R.; Dorich, S.; Banerjee, S.; Deschênes-Simard, B. *J. Org. Chem.* **2012**, *77*, 9458−9472.

(29) (a) Zhong, F.; Wang, Y.; Han, X.; Huang, K.-W.; Lu, Y. *Org. Lett.* **2011**, *13*, 1310−1313. (b) Xu, L.-W.; Lu, Y. *Org. Biomol. Chem.* **2008**, *6*, 2047−2053. (c) Wu, X.; Jiang, Z.; Shen, H.-M.; Lu, Y. *Adv. Synth. Catal.* **2007**, *349*, 812−816. (d) Xu, L.-W.; Luo, J.; Lu, Y. *Chem. Commun.* **2009**, 1807−1821. (e) Cheng, L.; Wu, X.; Lu, Y. *Org. Biomol. Chem.* **2007**, *5*, 1018−1020.

(30) Mlynarski, J.; Bas, S. *Chem. Soc. Rev.* **2014**, *43*, 577−587.

(31) (a) Jung, M. E.; Jung, Y. H. *Tetrahedron Lett.* **1989**, *30*, 6637−6640. (b) Shao, H.; Goodman, M. *J. Org. Chem.* **1996**, *61*, 2582−2583. (c) Schmidt, U.; Respondek, M.; Lieberknecht, A.; Werner, J.; Fischer, P. *Synthesis* **1989**, 256−261.

(32) (a) Makino, K.; Goto, T.; Hiroki, Y.; Hamada, Y. *Tetrahedron: Asymmetry* **2008**, *19*, 2816−2828. (b) Liu, Z.; Shultz, C. S.; Sherwood, C. A.; Krska, S.; Dormer, P. G.; Desmond, R.; Lee, C.; Sherer, E. C.; Shpungin, J.; Cuff, J.; Xu, F. *Tetrahedron Lett.* **2011**, *52*, 1685−1688.

(33) (a) Singjunla, Y.; Baudoux, J.; Rouden, J. *Org. Lett.* **2013**, *15*, 5770−5773. (b) MacMillan, J. B.; Molinski, T. F. *Org. Lett.* **2002**, *4*, 1883−1886. (c) Horikawa, M.; Busch-Petersen, J.; Corey, E. J. *Tetrahedron Lett.* **1999**, *40*, 3843−3846. (d) Yoshikawa, N.; Shibasaki, M. *Tetrahedron* **2002**, *58*, 8289−8298. (e) Lin, N.; Deng, Y.-Q.; Zhang, Z.-W.; Wang, Q.; Lu, G. *Tetrahedron: Asymmetry* **2014**, *25*, 650−657.

(34) (a) Kambourakis, S.; Rozzell, J. D. *Tetrahedron* **2004**, *60*, 663−669. (b) Fesko, K.; Giger, L.; Hilvert, D. *Bioorg. Med. Chem. Lett.* **2008**, *18*, 5987−5990. (c) Makart, S.; Bechtold, M.; Panke, S. *J. Biotechnol.* **2007**, *130*, 402−410. (d) Steinreiber, J.; Fesko, K.; Reisinger, C.; Schürmann, M.; van Assema, F.; Wolberg, M.; Mink, D.; Griengl, H. *Tetrahedron* **2007**, *63*, 918−926.

(35) (a) Andrés, J. M.; Martínez, M. a. A.; Pedrosa, R.; Pérez-Encabo, A. *Tetrahedron: Asymmetry* **2001**, *12*, 347−353. (b) Seo, Y.; Kim, H.; Chae, D. W.; Kim, Y. G. *Tetrahedron: Asymmetry* **2014**, *25*, 625−631.
(36) (a) Swift, M. D.; Sutherland, A. *Tetrahedron Lett.* **2007**, *48*, 3771−3773. (b) Jamieson, A. G.; Sutherland, A. *Tetrahedron* **2007**, *63*, 2123−2131.
(37) Kikuchi, M.; Konno, H. *Tetrahedron* **2013**, *69*, 7098−7101.
(38) (a) Horner, L.; Hoffmann, H. M. R.; Wippel, H. G. *Chem. Ber.* **1958**, *91*, 61−63. (b) Horner, L.; Hoffmann, H. M. R.; Wippel, H. G.; Klahre, G. *Chem. Ber.* **1959**, *92*, 2499−2505. (c) Wadsworth, W. S.; Emmons, W. D. *J. Am. Chem. Soc.* **1961**, *83*, 1733−1738. (d) Boutagy, J.; Thomas, R. *Chem. Rev.* **1974**, *74*, 87−99. (e) Maryanoff, B. E.; Reitz, A. B. *Chem. Rev.* **1989**, *89*, 863−927.
(39) (a) Corey, E. J.; Bakshi, R. K.; Shibata, S. *J. Am. Chem. Soc.* **1987**, *109*, 5551−5553. (b) Corey, E. J.; Bakshi, R. K.; Shibata, S.; Chen, C. P.; Singh, V. K. *J. Am. Chem. Soc.* **1987**, *109*, 7925−7926.
(40) (a) Nakamura, K.; Matsuda, T. Enzymatic Kinetic Resolution. In *Enantiomer Separation*; Toda, F., Ed.; Springer: Netherlands, 2004; pp 231−266. (b) Vulfson, E. N.; Halling, P. J.; Holland, H. L. *Enzymes in Nonaqueous Solvents: Methods and Protocols*; Humana Press: New York, 2001.
(41) (a) Luche, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 2226−2227. (b) Gemal, A. L.; Luche, J. L. *J. Am. Chem. Soc.* **1981**, *103*, 5454−5459.
(42) Stecko, S. *J. Org. Chem.* **2014**, *79*, 6342−6346.
(43) (a) Ichikawa, Y. *Synlett* **1991**, 238−240. (b) Ichikawa, Y.; Tsuboi, K.; Isobe, M. *J. Chem. Soc., Perkin Trans. 1* **1994**, 2791−2796. (c) Ichikawa, Y.; Kobayashi, C.; Isobe, M. *J. Chem. Soc., Perkin Trans. 1* **1996**, 377−382. (d) Ichikawa, Y.; Osada, M.; I. Ohtani, I.; Isobe, M. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1449−1456. (e) Ichikawa, Y. *Synlett* **2007**, 2927−2936.
(44) (a) Overman, L. E. *J. Am. Chem. Soc.* **1974**, *96*, 597−599. (b) Overman, L. E. *J. Am. Chem. Soc.* **1976**, *98*, 2901−2910. (c) Nishikawa, T.; Asai, M.; Ohyabu, N.; Isobe, M. *J. Org. Chem.* **1998**, *63*, 188−192. (d) Overman, L. E.; Carpenter, N. E. The Allylic Trihaloacetimidate Rearrangement. In *Organic Reactions*; John Wiley & Sons, Inc.: Hoboken, NJ, 2004.
(45) Marshall, J. A.; Garofalo, A. W.; Sedrani, R. C. *Synlett* **1992**, 643−645.
(46) Massad, S. K.; Hawkins, L. D.; Baker, D. C. *J. Org. Chem.* **1983**, *48*, 5180−5182.
(47) Ren, H.; Wulff, W. D. *Org. Lett.* **2012**, *15*, 242−245.
(48) Kobayashi, Y.; Takemoto, Y.; Kamijo, T.; Harada, H.; Ito, Y.; Terashima, S. *Tetrahedron* **1992**, *48*, 1853−1868.
(49) Kalesse, M.; Chary, K. P.; Quitschalle, M.; Burzlaff, A.; Kasper, C.; Scheper, T. *Chem.—Eur. J.* **2003**, *9*, 1129−1136.
(50) Tartaglia, S.; Padula, D.; Scafato, P.; Chiummiento, L.; Rosini, C. *J. Org. Chem.* **2008**, *73*, 4865−4873.
(51) Jackson, R. F. W.; Palmer, N. J.; Wythes, M. *J. Tetrahedron Lett.* **1994**, *35*, 7433−7434.
(52) Kuwano, R.; Okuda, S.; Ito, Y. *J. Org. Chem.* **1998**, *63*, 3499−3503.
(53) Muir, J. C. *Synthesis* **1998**, 613−618.