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Formal α-Vinylation of Amino Acids. Use of a New Benzeneselenolate Equivalent

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A new synthetic approach to the formal α-vinylation of α-amino acids is described, in which the readily available electrophile, ethylene oxide, serves as the vinyl cation equivalent. *N*-Benzoyl α-amino esters bearing appropriate side-chain protecting groups are deprotonated with lithium diisopropylamide in THF/TMEDA at −78 °C to generate the corresponding dianions. Exposure of these to ethylene oxide results in C-alkylation and lactonization to give the corresponding racemic, α-substituted homoserine lactones **2a–j** in 61–85% yield. Next, reduction of diphenyl diselenide with sodium trimethoxyborohydride generates a benzeneselenolate anion equivalent which efficiently cleaves the α-substituted homoserine lactones without competing lactone reduction (69–97% yields for **3a–j** following diazomethane workup). The protected α-[2-(phenylseleno)ethyl] amino acids thereby obtained are oxidized to the corresponding selenoxides through the agency of ozone at −78 °C. Pyrolysis of these in refluxing benzene or carbon tetrachloride gives the protected α-vinyl amino acids **4a–c** and **4e–j** in 95–100% yield. In the case of methyl N^{α}-benzoyl-2-[2′-(phenylseleno)ethyl]-N^{τ}-tritylhistidinate (**3d**), oxidation and pyrolysis (80%) are carried out in one pot by refluxing with tetrabutylammonium periodate in chloroform. Finally, deprotection is achieved by acidic hydrolysis. This methodology has been successfully applied to the synthesis, in racemic form, of the α-vinyl amino acids derived from phenylalanine (**5a**), DOPA (**5b**), histidine (**5c**), lysine (**5d**), ornithine (**5e**), valine (**5f**), alanine (**5g**), and homoserine (**5h**). In addition, α-vinylaspartic acid (**9**) and α-vinylarginine (**10**) could be obtained from α-vinylhomoserine derivative **4j** and α-vinylornithine (**5f**), respectively.

Introduction

α-Vinyl amino acids[1-5] are an important class of mechanism based inhibitors for enzymes of the amino acid decarboxylase class. For example, DOPA decarboxylase,[1] ornithine decarboxylase,[2] and glutamate decarboxylase,[3] all important medicinal targets, are irreversibly inhibited by the corresponding α-vinyl amino acids. α-Vinylhistidine reversibly inhibits histidine decarboxylase.[1a] Indeed, a large number of amino acid decarboxylases are known,[6] for which the corresponding α-vinyl amino acids might be expected to act as inhibitors. In the case of α-vinyl-DOPA, the "mechanism-based" nature of the inhibition has been borne out, as inactivation is known to require enzymatic decarboxylation.[1a] Hence, there is considerable interest in α-vinyl amino acids, both from a pharmaceutical and from a mechanistic point of view.

Among the synthetic approaches to α-vinyl amino acids, the α-vinylation of protected amino acids is arguably the most direct.[7-10] This approach begins with the amino acid side chain in place, as provided by Nature or a Strecker synthesis, and utilizes the intrinsic acidity of the α-proton to access an α-carbanion, which is then alkylated with a vinyl cation equivalent. There are several examples of this strategy in the literature, in which an amino acid derivative is deprotonated and then alkylated with either a phenylsulfonyl-activated Michael acceptor or an α-silyl acetaldehyde as vinyl cation equivalent.[7] However, these

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(3) Metcalf, B.; Jung, M. U. S. Patent 4,147,873, April 3, 1979.

(4) Tendler, S. J. B.; Threadgill, M. D.; Tisdale, M. J. *J. Chem. Soc., Perkin Trans. I* **1987**, 2617–2623.

(5) (a) Cho, C.; Ishii, R.; Hyeon, S.; Suzuki, A. *Agric. Biol. Chem.* **1987**, *51*, 2597–2598. (b) Soper, T. S.; Manning, J. M.; Marcotte, P. A.; Walsh, C. T. *J. Biol. Chem.* **1977**, *252*, 1571–1575. (c) Rando, R. R.; Relyea, N.; Cheng, L. *Ibid.* **1976**, *251*, 3306–3312.

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(7) For α-vinylation approaches, see: (a) Sawada, S.; Nakayama, T.; Esaki, N.; Tanaka, H.; Soda, K.; Hill, R. K. *J. Org. Chem.* **1986**, *51*, 3384–3386. (b) Steglich, W.; Wegmann, H. *Synthesis* **1980**, 481–483. (c) Huldrik, P. F.; Kulkarni, A. S. *J. Am. Chem. Soc.* **1981**, *103*, 6251–6253. (d) Metcalf, B. W.; Bonilavri, E. *J. Chem. Soc., Chem. Commun.* **1978**, 914–915.

(8) For alternative approaches, see: (a) Castelhano, A. L.; Horne, S.; Taylor, G. J.; Billedeau, R.; Krantz, A. *Tetrahedron*, **1988** *44*, 5451–5466. (b) Münster, P.; Steglich, W. *Synthesis* **1987**, 223–225. (c) Weber, T.; Aeschimann, R.; Maetzke, T.; Seebach, D. *Helv. Chim. Acta* **1986**, *69*, 1365–1377. (d) Castelhano, A. L.; Horne, S.; Billedeau, R.; Krantz, A. *Tetrahedron Lett.* **1986**, *27*, 2435–2438. (e) Greenlee, W. J.; Taub, D.; Patchett, A. A. *Tetrahedron Lett.* **1978**, 3999–4002. (f) Metcalf, B. W.; Jund, K. *Ibid.* **1978**, 3689–3692. (g) Taub, D.; Patchett, A. A. *Ibid.* **1977**, 2745–2748.

(9) For syntheses of (±)-α-vinylglycine see: (a) Fitzner, J. F.; Pratt, D. V.; Hopkins, P. B. *Tetrahedron Lett.* **1985**, *26*, 1959–1962. (b) Vyas, D. M.; Chiang, Y.; Doyle, T. W. *J. Org. Chem.* **1984**, *49*, 2037–2039. (c) Greenlee, W. J. *J. Org. Chem.* **1984**, *49*, 2632–2634. (d) Baldwin, J. E.; Haber, S. B.; Hoskins,C.; Kruse, L. I. *J. Org. Chem.* **1977**, *42*, 1239–1241. (e) Friis, P.; Helboe, P.; Larsen, P. O. *Acta Chem. Scand., Ser. B* **1974**, *28*, 317–321 and ref 7c.

(10) For syntheses of α-vinylglycine in enantiomerically enriched form see: (a) Pellicciari, R.; Natalini, B.; Marinozzi *Synth. Commun.* **1988**, *18*, 1715–1721. (b) Hanessian, S.; Sahoo, S. P. *Tetrahedron Lett.* **1984**, *25*, 1425–1428. (c) Schollkopf, U.; Nozulak, J.; Groth, U. *Tetrahedron* **1984** *40*, 1409–1417. (d) Afzali-Ardakani, A.; Rapoport, H. *J. Org. Chem.* **1980**, *45*, 4817 and ref 19.

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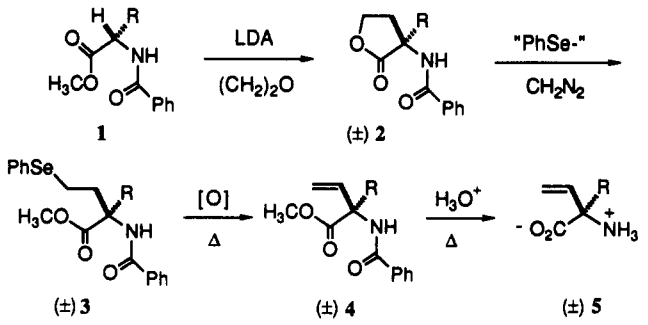
Scheme I



vinyl cation equivalents are not commercially available and the scope of these methods, with regard to side chain compatibility, remains to be demonstrated.

We have taken a conceptually different approach to the formal α-vinylation of amino acids, in which a readily available electrophile, ethylene oxide, serves as the vinyl cation equivalent (Scheme I).[11] Alkylation of a suitable α-carbanion with ethylene oxide is expected to proceed with facile *5-exo-trig* cyclization to give an α-substituted homoserine lactone directly. The necessary two-carbon fragment thereby becomes attached to the α-carbon. Its elaboration to a vinyl group follows from the sequence benzeneselenolate-mediated lactone cleavage, selenide oxidation and selenoxide pyrolysis. Herein, we report on the workability of this scheme and its compatibility with various amino acid side chains.

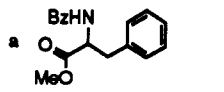
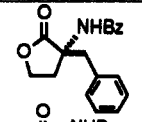
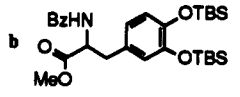
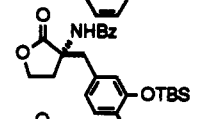
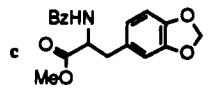
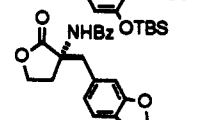
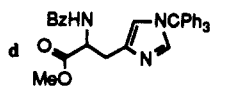
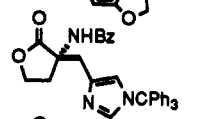
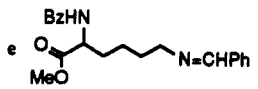
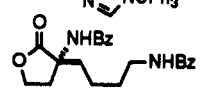
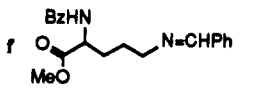
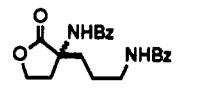
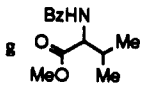
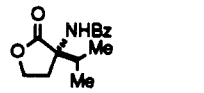
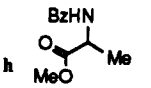
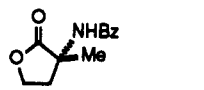
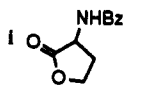
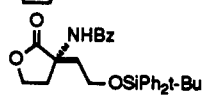
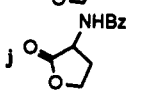
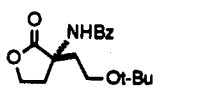
Results and Discussion

We initially observed that the α-monoanion of *N*-benzylidene-protected amino acid esters[12] is not sufficiently nucleophilic to react with ethylene oxide at an acceptable rate at room temperature. Rather, conversion to the homoserine lactone is inefficient and requires heating a solution of this monoanion with excess ethylene oxide in a sealed vessel overnight. On the other hand, the corresponding dianions, generated from *N*-benzoyl-protected α-amino esters,[13] react readily with ethylene oxide at or below room temperature. The desired homoserine lactones **2**, in racemic form, were obtained in good to very good yield in all cases studied (Table I). Evidently then, under these conditions, C-alkylation of the benzamido ester dianions is favored over N-alkylation and, even in the presence of excess ethylene oxide, monoalkylation predominates. Also noteworthy here is the ability to generate and effectively use dianions bearing silyl aryl ether (**1b**), *N*-tritylimidazole (**1d**), and imine (**1e**, **1f**) functional groups on the side chains.

Having developed conditions for the introduction of a two carbon fragment at the α-position, it remained to convert that fragment into a vinyl group. Both Smith[14] and Liotta[15] had reported nucleophilic benzeneselenolate equivalents capable of efficiently cleaving simple γ-lactones.[16] Smith and co-workers reduced diphenyl diselenide with sodium borohydride in dimethylformamide. Liotta and co-workers pointed out that Smith actually must have a sodium benzeneselenolate–diborane complex ($NaPhSeBH_3$) and reported lactone cleavage with sodium benzeneselenolate generated from sodium metal and diphenyl diselenide or from sodium hydride and benzeneselenol.

Screening of these benzeneselenolate reagents indicated that, for cleaving *N*-benzamido-α-substituted homoserine lactones, the Smith conditions were superior to the Liotta conditions in terms of both rate and yield. So, for example, in the case of α-methylhomoserine lactone **2h**, we obtained only 18–30% of the desired phenyl selenide using the Liotta conditions as compared with 86% under the conditions of Smith.[11] In each case, the intermediate carboxylate was

Table I. Dianion Alkylation with Ethylene Oxide

	protected amino acid	*t* (h)	product	yield
a		1		85%
b		1		84%
c		1		82%
d		2		80%
e		2		61%[a]
f		3		78%[a]
g		1		84%
h		0.5		72%[b]
i		8		52%[c] (62%)[d]
j		8		52%[c] (62%)[d]

[a] Overall yield for 3 steps: (i) LDA, $(CH_2)_2O$; (ii) 3 N HCl, THF; (iii) $PhCOCl$, NEt_3, CH_2Cl_2. [b] Reference 11. [c] Overall yield for 2 steps: (i) LDA, $(CH_2)_2O$; (ii) Ph-*t*-BuSiCl, imidazole, DMF. [d] Yield based on recovered **1i** in the first step. [e] Overall yield for 2 steps: (i) LDA, $(CH_2)_2O$; (ii) isobutylene, CH_2Cl_2, H_2SO_4.

(11) A preliminary communication of this α-vinylation methodology (one example) has appeared: Berkowitz, D. B. *Synth. Commun.* **1990**, *20*, 1819–1829.

(12) Stork, G.; Leong, A. Y. W.; Touzin, A. M. *J. Org. Chem.* **1976**, *41*, 3491-3493.

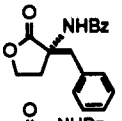
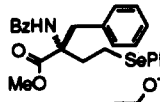
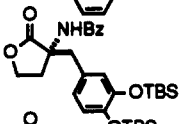
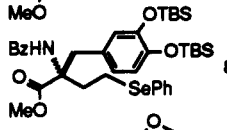
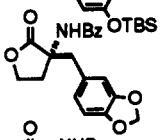
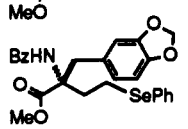
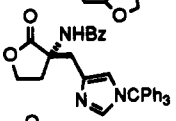
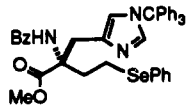
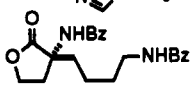
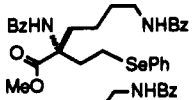
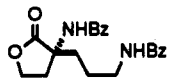
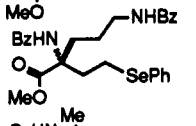
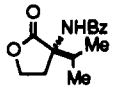
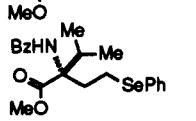
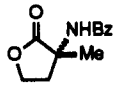
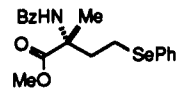
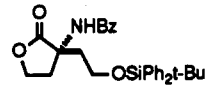
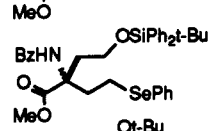
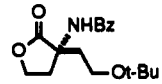
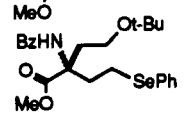
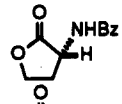
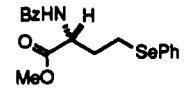
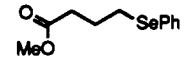
(13) (a) McIntosh, J. M.; Thangarasa, R.; Ager, D. J.; Zhi, B. *Tetrahedron* **1992**, *48*, 6219–6224. (b) Krapcho, A. P.; Dundulis, E. A. *Tetrahedron Lett.* **1976**, *26*, 2205–2208.

(14) (a) Scarborough, R. M., Jr.; Toder, B. H.; Smith, A. B., III. *J. Am. Chem. Soc.* **1980**, *102*, 3904–3913. (b) Scarborough, R. M., Jr.; Smith, A. B., III. *Tetrahedron Lett.* **1977**, 4361–4364.

(15) (a) Ley, S. V.; O'Neill, I. A.; Low, C. M. R. *Tetrahedron* **1986**, *46*, 5363-5368. (b) Liotta, D.; Sunay, U.; Santiesteban, H.; Markiewicz, W. Yoneda, F.; Kuroda, K. *J. Org. Chem.* **1981**, *46*, 2605–2610. (c) Liotta, D.; Santiesteban, H. *Tetrahedron Lett.* **1977**, 4369–4372.

(16) For other examples of the cleavage of lactones with benzeneselenolate anion, see: (a) Soucy, F.; Wernic, D.; Beaulieu, P. *J. Chem. Soc., Perkin Trans. I* **1991**, 2885–2887. (b) Dowd, P.; Kennedy, P. *Synth. Commun.* **1981**, *11*, 935–941. (c) Hoye, T. R.; Caruso, A. J. *Tetrahedron Lett.* **1978**, 4611–4614.

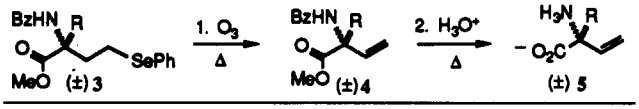
Table II. Lactone Cleavage with "NaPhSeB(OMe)$_3$"

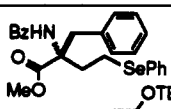
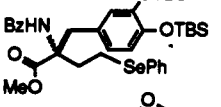
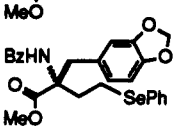
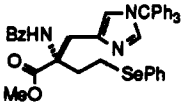
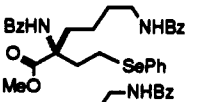
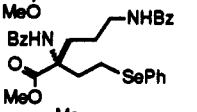
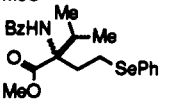
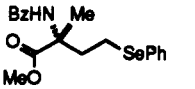
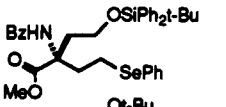
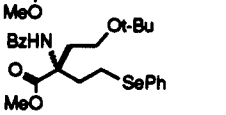
lactone		t (h)	product	yield
a	(±) 	1		97%
b	(±) 	2		81%
c	(±) 	1.3		83%
d	(±) 	3		68%
e	(±) 	1		88%
f	(±) 	1		79%
g	(±) 	1.5		96%
h	(±) 	1		89%
i	(±) 	2		90%
j	(±) 	2.5		93%
k	(±) 	1		85%
l		4.5		92%

protonated and esterified with diazomethane to give an α-[2-(phenylseleno)ethyl] α-amino ester. Unfortunately, attempts to apply this procedure to homoserine lactones bearing bulky α-substituents met with unsatisfactory results. Thus, with homoserine lactone **2i**, bearing an α-[2-[(*tert*-butyldiphenylsilyl)oxy]ethyl] side chain, lactone reduction (49%) was seen to compete with lactone cleavage (51%) under the Smith conditions. This problem was solved by developing a new benzeneselenolate equivalent.[17]

We reasoned that a phenyl selenide reagent possessing a potentially Lewis acidic, oxophilic boron component as in the Smith reagent,[14,15] but lacking reducing equivalents, might display both the reactivity and selectivity required. Accordingly, diphenyl diselenide was reduced with 2 equiv of sodium trimethoxyborohydride in DMF (60 °C, 1 h). Treatment of lactone **2h** with this reagent gave the desired α-[2-(phenylseleno)ethyl] amino ester **3i** in 90% yield. These conditions have been successfully applied to the cleavage of a variety of α-substituted *N*-benzoylhomoserine lactones (Table II).[17] These results suggest that the benzeneselenolate equivalent generated by the reduction of diphenyl diselenide with sodium trimethoxyborohydride may well be the reagent of choice of the cleavage of α-substituted homoserine lactones.

Table III. Selenide Oxidation/Pyrolysis and Deprotection



	selenide	yield step 1	yield step 2	product
a	(±) 	99%	70%	α-vinyl-phenylalanine
b	(±) 	97%	77%	α-vinyl-DOPA[a]
c	(±) 	95%	[b]	
d	(±) 	80%[c]	73%	α-vinyl-histidine
e	(±) 	99%	60%	α-vinyl-lysine
f	(±) 	100%	84%	α-vinyl-ornithine
g	(±) 	99%	85%	α-vinyl-valine
h	(±) 	100%[d]	89%	α-vinyl-alanine
i	(±) 	100%	78%	α-vinyl-homoserine
j	(±) 	99%	88%	α-vinyl-homoserine

[a] Isolated as the HCl salt. [b] Side-chain deprotection unsuccessful. [c] Bu_4NIO_4 (1 equiv), $CHCl_3$, reflux. [d] Reference 11.

Oxidation of the selenides **3** to the required selenoxides was next undertaken. Several oxidants, including hydrogen peroxide, sodium periodate, Chloramine T,[18] and ozone were examined. Oxidation with ozone at −78 °C in methylene chloride proved to be the best method in all but one case. The intermediate selenoxides were not isolated but rather were pyrolyzed directly to the protected α-vinyl amino acids. Addition of 1-hexene to the selenoxide solution prior to pyrolysis, as described by Barton and Crich,[19] resulted in nearly quantitative yields for the oxidation/pyrolysis sequence (Table III). Failure to include the 1-hexene gave markedly reduced yields.

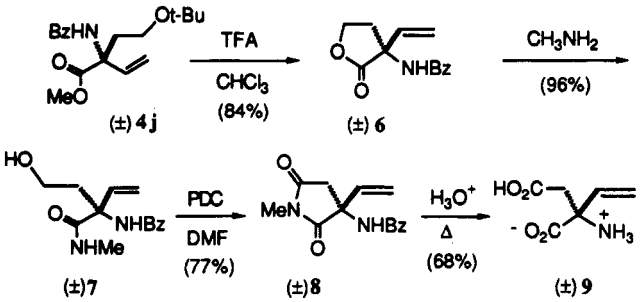
In the case of **3d**, however, all attempts at ozone-mediated selenoxide oxidation resulted in destruction of

(17) Pedersen, M. L.; Berkowitz, D. B. *Tetrahedron Lett.* **1992**, *33*, 7315-7318.

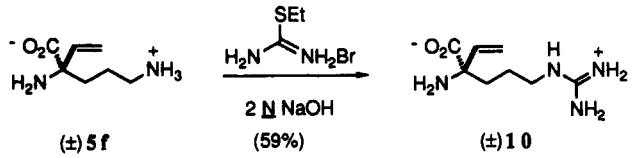
(18) Sharpless, K. B.; Gordon, K. M.; Lauer, P. F.; Patrick, D. W.; Singer, S. P.; Young, M. W. *Chem. Scr.* **1975**, *8A*, 9–13.

(19) Barton, D. H. R.; Crich, D.; Herve, Y.; Potier, P.; Thiery, J. *Tetrahedron* **1985**, *41*, 4347–4357.

Scheme II



Scheme III



the imidazole ring of the side chain. A convenient one-pot oxidation/pyrolysis procedure was found to solve this problem. Simply refluxing **3d** with 1 equiv of tetrabutylammonium periodate in chloroform gave **4d** directly in 80% isolated yield.

Finally, amino group, carboxyl group and side-chain deprotection were achieved simultaneously by refluxing the protected α-vinyl amino acids **4** with 6 N HCl (Table III). Only the methylenedioxy side chain of α-vinyl-DOPA derivative **4c** resisted cleavage under these conditions. This case was not pursued further as the alternative α-vinyl-DOPA derivative **4b**, bearing *tert*-butyldimethylsilyl (TBS) ether catechol protecting groups, was readily deprotected. We note that *installation* of the side chain protecting groups was also much more facile for **1b** (TBS ethers) than for **1c** (methylenedioxy, *vide infra*), giving the **b** series considerable advantage over the **c** series for the α-vinylation of DOPA. On the other hand, in the case of homoserine, both *tert*-butyl ether (**j** series) and *tert*-butyldiphenylsilyl ether (**i** series) side-chain protecting groups were nicely compatible with this chemistry and easily hydrolytically cleaved in the final step.

In addition, α-vinylaspartic acid (**9**) could be synthesized in four steps from the protected α-vinylhomoserine derivative **4j** (Scheme II). Thus, *tert*-butyl ether deprotection readily gave γ-lactone **6**. The pendant hydroxyethyl side chain could be released from lactone **6** by treatment with methylamine. The hydroxy amide **7** then underwent smooth four-electron oxidation to imide **8**. Acidic hydrolysis provided α-vinylaspartic acid.

Finally, α-vinylarginine **10** could be obtained from α-vinylornithine **5f**, in a single step, employing *S*-ethylisothiouronium bromide as formal amidine donor (Scheme III).[20]

Conclusions

A new procedure for the formal α-vinylation of α-amino acids has been developed. Key features include the use of the readily available electrophile ethylene oxide as a vinyl cation equivalent and the introduction of a new, chemoselective benzeneselenolate equivalent for α-substituted homoserine lactone cleavage. The overall yields obtained for this four step sequence [(i) lactone formation with ethylene oxide, (ii) lactone cleavage with benzeneselenolate anion, (iii) oxidation/pyrolysis, and (iv) deprotection] compare favorably to previously reported yields for the α-vinylation of protected amino acids.[7] However, the need to synthesize a vinyl cation equivalent is circumvented here. Furthermore, this methodology has been shown to be compatible with a considerable variety of side-chain functionality (β-branched alkyl, aryl, imine, benzamide, *N*-tritylimidazole, *tert*-butyl ether, alkyl silyl ether, aryl silyl ether, and acetal) and to provide ready access to the α-vinyl amino acids derived from alanine, phenylalanine, valine, homoserine, DOPA, ornithine, lysine, histidine, arginine, and aspartate.

Experimental Section

General. All reactions were conducted under an argon atmosphere using oven-dried glassware unless otherwise noted. Methylene chloride, pyridine, and diisopropylamine were distilled from CaH_2. THF, Et_2O and benzene were distilled from sodium benzophenone ketyl. Methanol was distilled from Mg. Other reagents were obtained from commercial sources and used without further purification. Flash chromatography was performed using Merck silica gel 60 (230-400 mesh). ^1H NMR spectra were recorded on a GE Omega-500, GE Omega-300, NT-360, or VXR-200 instrument. Proton-decoupled ^{13}C NMR spectra were acquired on a GE Omega-500, GE Omega-300, or VXR-200 instrument. Infrared spectra were obtained using an Analect RFX-65 FTIR spectrometer. Mass spectra were acquired at the Midwest Center for Mass Spectrometry (University of Nebraska—Lincoln) and are reported as *m/z* (relative intensity). Elemental analyses were carried out by M-H-W Labs (Phoenix, AZ). Melting points were determined using a Meltemp II (Laboratory Devices) apparatus and are uncorrected.

Methyl *N*-Benzoyl-3′,4′-bis(benzoyloxy)phenylalaninate. To a solution of (D,L)-DOPA methyl ester hydrochloride[21] (22.0 g, 88.8 mmol) and 4-(dimethylamino)pyridine (1.08 g, 8.88 mmol) in pyridine (440 mL) at 0 °C was added benzoyl chloride (30.9 mL, 266 mmol). After being stirred at rt for 1 h, the reaction mixture was filtered and then evaporated in vacuo. Flash chromatography [EtOAc/hexane/CH_2Cl_2 (50:50:5)] afforded the title compound (41.0 g, 88%) as a white solid: mp 173–175 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.32–3.34 (app d, J = 5 Hz, 2 H), 3.80 (s, 3 H), 5.11–5.17 (app dt, J = 5, 7 Hz, 1 H), 6.71–6.73 (d, J = 7 Hz, 1 H), 7.10–7.20 (m, 3 H), 7.30–7.57 (m, 9 H), 7.78–7.82 (m, 2 H), 8.00–8.05 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.3, 52.6, 53.5, 123.6, 124.7, 127.2, 127.2, 127.5, 128.5, 128.7, 128.7, 128.7, 130.1, 131.8, 133.7, 134.8, 141.6, 142.5, 164.1, 164.2, 166.9, 171.7; IR (film) 3420–3200, 1740, 1645 cm^{-1}; MS (FAB, 3-NOBA) 524 (20, MH^+), 464 (6), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{31}H_{26}NO_7$ (MH^+) 524.1709, obsd 524.1718. Anal. Calcd for $C_{31}H_{25}NO_7$: C, 71.12; H, 4.81; N, 2.67. Found: C, 71.38; H, 4.88; N, 2.71.

Methyl *N*-Benzoyl-3′,4′-dihydroxyphenylalaninate. To a suspension containing methyl *N*-benzoyl-3′,4′-bis(benzoyloxy)-phenylalaninate (20.1 g, 38.4 mmol) in MeOH (425 mL) and THF (85 mL) at rt was added K_2CO_3 (5.31 g, 38.4 mmol). After 2 h at rt, Dowex 50 × 8 (7.70 g, ca. 40 molar equiv) was added and the reaction mixture stirred for 1 h. Following filtration and evaporation of the solvent, flash chromatography (20–50% EtOAc/hexane) yielded the title compound (9.80 g, 81%) as a white solid: mp 142–143 °C; ^1H NMR (500 MHz, DMSO-d_6) δ 2.88-2.98 (m, 2 H), 3.62 (s, 3 H), 4.52–4.57 (m, 1 H), 6.51–6.66 (m, 3 H), 7.43–7.54 (m, 3 H), 7.79–7.81 (m, 2 H), 8.65–8.69 (br s, 1 H), 8.71 (s, 1 H), 8.73 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.7, 51.7, 54.6, 115.3, 116.3, 119.7, 127.3, 128.2, 128.3, 131.3, 133.7, 143.8, 144.9, 166.4, 172.3; IR (film) 3345–3200, 1735, 1635 cm^{-1}; MS (FAB, 3-NOBA) 316 (100, MH^+), 256 (13), 105 (58); HRMS (FAB, 3-NOBA) calcd for $C_{17}H_{18}NO_5$ (MH^+) 316.1185, obsd 316.1190. Anal. Calcd for $C_{17}H_{17}NO_5$: C, 64.76; H, 5.43; N, 4.44. Found: C, 64.86; H, 5.51; N, 4.26.

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Methyl *N*-Benzoyl-3′,4′-bis[(*tert*-butyldimethylsilyl)oxy]-phenylalaninate (1b). To a solution of methyl *N*-benzoyl-3′,4′-dihydroxyphenylalaninate (9.80 g, 31.1 mmol), imidazole (8.50 g, 124 mmol) and 4-(dimethylamino)pyridine (380 mg, 3.11 mmol) in DMF (200 mL) was added *tert*-butyldimethylsilyl chloride (11.7 g, 77.8 mmol). The resulting reaction mixture was heated at 50 °C for 3 h and then poured into $NaHCO_3$ (aq, 300 mL) and Et_2O (200 mL). The organic layer was further extracted with Et_2O (2 × 200 mL) and the combined extracts were dried ($MgSO_4$) and evaporated. Chromatrography (33% EtOAc/hexane) afforded **1b** (12.5 g, 74%) as a white solid: mp 72–73 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 0.11 (s, 6 H), 0.16 (s, 3 H), 0.17 (s, 3 H), 0.92 (s, 9 H), 0.95 (s, 9 H), 3.07–3.13 (dd, *J* = 5.5, 13 Hz, 1 H), 3.12–3.19 (dd, *J* = 6, 14 Hz, 1 H), 3.74 (s, 3 H), 4.97–5.04 (app dt, *J* = 6, 8 Hz, 1 H), 6.53–6.60 (m, 3 H), 6.72–6.75 (d, *J* = 8 Hz, 1 H), 7.37–7.51 (m, 3 H), 7.69–7.71 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.2 (2 C), −4.14, −4.11, 18.3, 18.4, 25.8, 25.9, 37.1, 52.3, 53.4, 121.0, 122.1, 122.3, 127.0, 128.5, 128.7, 131.7, 133.9, 146.1, 146.9 166.8, 172.1; IR (film) 3350–3310, 1745, 1645 cm^{-1}; MS (FAB, 3-NOBA) 544 (48, MH^+), 486 (75), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{29}H_{46}NO_5Si_2$ (MH^+) 544.2914, obsd 544.2908. Anal. Calcd for $C_{29}H_{45}NO_5Si_2$: C, 64.03; H, 8.34; N, 2.58. Found: C, 64.02; H, 8.20; N, 2.55.

Methyl *N*-Benzoyl-3′,4′-(methylenedioxy)phenylalaninate (1c). A solution of methyl *N*-benzoyl-3′,4′-dihydroxyphenylalaninate (10.3 g, 32.7 mmol) and CsF (24.8 g, 164 mmol) in DMF (20 mL) was shaken at rt for 1 h. Then CH_2Cl_2 (9.40 mL, 147 mmol) was added and the resulting reaction mixture heated at 115 °C for 2 h. The cooled (rt) reaction mixture was diluted with Et_2O (300 mL) and extracted with cold $NaHCO_3$ (3 × 200 mL). The organic layer was dried ($MgSO_4$), filtered, and evaporated. Flash chromatography (40% EtOAc/hexane) gave **1c** (4.20 g, 40%) as a white solid: mp 126–128 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 3.09–3.16 (dd, *J* = 5, 14 Hz, 1 H), 3.17–3.23 (dd, *J* = 5, 14 Hz, 1 H), 3.76 (s, 3 H), 4.99–5.05 (app dt, *J* = 5, 7 Hz, 1 H), 5.92 (s, 2 H), 6.55–6.57 (d, *J* = 7 Hz, 1 H), 6.55–6.72 (m, 3 H), 7.39–7.53 (m, 3 H), 7.72–7.75 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 37.6, 52.4, 53.6, 101.0, 108.3, 109.5, 122.4, 127.0, 128.6, 129.4, 131.8, 133.8, 146.7, 147.8, 166.8, 172.0; IR (film) 3330, 1740, 1640 cm^{-1}; MS (FAB, 3-NOBA) 328 (100, MH^+), 268 (22), 206 (76); HRMS (FAB, 3-NOBA) calcd for $C_{18}H_{18}NO_5$ (MH^+) 328.1185, obsd 328.1183. Anal. Calcd for $C_{18}H_{17}NO_5$: C, 66.05; H, 5.23; N, 4.28. Found: C, 66.08; H, 5.30; N, 4.22.

Methyl N^{α}-Benzoyl-N^{ν}-tritylhistidinate (1d). To a solution of methyl *N*-benzoylhistidinate[22] (7.77 g, 28.4 mmol) and triphenylmethyl chloride (15.7 g, 56.9 mmol) in CH_2Cl_2 (120 mL) at rt was added NEt_3 (17.0 mL, 122 mmol). After 4.5 h, the volatiles were removed in vacuo and the residue was purified by column chromatography (30% acetone/$CHCl_3$) to yield **1d** (14.3 g, 98%) as a light yellow solid: mp 74–76 °C; ^1H NMR (300 MHz, DMSO-d_6) δ 3.07–3.14 (dd, *J* = 4, 14 Hz, 1 H), 3.15–3.21 (dd, *J* = 5, 14 Hz, 1 H), 3.63 (s, 3 H), 4.98–5.04 (app dt, *J* = 5, 8 Hz, 1 H), 6.60–6.60 (m, 1 H), 7.08–7.14 (m, 6 H), 7.27–7.51 (m, 13 H), 7.89–7.93 (m, 2 H), 8.38–8.41 (d, *J* = 8 Hz, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.6, 52.0, 52.9, 75.2, 119.6, 127.2, 128.0 (2 C), 128.3, 129.6, 131.3, 134.0, 136.6, 138.7, 142.2, 166.8, 171.7; IR (film) 3380–3260, 1745, 1660 cm^{-1}; MS (FAB, 3-NOBA) 516 (50, MH^+), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{33}H_{30}N_3O_3$ (MH^+) 516.2287, obsd 516.2282. Anal. Calcd for $C_{33}H_{29}N_3O_3$: C, 76.87; H, 5.67; N, 8.15. Found: C, 77.00; H, 5.82; N, 7.96.

Methyl N^{α}-Benzoyl-N^{ϵ}-benzylidenelysinate (1e). To a suspension of N^{α}-benzoyllysine[23] (4.00 g, 16.0 mmol) in MeOH (14 mL) at 0 °C was added, dropwise, thionyl chloride (1.28 mL, 17.6 mmol). After heating at 40 °C for 1 h and evaporation of the volatiles in vacuo, methyl N^{α}-benzoyllysinate hydrochloride salt (4.81 g) was obtained of sufficient purity to be used directly for the next step: ^1H NMR (300 MHz, DMSO-d_6) δ 1.38–1.82 (m, 6 H), 2.74 (m, 2 H), 3.62 (s, 3 H), 4.05–4.05 (m, 1 H), 7.45–7.52 (m, 3 H), 7.93–8.07 (m, 2 H), 8.15 (br s, 3 H), 8.82–8.84 (d, 1 H); ^{13}C NMR (75 MHz, DMSO-d_6) δ 22.6, 26.3, 29.7, 38.2, 51.8, 52.6, 127.5, 128.1, 131.4, 133.5, 166.6, 172.6. To a suspension of this hydrochloride salt and benzaldehyde (1.54 mL, 15.1 mmol) in CH_2Cl_2 (23 mL) at 0 °C was added NEt_3 (2.22 mL, 15.94 mmol). The reaction mixture was stirred for 21 h at rt and then diluted with Et_2O (150 mL) and washed with H_2O (2 × 100 mL) and brine (100 mL). The organic layer was dried ($MgSO_4$) and evaporated to give **1e** (4.58 g, 81% for 2 steps) as an oil: ^1H NMR (500 MHz, $CDCl_3$) δ 1.41–1.59 (m, 2 H), 1.63–2.07 (m, 4 H), 3.58–3.63 (m, 2 H), 3.74 (s, 3 H), 4.82–4.86 (m, 1 H), 6.68-6.70 (d, *J* = 8 Hz, 1 H), 7.34–7.51 (m, 6 H), 7.67–7.78 (m, 4 H), 8.25 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.9, 30.2, 32.2, 52.3, 52.5, 61.0, 127.0, 128.0, 128.4, 128.5, 130.4, 131.6, 134.0, 136.2, 161.0, 167.0, 173.1; IR (film) 3320, 1740, 1640 cm^{-1}; MS (FAB, 3-NOBA) 353 (88, MH^+), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{21}H_{25}N_2O_3$ (MH^+) 353.1865, obsd 353.1861. Anal. Calcd for $C_{21}H_{24}N_2O_3$: C, 71.57; H, 6.86; N, 7.95. Found: C, 71.44; H, 6.90; N, 7.80.

Methyl N^{α}-Benzoyl-N^{δ}-benzylideneornithinate (1f). From N^{α}-benzoylornithine[23] (5.00 g, 21.2 mmol) and thionyl chloride (1.7 mL, 23.3mmol), according to the procedure for **1e**, was obtained methyl N^{α}-benzoylornithinate hydrochloride salt (6.07 g) of sufficient purity to be used directly for the next step: ^1H NMR (300 MHz, DMSO-d_6) δ 1.64–1.71 (m, 2 H), 1.85–1.91 (m, 2 H), 2.77-2.78 (m, 2 H), 3.63 (s, 3 H), 4.39–4.47 (m, 1 H), 7.44–7.57 (m, 3 H), 7.91–7.93 (m, 2 H), 8.11 (s, br), 8.87–8.90 (d, 1 H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 22.4, 25.9, 36.8, 51.0, 51.1, 126.0, 127.1, 130.5, 131.7, 166.6, 171.3. Treatment of this hydrochloride salt with benzaldehyde (1.91 mL, 18.8 mmol) and triethylamine (2.92 mL, 20.9 mmol), as for **1e**, gave **1f** (6.02 g, 84% for 2 steps) as an off-white solid: mp 80–81 °C; ^1H NMR (500 MHz, $CDCl_3$): δ 1.78–1.84 (app quintet, *J* = 7 Hz, 2 H), 1.93–2.08 (m, 2 H), 3.63–3.68 (app t, *J* = 7 Hz, 2 H), 3.75 (s, 3 H), 4.86-4.90 (app dt, *J* = 5, 7 Hz, 1 H), 7.21–7.22 (d, *J* = 7 Hz, 1 H), 7.35–7.48 (m, 6 H), 7.68–7.81 (m, 4 H), 8.28 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.8, 30.1, 52.4, 52.4, 60.6, 127.1, 128.1, 128.5, 128.6, 130.7, 131.6, 133.9, 136.0, 161.5, 167.1, 172.9; IR (film) 3330, 1740, 1640 cm^{-1}; MS (FAB, 3-NOBA) 339 (100, MH^+), 105 (75); HRMS (FAB, 3-NOBA) calcd for $C_{20}H_{23}N_2O_3$ (MH^+) 339.1709, obsd 339.1709. Anal. Calcd for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 8.27. Found: C, 70.91; H, 6.71; N, 8.40.

General Procedure A. *N*-Benzoyl-2-benzylhomoserine Lactone (2a). All solutions were deoxygenated by freezing (liquid N_2), six cycles of evacuation, and purging with Ar. To a solution of diisopropylamine (22.4 mL, 160 mmol) and TMEDA (36.2 mL, 240 mmol) in THF (800 mL) at −78 °C was added *n*-butyllithium (100 mL, 1.6 M in *n*-hexane), and the resulting solution was stirred for 30 min at 0 °C. The LDA solution thereby generated was cooled to −78 °C and a solution of **1a**[24] (14.6 g, 52.0 mmol) in THF (350 mL) at −78 °C was added via cannula. The resulting bright orange solution was stirred for 1 h at −78 °C. Then the cooling bath was removed and excess ethylene oxide (ca. 25 g) was bubbled into the solution with stirring over a period of 45 min. The reaction mixture was poured into ether (500 mL) and NH_4Cl (aq, 500 mL) and vigorously stirred for 15 min. After further extraction with ether (3 × 300 mL), the combined organics were dried ($MgSO_4$), filtered, evaporated, and chromatographed (50% EtOAc/hexane) to give **2a** (13.0 g, 85%) as a white solid: mp 170–172 °C; ^1H NMR (200 MHz, $CDCl_3$) δ 2.66–2.77 (m, 2 H), 3.12–3.19 (d, *J* = 13 Hz, 1 H), 3.22–3.29 (d, *J* = 13 Hz, 1 H), 3.44–3.57 (app dt, *J* = 8, 9 Hz, 1 H), 4.22–4.32 (app dt, *J* = 3, 9 Hz, 1 H), 6.61 (s, 1 H), 7.15-7.68 (m, 10 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 33.5, 41.6, 66.0, 127.0, 127.9, 128.7, 128.9, 130.0, 132.1, 176.7, 178.1; IR (film) 3320, 1760, 1650 cm^{-1}; MS (EI) 295 (8.6, M^+), 204 (100); HRMS (EI) calcd for $C_{18}H_{17}NO_3$ (M^+) 295.1208, obsd 295.1203. Anal. Calcd for $C_{18}H_{17}NO_3$: C, 73.21; H, 5.80; N, 4.74. Found: C, 73.33; H, 5.95; N, 4.66.

***N*-Benzoyl-2-[3′,4′-bis[(*tert*-butyldimethylsilyl)oxy]benzyl]homoserine Lactone (2b).** From **1b** (4.88 g, 8.98 mmol), following General Procedure A, was obtained **2b** (4.18 g, 84%), as a white solid, after flash chromatography (0–50% EtOAc/hexane): mp 138–140 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 0.17 (s, 6 H), 0.18 (s, 3 H), 0.19 (s, 3 H), 0.97 (s, 18 H), 2.73–2.80 (m, 2 H), 3.11–3.13 (d, *J* = 13 Hz,1 H), 3.14–3.17 (d, *J* = 13 Hz, 1 H), 3.52–3.55 (app dt, *J* = 8, 9 Hz, 1 H), 4.30-4.35 (app dt, *J* = 3, 9 Hz, 1 H), 6.62 (s, 1 H), 6.71–6.80 (m, 3 H), 7.40–7.43 (m,

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2 H), 7.49–7.52 (m, 1 H), 7.71–7.73 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.17, −4.13 (2 C), −4.07, 18.4, 18.5, 25.87, 25.90, 33.2, 41.5, 60.1, 65.9, 121.3, 122.7, 122.9, 126.7, 127.0, 128.6, 132.0, 133.4, 147.2, 166.6, 177.3; IR (film) 3340, 1775, 1640 cm^{-1}; MS (FAB, 3-NOBA) 556 (58, MH$^+$), 351 (96), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{30}H_{46}NO_5Si_2$ (MH$^+$) 556.2914, obsd 556.2914. Anal. Calcd for $C_{30}H_{45}NO_5Si_2$: C, 64.83; H, 8.16; N, 2.52. Found: C, 64.64; H, 8.29; N, 2.50.

***N*-Benzoyl-2-[3′,4′-(methylenedioxy)benzyl]homoserine Lactone (2c).** From **1c** (1.80 g, 5.50 mmol), following General Procedure A, was obtained **2c** (1.53 g, 82%), as a white solid, following chromatography (50% EtOAc/hexane): mp 185–187 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.72–2.85 (m, 2 H), 3.12–3.16 (d, J = 13 Hz, 1 H), 3.20–3.24 (d, J = 13 Hz, 1 H), 3.65–3.73 (app dt, J = 7, 9 Hz, 1 H), 4.33–4.40 (app dt, J = 3, 9 Hz, 1 H), 5.94 (s, 2 H), 6.66 (s, 1 H), 6.68–6.77 (m, 3 H), 7.39–7.54 (m, 3 H), 7.71–7.78 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 33.4, 41.3, 60.1, 66.1, 101.2, 108.5, 110.2, 123.3, 127.0, 127.3, 128.7, 132.1, 133.4, 147.3, 148.0, 166.8, 177.1; IR (film) 3410–3340, 1770, 1650 cm^{-1}; MS (FAB, 3-NOBA) 340 (100, MH$^+$), 218 (33), 105 (89); HRMS (FAB, 3-NOBA) calcd for $C_{19}H_{18}NO_5$ (MH$^+$) 340.1185, obsd 340.1185. Anal. Calcd for $C_{19}H_{17}NO_5$: C, 67.25; H, 5.05; N, 4.13. Found: C, 67.00; H, 5.20; N, 4.14.

***N*-Benzoyl-2-[(1′-trityl-4′-imidazolyl)methyl]homoserine Lactone (2d).** General Procedure A was followed, except that $NaHCO_3$ (aq) was substituted for NH_4Cl (aq) in the workup. From **1d** (1.80 g, 5.50 mmol) was obtained **2d** (1.48 g, 80%), as a white solid, after flash chromatography (45:45:10 $CHCl_3$/hexane/acetone): mp 104–106 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.18–2.23 (ddd, J = 4, 8, 13 Hz, 1 H), 2.67–2.73 (app dt, J = 9, 13 Hz, 1 H), 2.78–2.81 (d, J = 14 Hz, 1 H), 3.15–3.18 (d, J = 14 Hz, 1 H), 4.19–4.24 (app q, J = 9 Hz, 1 H), 4.56–4.61 (app dt, J = 4, 9 Hz, 1 H), 6.75 (s, 1 H), 7.08–7.18 (m, 6 H), 7.22–7.49 (m, 13 H), 7.90–7.92 (m, 2 H), 9.18 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 31.5, 33.6, 58.9, 64.9, 75.5, 120.7, 127.3, 128.1 (2 C), 128.2, 128.4, 129.7, 131.6, 133.2, 135.4, 139.1, 142.1, 166.1,.176.0; IR (film) 3380–3200, 1770, 1660 cm^{-1}; MS (FAB, 3-NOBA) 528 (100, MH$^+$), 243 (100); HRMS (FAB, 3-NOBA) calcd for $C_{34}H_{30}N_3O_3$ (100, MH$^+$) 528.2287, obsd 528.2298. Anal. Calcd for $C_{34}H_{29}N_3O_3$: C, 77.40; H, 5.54; N, 7.96. Found: C, 77.20; H, 5.35; N, 7.65.

***N*-Benzoyl-2-(4′-benzamidobutyl)homoserine Lactone (2e).** Starting from **1e** (4.11 g, 11.7 mmol), General Procedure A was followed, except that $NaHCO_3$ (aq) was substituted for NH_4Cl (aq) in the workup. The crude N^6-benzylidene lactone was taken up in THF (48 mL) and 3 N HCl (48 mL), stirred at rt for 23 h, and then evaporated. The residue was taken up in CH_2Cl_2 (230 mL) and benzoyl chloride (3.38 mL, 29.1 mmol) and cooled to 0 °C. After addition of NEt_3 (4.06 mL, 29.1 mmol), the reaction mixture was stirred for 15 h at rt and then poured into $NaHCO_3$ (300 mL) and EtOAc (300 mL). The organic layer was further washed with 1 N HCl (300 mL) and brine (300 mL), then dried ($MgSO_4$), filtered, and evaporated. Flash chromatography (50–75% EtOAc/hexane) yielded **2e** (2.70 g, 61%) as a white solid: mp 154–155 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.51–1.69 (m, 4 H), 1.86-1.96 (m, 1 H), 2.14–2.24 (m, 1 H), 2.31–2.38 (ddd, J = 3, 8, 13 Hz, 1 H), 2.82–2.93 (app dt, J = 9, 13 Hz, 1 H), 3.33–3.41 (m, 1 H), 3.55–3.65 (m, 1 H), 4.24–4.32 (app dt, J = 8, 9 Hz, 1 H), 4.51–4.59 (app dt, J = 3, 9 Hz, 1 H), 6.57–6.61 (m, 1 H), 7.27-7.50 (m, 6 H), 7.55 (s, 1 H), 7.67–7.90 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 29.6, 33.4, 34.2, 38.1, 58.7, 65.2, 126.9, 127.5, 128.3, 128.5, 131.5, 131.6, 133.2, 134.3, 167.3, 168.8, 176.5; IR (film): 3390–3185, 1765, 1640 cm^{-1}; MS (FAB, 3-NOBA) 381 (61, MH$^+$), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{22}H_{25}N_2O_4$ (MH$^+$) 381.1814, obsd 381.1819. Anal. Calcd for $C_{22}H_{24}N_2O_4$: C, 69.46; H, 6.36; N, 7.36. Found: C, 69.24; H, 6.37; N, 7.23.

***N*-Benzoyl-2-(3′-benzamidopropyl)homoserine Lactone (2f).** From **1f** (5.80 g, 17.1 mmol), according to the procedure for the synthesis of **1e**, was obtained **2f** (4.91 g, 78%), as a white solid, following flash chromatography (50–75% EtOAc/hexane): mp 179–181°C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.77–1.98 (m, 3 H), 2.14–2.23 (m, 1 H), 2.48–2.56 (ddd, J = 3, 8, 13 Hz, 1 H), 2.76–2.87 (app dt, J = 9, 13 Hz, 1 H), 3.42–3.51 (m, 1 H), 3.54–3.63 (m, 1 H), 4.26–4.35 (app dt, J = 8, 9 Hz, 1 H), 4.53–4.60 (app dt, J = 3, 9 Hz, 1 H), 6.39–6.43 (m, 1 H), 7.27–7.53 (m, 6 H), 7.74–7.88 (m, 4 H); ^{13}C NMR [75 MHz, DMSO-d_6/$CDCl_3$ (1:1)] δ 23.1, 31.9, 32.9, 39.1, 58.4, 64.5, 127.1, 127.5, 128.0 (2 C), 130.8, 131.4, 133.3, 134.5, 166.3, 166.4, 176.1; IR (film) 3360, 3290, 1750, 1640 cm^{-1}; MS (FAB, 3-NOBA) 367 (54, MH$^+$), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{21}H_{23}N_2O_4$ (MH$^+$) 367.1658, obsd 367.1654. Anal. Calcd for $C_{21}H_{22}N_2O_4$: C, 68.84; H, 6.05; N, 7.64. Found: C, 69.02; H, 6.06; N, 7.43.

***N*-Benzoyl-2-isopropylhomoserine Lactone (2g).** From **1g**[25] (10.2 g, 43.2 mmol), following General Procedure A, was obtained **2g** (8.97 g, 84%), as a white solid, following chromatography (20–60% EtOAc/hexane): mp 125–127 °C; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.93–0.96 (d, J = 7 Hz, 3 H), 1.08–1.11 (d, J = 7 Hz, 3 H), 2.19–2.26 (app heptet, J = 7 Hz, 1 H), 2.45–2.64 (m, 2 H), 4.18–4.31 (app dt, J = 7, 9 Hz, 1 H), 4.57–4.68 (ddd, J = 4, 9, 10 Hz, 1 H), 6.60 (s, 1 H), 7.36–7.50 (m, 3 H), 7.72–7.76 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 16.6 (2 C), 28.4, 33.5, 62.7, 66.0, 127.1, 128.4, 131.8, 133.1, 167.2, 177.4; IR (film) 3340, 1760, 1660 cm^{-1}; MS (EI) 247 (1.5, M$^+$), 105 (100); HRMS (EI) calcd for $C_{14}H_{17}NO_3$ (M$^+$) 247.1208, obsd 247.1203. Anal. Calcd for $C_{14}H_{17}NO_3$: C, 68.00; H, 6.93; N, 5.66. Found: C, 68.12; H, 6.86; N, 5.39.

***N*-Benzoyl-2-(2′-hydroxyethyl)homoserine Lactone.** General Procedure A was followed except that, after bubbling excess ethylene oxide into the solution of the dianion, the reaction mixture was capped and stirred at rt overnight. From **1i**[26] (14.0 g 68.2 mmol) were obtained (recovered) **1i** (2.20 g) and the title compound [9.80 g, 58% (68% based on recovered **1i**)], as a white solid, following flash chromatography (50–75% EtOAc/hexane): mp 103–105 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.98–2.03 (ddd, J = 2, 7, 15 Hz, 1 H), 2.10–2.15 (ddd, J = 3, 8, 15 Hz, 1 H), 2.32–2.37 (ddd, J = 3, 8, 13 Hz, 1 H), 2.88 (s, 1 H), 2.90–2.94 (m, 1 H), 3.89–3.93 (m, 1 H), 4.08–4.12 (m, 1 H), 4.23–4.29 (m, 1 H), 4.57–4.61 (app dt, J = 3, 9, 12 Hz, 1 H), 7.37–7.40 (m, 2 H), 7.42–7.49 (m, 1 H), 7.77–7.81 (m, 2 H), 8.41 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 33.0, 37.0, 59.08 59.13, 65.3, 127.1, 128.6, 132.0, 133.1, 166.8, 176.8; IR (film) 3670–3300, 1771, 1653 cm^{-1}; MS (EI): 249 (13, M$^+$), 105 (100); HRMS (EI) calcd for $C_{13}H_{15}NO_4$ (M$^+$) 249.1001, obsd 249.0993. Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.64; H, 6.06; N, 5.62. Found: C, 62.63; H, 6.17; N, 5.50.

***N*-Benzoyl-2-[2′-[(*tert*-butyldiphenylsilyl)oxy]ethyl]homoserine Lactone (2i).** To a solution of *N*-benzoyl-2-(2′-hydroxyethyl)homoserine lactone (1.60 g, 6.42 mmol) and imidazole (960 mg, 14.1 mmol) in DMF (25 mL) was added a solution of *tert*-butyldiphenylsilyl chloride (1.84 mL, 7.06 mmol) in DMF (5mL). After being stirred 16 h at rt, the reaction mixture was poured into $NaHCO_3$ (20 mL) and extracted with Et_2O (4 × 150 mL). The combined extracts were dried ($MgSO_4$), filtered, evaporated, and chromatographed to give **2i** (2.79 g, 89%) as a white solid: mp 132–134 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.04 (s, 9 H), 1.99–2.04 (ddd, J = 3, 7, 11 Hz, 1 H), 2.22–2.27 (ddd, J = 3, 8, 11 Hz, 1 H), 2.31–2.35 (ddd, J = 3, 8, 11 Hz, 1 H), 2.86–2.93 (m, 1 H), 3.92–3.96 (ddd, J = 3, 8, 11 Hz, 1 H), 4.11–4.15 (ddd, J = 3, 7,11 Hz, 1 H), 4.20–4.25 (app q, J = 9 Hz, 1 H), 4.57–4.62 (app dt, J = 3, 9 Hz, 1 H), 7.22–7.25 (m, 2 H), 7.32–7.45 (m, 7 H), 7.61–7.71 (m, 6 H), 7.99 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1, 26.8, 32.5, 37.6, 59.0, 60.8, 65.0, 127.3, 127.9 (2 C), 128.4, 130.1 (2 C), 131.7, 132.4, 132.7, 133.3, 135.4, 135.4, 167.2, 176.3; IR (film) 3375, 1780, 1660 cm^{-1}; MS (FAB, 3-NOBA) 488 (45, MH$^+$), 232 (90), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{29}H_{34}NO_4Si$ (MH$^+$) 488.2257, obsd 488.2237. Anal. Calcd for $C_{29}H_{33}NO_4Si$: C, 71.43; H, 6.82; N 2.87. Found: C, 71.43; H, 6.87; N, 2.71.

***N*-Benzoyl-2-[2′-(*tert*-butyloxy)ethyl]homoserine Lactone (2j).** Isobutylene was bubbled into a solution of *N*-benzoyl-2-(2′-hydroxyethyl)homoserine lactone (2.00 g, 8.02 mmol) and H_2SO_4 (0.52mL) in CH_2Cl_2 (65 mL) for 1 h. The flask was stoppered and the reaction mixture stirred at rt for 10 h. After dilution (50 mL CH_2Cl_2), the reaction was quenched with $NaHCO_3$ (aq, 100 mL). The organic layer was further extracted with H_2O (100 mL), 1 N HCl (100 mL), and H_2O (100 mL) and then dried (Na_2SO_4), filtered, and evaporated to provide **2j** (2.17 g, 89%) as an off white solid: mp 106–108 °C; ^{1}H NMR (500 MHz, $CDCl_3$)

(25) Applewhite, T. H.; Waite, H.; Niemann, C. *J. Am. Chem. Soc.* **1958**, *80*, 1465–1469.
(26) Knobler, Y.; Frankel, M. *J. Chem. Soc.* **1958**, 1629–1631.

δ 1.22 (s, 9 H), 1.95–2.00 (app dd, J = 7, 15 Hz, 1 H), 2.17–2.27 (m, 2 H), 2.90–2.97 (app dt, J = 9, 12 Hz, 1 H), 3.62–3.66 (m, 1 H), 3.84–3.87 (m, 1 H), 4.24–4.29 (app q, J = 8 Hz, 1 H), 4.59–4.64 (app dt, J = 3, 9 Hz, 1 H), 7.25–7.41 (m, 2 H), 7.47–7.50 (m, 1 H), 7.79–7.81 (m, 2 H), 8.53 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 27.4, 32.4, 35.7, 58.1, 58.9, 64.8, 74.4, 127.1, 128.3, 131.7, 133.3, 166.4, 176.3; IR (film) 3350, 1770, 1663 cm^{-1}; MS (EI) 305 (0.2, M$^+$), 232 (28), 105 (100); HRMS (EI) calcd for $C_{17}H_{23}NO_4$ (M$^+$) 305.1627, obsd 305.1617. Anal. Calcd for $C_{17}H_{23}NO_4$: C, 66.87; H, 7.59; N 4.58. Found: C, 66.83; H, 7.48; N, 4.34.

General Procedure B. Methyl *N*-Benzoyl-2-[2′-(phenylseleno)ethyl]phenylalaninate (3a). All solutions were deoxygenated by freezing (liquid N_2), six cycles of evacuation, and purging with Ar. To an argon-purged flask containing sodium trimethoxyborohydride (563 mg, 4.41 mmol) was added a solution of diphenyl diselenide (687 mg, 2.20 mmol) in DMF (30 mL). The resulting orange suspension was heated to 65 °C for 1 h, whereby a clear, colorless solution resulted. To this solution at rt was added a solution of lactone **2a** (1.00 g, 3.39 mmol) in DMF (30 mL), and the reaction mixture was heated at 110 °C (preheated oil bath) for 2 h. After the solution was cooled to rt, the solvent was removed in vacuo, and the residue was diluted with Et_2O (200 mL) and brought to pH 4 with 1 N HCl (aq). The aqueous layer was extracted twice more with Et_2O (200 mL) and the combined organics were dried ($MgSO_4$), filtered, and esterified with diazomethane. Evaporation of the solvent and chromatography (0–10% EtOAc/hexane) yielded **3a** (1.52 g, 97%) as a white solid. In another run, lactone **2a** (1.23 g, 9.59 mmol) gave selenide **3a** (3.10 g, 90%): mp 124–126 °C; ^{1}H NMR (360 MHz, $CDCl_3$) δ 2.24–2.32 (ddd, J = 6, 11, 14 Hz, 1 H), 2.43–2.51 (ddd, J = 6, 11, 12 Hz, 1 H), 2.73–2.79 (ddd, J = 5, 11, 12 Hz, 1 H), 2.97–3.01 (d, J = 13 Hz, 1 H), 3.14–3.21 (ddd, J = 5, 11, 14 Hz, 1 H), 3.64 (s, 3 H), 3.76–3.80 (d, J = 13 Hz, 1 H), 6.84–6.86 (m, 3 H), 7.01–7.14 (m, 6 H), 7.24–7.39 (m, 5 H), 7.51–7.55 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 21.9, 36.1, 40.6, 52.8, 66.8, 126.9, 126.9, 127.0, 128.3, 128.6, 129.1, 129.3, 129.6, 131.6, 132.4, 134.9, 135.9, 166.7, 173.4; IR (film) 3410, 1735, 1663 cm^{-1}; MS (EI) 467 (0.4, M$^+$), 310 (33), 105 (100); HRMS (EI) calcd for $C_{25}H_{25}NO_3Se$ (M$^+$) 467.0999, obsd 467.0980. Anal. Calcd for $C_{25}H_{25}NO_3Se$: C, 64.38; H, 5.40; N, 3.00. Found: C, 64.42; H, 5.30; N, 2.91.

Methyl *N*-Benzoyl-2-[2″-(phenylseleno)ethyl]-3′,4′-bis[(*tert*-butyldimethylsilyl)oxy]phenylalaninate (3b). From lactone **2b** (4.00 g, 720 mmol), following General Procedure B, was obtained **3b** (4.24 g, 81%) as an oil, after flash chromatography (0–10% EtOAc/hexane): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.028 (s, 3 H), 0.031 (s, 3 H), 0.16 (s, 6 H), 0.88 (s, 9 H), 0.95 (s, 9 H), 2.33–2.43 (ddd, J = 5, 11, 14 Hz, 1 H), 2.55–2.65 (ddd, J = 5, 11, 12 Hz, 1 H), 2.85–2.94 (ddd, J = 5, 11, 12 Hz, 1 H), 2.99–3.04 (d, J = 14 Hz, 1 H), 3.24–3.34 (ddd, J = 5, 11, 14 Hz, 1 H), 3.77 (s, 3 H), 3.76–3.80 (d, J = 14 Hz, 1 H), 6.43–6.65 (m, 3 H), 7.06 (s, 1 H), 7.21–7.28 (m, 3 H), 7.38–7.53 (m, 5 H), 7.67–7.71 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.31, −4.26, −4.1 (2 C), 18.2, 18.4, 21.8, 25.7, 25.9, 36.0, 40.0, 52.7, 66.7, 120.6, 122.3, 122.6, 126.8, 126.9, 128.5, 128.9, 129.0, 130.1, 131.5, 132.2, 134.8, 145.9, 146.4, 166.4,.173.4; IR (film) 3410, 1735, 1670 cm^{-1}; MS (FAB, 3-NOBA) 728 (6, MH$^+$), 351 (72), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{37}H_{54}NO_5Si_2Se$ (MH$^+$) 728.2705, obsd 728.2681. Anal. Calcd for $C_{37}H_{53}NO_5Si_2Se$: C, 61.13; H, 7.35; N, 1.93. Found: C, 61.07; H, 7.38; N, 1.88.

Methyl *N*-Benzoyl-2-[2″-(phenylseleno)ethyl]-3′,4′-(methylenedioxy)phenylalaninate (3c). From lactone **2c** (500 mg, 1.47 mmol), following General Procedure B, was obtained **3c** (621 mg, 83%), as a white solid, after flash chromatography (0–10% EtOAc/hexane): mp 110–111 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.31–2.41 (ddd, J = 6, 11, 14 Hz, 1 H), 2.52–2.62 (ddd, J = 6, 11, 12 Hz, 1 H), 2.83–2.92 (ddd, J = 5, 11, 12 Hz, 1 H), 2.98–3.03 (d, J = 14 Hz, 1 H), 3.22–3.32 (ddd, J = 5, 11, 14 Hz, 1 H), 3.77 (s, 3 H), 3.81–3.86 (d, J = 14 Hz, 1 H), 5.86 (s, 2 H), 6.42–6.61 (m, 3 H), 7.02 (s, 1 H), 7.21–7.27 (m, 3 H), 7.39–7.53 (m, 5 H), 7.67–7.71 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.9, 36.0, 40.3, 52.9, 67.0, 100.9, 108.1, 109.7, 122.8, 126.8, 126.9, 128.6, 129.0 (2 C), 129.4, 131.6, 132.3, 134.9, 146.5, 147.5, 166.7, 173.4; IR (film) 3410, 1730, 1660 cm^{-1}; MS (FAB, 3-NOBA) 512 (14, MH$^+$), 354 (47), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{26}H_{26}NO_5Se$ (MH$^+$) 512.0979, obsd 512.0977. Anal. Calcd for $C_{26}H_{25}NO_5Se$: C, 61.18; H, 4.94; N, 2.74. Found: C, 61.06; H, 4.98; N, 2.72.

Methyl N^{α}-Benzoyl-2-[2′-(phenylseleno)ethyl]-N^{τ}-trityl-histidinate (3d). General Procedure B was followed except that 100 mM NaOAc/HOAc buffer (aq, pH 5) was substituted for 1 N HCl in the acidification step. From lactone **2d** (1.44 g, 2.73 mmol) was obtained **3d** (1.32 g, 69%) as a white solid, after flash chromatography (0–50% EtOAc/hexane): mp 66–68 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.46–2.51 (m, 1 H), 2.68–2.74 (m, 1 H), 2.85–2.96 (m, 2 H), 3.10–3.13 (d, J = 14 Hz, 1 H), 3.62–3.65 (d, J = 14 Hz, 1 H), 3.73 (s, 3 H), 6.50 (s, 1 H), 6.97–6.98 (m, 6 H), 7.14–7.29 (m, 12 H), 7.34–7.49 (m, 6 H), 7.63–7.67 (m, 3 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 21.9, 34.1, 36.1, 52.8, 64.8, 76.3, 120.5, 126.7, 127.0, 128.0 (2 C), 128.03, 128.5, 129.0, 129.6, 130.4, 131.4, 132.1, 134.5, 138.4, 142.1, 166.2, 173.6; IR (film) 3415–3240, 1735, 1665 cm^{-1}; MS (FAB, 3-NOBA) 700 (4, MH$^+$), 243 (100); HRMS (FAB, 3-NOBA) calcd for $C_{41}H_{38}N_3O_3Se$ 700.2078 (MH$^+$), obsd 700.2062. Anal. Calcd for $C_{41}H_{37}N_3O_3Se$: C, 70.48; H, 5.34; N, 6.01. Found: C, 70.34; H, 5.40; N, 5.86.

Methyl N^{α},N^{ϵ}-Dibenzoyl-2-[2′-(phenylseleno)ethyl]lysinate (3e). From lactone **2e** (421 mg, 1.11 mmol), following General Procedure B, was obtained **3e** (539 mg, 88%), as a white solid, after flash chromatography (0–25% EtOAc/hexane). In another run, lactone **2e** (8.00 g, 21.0 mmol) gave selenide **3e** (9.90 g, 85%): mp 48–49 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.04–1.10 (m, 1 H), 1.32–1.68 (m, 3 H), 1.78–1.88 (m, 1 H), 2.21–2.31 (ddd, J = 6, 11, 14 Hz, 1 H), 2.53–2.63 (ddd, J = 6, 11, 12 Hz, 1 H), 2.70–2.94 (m, 2 H), 2.97–3.06 (ddd, J = 5, 11, 14 Hz, 1 H), 3.32–3.46 (m, 2 H), 3.76 (s, 3 H), 6.21–6.25 (m, 1 H), 7.19–7.24 (m, 3 H), 7.30 (s, 1 H), 7.31–7.53 (m, 8 H), 7.64–7.77 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.0, 21.8, 28.8, 34.3, 36.3, 39.0, 53.1, 65.4, 126.8, 126.9, 127.0, 128.4, 128.6, 128.9, 129.0, 131.2, 131.7, 132.3, 134.5, 134.6, 166.3, 167.5, 174.3; IR (film) 3410–3300, 1735, 1640 cm^{-1}; MS (FAB, 3-NOBA) 553 (16, MH$^+$), 395 (50), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{29}H_{33}N_2O_4Se$ (MH$^+$) 553.1606, obsd 553.1613. Anal. Calcd for $C_{29}H_{32}N_2O_4Se$: C, 63.15; H, 5.85; N, 5.08. Found: C, 63.20; H, 5.75; N, 4.98.

Methyl N^{α},N^{δ}-Dibenzoyl-2-[2′-(phenylseleno)ethyl]ornithinate (3f). From lactone **2f** (600 mg, 1.64 mmol), following General Procedure B, was obtained **3f** (695 mg, 79%), as a white solid, after flash chromatography (0–25% EtOAc/hexane). In another run, lactone **2f** (4.19 g, 11.4 mmol) gave selenide **3f** (4.43 g, 72%): mp 180–182 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.40–1.53 (m, 2 H), 1.88-1.98 (ddd, J = 6, 11, 14 Hz, 1 H), 2.20–2.30 (ddd, J = 6, 11, 14 Hz, 1 H), 2.53–2.63 (ddd, J = 6, 11, 12 Hz, 1 H), 2.76–2.89 (m, 2 H), 2.98–3.08 (ddd, J = 5, 11, 14 Hz, 1 H), 3.28–3.48 (m, 2 H), 3.77 (s, 3 H), 6.27–6.31 (m, 1 H), 7.18–7.24 (m, 3 H), 7.33 (s, 1 H), 7.35–7.54 (m, 8 H), 7.73–7.79 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 21.7, 23.9, 32.2, 36.2, 39.3, 53.2, 65.2, 126.8, 126.86, 126.91, 128.4, 128.6, 129.0, 129.9, 131.3, 131.8, 132.2, 134.2, 134.4, 166.3, 167.5, 174.1; IR (film) 3330, 1735, 1640 cm^{-1}; MS (FAB, 3-NOBA) 539 (MH$^+$, 10), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{28}H_{31}N_2O_4Se$ 539.1452, obsd 539.1436. Anal. Calcd for $C_{28}H_{30}N_2O_4Se$: C, 62.57; H, 5.62; N, 5.21. Found: C, 62.70; H, 5.80; N, 5.37.

Methyl *N*-Benzoyl-2-[2′-(phenylseleno)ethyl]valinate (3g). From lactone **2g** (500 mg, 2.02 mmol), following General Procedure B, was obtained **3g** (814 mg, 96%) as an oil after flash chromatography (0–10% EtOAc/hexane). In another run, lactone **2g** (2.40 g, 9.71 mmol) gave selenide **3g** (3.57 g, 88%): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89–0.90 (d, J = 7 Hz, 3 H), 0.99–1.00 (d, J = 7 Hz, 3 H), 2.44-2.50 (ddd, J = 5, 11, 14 Hz, 1 H), 2.55–2.61 (ddd, J = 5, 11, 12 Hz, 1 H), 2.75–2.81 (m, 1 H), 2.88–2.93 (ddd, J = 5, 11, 12 Hz, 1 H), 3.22–3.28 (ddd, J = 5, 11, 14 Hz, 1 H), 3.75 (s, 3 H), 7.18–7.24 (m, 3 H), 7.29 (s, 1 H), 7.42–7.52 (m, 5 H), 7.77–7.78 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.7, 18.1, 22.7, 33.2, 33.8, 52.7, 69.0, 126.7, 126.8, 128.6, 129.0, 130.5, 131.6, 132.1, 135.0, 166.0, 173.7; IR (film) 3400, 1730, 1660 cm^{-1}; MS (EI) 419 (1.3, M$^+$), 262 (100); HRMS (EI) calcd for $C_{21}H_{25}NO_3Se$ (M$^+$) 419.0999, obsd 419.1001. Anal. Calcd for $C_{21}H_{25}NO_3Se$: C, 60.29; H, 6.02; N, 3.35. Found: C, 60.31; H, 6.11; N, 3.10.

Methyl *N*-Benzoyl-4-*O*-(*tert*-butyldiphenylsilyl)-2-[2′-(phenylseleno)ethyl]homoserinate (3i). From lactone **2i** (3.15 g, 6.46 mmol), following General Procedure B, was obtained **3i** (3.83 g, 90%), as a colorless oil, after flash chromatography (0–10% EtOAc/hexane): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.99 (s, 9 H),

2.28–2.38 (m, 2 H), 2.58–2.64 (app dt, J = 5, 12 Hz, 1 H), 2.71–2.75 (app dt, J = 4, 8 Hz, 1 H), 2.83–2.88 (app dt, J = 5, 12 Hz, 1 H), 3.04–3.11 (ddd, J = 5, 11, 14 Hz, 1 H), 3.62–3.66 (m, 2 H), 3.68 (s, 3 H), 7.21–7.59 (m, 19 H), 7.76–7.78 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 19.1, 21.5, 26.8, 36.6, 37.4, 52.9, 60.1, 63.3, 126.8, 126.9, 127.6 (2 C), 127.7, 128.6, 129.0, 129.6, 131.6, 132.2 (2 C), 133.16, 133.21, 134.5, 135.4, 135.5, 166.2, 174.3; IR (film) 3410, 1730, 1665 cm^{-1}; MS (EI) 659 (1.0, M$^+$), 602 (41), 105 (100); HRMS (EI) calcd for $C_{36}H_{41}NO_4SiSe$ (M$^+$) 659.1970, obsd 659.1941. Anal. Calcd for $C_{36}H_{41}NO_4SiSe$: C, 65.64; H, 6.27; N, 2.13. Found: C, 65.79; H, 6.46; N, 1.88.

Methyl *N*-Benzoyl-4-*O*-*tert*-butyl-2-[2′-(phenylseleno)ethyl]homoserinate (3j). From lactone **2j** (3.80 g, 12.4 mmol), following General Procedure B, was obtained **3j** (5.52 g, 93%), as a white solid, after flash chromatography (0–10% EtOAc/hexane): mp. 65–67 °C; IR (film) 3410, 1730, 1665 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (s, 9 H), 2.13–2.19 (ddd, J = 5, 9, 14 Hz, 1 H), 2.29–2.35 (ddd, J = 5, 12, 14 Hz, 1 H), 2.60–2.65 (app dt, J = 5, 12 Hz, 1 H), 2.66–2.71 (app dt, J = 3, 7 Hz, 1 H), 2.81–2.87 (app dt, J = 5, 12 Hz, 1 H), 2.92–2.99 (ddd, J = 5, 12, 14 Hz, 1 H), 3.32–3.37 (m, 2 H), 3.74 (s, 3 H), 7.18–7.22 (m, 3 H), 7.40–7.45 (m, 5 H), 7.63 (s, 1 H), 7.80–7.82 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.2, 27.8, 36.1, 37.1, 53.1, 57.7, 63.9, 73.6, 127.4, 127.5, 129.3, 129.7, 132.2, 132.79, 132.83, 135.2, 166.6, 175.0; MS (EI) 477 (3, M$^+$), 320 (68), 105 (100); HRMS (EI) calcd for $C_{24}H_{31}NO_4Se$ 477.1418, obsd 477.1409. Anal. Calcd for $C_{24}H_{31}NO_4Se$: C, 60.50; H, 6.56; N, 2.94. Found: C, 60.28; H, 6.59; N, 2.83.

Methyl *N*-Benzoyl-2-[2′-(phenylseleno)ethyl]glycinate (3k). From 1i[23] (400 mg, 1.95 mmol), according to General Procedure B, was obtained **3k** (623 mg, 85%) as a white crystalline solid after flash chromatography (0–30% EtOAc/hexane): mp 96–98 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.14–2.23 (m, 1 H), 2.32-2.43 (m, 1 H), 2.87–2.99 (m, 2 H), 3.75 (s, 3 H), 4.89–4.96 (app dt, J = 5, 8 Hz, 1 H), 6.85–6.87 (d, J = 7 Hz, 1 H), 7.23–7.25 (m, 3 H), 7.40–7.49 (m, 5 H), 7.77–7.80 (m, 2 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.1, 33.1, 52.6, 52.7, 127.0, 127.2, 128.6, 129.1, 129.5, 131.9, 132.8, 133.6, 167.1, 172.4; IR (film) 3240–3390, 1740, 1640 cm^{-1}; MS (EI) 377 (6, M$^+$); 220 (99); 105 (100); HRMS (EI) calcd for $C_{18}H_{19}NO_3Se$ 377.0530, obsd 377.0527. Anal. Calcd for $C_{18}H_{19}NO_3Se$: C, 57.45 H, 5.09; N, 3.72. Found: C, 57.62; H, 5.15; N, 3.61.

Methyl 4-(Phenylseleno)butanoate (3l). From diphenyl diselenide (1.27 g, 4.07 mmol), sodium trimethoxyborohydride (1.04 g, 8.14 mmol), and γ-butyrolactone (447 μL, 5.82 mmol), according to General Procedure B, was obtained **3l**[14a] (1.37 g, 92%) after flash chromatography (100% hexane).

General Procedure C. Methyl *N*-Benzoyl-2-vinylphenylalaninate (4a). Ozone was bubbled into a solution of selenide **3a** (6.84 g, 14.7 mmol) in CH_2Cl_2 (150 mL) at −78 °C until a light blue color persisted. After addition of 1-hexene (31.7 mL, 255 mmol), this cold solution was added dropwise to refluxing CCl_4 (or PhH) (500 mL) and refluxing was continued for 30 min. Evaporation and flash chromatography (0–10% EtOAc/hexane) yielded **4a** (4.48g, 99%) as a white solid: mp 116–117 °C; IR (film) 3410–3265, 1740, 1650 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.40–3.45 (d, J = 14 Hz, 1 H), 3.82 (s, 3 H), 3.89–3.93 (d, J = 14 Hz, 1 H), 5.28–5.34 (d, J = 17 Hz, 1 H), 5.32–5.35 (d, J = 11 Hz, 1 H), 6.14–6.24 (dd, J = 11, 17 Hz, 1 H), 6.99 (s, 1 H), 7.06–7.09 (m, 2 H), 7.19–7.22 (m, 3 H), 7.39–7.50 (m, 3 H), 7.69–7.72 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 40.0, 53.0, 65.9, 116.3, 126.9, 127.1, 128.3, 128.6, 130.0, 131.6, 134.8, 135.7, 136.3, 166.4, 172.3; MS (EI) 309 (3, M$^+$), 218 (53), 105 (100); HRMS (EI) calcd for $C_{19}H_{19}NO_3$ (M$^+$) 309.1365, obsd 309.1362. Anal. Calcd for $C_{19}H_{19}NO_3$: C, 73.77; H, 6.19; N, 4.52. Found: C, 73.89; H, 6.24; N, 4.48.

Methyl *N*-Benzoyl-2-vinyl-3′,4′-bis[(*tert*-butyldimethylsilyl)oxy]phenylalaninate (4b). From selenide **3b** (825 mg, 1.14 mmol), following General Procedure C, was obtained **4b** (627 mg, 97%), as a white solid, after flash chromatography (10% EtOAc/hexane): mp 77–78 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.05 (s, 3 H), 0.06 (s, 3 H), 0.14 (s, 3 H), 0.15 (s, 3 H), 0.89 (s, 9 H), 0.94 (s, 9 H), 3.27–3.32 (d, J = 14 Hz, 1 H), 3.68–3.73 (d, 14 Hz, 1 H), 3.81 (s, 3 H), 5.23–5.29 (d, J = 17 Hz, 1 H), 5.32 (d, J = 11 Hz, 1 H), 6.12–6.22 (dd, J = 11, 17 Hz, 1 H), 6.52–6.68 (m, 3 H), 6.98 (s, 1 H), 7.36–7.48 (m, 3 H), 7.68–7.71 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ −4.24, −4.2, −4.14, −4.1, 18.2, 18.4, 25.8, 25.9, 39.8, 52.9, 65.6, 116.0, 120.7, 122.7, 123.0, 127.0, 128.5, 128.6, 131.5, 134.6, 136.4, 146.0, 146.5, 166.1, 172.4; IR (film) 3415–3250, 1740, 1660 cm^{-1}; MS (FAB, 3-NOBA) 570 (21, MH$^+$), 351 (100); HRMS (FAB, 3-NOBA) calcd for $C_{31}H_{48}NO_5Si_2$ (MH$^+$) 570.3071, obsd 570.3060. Anal. Calcd for $C_{31}H_{47}NO_5Si_2$: C, 65.34; H, 8.31; N, 2.45. Found: C, 65.12; H, 8.15; N, 2.31.

Methyl *N*-Benzoyl-2-vinyl-3′,4′-(methylenedioxy)phenylalaninate (4c). From selenide **3c** (500 mg, 0.979 mmol), following General Procedure C, was obtained **4c** (328 mg, 95%), as a white solid, after flash chromatography (10% EtOAc/hexane): mp 89–90 °C; IR (film) 3400–3320, 1740, 1650 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.31–3.34 (d, J = 14 Hz, 1 H), 3.82 (s, 3 H), 3.82–3.85 (d, J = 14 Hz, 1 H), 5.28–5.32 (d, J = 17 Hz, 1 H), 5.31–5.33 (d, J = 11 Hz, 1 H), 5.88 (s, 2 H), 6.13–6.19 (dd, J = 11, 17 Hz, 1 H), 6.54–6.65 (m, 3 H), 7.03 (s, 1 H), 7.40–7.50 (m, 3 H), 7.72–7.74 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 39.7, 53.0, 65.8, 100.8, 108.0, 110.0, 116.2, 123.0, 126.8, 128.5, 129.1, 131.6, 134.6, 136.1, 146.5, 147.4, 166.3,.172.2; MS (FAB, 3-NOBA): 354 (53, MH$^+$), 232 (18), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{20}H_{20}NO_5$ (MH$^+$) 354.1341, obsd 354.1331. Anal. Calcd for $C_{20}H_{19}NO_5$: C, 67.98; H, 5.42; N, 3.96. Found: C, 67.92; H, 5.52; N, 3.76.

Methyl N^{α}-Benzoyl-N^{τ}-trityl-2-vinylhistidinate (4d). A solution containing **3d** (995 mg, 1.43 mmol) and tetrabutylammonium periodate (803 mg, 1.85 mmol) in $CHCl_3$ (25 mL) was refluxed for 5 h and then evaporated and chromatographed (0-50% EtOAc/hexane) to give **4d** (618 mg, 80%) as a white solid: mp 73–75 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.09–3.12 (d, J = 14 Hz, 1 H), 3.25–3.27 (d, J = 14 Hz, 1 H), 3.75 (s, 3 H), 4.98–5.01 (d, J = 17 Hz, 1 H), 5.12–5.15 (d, J = 11 Hz, 1 H), 6.29–6.34 (dd, J = 11, 17 Hz, 1 H), 6.55 (s, 1 H), 7.05–7.09 (m, 6 H), 7.24–7.34 (m, 9 H), 7.39–7.49 (m, 4 H), 7.89–7.91 (m, 2 H), 8.79 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.4, 52.7, 64.4, 75.3, 114.5, 120.8, 127.3, 128.0, 128.1, 128.4, 129.7, 131.4, 134.2, 135.7, 135.9, 138.5, 142.2, 165.8, 172.6; IR (film) 3360–3270, 1740, 1670 cm^{-1}; MS (FAB, 3-NOBA) 542 (2, MH$^+$), 243 (100); HRMS (FAB, 3-NOBA) calcd for $C_{35}H_{32}N_3O_3$ (MH$^+$) 542.2443, obsd 542.2424. Anal. Calcd for $C_{35}H_{31}N_3O_3$: C, 77.61; H, 5.77; N, 7.76. Found: C, 77.48; H, 5.65; N, 7.65.

Methyl N^{α},N^{ϵ}-Dibenzoyl-2-vinyllysinate (4e). From selenide **3e** (9.50 g, 17.2 mmol), following General Procedure C, was obtained **4e** (6.70 g, 99%), as a white solid, after flash chromatography (10–50% EtOAc/hexane): mp 57–58 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.16–1.27 (m, 1 H), 1.38–1.74 (m, 3 H), 2.08–2.18 (app dt, J = 5, 13 Hz, 1 H), 2.62–2.72 (app dt, J = 4, 13 Hz, 1 H), 3.37–3.54 (m, 2 H), 3.79 (s, 3 H), 5.22–5.26 (d, J = 11 Hz, 1 H), 5.23–5.29 (d, J = 17 Hz, 1 H), 6.08–6.17 (dd, J = 11, 17 Hz, 1 H), 6.40–6.43 (m, 1 H), 7.25 (s, 1 H), 7.26–7.52 (m, 6 H), 7.67–7.83 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.8, 28.9, 34.0, 38.7, 53.1, 65.0, 115.2, 126.9, 127.0, 128.4, 128.6, 131.2, 131.6, 134.3, 134.5, 136.6, 166.4, 167.7, 172.9; IR (film) 3410–3220, 1740, 1640 cm^{-1}; MS (FAB, 3-NOBA) 395 (37, MH$^+$), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{23}H_{27}N_2O_4$ (MH$^+$) 395.1971, obsd 395.1970. Anal. Calcd for $C_{23}H_{26}N_2O_4$: C, 70.04; H, 6.64; N, 7.10. Found: C, 69.90; H, 6.59; N, 6.91.

Methyl N^{α},N^{δ}-Dibenzoyl-2-vinylornithinate (4f). From selenide **3f** (3.85 g, 7.16 mmol), according to General Procedure C, was obtained **4f** (2.71 g, 100%) as a white solid, after flash chromatography (10–50% EtOAc/hexane): mp 148–149 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.53–1.61 (m, 2 H), 2.19–2.29 (ddd, J = 7, 10, 14 Hz, 1 H), 2.76–2.86 (ddd, J = 6, 10, 14 Hz, 1 H), 3.36–3.56 (m, 2 H), 3.81 (s, 3 H), 5.25–5.29 (d, J = 11 Hz, 1 H), 5.27–5.32 (d, J = 17 Hz, 1 H), 6.03–6.12 (dd, J = 11, 17 Hz, 1 H), 6.39–6.43 (m, 1 H), 7.26–7.55 (m, 7 H), 7.77–7.84 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 23.8, 32.1, 39.4, 53.1, 64.7, 115.5, 126.9, 126.9, 128.3, 128.5, 131.1, 131.7, 133.9, 134.3, 136.2, 166.4, 167.6, 172.6; IR (film) 3380–3270, 1735, 1635 cm^{-1}; MS (FAB, 3-NOBA) 381 (39, MH$^+$), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{22}H_{25}N_2O_4$ (MH$^+$) 381.1814, obsd 381.1820. Anal. Calcd for $C_{22}H_{24}N_2O_4$: C, 69.46; H, 6.36; N, 7.36. Found: C, 69.25; H, 6.30; N, 7.26.

Methyl *N*-Benzoyl-2-vinylvalinate (4g). From selenide **3g** (1.50 g, 3.59 mmol), according to General Procedure C, was obtained **4g** (926 mg, 99%) as a white solid, after flash chromatography (10% EtOAc/hexane): mp 80–81 °C; ^{1}H NMR

(500 MHz, $CDCl_3$) δ 0.96–0.98 (d, J = 7 Hz, 3 H), 1.00–1.01 (d, J = 7 Hz, 3 H), 2.37–2.39 (app heptet, J = 7 Hz, 1 H), 3.77 (s, 3 H), 5.12–5.15 (d, J = 17 Hz, 1 H), 5.26–5.28 (d, J = 11 Hz, 1 H), 6.33–6.39 (dd, J = 11, 17 Hz, 1 H), 6.62 (s, 1 H), 7.41–7.44 (m, 2 H), 7.49–7.50 (m, 1 H), 7.79–7.80 (m, 2 H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 17.2, 17.8, 35.1, 52.5, 67.3, 115.3, 127.0, 128.6, 131.7, 133.2, 134.3, 166.3, 172.4; IR (film) 3370–3270, 1740, 1650 cm^{-1}; MS (FAB, 3-NOBA) 262 (61, MH^+), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{15}H_{20}NO_3$ (MH^+) 262.1443, obsd 262.1446. Anal. Calcd for $C_{15}H_{19}NO_3$: C, 68.94; H, 7.33; N, 5.36. Found: C, 68.76; H, 7.47; N, 5.28.

Methyl *N*-Benzoyl-4-*O*-(*tert*-butyldiphenylsilyl)-2-vinylhomoserinate (4i). From selenide **3i** (2.10 g, 3.19 mmol), according to General Procedure C, was obtained **4i** (1.57 g, 99%) as a white solid, after flash chromatography (100% hexane): mp 83–85 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 1.01 (s, 9 H), 2.37–2.41 (app dt, J = 4, 14.5 Hz, 1 H), 2.48–2.53 (m, 1 H), 3.74 (s, 3 H), 3.75–3.81 (m, 2 H), 5.24–5.28 (d, J = 17 Hz, 1 H), 5.26–5.28 (d, J = 11 Hz, 1 H), 6.16–6.21 (dd, J = 11, 17 Hz, 1 H), 7.27–7.48 (m, 9 H), 7.58–7.63 (m, 4 H), 7.76–7.77 (m, 2 H), 7.88 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.1, 26.9, 37.6, 52.9, 60.6, 63.7, 115.1, 127.1, 127.7, 127.7, 128.5, 129.8 (2 C), 131.5, 132.8, 132.9, 134.2, 135.4, 135.4, 136.0, 166.3, 173.0; IR (film) 3410, 1740, 1670 cm^{-1}; MS (FAB, 3-NOBA) 502 (11, MH^+), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{30}H_{35}NO_4Si$ (MH^+) 502.2413, obsd 502.2395. Anal. Calcd for $C_{30}H_{35}NO_4Si$: C, 71.82; H, 7.03; N, 2.79. Found: C, 71.60; H, 7.14; N, 2.60.

Methyl *N*-Benzoyl-4-*O*-*tert*-butyl-2-vinylhomoserinate (4j). From selenide **3j** (1.50 g, 3.15 mmol), according to General Procedure C, was obtained **4j** (1.00 g, 100%) as a white solid, after flash chromatography (0–10% EtOAc/hexane): mp 74–76 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 1.16 (s, 9 H), 2.15–2.22 (m, 1 H), 2.30–2.40 (m, 1 H), 3.48–3.54 (m, 2 H), 3.76 (s, 3 H), 5.16–5.22 (d, J = 17 Hz, 1 H), 5.24–5.27 (d, J = 11 Hz, 1 H), 6.17–6.27 (dd, J = 11, 17 Hz, 1 H), 7.39–7.52 (m, 3 H), 7.84- 7.87 (m, 2 H), 8.31 (s, 1 H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.3, 36.1, 52.6, 57.7, 63.9, 73.6, 114.8, 127.1, 128.4, 131.5, 134.2, 135.6, 165.8, 173.0; IR (film) 3370, 1740, 1670 cm^{-1}; MS (FAB, 3-NOBA) 320 (52, MH^+), 246 (53), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{18}H_{26}NO_4$ (MH^+) 320.1862, obsd 320.1858. Anal. Calcd for $C_{18}H_{25}NO_4$: C, 67.69; H, 7.89; N, 4.39. Found: C, 67.69; H, 7.95; N, 4.29.

α-Vinylphenylalanine (5a). A suspension of **4a** (500 mg, 1.62 mmol) in 6 N HCl (13 mL) was refluxed for 4 h. After extraction with CH_2Cl_2 (25 mL), the aqueous layer was evaporated in vacuo with mild heating ($T < 50$ °C). The residue was applied to a Dowex 50 × 8 ion exchange column. After the column was washed with several volumes of H_2O, elution with 1.3 M NH_4OH afforded **5a** (247 mg, 80%): ^1H NMR (500 MHz, D_2O) δ 2.99–3.04 (d, J = 14 Hz, 1 H), 3.31–3.36 (d, J = 14 Hz, 1 H), 5.19–5.25 (d, J = 17 Hz, 1 H), 5.32–5.36 (d, J = 11 Hz, 1 H), 6.05–6.15 (dd, J = 11, 17 Hz, 1 H), 7.17–7.20 (m, 2 H), 7.27–7.31 (m, 3 H); ^{13}C NMR (50 MHz, D_2O) δ 41.1, 65.9, 116.3, 127.6, 128.6, 129.9, 133.3, 134.9, 173.3; MS (EI) 191 (1, M^+), 146 (33), 100 (100); HRMS (EI) calcd for $C_{11}H_{13}NO_2$ (M^+) 191.0946, obsd 191.0942. Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 68.87; H, 6.84; N, 7.10.

α-Vinyl-3′,4′-dihydroxyphenylalanine Hydrochloride Salt (5b). A suspension of **4b** (100 mg, 0.175 mmol) in 6 N HCl (3 mL) was heated at 150 °C in a sealed glass vessel for 4 h. The cooled (rt) reaction mixture was extracted with CH_2Cl_2 (50 mL) and the aqueous layer evaporated in vacuo to provide **5b** (34.8 mg, 77%) as a tan solid [R_f = 0.31, *n*-BuOH/AcOH/H_2O (4:1:1)]: ^1H NMR (500 MHz, D_2O) δ 3.06–3.08 (d, J = 14 Hz, 1 H), 3.39–3.42 (d, J = 14 Hz, 1 H), 5.40–5.44 (d, J = 18 Hz, 1 H), 5.53–5.55 (d, J = 11 Hz, 1 H), 6.20–6.26 (dd, J = 11, 18 Hz, 1 H), 6.74–6.94 (m, 3 H); ^{13}C NMR (125 MHz, D_2O): δ 41.5, 66.8, 117.3, 118.2, 118.8, 123.6, 126.7, 135.4, 144.6, 145.0, 174.0; HRMS (FAB, 3-NOBA) calcd for $C_{11}H_{14}NO_4$ (HCl salt - Cl^-) 224.0923, obsd 224.0920. Anal. Calcd for $C_{11}H_{14}NO_4Cl$: C, 50.88; H, 5.43; N, 5.39. Found: C, 50.70; H, 5.46; N, 5.15.

α-Vinylhistidine (5d). A suspension of **4d** (200 mg, 0.369 mmol) in 6 N HCl (4 mL) was heated at 150 °C in a sealed glass vessel for 5 h and purified as for **5a** to give **5d** (48.7 mg, 73%) as a white solid: mp 179–181 °C; ^1H NMR (300 MHz, D_2O) δ 3.06–3.12 (d, J = 15 Hz, 1 H), 3.32–3.37 (d, J = 15 Hz, 1 H), 5.31–5.37 (d, J = 18 Hz, 1 H), 5.40–5.43 (d, J = 11 Hz, 1 H), 6.10–6.19 (dd, J = 11, 18 Hz, 1 H), 7.01 (s, 1 H), 7.70 (s, 1 H); ^{13}C NMR (75 MHz, D_2O) δ 33.9, 66.4, 117.6, 118.2, 131.9, 135.8, 136.8, 174.7; MS (FAB, 3-NOBA) 182 (100, MH^+); HRMS (FAB, 3-NOBA) calcd for $C_8H_{12}N_3O_2$ (MH^+) 182.0929, obsd 182.0932. Anal. Calcd for $C_8H_{11}N_3O_2$: C, 53.04; H, 6.12; N, 23.18. Found: C, 53.20; H, 6.30; N, 23.00.

α-Vinyllysine (5e). A suspension of **4e** (4.00 g, 10.1 mmol) in 6 N HCl (80 mL) was heated at 150 °C in a sealed glass vessel for 4.5 h. Purification was as for **5a**, except that elution from the Dowex 50 column was with a linear gradient of NH_4OH (0–1.3 M) to provide **5e** (1.05 g, 60%) as a white solid: mp 130–132 °C; ^1H NMR (300 MHz, D_2O) δ 1.22–1.32 (m, 1 H), 1.37–1.48 (m, 1 H), 1.59–1.72 (m, 3 H), 1.84–1.94 (app dt, J = 5, 14 Hz, 1 H), 2.95–3.00 (app t, J = 7 Hz, 2 H), 5.17–5.21 (d, J = 11 Hz, 1 H), 5.19–5.25 (d, J = 18 Hz, 1 H), 6.02–6.11 (dd, J = 11, 18 Hz, 1 H); ^{13}C NMR (125 MHz, D_2O) δ 20.1, 26.6, 36.6, 38.8, 63.7, 113.6, 139.3, 178.3; MS (FAB, 3-NOBA) 173 (MH^+, 100); HRMS (FAB, 3-NOBA) calcd for $C_8H_{17}N_2O_2$ (MH^+) 173.1290, obsd 173.1294.

α-Vinylornithine (5f). From **4f** (96.2 mg, 0.263mmol) in 6 N HCl (3 mL), according to the procedure for **5e**, was obtained **5f** (33.8 mg, 84%): mp 149–150 °C; ^1H NMR (500 MHz, D_2O) δ 1.63–1.69 (m, 1 H), 1.74–1.80 (m, 2 H), 1.96–2.01 (m, 1 H), 3.03–3.06 (app t, J = 7 Hz, 2 H), 5.28–5.30 (d, J = 11 Hz, 1 H), 5.29–5.33 (d, J = 18 Hz, 1 H), 6.10–6.16 (dd, J = 11, 18 Hz, 1 H); ^{13}C NMR (75 MHz, D_2O) δ 21.9, 34.5, 39.1, 63.3, 113.8, 139.6, 178.9; MS (FAB, 3-NOBA) 159 (100, MH^+); HRMS (FAB, 3-NOBA) calcd for $C_7H_{15}N_2O_2$ (MH^+) 159.1133, obsd 159.1128. Anal. Calcd for $C_7H_{14}N_2O_2$: C, 53.15; H, 8.92; N, 17.70. Found: C, 52.99; H, 8.74; N, 17.53.

α-Vinylvaline (5g). From **4g** (2.30 g, 8.80 mmol) in 6 N HCl (70 mL), according to the procedure for **5a**, was obtained **5g** (1.08 g, 85%) as a white solid: mp >245 °C; ^1H NMR (500 MHz, D_2O) δ 0.99–1.01 (d, J = 7 Hz, 3 H), 1.01–1.03 (d, J = 7 Hz, 3 H), 2.33–2.42 (app heptet, J = 7 Hz, 1 H), 5.27–5.31 (d, J = 18 Hz, 1 H), 5.43–5.45 (d, J = 11 Hz, 1 H), 6.10–6.16 (dd, J = 11 Hz, 18 Hz, 1 H); ^{13}C NMR (50 MHz, D_2O) δ 17.7, 18.6, 35.3, 72.0, 117.9, 137.9, 176.7; MS (EI) 143 (0.2, M^+), 100 (100); HRMS (EI) calcd for $C_7H_{13}NO_2$ (M^+) 143.0946, obsd 143.0942. Anal. Calcd for $C_7H_{13}NO_2$: C, 58.72; H, 9.15; N, 9.78. Found: C, 58.62; H, 9.06; N, 9.57.

α-Vinylalanine (5h). From **4h**[11] (500 mg, 2.14 mmol) in 6 N HCl (17 mL), according to the procedure for **5a**, was obtained **5h**[7b] (219 mg, 89%) as a white solid.

α-Vinylhomoserine (5i). From **4i** (500 mg, 0.997 mmol) in 6 N HCl (9 mL), according to the procedure for **5a**, was obtained **5i** (114 mg, 78%) as a white solid: mp 175 °C; ^1H NMR (500 MHz, D_2O) δ 2.16–2.25 (m, 2 H), 3.77–3.85 (m, 2 H), 5.38–5.41 (d, J = 17 Hz, 1 H), 5.45–5.47 (d, J = 11 Hz, 1 H), 6.08–6.14 (dd, J = 11, 17 Hz, 1 H); ^{13}C NMR (75 MHz, D_2O) δ 36.8, 58.6, 65.9, 117.5, 135.7, 174.6; MS (FAB, 3-NOBA) 146 (100, MH^+), 120 (15), 100 (26); HRMS (FAB, 3-NOBA) calcd for $C_6H_{12}NO_3$ (MH^+) 146.0817, obsd 146.0817. Anal. Calcd for $C_6H_{11}NO_3$: C, 49.65; H, 7.64; N, 9.64. Found: C, 49.53; H, 7.64; N, 9.60.

α-Vinylhomoserine (5i). From **4j** (500 mg, 1.57 mmol) in 6 N HCl (12 mL), according to the procedure for **5a**, was obtained **5i** (200 mg, 88%) identical in all aspects with the material obtained from **4i**.

***N*-Benzoyl-α-vinylhomoserine Lactone (6).** To a solution of **4j** (1.38 g, 4.32 mmol) in $CHCl_3$ (28 mL) at 0 °C was added CF_3CO_2H (33.0 mL, 432 mmol) and stirring continued for 30 h at rt. After dilution with CH_2Cl_2 (200 mL), $NaHCO_3$ (aq, 200 mL) was added carefully. After further extraction with CH_2Cl_2 (100 mL), the combined organics were dried ($MgSO_4$), filtered, and evaporated to yield **6** (837 mg, 84%) as a white solid: mp 145–146 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 2.82-2.88 (ddd, J = 9, 11, 13 Hz, 1 H), 2.93–2.97 (ddd, J = 1, 6, 13 Hz, 1 H), 4.27–4.32 (ddd, J = 6, 9, 11 Hz, 1 H), 4.54–4.58 (app dt, J = 1, 9 Hz, 1 H), 5.43–5.45 (d, J = 11 Hz, 1 H), 5.45–5.48 (d, J = 17 Hz, 1 H), 6.12–6.18 (dd, J = 11, 17 Hz, 1 H), 6.73–6.76 (m, 1 H), 7.44–7.47 (m, 2 H), 7.52–7.56 (m, 1 H), 7.79–7.85 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 34.3, 61.1, 65.9, 118.3, 127.0, 128.6, 132.1, 133.3 (2 C), 166.6, 175.2; IR (film) 3410–3220, 1770, 1655 cm^{-1}; MS (FAB, 3-NOBA) 232 (98, MH^+), 105 (100); HRMS (FAB, 3-NOBA) calcd for $C_{13}H_{14}NO_3$ (MH^+) 232.0974, obsd 232.0974. Anal. Calcd for $C_{13}H_{13}NO_3$: C, 67.52; H, 5.66; N, 6.06. Found: C, 67.34; H, 5.74; N, 5.91.

2-Benzamido-2-(hydroxyethyl)-*N*-methyl-3-butenamide (7). Lactone **6** (820 mg, 3.54 mmol) was taken up in ethanolic methylamine (4 ml, 8.0 M) and the reaction flask sealed. After 6 h of stirring at rt, the volatiles were removed in vacuo to provide **7** (897 mg, 96%) as a white solid: mp 140–141 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.25–2.37 (m, 2 H), 2.84 (s, 3 H), 2.85 (s, 3 H), 3.86–3.94 (m, 2 H), 5.30-5.34 (d, J = 17 Hz, 1 H), 5.35–5.37 (d, J = 11 Hz, 1 H), 6.16–6.22 (dd, J = 11, 17 Hz, 1 H), 6.87–6.87 (br s, 1 H), 7.41–7.44 (m, 2 H), 7.49–7.52 (m, 1 H), 7.83–7.85 (m, 2 H), 8.42 (s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 26.7, 38.3, 59.4, 64.9, 116.1, 127.1, 128.6, 131.8, 133, 137.8, 166.8, 172.8; IR (film) 3320, 1775, 1650 cm^{-1}; MS (FAB, 3-NOBA): 263 (100, MH^+), 204 (62); HRMS (FAB, 3-NOBA) calcd for $C_{14}H_{19}N_2O_3$ (MH^+) 263.1396, obsd 263.1404. Anal. Calcd for $C_{14}H_{18}N_2O_3$: C, 64.11; H, 6.92; N, 10.67. Found: C, 64.30; H, 6.86; N, 10.45.

2-Benzamido-*N*-methyl-2-vinylsuccinimide (8). A solution of **7** (856 mg, 3.05 mmol) and pyridinium dichromate (PDC) (4.01 g, 10.7 mmol) in DMF (8 mL) was stirred for 4 h at rt. Workup consisted of filtration through Celite, dilution with Et_2O (50 mL), and extraction with H_2O (10 × 30 mL). Flash chromatography (50–75% EtOAc/hexane) afforded **8** (654 mg, 77%) as a white solid: mp 114–115 °C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.05–3.09 (d, J = 18 Hz, 1 H), 3.09 (s, 3 H), 3.30-3.33 (d, J = 18 Hz, 1 H), 5.47–5.49 (d, J = 11 Hz, 1 H), 5.52–5.56 (d, J = 17 Hz, 1 H), 6.02–6.08 (dd, J = 11, 17 Hz, 1 H), 6.54 (s, 1 H), 7.43–7.46 (m, 2 H), 7.52–7.55 (m, 1 H), 7.75–7.77 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 25.2, 40.3, 61.0, 119.1, 127.1, 128.7, 132.4, 132.6, 134.7, 167.0, 173.9, 175.8; IR (film) 3340, 1780, 1705, 1660 cm^{-1}; MS (FAB, 3-NOBA) 259 (49, MH^+), 105 (COPh, 100); HRMS (FAB, 3-NOBA) calcd for $C_{14}H_{15}N_2O_3$ (MH^+) 259.1083, obsd 259.1083. Anal. Calcd for $C_{14}H_{14}N_2O_3$: C, 65.11; H, 5.46; N, 10.84. Found: C, 65.25; H, 5.60; N, 10.90.

α-Vinylaspartic Acid (9). A suspension of **8** (45.0 mg, 0.174 mmol) in 10 N HCl (2.5 mL) was heated in a sealed glass vessel at 150 °C for 5 h. After extraction with CH_2Cl_2 (50 mL), the aqueous layer was evaporated in vacuo. Purification by chromatography on polyethyleneimine-(PEI)–cellulose, washing with H_2O and elution with BuOH/H_2O/AcOH (4:1:1), afforded **9** (18.8 mg, 68%) as a white solid: ^{1}H NMR (500 MHz, D_2O) δ 2.98–3.02 (d, J = 18 Hz, 1 H), 3.24–3.28 (d, J = 18 Hz, 1 H), 5.49–5.52 (d, J = 18 Hz, 1 H), 5.52–5.55 (d, J = 11 Hz, 1 H), 6.04–6.09 (dd, J = 11, 18 Hz, 1 H); ^{13}C NMR (125 MHz, D_2O) δ 39.7, 63.3, 119.5, 134.1, 173.5, 174.6; HRMS (FAB, glycerol) calcd for $C_6H_{10}NO_4$ (MH^+) 160.0610, obsd 160.0604.

α-Vinylarginine (10). To a solution of α-vinylornithine **5f** (482 mg, 3.05 mmol) in 2 M NaOH (1.22 mL) was added *S*-ethylisothiouronium bromide (5.64 g, 30.5 mmol). The reaction mixture was maintained at ca. pH 10.5 by addition of 2 M NaOH and stirred at 45 °C for 36 h [TLC (R_f = 0.13; 20% NH_4OH/EtOH)]. The reaction mixture was then brought to pH 8 with 1 N HCl and the volatiles were removed in vacuo. Silica gel chromatography (20% NH_4OH/EtOH) gave **10** (360 mg, 59%) as a white solid: mp 179–181 °C; ^{1}H NMR (500 MHz, D_2O) δ 1.52–1.58 (m, 1 H), 1.66–1.82 (m, 2 H), 1.95–2.01 (m, 1 H), 3.24–3.27 (m, 2 H), 5.18–5.22 (d, J = 11 Hz, 1 H), 5.20–5.26 (d, J = 17.6 Hz, 1 H), 6.01–6.11 (dd, J = 11, 17.6 Hz, 1 H); ^{13}C NMR (125 MHz, D_2O) δ 23.6, 33.6, 41.5, 65.8, 117.6, 136.4, 157.7, 175.2; MS (FAB, 3-NOBA): 201 (100, MH^+); HRMS (FAB, 3-NOBA) calcd for $C_8H_{17}N_4O_2$ (MH^+) 201.1351, obsd 201.1350.

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Supplementary Material Available: ^{1}H NMR spectra for compounds **5a, 5b, 5d–i, 9** and **10** (10 pages). This material is contained in libraries on microfiche, immediately follows this article on the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.