magnitude mode. Generally 32 transients were acquired for each of 256 increments in t_1, which were zero-filled to a 2K × 1K matrix and transformed with pseudoecho weighting. The mixing time was set to 350 ms, and the recycle delay, to 3.0 s. NOESY cross-peak intensities as estimated by peak height were divided by peak intensities for the epindolidione aryl NH to H-1 and the heteroaryl NH to H-4 cross peaks in order to establish relative strengths of signals. The following rating system was used for these ratios: vs, >0.5; s, 0.15–0.5; m, 0.03–0.14; w, <0.03. For the derivatives discussed in the text, the following intensities were observed (heteroaryl NH to H-4 comparison appears in parentheses). For $d_{NN}(3,4)$: **8a**, m (w); **8b**, m (w); **8d**, s (s). For $d_{N_\alpha}(3,4)$: **8a**, vs (m); **8b**, s (m); **8d**, s (s). For $d_{N_\alpha}(2,3)$: **8a**, m (w); **8b**, m (w); **8d**, s (m).

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Supplementary Material Available: Experimental procedures for the preparation of substances **1a–m** and their precursors (19 pages). Ordering information is given on any current masthead page.

General Synthesis of β,γ-Alkynylglycine Derivatives

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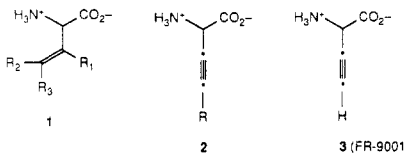
The coupling of α-haloglycinates **8** with alkynyltin reagents produces the fully protected β,γ-alkynylglycines **9**. Subsequent deprotection of the amino or carboxyl groups generates differentially protected β,γ-alkynylglycine derivatives **10–14**. The free amino acids were found to be too labile to isolate but can be generated in situ and trapped.

Introduction

β,γ-Unsaturated α-amino acids **1** have recently attracted considerable attention[1] due to their known ability[2] to pose as suicide inhibitors of pyridoxal-linked enzyme systems. The rarer β,γ-alkynyl α-amino acids **2** are represented by a single known[3] natural antibiotic, ethynylglycine (**3**, FR-900130), which is a suicide substrate for alanine racemase.



1 **2** **3** (FR-900130)

Both the vinyl (**1**) and ethynyl (**2**) amino acids are very challenging structures to prepare due to their chemical lability to racemization and tautomerization to unstable α,β-dehydro amino acids. While methodology to construct vinylglycines has been emerging,[4] comparable technology to construct the alkynyl systems has lagged[5] due to the greater relative chemical lability of these substances. As part of a general program aimed at embracing the most labile classes of amino acids, we have developed a mild alkynylation[6] of electrophilic glycinates[7] via organotin acetylides. We have recently communicated[8] the application of this methodology to construct *N*-acetylethynylglycine (*N*-acetyl-FR-900130) in racemic form. In this article, we disclose a full account of this general approach to differentially protected alkynylglycines.

Results and Discussion

The general approach that has been deployed is illustrated in Scheme I. Three different haloglycinates **8** were prepared according to the method of Ben-Ishai.[9] Both the carboxyl and amine protecting groups were varied in hopes of identifying suitable combinations for selective unmasking of the amine and carboxyl, respectively. We also hoped to be able to obtain the free amino acids, a task that has not yet been achieved due to the lability of the free amino acids themselves. The coupling reactions were

Scheme I

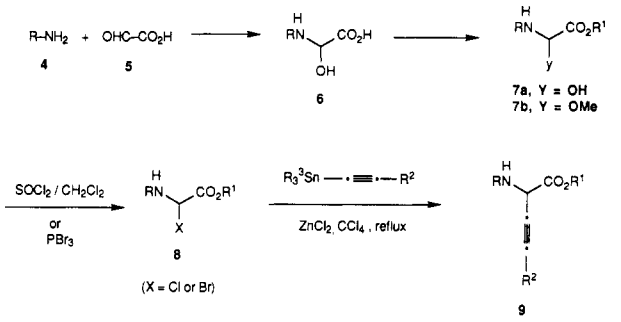


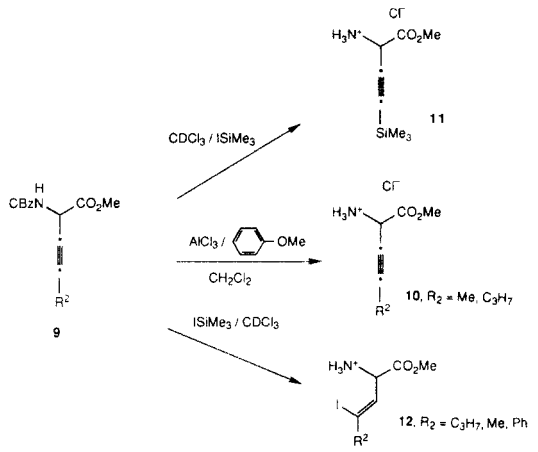
Table I

R	R^1	R^2	R^3	yield, % 7	8	9
CBz	Me			~quant.	~quant.	
		$SiMe_3$	Me			88
		Me	*n*-Bu			84
		n-C_3H_7	*n*-Bu			62
		n-C_4H_9	*n*-Bu			50
		n-C_6H_{13}	*n*-Bu			56
		Ph	*n*-Bu			64
		$CH_2CH_2OSiMe_2$-*t*-Bu	*n*-Bu			44
CBz	$CH(Ph)_2$			~quant.	~quant.	
		$SiMe_3$	Me			86
		Me	*n*-Bu			68
		n-C_3H_7	*n*-Bu			62
		n-C_4H_9	*n*-Bu			60
		n-C_6H_{13}	*n*-Bu			55
		Ph	*n*-Bu			80
		$CH_2CH_2OSiMe_2$-*t*-Bu	*n*-Bu			66
Ac	$CH(Ph)_2$			~quant.	~quant.	
		$SiMe_3$	Me			63
		Me	*n*-Bu			54
		n-C_3H_7	*n*-Bu			55
		n-C_4H_9	*n*-Bu			44
		n-C_6H_{13}	*n*-Bu			50
		Ph	*n*-Bu			58
		$CH_2CH_2OSiMe_2$-*t*-Bu	*n*-Bu			55

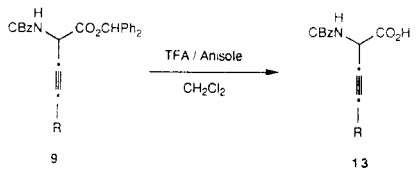
† Fellow of the Alfred P. Sloan Foundation 1986–90. NIH Research Career Development Awardee 1984–89.

0022-3263/90/1955-4657$02.50/0

Scheme II



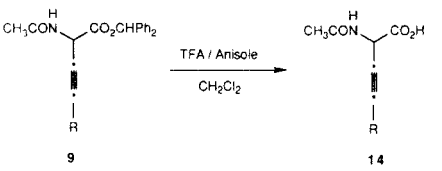
Scheme III



R	Yield (% 13)
TMS	quantitative
Me	75
C_3H_7	60
C_4H_9	quantitative
C_6H_{13}	40
Ph	58
CH_2CH_2OH	63

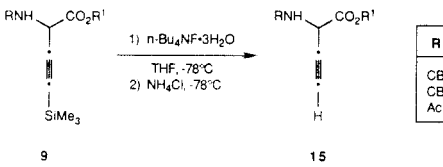
performed in refluxing carbon tetrachloride in the presence of $ZnCl_2$ (added as an anhydrous THF solution) to afford the fully protected alkynes **9**; the yields are given in Table I. The adducts **9** proved reasonably stable to normal chromatographic purification and handling.

Scheme IV



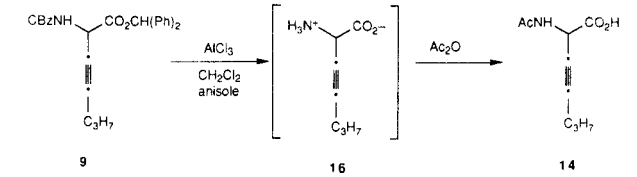
R	Yield (% 14)
TMS	quantitative
Me	50
C_3H_7	65
C_4H_9	quantitative
C_6H_{13}	69
Ph	60
H	84

Scheme V



R	R¹	Yield (% 15)
CBz	Me	67
CBz	$CH(Ph)_2$	92
Ac	$CH(Ph)_2$	~ quant

Scheme VI



Initial efforts were directed at selectively removing the amine protecting group. As shown in Scheme II, the *N*-carbobenzoxy (*N*-CBz) group could be removed with $AlCl_3$ in methylene chloride containing anisole as a tropylium ion scavenger. This procedure afforded the corresponding methyl ester amine hydrochloride salts (**10**). The use of trimethylsilyl iodide was also examined for removal of both the *N*-CBz and methyl ester groups in hopes of directly gaining access to the free amino acids. In the event, treatment of **9** with trimethylsilyl iodide (where $R_2 = SiMe_3$) cleanly effected removal of only the *N*-CBz group furnishing **11**. However, other substrates of **9** where R = aliphatic or aromatic groups, yielded the *unexpected* (*Z*)-vinyl iodides **12** as the sole identifiable products. It would seem that the HI produced in the removal of the *N*-CBz group readily adds across the acetylene, giving the observed HI addition products. The anomaly resides in the substrate **9**, where $R_2 = SiMe_3$. It is reasonable to postulate that the β-cation-directing influence of the trimethylsilyl substituent disfavors the (preferred, vide infra) direction of protonation of the alkyne at the β-position, which would place a developing partial positive charge adjacent to the silicon atom. This electronic perturbation thus results in an alkyne (**11**) that is recalcitrant to HI addition. The novel (*Z*)-γ-iodo amino acids produced constitute a new and potentially useful new class of derivatized β,γ-unsaturated amino acids. Chemical as well as biological studies are under way on these substances.

Despite extensive efforts to remove the methyl ester from **10** and **11** under a variety of acidic, basic, and nucleophilic conditions, extensive decomposition was the only common behavior that the methyl esters displayed.

Attention was then turned to the corresponding benzhydryl esters as shown in Schemes III and IV. Both the *N*-CBz and *N*-acetyl benzhydryl ester derivatives (**9**) were transformed into their corresponding *N*-acyl carboxylic acids in good yields by treatment with trifluoroacetic acid in methylene chloride containing anisole. The acids **13** and **14** represent potential substrates for preparing *N*-acyl peptides containing the β,γ-alkynyl side chain. Despite considerable effort, removal of the *N*-CBz group from **13**

(1) For a recent review on the synthesis of α-amino acids, see: Williams, R. M. *Synthesis of Optically Active α-Amino Acids*; Baldwin, J. E., Ed.; Organic Chemistry Series, Pergamon Press: Oxford, 1989.

(2) Walsh, C. *Tetrahedron* **1982**, *38*, 871.

(3) (a) Kuroda, Y.; Okuhara, M.; Goto, T.; Iguchi, E.; Kohsaka, M.; Aoki, H.; Imanaka, H. *J. Antibiot.* **1980**, *33*, 125. (b) Kuroda, Y.; Okuhara, M.; Goto, T.; Kohsaka, M.; Aoki, H.; Imanaka, H. *J. Antibiot.* **1980**, *33*, 132.

(4) (a) Williams, R. M.; Zhai, W. *Tetrahedron* **1988**, *44*, 5425. (b) Sasaki, N. A.; Hashimoto, C.; Pauly, R. *Tetrahedron Lett.* **1989**, *30*, 1943. (c) Sawada, S.; Nakayama, T.; Esaki, N.; Tanaka, H.; Soda, K.; Hill, R. K. *J. Org. Chem.* **1986**, *51*, 3384. (d) Baldwin, J. E.; Haber, S. B.; Hoskins, C.; Kruse, L. I. *J. Org. Chem.* **1977**, *42*, 1239. (e) Hudrlik, P. F.; Kulkarni, A. K. *J. Am. Chem. Soc.* **1981**, *103*, 6251. (f) Castelhano, A. L.; Horne, S.; Billedeau, R.; Krantz, A. *Tetrahedron Lett.* **1986**, *27*, 2435. (g) Lipshutz, B. H.; Huff, B.; Vaccaro, W. *Tetrahedron Lett.* **1986**, *27*, 4241. (h) Agouridas, K.; Girodeau, J. M.; Pineau, R. *Tetrahedron Lett.* **1985**, *26*, 3115. (i) Metcalf, B. W.; Bonilavri, E. *J. Chem. Soc., Chem. Commun.* **1978**, 914. (j) Greenlee, W. J.; Taub, D.; Patchett, A. A. *Tetrahedron Lett.* **1978**, 3999. (k) Paik, Y. H.; Dowd, P. *J. Org. Chem.* **1986**, *51*, 2910. (l) Steglich, W.; Wegmann, H. *Synthesis* **1980**, 481. (m) Thornberry, N. A.; Bull, H. G.; Taub, D.; Greenlee, W. J.; Patchett, A. A.; Cordes, E. H. *J. Am. Chem. Soc.* **1987**, *109*, 7543. (n) Fitzner, J. N.; Pratt, D. V.; Hopkins, P. B. *Tetrahedron Lett.* **1985**, *26*, 1959. (o) Schollkopf, U.; Groth, U. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 977. (p) Schollkopf, U.; Nozulak, J.; Groth, U. *Tetrahedron* **1984**, *40*, 1409. (q) Groth, U.; Schollkopf, U.; Chiang, Y.-C. *Synthesis* **1982**, 864. (r) Schollkopf, U.; Schroder, J. *Liebigs Ann. Chem.* **1988**, 87. (s) Weber, T.; Aeschimann, R.; Maetzke, T.; Seebach, D. *Helv. Chim. Acta* **1986**, *69*, 1365. (t) Keith, D. D.; Tortora, J. A.; Yang, R. *J. Org. Chem.* **1978**, *43*, 3711. (u) Keith, D. D.; Tortora, J. A.; Ineichen, K.; Leingrubber, W. *Tetrahedron* **1975**, *31*, 2633. (v) Kurokawa, N.; Ohfune, Y. *Tetrahedron Lett.* **1985**, *26*, 83. (w) Castelhano, A. L.; Pliura, D. H.; Taylor, G. J.; Hsieh, K. C.; Krantz, A. *J. Am. Chem. Soc.* **1984**, *106*, 2734. (x) Beaulieu, P. L.; Schiller, P. W. *Tetrahedron Lett.* **1988**, *29*, 2019. (y) For syntheses of vinylglycine itself, see ref 1.

(5) α-Substituted alkynylglycines: (a) Casara, P.; Metcalf, B. W. *Tetrahedron Lett.* **1978**, 1581. (b) Metcalf, B. W.; Casara, P. *J. Chem. Soc., Chem. Commun.* **1979**, 19. (c) Schollkopf, U.; Westphalen, K.-O.; Schroder, J.; Horn, K. *Liebigs Ann. Chem.* **1988**, 781. α-Unsubstituted alkynylglycines: (d) Castelhano, A. L.; Horne, S.; Taylor, G. J.; Billedeau, R.; Krantz, A. *Tetrahedron* **1988**, *44*, 5451.

(6) (a) Zhai, D.; Zhai, W.; Williams, R. M. *J. Am. Chem. Soc.* **1988**, *110*, 2501. (b) Williams, R. M.; Zhai, W. *Tetrahedron* **1988**, *44*, 5425.

(7) Williams, R. M.; Sinclair, P. J.; Zhai, D.; Chen, D. *J. Am. Chem. Soc.* **1988**, *110*, 1547 and references cited therein.

(8) Williams, R. M.; Aldous, D. J.; Aldous, S. C. *J. Chem. Soc., Perkin Trans. I* **1990**, 171.

(9) Bernstein, Z.; Ben-Ishai. *Tetrahedron* **1977**, *33*, 881.

($ISiMe_3$, $AlCl_3$, BCl_3, TFA, etc.) provided only extensive decomposition products and no isolable quantities of the corresponding free amino acids.

Removal of the *C*-trimethylsilyl residue to provide the parent acetylenic glycine derivatives proved to be a tricky undertaking. Eventually, it was found that careful treatment of these substrates (**9**, $R_2 = SiMe_3$) with tetra-*n*-butylammonium fluoride trihydrate in THF at −78 °C followed by a cold NH_4Cl (s) quench afforded the acetylenes **15** after a standard aqueous workup and flash column purification (Scheme V). It proved absolutely essential that the quench be conducted at low temperature; allowing the basic solution to warm above −78 °C resulted in extensive decomposition.

Although we were unable to isolate the free amino acids, preliminary evidence suggests that these substances can be generated in situ in solution and trapped. For example, treatment of **9** (R = CBz, $R^1 = CH(Ph)_2$) with $AlCl_3$ in methylene chloride followed by acetylation with acetic anhydride afforded the *N*-acetyl derivative **14** (Scheme VI). Authentic samples of **14** obtained by the route above (Scheme IV) confirmed the structure and the intermediacy of **16**.

Utility of these β,γ-alkynyl amino acids and derivatives for the preparation of small peptides and evaluation of their intrinsic antimicrobial properties are under active investigations in these laboratories.

Experimental Section

General Procedure for the Preparation of Alkynyltin Reagents.[10] To a solution of alkyne (0.43 mol) in THF (100 mL) at −78 °C under a nitrogen atmosphere was added *n*-butyllithium (2.0 M, 0.43 mol, 1 equiv) followed by the trialkyltin chloride (0.43 mol, 1 equiv) 5 min later. The reaction mixture was allowed to warm to room temperature and left stirring for 21 h. At this point the reaction was quenched by being filtered through Celite and concentrated in vacuo. The residue was distilled under reduced pressure yielding the alkynyltin in greater than 75% yield.

***N*-(Benzyloxycarbonyl)-α-hydroxyglycine (6, R = CBz).** Benzyl carbamate (6.4 g, 42.4 mmol) and glyoxylic acid monohydrate (**5**) (4.3 g, 46.7 mmol) were stirred together for 6 days in dry diethyl ether (50 mL). The product was filtered and used crude for further reactions. White solid (9.87 g, quantitative yield); ^1H NMR (270 MHz, $CDCl_3$, vs $CHCl_3$) δ 5.05 (s, 2 H), 5.25 (d, J = 8.8 Hz, 1 H), 7.35 (s, 5 H), 8.15 (d, J = 8.7 Hz, 1 H).

Methyl *N*-(Benzyloxycarbonyl)-α-methoxyglycinate (7b, R = CBz, R^1 = Me). To an ice-cooled solution of *N*-(benzyloxycarbonyl)-α-hydroxyglycine (**6**) (3.0 g, 13.3 mmol) in anhydrous methanol (50 mL) was added concentrated sulfuric acid (0.5 mL). The reaction was allowed to warm to room temperature and stirred for 48 h. At this point the reaction was quenched by being poured into ice-saturated $NaHCO_3$ (saturated aqueous, 100 mL). The product was extracted into EtOAc (5 × 50 mL) and the organic phase was dried over Na_2SO_4, filtered, and concentrated in vacuo, yielding **7b** as a powdery solid (97%). The product is used without further purification: ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 3.42 (s, 3 H), 3.76 (s, 3 H), 5.12 (s, 2 H), 5.33 (d, J = 9.52 Hz, 1 H), 6.02 (d, J = 9.3 Hz, 1 H), 7.3 (s, 5 H); mass spectrum (NH_3, CI) m/e 271 (M + NH_4, 7), 254 (M + H, 4.0).

Methyl *N*-(Benzyloxycarbonyl)-α-hydroxyglycinate (7a, R = CBz, R^1 = Me). A solution of methyl glyoxylate (10.2 g, 96 mmol) and benzyl carbamate (13.2 g, 87 mmol) was brought to reflux for 20 h. After this time the solution was concentrated to one-third the original volume and product crystallized out (15.2 g, 73%): ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 3.85 (br s, 3 H), 5.19 (br s, 2 H), 5.53 (d, J = 9.0 Hz, 1 H), 6.13 (d, J = 9.0 Hz, 1 H), 7.37 (s, 5 H); mass spectrum (NH_3, CI) m/e 239 (M, 1.4), 108 ($PhCH_2OH$, 100).

Methyl *N*-(Benzyloxycarbonyl)-α-chloroglycinate (8, R = CBz, R^1 = Me, X = Cl). To a suspension of methyl *N*-(benzyloxycarbonyl)-α-methoxyglycinate (**7b**) (0.5 g, 2 mmol) in carbon tetrachloride (25 mL), under a nitrogen atmosphere, was added phosphorus pentachloride (1.11 g, 4.4 mmol, 2.7 equiv). The reaction mixture was stirred at room temperature for 7 days; at this point the reaction was concentrated in vacuo and triturated with dry pentane (25 mL) for 24 h. The reaction mixture was then filtered, yielding a white solid (67% to quantitative yield): ^1H NMR (270 MHz, $CDCl_3$) δ 3.85 (s, 3 H), 5.2 (br s, 2 H), 6.15 (br s, 2 H), 7.35 (s, 5 H).

Methyl *N*-(Benzyloxycarbonyl)-α-bromoglycinate (8, R = CBz, R^1 = Me, X = Br). Same procedures as for the chloroglycinate were used only phosphorus tribromide replaced phosphorus pentachloride. The product in this case was a cream-colored solid (88% yield): ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 3.85 (s, 3 H), 5.2 (br s, 2 H), 6.2 (br, 1 H), 6.35 (br m, 1 H), 7.35 (s, 5 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 52.80 and 53.49 (m, overlapping d and q), 68.08 (t), 128.06–128.53 (m), 135.17 (s), 153.22 (s), 166.48 (s); IR (ν, cm^{-1}, $CHCl_3$) 3411, 3033, 2958, 1757, 1505; mp 92 °C (recrystallized from pentane).

General Preparation for the Protected α-Alkynylglycinates 9. To a refluxing solution of the α-haloglycinate (0.51 mmol) in CCl_4 (25 mL) was added alkynyltributylstannane (0.76 mmol, 1.3 equiv) followed by a solution of zinc chloride (1.6 M in THF, 0.4 mL, 1.1 equiv). Instantaneously the solution went turbid. The reaction was followed by TLC and generally was complete within 30 min. At this point the reaction was quenched by adding water (30 mL). The biphasic system was allowed to cool to room temperature; the organic phase was separated and the aqueous phase was washed with CH_2Cl_2 (2 × 15 mL). The combined organic phase was washed with brine (30 mL), dried over Na_2SO_4, filtered, concentrated in vacuo, and flash chromatographed, eluting with (see specific alkyne groups) yielding the alkynylglycinate.

Methyl 2-amino-*N*-(benzyloxycarbonyl)-4-(trimethylsilyl)-3-butynoate (9, R = CBz, R^1 = Me, R^2 = trimethylsilyl): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil; from 8 X = Cl (88%, based on a 0.07-mmol scale), X = Br (87%, based on a 0.51-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.14 (s, 9 H), 3.80 (s, 3 H), 5.11 (br s, 3 H), 5.40 (m, 1 H), 7.33 (s, 5 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ −0.63 (s), 46.63 (d), 52.87 (q), 67.05 (t), 89.87 (s), 97.95 (s), 127.80–128.25 (m), 135.98 (s), 155.00 (s), 167.80 (s); mass spectrum (NH_3, CI) m/e 320 (M + H, 41), 229 ([M + H − Bz], 43), 91 (Bz, 97.9); IR (ν, cm^{-1}) 3350, 3020, 2950, 2170, 1755, 1725.

Methyl 2-amino-*N*-(benzyloxycarbonyl)-3-pentynoate (9, R = CBz, R^1 = R^2 = Me): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil; from 8 X = Cl (84%, based on a 0.39-mmol scale), X = Br (65%, based on a 0.23-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 1.80 (s, 3 H), 3.78 (s, 3 H), 5.11 (br s, 3 H), 5.46 (m, 1 H), 7.33 (s, 5 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 3.36 (m), 46.23 (d), 53.00 (q), 67.22 (t), 72.52 (s), 81.23 (s), 127.96–128.64 (m), 136.10 (s), 155.23 (s), 168.60 (s); mass spectrum (NH_3, CI) m/e 279 (M + NH_4, 42), 2.62 (M + H, 27), 171 (M + H − Bz, 100); IR (ν, cm^{-1} neat) 3330, 3030, 2945, 2220, 1755, 1705.

Methyl 2-amino-*N*-(benzyloxycarbonyl)-3-heptynoate (9, R = CBz, R^1 = Me, R^2 = *n*-C_3H_7): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil; from 8 X = Cl (62%, based on a 0.28-mmol scale), X = Br (quantitative, based on a 0.33-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.93 (t, J = 7.4 Hz, 3 H), 1.49 (q, J = 7.2 Hz, 2 H), 2.14 (dt, J = 4.9 Hz and 2.0 Hz, 2 H), 3.78 (s, 3 H), 5.10 (br s, 3 H), 5.45 (m, 1 H), 7.33 (s, 5 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 13.20 (br s), 20.50 (distorted q), 21.61 (br s), 46.28 (d), 52.92 (distorted q), 67.17 (t), 73.56 (s), 85.56 (s), 127.96–128.42 (m), 136.15 (s), 155.19 (s), 168.39 (s); mass spectrum (NH_3, CI) m/e 290 (M + H, 79), 199 (M + H − Bz, 100); IR (ν, cm^{-1}) 3320, 3020, 2940, 2205, 1750, 1710.

Methyl 2-amino-*N*-(benzyloxycarbonyl)-3-octynoate (9, R = CBz, R^1 = Me, R^2 = *n*-C_4H_9): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil; from 8 X = Cl (50%, based on a 0.55-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.88 (m, 3 H), 1.37 (m, 4 H), 2.16 (m, 2 H),

(10) *CAUTION.* Extreme care should be taken in handling the organotin reagents; this is particularly important for the more volatile and more toxic trimethyltin acetylides. Proper gloves, eye protection, and an efficient fume hood should *always* be employed for the preparation, handling, and disposal of these toxic substances, see: Krigman, M. R.; Silverman, A. P. *Neurotoxicology* **1984**, *5*, 129.

3.75 (s, 3 H), 5.11 (br s, 3 H), 5.41 (br s, 1 H), 7.31 (s, 5 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 13.30 (s), 18.21 (t), 21.74 (br s), 30.24 (br s), 46.29 (d), 52.87 (q), 67.15 (s), 85.70 (s), 127.84–128.38 (m), 136.18 (s), 155.17 (s), 168.65 (s); mass spectrum (NH_3, CI) *m/e* 213 (M + H − Bz, 93); IR (ν, cm^{-1}, $CHCl_3$) 3330, 3030, 2945, 2220, 1750, 1700.

Methyl 2-amino-*N*-(benzyloxycarbonyl)-3-decynoate (9, R = CBz, R^1 = Me, R^2 = *n*-C_6H_{13}): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil; from 8 X = Cl (56%, based on a 1.20-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.88 (m, 3 H), 1.25 (m, 8 H), 2.13 (m, 2 H), 3.74 (br s, 3 H), 5.09 (s, 3 H), 5.52 (br m, 1 H), 7.30 (br s, 5 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 13.78 (br s), 18.50 (t), 22.33 (br s), 28.09 (m), 28.29 (m), 31.11 (br s), 46.23 (d), 52.86 (q), 67.11 (t), 73.36 (s), 85.70 (s), 127.92–128.30 (m), 136.15 (s), 155.13 (s), 168.62 (s); mass spectrum (NH_3, CI) *m/e* 349 (M + NH_4, 48) 332 (M + H, 31), 241 (M + H − Bz, 100); IR (ν, cm^{-1}; $CHCl_3$) 3300, 3010, 2915, 2835, 2200, 1780, 1700.

Methyl 2-amino-*N*-(benzyloxycarbonyl)-4-phenyl-3-butynoate (9, R = CBz, R^1 = Me, R^2 = C_6H_5): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil; from 8 X = Cl (94%, based on a 0.29-mmol scale), X = Br (78%, based on a 0.12-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 3.82 (s, 3 H), 5.14 (s, 2 H), 5.38 (br d, *J* = 8.4 Hz, 1 H), 5.63 (br d, *J* = 8.1 Hz, 1 H), 7.35 (m, 10 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 46.65 (d), 53.25 (q), 67.38 (t), 82.23 (s), 84.60 (s), 121.71 (s), 128.03–133.41 (m), 136.04 (s), 155.13 (s), 168.23 (s); mass spectrum (NH_3, CI) *m/e* 341 (M + NH_4, 6.4), 324 (M + H, 24), 233 (M + H − Bz, 37), 216 (M + H − Bz − OH, 61); IR (ν, cm^{-1} neat) 3310, 3020, 2940, 2220, 1750, 1710.

Methyl 2-amino-*N*-(benzyloxycarbonyl)-6-[(*tert*-butyldimethylsilyl)oxy]-3-hexynoate (9, R = CBz, R^1 = Me, R^2 = $CH_2CH_2OSiMe_2$-*t*-Bu): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil; From 8 X = Cl (44%, based on a 0.28-mmol scale); ^1H NMR (270 MHz, $CDCl_3$vs $CHCl_3$) δ 0.04 (s, 6 H), 0.86 (s, 9 H), 2.35 (m, 2 H), 3.64 (m, 2 H), 3.77 (br s, 3 H), 5.10 (br s, 3 H), 5.41 (m, 1 H), 7.33 (s, 5 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ −5.35 (s), 18.22 (s), 23.09 (br s), 25.83 (br s), 46.23 (d), 53.06 (q), 61.41 (t), 67.28 (t), 74.40 (s), 82.86 (s), 128.07–128.68 (m), 136.13 (s), 155.24 (s), 168.55 (s); mass spectrum (NH_3, CI) *m/e* 406 (M + H, 21), 31.5 (M + H − Bz, 79), 298 (M + H − Bz − OH, 100); IR (ν, cm^{-1}, neat) 3320, 3020, 2940, 2220.

Methyl 2-Amino-4-(trimethylsilyl)-3-butynoate Hydrochloride (11). To a stirred solution of CBz-protected glycine **9** (R_2 = $SiMe_3$) (0.082 mmol, 1 equiv) in $CDCl_3$ (2 mL) was added trimethylsilyl iodide (0.164 mmol, 2 equiv) at room temperature. After 30 min there was no starting material by TLC and the reaction was quenched by addition of hydrochloric acid (0.1 M, 4 × 15 mL). The aqueous phase was washed with CH_2Cl_2 (2 × 15 mL) and then concentrated in vacuo, yielding quantitatively product **11** as a brown solid: ^1H NMR (270 MHz, D_2O, vs HOD) δ 0.05 (s, 9 H), 3.73 (s, 3 H), 4.94 (s, 1 H); mass spectrum (NH_3, CI) *m/e* 186 (M^+, 100).

Methyl 2-Amino-3-pentynoate Hydrochloride (10, R^2 = Me). To a stirred solution of CBz glycinate **9** (R_2 = Me) (0.094 mmol, 1 equiv) in dry CH_2Cl_2 (3 mL) was added anisole (0.55 mmol, 5.8 equiv). The reaction mixture was then cooled to ice/water temperature, anhydrous $AlCl_3$ (0.28 mmol, 3 equiv) was added, and the solution was allowed to warm slowly to room temperature and left stirring for a total of 18 h. After this time the reaction was worked up by being washed with water (10 mL × 3). The combined aqueous phases were washed with CH_2Cl_2 (2 × 10 mL) and then concentrated in vacuo, producing the crude product (30 mg, quantitative) contaminated with $Al(OH)_2$: ^1H NMR (270 MHz, D_2O vs HOD) δ 1.64 (s, 3 H), 3.70 (s, 3 H), 4.80 (s, 1 H).

Methyl 2-amino-3-heptynoate hydrochloride (10, R^2 = *n*-C_3H_7): produced as for R^2 = Me crude product (60 mg, quantitative, based on a 0.10-mmol scale); ^1H NMR (270 MHz, D_2O vs HOD) δ 0.59 (distorted t, *J* = 7.2 Hz, 3 H), 1.15 (distorted q, *J* = 7.2 Hz, 2 H), 1.89 (m, 2 H), 3.53 (s, 3 H); mass spectrum (NH_3, CI) *m/e* 156 (M^+, 100).

Deprotection of Methyl 2-Amino-*N*-(benzyloxycarbonyl)-3-heptynoate (9, R^2 = C_3H_7). To a solution of alkynyl glycinate **9** (R^2 = *n*-C_3H_7) (0.104 g, 0.36 mmol) in CH_2Cl_2 was added anisole (0.222 g, 2.08 mmol, 5.8 equiv); the reaction mixture was cooled to 0 °C and $AlCl_3$ (0.148 g, 1.08 mmol, 3 equiv) was added. The mixture was allowed to warm slowly to room temperature and left stirring for 16 h. At this point sodium fluoride (0.182 g, 4.3 mol, 4.0 equiv (based on $AlCl_3$)) was added followed 30 min later by water (58 μL, 3.2 mmol, 3 equiv (based on $AlCl_3$)). After a further 30 min the reaction mixture was filtered and concentrated in vacuo to give the product **10** (R^2 = C_3H_7) in 14% yield (not contaminated with $Al(OH)_x$).

Methyl 2-amino-4-iodo-3-pentenoate hydrochloride (12, R = Me): same procedure as for **11** (R_2 = TMS); brown solid isolated (25 mg, quantitative, based on a 0.07 mmol-scale); ^1H NMR (270 MHz, D_2O vs HOD) δ 2.44 (s, 3 H), 3.73 (s, 3 H), 4.80 (d, *J* = 7.6 Hz, 1 H), 5.62 (d, *J* = 7.6 Hz, 1 H); mass spectrum (NH_3, CI) *m/e* 256 (M^+, 100) 156 (M − HI, 72).

Methyl 2-amino-4-iodo-3-heptenoate hydrochloride (12, R = *n*-C_3H_7): same procedure as for **11** (R_2 = TMS); brown solid isolated (20 mg, quantitative, based on a 0.04-mmol scale); ^1H NMR (270 MHz, D_2O vs HOD) vs 0.69 (t, *J* = 7.4 Hz, 3 H), 1.42 (distorted q, *J* = 7.2 Hz, 2 H), 2.44 (distorted t, *J* = 7.2 Hz, 1 H), 3.68 (s, 3 H), 4.84 (d, *J* = 9.9 Hz, 1 H), 5.66 (d, *J* = 9.9 Hz, 1 H); mass spectrum (NH_3, CI) *m/e* 284 (M^+, 100), 156 (M − HI, 72); IR (ν, cm^{-1}, Nujol mull) 3430, 2940, 2900, 2840, 1740, 1610.

Methyl 2-amino-4-iodo-4-phenyl-3-butenoate hydrochloride (12, R = C_6H_5): same procedure as for **11** (R_2 = TMS); brown solid isolated (20 mg, quantitative, based on a 0.04-mmol scale); ^1H NMR (270 MHz, D_2O vs HOD) δ 3.73 (overlapping s, 3 H), 6.02 (d, *J* = 7.8 Hz, 1 H), 6.45 (d, *J* = 7.8 Hz, 1 H), 7.32 (br s, 5 H); mass spectrum (NH_3, CI) *m/e* 317 (M^+, 8.6) 194 (100).

Diphenylmethyl *N*-(Benzyloxycarbonyl)-α-hydroxyglycinate (7, R = CBz, R^1 = $CH(Ph)_2$). To a stirred solution of *N*-(benzyloxycarbonyl)-α-hydroxyglycine (0.56 mmol, 1 equiv) was added dropwise diphenyldiazomethane (0.56 mmol, 1 equiv). The reaction mixture was stirred for 18 h until the purple color disappears; at this point workup simply involves concentration in vacuo, producing product (0.23 g, quantitative yield): ^1H NMR (270 MHz, $CDCl_3$) δ 5.05 (br s, 2 H), 5.58 (br d), 6.15 (br d, 1 H), 6.92 (br s, 1 H), 7.30 (br s, 15 H); ^{13}C NMR (69.73 MHz, $CDCl_3$) δ 67.40 (t), 73.87 (d), 79.09 (d), 127.06–128.56 (m), 135.76 (s), 139.04 (s), 155.49 (s), 168.49 (s); mass spectrum (NH_3, CI) *m/e* 183 ($OCHPh_2$), 22), 167 ($CHPh_2$, 100); IR (ν, cm^{-1}, Nujol mull) 3338, 2923, 2853, 1749, 1693, 1529; mp 128 °C (recrystallized from ethyl acetate and hexanes). Anal. Calcd for $C_{23}H_{21}NO_5$: C, 70.57; H, 5.41; N, 3.58. Found: C, 70.56; H, 5.29; N, 3.54.

Diphenylmethyl *N*-(Benzyloxycarbonyl)-α-chloroglycinate (8, R = CBz, R^1 = $CH(Ph)_2$, X = Cl). To a stirred solution of diphenylmethyl α-hydroxyglycinate (5.9 mmol, 1 equiv) in dry dichloromethane (150 mL) was added thionyl chloride (118.6 mmol, 20 equiv). The reaction mixture was brought to reflux for 1–2 h and concentrated in vacuo, yielding a brown oil, which was triturated for 18 h with dry pentane, producing a white solid after filtration (0.181 g, 75% yield): ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 5.30 (br s, 2 H), 6.63 (br s, 2 H), 7.10 (br s, 1 H), 7.50 (br s, 15 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 67.34 (t), 73.81 (d), 78.97 (d), 127.03–128.52 (m), 135.73 (s), 139.04 (s), 139.08 (s), 155.50 (s), 168.52 (s); mass spectrum (NH_3, CI) *m/e* 183 ($OCHPh_2$, 17), 169 (CBzNHCH + NH_4, 100), 167 ($CHPh_2$, 73); IR (ν, cm^{-1}, $CHCl_3$) 3425, 3034, 3012, 1729, 1507; mp 122 °C (recrystallized from pentane).

Diphenylmethyl 2-amino-*N*-(benzyloxycarbonyl)-4-(trimethylsilyl)-3-butynoate (9, R = CBz, R^1 = $CH(Ph)_2$, R^2 = $SiMe_3$): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil (0.2258 g, 86%, based on a 0.56-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.24 (s, 9 H), 5.15 (br s, 2 H), 5.36 (br d, 1 H), 5.64 (br d, 1 H, *J* = 8.5 Hz), 6.97 (s, 1 H), 7.37 (br s, 15 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ −0.52 (br s), 47.03 (d), 67.19 (t), 78.80 (d), 90.22 (s), 92.98 (s), 126.47–128.66 (m), 135.93 (s), 139.09 (s), 139.34 (s), 155.08 (s), 166.33 (s); mass spectrum (NH_3, CI) *m/e* 489 (M + 18, 2.1), 200 (Ph_2CHO + NH_4, 60), 183 (Ph_2CHO, 99), 167 (Ph_2CH, 100); IR (ν, cm^{-1}, neat) 3390, 3030, 2960, 2190, 1760, 1730.

Diphenylmethyl 2-amino-*N*-(benzyloxycarbonyl)-3-pentynoate (9, R = CBz, R^1 = $CH(Ph)_2$, R^2 = Me): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil (0.2037 g, 68%, based on a 0.73-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 1.82 and 1.83 (tight s, 3 H), 5.13 (br s, 2 H), 5.25 (br s, 1 H), 5.60 (br d, 1 H, *J* = 8.0 Hz), 6.94 (s, 1 H), 7.35

(br s, 15 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 3.11 (q), 46.41 (d), 66.98 (t), 72.48 (s), 78.57 (d), 81.36 (s), 126.39–128.00 (m), 135.45 (s), 139.10 (s), 139.29 (s), 155.23 (s), 167.00 (s); mass spectrum (NH_3, CI) *m/e* 431 (M + NH_4, 1.2), 200 (Ph_2CHO + NH_4, 87), 183 (Ph_2CHO, 100), 167 (Ph_2CH, 100); IR (ν, cm^{-1}, neat) 3420, 3330, 3100, 3070, 3040, 2960, 2940, 2860, 2240, 1770, 1710.

Diphenylmethyl 2-amino-*N*-(benzyloxycarbonyl)-3-heptynoate (9, R = CBz, R^1 = CH(Ph)$_2$, R^2 = *n*-C_3H_7): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil (0.2019 g, 62%, based on a 0.74-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.97 (t, *J* = 7.4 Hz, 3 H), 1.51 (q, *J* = 7.2 Hz, 2 H), 2.18 (dt, *J* = 4.9 Hz and 2.0 Hz, 2 H), 5.11 (br s, 2 H), 5.26 (br d, *J* = 2.2 Hz), 5.45 (br d, *J* = 2.7 Hz, 1 H), 6.92 (s, 1 H), 7.33 (br s, 15 × H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 13.24 (distorted t), 20.45 (q), 21.55 (distorted t), 46.53 (d), 67.09 (t), 73.50 (s), 78.60 (d), 85.70 (s), 126.48–129.86 (m), 136.04 (s), 139.19 (s), 139.38 (s), 155.15 (s), 167.09 (s); mass spectrum (NH_3, CI) *m/e* 459 (M + 18, 2.5), 167 (Ph_2CH, 100); IR (ν, cm^{-1}, neat), 3400, 3320, 3080, 3050, 3020, 2940, 2910, 2860, 2210, 1750, 1720.

Diphenylmethyl 2-amino-*N*-(benzyloxycarbonyl)-3-octynoate (9, R = CBz, R^1 = CH(Ph)$_2$, R^2 = *n*-C_4H_9): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil (0.32 g, 60%, based on a 0.70-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) 0.99 (m, 3 H), 1.47 (m, 4 H), 2.25 (br s, 2 H), 5.19 (br s, 2 H), 5.34 (br s, 1 H), 5.60 (br s, 1 H), 5.99 (s, 1 H), 7.38 (br s, 15 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 13.42 (distorted s), 18.18 (distorted q), 21.77 (br s), 30.21 (br s), 46.50 (d), 67.13 (t), 73.26 (s), 78.64 (d), 85.86 (s), 126.48–129.89 (m), 135.99 (s), 139.18 (s), 139.39 (s), 155.17 (s), 167.12 (s); mass spectrum (NH_3, CI) *m/e* 473 (M + 18, 9.8), 456 (M + H, 2.1), 183 (Ph_2CHO, 56), 167 (Ph_2CH, 100); IR (ν, cm^{-1}, $CHCl_3$) 3395, 3340, 3050, 3020, 2940, 2910, 2895, 2210, 1755, 1730, 1655, 1590.

Diphenylmethyl 2-amino-*N*-(benzyloxycarbonyl)-3-decynoate (9, R = CBz, R^1 = CH(Ph)$_2$, R^2 = *n*-C_6H_{13}): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil (0.1985 g, 55%, based on a 0.75-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.99 (m, 3 H), 1.55 (m, 8 H), 2.23 (m, 2 H), 5.15 (br s, 2 H), 5.25 (br s, 1 H), 5.62 (br s, 1 H), 6.95 (s, 1 H), 7.32 (s, 15 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 13.84 (m), 18.53 (m), 22.32 (br s), 28.16 (m), 28.37 (m), 31.14 (br s), 46.64 (d), 67.14 (t), 73.36 (s), 78.67 (d), 85.99 (s), 126.52–129.88 (m), 136.10 (s), 139.28 (s), 139.46 (s), 155.12 (s), 167.11 (s); mass spectrum (NH_3, CI) *m/e* 501 (M + NH_4, 1.2) 200 (Ph_2CHO + NH_4, 100); IR (ν, cm^{-1}, $CHCl_3$) 3370, 3300, 3030, 3000, 2920, 2890, 2820, 2195, 1780, 1735, 1705, 1648, 1580.

Diphenylmethyl 2-amino-*N*-(benzyloxycarbonyl)-4-phenyl-3-butynoate (9, R = CBz, R^1 = CH(Ph)$_2$, R^2 = C_6H_5): purified by flash chromatography, eluting with CH_2Cl_2 to give a colorless oil (0.3339 g, 80%, based on a 0.70-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 5.15 (br s, 2 H), 5.54 (m, 1 H), 5.65 (m, 1 H), 6.95 (s, 1 H), 7.32 (s, 20 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 46.92 (d), 67.21 (t), 78.88 (d), 82.42 (s), 84.77 (s), 121.64 (s), 126.45–128.78 (m), 131.75 (d), 135.95 (s), 139.05 (s), 139.29 (s), 155.22 (s), 166.58 (s); mass spectrum (NH_3, CI) *m/e* 200 (Ph_2CHO + NH_4, 49), 183 (Ph_2CHO, 50), 167 (Ph_2CH, 100); IR (ν, cm^{-1}) 3405, 3320, 3060, 3030, 2950, 2915, 2845, 2220, 1760, 1720.

Diphenylmethyl 2-amino-*N*-(benzyloxycarbonyl)-6-[(*tert*-butyldimethylsilyl)oxy]-3-hexynoate (9, R = CBz, R^1 = CH(Ph)$_2$, R^2 = $CH_2CH_2OSiMe_2t$-Bu): purified by flash chromatography, eluting with CH_2Cl_2; ^1H NMR (270 MHz, $CDCl_3$) δ 0.20 (s, 6 H), 0.95 (s, 9 H), 2.4 (2 × t overlapping, 2 H), 3.70 (t, 2 H), 5.15 (s, 2 H), 5.32 (m, 1 H), 5.45 (m, 1 H), 6.95 (s, 1 H), 7.35 (s, 15 H); ^{13}C NMR (270 MHz, $CDCl_3$) δ −5.32 (br s), 18.14 (br s), 22.98 (br s), 25.70 (br s), 46.54 (d), 61.40 (t), 67.18 (t), 74.55 (s), 78.74 (d), 82.80 (s), 126.52–128.44 (m), 136.07 (s), 139.22 (s), 139.39 (s), 155.22 (s), 166.92 (s); mass spectrum (NH_3, CI) *m/e* 575 (M + NH_4, 13.9), 558 (M + H, 2.0), 200 (Ph_2CHO + NH_4, 41), 183 (Ph_2CHO, 38); IR (ν, cm^{-1} neat) 3420, 3340, 3060, 3030, 2945, 2860, 2210, 1755, 1720, 1655, 1595, 1580.

***N*-Acetyl-α-hydroxyglycine (6, R = $COCH_3$)**. A solution of acetamide (6.1 g, 103.4 mmol) and glyoxylic acid monohydrate (**5**) (10.6 g, 115.2 mmol) in anhydrous acetone (150 mL) was brought to reflux for 20 h. At this point the reaction was quenched by simply concentrating in vacuo, yielding a thick oil (14 g, quantitative): ^1H NMR (270 MHz, DMSO-d_6 vs DMSO) δ 1.83 (s, 3 H), 5.37 (d, *J* = 8.4 Hz, 1 H), 8.66 (d, *J* = 8.4 Hz, 1 H); ^{13}C NMR (67.93 MHz, DMSO-d_6) δ 22.72 (t), 71.27 (d), 169.86 (s), 171.58 (s); mass spectrum (NH_3, CI) *m/e* no M^+; IR (ν, cm^{-1} neat) 3257, 3037, 2511, 2252, 2126, 1680, 1538.

Diphenylmethyl *N*-Acetyl-α-hydroxyglycinate (7, R = $COCH_3$, R^1 = CH(Ph)$_2$). Procedure used was as for the benzyloxycarbonyl derivative; the only modification was the use of 1:3 acetone/ethyl acetate as solvent: White solid (11.80 g, quantitative, based on a 37.60 mmol-scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 1.95 (s, 3 H), 4.63 (d, *J* = 6.21 Hz, 1 H), 5.69 (t, *J* = 7.3 Hz, 1 H), 6.89 (s, 1 H), 7.31 (s, 10 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 22.67 (t), 72.06 (d), 78.86 (d), 126.97–128.52 (m), 139.19 (2 × s), 168.85 (s), 171.25 (s); mass spectrum (NH_3, CI) *m/e* 167 (Ph_2CH), 100); IR (ν, cm^{-1}, $CHCl_3$) 3350, 2925, 2854, 1749, 1660, 1543; mp 124 °C (recrystallized from ethyl acetate and hexanes). Anal. Calcd for $C_{17}H_{17}NO_4$: C, 68.21; H, 5.73; N, 4.68. Found: C, 68.18; H, 5.69; N, 4.59.

Diphenylmethyl *N*-Acetyl-α-chloroglycinate (8, R = $COCH_3$, R^1 = $CHPh_2$). Procedure used was as for the benzyloxycarbonyl derivative: white solid (1.51 g, 75%, based on a 5.12 mmol-scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 1.97 (s, 3 H), 6.41 (d, *J* = 9.8 Hz, 1 H), 6.89 (s, 1 H), 7.16 (d, *J* = 9.8 Hz, 1 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 22.66 (t), 72.12 (d), 78.80 (d), 126.68–128.47 (m), 139.06 (s), 139.13 (s), 156.50 (s), 168.75 (s); IR (ν, cm^{-1}) 3418, 3033, 3012, 1748, 1698, 1497; mp 121 °C (recrystallized from pentane).

Diphenylmethyl 2-amino-*N*-acetyl-4-(trimethylsilyl)-3-butynoate (9, R = $COCH_3$, R^1 = CH(Ph)$_2$, R^2 = $SiMe_3$): purified by flash chromatography, eluting with 50:1 CH_2Cl_2/MeOH to give a white solid (0.94 g, 63%, based on a 3.92-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.21 (s, 9 H), 1.95 (s, 3 H), 5.54 (d, *J* = 8.0 Hz, 1 H), 6.53 (d, *J* = 6.0 Hz, 1 H), 6.92 (s, 1 H), 7.35 (s, 5 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ −0.38 (br s), 22.34 (br m), 45.17 (d), 79.01 (d), 90.09 (s), 98.24 (s), 126.83–128.57 (m), 139.54 (s), 166.69 (s), 169.07 (s); mass spectrum (NH_3, CI) *m/e* 379 (M^+, 2.4), 167 (Ph_2CH), 100); IR (ν, cm^{-1}, $CHCl_3$), 3445, 3088, 3069, 3050, 3022, 2956, 2900, 2176, 1756, 1699; mp 113 °C (recrystallized from ethyl acetate and hexanes). Anal. Calcd for $C_{22}H_{25}NO_3Si$: C, 69.62; H, 6.64; N, 3.69. Found: C, 69.53; H, 6.55; N, 3.68.

Diphenylmethyl 2-amino-*N*-acetyl-3-pentynoate (9, R = $COCH_3$, R^1 = CH(Ph)$_2$, R^2 = Me): purified by flash chromatography, eluting with 50:1 CH_2Cl_2/MeOH to give a white solid (0.254 g, 54%, based on a 1.48-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 1.78 (tight d, *J* = 2.3 Hz, 3 H), 1.94 (s, 3 H), 5.42 (dd, *J* = 2.5 Hz, 8.0 Hz, 1 H), 6.47 (d, *J* = 8.0 Hz, 1 H), 6.88 (s, 1 H), 7.32 (s, 10 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 3.32 (t), 22.65 (t), 44.68 (d), 72.69 (s), 78.83 (d), 81.13 (s), 126.88–128.51 (m), 139.25 (s), 139.49 (s), 167.28 (s), 169.23 (s); mass spectrum (NH_3, CI) *m/e* 322 (M + H, 2), 167 (Ph_2CH, 100); IR (ν, cm^{-1}, $CHCl_3$) 3441, 3066, 3075, 3011, 2960, 2924, 2873, 2855, 1750, 1680; mp 141.5 °C (recrystallized from ethyl acetate and hexanes). Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.74; H, 5.96; N, 4.36. Found: C, 74.48; H, 5.76; N, 4.3.

Diphenylmethyl 2-amino-*N*-acetyl-3-heptynoate (9, R = $COCH_3$, R^1 = CH(Ph)$_2$, R^2 = *n*-C_3H_7): purified by flash chromatography, eluting with 50:1 CH_2Cl_2/MeOH to give a white solid (0.3008 g, 55%, based on a 1.58-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.92 (t, *J* = 7.3 Hz, 3 H), 1.47 (q, *J* = 7.3 and 14.4 Hz, 2 H), 1.92 (s, 3 H), 2.13 (dt, *J* = 2.3 and 7.0 Hz, 2 H), 5.46 (m, 1 H), 6.66 (d, *J* = 7.7 Hz, 1 H), 6.89 (s, 1 H), 7.31 (br s, 10 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 13.24 (t), 20.42 (distorted t), 21.55 (m), 22.23 (m), 44.54 (d), 73.55 (s), 78.54 (d), 85.28 (s), 126.34–128.77 (m), 139.17 (s), 139.42 (s), 167.22 (s), 169.34 (s); mass spectrum (NH_3, CI) *m/e* 349 (M^+, 1.7), 167 (Ph_2CH, 100); IR (ν, cm^{-1}, $CHCl_3$) 3445, 3067, 3033, 3011, 2966, 2936, 2874, 1750, 1680; mp 109.5 °C (recrystallized from ethyl acetate and hexanes). Anal. Calcd for $C_{22}H_{23}NO_3$: C, 75.62; H, 6.63; N, 4.01. Found: 75.87; H, 6.47; N, 4.00.

Diphenylmethyl 2-amino-*N*-acetyl-3-octynoate (9, R = $COCH_3$, R^1 = CH(Ph)$_2$, R^2 = *n*-C_4H_9): purified by flash chromatography, eluting with 50:1 CH_2Cl_2/MeOH to give a white solid (0.254 g, 44%, based on a 1.60-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.88 (t, *J* = 7.2 Hz, 3 H), 1.42 (m, 4 H), 1.94 (s, 3 H), 2.16 (distorted t, 2 H), 5.45 (m, 1 H), 6.46 (d, *J* = 7.8 Hz, 1 H), 6.89 (s, 1 H), 7.32 (s, 10 H); ^{13}C NMR (67.93 MHz,

$CDCl_3$) δ 13.40 (m), 18.20 (distorted t), 21.77 (m), 22.61 (m), 30.28 (m), 44.70 (d), 73.49 (s), 78.68 (d), 85.54 (s), 126.46–128.86 (m), 139.29 (s), 139.53 (s), 167.30 (s), 169.22 (s); mass spectrum (NH_3, CI) *m/e* 363 (M^+, 6.2), 167 (Ph_2CH, 100); IR (ν, cm^{-1}, $CHCl_3$) 3444, 3067, 3033, 3011, 2961, 2935, 2874, 1750, 1681, 1497; mp 94 °C (recrystallized from ethyl acetate and hexanes). Anal. Calcd for $C_{23}H_{25}NO_3$: C, 76.00; H, 6.92; N, 3.85. Found: C, 76.25; H, 6.88; N, 3.65.

Diphenylmethyl 2-amino-*N*-acetyl-3-decynoate (9, R = $COCH_3$, R^1 = $CH(Ph)_2$, R^2 = *n*-C_6H_{13}): purified by flash chromatography, eluting with 50:1 CH_2Cl_2/MeOH to give a white solid (0.387 g, 50%, based on a 1.90-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.90 (m, 3 H), 1.24–1.49 (2 × m, 8 H), 1.93 (s, 3 H), 2.15 (distorted dt, 2 H), 5.46 (distorted dd, *J* = 8.0 Hz, 1 H), 6.52 (d, *J* = 8.0 Hz, 1 H), 6.88 (s, 1 H), 7.31 (s, 10 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 13.83 (br s), 18.56 (br s), 22.33 (br s), 22.57 (br s), 28.22 (br s), 28.40 (br s), 31.15 (br s), 44.65 (d), 73.40 (s), 78.70 (d), 85.63 (s), 126.44–128.90 (m), 139.27 (s), 139.54 (s), 167.31 (s), 169.23 (s); mass spectrum (NH_3, CI) *m/e* 391 (M^+, 3.0), 167 (Ph_2CH), 100); IR (ν, cm^{-1}, $CHCl_3$) 3446, 3033, 3011, 2933, 2861, 1750, 1681, 1497; mp 88 °C (recrystallized from ethyl acetate and hexanes). Anal. Calcd for $C_{25}H_{29}NO_3$: C, 76.69; H, 7.46; N, 3.50. Found: C, 76.94; H, 7.42; N, 3.59.

Diphenylmethyl 2-amino-*N*-acetyl-4-phenyl-3-butynoate (9, R = $COCH_3$, R^1 = $CH(Ph)_2$, R^2 = C_6H_5): purified by flash chromatography, eluting with 50:1 CH_2Cl_2/MeOH to give a white solid (0.3362 g, 58%, based on a 1.5-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 1.99 (s, 3 H), 5.75 (d, *J* = 8.0 Hz, 1 H), 6.65 (d, *J* = 8.0 Hz, 1 H), 6.95 (s, 1 H), 7.32 (m, 15 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 22.60 (m), 44.94 (d), 78.97 (d), 82.52 (s), 84.51 (s), 121.81 (s), 126.41–129.25 (m), 131.78 (d), 139.10 (s), 139.42 (s), 166.79 (s), 169.25 (s); mass spectrum (NH_3, CI) *m/e* 383 (M^+, 3.0), 167 (Ph_2CH, 100); IR (ν, cm^{-1}, $CHCl_3$) 3443, 3067, 3033, 3012, 1751, 1682, 1496; exact mass calcd for $C_{25}H_{21}NO_3$ 383.15214, found 383.1528; mp 139 °C (recrystallized from ethyl acetate and hexanes).

Diphenylmethyl 2-amino-*N*-acetyl-6-[(*tert*-butyldimethylsilyl)oxy]-3-hexynoate (9, R = $COCH_3$, R^1 = $CH(Ph)_2$, R^2 = $CH_2CH_2OSiMe_2$-*t*-Bu): purified by flash chromatography, eluting with 50:1 CH_2Cl_2/MeOH to give a light brown oil (0.54 g, 55%, based on a 2.11-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.03 (s, 6 H), 0.87 (s, 9 H), 1.90 (s, 3 H) 2.36 (br t, *J* = 7.2 Hz, 2 H), 3.65 (t, *J* = 7.0 Hz, 2 H), 5.43 (d, *J* = 8.0 Hz, 1 H), 6.47 (d, *J* = 8.0 Hz, 1 H), 6.86 (s, 1 H), 7.26 (br s, 10 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ −5.38 (br s), 18.14 (s), 22.51 (m), 22.97 (m), 25.76 (m), 44.57 (d), 61.40 (t), 74.63 (s), 78.73 (d), 82.42 (s), 126.41–128.85 (m), 139.19 (s), 139.45 (s), 167.05 (s), 169.14 (s); mass spectrum (NH_3, CI) *m/e* 466 (M + H, 1.2), 167 (Ph_2CH), 100); IR (ν, cm^{-1}, $CHCl_3$) 3436, 3033, 3011, 2958, 2930, 2858, 1750, 1683, 1498; exact mass calcd for $C_{27}H_{35}NO_3Si$ 465.2335, found 350.1396; fits $C_{21}H_{20}NO_4$ (M − TBDMS).

Diphenylmethyl 2-Amino-*N*-acetyl-6-hydroxy-3-hexynoate (9, R = $COCH_3$, R^1 = $CH(Ph)_2$, R^2 = CH_2CH_2OH). The above oxysilyl compound decomposes to the title compound as an oil on standing: ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 1.96 (s, 3 H), 2.39 (dt, *J* = 6.15 and 2.3 Hz, 2 H), 3.62 (br s, 2 H), 5.40 (d, *J* = 7.5 Hz, 1 H), 6.60 (d, *J* = 7.5 Hz, 1 H), 6.87 (s, 1 H), 7.31 (br s, 10 H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 22.70, 22.94, 44.60, 60.56, 75.11, 82.44, 78.91, 126.81–128.55, 138.98, 139.29, 167.13, 169.64; mass spectrum (NH_3, CI) *m/e* 352 (M + H, 6), 167 ($CHPh_2$, 100); IR (ν, cm^{-1}, $CHCl_3$) 3438, 3012, 2930, 1749, 1679, 1497; exact mass calcd for $C_{21}H_{21}NO_4$ 351.14706, found 351.1467.

Methyl 2-Amino-*N*-(benzyloxycarbonyl)-3-butynoate (15, R = CBz, R^1 = Me). To a solution of **9** (R = CBz, R^1 = Me, R^2 = TMS) (48.3 mg, 0.15 mmol) in dry THF (30 mL) at −78 °C was added *n*-$Bu_4NF{\cdot}3H_2O$ (1 M, 300 μL, 0.3 mmol, 2 equiv). The reaction was followed by tlc (eluting with 1:1 hexanes/EtOAc) and quenched at −78 °C by the addition of NH_4Cl (s) (5.0 g). At this point the reaction was concentrated in vacuo, extracted into EtOAc (5 × 50 mL) from H_2O (50 mL), washed with NaCl (saturated aqueous, 50 mL), dried over Na_2SO_4, filtered, concentrated in vacuo, and purified by flash chromatograhy (eluting with 3:1 hexanes/EtOAc), producing a white solid (30 mg, 80%): ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 2.38 (d, *J* = 2.8 Hz, 1 H), 3.80 (s, 3 H), 5.11 (br s, 3 H), 5.49 (br s, 1 H), 7.33 (s, 5 H); ^{13}C NMR (67.93 MHz, $CDCl_3$) δ 45.81 (d), 53.29 (q), 67.37 (t), 72.95 (d), 77.16 (s), 128.03–128.45 (m), 135.92 (s), 155.05 (s), 167.70 (s); mass spectrum (NH_3, CI) *m/e* 265 (M + NH_4, 37), 248 (M + H, 20), 108 ($PhCH_2OH$ 82), 106 (PhCHO, 100); IR (ν, cm^{-1}, $CHCl_3$) 3435, 3302, 3025, 2943, 1753, 1723; exact mass calcd for $C_{13}H_{13}NO_4$ 247.0845, found 247.0849; mp 68 °C (recrystallized from ethyl acetate and hexanes).

Diphenylmethyl 2-amino-*N*-(benzyloxycarbonyl)-3-butynoate (15, R = CBz, R^1 = $CH(Ph)_2$): procedure as for methyl 2-amino-*N*-(benzyloxycarbonyl)-3-butynoate; from **9** (R = CBz, R^1 = $CH(Ph_2)$, R^2 = TMS) (35.60 mg, 92%, based on a 0.01-mmol scale), clear glass; ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 2.42 (d, *J* = 2.6 Hz, 1 H), 5.11 (s, 2 H), 5.28 (d, *J* = 7.2 Hz, 1 H), 5.50 (d, *J* = 7.2 Hz, 1 H), 6.90 (s, 1 H), 7.32 (br s, 15 H); mass spectrum (NH_3, CI) *m/e* 418 (M + NH_4, 0.5), 400 (M + H, 0.8), 167 (Ph_2CH, 100); IR (ν, cm^{-1}, $CHCl_3$) 3608, 3457, 3326, 3098, 3044, 3000, 1761, 1728.

Diphenylmethyl 2-amino-*N*-acetyl-3-butynoate (15, R = $COCH_3$, R^1 = $CH(Ph)_2$): procedure as for methyl 2-amino-*N*-(benzyloxycarbonyl)-3-butynoate; from **9**, (R = $COCH_3$, R^1 = $CH(Ph_2)$, R^2 = TMS) (24.50 mg, quantitative, based on a 0.08-mmol scale), white solid; ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 2.01 (s, 3 H), 2.37 (d, *J* = 2.5 Hz, 1 H), 5.49 (dd, *J* = 2.5 Hz and 8.0 Hz, 1 H), 6.21 (d, *J* = 8.0 Hz, 1 H), 6.87 (s, 1 H), 7.32 (s, 10 H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 22.77, 44.12, 72.88, 77.14, 79.25, 126.72–128.60, 138.98, 139.19, 139.95, 166.46, 169.32; mass spectrum (NH_3, CI) *m/e* 308 (M + H, 3.1), 167 (Ph_2CH, 100); IR (ν, cm^{-1}, $CHCl_3$) 3436, 3304, 3069, 3031, 2965, 1754, 1699; exact mass calcd for $C_{19}H_{17}NO_3$ 307.1208, found 307.1215; mp 106 °C (recrystallized from ethyl acetate and hexanes).

General Procedure for the Protected 2-Amino-3-alkynoic Acids 13 and 14. To a solution of diphenylmethyl glycinate (**9**, R^1 = $CH(Ph)_2$) (0.081 mmol, 1 equiv) and anisole (0.24 mmol, 3 equiv) in dry CH_2Cl_2 (5 mL) at 0 °C was added TFA (0.86 mmol, 10 equiv). The reaction mixture was allowed to warm to room temperature and left stirring for 20 h. The reaction was worked up by washing with $NaHCO_3$ (aq) (3 × 15 mL) the aqueous phase acidified to pH 2–3 with 1 M HCl, and the product was extracted with EtOAc (4 × 20 mL). The combined organic phases were dried over Na_2SO_4, filtered, and concentrated.

2-Amino-*N*-(benzyloxycarbonyl)-4-(trimethylsilyl)-3-butynoic acid (13, R = $SiMe_3$): oil (67.30 mg, quantitative, based on a 0.20-mmol scale); ^1H NMR (300 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.15 (s, 9 H), 5.13 (m, 3 H), 5.64 (d, *J* = 7.4 Hz, 1 H), 7.32 (s, 5 H), 9.02 (br s, CO_2H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ −0.45, 46.90, 67.57, 90.69, 97.33, 126.18–130.33, 135.72, 155.74, 171.71; IR (ν, cm^{-1}, $CHCl_3$) 3446, 3010, 2986, 2961, 2359, 1718, 1685, 1506; exact mass calcd for $C_{15}H_{19}NO_4Si$ 305.10833, found 305.1086.

2-Amino-*N*-(benzyloxycarbonyl)-3-pentynoic acid (13, R = Me): white solid (63.00 mg, 75%, based on a 0.34-mmol scale); ^1H NMR (300 MHz, $CDCl_3$ vs $CHCl_3$) δ 1.81 (s, 3 H), 5.13 (br m, 3 H), 5.50 (d, *J* = 11.2 Hz, 1 H), 7.34 (s, 5 H), 8.56 (br s, CO_2H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 3.55, 46.11, 67.50, 71.87, 81.92, 126.19–130.34, 135.81, 155.61, 172.2; mass spectrum (NH_3, CI) *m/e* 265 (M + NH_4, 22), 248 (M + H, 28), 157 (M + H − Bz, 100), 108 (BzOH, 93), 91 (Bz, 85); IR (ν, cm^{-1}, $CHCl_3$) 3322, 3061, 3029, 2950, 2920, 2583, 2359, 2336, 2242, 1952, 1885, 1716, 1514; exact mass calcd for $C_{13}H_{13}NO_4$ 247.0845, found 247.0844; mp 76–77 °C (recrystallized from ethyl acetate and hexanes).

2-Amino-*N*-(benzyloxycarbonyl)-3-heptynoic acid (13, R = *n*-C_3H_7): solid/oil (49.50 mg, 60%, based on a 0.30-mmol scale); ^1H NMR (300 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.93 (t, *J* = 7.3 Hz, 3 H), 1.49 (q, *J* = 7.2 Hz, 2 H), 2.13 (dt, *J* = 6.9, 1.7 Hz, 2 H), 5.13 (m, 3 H), 5.63 (d, *J* = 7.7 Hz, 1 H), 7.33 (s, 5 H), 9.74 (br s, CO_2H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 13.35, 20.51, 21.60, 46.24, 67.49, 72.81, 86.12, 126.17–130.32, 135.76, 155.77, 172.46; mass spectrum (NH_3, CI) *m/e* 293 (M + NH_4, 26), 276 (M + H, 20), 185 (M + H − Bz, 100); IR (ν, cm^{-1}, $CHCl_3$) 3323, 3060, 3031, 2961, 2933, 2872, 2595, 1724, 1508; exact mass calcd for $C_{15}H_{17}NO_4$ 275.11576, found 275.1153.

2-Amino-*N*-(benzyloxycarbonyl)-3-octynoic acid (13, R = *n*-C_4H_9): glass (51.40 mg, quantitative, based on a 0.20-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.86 (t, *J* = 7.0 Hz, 3 H), 1.35 (m, 4 H), 2.15 (br s, 2 H), 5.12 (m, 3 H), 5.59 (br s, 1 H), 7.32 (s, 5 H), 9.20 (br s, CO_2H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 13.50, 18.28, 21.87, 30.24, 46.46, 67.39, 73.04, 85.98, 126.18–130.33, 135.89, 155.76, 172.44; mass spectrum (NH_3, CI)

m/e 307 (M + NH_4, 19), 390 (M + H, 40), 108 (BzOH, 86), 91 (Bz, 100); IR (ν, cm^{-1}, $CHCl_3$) 3320, 3065, 3032, 2956, 2928, 2867, 2580, 2232, 1952, 1721, 1509; exact mass calcd for $C_{16}H_{19}NO_4$ 289.13141, found 289.1317.

2-Amino-*N*-(benzyloxycarbonyl)-3-decynoic acid (13, R = *n*-C_6H_{13}): oil (29.20 mg, 40%, based on a 0.23-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.85 (m, 3 H), 1.30 (m, 8 H), 2.17 (m, 2 H), 5.12 (br s, 3 H), 5.48 (br s, 1 H), 7.32 (s, 5 H), 8.05 (br s, CO_2H); ^{13}C NMR (75.47 MHz, DMSO) δ 13.88, 17.97, 21.97, 27.81, 27.94, 30.72, 46.36, 65.50, 76.07, 83.10, 127.68–128.30, 136.91, 155.44, 168.87; mass spectrum (NH_3, CI) *m/e* 335 (M + NH_4, 18), 318 (M + H, 12), 227 (M + H − Bz, 100), 108 (BzOH, 45); IR (ν, cm^{-1}, $CHCl_3$) 3341, 3062, 3031, 2955, 2929, 2856, 2533, 1952, 1717, 1604, 1505; exact mass calcd for $C_{18}H_{23}NO_4$ 317.1627, found 317.1624.

2-Amino-*N*-(benzyloxycarbonyl)-4-phenyl-4-butynoic acid (13, R = C_6H_5): glass (35.80 mg, 58%, based on a 0.20-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 5.15 (br s, 2 H), 5.42 (d, *J* = 7.4 Hz, 1 H), 5.77 (d, *J* = 7.4 Hz, 1 H), 7.29 (br m, 10 H), 9.08 (br s, CO_2H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 46.75, 67.58, 81.88, 84.82, 121.62, 128.49–131.93, 135.74, 155.79, 171.79; mass spectrum (NH_3, CI) *m/e* 327 (M + NH_4, 100), 310 (M + H, 34); IR (ν, cm^{-1}, $CHCl_3$) 3437, 3032, 1757, 1504; exact mass calcd for $C_{18}H_{15}NO_4$ 309.1001, found 309.1009.

2-Amino-*N*-acetyl-3-butynoic acid (*N*-acetylethynylglycine) (14, R = H): white solid (13 mg, 84%, based on a 0.11-mmol scale); ^1H NMR (300 MHz, $CDCl_3$ vs $CHCl_3$) δ 2.12 (s, 3 H), 2.43 (d, *J* = 2.6 Hz, 1 H), 5.36 (dd, *J* = 2.6 and 7.4 Hz, 1 H), 6.73 (d, *J* = 7.4 Hz, 1 H), 8.0 (br s, CO_2H); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 21.97, 43.64, 74.81, 78.66, 168.60, 169.00; mass spectrum (NH_3, CI) *m/e* 142 (M + H, 100), 141 (M^+, 35); decomposes above 150 °C.

2-Amino-*N*-acetyl-4-(trimethylsilyl)-3-butynoic acid (14, R = $SiMe_3$): white solid (85.20 mg, quantitative, based on 0.40-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCL_3$) δ 0.15 (s, 9 H), 2.12 (s, 3 H), 5.34 (d, *J* = 7.2 Hz, 1 H), 6.66 (m, 1 H), 10.10 (br s, CO_2H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ −0.6, 22.10, 45.45, 91.42, 96.07, 170.62, 172.70; IR (ν, cm^{-1}, $CHCl_3$) 3446, 3010, 2986, 2961, 2359, 1718, 1685, 1506; exact mass calcd for $C_9H_{15}NO_3Si$ 213.08212, found 213.0828; decomposes above 110 °C (recrystallized from ethyl acetate and hexanes).

2-Amino-*N*-acetyl-3-pentynoic acid (14, R = Me): solid (18 mg, 50%, based on 0.23-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 1.82 (d, *J* = 2.7 Hz, 3 H), 2.07 (s, 3 H), 5.23 (br s, 1 H), 6.79 (br s, 1 H), 8.23 (br s, CO_2H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 3.40, 22.13, 45.06, 70.92, 82.55, 171.00, 172.53; mass spectrum (NH_3) *m/e* 156 (M + H, 100); IR (ν, cm^{-1}, $CHCl_3$) 3448, 3026, 1731, 1677, 1510; exact mass calcd for $C_7H_9NO_3$ 155.0583, found: 155.0589; mp 116 °C (recrystallized from ethyl acetate and hexanes).

2-Amino-*N*-acetyl-3-heptynoic acid (14, R = *n*-C_3H_7): white solid (53.50 mg, 65%, based on a 0.45-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.92 (t, *J* = 7.3 Hz, 3 H), 1.50 (m, 2 H), 2.03 (s, 3 H), 2.13 (br s, 2 H), 5.23 (d, *J* = 7.3 Hz, 1 H), 6.83 (d, *J* = 7.2 Hz, 1 H), 8.43 (br s, CO_2H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 13.38, 20.55, 26.66, 22.49, 44.97, 73.24, 85.72, 170.85, 171.02; mass spectrum (NH_3, CI) *m/e* 201 (M + NH_4), 28), 184 (M + H, 100), 140 (M + H − CO_2, 48); IR (ν, cm^{-1}, $CHCl_3$) 3446, 3046, 3011, 2976, 2950, 2891, 2543, 1727, 1673, 1509; exact mass calcd for $C_9H_{13}NO_3$ 183.0896, found 183.0893; mp 93 °C (recrystallized from ethyl acetate and hexanes).

2-Amino-*N*-acetyl-3-octynoic acid (14, R = *n*-C_4H_9): white solid (41.00 mg, quantitative, based on a 0.21-mmol scale); ^1H NMR (300 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.86 (t, *J* = 7.2 Hz, 3 H), 1.35 (m, 4 H), 2.03 (s, 3 H), 2.16 (dt, *J* = 7.3 and 2.0 Hz, 2 H), 5.22 (d, *J* = 6.8 Hz, 1 H), 6.89 (d, *J* = 6.8 Hz, 1 H), 9.20 (br s, CO_2H); ^{13}C NMR (75.47 MHz, $CDCl_3$) δ 13.49, 18.30, 21.88, 22.14, 30.29, 42.39, 72.94, 85.82, 171.09, 171.37; mass spectrum (NH_3, CI) *m/e* 215 (M + NH_4, 31), 198 (M + H, 100), 154 (M + H − CO_2, 55); IR (ν, cm^{-1}), $CHCl_3$) 3444, 2961, 1732, 1676, 1512; mp 98 °C (recrystallized from ethyl acetate and hexanes).

2-Amino-*N*-acetyl-3-decynoic acid (14, R = *n*-C_6H_{13}): oil (19.40 mg, 69%, based on a 0.13-mmol scale); ^1H NMR (270 MHz, $CDCl_3$ vs $CHCl_3$) δ 0.85 (m, 3 H), 1.24–1.48 (m, 8 H), 2.03 (s, 3 H), 2.15 (m, 2 H), 5.23 (d, *J* = 6.0 Hz, 1 H), 6.86 (d, *J* = 6.0 Hz, 1 H), 10.83 (br s, CO_2H); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 13.88, 17.98, 21.98, 22.17, 27.87, 28.00, 30.73, 44.54, 76.44, 82.72, 168.58, 169.24; mass spectrum (NH_3, CI) *m/e* 243 (M + NH_4, 26), 226 (M + H, 75), 182 (M + H − CO_2, 100); IR (ν, cm^{-1}, $CHCl_3$) 3441, 3010, 2932, 2860, 1725, 1674, 1512; exact mass calcd for $C_{12}H_{19}NO_3$ 225.1365, found 225.1364.

2-Amino-*N*-acetyl-4-phenyl-3-butynoic acid (14, R = C_6H_5): oil (15.60 mg, 60%, based on a 0.12-mmol scale); ^1H NMR (270 MHz, DMSO-d_6, vs DMSO) δ 1.90 (s, 3 H), 5.30 (d, *J* = 7.6 Hz, 1 H), 7.41 (s, 5 H), 8.89 (d, *J* = 7.6 Hz, 1 H); ^{13}C NMR (75.47 MHz, DMSO-d_6) δ 22.00, 44.29, 82.86, 84.37, 121.54, 128.57–131.40, 168.74, 168.99; mass spectrum (NH_3, CI) *m/e* 218 (M + H, 100), 174 (M + H − CO_2, 16), 85(100); IR (ν, cm^{-1}, $CHCl_3$) 3496, 3012, 2927, 2855, 1706, 1496; exact mass calcd for $C_{12}H_{11}NO_3$ 217.0739, found 217.0729.

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Registry No. **5**, 298-12-4; **6** (R = Cbz), 79002-45-2; **6** (R = Ac), 109125-47-5; **7a** (R = Cbz, R′ = Me), 127357-38-4; **7b** (R = Cbz, R′ = Me), 127357-37-3; **7** (R = Cbz, R′ = $CHPh_2$, Y = H), 127357-52-2; **7** (R = Ac, R′ = $CHPh_2$, Y = H), 127357-59-9; **8** (R = Cbz, R′ = Me, X = Cl), 127382-96-1; **8** (R = Cbz, R′ = Me, X = Br), 127382-97-2; **8** (R = Cbz, R′ = $CHPh_2$, X = Cl), 127382-98-3; **8** (R = Ac, R′ = $CHPh_2$, X = Cl), 127357-60-2; **9** (R = Cbz, R′ = Me, R^2 = $SiMe_3$), 127357-39-5; **9** (R = Cbz, R′ = R^2 = Me), 127357-40-8; **9** (R = Cbz, R′ = Me, R^2 = Pr), 127357-41-9; **9** (R = Cbz, R′ = Me, R^2 = Bu), 127357-42-0; **9** (R = Cbz, R′ = Me, R^2 = *n*-C_6H_{13}), 127357-43-1; **9** (R = Cbz, R′ = Me, R^2 = Ph), 127357-44-2; **9** (R = Cbz, R′ = Me, R^2 = $CH_2CH_2OSiMe_2(t\text{-Bu})$), 127357-45-3; **9** (R = Cbz, R′ = $CHPh_2$, R^2 = $SiMe_3$), 127382-99-4; **9** (R = Cbz, R′ = $CHPh_2$, R^2 = Me), 127357-53-3; **9** (R = Cbz, R′ = $CHPh_2$, R^2 = Pr), 127357-54-4; **9** (R = Cbz, R′ = $CHPh_2$, R^2 = Bu), 127357-55-5; **9** (R = Cbz, R′ = $CHPh_2$, R^2 = *n*-C_6H_{13}), 127357-56-6; **9** (R = Cbz, R′ = $CHPh_2$, R^2 = Ph), 127357-57-7; **9** (R = Cbz, R′ = $CHPh_2$, R^2 = $CH_2CH_2OSiMe_2(t\text{-Bu})$), 127357-58-8; **9** (R = Ac, R′ = $CHPh_2$, R^2 = $SiMe_3$), 127357-61-3; **9** (R = Ac, R′ = $CHPh_2$, R^2 = Me), 127357-62-4; **9** (R = Ac, R′ = $CHPh_2$, R^2 = Pr), 127357-63-5; **9** (R = Ac, R′ = $CHPh_2$, R^2 = Bu), 127357-64-6; **9** (R = Ac, R′ = $CHPh_2$, R^2 = *n*-C_6H_{13}), 127357-65-7; **9** (R = Ac, R′ = $CHPh_2$, R^2 = Ph), 127357-66-8; **9** (R = Ac, R′ = $CHPh_2$, R^2 = $CH_2CH_2OSiMe_2(t\text{-Bu})$), 127357-67-9; **9** (R = Ac, R′ = $CHPh_2$, R^2 = CH_2CH_2OH), 127357-68-0; **10** (R^2 = Me), 127357-47-5; **10** (R^2 = Pr), 127357-48-6; **11**, 127357-46-4; **12** (R^2 = Me), 127357-49-7; **12** (R^2 = Pr), 127357-50-0; **12** (R^2 = Ph), 127357-51-1; **13** (R^2 = $SiMe_3$), 127357-72-6; **13** (R^2 = Me), 127357-73-7; **13** (R^2 = Pr), 127357-74-8; **13** (R^2 = Bu), 127357-75-9; **13** (R^2 = *n*-C_6H_{13}), 127357-76-0; **13** (R^2 = Ph), 127383-00-0; **14** (R^2 = H), 127419-87-8; **14** (R = $SiMe_3$), 127357-77-1; **14** (R^2 = Me), 127357-78-2; **14** (R^2 = Pr), 127357-79-3; **14** (R^2 = Bu), 127357-80-6; **14** (R^2 = *n*-C_6H_13), 127357-81-7; **14** (R^2 = Ph), 127357-82-8; **15** (R = Cbz, R′ = Me), 127357-69-1; **15** (R = Cbz, R′ = $CHPh_2$), 127357-70-4; **15** (R = Ac, R′ = $CHPh_2$), 127357-71-5; $H_2NCOOCH_2Ph$, 621-84-1; OHCCOOMe, 922-68-9; $Bu_3SnC{\equiv}CSiMe_3$, 81353-38-0; $Bu_3SnC{\equiv}CMe$, 64099-82-7; $Bu_3SnC{\equiv}CPr$, 86633-17-2; $Bu_3SnC{\equiv}CBu$, 35864-20-1; $Bu_3SnC{\equiv}C(n\text{-}C_6H_{13})$, 113794-23-3; $Bu_3SnC{\equiv}CPh$, 3757-88-8; $Bu_3SnC{\equiv}CCH_2CH_2OSiMe_2(t\text{-Bu})$, 98155-22-7; $AcNH_2$, 60-35-5.