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A General Approach to Dehydro-Freidinger Lactams: Ex-Chiral Pool Synthesis and Spectroscopic Evaluation as Potential Reverse Turn Inducers†

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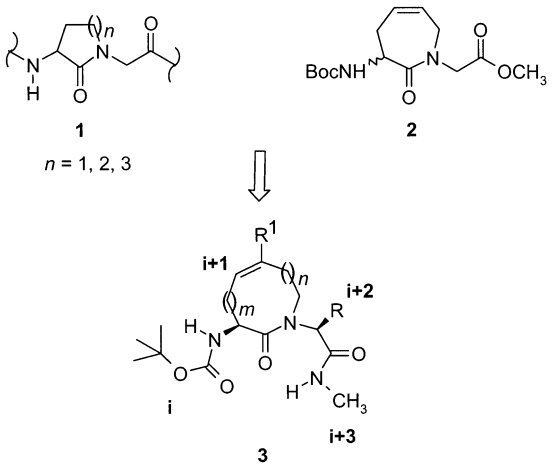
Starting from natural α-amino acids, a practical synthesis of the dehydro-Freidinger lactams **9a**−**h** based on the ring-closing olefin metathesis reaction was investigated. The presented examples comprise 6-, 7-, 8-, 9-, and 10-membered cyclic dipeptide mimics. Structural variations were demonstrated. We approached the metathesis precursors **8a**−**h** employing an N-alkylation/peptide-coupling strategy. Subsequent ring closure was promoted by the ruthenium-based catalyst **10a** or **10b**. The resulting tetraresidue **11d** was shown to undergo intramolecular hydrogen bonding based on NMR and FT-IR studies. Thus, the development of dehydro-Freidinger lactams as potential reverse turn inducers stabilizing an intramolecular $NH^{i+3}\cdots CO^{i}$ hydrogen-bond was demonstrated.

Introduction

The regulation of biological signal transduction involves interactions of peptide ligands with their receptors when the binding process of a highly flexible peptide ligand leads to an unfavorable loss of entropy due to the reduction of conformational freedom. Hence, the conformational restriction of the backbone of endogenic peptides offers a great challenge to increase the affinity and selectivity to a given receptor and provides indirect information about the bio-active conformation of the natural ligand. Extensive efforts have been made on the preparation of peptide mimics for the development of enzyme inhibitors and receptor modulators.[1] Reverse-turn templates have attracted particular attention since β- or γ-turn conformations are commonly found among bioactive peptides.[2] Freidinger developed γ-, δ-, and ϵ-lactams of type **1**[3] (Scheme 1) as molecular scaffolds that were assigned to stabilize type-βII turns.[4]

During the past decade, the ring-closing olefin metathesis reaction (RCM) emerged as an elegant manner of carbon−carbon-bond formation.[5] Initial results on the synthesis of rigidified peptides by RCM published by Grubbs and co-workers involved the α-amino ϵ-lactam **2**

SCHEME 1



employing an olefin linker to constrain the peptide backbone.[6] Recently, these findings were extended by Piscopio and co-workers describing lactam-bridged β-turn mimics based on a metathesis strategy.[7] The examples were limited to seven-membered heterocycles obtained as mixtures of diastereomers. On the other hand, the ability of cyclic templates to stabilize an intramolecular hydrogen bond strongly depends on both ring size and substitution pattern.[8] Complementary to our ongoing research concerning the design and conformational characterization of lactam-bridged β-amino acid analogues,[9]

† This paper is dedicated to the memory of Professor Henry Rapoport.

(1) (a) Giannis, A.; Kolter, T. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1244; *Angew. Chem.* **1993**, *105*, 1303. (b) Gante, J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 1699; *Angew. Chem.* **1994**, *106*, 1780. (c) Liskamp, R. M. J. *Recl. Trav. Chim. Pays-Bas* **1994**, *113*, 1.

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(4) Valle, G.; Crisma, M.; Toniolo, C.; Yu, K.-L.; Johnson, R. L. *J. Chem. Soc., Perkin Trans. 2* **1998**, 83.

(5) (a) Schuster, M.; Blechert, S. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 2036; *Angew. Chem* **1997**, *109*, 2124. (b) Fürstner, A. *Angew. Chem., Int. Ed.* **2000**, *39*, 3012; *Angew. Chem.* **2000**, *112*, 3140. (c) Armstrong, S. K. *J. Chem. Soc., Perkin Trans. 1* **1998**, 371.

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(7) Piscopio, A. D.; Miller, J. F.; Koch, K. *Tetrahedron* **1999**, *55*, 8189.

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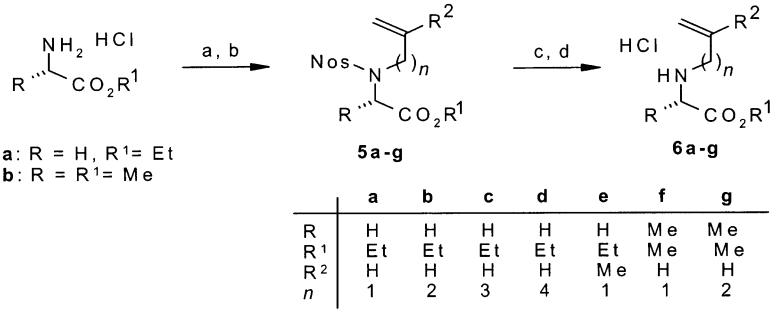
SCHEME 2[a]



4a: R = H, R^1 = Et
4b: R = R^1 = Me

5a-g **6a-g**

	a	b	c	d	e	f	g
R	H	H	H	H	H	Me	Me
R^1	Et	Et	Et	Et	Et	Me	Me
R^2	H	H	H	H	Me	H	H
n	1	2	3	4	1	1	2

[a] Reagents: (a) 4-nitrobenzenesulfonyl chloride, NEt_3, CH_2Cl_2, 0 °C (62−69%); (b) allyl bromide, K_2CO_3, DMF for **5a** (92%) and for **5f** (95%) 3-bromo-2-methyl-1-propane, K_2CO_3, DMF for **5e** (94%); DEAD, PPh_3, CH_2Cl_2, 3-buten-1-ol for **5b** (76%), 4-penten-1-ol for **5c** (66%), 5-hexen-1-ol for **5d** (55%); (c) PhSH, K_2CO_3, DMF (28−71%); (d) HCl, ether, 0 °C (99%).

we herein report a widely applicable and general protocol for the preparation of differently sized unsaturated lactams of type **3** (which we call dehydro-Freidinger lactams). The strategy is based on an ex-chiral pool approach involving N-alkylation, peptide-coupling, and ring-closing olefin metathesis as the key reaction step. Furthermore, the ability of the tetraresidue sequences to stabilize β-turn conformations is described.

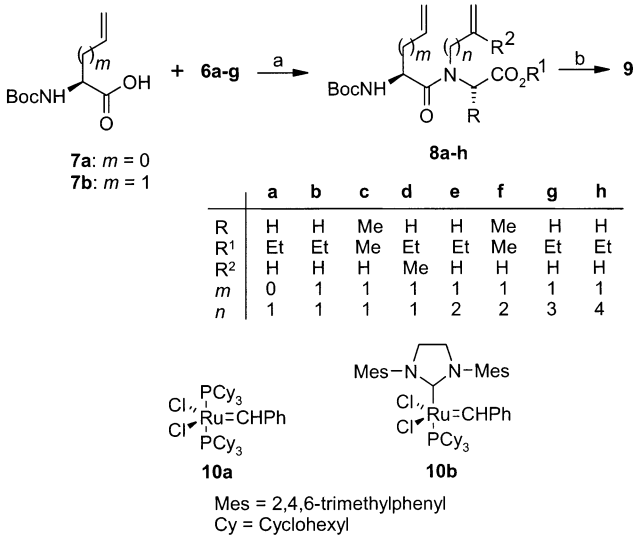
Results and Discussion

Metathesis Precursors. Based upon work published by Fukuyama[10] and Reichwein and Liskamp,[11] the protected building blocks **6a**−**g** (Scheme 2) were obtained from the glycine and alanine esters **4a** and **4b** by transformation into the corresponding sulfonamides and subsequent N-alkylation. Thiol-induced N-deprotection afforded the respective secondary amines that were isolated as their hydrochloride salts **6a**−**g**.[12]

The metathesis precursors **8b**−**h** were readily available employing DCC/HOBt-promoted peptide coupling of the secondary amines **6a**−**g** with the N-terminal-protected allyl glycine **7b**[13] (Scheme 3). The preparation of the diene **8a** starting from the vinyl glycine derivative **7a**[14] was achieved using the mixed anhydride method.

Metathesis Reaction and Synthesis of β-Turn Model Systems. Starting from the cyclization precursor **8a**, the ring-closing olefin metathesis reaction was elaborated. RCM-based transformations of vinyl glycine derivatives are described as problematic and strongly dependent on substitution patterns.[6,15] Employing 1,2-dichloroethane (DCE) at reflux temperature and a diene concentration of 5 mM, we obtained the aminopiperidinone **9a** in 53% yield after 48 h employing the ruthenium complex **10a**[16] (Table 1, entry 1). The metathesis of the *N*-allylglycine derived dienes **8b**−**d** also proceeded smoothly to furnish the corresponding seven-membered lactams **9b**−**d** (entry 2).

SCHEME 3[a]



7a: *m* = 0
7b: *m* = 1

8a-h

	a	b	c	d	e	f	g	h
R	H	H	Me	H	H	Me	H	H
R^1	Et	Et	Me	Et	Et	Me	Et	Et
R^2	H	H	H	Me	H	H	H	H
m	0	1	1	1	1	1	1	1
n	1	1	1	1	2	2	3	4

10a **10b**

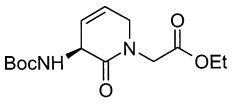
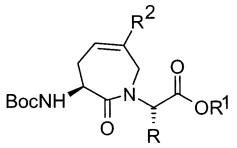
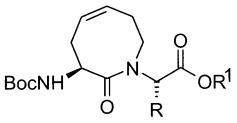
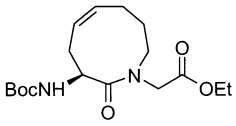
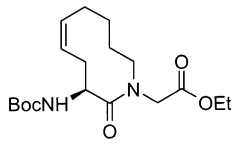
Mes = 2,4,6-trimethylphenyl
Cy = Cyclohexyl

[a] Reagents: (a) NMM/$ClCO_2$ ^{i}Bu, THF, −15 °C for **8a** (28%); DCC/HOBt, DIEA, CH_2Cl_2 for **8b**−**h** (19−83%); (b) **10a** (10 mol %) or **10b** (5 mol %), see Table 1.

Exchange of glycine by alanine in position $i + 2$ slightly lowered the yield. The highly active catalyst **10b**[16] was employed to promote the ring closure of the methyl-substituted diene **8d**, resulting in the formation of azepinone **9d** in 89% yield. For the synthesis of medium-sized rings being known as a remarkable challenge, the diene concentration for the RCM of **8e**−**g** was lowered to 2 mM, since previous results[8b] indicated this concentration to be sufficient to prevent possible oligomerization processes. As a consequence, the azocanone **9e** could be isolated in 70% yield (entry 3). No byproducts were detected. The alanine-derived diene **8f** led to the cycloolefin **9f** (60% yield). The synthetic potential of the strategy was demonstrated by the synthesis of the nine-membered azacycle **9g** which was isolated in 86% yield (entry 4). No side reactions were observed. According to the NMR spectra, only the cis isomer was formed. We attempted to enlarge the ring size of the lactam templates by the synthesis of a 10-membered ring compound. There are only a few examples in the literature that describe the

(10) Fukuyama, T.; Jow, C.-K.; Cheung, M. *Tetrahedron Lett.* **1995**, *36*, 6373.
(11) (a) Reichwein, J. F.; Liskamp, R. M. J. *Eur. J. Org. Chem.* **2000**, 2335. (b) Reichwein, J. F.; Versluis, C.; Liskamp, R. M. J. *J. Org. Chem.* **2000**, *65*, 6187. (c) Reichwein, J. F.; Liskamp, R. M. J. *Tetrahedron Lett.* **1998**, *39*, 1243.
(12) Hoffmann, T.; Gmeiner, P. *Synlett* **2002**, *6*, 1014.
(13) Prepared from commercially available (*S*)-allylglycine.
(14) (a) Afzali-Ardakani, A.; Rapoport, H. *J. Org. Chem.* **1980**, *45*, 4817. (b) Meffre, P.; Vo-Quang, L.; Vo-Quang, F. Le Goffic *Synth. Commun.* **1989**, *19*, 3457.
(15) Campagne, J.-M.; Ghosez, L. *Tetrahedron Lett.* **1998**, *39*, 6175.
(16) Trnka, T. M.; Grubbs, R. H. *Acc. Chem. Res.* **2001**, *34*, 18.

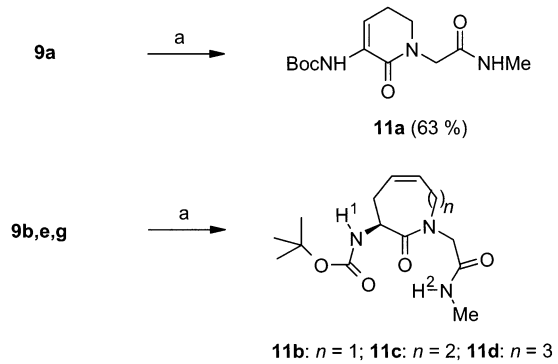
TABLE 1. Results of the Metathesis Reaction of the Dienes 8b−h (1,2-Dichloroethane, 81 °C)

entry	diene	cycloolefin	catalyst (yield)
1	8a	 **9a**	**10a** (53 %)
2	8b	 **9b**: R = R^2= H, R^1= Et	**10a** (68 %)
	8c	**9c**: R = R^1= Me, R^2= H	**10a** (42 %)
	8d	**9d**: R = H, R^1= Et, R^2= Me	**10b** (89 %)
3	8e	 **9e**: R = H, R^1= Et	**10a** (70 %)
	8f	**9f**: R = R^1= Me	**10a** (60 %)
4	8g	 **9g**	**10a** (86 %)
5	8h	 **9h**	**10b** (8 %)

synthesis of 10-membered rings by olefin metathesis.[17] When a high-dilution/slow addition strategy for the metathesis reaction of **8h** at a concentration of 0.5 mM was employed, the azacycle **9h** was isolated with 8% yield besides unreacted material and some polar byproducts. The NMR spectra of the chromatographic clean product **9h** displayed a minor impurity (likely the *E*-isomer, unambiguous assignment was impossible). Subsequent treatment of the representative lactams **9a**,**b**,**e**,**g** with methylamine furnished the model peptide mimics **11a**−**d** (Scheme 4). Due to an obvious deprotonation of the acidic α-proton of the vinyl glycine substructure, a migration of the double bond of the lactam **9a** occurred under the reaction conditions investigated when the α,*β*-unsaturated lactam **11a** was isolated. Nevertheless, the amides **11b**−**d** were obtained in 55−95 yield.

NMR Spectroscopy. To investigate the conformational preferences of the *β*-turn model systems, NMR studies were performed at 2 mM concentrations thus excluding intermolecular interactions.[18] Characteristic

SCHEME 4[a]



[a] Reagents: (a) $MeNH_2$, EtOH, rt (55-95%).

TABLE 2. ^{1}H NMR Data for Peptide Conjugates 8b−h (2 mM, $CDCl_3$)

compd	δNH^1 [a] (ppm)	δNH^2 [a] (ppm)	$\Delta\delta NH^2$ [b] (ppm) $CDCl_3 \rightarrow$ DMSO-d_6
11b	5.66	6.02	−1.69
11c	5.54	6.41	−1.18
11d	5.51	6.67	−0.86

[a] Designation as indicated in Scheme 4. [b] Difference of NH chemical shift.

NMR data are visualized in Table 2. The chemical shift value, the behavior upon addition of a competitive solvent, the temperature and concentration dependence of their chemical shift, and particularly NOE experiments are discussed as parameters reflecting the hydrogen-bonding states of amide protons.[19] To distinguish a hydrogen-bonded from a non-hydrogen-bonded population, all these parameters have to be considered.[20] The resonances for the amide protons NH^2 of all peptide analogues **11b**−**d** were observed at lower field when compared to the protons NH^1. Interestingly, the protons NH^2 resonate increasingly downfield when the ring size is enlarged (6.02 ppm for **11b**, 6.41 ppm for **11c**, 6.67 ppm for **11d**). Furthermore, when the hydrogen bond acceptor DMSO-d_6 was employed for NMR experiments, the signals for the protons NH^2 appeared at lower field. More important, the differences between the chemical shifts in $CDCl_3$ and the chemical shifts in DMSO-d_6 were decreased when the ring size is enlarged from **11b** to **11d** consistent with an increasing amount of intramolecular hydrogen bonding.[21] VT-NMR experiments displayed a strong chemical shift change of the NH^2 signal of the azonine-based peptide mimetic **11d** ($\delta/\Delta T$ −5.8 ppb/K) indicating a temperature-dependent equilibrium of hydrogen-bonded and nonbonded populations.

This deduction is independently reinforced by conformational analysis of the nine-membered azacycle **11d** based on NOE experiments (Figure 1).

(17) For examples, see: (a) Heinrich, M. R.; Steglich, W. *Tetrahedron Lett.* **2001**, *42*, 3287. (b) Fink, B. E.; Kym, P. R.; Katzenellenbogen, J. A. *J. Am. Chem. Soc.* **1998**, *120*, 4334. (c) Nevalainen, M.; Koskinen, A. M. P. *J. Org. Chem.* **2002**, *67*, 1554. (d) Fürstner, A.; Langemann, K. *Synlett* **1997**, *8*, 1010.

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(19) (a) Estiarte, M. A.; Rubiralta, M.; Diez, A. *J. Org. Chem.* **2000**, *65*, 6992. (b) Derrer, S.; Davies, J. E.; Holmes, A. B. *J. Chem. Soc., Perkin Trans. 1* **2000**, 2943. (c) Kessler, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 512; *Angew. Chem.* **1982**, *94*, 509.

(20) Belvisi, L.; Gennari, C.; Mielgo, A.; Potenza, D.; Scolastico, C. *Eur. J. Org. Chem.* **1999**, 389.

(21) Liang, G. B.; Rito, C. J.; Gellman, S. H. *J. Am. Chem. Soc.* **1992**, *114*, 4440.

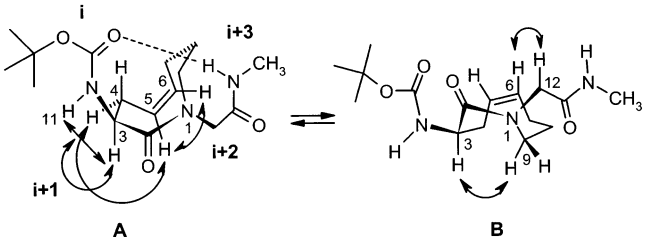

FIGURE 1. Diagnostic NOEs for the equilibrium between the conformations **A** and **B** for compound **11d**.

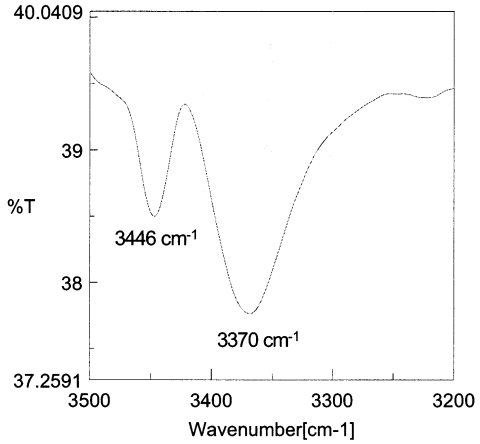

FIGURE 2. NH-stretch FT-IR data of **11d** (2 mM sample in $CHCl_3$) after subtraction of the spectrum of **9g**.

At room temperature, strong NOEs between H-6/H-5, H-5/H-4a, H-4a/H-3, and H-11/H-3 are indicative for the boatlike conformation **A** of the nine-membered lactam which enables the formation of an intramolecular hydrogen bond $NH^{i+3}\cdots CO^{i}$. The coexistence of conformation **B** was confirmed by diagnostic NOEs between H-3/H-9 and H-6/H-12 which are diminished by lowering the temperature (+5 °C) indicating an increase of **A**. This is consistent with the observed temperature coefficient (see above) indicating a substantially higher amount of intramolecular hydrogen bonding at low temperature.

FT-IR Spectroscopy. IR spectroscopy is believed as a more valuable tool for attributing hydrogen bonding to amide protons. Due to a much shorter time scale, a differentiation between N−H-stretching absorptions for hydrogen-bonded and non-hydrogen-bonded states is possible.

After subtraction of the spectrum of **9g** from the spectrum of **11d** and subsequent baseline correction, the NH region of the IR spectrum of **11d** at a 2 mM concentration in $CHCl_3$ displays only NH-stretch absorptions for NH^2 (Figure 2). The absorption band at 3446 cm^{-1} clearly results from a non-hydrogen-bonded amide NH^2.[22] The broad absorption at 3370 cm^{-1} represents the intramolecularly bonded portion of NH^2, which is in accordance to the results of the NMR-measurements. In summary, both NMR and FT-IR experiments strongly indicate the ability of the azoninone **11d** to stabilize intramolecularly hydrogen-bonded conformations.

(22) (a) Gellman, S. H.; Dado, G. P.; Liang, G. B.; Adams, R. B. *J. Am. Chem. Soc.* **1991**, *113*, 1164. (b) Gellman, S. H.; Desper, J. M.; Liang, G. B. *J. Am. Chem. Soc.* **1993**, *115*, 925.

Experimental Section

General Methods. All manipulations were carried out in dry solvents under an atmosphere of dry N_2. Commercially available reagents were used without further purification. DMF and 1,2-dichloroethane were purchased (0.005% water). Et_2O was freshly distilled from Na/benzophenone prior to use. Evaporations of solutions were done with a rotary evaporator. Flash chromatography was conducted on silica gel (230−400 mesh) using freshly distilled solvents. All ^1H NMR experiments were performed at 360 MHz and all ^{13}C NMR at 62.9 MHz with internal standard TMS (^1H NMR) and the solvent signal (^{13}C NMR), respectively; NOEs were obtained using difference spectroscopy with a pre-irradiation period of 4 s. Coupling constants are reported in hertz. Multiple irradiation points per resonance were used to suppress SPT. NOE samples were degassed by 5 freeze−pump−thaw cycles. MS were run by EI ionization (70 eV).

Nos-Gly-OEt (I). Obtained from **4a** (1.0 g, 7.16 mmol), Nos-Cl (1.75 g, 7.88 mmol), and NEt_3 (2.99 mL, 21.5 mmol) in CH_2Cl_2 (25 mL) as described for Nos-Gly-OMe in ref 11a. Purification by flash chromatography (ligroin-EtOAc, 1:1) yielded **I** (1.27 g, 62%) as a pale yellow solid: mp 114−115 °C; R_f 0.32 (ligroin−EtOAc, 1:1); IR (film) 3289, 1739, 1530 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (t, J = 7.1, 3H), 3.87 (d, J = 5.3, 2H), 4.12 (q, J = 7.1, 2H), 5.41 (m, 1H), 8.01−8.15 (m, 2H), 8.32−8.42 (m, 2H); ^{13}C NMR δ 13.9, 44.1, 62.2, 124.4, 128.5, 145.3, 150.2, 168.4; EIMS 288 (M^+). Anal. Calcd for $C_{10}H_{12}N_2O_6S$: C, 41.66; H, 4.20; N, 9.72; S, 11.12. Found: C, 41.55; H, 4.30; N, 9.58; S, 11.00.

Nos-(*S*)-Ala-OMe (II). Obtained from **4b** (1.0 g, 7.16 mmol), Nos-Cl (1.75 g, 7.88 mmol), and NEt_3 (2.99 mL, 21.5 mmol) in CH_2Cl_2 (25 mL) as described for Nos-Gly-OMe in ref 11a. Purification by flash chromatography (ligroin−EtOAc, 6:4) yielded **II** (1.42 g, 69%) as a pale yellow solid: mp 108−109 °C; R_f 0.33 (ligroin−EtOAc, 6:4); $[\alpha]^{20}_D$ +16.6 (c = 1.0, $CHCl_3$); IR (film) 3275, 1741, 1530 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.44 (d, J = 7.1, 3H), 3.60 (s, 3H), 4.12 (m, 1H), 5.49 (d, J = 8.2, 1H), 8.00−8.10 (m, 2H), 8.35−8.41 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 19.9, 51.6, 52.9, 124.3, 128.4, 145.9, 150.2, 172.1; EIMS 288 (M^+). Anal. Calcd for $C_{10}H_{12}N_2O_6S$: C, 41.66; H, 4.20; N, 9.72; S, 11.12. Found: C, 41.34; H, 4.24; N, 9.55; S, 10.38.

Nos-*N*-(allyl)-Gly-OEt (5a). Obtained from **I** (250 mg, 0.87 mmol), K_2CO_3 (360 mg, 2.61 mmol), and allyl bromide (151 μL, 1.74 mmol) in DMF (15 mL) as described for Nos-*N*-allyl-Phe-OMe in ref 11a. Purification by flash chromatography (ligroin−EtOAc, 8:2) furnished **5a** (263 mg, 92%) as a pale yellow solid: mp 69−71 °C; R_f 0.19 (ligroin−EtOAc, 8:2); IR (film) 1743, 1645, 1535 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (t, J = 7.3, 3H), 3.94 (d, J = 6.3, 2H), 4.09 (q, J = 7.2, 2H), 4.10 (s, 2H), 5.20−5.30 (m, 2H), 5.72 (dddd, J = 6.5, 16.8, 10.2, 6.5, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 46.9, 50.8, 61.5, 120.5, 124.1, 128.7, 131.5, 145.8, 150.0, 168.5; EIMS 255 ($M - CO_2Et^+$), M^+ not observed. Anal. Calcd for $C_{13}H_{16}N_2O_6S$: C, 47.56; H, 4.91; N, 8.53; S, 9.77. Found: C, 47.54; H, 4.93; N, 8.49; S, 9.60.

Nos-*N*-(3-butenyl)-Gly-OEt (5b). Obtained from **I** (100 mg, 0.35 mmol), PPh_3 (104 mg, 0.46 mmol), 3-buten-1-ol (39 μL, 0.46 mmol), and DEAD (209 μL, 40% in toluene, 0.46 mmol) in CH_2Cl_2 (20 mL) as described for Nos-*N*-(3-butenyl)-Gly-OMe in ref 11a. Purification by flash chromatography (ligroin−EtOAc, 8:2) yielded **5b** (104 mg, 87%) as a colorless solid: mp 51−53 °C; R_f 0.23 (ligroin−EtOAc, 8:2); IR (film) 1747, 1642, 1531 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (t, J = 7.1, 3H), 2.30−2.41 (m, 2H), 3.37 (t, J = 7.1, 2H), 4.09 (q, J = 7.1, 2H), 4.16 (s, 2H), 5.01−5.18 (m, 2H), 5.71 (m, 1H), 7.95−8.10 (m, 2H), 8.30−8.40 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.0, 32.4, 47.6, 47.9, 61.6, 117.8, 124.1, 128.7, 133.9, 145.7, 150.0, 168.5; EIMS 342 (M^+). Anal. Calcd for $C_{14}H_{18}N_2O_6S$: C, 49.11; H, 5.30; N, 8.18; S, 9.37. Found: C, 49.22; H, 5.37; N, 8.10; S, 8.97.

Nos-*N*-(4-pentenyl)-Gly-OEt (5c). Obtained from **I** (98 mg, 0.34 mmol), PPh_3 (100 mg, 0.44 mmol), 4-penten-1-ol (45 μL, 0.44 mmol), and DEAD (200 μL, 40% in toluene, 0.44 mmol)

in CH_2Cl_2 (20 mL) as described for **5b**. Purification by flash chromatography (ligroin−EtOAc, 8:2) yielded **5c** (80 mg, 66%) as a colorless solid: mp 73−75 °C; R_f 0.25 (ligroin−EtOAc, 8:2); IR (film) 1748, 1641, 1530 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.22 (t, J = 7.1, 3H), 1.65−1.78 (m, 2H), 2.05−2.17 (m, 2H), 3.29 (t, J = 7.5, 2H), 4.09 (q, J = 7.1, 2H), 4.14, (s, 2H), 4.95−5.10 (m, 2H), 5.76 (dddd, J = 6.7, 17.0, 10.3, 6.7, 1H), 8.00−8.10 (m, 2H), 8.30−8.41 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1, 26.9, 30.5, 47.6, 47.8, 61.6, 115.7, 124.1, 128.7, 136.9, 145.7, 150.0, 168.5; EIMS 356 (M^+). Anal. Calcd for $C_{15}H_{20}N_2O_6S$: C, 50.55; H, 5.66; N, 7.86; S, 8.99. Found: C, 50.54; H, 5.71; N, 7.81; S, 8.77.

Nos-*N*-(5-hexenyl)-Gly-OEt (5d). Obtained from **I** (150 mg, 0.52 mmol), PPh_3 (154 mg, 0.68 mmol), 5-hexen-1-ol (78 μL, 0.68 mmol), and DEAD (124 μL, 0.68 mmol) in CH_2Cl_2 (10 mL) at 0 °C as described for **5b**. Purification by flash chromatography (ligroin−EtOAc, 8:2) yielded **5d** (106 mg, 55%) as a pale yellow solid: mp 47−49 °C; R_f 0.30 (ligroin−EtOAc, 8:2); IR (film) 1749, 1639, 1531 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14 (t, J = 7.1, 3H), 1.25−1.40 (m, 2H,), 1.45−1.55 (m, 2H), 1.90−2.05 (m, 2H), 3.21 (t, J = 7.5, 2H), 4.01 (q, J = 7.1, 2H), 4.10 (s, 2H), 4.85−5.00 (m, 2H), 5.68 (dddd, J = 10.5, 13.2, 10.5, 6.5, 1H), 7.90−8.00 (m, 2H), 8.28−8.35 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.0, 25.6, 27.0, 33.1, 47.5, 48.0, 61.6, 115.1, 124.1, 128.6, 137.9, 145.7, 149.9, 168.5; EIMS 370 (M^+). Anal. Calcd for $C_{16}H_{22}N_2O_6S$: C, 51.88; H, 5.99; N, 7.56; S, 8.66. Found: C, 51.71; H, 6.10; N, 7.50; S, 8.47.

Nos-*N*-(2-methyl-2-propenyl)-Gly-OEt (5e). Obtained from **I** (2.0 g, 6.94 mmol), K_2CO_3 (1.92 g, 13.9 mmol), and 3-bromo-2-methyl-2-propene (1.40 mL, 13.9 mmol) in DMF (20 mL) as described for **6a**. Purification by flash chromatography (ligroin−EtOAc, 8:2) yielded **5e** (2.20 g, 94%) as a light yellow solid: mp 44−46 °C; R_f 0.29 (ligroin−EtOAc, 8:2); IR (film) 1743, 1662, 1535 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.19 (t, J = 7.1, 3H), 1.73 (s, 3H), 3.89 (s, 2H), 4.00−4.15 (m 2H), 4.05 (q, J = 7.1, 2H), 4.81−5.05 (m, 2H), 8.00−8.10 (m, 2H), 8.30−8.40 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.0, 19.6, 46.5, 53.9, 61.4, 116.3, 124.1, 128.6, 138.8, 145.7, 149.9, 168.3; EIMS 342 (M^+). Anal. Calcd for $C_{14}H_{18}N_2O_6S$: C, 49.11; H, 5.30; N, 8.18; S, 9.37. Found: C, 49.31; H, 5.30; N, 8.21; S, 9.34.

Nos-*N*-(allyl)-(*S*)-Ala-OMe (5f). Obtained from **II** (300 mg, 1.04 mmol), K_2CO_3 (287 mg, 2.08 mmol), and allyl bromide (180 μL, 2.08 mmol) in DMF (25 mL) as described for **5a**. Purification by flash chromatography (ligroin−EtOAc, 8:2) yielded **5f** (323 mg, 95%) as a pale yellow solid: mp 62−64 °C; R_f 0.20 (ligroin−EtOAc, 8:2); $[\alpha]^{22}_D$ −50.0 (c = 0.50, $CHCl_3$); IR (film) 1743, 1641, 1531 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.49 (d, J = 7.2, 3H), 3.58 (s, 3H), 3.75−4.01 (m, 2H), 4.71 (q, J = 7.2, 1H), 5.15−5.29 (m, 2H), 5.78 (m, 1H).; ^{13}C NMR ($CDCl_3$) δ 16.9, 48.7, 52.3, 55.6, 118.5, 124.1, 128.7, 134.2, 145.9, 149.9, 171.3; EIMS 328 (M^+). Anal. Calcd for $C_{13}H_{16}N_2O_6S$: C, 47.55; H, 4.91; N, 8.53; S, 9.77. Found: C, 47.87; H, 4.94; N, 8.49; S, 9.38.

Nos-*N*-(3-butenyl)-(*S*)-Ala-OMe (5g). Obtained from **II** (400 mg, 1.39 mmol), PPh_3 (410 mg, 1.81 mmol), 3-buten-1-ol (156 μL, 1.81 mmol), and DEAD (823 μL, 40% in toluene, 1.81 mmol) in CH_2Cl_2 (20 mL) as described for **5b**. Purification by flash chromatography (ligroin−EtOAc, 8:2) yielded **5g** (362 mg, 76%) as a colorless oil: R_f 0.21 (ligroin−EtOAc, 8:2); $[\alpha]^{23}_D$ −56.0 (c = 0.98, $CHCl_3$); IR (film) 1743, 1643, 1531 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.51 (d, J = 7.5, 3H), 2.25−2.40 (m, 1H), 2.36−2.60 (m, 1H), 3.15 (ddd, J = 15.3, 10.4, 5.4, 1H), 3.36 (ddd, J = 15.4, 10.5, 5.1, 1H), 3.55 (s, 3H), 4.69 (q, J = 7.5, 1H), 5.00−5.19 (m, 2H), 5.65−5.80 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 17.1, 35.4, 45.8, 52.3, 55.8, 117.4, 124.1, 128.6, 134.1, 145.6, 149.9, 171.3; EIMS 342 (M^+). Anal. Calcd for $C_{14}H_{18}N_2O_6S$: C, 49.11; H, 5.30; N, 8.18; S, 9.37. Found: C, 49.06; H, 5.42; N, 8.01; S, 9.15.

***N*-(Allyl)-Gly-OEt (6a).** Obtained from **5a** (150 mg, 0.46 mmol), K_2CO_3 (191 mg, 1.38 mmol), and PhSH (56 μL, 0.55 mmol) in DMF (6 mL) as described for *N*-allyl-Ph-OMe in ref 11a. Purification by flash chromatography (ligroin−EtOAc, 1:1) yielded **6a** (98 mg, 67%) as a colorless oil. Analytical data are in agreement with data previously published.[11a]

***N*-(3-Butenyl)-Gly-OEt·HCl (6b).** Obtained from **5b** (463 mg, 1.35 mmol), K_2CO_3 (560 mg, 4.05 mmol), and PhSH (166 μL, 1.62 mmol) in DMF (7 mL) as described for **6a**. Purification by flash chromatography (ligroin−EtOAc, 3:7) yielded a yellow oil. To a solution of this crude product in ether (3 mL) was added a saturated solution of HCl in ether (2 mL) at 0 °C. The resulting precipitate was filtered and dried (P_4O_{10}) to furnish **6b** (164 mg, 63%). **6b**: colorless needles; mp 176−179 °C; IR (KBr) 3487, 1753, 1643 cm^{-1}; ^1H NMR (CH_3OH-d_4) δ 1.31 (t, J = 7.2, 3H), 2.45−2.55 (m, 2H), 3.15 (t, J = 7.6, 2H,), 3.98 (s, 2H), 4.31 (q, J = 7.2, 2H), 5.20 (ddd, J = 10.4, 2.4, 1.2, 1H), 5.25 (ddd, J = 17.2, 3.1, 1.6, 1H), 5.82 (dddd, J = 6.8, 17.2, 10.4, 6.8, 1H); ^{13}C NMR (CH_3OH-d_4) δ 14.3, 31.3, 47.9, 48.3, 63.6, 119.3, 133.8, 167.7. Anal. Calcd for $C_8H_{16}NO_2Cl$: C, 49.61; H, 8.33; N, 7.23. Found: C, 49.74; H, 8.51; N, 7.10.

***N*-(4-Pentenyl)-Gly-OEt·HCl (6c).** Obtained from **5c** (1.13 g, 3.17 mmol), K_2CO_3 (1.10 g, 7.93 mmol), and PhSH (419 μL, 3.80 mmol) in DMF (7 mL) as described for **6b**. Yield: 184 mg (28%). **6c**: colorless solid; mp 186−188 °C; IR (KBr) 3448, 1747, 1641 cm^{-1}; ^1H NMR (CH_3OH-d_4) δ 1.31 (t, J = 7.2, 3H), 1.78−1.85 (m, 2H), 2.12−2.22 (m, 2H), 3.05−3.10 (m 2H), 3.97 (s, 2H), 4.31 (q, J = 7.1, 2H), 5.05 (ddd, J = 10.3, 2.9, 1.2, 1H), 5.11 (ddd, J = 17.1, 3.4, 1.7, 1H), 5.83 (dddd, J = 6.7, 17.1, 10.3, 6.7, 1H); ^{13}C NMR (CH_3OH-d_4) δ 14.3, 26.2, 31.5, 63.6, 74.3, 83.7, 116.7, 137.7, 167.8. Anal. Calcd for $C_9H_{18}NO_2Cl$: C, 52.05; H, 8.74; N, 6.74. Found: C, 51.62; H, 8.78; N, 6.64.

***N*-(5-Hexenyl)-Gly-OEt·HCl (6d).** Obtained from **5d** (930 mg, 2.51 mmol), K_2CO_3 (1.04 g, 7.53 mmol), and PhSH (309 μL, 3.01 mmol) in DMF (10 mL) as described for **6b**. Yield: 206 mg (37%). **6d**: colorless needles; mp 181−183 °C; IR (KBr) 3440, 1752, 1641 cm^{-1}; ^1H NMR (CH_3OH-d_4) δ 1.32 (t, J = 7.1, 3H), 1.45−1.55 (m, 2H), 1.69−1.79 (m, 2H), 2.07−2.20 (m, 2H), 3.00−3.10 (m, 2H), 4.30 (q, J = 7.1, 2H), 4.99 (dddd, J = 10.2, 1.1, 2.2, 1.1, 1H), 5.05 (ddd, J = 17.2, 3.6, 1.5, 1H), 5.82 (dddd, J = 6.7, 17.2, 10.2, 6.7, 1H); ^{13}C NMR (CH_3OH-d_4) δ 14.3, 24.2, 26.5, 26.8, 34.1, 63.6, 83.6, 115.8, 138.9, 167.7. Anal. Calcd for $C_{10}H_{20}NO_2Cl$: C, 54.17; H, 9.09; N, 6.32. Found: C, 53.88; H, 8.99; N, 6.27.

***N*-(2-Methyl-2-propenyl)-Gly-OEt·HCl (6e).** Obtained from **5e** (2.38 g, 6.94 mmol), K_2CO_3 (2.87 g, 20.8 mmol), and PhSH (852 μL, 8.30 mmol) in DMF (15 mL) as described for **6b**. Yield: 578 mg (43%). **6e**: pale yellow needles; mp 64−66 °C; IR (KBr) 3484, 1746, 1650 cm^{-1}; ^1H NMR (CH_3OH-d_4) δ 1.32 (t, J = 7.1, 3H), 1.45−1.55 (m, 2H), 1.69−1.79 (m, 2H), 2.07−2.20 (m, 2H), 3.00−3.10 (m, 2H), 4.30 (q, J = 7.1, 2H), 4.99 (dddd, J = 10.2, 1.1, 2.2, 1.1, 1H), 5.05 (ddd, J = 17.2, 3.6, 1.5, 1H), 5.82 (dddd, J = 6.7, 17.2, 10.2, 6.7, 1H); ^{13}C NMR (CH_3OH-d_4) δ 14.3, 24.2, 26.5, 26.8, 34.1, 63.6, 83.6, 115.8, 138.9, 167.7. Anal. Calcd for $C_8H_{16}NO_2Cl$: C, 49.61; H, 8.33; N, 7.23. Found: C, 49.56; H, 8.24; N, 7.02.

***N*-(Allyl)-(*S*)-Ala-OMe·HCl (6f).** Obtained from **5f** (3.60 g, 10.9 mmol), K_2CO_3 (4.54 g, 3.63 mmol), and PhSH (1.35 mL, 13.1 mmol) in DMF (20 mL) as described for **6b**. Yield: 935 mg (60%). **6f**: colorless needles; mp 144−146 °C; $[\alpha]^{23}_D$ −1.3 (c = 0.45, CH_3OH); IR (KBr) 3489, 1752, 1648 cm^{-1}; ^1H NMR (CH_3OH-d_4) δ 1.58 (d, J = 7.1, 3H), 3.68−3.75 (m, 2H), 3.86 (s, 3H), 4.13 (q, J = 7.1, 1H), 5.52 (ddd, J = 10.3, 1.8, 0.9, 1H), 5.57 (ddd, J = 17.2, 2.5, 1.3, 1H), 5.95 (dddd, J = 6.9, 17.2, 10.3, 6.9, 1H); ^{13}C NMR (CH_3OH-d_4) δ 14.9, 49.2, 53.9, 55.8, 124.6, 128.9, 170.9. Anal. Calcd for $C_7H_{14}NO_2Cl$: C, 46.80; H, 7.86; N, 7.80. Found: C, 46.54; H, 7.99; N, 7.79.

***N*-(3-Butenyl)-(*S*)-Ala-OMe·HCl (6g).** Obtained from **5g** (1.74 g, 5.08 mmol), K_2CO_3 (2.11 g, 15.2 mmol), and PhSH (626 μL, 6.09 mmol) in DMF (10 mL) as described for **6b**. Yield: 696 mg (71%). **6g**: colorless needles; mp 139−141 °C; $[\alpha]^{21}_D$ +4.8° (c = 0.17, CH_3OH); IR (KBr) 3477, 1747, 1644 cm^{-1}; ^1H NMR (CH_3OH-d_4) δ 1.58 (d, J = 7.2, 3H), 2.45−2.56 (m, 2H), 3.10−3.20 (m, 2H), 3.86 (s, 3H), 4.15 (q, J = 7.2, 1H), 5.19 (ddd, J = 17.1, 3.11, 1.5, 1H), 5.25 (ddd, J = 10.2, 2.8, 1.3, 1H), 5.83 (dddd, J = 6.8, 17.1, 10.2, 6.8, 1H); ^{13}C NMR (CH_3-

OH-d_4) δ 14.9, 31.5, 46.4, 53.9, 56.6, 119.2, 133.8, 170.9. Anal. Calcd for $C_8H_{15}NO_2Cl$: C, 49.61; H, 8.33; N, 7.23. Found: C, 49.59; H, 7.99; N, 7.38.

***N*-(Allyl)-N-[(2*S*)-*tert*-butoxycarbonylamino-3-butenoyl]-glycine Ethyl Ester (8a).** A solution of **7a** (50 mg, 0.25 mmol), *N*-methylmorpholine (27 μL, 0.25 mmol), and $ClCO_2{}^iBu$ (32 μL, 0.25 mmol) in THF at −15 °C was stirred for 10 min, and then a solution of **6a** (36 mg, 0.25 mmol) in THF (2 mL) was added. After slow warming to room temperature, the mixture was stirred overnight. Evaporation and flash chromatography (ligroin−EtOAc, 8:2) of the resulting residue yielded **8a** (23 mg, 28%) as a colorless oil. **8a**: R_f 0.11 (ligroin−EtOAc, 8:2); $[\alpha]^{23}_D$ +2.1 (c = 1.01, $CHCl_3$); IR (film) 3339, 1789, 1682, 1619 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.1, 3H), 1.44 (s, 9H), 3.80 (d, J = 17.0, 1H), 4.05−4.15 (m, 2H), 4.19 (q, J = 7.1, 2H), 4.33 (d, J = 17.0, 1H), 5.05−5.15 (m, 1H), 5.20−5.45 (m, 4H), 5.58 (br d, J = 7.8, 1H), 5.70−5.90 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1, 19.0, 27.8, 47.0, 51.0, 61.3, 79.8, 118.5, 118.6, 131.9, 133.3, 154.9, 168.9, 170.5; EIMS 326 (M^+). Anal. Calcd for $C_{16}H_{26}N_2O_5$: C, 58.88; H, 8.03; N, 8.58. Found: C, 58.68; H, 7.94; N, 8.50.

***N*-(Allyl)-*N*-[(2*S*)-*tert*-butoxycarbonylamino-4-pentenoyl]glycine Ethyl Ester (8b).** At 0 °C, DCC (47 mg, 0.23 mmol) and HOBt (31 mg, 0.23 mmol) were added to a solution of **7b** (50 mg, 0.23 mmol) in CH_2Cl_2 (20 mL). After 1 h of stirring, a solution of **6a** (33 mg, 0.23 mmol) in CH_2Cl_2 (2 mL) was added. Warming to room temperature and stirring overnight was followed by evaporation and subsequent flash chromatography (ligroin−EtOAc, 8:2) of the resulting residue yielding **8b** (66 mg, 84%) as a colorless solid. **8b**: mp 74−76 °C; R_f 0.13 (ligroin−EtOAc, 8:2); $[\alpha]^{23}_D$ +4.2 (c = 0.21, $CHCl_3$); IR (film) 3325, 1747, 1704, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.1, 3H), 1.43 (s, 9H), 2.32−2.45 (m, 1H), 2.49−2.60 (m, 1H), 3.83 (d, J = 17.4, 1H), 3.99−4.10 (m, 2H), 4.18 (q, J = 7.1, 2H), 4.26 (d, J = 17.0, 1H), 4.65−4.75 (m, 1H), 5.09−5.20 (m, 3H), 5.25−5.32 (m, 2H), 5.60−5.90 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1, 28.3, 37.7, 47.1, 49.8, 51.3, 61.2, 83.3, 118.2, 118.7, 132.3, 132.7, 155.1, 168.9, 172.3; EIMS 340 (M^+). Anal. Calcd for $C_{17}H_{28}N_2O_5$: C, 59.98; H, 8.29; N, 8.23. Found: C, 60.29; H, 8.43; N, 8.37.

(*S*)-*N*-(Allyl)-*N*-[(2*S*)-*tert*-butoxycarbonylamino-4-pentenoyl]alanine Methyl Ester (8c). Obtained from DCC (95 mg, 0.46 mmol), HOBt (62 mg, 0.46 mmol), and **7b** (100 mg, 0.46 mmol) in CH_2Cl_2 (15 mL) as described for **8b**. A solution of **6f** (83 mg, 0.46 mmol) and DIEA (88 μL, 0.51 mmol) in CH_2Cl_2 (2 mL) was added. Stirring overnight at room temperature and workup as mentioned for **8b** yielded **8c** (67 mg, 43%) as a colorless oil. **8c**: R_f 0.14 (ligroin−EtOAc, 8:2); $[\alpha]^{23}_D$ −46.3 (c = 0.43, $CHCl_3$); IR (film) 3429, 1747, 1712, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.41 (d, J = 7.4, 3H), 1.42 (s, 9H), 2.30−2.39 (m, 1H), 2.45−2.56 (m, 1H), 3.70 (s, 3H), 3.90−4.15 (m, 2H), 4.55−4.61 (m, 1H), 4.74 (q, J = 7.4, 1H), 5.08−5.19 (m, 2H), 5.22−5.30 (m, 3H), 5.76 (dddd, J = 7.1, 17.1, 9.9, 7.1, 1H), 5.90 (dddd, J = 5.4, 17.0, 10.6, 5.3, 1H); ^{13}C NMR ($CDCl_3$) δ 14.7, 28.3, 37.9, 48.9, 50.3, 52.2, 53.7, 54.9, 117.9, 118.7, 132.7, 133.7, 155.1, 172.0, 172.3; EIMS 340 (M^+). Anal. Calcd for $C_{17}H_{28}N_2O_5$: C, 59.98; H, 8.29; N, 8.23. Found: C, 60.17; H, 8.28; N, 8.26.

***N*-(2-Methyl-2-propenyl)-*N*-[(2*S*)-*tert*-butoxycarbonylamino-4-pentenoyl]glycine Ethyl Ester (8d).** Obtained from a solution of DCC (47 mg, 0.23 mmol), HOBt (31 mg, 0.23 mmol) and **7b** (50 mg, 0.23 mmol) in CH_2Cl_2 (10 mL) and a solution of **6e** (45 mg, 0.23 mmol) and DIEA (44 μL, 0.25 mmol) in CH_2Cl_2 (2 mL) as described for **8c**. **8d** (66 mg, 81%): colorless oil; R_f 0.15 (ligroin−EtOAc, 8:2); $[\alpha]^{21}_D$ −20.0 (c = 0.14, $CHCl_3$); IR (film) 3318, 1747, 1708, 1651, 1643 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.1, 3H), 1.42 (s, 9H), 1.73 (s, 3H), 2.37 (ddd, J = 6.9, 14.0, 6.9, 1H), 2.52 (ddd, J = 6.5, 14.0, 6.5, 1H), 3.82 (d, J = 17.0, 1H), 3.97 (d, J = 10.7, 1H), 4.06 (d, J = 10.7, 1H), 4.18 (q, J = 7.1 Hz, 2H), 4.60−4.75 (m, 1H), 4.75−5.00 (m, 2H), 5.05−5.20 (m, 2H), 5.13 (d, J = 17.0, 1H), 5.27 (d, J = 8.2, 1H), 5.78 (dddd, J = 7.2, 17.1, 10.0, 7.2, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 19.9, 28.3, 37.8, 48.2, 49.9, 61.2, 61.6, 79.6, 113.3, 118.6, 132.8, 139.5, 155.1, 168.9, 172.6; EIMS 354 (M^+). Anal. Calcd for $C_{18}H_{30}N_2O_5$: C, 60.99; H, 8.53; N, 7.90. Found: C, 60.92; H, 8.68; N, 7.98.

***N*-(3-Butenyl)-*N*-[(2*S*)-*tert*-butoxycarbonylamino-4-pentenoyl]glycine Ethyl Ester (8e).** Obtained from a solution of DCC (124 mg, 0.60 mmol), HOBt (81 mg, 0.60 mmol), and **7b** (129 mg, 0.60 mmol) in CH_2Cl_2 (20 mL) and a solution of **6b** (116 mg, 0.60 mmol) and DIEA (115 μL, 0.66 mmol) in CH_2Cl_2 (2 mL) as described for **8c**. **8e** (168 mg, 79%): colorless oil; R_f 0.16 (ligroin−EtOAc, 8:2); $[\alpha]^{20}_D$ −6.3 (c = 0.48, $CHCl_3$); IR (film) 3324, 1747, 1708, 1654 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.3, 3H), 1.43 (s, 9H), 2.25−2.40 (m, 3H), 2.44−2.59 (m, 1H), 3.35 3.42 (m 1H), 3.50−3.62 (m, 1H), 3.77 (d, J = 17.4, 1H), 4.19 (q, J = 7.3, 2H), 4.34 (d, J = 17.0, 1H), 4.65−4.75 (m, 1H), 5.02−5.20 (m, 5H), 5.70−5.85 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1, 28.3, 33.1, 37.9, 47.9, 48.4, 49.7, 61.2, 61.8, 118.1, 118.4, 132.9, 133.8, 155.1, 168.9, 172.3; EIMS 354 (M^+). Anal. Calcd for $C_{18}H_{30}N_2O_5$: C, 60.99; H, 8.53; N, 7.90. Found: C, 61.00; H, 8.20; N, 8.11.

(*S*)-*N*-(3-Butenyl)-*N*-[(2*S*)-*tert*-butoxycarbonylamino-4-pentenoyl]alanine Methyl Ester (8f). Obtained from a solution of DCC (142 mg, 0.69 mmol), HOBt (93 mg, 0.69 mmol), and **7b** (150 mg, 0.69 mmol) in CH_2Cl_2 (40 mL) and a solution of **6g** (134 mg, 0.69 mmol) and DIEA (120 μL, 0.69 mmol) in CH_2Cl_2 (2 mL) as described for **8c**. Yield: (46 mg, 19%). **8f**: colorless oil; R_f 0.19 (ligroin−EtOAc, 8:2); $[\alpha]^{20}_D$ −37.7 (c = 0.13, $CHCl_3$); IR (film) 3324, 1743, 1710, 1645 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.43 (s, 9H), 1.46 (d, J = 7.1, 3H), 2.30−2.41 (m, 2H), 2.43−2.56 (m, 2H), 3.30 (ddd, J = 15.3, 10.0, 5.4, 1H), 3.50 (ddd, J = 15.3, 10.1, 6.0, 1H), 3.70 (s, 3H), 4.48 (q, J = 7.1, 1H), 4.64 (ddd, J = 13.9, 8.0, 6.8, 1H), 5.08−5.19 (m, 4H), 5.24 (br d, J = 8.5, 1H), 5.66−5.83 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.8, 19.1, 28.4, 38.4, 47.7, 49.2, 52.2, 53.6, 79.0, 116.2, 117.3, 134.2, 136.2, 155.5, 171.7, 176.1; EIMS 354 (M^+). Anal. Calcd for $C_{18}H_{30}N_2O_5$: C, 60.99; H, 8.53; N, 7.90. Found: C, 61.13; H, 8.65; N, 7.72.

***N*-(4-Pentenyl)-*N*-[(2*S*)-*tert*-butoxycarbonylamino-4-pentenoyl]glycine Ethyl Ester (8g).** Obtained from a solution of DCC (47 mg, 0.23 mmol), HOBt (31 mg, 0.23 mmol), and **7b** (50 mg, 0.23 mmol) in CH_2Cl_2 (10 mL) and a solution of **6c** (48 mg, 0.23 mmol) and DIEA (44 μL, 0.25 mmol) in CH_2Cl_2 (2 mL) as described for **8c**. Yield: (56 mg, 66%). **8g**: colorless oil; R_f 0.22 (ligroin−EtOAc, 8:2); $[\alpha]^{20}_D$ +5.5 (c = 0.15, $CHCl_3$); IR (film) 3421, 1747, 1708, 1650 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.1, 3H), 1.43 (s, 9H), 1.59−1.80 (m, 2H), 2.05−2.17 (m, 2H), 2.31−2.40 (m, 1H), 2.45−2.58 (m, 2H), 3.26−3.50 (m, 2H), 3.77 (d, J = 17.0, 1H), 4.19 (q, J = 7.1, 2H), 4.32 (d, J = 17.0, 1H), 4.65−4.75 (m, 1H), 4.96−5.20 (m, 4H), 5.26 (d, J = 8.5, 1H), 5.79 (dddd, J = 13.5, 17.1, 7.0, 3.5, 1H), 5.80 (dddd, J = 10.3, 17.1, 10.3, 3.8, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 27.7, 28.3, 30.6, 37.9, 47.8, 48.4, 49.7, 61.2, 79.6, 115.9, 118.6, 132.8, 136.9, 155.1, 168.9, 172.3; EIMS 368 (M^+). Anal. Calcd for $C_{19}H_{32}N_2O_5$: C, 61.93; H, 8.75; N, 7.60. Found: C, 62.06; H, 8.87; N, 7.61.

***N*-(4-Hexenyl)-*N*-[(2*S*)-*tert*-butoxycarbonylamino-4-pentenoyl]glycine Ethyl Ester (8h).** Obtained from a solution of DCC (47 mg, 0.23 mmol), HOBt (31 mg, 0.23 mmol), and **7b** (50 mg, 0.23 mmol) in CH_2Cl_2 (10 mL) and a solution of **6d** (51 mg, 0.23 mmol) and DIEA (44 μL, 0.25 mmol) in CH_2Cl_2 (2 mL) as described for **8c**. Yield: (73 mg, 83%). **8h**: colorless oil; R_f 0.20 (ligroin−EtOAc, 8:2); $[\alpha]^{22}_D$ −12.2 (c = 0.09, $CHCl_3$); IR (film) 3318, 1749, 1708, 1648 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.27 (t, J = 7.1, 3H), 1.43 (s, 9H), 1.37−1.70 (m, 4H), 2.01−2.12 (m, 2H), 2.30−2.42 (m, 1H), 2.45−2.60 (m, 1H), 3.28−3.50 (m, 2H), 3.77 (d, J = 17.0, 1H), 4.18 (q, J = 7.1, 2H), 4.32 (d, J = 17.0, 1H), 4.65−4.72 (m, 1H), 4.90−5.20 (m, 4H), 5.26 (d, J = 8.5, 1H), 5.70−5.85 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.1, 25.8, 26.5, 28.2, 37.5, 37.9, 47.7, 49.7, 61.1, 79.5, 115.1, 118.5, 132.8, 137.9, 155.1, 168.9, 172.1; EIMS 382 (M^+). Anal. Calcd for $C_{20}H_{34}N_2O_5$: C, 62.80; H, 8.96; N, 7.32. Found: C, 62.61; H, 8.85; N, 7.31.

(*S*)-(3-*tert*-Butoxycarbonylamino-2-oxo-3,6-dihydro-2*H*-pyridin-1-yl)acetic Acid Ethyl Ester (9a). The catalyst **10a** (6 mg, 0.007 mmol) was added to a solution of **8a** (23 mg, 0.07 mmol) in DCE (35 mL) employing flame-dried glassware. The mixture was heated to reflux until TLC indicated completion of the reaction. After cooling, the solution was evaporated and the resulting residue purified by flash chromatography (ligroin−ETOAc, 1:1) to yield **9a** (11 mg, 53%). **9a**: colorless oil; R_f 0.15 (ligroin−EtOAc, 1:1); $[\alpha]^{24}_D$ −12.4 (c = 0.21, $CHCl_3$); IR (film) 3336, 1743, 1712, 1658 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (t, J = 7.1, 3H), 1.46 (s, 9H), 3.85−3.95 (m, 1H), 4.05−4.15 (m, 2H), 4.20 q, J = 7.1, 2H), 4.19−4.25 (m, 1H), 4.65−4.72 (m, 1H), 5.20−5.30 (br s, 1H), 5.81−5.90 (m, 1H), 5.95−6.10 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 28.3, 48.4, 49.6, 61.4, 77.2, 79.9, 127.2, 121.5, 155.9, 167.5, 168.5; EIMS 298 (M^+). Anal. Calcd for $C_{14}H_{22}N_2O_5$: C, 56.36; H, 7.43; N, 9.39. Found: C, 56.13; H, 7.44; N, 9.37.

(*S*)-(3-*tert*-Butoxycarbonylamino-2-oxo-2,3,4,7-tetrahydroazepin-1-yl)acetic Acid Ethyl Ester (9b). Obtained from **8b** (123 mg, 0.36 mmol) and **10a** (30 mg, 0.036 mmol) in DCE (72 mL) as described for **9a**. Purification by flash chromatography (ligroin−EtOAc, 6:4) yielded **9b** (76 mg, 68%). **9b**: colorless oil; R_f 0.25 (ligroin−EtOAc, 6:4); $[\alpha]^{20}_D$ +20.6 (c = 1.27, $CHCl_3$); IR (film) 3413, 1751, 1712, 1658 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (t, J = 7.3, 3H), 1.45 (s, 9H), 2.20−2.30 (m, 1H), 2.63−2.75 (m, 1H), 3.36 (dd, J = 17.7, 6.7, 1H), 4.09 (d J = 17.4, 1H), 4.19 (q, J = 7.1, 2H), 4.35 (d, J = 17.4, 1H), 4.50−4.60 (m, 1H), 4.96 (ddd, J = 12.1, 6.7, 4.5, 1H), 5.70−5.82 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 14.1, 28.4, 33.3, 47.4, 50.1, 50.3, 55.8, 61.4, 123.6, 129.9, 154.9, 168.9, 172.9; EIMS 239 (($M - CO_2$-Et)$^+$), M^+ not observed. Anal. Calcd for $C_{15}H_{24}N_2O_5$: C, 57.68; H, 7.74; N, 8.97. Found: C, 57.10; H, 7.88; N, 9.02.

(2*S*)-[(3*S*)-*tert*-Butoxycarbonylamino-2-oxo-2,3,4,7-tetrahydroazepin-1-yl)propionic Acid Methyl Ester (9c). Obtained from **8c** (34 mg, 0.10 mmol) and **10a** (8 mg, 0.01 mmol) in DCE (21 mL) as described for **9a**. Purification by flash chromatography (ligroin−EtOAc, 6:4) yielded **9c** (13 mg, 42%). **9c**: colorless oil; R_f 0.28 (ligroin−EtOAc, 6:4); $[\alpha]^{23}_D$ −33.6 (c = 0.62, $CHCl_3$); IR (film) 3413, 1743, 1712, 1654 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.39 (d, J = 7.5, 3H), 1.45 (s, 9H), 2.21−2.32 (m, 1H), 2.65 (ddd, J = 18.0, 7.4, 3.6, 1H), 3.42−3.58 (m, 1H, 3.68 (s, 3H), 4.19−4.31 (m, 1H), 4.92 (ddd, J = 12.1, 7.3, 4.4, 1H), 5.27 (q, J = 7.2, 1H), 5.69−5.82 (m, 3H); ^{13}C NMR ($CDCl_3$) δ 14.8, 28.3, 30.9, 33.3, 41.9, 50.1, 52.1, 52.7, 124.1, 129.5, 155.0, 171.9, 172.3; EIMS 312 (M^+). Anal. Calcd for $C_{15}H_{24}N_2O_5 \cdot {}^1/_3H_2O$: C, 56.06; H, 7.84; N, 8.72. Found: C, 55.95; H, 7.87; N, 8.51.

(*S*)-(3-*tert*-Butoxycarbonylamino-6-methyl-2-oxo-2,3,4,7-tetrahydroazepin-1-yl)acetic Acid Ethyl Ester (9d). Obtained from **8d** (45 mg, 0.12 mmol) and **10b** (5 mg, 0.006 mmol) in DCE (24 mL) as described for **9a**. Purification by flash chromatography (ligroin−EtOAc, 6:4) yielded **9d** (35 mg, 89%). **9d**: colorless oil; R_f 0.29 (ligroin−EtOAc, 6:4); $[\alpha]^{21}_D$ +58.5 (c = 0.13, $CHCl_3$); IR (film) 3417, 1749, 1714, 1662 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (t, J = 7.1, 3H), 1.44 (s, 9H), 1.74 (s, 3H), 2.16−2.28 (m, 1H), 2.55.2.65 (m, 1H), 3.15 (d, J = 17.7, 1H), 4.08−4.14 (m, 1H), 4.19 (q, J = 7.1, 2H), 4.32 (d, J = 17.1, 1H), 4.58−4.65 (m, 1H), 4.91 (ddd, J = 12.3, 6.6, 4.2, 1H), 5.45−5.52 (m, 1H), 5.76 (d, J = 6.6, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 24.6, 28.3, 33.1, 50.2, 50.4, 52.1, 61.3, 79.5, 123.3, 132.3, 155.0, 168.9, 172.9; EIMS 326 (M^+). Anal.Calcd for $C_{16}H_{26}N_2O_5$: C, 58.88; H, 8.03; N, 8.58. Found: C, 58.49; H, 8.04; N, 8.26.

(*S*)-3-*tert*-Butoxycarbonylamino-2-oxo-3,4,7,8-tetrahydro-2*H*-azocin-1-yl)acetic Acid Ethyl Ester (9e). Obtained from **8e** (50 mg, 0.14 mmol) and **10a** (12 mg, 0.014 mmol) in DCE (70 mL) as described for **9a**. Purification by flash chromatography (ligroin−EtOAc, 6:4) yielded **9e** (32 mg, 70%). **9e**: colorless oil; R_f 0.20 (ligroin−EtOAc, 6:4); $[\alpha]^{23}_D$ +33.1 (c = 0.16, $CHCl_3$); IR (film) 3405, 1747, 1712, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.27 (t, J = 7.1, 3H), 1.44 (s, 9H), 2.27 2.35 (m, 2H), 2.49−2.60 (m, 1H), 2.80−2.91 (m, 1H), 3.22 (ddd, J = 15.6, 5.7, 5.7, 1H), 3.75 (d, J = 17.0, 1H), 3.99−4.10 (m, 1H), 4.19 (q, J = 7.1, 2H), 4.39 (d, J = 17.0, 1H), 4.81−4.95 (m, 1H), 5.56 (ddd, J = 11.8, 6.1, 5.8, 1H), 5.70 (ddd, J = 11.5, 6.0, 6.0, 1H), 5.84 (d, J = 6.0, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 27.6, 27.9, 28.4, 35.9, 47.4, 49.1, 51.3, 61.3, 126.7, 127.8, 159.8, 168.9, 172.7; EIMS 326 (M^+). Anal. Calcd for $C_{16}H_{26}N_2O_5 \cdot {}^1/_3H_2O$: C, 57.30; H, 8.11; N, 8.35. Found: C, 57.32; H, 7.81; N, 8.30.

(2*S*)-[(3*S*)-*tert*-Butoxycarbonylamino-2-oxo-3,4,7,8-tetrahydro-2*H*-azocin-1-yl]propionic Acid Methyl Ester (9f). Obtained from **8f** (20 mg, 0.056 mmol) and **10a** (5 mg, 0.006 mmol) in DCE (28 mL) as described for **9a**. Purification by flash chromatography (ligroin−EtOAc, 6:4) yielded **9f** (11 mg, 60%). **9f**: colorless oil; R_f 0.21 (ligroin−EtOAc, 6:4); $[\alpha]^{23}_D$ −34.7 (c = 1.0, $CHCl_3$); IR (film) 3413, 1747, 1700, 1650 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.41 (d, J = 7.1, 3H), 1.44 (s, 9H), 2.27 (ddd, J = 8.1, 16.0, 8.1, 1H), 2.42 (ddd, J = 15.5, 7.5, 7.5, 1H), 2.56−2.65 (m, 1H), 2.78−2.85 (m, 1H), 3.34 (ddd, J = 14.9, 7.4, 7.0, 1H), 3.69 (s, 3H), 3.86 (ddd, J = 14.8, 7.1, 7.0, 1H), 4.80 (q, J = 7.1 Hz, 1H), 4.80−4.90 (m, 1H), 5.50−5.60 (m, 1H), 5.64−5.77 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.9, 28.2, 28.4, 35.5, 44.1, 51.2, 52.0, 54.4, 79.6, 126.8, 127.6, 155.2, 171.8, 172.4; EIMS 326 (M^+). Anal. Calcd for $C_{16}H_{26}N_2O_5$: C, 58.88; H, 8.03; N, 8.58. Found: C, 58.62; H, 7.67; N, 8.51.

(*S*)-(3-*tert*-Butoxycarbonylamino-2-oxo-2,3,4,7,8,9-hexahydroazonin-1-yl)acetic Acid Ethyl Ester (9g). Obtained from **8g** (100 mg, 0.27 mmol) and **10a** (22 mg, 0.027 mmol) in DCE (135 mL) as described for **9a**. Purification by flash chromatography (ligroin−EtOAc, 6:4) yielded **9g** (82 mg, 86%). **9g**: colorless oil; R_f 0.29 (ligroin−EtOAc, 6:4); $[\alpha]^{26}_D$ −15.2 (c = 0.65, $CHCl_3$); IR (film) 3419, 1751, 1710, 1643 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.21 (t, J = 7.1, 3H), 1.38 (s, 9H), 1.40−1.50 (m, 1H), 1.80 (dddd, J = 14.1, 13.7, 6.9, 3.7, 1H), 1.92 (dddd, J = 13.4, 13.0, 10.8, 2.8, 1H), 2.57 (ddd, J 8.3, 14.2, 8.3, 1H), 3.00 (ddd, J = 14.5, 2.5, 2.4, 1H), 3.63−3.75 (m, 1H), 3.93 (s, 2H), 4.14 (q, J = 7.1, 2H), 4.30−4.39 (m, 1H), 5.51 (ddd, J = 10.6, 10.0, 6.2, 1H), 5.91 (br d, J = 6.7, 1H), 6.01 (ddd, J = 9.2, 8.8, 10.0, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 21.0, 22.4, 28.4, 34.4, 45.6, 47.6, 51.2, 61.2, 79.4, 129.1, 130.4, 154.9, 172.9, 180.9; EIMS 340 (M^+). Anal. Calcd for $C_{17}H_{28}N_2O_5$: C, 59.98; H, 8.29; N, 8.22. Found: C, 59.50; H, 8.31; N, 8.17.

(*S*)-(9-*tert*-Butoxycarbonylamino-10-oxo-3,4,5,8,9,10-hexahydro-2*H*-azecin-1-yl)acetic Acid Ethyl Ester (9h). A solution of **8h** (30 mg, 0.078 mmol) in DCE (16 mL) was added dropwise to a solution of **10b** (3 mg, 0.004 mmol) in DCE (140 mL) at 60 °C. Subsequent heating to reflux and workup was done as described for **9a**. Purification by flash chromatography (ligroin−EtOAc, 6:4) yielded **9h** (2 mg, 8%). **9h**: colorless oil; R_f 0.32 (ligroin−EtOAc, 6:4); $[\alpha]^{22}_D$ −21.2 (c = 0.34, $CHCl_3$); IR (film) 3431, 1749, 1711, 1639 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.28 (t, J = 7.2, 3H), 1.45 (m, 1H), 1.44 (s, 9H), 1.60−2.10 (m, 4H), 2.23 (dd, J = 14.0, 9.0, 1H), 2.34 (dddd, J = 13.2, 13.2, 10.5, 2.7, 1H), 2.64 (ddd, J = 14.0, 8.3, 7.5 1H), 3.07 (dd, J = 13.0, 1.5, 1.5, 1H), 3.77 (dd, 13.0, 13.0, 1H), 4.00 (s, 2H), 4.21 (q, J = 7.2, 2H), 4.40 (dd, J = 7.5, 7.1, 1H), 5.58 (ddd, J = 10.5, 10.5, 6.2, 1H), 5.99 (brd, J = 7.1, 1H), 6.08 (ddd, J = 10.5, 9.0, 8.3, 1H); ^{13}C NMR ($CDCl_3$) δ 14.1, 22.4, 27.2, 28.4, 27.0, 34.5, 45.6, 47.6, 51.6, 61.1, 79.4, 129.3, 130.4, 155.0, 168.8, 172.9; EIMS 354 (M^+); HRMS m/z calcd for $C_{18}H_{30}N_2O_5$ 354.2155, found 354.2157.

(5-*tert*-Butoxycarbonylamino-6-oxo-3,6-dihydro-2*H*-pyridin-1-yl)acetic Acid Methyl Amide (11a). Compound **9a** (41 mg, 0.41 mmol) was added to a solution of methylamine in EtOH (5 mL, 8.03 M). The mixture was stirred overnight when evaporation followed by flash chromatography (CH_2Cl_2−MeOH, 95:5) of the resulting residue yielded **11a** (25 mg, 63%). **11a**: colorless oil; R_f 0.33 (CH_2Cl_2−MeOH, 95:5); IR (film) 3398, 1718, 1697, 1666, 1639 cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.47 (s, 9H), 2.51 (td, J = 7.3, 4.8, 2H), 2.81 (d, J = 4.5, 3H), 3.52 (t, J = 7.3, 2H), 4.03 (s, 2H), 6.09 (br s, 1H), 6.88 (t, J = 4.8, 1H), 7.38 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 22.4, 26.3, 28.2, 47.1, 52.1, 80.4, 115.3, 127.3, 152.9, 162.8, 168.9; EIMS 283 (M^+); HRMS m/z calcd for $C_{13}H_{21}N_3O_4$ 283.1532, found 283.1542.

(*S*)-(3-*tert*-Butoxycarbonylamino-2-oxo-2,3,4,7-tetrahydroazepin-1-yl)acetic Acid Methyl Amide (11b). Obtained from **9b** (20 mg, 0.064 mmol) and a solution of methylamine in EtOH (6 mL, 8.03 M) as described for **11a**. Purification by flash chromatography (CH_2Cl_2−MeOH, 95:5) yielded **11b** (18 mg, 95%). **11b**: colorless solid; mp 63−65 °C; R_f 0.33 (CH_2Cl_2−MeOH, 95:5); $[\alpha]^{22}_D$ +23.0 (c = 0.34, $CHCl_3$); IR (film) 3417, 3324, 1706, 1654 cm^{-1}; ^1H NMR (2 mM, $CDCl_3$) δ 1.45 (s, 9H), 2.24 (ddd, J = 17.1, 12.8, 3.9, 1H), 2.70 (ddd, J = 18.4, 6.7, 2.9, 1H), 2.79 (d, J = 4.9, 3H), 3.55−3.60 (m, 1H), 4.05 (d, J = 15.6, 1H), 4.14 (d, J = 15.6, 1H), 4.51 (ddd, J = 17.7, 3.7, 3.7, 1H), 4.98 (ddd, J = 12.1, 7.0, 4.6, 1H) 5.66 (d, J = 6.9, 1H), 5.75−5.88 (m, 2H), 6.02 (br s, 1H); ^1H NMR (2 mM, DMSO-d_6) δ 1.39 (s, 9H), 2.10−2.22 (m, 1H), 2.30−2.44 (m, 1H), 2.58 (d, J = 4.6, 3H), 3.47 (dd, J = 17.9, 7.3, 1H), 3.71 (d, J = 16.3, 1H), 4.19 (d, J = 16.3, 1H), 4.38−4.51 (m, 1H), 4.79 (ddd, J = 12.1, 7.1, 4.4, 1H), 5.60−5.80 (m, 2H), 6.49 (d, J = 7.1, 1H), 7.71 (br q, J = 4.4, 1H); ^{13}C NMR ($CDCl_3$) δ 26.2, 28.3, 33.1, 47.2, 50.1, 53.0, 79.9, 124.1, 130.3, 155.1, 168.9, 173.3; EIMS 297 (M^+); HRMS m/z calcd for $C_{14}H_{23}N_3O_4$ 297.1689, found 297.1670.

(*S*)-(3-*tert*-Butoxycarbonylamino-2-oxo-3,4,7,8-tetrahydro-2*H*-azocin-1-yl)acetic Acid Methyl Amide (11c). Obtained from **9e** (139 mg, 0.43 mmol) and a solution of methylamine in EtOH (8 mL, 8.03 M) as described for **11a**. Purification by flash chromatography (CH_2Cl_2−MeOH, 95:5) yielded **11c** (74 mg, 55%). **11c**: colorless solid; mp 46−48 °C; R_f 0.33 (CH_2Cl_2-MeOH, 95:5); $[\alpha]^{16}_D$ +86.7 (c = 0.03, $CHCl_3$); IR (film) 3328, 1700, 1650 cm^{-1}; ^1H NMR (2 mM, $CDCl_3$) δ 1.45 (s, 9H), 2.30 (ddd, J = 7.9, 16.1, 7.9, 1H), 2.40−2.62 (m, 2H), 2.78 (d, J = 4.9, 3H), 2.80−2.82 (m, 1H), 3.31 (ddd, J = 6.5, 14.9, 6.5, 1H), 3.86 (d, J = 15.3, 1H), 4.03 (ddd, J = 7.5, 14.9, 7.5, 1H), 4.13 (d, J = 15.3, 1H), 4.87 (dd, J = 14.7, 7.3, 1H), 5.50−5.61 (m, 2H), 5.66−5.75 (m, 1H), 6.41 (br s, 1H); ^1H NMR (2 mM, DMSO-d_6) δ 1.39 (s, 9H), 2.10−2.20 (m, 1H), 2.32−2.45 (m, 2H), 2.57 (d, J = 4.3, 3H), 2.61−2.75 (m, 1H), 3.40−3.50 (m, 1H), 3.49 (d, J = 16.3, 1H), 3.86 (ddd, J = 15.9, 14.1, 6.7, 1H,), 4.09 (d, J = 16.3, 1H), 4.68 (ddd, J = 9.3, 7.1, 4.9, 1H), 5.48 (ddd, J = 5.8, 11.3, 5.6, 1H), 5.61 (ddd, J = 6.7, 11.3, 6.7, 1H), 6.81 (d, J = 7.1, 1H), 7.59 (br s, 1H); ^{13}C NMR ($CDCl_3$) δ 18.1, 25.5, 26.8, 28.2, 33.9, 47.1, 51.6, 80.1, 126.6, 127.4, 155.6, 169.0, 174.8; EIMS 311 (M^+). Anal. Calcd for $C_{15}H_{25}N_3O_4 \cdot {}^1/_4H_2O$: C, 56.76; H, 8.15; N, 13.24. Found: C, 56.07; H, 8.04; N, 13.04.

(*S*)-(3-*tert*-Butoxycarbonylamino-2-oxo-2,3,4,7,8,9-hexahydroazonin-1-yl)acetic Acid Methyl Amide (11d). Obtained from **9g** (82 mg, 0.23 mmol) and a solution of methylamine in EtOH (6 mL, 8.03M) as described for **11a**. Purification by flash chromatography (CH_2Cl_2−MeOH, 95:5) yielded **11d** (83 mg, 84%). **11d**: colorless solid; mp 54−56 °C; R_f 0.25 (CH_2Cl_2−MeOH, 95:5); $[\alpha]^{16}_D$ +6.0 (c = 0.05, $CHCl_3$); IR (film) 3332, 1700, 1670, 1637 cm^{-1}; IR (2 mM, $CHCl_3$, background: **9g**) 3430, 3370, 1708, 1670, 1648 cm^{-1}; ^1H NMR (2 mM, $CDCl_3$) δ 1.39 (s, 9H), 1.85−2.00 (m, 3H), 2.17 (ddd, J = 14.4, 7.8, 1.6, 1H), 2.38−2.50 (m, 1H), 2.71 (d, J = 4.9, 3H), 3.08 (d, J = 15.3, 1H), 3.65−3.80 (m, 2H), 4.18 (d, J = 15.3, 1H), 4.34−4.43 (m, 1H), 5.43 (d, J = 6.4, 1H), 5.50 (ddd, J = 8.5, 9.8, 8.9, 1H), 5.82 (ddd, J = 9.8, 8.9, 8.9, 1H), 6.59 (br s, 1H); ^1H NMR (2 mM, DMSO-d_6) δ 1.38 (s, 9H), 1.79−2.00 (m, 2H), 2.05−2.20 (m, H), 2.31−2.40 (m, 1H), 2.57 (d, J = 4.5, 3H), 3.00−3.12 (m, 1H), 3.62 (d, J = 16.3, 1H), 3.60−3.70 (m, 1H), 3.99 (d, J = 16.3, 1H), 4.30−4.40 (m, 1H), 5.49−5.61 (m, 1H), 5.72−5.85 (m, 1H), 6.91 (d, J = 6.4, 1H), 7.53 (br q, J = 4.5, 1H); ^{13}C NMR ($CDCl_3$) δ 23.3, 26.4, 26.8, 28.5, 31.8, 46.3, 49.6, 51.2, 79.9, 127.2, 131.6, 155.8, 169.1, 173.9; EIMS 325 (M^+). Anal. Calcd for $C_{16}H_{27}N_3O_4$: C, 59.06; H, 8.36; N, 12.91. Found: C, 59.02; H, 8.52; N, 12.76.

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Supporting Information Available: ^1H NMR spectra for **8a**−**h**, **9a**−**h**, and **11a**−**d** and ^{13}C NMR, $^1H/^1H$ COSY, HMQC, and NOE spectra for **11d**. This material is available free of charge via the Internet at http://pubs.acs.org.

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