Conversion of β-Amino Esters to β-Lactams via Tin(II) Amides

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Abstract: Addition of $Sn[N(TMS)_2]_2$ to β-amino esters with sterically nondemanding substituents at C3 or on nitrogen gave β-lactams in 76–100% yield. More sterically demanding β-amino esters could be converted to β-lactams in excellent yield using unsymmetrical tin(II) amide reagents which were prepared *in situ*. Optimal results for the *in situ* procedure involved addition of $Sn[N(TMS)_2]_2$ to a β-amino ester, followed by addition of either pivalic acid or *N-tert*-butylacetamide.

Introduction

β-Lactam-based antibiotics include penicillins, cephalosporins, carbapenems, norcardins, and monobactams.[1] These compounds constitute a large class of broad spectrum antibiotics that effectively combat bacterial infections. Their primary mode of action is to inhibit the cross-linking of peptidoglycan strands in the final stage of bacterial cell-wall synthesis.[2] Since the peptidoglycan layer determines the shape of the bacterial cell and prevents osmotic lysis, a structurally weakened cell wall ultimately results in rupture and death of the cell. It is important to note that the β-lactam moiety is critical to the efficacy of these antibiotics; splitting the ring via hydrolysis with acid or by the action of β-lactamases yields products that do not inhibit bacterial growth.

Given the pharmacological importance of these antibiotics, it is not surprising that synthetic chemists have developed several routes to β-lactams. These methodologies can be generally categorized as follows: (i) [2 + 2] cycloadditions,[3] (ii) cyclization reactions,[4] and (iii) carbene insertion reactions.[5,6] The methodology that we have developed falls into the category of cyclization reactions.

Our interest in β-lactams stems from our work with divalent tin reagents. In particular, we have found that tin(II) amides serve as a new and useful source of nucleophilic amines. We have shown, for example, that tin(II) amides can be used for the stereoselective synthesis of *trans*-enamines from either aldehydes or ketones.[7] More recently, we published a new procedure for the direct conversion of esters to amides using tin(II) reagents.[8,9] After successfully developing these intermolecular reactions, we next turned our attention to similar *intramolecular* procedures.

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Herein, we describe the use of tin(II) amide reagents for the facile conversion of β-amino esters to β-lactams.

Tin(II) amides, otherwise known as stannylenes, are isoelectronic to singlet carbenes.[10] The most conveniently prepared tin(II) amide is bis(bis(trimethylsilyl)amino)tin(II), $Sn[N(SiMe_3)_2]_2$, which is synthesized from tin(II) chloride and lithium bis(trimethylsilyl)amide.[11,12] Bis(bis(trimethylsilyl)amino)tin(II) is a diamagnetic, thermally stable, distillable red liquid which solidifies to an orange solid and is readily soluble in organic solvents. Other symmetrical tin(II) amides can be prepared *in situ* via addition of 2 equiv of a lithium amide to $SnCl_2$.[13,14] There is also literature precedent for the conversion of tin(II) amides to tin(II) alkoxides by reaction with alcohols.[15]

Results and Discussion

We have found that $Sn[N(TMS)_2]_2$ is readily prepared in 86% isolated yield on a 75-g scale according to the literature procedure (eq 1).[11,16] Since it is one of the few tin(II) amides that can be

$$SnCl_2 \xrightarrow[Et_2O,\ r.t.,\ 86\%]{2\ equiv\ LiN(TMS)_2} Sn[N(TMS)_2]_2 \qquad (1)$$

purified by distillation, we attempted to use bis(bis(trimethylsilyl)amino)tin(II) as the starting material for other transformations. We were pleased to find that addition of 1 equiv of a primary or secondary amine to $Sn[N(TMS)_2]_2$ generates an unsymmetrical tin(II) amide via a metathesis reaction (eq 2).[17] Furthermore,

$$Sn[N(TMS)_2]_2 \xrightarrow[-HN(TMS)_2]{R_2NH} R_2N\text{-}Sn\text{-}N(TMS)_2 \qquad (2)$$

1

these unsymmetrical R_2N–Sn–$N(TMS)_2$ amides also proved to be more reactive than bis(bis(trimethylsilyl)amino)tin(II). Whereas $Sn[N(TMS)_2]_2$ did not react with secondary aldehydes, tertiary aldehydes, cinnamaldehyde, ketones, acetals, esters, nitriles, acetylenes, olefins, epoxides, or nitro groups, our unsymmetrical tin(II) reagents readily converted carbonyl compounds to enamines and esters to amides. Most importantly, the alkyl amido ligand was selectively transferred in all cases we examined.

As an extension of these studies, we decided to examine whether lactams could be similarly prepared from amino esters using an *intramolecular* variant of this methodology.[18] Addition of $Sn[N(TMS)_2]_2$ to a β-amino ester, for example, would be expected

Scheme I

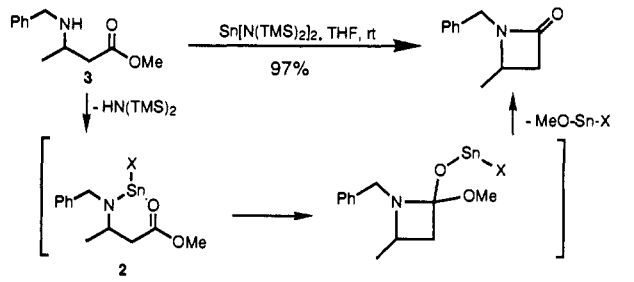
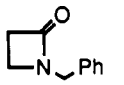
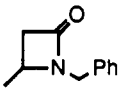
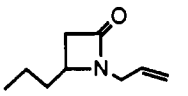
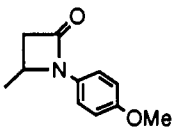
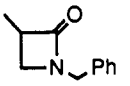
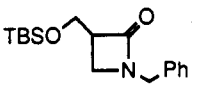
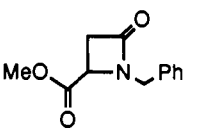


Table I. β-Lactams via Tin(II) Amides

entry	β-lactam	yield, % (method A)
1		90
2		97
3		90
4		85 (100)[a]
5		100
6		94
7		76

[a] The reaction mixture was heated at reflux.

to give tin(II) amide **2** via a metathesis reaction (Scheme I, X = $N(TMS)_2$). Since the silazane ligand does not transfer relative to other amido ligands and tin could activate the proximal ester functionality, we reasoned that β-lactam formation might occur. In fact, when a THF solution of methyl 3-(*N*-benzylamino)butanoate (**3**) was treated with $Sn[N(TMS)_2]_2$ at room temperature, the corresponding β-lactam was obtained in 97% isolated yield (Table I, entry 2).

The cyclization also proceeded smoothly when there were substituents at the α-position of the β-amino ester. For example, substrates with α-methyl or α-CH_2OTBS were converted in good yield to the corresponding C3-substituted β-lactams (Table I, entries 5 and 6). Furthermore, we found that the substituent on the amino group could be varied from allyl to benzyl to *p*-methoxyphenyl (entries 1–4). Substrates with large substituents on either the amino group or at the β-position, however, were converted to β-lactams in poor yield.

It appeared that the diminished yields in the latter cases were caused by unfavorable steric interactions between these substituents and the bulky silazane ligand on tin. We then sought to evaluate whether the yields of the cyclization could be improved by modifying the size and/or electronegativity of the nontransferrable ligand (Table II). Using methyl 3-(*N*-benzylamino)hexanoate as our model system, we determined the impact of

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(14) The stability of these compounds varies greatly with the nature of the amino group. Bis(diisopropylamino)tin(II), for example, decomposes at room temperature. Bis(piperidino)tin(II) is stable at room temperature, but decomposes upon attempted distillation.

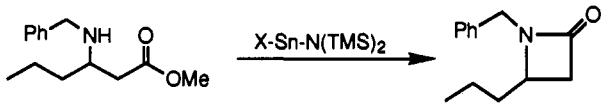
(15) Cetinkaya, B.; Gumrukcu, I.; Lappert, M. F.; Atwood, J. L.; Rogers, R. D.; Zaworotko, M. J. *J. Am. Chem. Soc.* **1980**, *102*, 2088.

(16) Storing $Sn[N(SiMe_3)_2]_2$ as a hexane solution permits subsequent transfer via standard syringe techniques.

(17) NMR experiments have shown that the unsymmetrical tin(II) amides exist in equilibrium with $Sn[N(TMS)_2]_2$ and $Sn[NR_2]_2$. For example, addition of 1 equiv of piperidine to $Sn[N(TMS)_2]_2$ leads to a 1:2:1 mixture of $Sn[N(TMS)_2]_2$:[piperidino–Sn–$N(TMS)_2]_2$:$Sn[(piperidino)_2]_2$. The same equilibrium mixture is obtained when $Sn[N(TMS)_2]_2$ is added to $Sn[NR_2]_2$. Addition of 2 equiv of piperidine to $Sn[N(TMS)_2]_2$ gives $Sn[(piperidino)_2]_2$, exclusively. When 1 equiv of alcohol or pivalic acid is added to $Sn(piperidino)_2$, the unsymmetrical alkoxy–Sn–piperidino compound is the major product. The solution studies of tin(II) amides will be reported in due course.

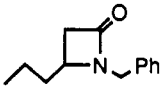
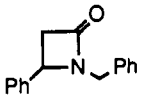
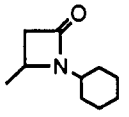
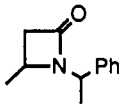
(18) Macrocyclic lactams are formed in poor yields as a mixture of monomeric and dimeric products. For example, cyclization of methyl 12-(methylamino)dodecanoate gave a 1:3 mixture of the desired product (12-membered ring) and dimer (24-membered ring) in 20% yield.

Table II. Effect of Ligands on β-Lactam Formation



X	solvent	yield, %
$(TMS)_2N$	THF	28
$(iPr)_2N$	THF	50
$c\text{-}C_5H_{10}N$	THF	34
$(TMS)_2N$, nBu_4NBr	THF	8
ArO	THF	26
$tBuCO_2$	THF	69
$(TMS)_2N$	hexane	57
$tBuCO_2$	hexane	89
MeC(O)NnBu	hexane	60
MeC(O)NtBu	hexane	100

Table III. β-Lactams via Modified Tin(II) Amides

entry	β-lactam	yield, % method A[a]	yield, % method B[b]
1		28	89
2		31	95
3		5 (45)[c]	99
4		0	97

[a] Method A: $Sn[N(TMS)_2]_2$/THF/room temperature. [b] Method B: $Sn[N(TMS)_2]_2$/pivalic acid/hexane/room temperature. [c] The reaction mixture was heated at reflux.

smaller ligands (Scheme I, X = $N(iPr)_2$, $c\text{-}C_5H_{10}N$), an extra ligand (X = Br^-), and electron-withdrawing ligands such as alkoxides, carboxylates, and amides (X = ArO, $tBuCO_2$, MeC(O)NnBu, MeC(O)NtBu).

Overall, reactions run in hexanes using pivalate or *tert*-butylacetamide as the nontransferable ligand gave the best results. Experiments run with pivalate proved operationally simpler, however, since pivalic acid could be easily removed by simple extraction instead of column chromatography.

With an optimized procedure for the cyclization of β-amino esters in hand, we then re-evaluated reactions that had proceeded in poor yield under our original conditions (Table III, method A). We were gratified to find that substrates with large substituents on nitrogen or at the β-position of the amino ester could now be smoothly converted to β-lactams (method B). Thus, a simple modifications in the reaction conditions resulted in dramatically improved yields of the desired cyclization products.

Conclusion

Unsymmetrical tin(II) amides can be generated *in situ* by addition of either a primary or secondary alkyl amine to $Sn[N(TMS)_2]_2$. When the amino group is situated β to an ester, the resultant tin(II) amide cyclizes to give a β-lactam. Simple substrates that lack sterically demanding substituents on the amino group or at the β-position give β-lactams in 76–100% yield. This procedure can be easily modified to accommodate more sterically demanding substrates by changing the nontransferable ligand from silazane to pivalate. Thus, the reactivity of these reagents can be deliberately and predictably modified by the selection of the two ligands on tin.

Experimental Section

General Procedure. Spectra were recorded on a Varian XLA-400 MHz or Gemini 300 MHz spectrometer at the frequencies indicated: ^1H NMR, 400 or 300 MHz; ^{13}C NMR, 100 or 75 MHz. Chemical shifts are reported in parts per million (δ) relative to tetramethylsilane, $CDCl_3$ with $CHCl_3$ as an internal reference (7.26 ppm for ^1H NMR and 77.0 ppm for ^{13}C NMR), or C_6D_6 with C_6D_5H as an internal reference (7.15 ppm for ^1H NMR). Coupling constants are reported in hertz (Hz). Spectral splitting patterns are designated as s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet), and br (broad). Electron impact mass spectra were recorded on a VG-70-250SE high-resolution mass spectrometer with ionization voltages of 70 or 10 eV. Data are reported in the form *m/z* (intensity relative to base = 100%).

Unless otherwise indicated, all reagents were obtained from commercial suppliers and were used without further purification. Tetrahydrofuran (THF) and diethyl ether were distilled from sodium metal/benzophenone ketyl. Hexanes and benzene were distilled from sodium metal. Air- and/or moisture-sensitive reactions were carried out under an atmosphere of nitrogen in flame-dried glassware using standard Schlenk line techniques or in a Vacuum Atmospheres drybox.

The following procedures are representative of the preparation of β-lactams.

Method A. To a 100-mL THF solution of $Sn[N(TMS)_2]_2$ (0.530 g, 1.20 mmol), at room temperature and under a nitrogen atmosphere, was added 0.207 g of methyl 3-(benzylamino)-butanoate[19] (1.00 mmol). The reaction mixture was then stirred at room temperature and followed by TLC or GC until the reaction had gone to completion. After 12 h, the reaction solution was quenched with 1 mL of methanol in order to precipitate $[Sn(OMe)_2]_n$. The solvent was evaporated, the residue diluted with 100 mL of ethyl ether and then decanted. The ether layer was washed consecutively with two 10-mL portions of 15% NaOH solution, two 10-mL portions of 5 M aqueous KF, and one 10-mL portion of brine. It was then dried over anhydrous magnesium sulfate, filtered, and concentrated at reduced pressure. Purification of the crude product by column chromatography (1:1 hexanes/ethyl acetate) gave 0.170 g (97%) of 1-benzyl-4-methyl-2-azetidinone:[22] IR (neat) 1736, 910 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.26 (m, 5H), 4.55 (d, *J* = 15.1 Hz, 1H), 4.07 (d, *J* = 15.3 Hz, 1H), 3.54 (m, 1H), 3.35 (dd, *J* = 14.6, 5.0 Hz, 1H), 2.50 (dd, *J* = 14.3, 1.9 Hz, 1H), 1.18 (d, *J* = 6.1 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 166.6, 135.9, 128.5, 128.2, 127.4, 46.8, 44.1, 43.9, 18.3; MS *m/z* (relative intensity) 176 (8, M^+ + 1), 175 (23, M^+), 133 (51), 119 (14), 105 (23), 91 (62), 43 (100).

Method B. To a 100-mL hexanes solution of $Sn[N(TMS)_2]_2$ (0.530 g, 1.20 mmol), at room temperature and under a nitrogen atmosphere, was added 0.235 g of methyl 3-(benzylamino)-hexanoate[20] (1.00 mmol). After stirring for 15 min, by which time the orange color of the solution had turned to pale yellow, 2 mL of a hexanes solution of pivalic acid (0.112 g, 1.10 mmol) was added.[21] The resulting colorless solution was stirred at room temperature and monitored by TLC or GC until the reaction had gone to completion. The reaction mixture was then worked up as in method A to give 0.180 g (89%) 1-benzyl-4-propyl-2-

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(21) Upon addition of the acid, the reaction mixture should be clear and colorless. We have obtained dark red mixtures when the acid is added neat or too quickly.

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azetidinone:[22] IR (neat) 1741, 1402, 912 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 5H), 4.60 (d, J = 15.2 Hz, 1H), 4.10 (d, J = 15.3 Hz, 1H), 3.45 (m, 1H), 3.00 (dd, J = 14.6, 4.9 Hz, 1H), 2.56 (dd, J = 14.6, 1.9 Hz, 1H), 1.68 (m, 1H), 1.25 (m, 3H), 0.85 (m, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 167.1, 136.1, 128.6, 128.0, 127.5, 51.2, 44.5, 42.3, 34.8, 18.7, 13.9; MS m/z (relative intensity) 204 (14, M^+ + 1), 203 (36, M^+), 175 (5), 160 (11), 133 (95), 105 (32), 91 (100), 77 (11), 65 (19), 55 (13).

1-Benzyl-2-azetidinone[23] [4458-64-4]. Ethyl 3-(benzylamino)-propionate[24] (207 mg, 1.00 mmol) was converted to 1-benzyl-2-azetidinone (145 mg, 90%) according to method A: IR (neat) 1734, 1406 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31 (m, 5H), 4.35 (s, 2H), 3.11 (m, 2H), 2.93 (m, 2H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 167.4, 135.5, 128.6, 128.0, 127.6, 46.0, 38.4, 36.7; MS m/z (relative intensity) 162 (12, M^+ + 1), 161 (43, M^+), 133 (31), 105 (12), 91 (100).

1-Benzyl-3-methyl-2-azetidinone[23] [34317-15-2]. Methyl 2-methyl-3-(benzylamino)propionate[19] (207 mg, 1.00 mmol) was converted to 1-benzyl-3-methyl-2-azetidinone (175 mg, 100%) according to method A: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.29 (m, 5H), 4.35 (d, J = 15.1 Hz, 1H), 4.30 (d, J = 15.1 Hz, 1H), 3.26 (dd, J = 6.2, 5.2 Hz, 1H), 3.15 (m, 1H), 2.73 (dd, J = 5.3, 2.2 Hz, 1H), 1.27 (d, J = 7.4 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 171.2, 135.8, 128.8, 128.1, 127.6, 46.7, 45.8, 44.5, 13.7; MS m/z (relative intensity) 176 (27, M^+ + 1), 175 (43, M^+), 133 (95), 105 (28), 91 (100), 77 (11), 65 (16).

1-(1-Phenylethyl)-4-methyl-2-azetidinone[25] [89578-36-9 and 26757-80-2]. Methyl 3-(1-(phenylethyl)amino)butanoate[26] (221 mg, 1.00 mmol) was converted to 1-(1-phenylethyl)-4-methyl-2-azetidinone (183 mg, 97%) according to method B: IR (neat) 1734, 912 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (m, 10H), 4.86 (q, J = 7.2 Hz, 1H), 4.62 (q, J = 7.1 Hz, 1H), 3.50 (m, 2H), 2.96 (dd, J = 12.1, 5.0 Hz, 1H), 2.91 (dd, J = 14.4, 5.1 Hz, 1H), 2.40 (dd, J = 14.4, 2.2 Hz, 2H), 1.65 (d, J = 7.1 Hz, 3H), 1.58 (d, J = 7.3 Hz, 3H), 1.20 (d, J = 6.1 Hz, 3H), 1.03 (d, J = 6.1 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 166.7, 166.6, 140.5, 128.7, 128.6, 127.6 127.5, 126.9, 126.8, 52.4, 51.9, 47.3, 46.2, 43.6, 20.8, 19.5, 19.3, 19.1; MS m/z (relative intensity) 189 (21, M^+), 174 (29), 147 (38), 132 (70), 105 (100), 84 (73). Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 75.81; H, 7.95; N, 7.19.

1-Benzyl-4-phenyl-2-azetidinone[27] [19340-71-7]. Methyl 3-(benzylamino)hydrocinnamate[29] (269 mg, 1.00 mmol) was converted to 1-benzyl-4-phenyl-2-azetidinone according to method A (74 mg, 31%) and according to method B (225 mg, 95%): IR (neat) 1749, 1456, 912 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35 (m, 10H), 4.81 (d, J = 14.9 Hz, 1H), 4.41 (dd, J = 5.2, 2.2 Hz, 1H), 3.76 (d, J = 15.1 Hz, 1H), 3.35 (dd, J = 14.7, 5.1 Hz, 1H), 2.88 (dd, J = 14.6, 2.3 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 167.2, 137.8, 135.5, 128.9, 128.6, 128.5, 127.6, 126.4, 53.4, 46.8, 44.6, 29.6; MS m/z (relative intensity) 237 (10, M^+), 194 (5), 104 (100), 91 (28), 78 (10). Anal. Calcd for $C_{16}H_{15}NO$: C, 80.98; H, 6.37; N, 5.90. Found: C, 80.54; H, 6.71; N, 5.84.

1-Cyclohexyl-4-methyl-2-azetidinone[23] [78159-35-0]. Methyl 3-(cyclohexylamino)butanonate[28] (200 mg, 1.00 mmol) was converted to 1-cyclohexyl-4-methyl-2-azetidinone by method A (8 mg, 5%) and by method B (165 mg, 98%): ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.66 (m, 1H), 3.36 (m, 1H), 2.90 (dd, J = 14.3, 5.0 Hz, 1H), 2.35 (dd, J = 14.3, 2.0 Hz, 1H), 1.50 (m, 10H), 1.28 (d, J = 6.1 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 166.1, 51.7, 46.1, 43.2, 32.0, 30.5, 25.2, 25.1, 20.6; MS m/z (relative intensity) 168 (22, M^+ + 1), 167 (100), 156 (27), 124 (79), 110 (22), 96 (24), 83 (90), 69 (28), 55 (43). HRMS (M^+): calcd for $C_{10}H_{17}NO$, 167.1310; found, 167.1308.

1-(4-Methoxyphenyl)-4-methyl-2-acetidinone[29] [61999-49-3]. Methyl 3-(*p*-(methyloxy)anilino)butanonate[30] (223 mg, 1.00 mmol) was converted to 1-(4-methoxyphenyl)-4-methyl-2-azetidinone (162 mg, 85%) according to method A: IR (neat) 1734, 1512, 912 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (d, J = 9.0 Hz, 2H), 6.85 (d, J = 9.0 Hz, 2H), 4.08 (m, 1H), 3.75 (s, 3H), 3.17 (dd, J = 14.9, 5.3 Hz, 1H), 2.62 (dd, J = 14.9, 2.4 Hz, 1H), 1.45 (d, J = 6.1 Hz, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 163.6, 155.7, 130.8, 118.0, 114.2, 55.3, 46.9, 43.7, 18.4; MS m/z (relative intensity) 192 (15, M^+ + 1), 191 (81, M^+), 149 (100), 134 (70), 106 (10), 92 (8), 77 (11), 64 (8), 51 (5). Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.13; H, 6.77; N, 7.28.

1-Benzyl-3-((*tert*-butyldimethylsiloxy)methyl)-2-azetidinone. Methyl 3-(*N*-benzylamino)-2-((*tert*-butylidmethylsiloxy)-methyl)propionate[31] (337 mg, 1.00 mmol) was converted to 1-benzyl-3((*tert*-butyldimethylsiloxy)methyl)-2-azetidinone (286 mg, 94%) according to method A: IR (neat) 1743, 910 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.28 (m, 5H), 4.45 (d, J = 15.1 Hz, 1H), 4.30 (d, J = 15.2 Hz, 1H), 3.96 (dd, J = 11.0, 4.7 Hz, 1H), 3.82 (dd, J = 10.8, 3.1 Hz, 1H), 3.32 (m, 1H), 3.17 (m, 2H), 0.85 (s, 9H), 0.05 (d, 6H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 168.2, 135.6, 128.6, 128.0, 127.5, 59.3, 52.2, 45.7, 41.9, 29.6, 25.8, 18.2; MS m/z (relative intensity) 290 (6), 248 (100), 218 (6), 191 (8), 156 (4), 115 (11), 91 (53), 75 (8), 59 (7). Anal. Calcd for $C_{17}H_{27}NO_2Si$: C, 66.52; H, 8.91; N, 4.58. Found: C, 66.52; H, 9.25; N, 4.51.

Methyl 3-(*N*-Allylamino)hexanoate. A solution of methyl *trans*-2-hexenonate (12.8 g, 0.10 mol) and allylamine (6.0 g, 0.11 mol) in methanol (20 mL) was heated under reflux for 8 h, then concentrated. Distillation of the residue gave 14.5 g (80%) of methyl 3-(allylamino)hexanoate as a colorless oil: ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.87 (m, 1H), 5.18 (d, J = 15.6, 1.6 Hz, 1H), 5.05 (d, J = 10.2, 1.5 Hz, 1H), 3.68 (s, 3H), 3.24 (d, J = 6.0 Hz, 2H), 3.02 (m, 1H), 2.42 (d, J = 6.1 Hz, 2H), 1.41 (m, 4H), 0.92 (t, J = 8.9 Hz); ^{13}C NMR (300 MHz, $CDCl_3$) δ 172.9, 136.8, 53.7, 51.4, 49.4, 38.9, 36.5, 18.8, 14.0.

1-Allyl-4-propyl-2-acetidinone. 3-(*N*-Allylamino)hexanoate (185 mg, 1.00 mmol) was converted to 1-allyl-4-propyl-2-azetidinone (138 mg, 90%) according to method A: IR (neat) 1736, 910 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.69 (m, 1H), 5.12 (m, 2H), 3.91 (dd, J = 15.7, 5.4 Hz, 1H), 3.56 (dd, J = 15.9, 6.6 Hz, 1H), 3.50 (m, 1H), 2.93 (dd, J = 14.6, 5.0 Hz, 1H), 2.46 (dd, J = 14.6, 2.2 Hz, 1H), 1.72 (m, 1H), 1.30 (m, 3H), 0.98 (m, 3H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 166.8, 132.2, 117.8, 51.3, 43.0, 42.1, 35.0, 18.7, 13.8; MS m/z (relative intensity) 154 (19 M^+ + 1), 153 (58, M^+), 138 (8), 110 (24), 96 (8), 84 (14), 70 (100), 68 (51), 55 (71), 42 (77). HRMS (M^+): calcd for $C_9H_{15}NO$, 153.1154; found, 153.1162.

1-Benzyl-4-(methoxycarbonyl)-2-azetidinone. Methyl *N*-benzylaspartate (251 mg, 1.00 mmol) was converted to 1-benzyl-4-(methoxycarbonyl)-2-azetidinone (175 mg, 76%) according to method A: IR (neat) 1755, 912 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30 (m, 5H), 4.74 (d, J = 15.0 Hz, 1H), 4.15 (d, J = 15.1, 1H), 3.94 (m, 1H), 3.69 (s, 3H), 3.21 (dd, J = 14.4, 5.7 Hz, 1H), 3.03 (dd, J = 14.5, 2.4 Hz, 1H); ^{13}C NMR (300 MHz, $CDCl_3$) δ 170.5, 165.4, 134.6, 128.7, 128.4, 127.8, 52.4, 49.9, 45.9, 42.0.

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