Synthesis and Reactions of Some 1,2-Disubstituted 1,2-Diazetidin-3-ones: An Intramolecular Aldol Approach to Bicyclic Systems

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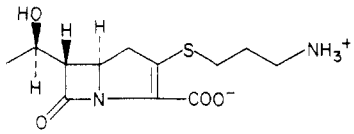
Several procedures have been developed for alkylation at N-2 of a variety of 1,2-diazetidin-3-ones with N-1 substituents carrying an olefinic bond. Ozonolysis yielded aldehydes which were subjected to aldol cyclization conditions. The products proved to be rearranged bicyclic products arising from intramolecular ring opening of the 1,2-diazetidin-3-one lactam bond by the secondary hydroxyl group formed in the aldol reaction.

There is intense current interest in the synthesis of new carbapenems since the discovery of the potent β-lactam antibiotic thienamycin (**1**).[1] Efficient procedures for the synthesis of such bicyclic systems have recently been developed based on intramolecular aldol[2] or Dieckmann[3] reactions. We are currently engaged in a program aimed



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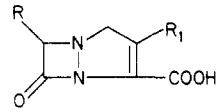

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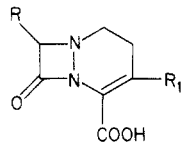

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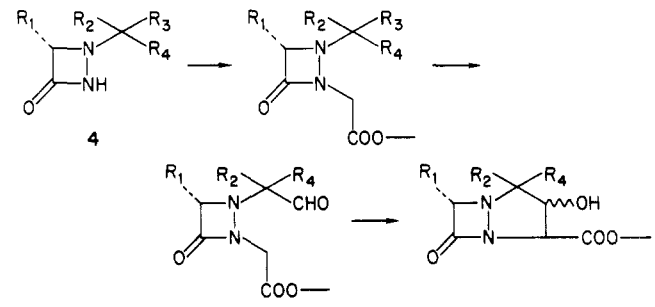
at the synthesis of highly strained aza analogues of bicyclic β-lactam antibiotics (e.g., **2** and **3**) and report in this paper our results from attempts to extend such intramolecular cyclizations to the aza β-lactam system.

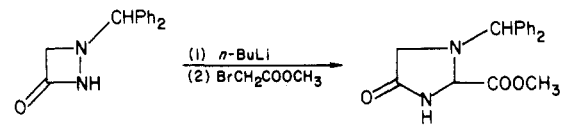
A generalized presentation of our proposed synthetic strategy is outlined in Scheme I. 1,2-Diazetidin-3-ones possessing a latent N-1 aldehydic functionality in the form of a double bond (**4**, R_3 = CH=CHR′) were available from previous work.[4] We hoped that further modification of **4** by regioselective N-2 alkylation with alkyl haloacetates, followed by ozonolysis and subsequent treatment with base, would provide entry into the desired bicyclic systems.

The anion of 1-benzhydryl-1,2-diazetidin-3-one (**5**), generated by either thallium(I) ethoxide or *n*-butyllithium, is readily alkylated by alkyl halides.[5] However, attempts to alkylate 1,2-diazetidin-3-ones with less bulky substituents at N-1 resulted in decomposition and/or polymerization, and the desired products were not obtained. It was observed in earlier work that treatment of 1,2-disubstituted 1,2-diazetidin-3-ones with strong base (i.e., LDA) resulted in proton abstraction from the α-carbon atom of the N-2 substituent and a subsequent extremely rapid ring expansion to give an imidazolidinone.[5] This reaction was also observed in the present work. For example, attempted alkylation of the anion of **5** with methyl bromoacetate gave only the imidazolidinone **6** (Scheme II). A possible way to avoid this ring-expansion problem would be to alkylate

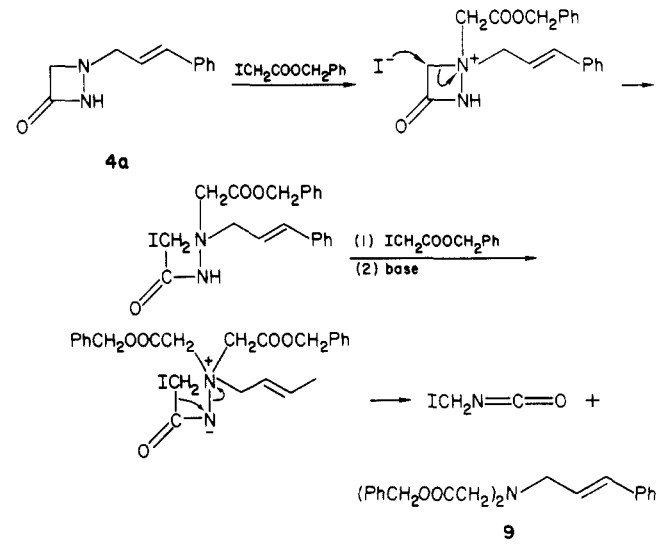
Scheme I



Scheme II



Scheme III

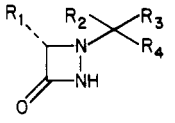


the 1-substituted 1,2-diazetidin-3-one in the presence of a *weak* base. Our results with alkylation of a range of 1-substituted 1,2-diazetidin-3-ones with benzyl and 2-(trimethylsilyl)ethyl iodoacetate and with methyl iodide in the presence of sodium bicarbonate as the base are summarized in Table I. For example, alkylation of **4d** with excess benzyl iodoacetate in DMF in the presence of sodium bicarbonate did result in slow formation of the desired alkylation product **7d**. The best yield of **7d** (40%) by this procedure was obtained by using 3 equiv of benzyl iodoacetate and allowing the reaction to run for 3 days at room temperature. When the reaction was repeated with DBU as the base, the imidazolidinone **8a** was isolated in

(1) Durckheimer, W.; Blumbach, J.; Lattrell, R.; Scheunemann, K. H. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 180.
(2) Shibuya, M.; Kubota, S. *Tetrahedron Lett.* **1980**, *21*, 4009.
(3) Shibuya, M.; Kubota, S. *Tetrahedron Lett.* **1981**, *22*, 3011.
(4) For preliminary work in this area, see: Taylor, E. C.; Davies, H. M. L. *J. Org. Chem.* **1984**, *49*, 4415.
(5) Taylor, E. C.; Clemens, R. J.; Davies, H. M. L.; Haley, N. F. *J. Am. Chem. Soc.* **1981**, *103*, 7659.

0022-3263/86/1951-1530$01.50/0

Table I. Preparation of 1,2-Disubstituted 1,2-Diazetidin-3-ones



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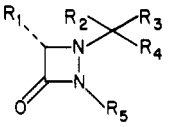

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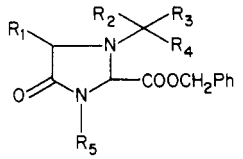
substrate	product	R_1	R_2	R_3	R_4	R_5	procedure	yield, %
4a	7a	H	H	CH=CHPh	H	CH_2COOCH_2Ph	A	0
4b	7b	CH_3	H	CH=CHPh	H	CH_2COOCH_2Ph	A	10
4c	7c	CH_2CH_3	H	CH=CHPh	H	CH_2COOCH_2Ph	A	45
4d	7d	H	CH_3	CH=CHPh	CH_3	CH_2COOCH_2Ph	A	40
4e	7e	CH_3	CH_3	CH=CHPh	CH_3	CH_2COOCH_2Ph	A	85
4c	7f	CH_2CH_3	H	CH=CHPh	H	$CH_2COOCH_2CH_2Si(CH_3)_3$	A	37
4e	7g	CH_3	CH_3	CH=CHPh	CH_3	$CH_2COOCH_2CH_2Si(CH_3)_3$	A	76
4f	7h	CH_3	Ph	Ph	CH_3	CH_3	B	77
4f	7i	CH_3	Ph	Ph	CH_3	CH_2COOCH_2Ph	A	37
							B	61
4g	7j	CH_3	Ph	Ph	$CH_2CH=CH_2$	CH_3	B	70
4g	7k	CH_3	Ph	Ph	$CH_2CH=CH_2$	CH_2COOCH_2Ph	A	55
4h	7l	CH_3	Ph	Ph	$CH=CH_2$	CH_3	A	10
							B	64
4i	7m	CH_3	CH_3	CH_3	$CH=CH_2$	CH_3	A	13
							B	2
4j	7n	CH_3	CH_3	CH_3	$CH_2CH=CH_2$	CH_2COOCH_2Ph	A	52
							B	23
4e	7o	CH_3	CH_3	CH=CHPh	CH_3	CH_3	A	72
							B	25

60% yield, indicating that DBU is sufficiently basic not only to deprotonate N-2 of **4d** but also the carbon α to N-2 in the alkylation product **7d**. The success of the alkylation

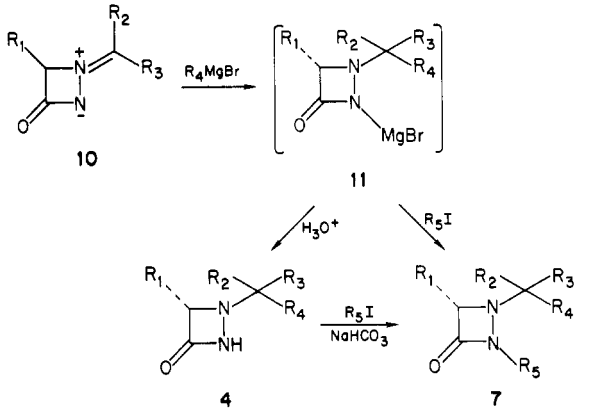


8a, $R_1=R_5=H$, $R_2=R_4=CH_3$, $R_3=CH=CHPh$
b, $R_1=CH_3$, $R_2=R_3=Ph$, $R_4=CH_3$, $R_5=CH_2COOCH_2Ph$
c, $R_1=CH_3$, $R_2=R_3=Ph$, $R_4=CH_2CH=CH_2$, $R_5=CH_2COOCH_2Ph$
d, $R_1=R_2=R_3=CH_3$, $R_4=CH_2CH=CH_2$, $R_5=H$
e, $R_1=R_2=R_3=CH_3$, $R_4=CH_2CH=CH_2$, $R_5=CH_2COOCH_2Ph$

reaction was found to be highly dependent on the degree of steric crowding about N-1 (because of competition between alkylation at N-2 vs. N-1). In the case of **4a**, for example, none of the desired product **7a** was formed, and the tertiary amine **9** was isolated in very low yield (3%). The amine **9** was also formed in alkylation reactions of **4b** and **4c**. As steric crowding about N-1 increases, the yield of N-2 alkylation improves until, with **4e**, it was possible to isolate the N-2 alkylation product **7e** in 85% yield. Scheme III depicts a reasonable pathway for the generation of the tertiary amine **9** from **4a**.

An alternate approach to N-2 alkylation was then investigated. 1,2-Diazetidin-3-ones with bulky N-1 substituents can be prepared by addition of Grignard reagents to the ylides **10** (see Scheme IV).[4] Direct alkylation of the immediate product of the Grignard addition (i.e., the magnesium salt **11**) should lead to N-2 alkylation in the absence of an added strong base capable of deprotonating the carbon α to N-2 in the product. Addition of alkyl halides to the crude intermediates obtained from addition of Grignard reagents to the ylides **10** indeed provided N-2 alkylated products in excellent yield. In fact, overall yields of N-2 alkylation products were in general better than isolated yields of the Grignard adducts themselves. However, the less bulky the N-1 substituent in the 1,2-diazetidin-3-one, the less satisfactory was the N-2 alkylation reaction, in line with our earlier observations. Furthermore, when benzyl iodoacetate was used in the N-2

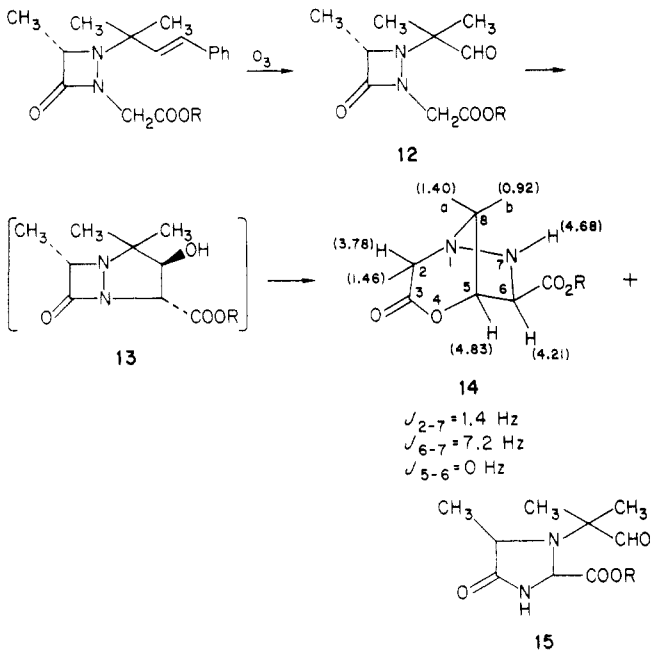
Scheme IV



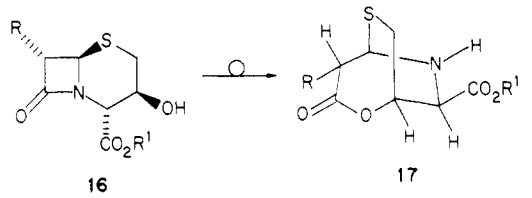
alkylation step, imidazolidinones (**8a,d**) were again formed, along with additional products (**8b,c,e**) from alkylation of initially formed N-3-unsubstituted imidazolidinones. Shorter reaction times increased the yields of the 1,2-diazetidin-3-ones relative to the imidazolidinones, but conditions were not optimized. Results are detailed in the Experimental Section.

Ozonolysis of **7e** in methylene chloride at −78 °C, followed by quenching with methyl sulfide and purification by column chromatography, gave the aldehyde **12a** in 36% yield. Treatment of **12a** with LDA yielded several products, among which were the imidazolidinone **15a** and an *apparent* aldol product (**13a**) as a single diastereoisomer (see Scheme V). The first indication that this latter compound might not be the anticipated aldol product was its inertness under a variety of dehydrating conditions. Furthermore, data from NOE experiments (vide infra) were inconsistent with any reasonable stereochemistry for **13a**. A careful analysis of NMR and NOE spectral data have led us to propose structure **14a** for this "aldol" product. ^1H NMR assignments from expected chemical shifts and coupling data are given in Scheme V. Irradiation at the frequency of the C-8a methyl signal (1.40 ppm) shows NOE in the C-2 (3.78 ppm) and C-5 (4.83 ppm) hydrogen signals, confirming the assigned stereochemistry about C-2. Irradiation of the C-8b methyl signal (0.92

Scheme V



Scheme VI



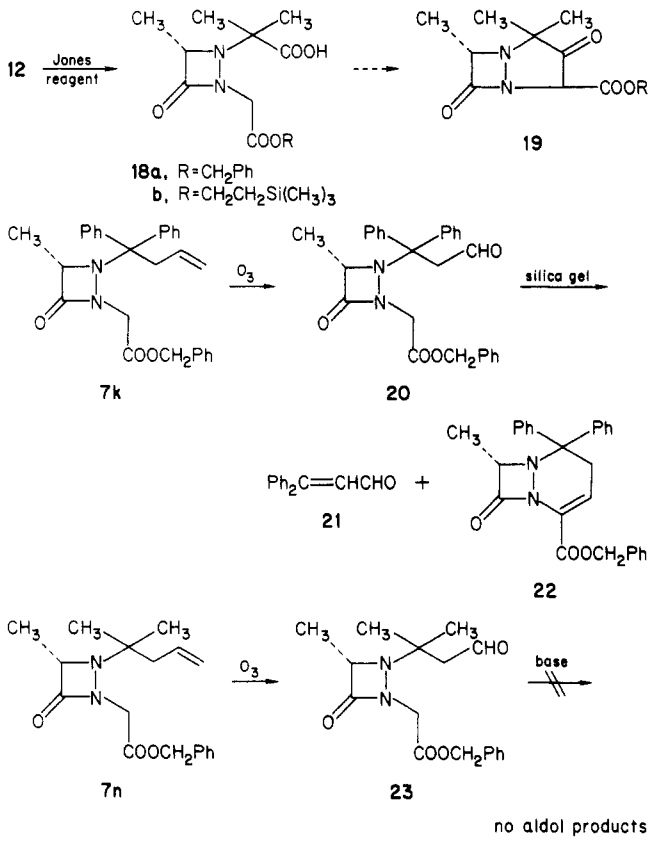
ppm) gives NOE in the C-5 (4.83 ppm) and N-7 (4.68 ppm) hydrogen signals, showing the configuration at N-7. There is long range four-bond coupling from the C-2 hydrogen to the N-7 hydrogen ($^4J_{2\text{-}7}$), confirming the configuration at N-7. The lack of NOE in the C-6 hydrogen (4.21 ppm) signal indicates that this hydrogen is oriented away from the C-8 methyl group. This relative stereochemistry is confirmed by the lack of coupling from the C-5 to C-6 hydrogens (models indicate nearly a 90° torsional angle) and the large coupling from the C-6 to C-7 hydrogens (models indicate approximately a 120° torsional angle). These structural and stereochemical assignments have been confirmed by single-crystal X-ray analysis.

A reasonble pathway for the formation of this unexpected "aldol" product involves intramolecular opening of the aza-β-lactam ring by the secondary hydroxyl group (which models indicate is forced extremely close to the lactam carbonyl group). An extremely unstable compound with a high-frequency IR carbonyl absorption band was also formed in this "aldol" reaction, but it decomposed on column chromatography; it may have been the aldol product with opposite stereochemistry. Precedent for the transformation of **13a** to **14a** is found in the rearrangement of **16** to **17** (Scheme VI).[6]

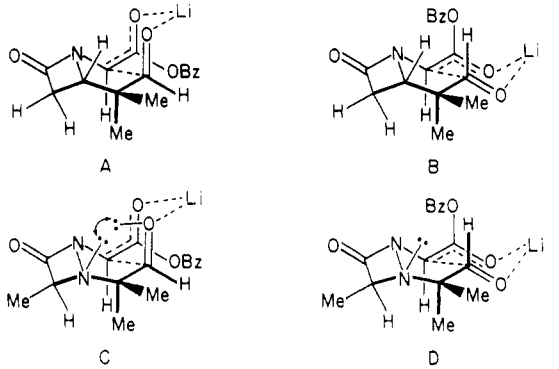
Related aldol condensations in β-lactam chemistry do not provide rearrangement products corresponding to **14a** apparently because the stereochemistry of the aldol products is opposite to that presumed for **13a**, the putative precursor to **14a**. The stereospecificity of the aldol reaction in β-lactam systems was reported to be due to the greater

(6) Gutowski, G. E.; Daniels, C. M.; Cooper, R. D. G. *Tetrahedron Lett.* **1971**, *37*, 3429.

Scheme VII



stability of transition-state A as contrasted with B (presumably because it led to the observed stereochemistry).[2]



In the 1,2-diazetidin-3-one case, the comparable transition-state C might be expected to be less stable than transition-state D because of the anomeric effect of N-1 (lone pair–aldehyde oxygen interaction) which is avoided in D; N-1 to lithium coordination, also not possible in the β-lactam case, may also affect transition-state geometries and favor D over C.

This "aldol" condensation was also examined with the 2-(trimethylsilyl)ethyl ester **12b**, which was prepared by alkylation of **4e** with 2-(trimethylsilyl)ethyl iodoacetate to give **7g**, followed by ozonolysis. The abnormal aldol product **14b** (24%), along with the imidazolidinone **15b**, was obtained upon treatment of **12b** with LDA. The free acid **14c** was obtained by deprotection of **14b** with fluoride ion; it proved to have no biological activity.

Numerous additonal attempts to form bicyclic systems from these 1,2-diazetidin-3-one precursors by classical procedures were made. Oxidation of the crude aldehydes **12a,b** with Jones reagent afforded the corresponding acids **18a,b**, which were converted to their respective acid chlorides with oxalyl chloride (Scheme VII). Without

purification, these acid chlorides (which were very unstable) were treated with LDA or with DBU, but only colorless gums were obtained which could not be satisfactorily characterized. ^1H and ^{13}C NMR data on these products were not consistent with the expected β-keto ester structures **19a,b**. Extensions of the above reactions to homologous precursors, with the intent of preparing fused six-membered rings, were only partially successful. For example, ozonolysis of the 1,2-diazetidin-3-one **7k** yielded the aldehyde **20**, but attempts to isolate it by silica gel chromatography led surprisingly to a mixture of β-phenylcinnamaldehyde (**21**) and the dehydrated aldol product **22**. Since the conversion of **20** to **22** appeared to take place in the presence of the acidic silica gel, attempts were made to effect an acid-catalyzed aldol condensation with **20** but without success. Aldehyde **23** was prepared by ozonolysis of **7n**, but no aldol condensation of **23** could be effected under any of the many conditions attempted, including treatment with silica gel.

The above results, coupled with past findings, provide further evidence that the structural similarity of 1,2-diazetidin-3-ones with β-lactams is more apparent than real and that even simple extensions of standard β-lactam chemistry to its aza analogues can be fraught with unexpected chemistry.

Experimental Section

Commercial reagents were utilized (Aldrich, Fluka) without further purification unless otherwise noted. Methylene chloride and DMF were dried over 4-Å molecular sieves, THF was freshly distilled over sodium benzophenone ketyl, and diisopropylamine was freshly distilled from barium oxide. Ozonolyses were carried out with a Welsbach Ozonator, Model T816, operating at 115 V, 4.5 A, and 195 W, with a supply oxygen pressure of 8 psig, a total ozone flow rate of 1.0 slpm, and an ozone flow rate to the sample of 0.4 slpm. The ozone was introduced to the reaction mixture via a sintered-glass aerator and with efficient stirring from a magnetic stirrer.

Melting points were determined in open capillaries with a Thomas-Hoover apparatus and are uncorrected. Boiling ranges were obtained during distillation at atmospheric pressure (or at the pressure indicated) and are uncorrected. Infrared data were obtained from a Perkin-Elmer Model 457 or 1320 spectrophotometer. ^1H NMR data were obtained on JEOL FX-90Q 90-MHz, Perkin-Elmer R32 90-MHz, and Bruker WM250 255-MHz spectrometers and are expressed as δ values. ^{13}C NMR data were obtained on the JEOL FX-90Q spectrometer operating at 22.5 MHz [heteronuclear decoupling was used unless multiplicities are indicated (obtained by off-resonance decoupling)] and are expressed as δ values. Mass spectral data were obtained on an AEI MS-902 instrument at 70 eV. TLC data were obtained on 2.5 × 7.5 cm silica gel plates (Bakerflex IB2-F), and products were detected by UV and/or iodine staining. The silica used in column chromatography was Merck 60 (230–400 mesh ASTM, catalog number 9385). 3-Oxo-1,2-diazetidinium tosylates employed as starting materials were prepared as described in ref 5.

2-(Trimethylsilyl)ethyl Chloroacetate. A solution of 10.1 mL (125 mmol) of chloroacetyl chloride in 20 mL of methylene chloride was dripped into a solution of 14.93 g (125 mmol) of 2-(trimethylsilyl)ethanol in 50 mL of methylene chloride at 0 °C under nitrogen. The reaction mixture was slowly warmed to room temperature, stirred for 24 h, then washed with three 100-mL portions of 0.5 N hydrochloric acid and three 100-mL portions of saturated ammonium chloride, then dried ($MgSO_4$), and evaporated under reduced pressure. The residual oil was distilled to give 24.1 g (99%) of the product as a colorless liquid: bp 72–75 °C (0.5 mm); IR (neat) 2945, 2895, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) 4.3–4.2 (m, 2 H), 4.01 (s, 2 H), 1.05–0.95 (m, 2 H), 0.03 (s, 9H).

Anal. Calcd for $C_7H_{15}ClO_2Si$: C, 43.18; H, 7.75; Cl, 18.21. Found: C, 42.84; H, 7.84; Cl, 18.39.

2-(Trimethylsilyl)ethyl Iodoacetate. A mixture of 24.34 g (125 mmol) of 2-(trimethylsilyl)ethyl chloroacetate and 30 g of sodium iodide in 100 mL of acetone was heated at 60 °C for 3 h, cooled to room temperature, filtered, and evaporated under reduced pressure. The residue was taken up in methylene chloride, washed with three 100-mL portions of water, dried ($MgSO_4$), and evaporated. The residual oil was distilled to give 33.67 g (94%) of the product as a pale pink liquid: bp 68–69 °C (0.35 mm); IR (neat) 1730 cm^{-1}; ^1H NMR ($CDCl_3$) 4.25–4.15 (m, 2 H), 3.65 (s, 2 H), 1.05–0.95 (m, 2 H), 0.03 (s, 9 H).

Anal. Calcd for $C_7H_{15}IO_2Si$: C, 29.38; H, 5.28; I, 44.34. Found: C, 29.70; H, 5.09; I, 44.11.

1-Isopropylidene-4-methyl-3-oxo-1,2-diazetidinium Inner Salt. Potassium carbonate (4 g, pellets freshly ground into powder) was added to a mixture of 1.29 g (5 mmol) of 4-methyl-3-oxo-1,2-diazetidinium tosylate in 25 mL of reagent grade acetone, and the mixture was stirred for 1 h. It was then filtered through Celite, and the filtrate was evaporated under reduced pressure to give an oil. The oil was taken up in methylene chloride, dried ($MgSO_4$), and filtered through Celite and the filtrate evaporated under reduced pressure to give 0.45 g (71%) of the product as a hydroscopic oil, which crystallized upon standing in a desiccator. The material decomposed upon exposure to moist air but was slightly more stable than the 4-unsubstituted material: IR (neat) 3480 (br), 2980, 2940, 1760, 1649, 1450, 1379, 1319, 1259, 1218, 1139, 1115, 1070, 1009, 903, 802, 732 cm^{-1}; ^1H NMR ($CDCl_3$) 5.56 (q, J = 7.0 Hz, 1 H), 2.27 and 2.24 (2 s, 6 H), 1.71 (d, J = 7.0 Hz, 3 H); LRMS (70 eV), m/z (relative intensity) 126 (M^+, 25), 99 (30), 98 (25), 84 (100); HRMS calcd for $C_6H_{10}N_2O$ m/z 126.0793, found m/z 126.0788 ± 0.0013.

N-2 Alkylation Procedure A. The requisite alkyl iodide (3 equiv) and the corresponding isolated N-1-substituted 1,2-diazetidin-3-one in DMF or THF (5 mL/mol) were stirred at room temperature with an excess of sodium bicarbonate (3 g/5 mmol) for 3 days. Products were isolated by column chromatography on silica gel with the solvent mixture and R_f values indicated.

2-[((Benzyloxy)carbonyl)methyl]-4-methyl-1-(3-phenylprop-2-en-1-yl)-1,2-diazetidin-3-one (7b): by procedure A (in DMF); yield 10% (R_f 0.25 in 2:3 ether/petroleum ether), along with 19% of recovered starting material; IR (neat) 1780, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) 7.33 (s, 10 H), 6.64 (d, J = 16 Hz, 1 H), 6.24 (dt, J_1 = 16 Hz, J_2 = 6 Hz, 1 H), 5.16 (s, 2 H), 4.13 (m, 2 H), 3.96 (q, J = 8 Hz, 1 H), 3.62 (m, 2 H), 1.44 (d, J = 8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 171.5, 167.4, 136.5, 135.0, 128.7, 128.6, 128.1, 126.5, 123.6, 75.2, 67.4, 65.2, 48.0, 14.3; HRMS calcd for $C_{21}H_{22}N_2O_3$ m/z 350.1630, found m/z 350.1638 ± 0.0035.

2-[((Benzyloxy)carbonyl)methyl]-4-ethyl-1-(3-phenylprop-2-en-1-yl)-1,2-diazetidin-3-one (7c): by procedure A (in DMF); yield 45% of a pale yellow oil (R_f = 0.3 in 30:70 ether/petroleum ether); IR (neat) 1770, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) 7.31 (s, 10 H), 6.61 (d, J = 16.1 Hz, 1 H), 6.21 (dt, J_1 = 16.1 Hz, J_2 = 6 Hz, 1 H), 5.13 (s, 2 H), 4.13, 4.11 (2 s, 2 H), 3.84 (t, J = 7.25 Hz, 1 H), 3.7–3.4 (m, 2 H), 1.84 (quintet, J = 7.25 Hz, 2 H), 0.99 (t, J = 7.25 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 170.6, 167.3, 136.4, 135.1, 134.8, 128.7, 128.6, 128.4, 128.0, 126.4, 123.8, 80.6, 67.2, 62.5, 47.8, 22.6, 10.1; HRMS calcd for $C_{22}H_{24}N_2O_3$ m/z 364.1787, foumd m/z 364.1770 ± 0.0036.

2-[((Benzyloxy)carbonyl)methyl]-1-(2-methyl-4-phenylbut-3-en-2-yl)-1,2-diazetidin-3-one (7d): by procedure A (in DMF); yield 40%; mp 73–78 °C (R_f 0.6 in ether/petroleum ether 1:1); IR (Nujol) 1770, 1738 cm^{-1}; ^1H NMR ($CDCl_3$) 7.33 (s, 10 H), 6.55, 6.31 (2 d, J = 16 Hz, 2 H), 5.15 (s, 2 H), 4.10 (m, 4 H), 1.31 (s, 6 H); ^{13}C NMR ($CDCl_3$) 170.2, 167.5, 136.6, 135.2, 132.5, 130.7, 128.7, 128.0, 126.5, 67.3, 61.5, 60.9, 50.4, 24.9, 21.1.

Anal. Calcd for $C_{22}H_{24}N_2O_3$: C, 72.51; H, 6.64; N, 7.69. Found: C, 72.29; H, 6.78; N, 7.42.

2-[((Benzyloxy)carbonyl)methyl]-4-methyl-1-(2-methyl-4-phenylbut-3-en-2-yl)-1,2-diazetidin-3-one (7e): by procedure A (in DMF) from **4e**; yield 85% (yellow oil, R_f = 0.5 in 50:50 ether/petroleum ether); IR (neat) 1780, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) 7.32 (s, 10 H), 6.57, 6.36 (2 d, J = 16 Hz, 2 H), 5.21, 5.06 (2 d, J = 11.5 Hz, 2 H), 4.27, 3.99 (2 d, J = 17.8 Hz, 2 H), 4.12 (q, superimposed, J = 7.2 Hz, 1 H), 1.42 (d, J = 7.2 Hz, 3 H), 1.31, 1.25 (2 s, 6 H); ^{13}C NMR ($CDCl_3$) 172.8, 167.3, 136.5, 135.0, 133.0, 130.1, 128.5, 128.4, 128.3, 127.5, 126.3, 68.4, 67.0, 60.7, 49.6, 25.2, 21.0, 15.1; HRMS calcd for $C_{23}H_{26}N_2O_3$ m/z 378.1943; found m/z 378.1922 ± 0.0038.

4-Ethyl-1-(3-phenylprop-2-enyl)-2-[((2-(trimethylsilyl)-ethoxy)carbonyl)methyl]-1,2-diazetidin-3-one (7f): by pro-

cedure A (in DMF); 37% yield; IR (neat) 1778, 1745 cm^{-1}; ^1H NMR ($CDCl_3$) 7.31 (m, 5 H), 6.60 (d, J = 16 Hz, 1 H), 6.22 (dt, J_1 = 16 Hz, J_2 = 6 Hz, 1 H), 4.18 (m, 2 H), 4.04 (br s, 2 H), 3.82 (t, J = 7 Hz, 1 H), 3.64–3.54 (m, 2 H), 1.89 (q, J = 7 Hz, 2 H), 1.01 (t, J = 7 Hz, 3 H), 0.92 (m, 2 H), 0.00 (s, 9 H); ^{13}C NMR ($CDCl_3$) 170.4 (s), 167.3 (s), 136.2 (d), 134.6 (d), 128.4 (d), 127.7 (s), 126.2 (d), 123.6 (d), 80.3 (d), 63.6 (t), 62.3 (t), 47.6 (t), 22.5 (t), 17.1 (t), 9.9 (q), −1.8 (q); HRMS calcd for $C_{20}H_{30}N_2O_3Si$ m/z 374.2025, foumd m/z 374.2039 ± 0.004.

4-Methyl-1-(2-methyl-4-phenylbut-3-en-2-yl)-2-[((2-(trimethylsilyl)ethoxy)carbonyl)methyl]-1,2-diazetidin-3-one (7g): by procedure A (in DMF); 76% yield of **7g** as a pale yellow oil; IR (neat) 1775, 1740 cm^{-1}; ^1H NMR ($CDCl_3$) 7.32 (m, 5 H), 6.45 (s, 2 H), 4.3–4.0 (m, 5 H), 1.44 (d, J = 7.03 Hz, 3 H), 1.30, 1.25 (2 s, 6 H), 0.89 (m, 2 H), 0.00 (s, 9 H); HRMS calcd for $C_{21}H_{32}N_2O_3Si$ m/z 388.2182, found m/z 388.2204 ± 0.004.

2-[(Benzyloxy)carbonyl]-1-(2-methyl-4-phenylbut-3-en-2-yl)imidazolidin-4-one (8a). To a stirred solution of 0.202 g (1 mmol) of 1-(2-methyl-4-phenylbut-3-en-2-yl)]-1,2-diazetidin-3-one[4] and 0.572 g (2 mmol) of benzyl iodoacetate in 20 mL of methylene chloride was added 0.304 g (2 mmol) of DBU. After 5 min, the solvent was evaported under reduced pressure, and the residue was chromatographed on silica gel with ether/petroleum ether (2:3) to give **8a** as a colorless gum (60%): IR (neat) 3200 (br), 1750–1700 (br) cm^{-1}; ^1H NMR ($CDCl_3$) 7.28 (s, 10 H), 6.45, 6.17 (2 d, J = 16 Hz, 2 H), 5.09 (s, 2 H), 4.90 (s, 1 H), 3.48 (s, 2 H), 1.24 (s, 6 H); ^{13}C NMR ($CDCl_3$) 176.3, 170.8, 136.7, 135.2, 134.8, 129.1, 128.4, 128.2, 128.0, 127.5, 126.3, 71.0, 67.1, 58.9, 48.9, 25.1, 23.2; HRMS calcd for $C_{22}H_{24}N_2O_3$ m/z 364.1787, found m/z 364.1784 ± 0.004.

***N*,*N*-Bis[((benzyloxy)carbonyl)methyl]-*N*-(3-phenylprop-2-en-1-yl)amine (9).** Sodium bicarbonate (1.20 g) was added to a stirred solution of 0.60 g of 1-(3-phenylprop-2-en-1-yl)-1,2-diazetidin-3-one[4] and 0.90 g of benzyl iodoacetate in 6 mL of DMF. The mixture was stirred for 12 h, water was added, and the mixture was extracted with three 100-mL portions of ether. The ether extracts were washed with water and dried ($MgSO_4$), and the solvent was evaporated. The residue was chromatographed on silica gel with ether/petroleum ether (7:13) to give **9** as a colorless gum: yield 0.04 g (3%) (R_f 0.5 in 1:3 ether/petroleum ether). When this reaction was carried with 4-methyl-1-(3-phenylprop-2-en-1-yl)-1,2-diazetidin-3-one, compound **9** was formed in 13% yield: IR (neat) 1750 cm^{-1}; ^1H NMR ($CDCl_3$) 7.32 (s, 15 H), 6.33 (d, J = 16 Hz, 1 H), 6.24 (dt, J_1 = 16 Hz, J_2 = 7 Hz, 1 H), 5.12 (s, 4 H), 3.66 (s, 4 H), 3.54 (d, J = 7 Hz, 2 H); ^{13}C NMR ($CDCl_3$) 171.0, 136.7, 135.8, 133.4, 128.6, 128.3, 127.7, 126.6, 126.4, 66.3, 56.8, 54.4; HRMS calcd for $C_{27}H_{27}NO_4$ m/z 429.1940, found m/z 429.1947 ± 0.004.

1-(1,1-Diphenylethyl)-4-methyl-1,2-diazetidin-3-one (4f). Methylmagnesium bromide (7.0 mL of a 2.9 M solution in ether, 20.7 mmol) was added to a mixture of 2.50 g (10 mmol) of 1-(1,1-diphenylmethylene)-4-methyl-3-oxo-1,2-diazetidinium inner salt in 40 mL of THF at 0 °C. After 1 h, saturated ammonium chloride was added, and the mixture was extracted with three 20-mL portions of ether. The combined ether extracts were dried ($MgSO_4$) and evaporated, and the residue was chromatographed on silica gel with 30:70 ether/petroleum ether (R_f = 0.45 in 50:50 ether/petroleum ether) to give 1.92 g (72%) of **4f** as a white foam: mp 118–121 °C; IR (KBr) 3200, 1765 cm^{-1}; ^1H NMR ($CDCl_3$) 7.6–7.2 (m, 11 H), 3.89 (q, J = 7.0 Hz, 1 H), 1.83 (s, 3 H), 1.27 (d, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 170.9, 144.6, 142.4, 128.0, 127.8, 127.3, 68.6, 68.3, 22.0, 15.3.

Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.44; H, 7.10; N, 10.47.

1-(1,1-Diphenylbut-3-enyl)-4-methyl-1,2-diazetidin-3-one (4g). A mixture of 7.5 mL of 2 M allylmagnesium chloride in THF (1.5 equiv) and 2.50 g (10 mmol) of 1-(1,1-diphenylmethylene)-4-methyl-3-oxo-1,2-diazetidinium inner salt in 50 mL of THF at 0 °C under nitrogen was stirred for 1 h and then quenched with 25 mL of saturated ammonium chloride solution. The mixture was then extracted with three 25-mL portions of ether, and the combined extracts were dried ($MgSO_4$) and evaporated. Column chromatography of the residual oil over silica gel with 30:70 ether/petroleum ether (R_f = 0.25) gave 1.09 g (37%) of **4g** as a crystalline solid: mp 132–136 °C; IR (KBr) 1770, 1490, 1440 cm^{-1}; ^1H NMR ($CDCl_3$) 8.08 (s, 1 H), 7.28–7.22 (m, 10 H), 5.9–5.4 (m, 1 H), 5.0–4.7 (m, 2 H), 3.71 (q, J = 7.0 Hz, 1 H), 2.85 (d, J = 6.6 Hz, 2 H), 1.20 (d, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 170.1, 142.2, 137.7, 133.2, 130.0, 128.4, 127.4, 126.8, 117.5, 71.9, 68.2, 43.3, 15.0.

Anal. Calcd for $C_{19}H_{20}N_2O$: C, 78.05; H, 6.89; N, 9.58. Found: C, 77.77; H, 6.76; N, 9.58.

1-(1,1-Diphenylprop-2-en-1-yl)-4-methyl-1,2-diazetidin-3-one (4h). A solution of 40 mL of 1 M vinylmagnesium bromide in THF, 6.43 g (25.7 mmol) of 1-(1,1-diphenylmethylene)-4-methyl-3-oxo-1,2-diazetidinium inner salt, and 175 mL of dry THF at 0 °C was stirred for 2 h and allowed to warm to room temperature, saturated ammonium chloride added, and the mixture extracted with three 100-mL portions of ether. The combined ether extracts were dried ($MgSO_4$) and evaporated, and the residual oil was chromatographed on silica gel with 50:50 ether/petroleum ether. The material with R_f 0.45 was collected and rechromatographed with 20:80 ether/petroleum ether to give 0.35 g (5%) of **4h** (R_f = 0.45 in 50:50 ether/petroleum ether): IR (neat) 3000, 1765 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–7.2 (m, 11 H), 6.51 (dd, J_1 = 17.4, J_2 = 11.0 Hz, 1 H), 5.61 (dd, J_1 = 11.0 Hz, J_2 = 1.3 Hz, 1 H), 5.21 (dd, J_1 = 17.4 Hz, J_2 = 1.3 Hz, 1 H), 4.03 (q, J = 7.25 Hz, 1 H), 1.45 (d, J = 7.25 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 170.2, 141.3, 137.3, 128.6, 128.5, 127.9, 127.7, 127.5, 127.2, 120.5, 78.5, 69.4, 15.6; LRMS (70 eV), m/z (relative intensity) 278 (M^+, 5), 193 (100), 178 (15), 165 (13), 115 (47), 105 (16), 91 (24), 77 (18); HRMS calcd for $C_{18}H_{18}N_2O$ m/z 278.1419, found m/z 278.1397 ± 0.0028.

4-Methyl-1-(2-methylbut-3-en-2-yl)-1,2-diazetidin-3-one (4i). Vinylmagnesium bromide (6 mL, 1.2 equiv) was added to a solution of 0.63 g (5 mmol) of 1-isopropylidene-4-methyl-3-oxo-1,2-diazetidinium inner salt in 25 mL of THF at 0 °C under nitrogen and the reaction mixture stirred for 1 h and then worked up as described above to give 0.28 g (36%) of **4i** as an oil (R_f = 0.45 in 50:50 ether/petroleum ether): IR (neat) 1765 cm^{-1}; ^1H NMR ($CDCl_3$) 6.16–5.84 (m, 1 H), [5.3–4.8 (br s) with 5.25–5.05 (m), superimposed, total 3 H], 4.01 (q, J = 7.25 Hz, 1 H), 1.36 (d, J = 7.25 Hz, 3 H), 1.31 (s, 6 H); ^{13}C NMR ($CDCl_3$) 171.9, 140.1, 115.8, 68.8, 60.3, 23.7, 21.7, 15.5; LRMS (70 eV), m/z (relative intensity) 154 (M^+, 6), 139 (7), 111 (9), 97 (8), 96 (12), 69 (100); HRMS calcd for $C_8H_{14}N_2O$ m/z 154.1106, found m/z 154.1108 ± 0.0015.

4-Methyl-1-(2-methylpent-4-en-2-yl)-1,2-diazetidin-3-one (4j). This material was prepared from 0.50 g (4 mmol) of 1-isopropylidene-4-methyl-3-oxo-1,2-diazetidinium inner salt and 12 mL of 1 M allylmagnesium chloride in ether as described above: yield 0.95 g (63%) (R_f = 0.25 in 50:50 ether/petroleum ether); IR (neat) 3200 (br), 2970, 1770, 1639 cm^{-1}; ^1H NMR ($CDCl_3$) 8.0 (br s, 1 H), 5.96–5.54 (m, 1 H), 5.17–5.03 (m, 1 H), 4.95–4.87 (m, 1 H), 4.07 (q, J = 7.0 Hz, 1 H), 2.04 (d, J = 7.0 Hz, 2 H), 1.30 (d, J = 7.0 Hz, 3 H), 0.95 (s, 6 H); ^{13}C NMR ($CDCl_3$) 171.4, 133.7, 117.4, 67.0, 58.6, 42.9, 20.5, 20.3, 15.0; LRMS (70 eV), m/z (relative intensity) 168 (M^+, 2), 153 (2), 127 (100), 110 (4), 99 (7), 84 (100); HRMS calcd for $C_9H_{16}N_2O$ m/z 168.1262, found m/z 168.1256 ± 0.0017.

N-2 Alkylation Procedure B. The requisite Grignard reagent was added to a solution of the appropriate diazetidinium inner salt in dry THF (5 mL/mol) at 0 °C under nitrogen. The reaction mixture was stirred for 1 h at 0 °C and then quenched with the alkyl iodide (3 equiv). The mixture was stirred at room temperature for 1–3 h (the course of the alkylation reaction was followed by TLC); longer reaction times often resulted in the formation of greater amounts of imidazolidinone ring-expansion byproducts. N-2-alkylated products were isolated by column chromatography on silica gel with the solvent mixture and R_f values indicated.

2,4-Dimethyl-1-(1,1-diphenylethyl)-1,2-diazetidin-3-one (7h): by procedure B; yield 77% (R_f = 0.55 in 50:50 ether/petroleum ether); mp 126–128 °C; IR (KBr) 1765 cm^{-1}; ^1H NMR ($CDCl_3$) 7.5–7.2 (m, 10 H), 3.80 (q, J = 7 Hz, 1 H), 2.77, 2.76 (s, total 3 H), 1.82 (s, 3 H), 1.27 (d, J = 7 Hz, 3 H).

Anal. Calcd for $C_{18}H_{20}N_2O$: C, 77.11; H, 7.19; N, 9.99. Found: C, 76.85; H, 7.28; N, 10.12.

2-[((Benzyloxy)carbonyl)methyl]-1-(1,1-diphenylethyl)-4-methyl-1,2-diazetidin-3-one (7i): by procedure B, yield 61%; by procedure A, yield 37% (R_f = 0.25 in 30:70 ether/petroleum ether); mp 92–94 °C; IR (neat) 1782, 1751 cm^{-1}; ^1H NMR ($CDCl_3$) 7.60–7.15 (m, 15 H), 5.30, 5.13 (2 d, J = 12.2 Hz, 2 H), 4.23, 3.32

(2 d, J = 18.0 Hz, 2 H), 3.92 (q, J = 7.0 Hz, 1 H), 1.87 (s, 3 H), 1.37 (d, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 172.0, 166.9, 144.5, 142.3, 129.1, 128.4, 127.9, 127.8, 127.1, 69.3, 67.7, 66.9, 47.6, 21.1, 15.0; LRMS (70 eV), m/z (relative intensity) 414 (M^+, 4), 399 (1), 353 (2), 337 (1), 291 (2), 279 (2), 235 (10), 207 (10), 181 (100), 165 (100); HRMS calcd for $C_{26}H_{26}N_2O_3$ m/z 414.1943, found m/z 414.1926 ± 0.0041.

Anal. Calcd: C, 75.34; H, 6.32; N, 6.76. Found: C, 75.54; H, 6.05; N, 6.68.

1-(1,1-Diphenylethyl)-2-[(benzyloxy)carbonyl]-3-[((benzyloxy)carbonyl)methyl]-5-methyl-4-imidazolidinone (8b). This compound was also obtained during the above silica gel chromatography (R_f = 0.15 in 30:70 ether/petroleum ether): IR (neat) 3060, 3035, 2985, 1750, 1723 cm^{-1}; mixture of diastereoisomers A and B (3:1 ratio). Isomer A: ^{1}H NMR ($CDCl_3$) 7.6–7.2 (m, 20 H), 5.2–3.5 (m, 8 H), 2.00 (s, 3 H), 1.40 (d, J = 6.8 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 175.6, 169.7, 167.7, 144.7, 134.9, 128.5–126.8 (Ar m), 75.2, 67.1, 63.8, 57.0, 42.2, 21.6, 19.7. Isomer B: ^{1}H NMR ($CDCl_3$) 7.6–7.2 (m, 20 H), 5.2–3.5 (m, 8 H), 2.18 (s, 3 H), 1.13 (d, J = 6.6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 174.7, 170.8, 167.5, 144.2, 134.7, 128.5–126.8 (Ar m), 75.2, 68.7, 63.8, 55.3, 41.7, 25.0, 18.3; LRMS (70 eV), m/z (relative intensity) 562 (M^+, 0.5), 547 (2), 427 (50), 247 80), 207 (80), 181 (100), 165 (90); HRMS calcd for $C_{35}H_{34}N_2O_5$ m/z 547.2233, found m/z 547.2168 ± 0.0055.

2,4-Dimethyl-1-(1,1-diphenylbut-3-en-1-yl)-1,2-diazetidin-3-one (7j): by procedure B; yield 70% (R_f = 0.7 in 50:50 ether/petroleum ether); mp 121–124 °C; IR (neat) 3050, 2960, 2909, 1771, 1491, 1442 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.6–7.2 (m, 10 H), 5.8–5.3 (m, 1 H), 4.95 (m, 1 H), 4.80 (m, 1 H), 3.74 (q, J = 7.0 Hz, 1 H), 2.94–2.84 (m, 2 H), 2.84, 2.83 (2 s, 3 H), 1.46 (d, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 170.4 (s), 142.3 (s), 136.1 (s), 132.9 (d), 130.3 (d), 129.2 (d), 127.7 (d), 127.2 (d), 117.9 (t), 72.2 (s), 68.5 (d), 42.9 (t), 34.1 (q), 15.4 (q).

Anal. Calcd for $C_{20}H_{22}N_2O$: C, 78.40; H, 7.24; N, 9.14. Found: C, 78.26; H, 7.24; N, 8.96.

2-[((Benzyloxy)carbonyl)methyl]-1-(1,1-diphenylbut-3-en-1-yl)-4-methyl-1,2-diazetidin-3-one (7k): by procedure A; yield 55% (R_f = 0.5 in 50:50 ether/petroleum ether); mp 95–99 °C; IR ($CHBr_3$) 1785, 1750, 1492, 1445 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.4–7.1 (m, 15 H), 5.7–5.2 (m, 1 H), 5.31, 5.14 (2 d, J = 12 Hz, 2 H), 5.0–4.6 (m, 2 H), 4.26, 3.40 (2 d, J = 18 Hz, 2 H), 3.81 (q, J = 7.0 Hz, 1 H), 2.84 (br t, J = 6.7 Hz, 2 H), 1.52 (d, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 171.5, 166.8, 142.4, 135.8, 135.1, 132.7, 130.4, 128.8, 128.4, 127.7, 127.3, 127.2, 127.0, 117.9, 72.1, 69.1, 67.0, 47.9, 42.6, 14.9; LRMS (70 eV), m/z (relative intensity) 440 (M^+, 1), 399 (6), 207 (100), 191 (8), 178 (9), 167 (11), 165 (22), 129 (100), 91 (100); HRMS calcd for $C_{28}H_{28}N_2O_3$ m/z 440.2100, found m/z 440.2089 ± 0.0044.

2-[(Benzyloxy)carbonyl]-3-[((benzyloxy)carbonyl)methyl]-1-(1,1-diphenylbut-3-en-1-yl)-5-methyl-4-imidazolidinone (8c). This compound was obtained in 37% yield during the silica gel chromatography above (R_f = 0.4 in 50:50 ether/petroleum ether): IR (neat) 1752, 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.65–7.15 (m, 20 H), 5.9–5.3 (m, 2 H), 5.25–4.82 (m, 6 H), 4.10, 3.70 (2 d, J = 17.8 Hz, 2 H), 3.85 (q, J = 7.0 Hz, 1 H), 3.20 (br d, J = 6.4 Hz, 2 H), 1.51 (d, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 175.3, 169.8, 167.5, 141.8, 141.0, 135.0, 133.9, 128.8, 128.6, 128.4, 128.3, 128.0, 127.9, 127.4, 126.1, 117.8, 75.9, 72.0, 67.2, 67.0, 57.0, 45.1, 42.6, 20.2; LRMS (70 eV), m/z (relative intensity) 588 (M^+, 0.5), 547 (9), 453 (5), 247 (22), 207 (56), 165 (6), 129 (90), 115 (5), 105 (8), 91 (100); HRMS calcd for $C_{34}H_{31}N_2O_5$ (M^+ – allyl) m/z 547.2233, found m/z 547.2241 ± 0.0055.

2,4-Dimethyl-1-(1,1-diphenylprop-2-en-1-yl)-1,2-diazetidin-3-one (7l): by procedure B, yield 6.4%; by procedure A, yield 10% (R_f = 0.5 in 50:50 ether/petroleum ether); IR (neat) 1770 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.7–7.1 (m, 10 H), 6.46 (dd, J = 17.35, 10.99 Hz, 1 H), 5.58 (dd, J = 10.99, 1.32 Hz, 1 H), 5.14 (dd, J = 17.35, 1.32 Hz, 1 H), 3.91 (q, J = 7.03 Hz, 1 H), 2.65, 2.64 (2 s, 3 H), 1.42 (d, J = 7.03 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 170.3, 142.4, 137.3, 132.3, 130.0, 128.8, 128.4, 127.9, 127.8, 127.3, 127.1, 120.8, 73.8, 69.9, 33.6, 15.9; LRMS (70 eV), m/z (relative intensity) 292 (M^+, 2), 193 (100), 178 (31), 165 (18), 115 (100), 105 (19), 91 (5); HRMS calcd for $C_{19}H_{20}N_2O$ m/z 292.1575, found m/z 292.1557 ± 0.0030.

2,4-Dimethyl-1-(2-methylbut-3-en-2-yl)-1,2-diazetidin-3-one (7m): by procedure B, yield 2%; by procedure A, yield 13% (R_f = 0.5 in 50:50 ether/petroleum ether); IR (neat) 2980, 1778 cm^{-1}; ^{1}H NMR ($CDCl_3$) 5.95 (dd, J = 18.02, 10.11 Hz, 1 H) [5.13 (dd, J = 10.11, 1.32 Hz), 5.10 (dd, J = 18.02, 1.32 Hz), total 2 H], 3.89 (q, J = 7.03 Hz, 1 H), 2.96, 2.95 (2 s, 3 H), 1.85 (d, J = 7.03 Hz, 3 H), 1.15, 1.11 (2 s, 6 H); ^{13}C NMR ($CDCl_3$) 171.6, 141.1, 115.2, 68.0, 60.8, 35.0, 24.7, 21.9, 15.5; LRMS (70 eV), m/z (relative intensity) 168 (M^+, 3), 141 (3), 115 (8), 98 (20), 69 (39), 59 (100); HRMS calcd for $C_9H_{16}N_2O$ m/z 168.1262, found m/z 168.1258 ± 0.0017.

2-[((Benzyloxy)carbonyl)methyl]-4-methyl-1-(2-methylpent-4-en-2-yl)-1,2-diazetidin-3-one (7n): by procedure B, yield 23%; by procedure A, yield 50% (R_f = 0.6 in 50:50 ether/petroleum ether); IR (neat) 2975, 2930, 1786, 1755 (sh) cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.33 (s, 5 H), 6.02–5.56 (m, 1 H), 5.18–4.92 (m, 4 H), 4.28, 3.93 (2 d, J = 17.6 Hz, 2 H), 4.12 (q, J = 7.0 Hz, 1 H), 2.11 (d, J = 6.8 Hz, 2 H), 1.38 (d, J = 7.0 Hz, 3 H), 1.03, 1.01 (2 s, 6 H); ^{13}C NMR ($CDCl_3$) 173.4, 167.2, 135.0, 133.7, 128.2, 117.7, 67.4, 67.0, 59.8, 49.9, 43.3, 21.9, 21.5, 15.1; LRMS (70 eV), m/z (relative intensity) 316 (M^+, 2), 301 (0.5), 275 (100), 247 (2), 217 (20), 206 (4), 149 (5), 148 (10), 91 (100); HRMS calcd for $C_{18}H_{24}N_2O_3$ m/z 316.1787, found m/z 316.1766 ± 0.0032.

2-[(Benzyloxy)carbonyl]-5-methyl-1-(2-methylpent-4-en-2-yl)-4-imidazolidinone (8d). By procedure B, using 1-isopropylidene-4-methyl-1,2-diazetidinium inner salt, the above imidazolidinone was obtained in 25% yield from column chromatography on silica gel with 50:50 ether/petroleum ether (R_f = 0.25), along with the corresponding 3-((benzyloxy)carbonyl)-methyl derivative **8e** (see below) and **7n** (23%): IR (neat) 3240 (br), 2978, 1750, 1718 (br) cm^{-1}; ^{1}H NMR ($CDCl_3$) 8.08 (br s, 1 H), 7.32 (s, 5 H), 6.00–5.40 (m, 1 H), 5.15–4.90 (m, 5 H), 3.57 (q, J = 7.0 Hz, 1 H), 2.13 (d, J = 6.8 Hz, 2 H), 1.29 (d, J = 7.0 Hz, 3 H), 1.03 (s, 6 H); ^{13}C NMR ($CDCl_3$) 179.1, 171.3, 135.2, 134.1, 128.3, 128.1, 127.9, 117.5, 69.1, 66.9, 57.7, 54.7, 43.6, 24.2, 20.7.

Anal. Calcd for $C_{18}H_{24}N_2O_3$: C, 68.33; H, 7.65; N, 8.85. Found: C, 68.69, 7.61; N, 8.54.

2-[(Benzyloxy)carbonyl]-3-[((benzyloxy)carbonyl)-methyl]-5-methyl-1-(2-methylpent-4-en-2-yl)-4-imidazolidinone (8e). This compound was also obtained in the above preparation during the silica gel chromatography: yield 27% (R_f = 0.50); IR (neat) 2978, 1749, 1721 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.36 (s, 10 H), 6.0–5.4 (m, 1 H), 5.19, 5.15 (2 s, 4 H), 5.19–4.40 (m, 3 H), 4.65 (s, 2 H), 3.69 (q, J = 7.0 Hz, 1 H), 2.19 (br d, J = 6.8 Hz, 2 H), 1.32 (d, J = 7.0 Hz, 3 H), 1.07 (s, 6 H); ^{13}C NMR ($CDCl_3$) 175.4, 170.1, 167.8, 134.9, 134.3, 134.1, 128.3, 127.9, 127.1, 126.6, 117.4, 74.3, 72.8, 67.0, 64.6, 54.8, 43.6, 41.9, 23.9, 23.7, 20.4; LRMS (70 eV), m/z (relative intensity) 464 (M^+, 1), 449 (3), 423 (16), 373 (17), 329 (67), 279 (8), 247 (57), 197 (9), 91 (100); HRMS calcd for $C_{26}H_{29}N_2O_5$ m/z 449.2078, found m/z 449.2085 ± 0.0045.

2,4-Dimethyl-1-(2-methyl-4-phenylbut-3-en-2-yl)-1,2-diazetidin-3-one (7o): by procedure B, yield 25%; by procedure A, yield 72% (R_f = 0.4 in 50:50 ether/petroleum ether); IR (neat) 2971, 2921, 1772 cm^{-1}; ^{1}H NMR ($CDCl_3$) 7.41–7.22 (m, 5 H), 6.58, 6.36 (2 d, J = 16.3 Hz, 2 H), 4.03 (q, J = 7.25 Hz, 1 H), 3.04, 3.03 (2 s, 3 H), 1.38 (d, J = 7.25 Hz, 3 H), 1.31 (s, 6 H); ^{13}C NMR ($CDCl_3$) 171.5, 136.5, 132.6, 130.0, 128.4, 127.5, 126.2, 67.8, 60.5, 34.9, 25.0, 22.1, 15.4; HRMS calcd for $C_{15}H_{20}N_2O$ m/z 244.1575, found m/z 244.1566 ± 0.0024.

2-[((Benzyloxy)carbonyl)methyl]-4-methyl-1-(2-methyl-1-oxoprop-2-yl)-1,2-diazetidin-3-one (12a). Oxygen was bubbled through a colution of 1.38 g (3.7 mmol) of **7e** in 40 mL of methylene chloride while the solution was being cooled to −78 °C. Ozone was bubbled through the stirred, cold solution until it became blue. Dimethyl sulfide was then added and the reaction mixture was stirred for 30 min at −78 °C and then at room temperature for 2 h. The mixture was then evaporated under reduced pressure to give an oil, which was chromatographed on silica gel with 50:50 ether/petroleum ether to give 0.41 g (36%) of **12a** as a colorless oil (R_f = 0.4): IR (neat) 1788, 1750 cm^{-1}; ^{1}H NMR ($CDCl_3$) 9.48 (s, 1 H), 7.32 (s, 5 H), 5.15 (s, 2 H), 4.26, 3.87 (2 d, J = 18 Hz, 2 H), 4.23 (q, J = 7.0 Hz, 1 H), 1.43 (d, J = 7.0 Hz, 3 H), 1.22, 1.17 (s, 6 H); ^{13}C NMR ($CDCl_3$) 201.9, 172.1, 167.0, 134.9, 133.0, 129.8, 128.2, 69.0, 67.1, 60.4, 48.9, 19.3, 15.0, 14.6; HRMS calcd for $C_{16}H_{20}N_2O_4$ m/z 304.1423, found m/z 304.1412 ± 0.0030.

6-[(Benzyloxy)carbonyl]-2,8,8-trimethyl-3-oxo-1,7-diaza-4-oxabicyclo[3.2.1]octane (14a). The crude product from the

ozonolysis of **7e** (1.0 g), as described above, was dissolved in 50 mL of dry THF and added to a solution of LDA (1.7 mL of *n*-butyllithium, 1.6 M in hexane, and 0.41 mL of diisopropylamine) in 10 mL of dry THF at −78 °C under nitrogen. After 10 min, saturated ammonium chloride was added, the mixture was extracted with ether, and the ether layers were dried ($MgSO_4$) and evaporated. Chromatography of the residual oil on silica gel with 50:50 ether/petroleum ether gave 0.08 g (5%) of **14a** as a white solid (R_f = 0.4): mp 80–84 °C; IR (KBr) 3280, 1740 cm^{-1}; 250-MHz ^1H NMR ($CDCl_3$) 7.35 (s, 5 H), 5.24 (d, J = 11.9 Hz, 1 H), 5.16 (d, J = 11.9 Hz, 1 H), 4.83 (s, 1 H), 4.68 (dd, J_1 = 6.0 Hz, J_2 = 1.4 Hz, 1 H), 4.21 (d, J = 6.0 Hz, 1 H), 3.78 (qd, J_1 = 7.2 Hz, J_2 = 1.4 Hz, 1 H), 1.46 (d, J = 7.2 Hz, 3 H), 1.40 (s, 3 H), 0.92 (s, 3 H); ^{13}C NMR ($CDCl_3$) 171.4 (s), 169.9 (s), 134.7 (s), 128.8 (d), 128.7 (d), 128.6 (d), 87.4 (d), 67.9 (t), 67.9 (d), 64.0 (s), 59.2 (d), 22.4 (q), 19.2 (q), 15.8 (q); LRMS (70 eV), m/z (relative intensity) 304 (M^+, 1), 275 (20), 260 (2), 125 (100); HRMS calcd for $C_{16}H_{20}N_2O_4$ m/z 304.1423, found m/z 304.1435 ± 0.003. The structure of **14a** was confirmed by single-crystal X-ray crystallography.

2-[(Benzyloxy)carbonyl]-5-methyl-1-(2-methyl-1-oxoprop-2-yl)-4-imidazolidinone (15a). This material was obtained during the silica gel chromatography above: yield 24% (R_f = 0.6 in ether); IR (neat) 1700 cm^{-1}; ^1H NMR ($CDCl_3$) 9.45 (s, 1 H), 7.33 (s, 5 H), 7.06 (br s, 1 H), 5.18 (s, 2 H), 4.68 (s, 1 H), 3.42 (q, J = 7.0 Hz, 1 H), 1.29 (d, J = 7.0 Hz, 3 H), 1.19 (s, 6 H); ^{13}C NMR ($CDCl_3$) 201.9, 179.2, 169.8, 128.6, 128.2, 69.8, 67.5, 67.0, 55.3, 20.7, 19.9, 18.9; LRMS (70 eV), m/z (relative intensity) 304 (M^+, 0.5), 275 (25), 205 (16), 169 (60), 141 (13), 139 (10), 122 (90), 105 (100); HRMS calcd for $C_{15}H_{19}N_2O_3$ (M^+ − CHO) m/z 275.1395, found m/z 275.1389 ± 0.0028.

4-Methyl-1-(2-methyl-1-oxoprop-2-yl)-2-[((2-(trimethylsilyl)ethoxy)carbonyl)methyl]-1,2-diazetidin-3-one (12b). Ozonolysis of compound **7g** (1.02 g, 2.6 mmol) as described above for the preparation of **12a** gave 0.31 g (38%) of the aldehyde **12b** as a colorless oil (R_f = 0.4 in 50:50 ether/petroleum ether): IR (neat) 1770, 1732 cm^{-1}; ^1H NMR ($CDCl_3$) 9.54 (s, 1 H), 4.30–3.65 [m, total 5 H, including superimposed doublets at 4.14, 3.76 (J = 16.1 Hz, 2 H)], 1.49 (d, J = 7.0 Hz, 3 H), 1.25, 1.20 (2 s, 6 H), 1.05–0.80 (m, 2 H), 0.02 (s, 9 H); LRMS (70 eV), m/z (relative intensity) 314 (M^+, 5), 285 (10), 257 (15), 185 (45), 84 (95), 73 (100): HRMS calcd for $C_{14}H_{26}N_2O_4Si$ m/z 314.1662, found m/z 314.1661 ± 0.003.

2,8,8-Trimethyl-6-[((2-(trimethylsilyl)ethoxy)carbonyl)methyl]-3-oxo-1,7-diaza-4-oxabicyclo[3.2.1]octane (14b). Treatment of **12b** with LDA, as described above in the preparation of **14a**, gave the title compound in 24% yield (R_f = 0.75 in 50:50 ether/petroleum ether): IR (neat) 3335, 2950, 1735 (br) cm^{-1}; ^1H NMR ($CDCl_3$) 4.77 (s, 1 H), 3.58 (br s, 1 H), 4.32–4.06 (m, 3 H), 3.73 (q, J = 7.0 Hz, 1 H), 1.44 (d, J = 7.0 Hz, 3 H), 1.39, 0.99 (2 s, 6 H), 1.05–0.76 (m, 2 H), 0.00 (s, 9 H); ^{13}C NMR ($CDCl_3$) 171.5 (s), 170.1 (s), 87.5 (d), 68.0 (d), 64.7 (s), 63.9 (t), 59.2 (d), 22.5 (q), 19.2 (q), 17.4 (t), 15.8 (q), −1.6 (q); LRMS (70 eV), m/z (relative intensity) 314 (M^+, 3), 285 (8), 270 (10), 125 (100), 84 (80), 73 (70); HRMS calcd for $C_{14}H_{26}N_2O_4Si$ m/z 314.1662, found m/z 314.1643 ± 0.0030.

Sodium 2,8,8-Trimethyl-3-oxo-1,7-diaza-4-oxabicyclo[3.2.1]octane-6-carboxylate (14c). Tetrabutylammonium fluoride (0.42 mL, 1 M in THF) was added to a stirred solution of 0.13 g of **14b** in 10 mL of THF, and the mixture was stirred for 12 h. Solvent was evaporated under reduced pressure, and the residue was triturated with ether/pentane (1:2). The residual solid was then passed through an Amberlite CG-120 (strongly acidic sulfonated polystyrene-type $RSO_3^-Na^+$) cation-exchange column to give 0.09 g of **14c**: ^1H NMR ($CDCl_3$) 4.75 (s, 1 H), 3.88 (q, J = 7 Hz, 1 H), 3.87 (s, 1 H), 1.23 (d, J = 7 Hz, 3 H), 1.26, 0.96 (2 s, 6 H).

2-[((Benzyloxy)carbonyl)methyl]-1-(2-carboxyprop-2-yl)-4-methyl-1,2-diazetidin-3-one (18a). The crude product from the ozonolysis of **7e** (1.01 g) was dissolved in 20 mL of acetone, cooled to 0 °C, and Jones reagent added dropwise until a definite orange color persisted for 5 min. Sodium bisulfite was added, the solution stirred for 10 min, and the acetone layer decanted. The residual solid was washed with ether, and the combined organic layers were then dried ($MgSO_4$). Chromatography on silica gel with 50:50 ether/petroleum ether gave 0.17 g (10%) of **18a** as a colorless oil (R_f = 0.25 in 50:50 ether/petroleum ether): IR (neat) 1780 (sh), 1750 (br) cm^{-1}; ^1H NMR ($CDCl_3$) 9.4 (br s, 1 H), 7.31 (s, 5 H), 5.14 (s, 2 H), 4.36 (q, J = 7.25 Hz, 1 H), 4.33, 3.98 (2 d, J = 17.5 Hz, 2 H), 1.34 (d, J = 7.25 Hz, 3 H), 1.33 (s, 6 H); ^{13}C NMR ($CDCl_3$) 177.1 (s), 172.7 (s), 167.3 (s), 134.9 (s), 128.3 (d), 128.1 (d), 69.5 (d), 67.0 (t), 64.4 (s), 48.9 (t), 23.0 (q), 19.0 (q), 15.0 (q); HRMS calcd for $C_{16}H_{20}N_2O_5$ m/z 320.1372, found m/z 320.1364 ± 0.0033.

1-(2-Carboxyprop-2-yl)-4-methyl-2-[((2-(trimethylsilyl)ethoxy)carbonyl)methyl]-1,2-diazetidin-3-one (18b). This compound was prepared in 42% yield in the same manner as the benzyl ester **18a** described above (R_f = 0.2 in 50:50 ether/petroleum ether): IR (neat) 3500 (br), 3150 (br) 2950, 1770 (sh), 1730 (br) cm^{-1}; ^1H NMR ($CDCl_3$) 7.47 (br s, 1 H), 4.4–3.8 (m, 5 H), 1.49 (d, J = 7.0 Hz, 3 H), 1.38 (s, 6 H), 1.08–0.89 (m, 2 H), 0.01 (s, 9 H); ^{13}C NMR ($CDCl_3$) 177.2 (s), 172.7 (s), 167.5 (s), 69.6 (d), 64.5 (s), 63.8 (t), 49.0 (t), 23.0 (q), 19.4 (q), 17.1 (t), 15.1 (q), −1.77 (q); HRMS calcd for $C_{14}H_{26}N_2O_5Si$ m/z 330.1579, found m/z 330.1584 ± 0.0003.

2-[(Benzyloxy)carbonyl]-5,5-diphenyl-7-methyl-8-oxo-1,6-diazabicyclo[4.2.0]oct-2-ene (22). A solution of 0.75 g (1.7 mmol) of **7k** in 60 mL of methylene chloride was cooled to −78 °C, and ozone was bubbled through the solution until it became blue (about 5–7 min). Dimethyl sulfide (2 mL) was added, the mixture was stirred at −78 °C for 2 h and evaporated under reduced pressure, and the residue was purified by column chromatography on silica gel with 30:70 ether/petroleum ether to give 0.19 g (26%) of **22** as an oil (R_f = 0.45 in 30:70 ether/petroleum ether) [a second product, β-phenylcinnamaldehyde (**21**), was isolated in 62% yield, R_f = 0.55]: IR (neat) 3043, 3018, 1780, 1749, 1662 cm^{-1}; ^1H NMR ($CDCl_3$) 7.45–7.20 (m, 15 H), 4.95–4.85 (m, 2 H), 4.5–3.3 (m, 2 H), 2.65–2.40 (m, 2 H), 1.55 (d, J = 6.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 171.6, 166.9, 141.4, 135.6, 130.1, 128.7, 128.6, 128.2, 127.9, 127.3, 101.1, 93.5, 69.5, 67.2, 48.2, 40.9, 14.9; LRMS (70 eV), m/z (relative intensity) 424 (M^+, 5), 355 (100), 331 (5), 324 (5).

Anal. Calcd for $C_{27}H_{24}N_2O_3$: C, 76.40; H, 5.70; N, 6.60. Found: C, 76.66; H, 5.82; N, 6.38.

2-[((Benzyloxy)carbonyl)methyl]-4-methyl-1-(2-methyl-4-oxobut-2-yl)-1,2-diazetidin-3-one (23). Ozonolysis of **7n**, as described above for the ozonolysis of **7k**, gave the aldehyde **23** in 61% yield (R_f = 0.2 in 50:50 ether/petroleum ether): IR (neat) 2975, 2955, 1785, 1750, 1719 cm^{-1}; ^1H NMR ($CDCl_3$) 9.76 (dd, J_1 = 3.3 Hz, J_2 = 2.6 Hz, 1 H), 7.32 (s, 5 H), 5.15 (s, 2 H), 4.24, 3.93 (2 d, J = 17.8 Hz, 2 H), 4.11 (q, J = 7.0 Hz, 1 H), 2.52 (dd, J_1 = 14.8 Hz, J_2 = 3.3 Hz, 1 H), 2.27 (dd, J_1 = 14.8 Hz, J_2 = 2.6 Hz, 1 H), 1.36 (d, J = 7.0 Hz, 3 H), 1.22, 1.18 (2 s, 6 H); ^{13}C NMR ($CDCl_3$) 200.8, 172.7, 167.3, 135.0, 128.5, 68.0, 67.4, 59.7, 51.5, 23.2, 22.8, 15.1; LRMS (70 eV), m/z (relative intensity) 318 (M^+, 4), 276 (14), 235 (9), 207 (22), 162 (14), 91 (100); HRMS calcd for $C_{17}H_{22}N_2O_4$ m/z 318.1579, found m/z 318.1574 ± 0.0032.

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Registry No. **4a**, 79559-06-1; **4b**, 92184-58-2; **4c**, 92184-59-3; **4d**, 89773-81-9; **4e**, 92184-64-0; **4f**, 100311-49-7; **4g**, 100297-91-4; **4h**, 100297-92-5; **4i**, 100297-93-6; **4j**, 100297-94-7; **7a**, 100297-95-8; **7b**, 100297-96-9; **7c**, 100297-97-0; **7d**, 100297-98-1; **7e**, 100297-99-2; **7f**, 100298-00-8; **7g**, 100298-01-9; **7h**, 100298-02-0; **7i**, 100298-03-1; **7j**, 100298-04-2; **7k**, 100298-05-3; **7l**, 100298-06-4; **7m**, 100298-07-5; **7n**, 100298-08-6; **7o**, 100298-09-7; **8a**, 100298-10-0; **8b**, 100298-13-3; **8c**, 100298-14-4; **8d**, 100298-15-5; **8e**, 100298-16-6; **9**, 100298-11-1; **10** (R_1 = Me, R_2 = R_3 = Ph), 79289-32-0; **10** (R_1 = R^2 = R^3 = Me), 100298-12-2; **12a**, 100298-17-7; **12b**, 100298-20-2; **14a**, 100298-18-8; **14b**, 100298-21-3; **14c**, 100298-22-4; **15a**, 100298-19-9; **18a**, 100298-23-5; **18b**, 100298-24-6; **22**, 100298-25-7; **23**, 100298-26-8; $ClCH_2C(O)Cl$, 79-04-9; $Me_3Si(CH_2)_2OH$, 2916-68-9; $CH_2ClC(O)O(CH_2)_2SiMe_3$, 100297-89-0; $CH_2IC(O)O(CH_2)_2SiMe_3$, 100297-90-3; 4-methyl-3-oxo-1,2-diazetidinium tosylate, 79289-51-3.