JOC Article

Rearrangement of 4-(1-Haloalkyl)- and 4-(2-Haloalkyl)-2-azetidinones into Methyl ω-Alkylaminopentenoates via Transient Aziridines and Azetidines

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The synthesis of 4-(1-haloalkyl)-2-azetidinones and 4-(2-haloalkyl)-2-azetidinones was investigated with use of the Staudinger reaction between in situ generated ketenes and α-haloimines or β-haloimines. This new class of functionalized 2-azetidinones was further evaluated for its potential use as intermediates in the synthesis of highly functionalized compounds. The reaction of 4-(1-haloalkyl)-2-azetidinones and 4-(2-haloalkyl)-2-azetidinones with sodium methoxide in methanol yielded ring-opened products, i.e., methyl 2-alkoxy-4-(alkylamino)pentenoate and methyl 5-(alkylamino)pentenoate, respectively. Further attention was paid in detail to the reaction mechanism involved in this peculiar transformation. It was proven that these reactions proceeded via intermediate aziridines or azetidines.

Introduction

The synthesis of halogen-substituted 2-azetidinones has been sporadically reported in the literature, and synthetic methodologies toward these compounds include cycloaddition of alkenes and chlorosulfonylisocyanate,[1] ester enolate-imine condensation,[2] electrophile-induced cyclizations of amides and hydroxamates,[3] ring transformation of aziridines,[4] Staudinger reaction between ketenes and imines,[5a,b,6] or transformation of other functional groups after β-lactam synthesis.[5c,7]

Although the incorporation of a halogen functionality into 2-azetidinones opens various possibilities for further transformations, no real reactivity study has yet been undertaken. Several halogen-functionalized azetidin-2-ones were synthesized to investigate their antibacterial activity as such[8] or as intermediates in the synthesis of bicyclic 2-azetidinones,[9] e.g. isocephem derivatives.[6]

However, several efforts were directed toward the synthesis of β-lactams, containing fluorinated substituents at the C-4 position of the β-lactam ring. Several 4-trifluoromethyl- and 4-difluoromethylazetidin-2-ones

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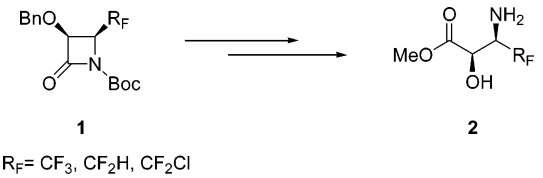
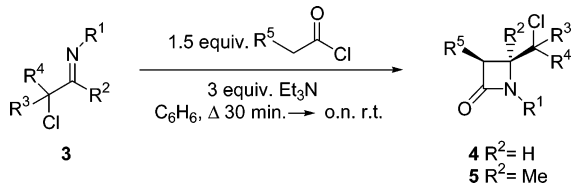
SCHEME 1



1 **2**

R_F= CF_3, CF_2H, CF_2Cl

SCHEME 2



3

4 R^2= H
5 R^2= Me

were synthesized for side-chain modification in taxol derivatives.[5c,10] The former compounds have also been assigned antiinflammatory, analgetic, and blood platelet aggregation inhibitory activity.[8a] Another example is the *β*-lactam mediated synthesis of isoserinates **2** (Scheme 1).[5a,b] Fluorinated isoserinates can be potentially used as peptidomimetic units and their incorporation into peptides can alter the behavior of the latter compounds, due to specific features of the fluoroalkyl moiety.[5c] For example, fluoroalkyl groups are known to weaken the basicity of the amino group, modifying solubility and solvation properties.[11] The incorporation of these peptidomimetics into peptides can lead to the identification of new protease inhibitors.

In this work, the synthesis of a series of novel 4-(1-haloalkyl)- and 4-(2-haloalkyl)-substituted 2-azetidinones was accomplished by the Staudinger reaction. The application of this method to α-, *β*-, or *ω*-haloimines is only very poorly documented and mainly concerns the use of the 2-azetidinones obtained as intermediates for the further synthesis of bicyclic *β*-lactams.[5a,b,6] For the first time, the condensation of α-haloimines and *β*-haloimines with in situ generated ketenes in a Staudinger reaction, to afford 4-(1-haloalkyl)-2-azetidinones and 4-(2-haloalkyl)-2-azetidinones in a stereochemical way, is extensively documented. In principle, such functionalized *β*-lactams lend themselves to ring transformations.

Results and Discussion

The results, obtained by application of the Staudinger reaction to α- and *β*-haloimines, are summarized in Scheme 2 and Table 1, and Scheme 3 and Table 2, respectively.

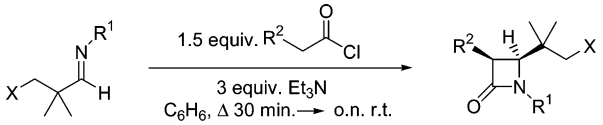
α-Haloimines **3** and *β*-haloimines **6** were reacted with different types of acid chlorides in benzene in the presence of triethylamine to generate the intermediate ketenes. [2+2]-Cycloaddition of the in situ generated ketenes with the appropriate imine yielded the corresponding new *β*-lactams **4**, **5** and **7**, **8**, respectively. The general usefulness has been demonstrated by application of this methodology to numerous α-haloimines **3** and *β*-haloimines **6**.

TABLE 1. Overview of the Synthesized 4-(1-Haloalkyl)azetidin-2-ones 4 and 5

compd no.	R^1	R^2	R^3	R^4	R^5	yield (%)[a]
4a	^{i}Pr	H	Me	Me	OBn[b]	82
4b	cHex	H	Me	Me	OBn	79
4c	allyl	H	Me	Me	OBn	97
4d	Et	H	Me	Me	OBn	85
4e	PMP[c]	H	Me	Me	OBn	65
4f	^{i}Pr	H	Me	Me	OC_6H_5	60
4g	allyl	H	Me	Me	OC_6H_5	85
4h	^{i}Pr	H	Me	Me	OMe	72
4i	cHex	H	Me	Me	OMe	82
4j	allyl	H	Me	Me	OMe	65
5a	^{i}Pr	Me	Me	Me	OBn	50
5b	^{i}Pr	Me	Cl	H	OBn	84

[a] Yield after purification by flash chromatography or recrystallization. [b] Bn = $CH_2C_6H_5$. [c] PMP= 4-methoxyphenyl.

SCHEME 3



6 **7** or **8**

TABLE 2. Overview of the Synthesized 4-(2-haloalkyl)-azetidin-2-ones 7 and 8

compd no.	R^1	X	R^2	yield (%)[a]
7a	^{i}Pr	Cl	OBn[b]	70
7b	cHex	Cl	OBn	65
7c	allyl	Cl	OBn	97
7d	allyl	Cl	OC_6H_5	45
7e	^{i}Pr	Cl	OMe	73
7f	allyl	Cl	OMe	68
8a	^{i}Pr	Br	OBn	75
8b	cHex	Br	OBn	99
8c	allyl	Br	OBn	90
8d	Et	Br	OBn	75
8e	n-Pr	Br	OBn	67
8f	$CH_2CH{=}CHC_6H_5$	Br	OBn	78
8g	^{i}Pr	Br	OMe	76
8h	allyl	Br	OMe	90
8i	Et	Br	OMe	61
8j	CH_2CH_2Br	Br	OMe	77
8k	CH_2CH_2OBn	Br	OMe	85
8l	$CH_2CH{=}CHC_6H_5$	Br	OMe	63
8m	$CH_2C(CH_3)CH{=}CH_2$	Br	OMe	90
8n	$C(CH_2CH_2)CH{=}CH_2$	Br	OMe	77
8o	$CH(C_6H_5)CH{=}CH_2$	Br	OMe	90
8p	^{i}Pr	Br	Phth[c]	76

[a] Yield after purification by flash chromatography or recrystallization. [b] Bn = $CH_2C_6H_5$. [c] Phth = phthalimidoyl.

In all the presented examples of 2-azetidinones **4**, **5**, **7**, and **8**, the stereochemical outcome of this reaction was shown to be cis. The stereochemistry was easily determined for compounds **4**, **7**, and **8** by the coupling constants between the protons at C-3 and C-4 of the azetidin-2-one ring. Such coupling constants of C-3 and C-4 vicinal protons of 2-azetidinones are reported to be 5−6 Hz for the cis derivative and 0−2 Hz for the trans derivative.[12] For compound **5a**, the cis stereochemical relationship was confirmed by nOe experiments, which revealed a nOe effect of 8.0% between the C-3 proton and

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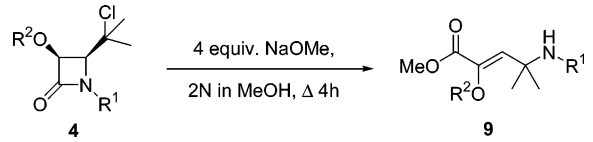
the C-4 methyl group. For analogous reasons, **5b** was also considered to possess the cis stereorelationship as similar NMR spectroscopic data were obtained. These results for the 4,4-disubstituted 2-azetidinones **5** are in agreement with literature data.[13a] The synthesis of β-lactams with quaternary centers at the C-4 position has been reported to be of particular interest.[13a,b] The latter compounds might provide new opportunities for the study of structure−activity relationships and further insight into the design of new antibiotics and enzyme inhibitors.[13c]

The starting materials, i.e., halogenated imines, were easily synthesized from the corresponding halogenated aldehydes and ketones. α-Haloimines **3** (R^2 = H) were derived from isobutyraldehyde, which was chlorinated at the α-position with sulfuryl chloride and subsequently condensed with the appropriate amines in the presence of magnesium sulfate. β-Halogenated imines for the synthesis of β-lactams **7** and **8** were derived from 3-bromo- or 3-chloro-2,2-dimethyl alcohols. Oxidation of the alcohols with pyridinium chlorochromate yielded the corresponding aldehydes, which were used for the imine synthesis.[14] β-Lactam **5a** was derived from 3-methyl-2-butanone, which was chlorinated with sulfuryl chloride[15] and condensed with isopropylamine in the presence of titanium(IV) chloride.[16] β-Lactam **5b** was derived from commercially available 1,1-dichloroacetone. Phthaloylglycyl chloride was easily obtained from the reaction of phthaloylglycine and thionyl chloride.[17]

β-Lactams have been widely applied in the synthesis of various classes of compounds, since ring opening of 2-azetidinones gave immediate access to nonproteogenic β-amino acids and further on to peptides.[18] The ring opening of β-lactams by nucleophiles is well-studied[19] and the application of this methodology to 4-(1-haloalkyl)-2-azetidinones **4** and **5** and 4-(2-haloalkyl)-2-azetidinones **7** and **8** may lead to ring transformation. Functionalized aziridines should be accessible from 4-(1-chloro-1-methylethyl)-2-azetidinones **4**, while functionalized azetidines should be accessible from 4-(2-chloro-1,1-dimethylethyl)-2-azetidinones **7** and 4-(2-bromo-1,1-dimethylethyl)-2-azetidinones **8**. The results obtained in this area are summarized hereafter.

SCHEME 4



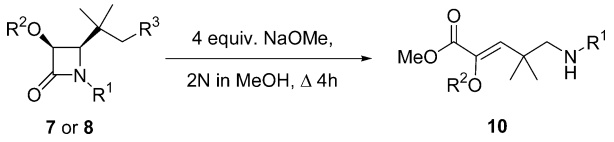
4 **9**

TABLE 3. Substitution Pattern and Yields of (*Z*)-2-Alkoxy-4-(alkylamino)pent-2-enoates 9

compd **9**	starting product	R^1	R^2	yield (%)[a]
a	**4a**	^{i}Pr	Bn	65 (45)
b	**4c**	allyl	Bn	60 (45)
c	**4h**	^{i}Pr	Me	55 (46)

[a] Yields after flash chromatography are given in parentheses.

SCHEME 5



7 or **8** **10**

TABLE 4. Substitution Pattern and Yields of (*Z*)-Methyl 2-alkoxy-5-(alkylamino)pent-2-enoates 10

compd **10**	starting product	R^1	R^2	R^3	yield (%)[a]
a	**7a**, **8a**	^{i}Pr	Bn	Cl or Br	80 (65)
b	**8d**	Et	Bn	Br	75 (66)
c	**7c**, **8c**	allyl	Bn	Cl or Br	86 (60)
d	**8e**	nPr	Bn	Cl or Br	94 (75)
e	**7e**, **8g**	^{i}Pr	Me	Cl or Br	74 (68)
f	**7f**, **8h**	allyl	Me	Cl or Br	85 (70)
g	**8i**	Et	Me	Br	68 (50)
h	**8l**	$CH_2CH{=}CHC_6H_5$	Me	Br	90 (68)
i	**8m**	$CH_2(CH_3)C{=}CH_2$	Me	Br	60 (45)

[a] Yields after flash chromatography are given in parentheses.

4-(1-Chloro-1-methylethyl)-2-azetidinones **4** were treated with an excess of 2N sodium methoxide in methanol at reflux temperature for 4 h (Scheme 4). In the reaction mixture, no cyclized product, i.e., aziridines, could be detected, but only ring-opened products (*Z*)-**9** were isolated and purified by flash chromatography (Table 3), although the reaction products **9** were of very high purity in the reaction mixture. Intermediate workup of the reaction (e.g., after 1 h) results in the isolation of a mixture of 4-(1-chloro-1-methylethyl)-2-azetidinones **4** and reaction products **9**.

Similar observations as for 4-(1-chloro-1-methylethyl)-2-azetidinones **4** were obtained for 4-(2-halo-1,1-dimethylethyl)-2-azetidinones **7** and **8**. Also in this case the only products obtained were the ring-opened (*Z*)-methyl 2-alkoxy-4,4-dimethyl-5-(alkylamino)pent-2-enoates **10** (Scheme 5, Table 4).

The same results were obtained from both 4-(2-bromoalkyl)- and 4-(2-chloroalkyl)-2-azetidinones **7** and **8**, respectively. Although not completely documented here, this transformation is valid for all 2-azetidinones **4a**−**e**,**h**−**j**, **7**, and **8**. The proposed reaction mechanism starts with nucleophilic attack of sodium methoxide at the amide functionality of β-lactam **11**, resulting in ring opening (Scheme 6).

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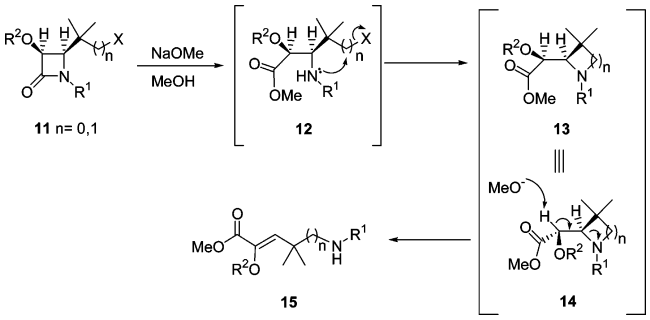
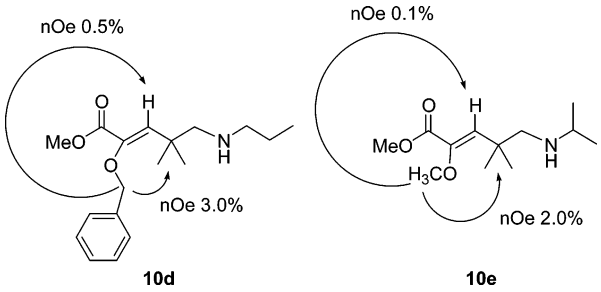
SCHEME 6



SCHEME 7

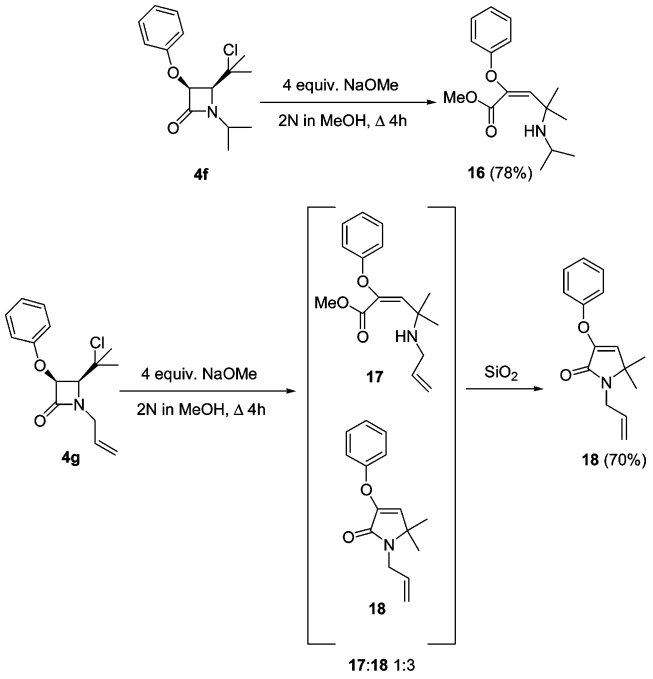


The secondary amine thus formed then attacks the halogenated carbon leading to ring closure by intramolecular nucleophilic substitution. The ring-closed products **13** are the originally expected aziridine ($n = 0$) and azetidine ($n = 1$) derivatives. However, in the presence of excess sodium methoxide, deprotonation at the α-position of the ester **13** occurs and anti elimination leads unexpectedly to the stereospecific formation of alkenoates **15**. The ring opening by this mechanism is quite understandable for the more strained aziridines **13** ($n = 0$), while this result is more surprising for the more stable azetidines **13** ($n = 1$). To the best of the authors' knowledge, no similar ring opening of *N*-alkyl-functionalized azetidines has been reported. According to the reaction mechanism, the products obtained should be the *Z*-alkenoates **15**, if no isomerization occurs during the reaction. Experimentally obtained products consisted of one isomer exclusively and the geometry was firmly established by the performance of nOe experiments on derivatives **10d** and **10e** (Scheme 7).

These nOe experiments clearly showed the closer proximity between the benzylic CH_2 **(10d**) and methoxy (**10e**) protons and the geminal dimethyl group. In both compounds, weak nOe effects were obtained toward the vinylic protons. The olefinic protons of the 4-alkylamino- and 5-alkylaminopentenoates **9** and **10** all appear in the range of 6.13−6.25 ppm in ^{1}H NMR ($CDCl_3$, 270 MHz). Because of this fact, alkenoates **9** also were assumed to possess the *Z*-geometry. However, additional evidence for this fact was found in the reaction of 3-phenoxy-*β*-lactams **4f** and **4g** with sodium methoxide in methanol (Scheme 8).

Reacting 2-azetidinone **4f** with excess 2 N sodium methoxide in methanol for 4 h under reflux led to the formation of a ring-opened product, similar to the previously isolated compounds **9**. However, the chemical shift of the double bond proton of this product was higher than that for compounds **9**, i.e., 6.60 ppm ($CDCl_3$, 270 MHz). When the same reaction was performed with 1-allyl-2-

SCHEME 8



azetidinone **4g**, a mixture of two compounds was obtained. One compound was also believed to be the ring-opened product **17** because of the appearance of the double bond proton at 6.55 ppm ($CDCl_3$, 270 MHz). The main product, however, was pyrrolinone **18**, derived from the *E* isomer **17** after ring closure. The ratio **17**:**18** in the reaction mixture was 1:3, based on signal integration of the double bond protons in the ^{1}H NMR spectrum. Although (*E*)-methyl 4-(allylamino)-4-methyl-2-phenoxypent-2-enoate **17** was clearly present in the reaction mixture, after flash chromatography only the cyclized 1-allyl-5,5-dimethyl-3-phenoxypyrrolinone **18** could be isolated in 70% yield.

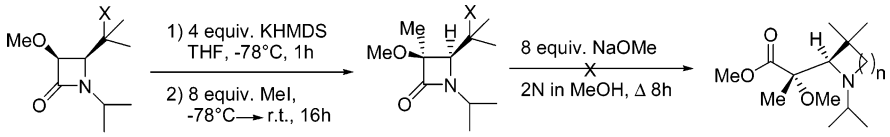
Apparently, in the case of the 3-phenoxy substitution at the *β*-lactams **4**, isomerization took place during the reaction, which led to the formation of the corresponding *E*-alkenoates. Stopping the reaction before completion gave no clear indication of this epimerization. Previously, ring opening of 3-azido-4-chloro-2-azetidinones with sodium methoxide gave rise to the formation of the corresponding α,*β*-unsaturated *β*-aminoesters as a mixture of *E* and *Z* isomers.[20] However, it is not clear from these data which stereochemistry was involved in the starting materials.

β-Lactams **5**, with a quaternary C4 carbon atom, were not susceptible to this transformation with sodium methoxide in methanol and starting products were recovered. Even **5b**, which has a 4-(dichloromethyl) substituent, did not react at all and could be almost quantitatively recovered after several hours of reaction under reflux with 2 N sodium methoxide (up to 10 equiv).

Two strategies to block the rearrangement of 4-(1-haloalkyl) or 4-(2-haloalkyl)-2-azetidinones were developed to stop the reaction at an intermediate stage in order to isolate the intermediate aziridines and azetidines. The first strategy implied alkylation of the

(20) Rao, S. N.; O'Ferrall, R. A. M. *J. Org. Chem.* **1990**, *55*, 3244.

SCHEME 9



β-lactam at the C3 position, generating a quaternary center at this position. During reaction with sodium methoxide, deprotonation adjacent to the ester functionality cannot occur any longer because of the absence of a proton at the α position. Potassium and lithium hexamethyldisilazides have been used as strong nonnucleophilic bases in β-lactam chemistry.[21,22] These reagents were also evaluated in the alkylations under investigation. Application of potassium hexamethyldisilazide (KHMDS) at −78 °C for 1 h to both β-lactams **4h** and **8g** in tetrahydrofuran, followed by quenching with excess iodomethane and warming to room temperature overnight, yielded the desired alkylated compounds **19** and **20**, respectively, in moderate yields (Scheme 9).

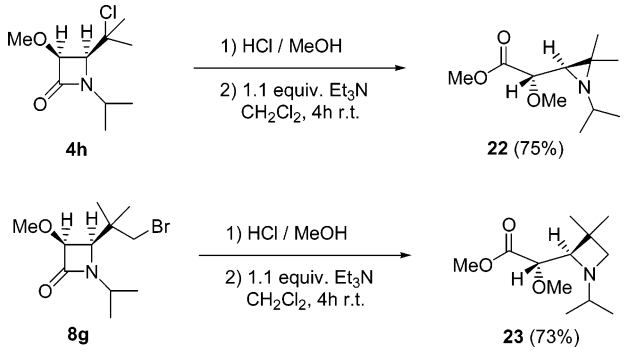
When performing the same alkylation on the latter β-lactam under the same conditions (−78 °C for 1 h, quenching with iodomethane, and gradually warming to room temperature) but with lithium hexamethyldisilazide (LiHMDS) no alkylation was observed and the starting material was recovered.

The stereochemical outcome of this alkylation is consistent with literature data, with the electrophile coming in from the opposite site of the C4 substituent.[21,23] This was additionally checked and confirmed by nOe experiments showing a nOe effect of 4% between the C3 methyl group and the C4 proton for 2-azetidinone **19** and 5% for 2-azetidinone **20**.

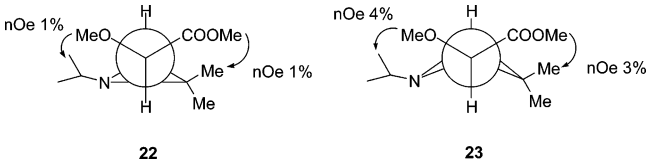
Reaction of the C3-disubstituted β-lactams **19** and **20** with sodium methoxide in methanol did not lead to ring opening and isolation of the corresponding aziridine or azetidine (Scheme 9). Even application of the double number of equivalents compared to previous reactions gave no better results and in all cases the starting material was isolated. As in the case of C4-disubstituted β-lactams **5** sterical hindrance can play a role in these negative results. Attempts to effect this ring opening under acidic conditions (bubbling gaseous hydrochloric acid through a methanol solution of the 2-azetidinones) also failed. This was also the case for attempted ring opening of C4-disubstituted β-lactams **5**.

The second strategy to block the rearrangement of 4-(1-haloalkyl)- and 4-(2-haloalkyl)-2-azetidinones at an intermediate stage involved ring opening of the 2-azetidinones with acidic methanolysis. Gaseous hydrogen chloride was bubbled through a solution of 2-azetidinones **4h** and **8g** in methanol. This reaction mixture was kept in a closed vessel for 24 h and methanol was subsequently evaporated. The intermediate salt was not characterized, but was taken up in dichloromethane and the mixture stirred in the presence of triethylamine for 4 h at room

SCHEME 10



SCHEME 11



temperature. The resulting aziridine **22** and azetidine **23** were isolated in 75 and 73% yield, respectively (Scheme 10).

The coupling constants between the NC*H* and MeOC*H* proton were rather large, i.e., 8.9 Hz in the case of the aziridine **21** and 8.6 Hz for the azetidine **23** ($CDCl_3$, 270 MHz). With use of the Karplus equation,[24] this corresponds to dihedral angles, as indicated in Scheme 11, of approximately 175°.

Calculation of the minimal energy conformation of these compounds, using the MOPAC utility of the ChemPro 3D software, gave similar values for the dihedral angles, i.e., 171° for the aziridine **22** and 179° for the azetidine **23**. To confirm these results, nOe experiments were performed and results were found in agreement with the suggested conformation.

In both cases, clear nOe effects were observed between the methoxy and methyl groups of the isopropyl group, and between the methoxy group of the ester moiety and the dimethyl substituent on the nitrogen heterocycle. Further nOe effects were not significant. Analogous aziridines of compound **22**, i.e., 2-(2-aziridinyl)-3-phenylpropanoic acids, were recently evaluated as carboxypeptidase A inhibitors.[25] Having established this structure, no izomerization took place during the acidic methanolysis and the subsequent basic workup. Further reaction of the isolated heterocyclic intermediates **22** and **23** with

(21) Ojima, I. β-Lactam Synthon Method: Enantiomerically Pure β-Lactams as Synthetic Intermediates. In *The Organic Chemistry of β-Lactams*; Georg, G. I., Ed.; VCH: New York, 1993; Chapter 4, pp 197−255 and references cited therein.

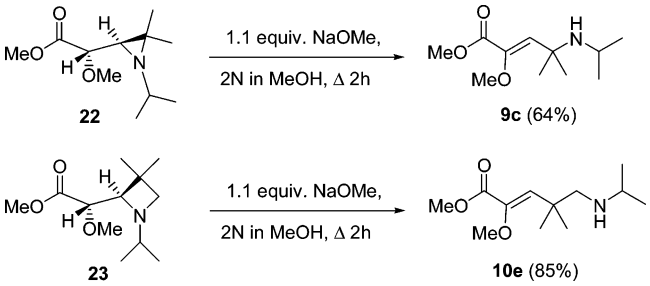
(22) Colson, P.-J.; Hegedus, L. S. *J. Org. Chem.* **1993**, *58*, 5918.

(23) Ojima, I.; Wang, T.; Delaloge, F. *Tetrahedron Lett.* **1998**, *39*, 3663.

(24) (a) Haasnoot, C. A. G.; De Leeuw, F. A. A. M.; Altona, C. *Tetrahedron* **1980**, *36*, 2783. (b) http://www.spectroscopynow.com/Spy/tools/proton−proton.html.

(25) Park, J.-I.; Kim, D. H. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2967.

SCHEME 12



1 equiv of sodium methoxide in methanol yielded the expected ring-opened products **9c** and **10e** in acceptable yields (Scheme 12). This conversion clearly showed the intermediacy of the nitrogen-containing heterocycles during this ring opening under the action of sodium methoxide in methanol under reflux.

In conclusion, the synthesis of 4-(1-haloalkyl)-2-azetidinones and 4-(2-haloalkyl)-2-azetidinones was achieved and further ring opening to methyl 2-alkoxy-4-alkylamino- and 5-alkylaminopentenoates was accomplished after reaction with sodium methoxide in methanol. It was proven that the reaction mechanism passed via intermediate aziridines and azetidines, which could be isolated and further transformed into the previously isolated ring-opened products.

Experimental Section

Spectroscopic data were recorded as follows: ^{1}H NMR and ^{13}C NMR spectra were run at 270 and 68 MHz, respectively. Peak assignments were performed with the aid of the DEPT technique, 2D-COSY, and HETCOR spectra. IR spectra were obtained from an infrared spectrophotometer. Mass spectra were recorded on a mass spectrometer (70 eV), using either GC-MS coupling or a direct inlet system. Melting points were measured with a melting point apparatus and are uncorrected. Flash chromatography was carried out with use of a glass column with silica gel (particle size 0.035−0.070 mm, pore diameter ca. 6 nm). Solvent systems were determined via initial TLC analysis (Kieselgel 60F_{254}, precoated 0.25 mm). Tetrahydrofuran was distilled from sodium benzophenone ketyl, while dichloromethane was distilled from calcium hydride before use. Methanol was dried with magnesium and distilled. A stock solution of 4 N sodium methoxide in methanol was prepared and stored, shielded from light. All compounds were obtained as colorless to yellow oils, except where melting points are mentioned. These latter compounds were obtained as white to slightly yellow crystals.

Synthesis of 4-(1-Haloalkyl)- and 4-(2-Haloalkyl)-2-azetidinones. A generalized procedure, representative for the synthesis of both 4-(1-haloalkyl)- and 4-(2-haloalkyl)-azetidin-2-ones, is given. A solution of 10 mmol of the α-haloimine or *β*-haloimine and 30 mmol of triethylamine in 50 mL of benzene was heated. To this refluxing solution was added dropwise 15 mmol of acid chloride in 50 mL of benzene. The resulting solution was kept at reflux temperature for 30 min, and subsequently stirred overnight at room temperature. The reaction mixture was diluted with 100 mL of chloroform and washed with a saturated sodium bicarbonate solution and brine. After drying (magnesium sulfate) and evaporation of the solvent, the crude reaction product was obtained. Further purification was performed by flash chromatography or recrystallization.

***cis*-3-Benzyloxy-4-[(1-chloro-1-methyl)ethyl]-1-isopropylazetidin-2-one (4a):** mp 48.0−49.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.32 and 1.48 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 1.72 and 1.76 (2 × 3H, 2 × s, Me_2C_q), 3.92 (1H, septet, J = 6.6 Hz, C*H*Me_2), 4.04 (1H, d, J = 5.3 Hz, NCHC$_q$), 4.56 (1H, d, J = 5.3 Hz, OCH), 4.67 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.91 (1H, d, J = 11.9 Hz, OCH(*H*)), 7.29−7.39 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 20.32 and 20.72 (Me_2CH), 27.55 and 29.47 (Me_2C_q), 46.54 (*C*HMe_2), 66.92 (N*C*HC$_q$), 71.66 (C_qCl), 73.17 (O*C*H$_2$C$_6$H$_5$), 80.77 (OCH), 127.73, 127.96 and 128.46 (C$_o$, C$_m$, C$_p$), 136.96 (C$_q$), 168.10 (C=O); IR (KBr) 1743 cm^{-1} (C=O); MS *m*/*z* no M$^+$, 260 (6, M$^+$ − Cl), 178 (11), 175 (19), 161 (13), 158 (13), 144 (28), 138 (36), 118 (38), 111 (16), 91 (100), 75 (13), 65 (15). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.25, yield 82%. Anal. Calcd for $C_{16}H_{22}ClNO_2$: C, 64.97; H, 7.50; N, 4.74. Found: C, 64.75; H, 7.60; N, 4.67.

***cis*-3-Benzyloxy-4-[(1-chloro-1-methyl)ethyl]-1-cyclohexylazetidin-2-one (4b):** mp 87.2−89.0 °C; ^{1}H NMR ($CDCl_3$) δ 1.14−2.17 (10H, m, $(CH_2)_5$), 1.71 and 1.75 (2 × 3H, 2 × s, Me_2C_q), 3.45−3.57 (1H, m, NC*H*), 4.06 (1H, d, J = 5.3 Hz, NCHC$_q$), 4.56 (1H, d, J = 5.3 Hz, OCH), 4.67 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.91 (1H, d, J = 11.9 Hz, OCH(*H*)), 7.26−7.38 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 25.30, 25.75 and 30.64 ($(CH_2)_5$), 27.62 and 29.51 (Me_2C_q), 54.57 (N*C*H), 66.76 (N*C*HC$_q$), 71.86 (C_qCl), 73.15 (O*C*H$_2$C$_6$H$_5$), 80.68 (OCH), 127.71, 127.92 and 128.44 (C$_o$, C$_m$, C$_p$), 137.00 (C$_q$), 168.00 (C=O); IR (KBr) 1723 cm^{-1} (C=O); MS *m*/*z* no M$^+$, 260 (15), 258 (14), 178 (27), 159 (16), 158 (29), 144 (60), 143 (12), 140 (37), 138 (100), 118 (99), 113 (14), 111 (39), 91 (63), 75 (27), 65 (20). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.37, yield 79%. Anal. Calcd for $C_{19}H_{26}ClNO_2$: C, 67.94; H, 7.80; N, 4.17. Found: C, 68.19; H, 7.87; N, 4.27.

***cis*-1-Allyl-3-benzyloxy-4-[(1-chloro-1-methyl)ethyl]azetidin-2-one 4c:** mp 48.7−50.3 °C; ^{1}H NMR ($CDCl_3$) δ 1.70 and 1.74 (2 × 3H, 2 × s, Me_2C_q), 3.86 (1H, d × d, J = 15.0 Hz, J = 8.0 Hz, NC*H*(H)), 4.08 (1H, d, J = 5.3 Hz, NCHC$_q$), 4.25 (1H, d × d, J = 15.0 Hz, J = 4.0 Hz, NCH(*H*)), 4.65 (1H, d, J = 5.3 Hz, OCH), 4.68 (1H, d, J = 11.5 Hz, OC*H*(H)), 4.92 (1H, d, J = 11.5 Hz, OCH(*H*)), 5.21−5.29 (2H, m, CHC*H*$_2$), 5.75−5.85 (1H, m, C*H*CH$_2$), 7.26−7.38 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 27.76 and 29.27 (Me_2C_q), 43.65 (N*C*H$_2$), 66.47 (N*C*HC$_q$), 71.52 (C_qCl), 73.30 (O*C*H$_2$C$_6$H$_5$), 81.42 (OCH), 119.19 (=CH), 127.73, 128.01 and 128.48 (C$_o$, C$_m$, C$_p$), 131.12 (=CH$_2$), 136.84 (C$_q$), 168.08 (C=O); IR (KBr) 1758 cm^{-1} (C=O); LC-MS *m*/*z* 316/318 (14, [M + Na]$^+$), 294/296 (100, [M + H]$^+$), 91 (36). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.28, yield 97%. Anal. Calcd for $C_{16}H_{20}ClNO_2$: C, 65.41; H, 6.86; N, 4.77. Found: C, 65.65; H, 6.96; N, 4.67.

***cis*-3-Benzyloxy-4-[(1-chloro-1-methyl)ethyl]-1-ethylazetidin-2-one (4d):** mp 61.9−63.0 °C; ^{1}H NMR ($CDCl_3$) δ 1.21 (3H, t, J = 7.3 Hz, C*H*$_3$CH), 1.70 and 1.73 (2 × 3H, 2 × s, Me_2C_q), 3.30 (1H, d × d, J = 14.2 Hz, J = 7.3 Hz, NC*H*(H)), 3.64 (1H, d × d, J = 14.2 Hz, J = 7.3 Hz, NCH(*H*)), 4.07 (1H, d, J = 5.3 Hz, NCHC$_q$), 4.61 (1H, d, J = 5.3 Hz, OCH), 4.66 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.91 (1H, d, J = 11.9 Hz, OCH(*H*)), 7.26−7.37 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 12.54 (*C*H$_3$CH$_2$), 27.51 and 29.29 (Me_2C_q), 35.97 (CH$_3$*C*H$_2$), 66.29 (N*C*HC$_q$), 71.68 (C_qCl), 73.19 (O*C*H$_2$C$_6$H$_5$), 81.29 (OCH), 127.67, 127.94 and 128.43 (C$_o$, C$_m$, C$_p$), 136.87 (C$_q$), 167.90 (C=O); IR (KBr) 1715 cm^{-1} (C=O); MS *m*/*z* 281/283 (M$^+$, 20), 222 (23), 221 (35), 207 (38), 148 (19), 147 (55), 86/88 (36), 73/75 (100), 51/53 (33), 47/49 (39), 44 (49). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.24, yield 85%. Anal. Calcd for $C_{15}H_{20}ClNO_2$: C, 63.94; H, 7.15; N, 4.97. Found: C, 64.15; H, 7.26; N, 4.87.

***cis*-3-Benzyloxy-4-[(1-chloro-1-methyl)ethyl]-1-(4-methoxyphenyl)azetidin-2-one (4e):** mp 97.2−100.0 °C; ^{1}H NMR ($CDCl_3$) δ 1.71 and 1.76 (2 × 3H, 2 × s, Me_2C_q), 3.78 (3H, s, OMe), 4.63 (1H, d, J = 5.28 Hz, NCHC$_q$), 4.84 (1H, d, J = 5.28 Hz, OCH), 4.80 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.94 (1H, d, J = 11.9 Hz, OCH(*H*)), 6.85−6.89 and 7.33−7.40 (9H, m, C_6H_5 and C_6H_4); ^{13}C NMR ($CDCl_3$) δ 28.81 and 29.43 (Me_2C_q), 55.40 (OMe), 67.10 (N*C*HC$_q$), 70.44 (C_qCl), 73.71 (O*C*H$_2$C$_6$H$_5$), 81.24 (OCH), 114.01, 122.33, 127.76, 128.03 and 128.50 (C$_o$, C$_m$, C$_p$), 129.20, 136.78, 157.12 (C$_q$), 166.21 (C=O); IR (KBr) 1733 cm^{-1}

(C═O); MS *m*/*z* 359/361 (M^+, 2), 175/177 (3), 165 (8), 164 (8), 149 (15), 134 (18), 107 (57), 91 (100), 86 (15), 79 (27), 77 (17), 65 (30), 60 (15), 56 (16). Recrystallized from methanol, yield 65%. Anal. Calcd for $C_{20}H_{22}ClNO_3$: C, 66.75; H, 6.16; N, 3.89. Found: C, 66.92; H, 6.32; N, 3.80.

***cis*-4-[(1-Chloro-1-methyl)ethyl]-1-isopropyl-3-phenyloxyazetidin-2-one (4f):** mp 108.0−109.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.38 and 1.53 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 1.77 and 1.84 (2 × 3H, 2 × s, Me_2C_q), 3.99 (1H, septet, J = 6.6 Hz, C*H*Me$_2$), 4.22 (1H, d, J = 5.3 Hz, NCHC$_q$), 5.16 (1H, d, J = 5.3 Hz, OCH), 6.99−7.32 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 20.34 and 20.68 (Me_2CH), 27.37 and 29.74 (Me_2C_q), 46.95 (*C*HMe$_2$), 67.06 (N*C*HC$_q$), 71.30 (C_qCl), 80.43 (OCH), 116.03, 122.59 and 129.63 (C_o, C_m, C_p), 157.61 (C_q), 166.47 (C═O); IR (KBr) 1739 cm^{-1} (C═O); MS *m*/*z* no M^+, 196 (12), 175 (17), 161 (100), 144 (11), 138 (16), 132 (6), 118 (13), 111 (8), 110 (10), 107 (9), 103 (8), 94 (40), 91 (60), 83 (6), 77 (17), 70 (5), 65 (10),54 (11). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.40, yield 60%. Anal. Calcd for $C_{15}H_{20}ClNO_2$: C, 63.94; H, 7.15; N, 4.97. Found: C, 63.81; H, 7.26; N, 4.85.

***cis*-1-Allyl-4-[(1-chloro-1-methyl)ethyl]-3-phenyloxyazetidin-2-one (4g):** mp 88.5−89.1 °C; ^{1}H NMR ($CDCl_3$) δ 1.76 and 1.82 (2 × 3H, 2 × s, Me_2C_q), 3.94 (1H, d × d, J = 15.2 Hz, J = 7.3 Hz, NC*H*(H)), 4.26 (1H, d, J = 5.3 Hz, NCHC$_q$), 4.32 (1H, d × d, J = 15.2 Hz, J = 6.6 Hz, NCH(*H*)), 5.24 (1H, d, J = 5.3 Hz, OCH), 5.26−5.34 (2H, m, CHC*H*$_2$), 5.78−5.88 (1H, m, C*H*CH$_2$), 7.01−7.33 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 27.57 and 29.56 (Me_2C_q), 44.02 (N*C*H$_2$), 66.59 (N*C*HC$_q$), 71.21 (C_qCl), 80.99 (OCH), 119.53 (═CH), 115.99, 122.71 and 129.68 (C_o, C_m, C_p), 130.93 (═CH$_2$), 157.55 (C_q), 166.56 (C═O); IR (KBr) 1745 cm^{-1} (C═O); MS *m*/*z* 279 (2, M^+), 196 (13), 161 (100), 107 (5), 105 (8), 103 (11), 94 (70), 91 (12), 77 (23), 68 (6), 67 (10), 65 (5), 55 (10), 53 (6), 51 (12). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.41, yield 85%. Anal. Calcd for $C_{15}H_{18}ClNO_2$: C, 64.40; H, 6.49; N, 5.01. Found: C, 64.52; H, 6.62; N, 5.13.

***cis*-4-[(1-Chloro-1-methyl)ethyl]-1-isopropyl-3-methoxyazetidin-2-one (4h):** mp 53.2−53.5 °C; ^{1}H NMR ($CDCl_3$) δ 1.31 and 1.46 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 1.68 and 1.70 (2 × 3H, 2 × s, Me_2C_q), 3.53 (OMe), 3.89 (1H, septet, J = 6.6 Hz, C*H*Me$_2$), 4.04 (1H, d, J = 5.3 Hz, NCHC$_q$), 4.38 (1H, d, J = 5.3 Hz, OCH); ^{13}C NMR ($CDCl_3$) δ 20.31 and 20.72 (Me_2CH), 27.49 and 29.38 (Me_2C_q), 46.47 (*C*HMe$_2$), 59.53 (OMe), 67.04 (N*C*HC$_q$), 71.66 (C_qCl), 83.34 (OCH), 168.12 (C═O); IR (KBr) 1732 cm^{-1} (C═O); MS *m*/*z* no M^+, 184 (2, M^+ − Cl), 156 (6), 148 (6), 134/136 (28), 114 (11), 99 (100), 98 (10), 83 (12), 72 (10), 70 (24), 69 (10), 67 (21), 55 (18). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.24, yield 72%. Anal. Calcd for $C_{10}H_{18}ClNO_2$: C, 54.67; H, 8.26; N, 6.38. Found: C, 54.83; H, 8.39; N, 6.27.

***cis*-4-[(1-Chloro-1-methyl)ethyl]-1-cyclohexyl-3-methoxyazetidin-2-one (4i):** mp 107.6−108.3 °C; ^{1}H NMR ($CDCl_3$) δ 1.18−2.04 (10H, m, $(CH_2)_5$), 1.67 and 1.71 (2 × 3H, 2 × s, Me_2C_q), 3.44−3.61 (1H, m, NC*H*), 3.53 (OMe), 4.05 (1H, d, J = 5.3 Hz, NCHC$_q$), 4.36 (1H, d, J = 5.3 Hz, OCH); ^{13}C NMR ($CDCl_3$) δ 25.25, 25.30, 25.73, 30.53 and 30.64 ($(CH_2)_5$), 27.55 and 29.40 (Me_2C_q), 54.48 (N*C*H), 59.57 (OMe), 66.88 (N*C*HC$_q$), 71.86 (C_qCl), 83.23 (OCH), 168.03 (C═O); IR (KBr) 1730 cm^{-1} (C═O); MS *m*/*z* 259/261 (0.1, M^+), 224 (1, M^+ − Cl), 136 (5), 134 (15), 99 (100), 98 (4), 86 (5), 84 (9), 83 (8), 67 (11), 55 (17), 49 (12). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.29, yield 82%. Anal. Calcd for $C_{13}H_{22}ClNO_2$: C, 60.11; H, 8.54; N, 5.39. Found: C, 59.94; H, 8.67; N, 5.30.

***cis*-1-Allyl-4-[(1-chloro-1-methyl)ethyl]-3-methoxyazetidin-2-one (4j):** ^{1}H NMR ($CDCl_3$) δ 1.67 and 1.70 (2 × 3H, 2 × s, Me_2C_q), 3.55 (OMe), 3.85 (1H, d × d, J = 15.0 Hz, J = 7.0 Hz, NC*H*(H)), 4.08 (1H, d, J = 5.3 Hz, NCHC$_q$), 4.24 (1H, d × d, J = 15.0 Hz, J = 4.0 Hz, NCH(*H*)), 4.47 (1H, d, J = 5.3 Hz, OCH), 5.21−5.28 (2H, m, CHC*H*$_2$), 5.75−5.88 (1H, m, C*H*CH$_2$); ^{13}C NMR ($CDCl_3$) δ 27.39 and 28.88 (Me_2C_q), 43.25 (N*C*H$_2$), 59.35 (OMe), 66.22 (N*C*HC$_q$), 71.20 (C_qCl), 83.67 (OCH), 118.76 (═CH), 130.87 (═CH$_2$), 167.78 (C═O); IR (NaCl) 1760 cm^{-1} (C═O); MS *m*/*z* 217/219 (0.1, M^+), 182 (0.1, M^+ − Cl), 134 (2), 131 (3), 121 (1), 99 (100), 98 (1), 91 (2), 86 (7), 84 (11), 83 (6), 77 (3), 71 (4), 69 (5), 67 (11), 55 (10), 49 (23). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.30, yield 65%. Anal. Calcd for $C_{10}H_{16}ClNO_2$: C, 55.17; H, 7.41; N, 6.43. Found: C, 54.87; H, 7.60; N, 6.57.

***cis*-3-Benzyloxy-4-[(1-chloro-1-methyl)ethyl]-1-isopropyl-4-methylazetidin-2-one (5a):** ^{1}H NMR ($CDCl_3$) δ 1.36 and 1.50 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 1.61 (3H, s, C_qCH_3), 1.70 and 1.87 (2 × 3H, 2 × s, Me_2C_q), 3.60 (1H, septet, J = 6.6 Hz, C*H*Me$_2$), 4.29 (1H, s, OCH), 4.67 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.90 (1H, d, J = 11.9 Hz, OCH(*H*)), 7.26−7.38 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 20.40, 21.17 and 21.69 (3 × CH_3), 29.03 and 30.08 (Me_2C_qCl), 45.88 (*C*HMe$_2$), 70.48 (NC$_q$ and C_qCl), 73.49 (O*C*H$_2$C$_6$H$_5$), 88.17 (OCH), 127.62, 127.94 and 128.48 (C_o, C_m, C_p), 137.03 (C_q), 166.88 (C═O); IR (NaCl) 1737 cm^{-1} (C═O); MS *m*/*z* no M^+, 223 (2), 188 (12), 166 (50), 160 (10), 151 (100), 124 (2), 112 (4), 110 (15), 106 (4), 105 (5), 99 (9), 98 (7), 97 (3), 91 (75), 84 (3), 83 (3), 77 (6), 70 (3), 69 (9), 68 (5), 67 (5), 55 (3), 53 (2), 51 (2). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.29, yield 50%. Anal. Calcd for $C_{17}H_{24}ClNO_2$: C, 65.90; H, 7.81; N, 4.52. Found: C, 65.75; H, 7.94; N, 4.67.

***cis*-3-Benzyloxy-4-dichloromethyl-1-isopropyl-4-methylazetidin-2-one (5b):** mp 78.6−80.1 °C; ^{1}H NMR ($CDCl_3$) δ 1.35 and 1.41 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 1.63 (3H, s, C_qCH_3), 3.50 (1H, septet, J = 6.6 Hz, C*H*Me$_2$), 4.30 (1H, s, OCH), 4.75 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.78 (1H, d, J = 11.9 Hz, OCH(*H*)), 6.01 (1H, s, $CHCl_2$), 7.26−7.39 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 15.20 (C_qCH_3), 21.31 and 21.64 (Me_2CH), 46.02 (*C*HMe$_2$), 68.23 (N*C*$_q$), 73.94 (O*C*H$_2$C$_6$H$_5$), 75.67 ($CHCl_2$), 88.00 (OCH), 127.69, 128.03 and 128.48 (C_o, C_m, C_p), 136.80 (C_q), 165.66 (C═O); IR (NaCl) 1748 cm^{-1} (C═O); MS *m*/*z* no M^+, 280/282 (0.1, M^+ − Cl), 245 (0.1, M^+ − Cl_2), 232 (8), 230 (13), 220 (4), 195 (6), 128 (2), 126 (6), 105 (4), 91 (100), 65 (13), 63 (2). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.31, yield 84%. Anal. Calcd for $C_{15}H_{19}Cl_2NO_2$: C, 56.97; H, 6.06; N, 4.43. Found: C, 56.75; H, 6.20; N, 4.37.

***cis*-3-Benzyloxy-4-[(2-chloro-1,1-dimethyl)ethyl]-1-isopropylazetidin-2-one (7a):** ^{1}H NMR ($CDCl_3$) δ 1.16 and 1.19 (2 × 3H, 2 × s, Me_2C_q), 1.28 and 1.45 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 3.44 (1H, d, J = 10.9 Hz, C*H*(H)Cl), 3.51 (1H, septet, J = 6.6 Hz, C*H*Me$_2$), 3.78 (1H, d, J = 10.9 Hz, CH(*H*)Cl), 3.84 (1H, d, J = 5.3 Hz, NCHC$_q$), 4.59 (1H, d, J = 5.3 Hz, OCH), 4.68 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.94 (1H, d, J = 11.9 Hz, OCH(*H*)), 7.28−7.35 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 20.74 (Me_2CH), 21.96 and 23.81 (Me_2C_q), 37.84 ($C_q(CH_3)_2$), 47.19 (*C*HMe$_2$), 53.51 (CH_2Cl), 62.77 (N*C*HC$_q$), 73.10 (O*C*H$_2$C$_6$H$_5$), 80.99 (OCH), 127.60, 127.80 and 128.41 (C_o, C_m, C_p), 137.25 (C_q), 168.78 (C═O); IR (NaCl) 1741 cm^{-1} (C═O); MS *m*/*z* no M^+, 224/226 (58), 175 (74), 133 (10), 98 (4), 96 (4), 93 (6), 91 (100), 86 (5), 84 (6), 83(19), 77 (6), 70 (17), 69 (7), 65 (43), 63 (7), 56 (8), 55 (16). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.33, yield 70%. Anal. Calcd for $C_{17}H_{24}ClNO_2$: C, 65.90; H, 7.81; N, 4.52. Found: C, 65.82; H, 7.96; N, 4.67.

***cis*-3-Benzyloxy-4-[(2-chloro-1,1-dimethyl)ethyl]-1-cyclohexylazetidin-2-one (7b):** ^{1}H NMR ($CDCl_3$) δ 1.19−2.04 (10H, m, $(CH_2)_5$), 1.16 and 1.19 (2 × 3H, 2 × s, Me_2C_q), 3.04−3.10 (1H, m, NC*H*), 3.44 (1H, d, J = 10.9 Hz, C*H*(H)Cl), 3.79 (1H, d, J = 10.9 Hz, CH(*H*)Cl), 3.87 (1H, d, J = 5.3 Hz, NCHC$_q$), 4.59 (1H, d, J = 5.3 Hz, OCH), 4.68 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.94 (1H, d, J = 11.9 Hz, OCH(*H*)), 7.25−7.39 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 22.07 and 23.88 (Me_2C_q), 25.25, 25.34, 25.82, 30.75 and 31.05 ($(CH_2)_5$), 38.02 ($C_q(CH_3)_2$), 53.58 (CH_2Cl), 55.49 (NCH), 62.71 (N*C*HC$_q$), 73.15 (O*C*H$_2$C$_6$H$_5$), 80.95 (OCH), 127.65, 127.81 and 128.43 (C_o, C_m, C_p), 137.34 (C_q), 168.71 (C═O); IR (NaCl) 1720 cm^{-1} (C═O); LC-MS *m*/*z* 350/352 (100, $[M + H]^+$). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.41, yield 65%. Anal. Calcd for $C_{20}H_{28}ClNO_2$: C, 68.65; H, 8.07; N, 4.00. Found: C, 68.75; H, 7.99; N, 4.12.

***cis*-1-Allyl-3-benzyloxy-4-[(2-chloro-1,1-dimethyl)ethyl]-azetidin-2-one (7c):** ^{1}H NMR ($CDCl_3$) δ 1.15 and 1.16 (2 × 3H, 2 × s, Me_2C_q), 3.44 (1H, d, J = 10.9 Hz, C*H*(H)Cl), 3.63 (1H, d × d, J = 15 Hz, J = 7 Hz, NC*H*(H)), 3.76 (1H, d, J = 10.9 Hz, CH(*H*)Cl), 3.87 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.19 (1H, d × d, J = 15 Hz, J = 5 Hz, NCH(*H*)), 4.70 (1H, d, J = 5.3 Hz, OCH), 4.70 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.95 (1H, d, J = 11.9 Hz, OCH(*H*)), 5.19−5.25 (2H, m, $CHCH_2$), 5.67−5.80 (1H, m, $CHCH_2$), 7.26−7.36 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 21.89 and 23.65 (Me_2C_q), 37.86 ($C_q(CH_3)_2$), 44.33 (NCH_2), 53.12 (CH_2-Cl), 62.89 ($NCHC_q$), 73.12 ($OCH_2C_6H_5$), 81.89 (OCH), 119.06 (=CH), 127.53, 127.81 and 128.39 (C_o, C_m, C_p), 131.55 (=CH_2), 137.09 (C_q), 168.55 (C=O); IR (NaCl) 1756 cm^{-1} (C=O); MS *m*/*z* no M$^+$, 224 (10), 175 (23), 133 (2), 91 (100), 89 (2), 84 (2), 83 (2), 65 (7), 55 (3). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.29, yield 97%. Anal. Calcd for $C_{17}H_{22}$-$ClNO_2$: C, 66.33; H, 7.20; N, 4.55. Found: C, 66.45; H, 7.33; N, 4.44.

***cis*-1-Allyl-4-[(2-chloro-1,1-dimethyl)ethyl]-3-phenyloxyazetidin-2-one (7d):** ^{1}H NMR ($CDCl_3$) δ 1.21 and 1.23 (2 × 3H, 2 × s, Me_2C_q), 3.51 (1H, d, J = 10.9 Hz, C*H*(H)Cl), 3.71 (1H, d × d, J = 16 Hz, J = 7 Hz, NC*H*(H)), 3.75 (1H, d, J = 10.9 Hz, CH(*H*)Cl), 4.08 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.24 (1H, d × d, J = 16 Hz, J = 6 Hz, NCH(*H*)), 5.25 (1H, d, J = 5.3 Hz, OCH), 5.25−5.30 (2H, m, $CHCH_2$), 5.72−5.87 (1H, m, $CHCH_2$), 7.00−7.45 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 21.98 and 23.63 (Me_2C_q), 38.13 ($C_q(CH_3)_2$), 44.89 (NCH_2), 53.23 (CH_2Cl), 63.11 ($NCHC_q$), 81.42 (OCH), 119.57 (=CH), 115.99, 122.51, 129.49 and 129.63 (C_o, C_m, C_p), 131.32 (=CH_2), 157.72 (C_q), 167.33 (C=O); IR (NaCl) 1742 cm^{-1} (C=O); MS *m*/*z* no M$^+$, 209/211 (23), 158 (2), 145 (2), 160 (100), 112 (2), 108 (3), 107 (9), 105 (3), 99 (3), 94 (17), 91 (7), 79 (4), 78 (3), 77 (16), 67 (3), 66 (6), 65 (8), 55 (7). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.29, yield 97%. Anal. Calcd for $C_{16}H_{20}ClNO_2$: C, 65.41; H, 6.86; N, 4.77. Found: C, 65.54; H, 6.94; N, 4.65.

***cis*-4-[(2-Chloro-1,1-dimethyl)ethyl]-1-isopropyl-3-methoxyazetidin-2-one (7e):** ^{1}H NMR ($CDCl_3$) δ 1.13 and 1.16 (2 × 3H, 2 × s, Me_2C_q), 1.29 and 1.45 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 3.44 (1H, d, J = 10.9 Hz, C*H*(H)Cl), 3.51 (1H, septet, J = 6.6 Hz, C*H*Me_2), 3.55 (3H, s, OMe), 3.73 (1H, d, J = 10.9 Hz, CH(*H*)Cl), 3.84 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.40 (1H, d, J = 5.3 Hz, OCH); ^{13}C NMR ($CDCl_3$) δ 20.72 (Me_2CH), 21.89 and 23.65 (Me_2C_q), 37.93 ($C_q(CH_3)_2$), 47.13 (*C*HMe_2), 53.40 (CH_2Cl), 59.44 (OMe), 62.96 ($NCHC_q$), 83.54 (OCH), 168.80 (C=O); IR (NaCl) 1751 cm^{-1} (C=O); MS *m*/*z* 233/235 (0.1, M$^+$), 198 (0.2, M$^+$ − Cl), 163 (2), 149 (11), 133 (3), 124 (1), 114 (2), 99 (100), 98 (2), 84 (1), 83 (4), 72 (1), 70 (2), 67 (3), 56 (1), 55 (4), 53 (1). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.30, yield 73%. Anal. Calcd for $C_{11}H_{20}ClNO_2$: C, 56.52; H, 8.52; N, 5.99. Found: C, 56.38; H, 8.63; N, 5.77.

***cis*-1-Allyl-4-[(2-chloro-1,1-dimethyl)ethyl]-3-methoxyazetidin-2-one (7f):** ^{1}H NMR ($CDCl_3$) δ 1.11 and 1.13 (2 × 3H, 2 × s, Me_2C_q), 3.44 (1H, d, J = 10.9 Hz, C*H*(H)Cl), 3.57 (3H, s, OMe), 3.60 (1H, m, NC*H*(H)), 3.71 (1H, d, J = 10.9 Hz, CH(*H*)Cl), 3.86 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.20 (1H, m, NCH-(*H*)), 4.51 (1H, d, J = 5.3 Hz, OCH), 5.19−5.26 (2H, m, $CHCH_2$), 5.70−5.80 (1H, m, $CHCH_2$); ^{13}C NMR ($CDCl_3$) δ 21.94 and 23.68 (Me_2C_q), 38.04 ($C_q(CH_3)_2$), 44.42 (NCH_2), 53.14 (CH_2-Cl), 59.57 (OMe), 63.16 ($NCHC_q$), 84.53 (OCH), 119.15 (=CH), 131.61 (=CH_2), 168.75 (C=O); IR (NaCl) 1738 cm^{-1} (C=O); MS *m*/*z* 231/233 (0.03, M$^+$), 148/150 (7), 133/135 (2), 99 (100), 91 (2), 85 (3), 84 (2), 83 (3), 71 (2), 69 (3), 67 (6), 65 (3), 56 (3), 55 (11), 53 (4). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.24, yield 68%. Anal. Calcd for $C_{11}H_{18}ClNO_2$: C, 57.02; H, 7.83; N, 6.04. Found: C, 57.26; H, 7.94; N, 6.16.

***cis*-3-Benzyloxy-4-[(2-bromo-1,1-dimethyl)ethyl]-1-isopropylazetidin-2-one (8a):** ^{1}H NMR ($CDCl_3$) δ 1.19 and 1.21 (2 × 3H, 2 × s, Me_2C_q), 1.28 and 1.46 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 3.34 (1H, d, J = 10.9 Hz, C*H*(H)Br), 3.51 (1H, septet, J = 6.6 Hz, C*H*Me_2), 3.74 (1H, d, J = 10.9 Hz, CH(*H*)-Br), 3.85 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.59 (1H, d, J = 5.3 Hz, OCH), 4.69 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.94 (1H, d, J = 11.9 Hz, OCH(*H*)), 7.32−7.36 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 20.75 and 20.79 (Me_2CH), 22.70 and 24.76 (Me_2C_q), 37.14 ($C_q(CH_3)_2$), 44.06 (CH_2Br), 47.28 (*C*HMe_2), 63.52 ($NCHC_q$), 73.17 ($OCH_2C_6H_5$), 81.10 (OCH), 127.65, 127.83 and 128.43 (C_o, C_m, C_p), 137.27 (C_q), 168.77 (C=O); IR (NaCl) 1739 cm^{-1} (C=O); MS *m*/*z* no M$^+$, 224/226 (4), 208 (3), 196 (8), 194 (27), 192 (19), 177/179 (8), 175 (6), 114 (8), 105 (49), 99 (100), 98 (13), 91 (49), 88 (90), 86 (17), 84 (29), 83 (11), 81 (9), 69 (15), 67 (12), 59 (25), 56 (16), 55 (27), 53 (8). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.35, yield 75%. Anal. Calcd for $C_{17}H_{24}BrNO_2$: C, 57.63; H, 6.83; N, 3.95. Found: C, 57.75; H, 6.94; N, 3.79.

***cis*-3-Benzyloxy-4-[(2-bromo-1,1-dimethyl)ethyl]-1-cyclohexylazetidin-2-one (8b):** ^{1}H NMR ($CDCl_3$) δ 1.20−2.01 (10H, m, $(CH_2)_5$), 1.18 and 1.20 (2 × 3H, 2 × s, Me_2C_q), 3.01−3.10 (1H, m, NC*H*), 3.33 (1H, d, J = 10 Hz, C*H*(H)Br), 3.73 (1H, d, J = 10 Hz, CH(*H*)Br), 3.85 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.57 (1H, d, J = 5.3 Hz, OCH), 4.67 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.92 (1H, d, J = 11.9 Hz, OCH(*H*)), 7.26−7.34 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 22.68 and 24.69 (Me_2C_q), 25.18, 25.23, 25.73, 30.64 and 31.00 ($(CH_2)_5$), 37.18 ($C_q(CH_3)_2$), 44.06 (CH_2Br), 55.36 (NCH), 63.27 ($NCHC_q$), 73.04 ($OCH_2C_6H_5$), 80.86 (OCH), 127.53, 127.74 and 128.34 (C_o, C_m, C_p), 137.19 (C_q), 168.51 (C=O); IR (NaCl) 1737 cm^{-1} (C=O); MS *m*/*z* no M$^+$, 267/269 (58), 176 (100), 134 (14), 99 (12), 92 (50), 91 (89), 86 (13), 84 (18), 83 (48), 65 (27), 55 (36). Flash chromatography petroleum ether/EtOAc 8/2, R_f 0.38, yield 99%. Anal. Calcd for $C_{20}H_{28}BrNO_2$: C, 60.91; H, 7.16; N, 3.55. Found: C, 60.75; H, 6.94; N, 3.59.

***cis*-1-Allyl-3-benzyloxy-4-[(2-bromo-1,1-dimethyl)ethyl]-azetidin-2-one (8c):** ^{1}H NMR ($CDCl_3$) δ 1.17 (2 × 3H, 2 × s, Me_2C_q), 3.33 (1H, d, J = 10.9 Hz, C*H*(H)Br), 3.66 (1H, d × d, J = 15 Hz, J = 7 Hz, NC*H*(H)), 3.71 (1H, d, J = 10.9 Hz, CH-(*H*)Br), 3.87 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.19 (1H, d × d, J = 15 Hz, J = 3 Hz, NCH(*H*)), 4.69 (1H, d, J = 5.3 Hz, OCH), 4.69 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.95 (1H, d, J = 11.9 Hz, OCH(*H*)), 5.18−5.25 (2H, m, $CHCH_2$), 5.67−5.79 (1H, m, $CHCH_2$), 7.30−7.35 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 22.70 and 24.78 (Me_2C_q), 37.23 ($C_q(CH_3)_2$), 43.65 (CH_2Br), 44.47 (NCH_2), 63.67 ($NCHC_q$), 73.30 ($OCH_2C_6H_5$), 81.99 (OCH), 119.23 (=CH), 127.67, 127.90 and 128.46 (C_o, C_m, C_p), 131.61 (=CH_2), 137.10 (C_q), 168.73 (C=O); IR (NaCl) 1751 cm^{-1} (C=O); MS *m*/*z* 351/353 (0.1, M$^+$), 267/269 (21), 261 (10), 175 (56), 133 (8), 115 (5), 103 (11), 92 (42), 91 (100), 83 (14), 77 (8), 68 (8), 65 (30), 56 (11), 55 (15), 51 (14), 49 (13). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.31, yield 90%. Anal. Calcd for $C_{17}H_{22}BrNO_2$: C, 57.96; H, 6.29; N, 3.98. Found: C, 57.75; H, 6.42; N, 3.87.

***cis*-3-Benzyloxy-4-[(2-bromo-1,1-dimethyl)ethyl]-1-ethylazetidin-2-one (8d):** ^{1}H NMR ($CDCl_3$) δ 1.18 (3H, t, J = 7.3 Hz, CH_3CH_2), 1.18 and 1.20 (2 × 3H, 2 × s, Me_2C_q), 2.95−3.09 (1H, m, CH_3CH(H)), 3.33 (1H, d, J = 10.2 Hz, C*H*(H)Br), 3.59−3.73 (1H, m, CH_3CH(*H*)), 3.73 (1H, d, J = 10.2 Hz, CH-(*H*)Br), 3.89 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.65 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.67 (1H, d, J = 5.3 Hz, OCH), 4.94 (1H, d, J = 11.9 Hz, OCH(*H*)), 7.26−7.36 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 12.65 (CH_3CH_2), 22.55 and 24.76 (Me_2C_q), 36.46 (CH_3CH_2), 37.27 ($C_q(CH_3)_2$), 43.65 (CH_2Br), 62.80 ($NCHC_q$), 73.22 (OCH_2-C_6H_5), 81.72 (OCH), 127.62, 127.85 and 128.43 (C_o, C_m, C_p), 137.12 (C_q), 168.66 (C=O); IR (NaCl) 1753 cm^{-1} (C=O); MS *m*/*z* no M$^+$, 268/270 (31), 194/196 (5), 177 (100), 135 (13), 115 (13), 108 (30), 99 (11), 93 (56), 92 (92), 90 (12), 84 (25), 65 (40), 57 (29), 56 (22). Flash chromatography petroleum ether/EtOAc 8/2, R_f 0.15, yield 75%. Anal. Calcd for $C_{16}H_{22}BrNO_2$: C, 56.48; H, 6.52; N, 4.12. Found: C, 56.60; H, 6.66; N, 4.03.

***cis*-3-Benzyloxy-4-[(2-bromo-1,1-dimethyl)ethyl]-1-*n*-propylazetidin-2-one (8e):** ^{1}H NMR ($CDCl_3$) δ 0.90 (3H, t, J = 7.3 Hz, CH_3CH_2), 1.19 and 1.20 (2 × 3H, 2 × s, Me_2C_q), 1.49−1.70 (2H, m, CH_2CH_3), 2.90−3.00 (1H, m, NC*H*(H)), 3.33 (1H, d, J = 10 Hz, C*H*(H)Br), 3.50−3.61 (1H, m, NCH(*H*)), 3.73 (1H, d, J = 10 Hz, CH(*H*)Br), 3.87 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.69 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.69 (1H, d, J =

5.3 Hz, OCH), 4.96 (1H, d, J = 11.9 Hz, OCH(*H*)), 7.23−7.39 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 11.39 (CH_3CH_2), 20.58 (CH_3CH_2), 22.57 and 24.78 (Me_2C_q), 37.29 ($C_q(CH_3)_2$), 43.32 (NCH_2), 43.68 (CH_2Br), 63.05 ($NCHC_q$), 73.17 ($OCH_2C_6H_5$), 81.62 (OCH), 127.56, 127.81 and 128.41 (C_o, C_m, C_p), 137.14 (C_q), 168.84 (C=O); IR (NaCl) 1753 cm^{-1} (C=O); MS *m*/*z* 353/355 (2, M^+), 269/271 (82), 207 (11), 182 (24), 176 (100), 146 (8), 133 (34), 128 (25), 98 (13), 92 (44), 91 (77), 90 (10), 89 (12), 83 (21), 70 (11), 65 (21), 55 (10). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.29, yield 67%. Anal. Calcd for $C_{17}H_{24}BrNO_2$: C, 57.63; H, 6.83; N, 3.95. Found: C, 57.67; H, 6.96; N, 3.82.

***cis*-3-Benzyloxy-4-[(2-bromo-1,1-dimethyl)ethyl]-1-cinnamylazetidin-2-one (8f):** ^{1}H NMR ($CDCl_3$) δ 1.20 and 1.21 (2 × 3H, 2 × s, Me_2C_q), 3.37 (1H, d, J = 9.9 Hz, C*H*(H)Br), 3.70 (1H, d, J = 9.9 Hz, CH(*H*)Br), 3.79 (1H, d × d, J = 15 Hz, J = 7 Hz, NC*H*(H)), 3.92 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.34 (1H, d × d, J = 15 Hz, J = 6 Hz, NCH(*H*)), 4.71 (1H, d, J = 11.9 Hz, OC*H*(H)), 4.72 (1H, d, J = 5.3 Hz, OCH), 4.96 (1H, d, J = 11.9 Hz, OCH(*H*)), 6.05−6.15 (1H, m, =CH), 6.52−6.58 (1H, m, =CH), 7.23−7.38 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 22.73 and 24.67 (Me_2C_q), 37.23 ($C_q(CH_3)_2$), 43.74 (CH_2Br), 49.97 (NCH_2), 63.63 ($NCHC_q$), 73.31 ($OCH_2C_6H_5$), 82.05 (OCH), 122.62 (=CH), 126.49, 127.67, 127.90, 128.08, 128.46 and 128.64 (C_o, C_m, C_p), 134.43 (=CH_2), 136.08 and 137.07 (C_q), 168.75 (C=O); IR (NaCl) 1751 cm^{-1} (C=O); LC-MS *m*/*z* 428/430 (100, $[M + H]^+$). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.34, yield 78%. Anal. Calcd for $C_{23}H_{26}BrNO_2$: C, 64.49; H, 6.12; N, 3.27. Found: C, 64.61; H, 6.26; N, 3.19.

***cis*-4-[(2-Bromo-1,1-dimethyl)ethyl]-1-isopropyl-3-methoxyazetidin-2-one (8g):** ^{1}H NMR ($CDCl_3$) δ 1.16 and 1.19 (2 × 3H, 2 × s, Me_2C_q), 1.29 and 1.45 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 3.34 (1H, d, J = 9.9 Hz, C*H*(H)Br), 3.51 (1H, septet, J = 6.6 Hz, C*H*Me_2), 3.56 (3H, s, OMe), 3.68 (1H, d, J = 9.9 Hz, CH(*H*)Br), 3.84 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.40 (1H, d, J = 5.3 Hz, OCH); ^{13}C NMR ($CDCl_3$) δ 20.72 and 20.75 (Me_2-CH), 22.64 and 24.60 (Me_2C_q), 37.20 ($C_q(CH_3)_2$), 43.97 (CH_2-Br), 47.17 (*C*HMe_2), 59.48 (OMe), 63.63 ($NCHC_q$), 83.57 (OCH), 168.77 (C=O); IR (NaCl) 1749 cm^{-1} (C=O); MS *m*/*z* 277/279 (2, M^+), 263/265 (2), 233/235 (2), 225 (10), 223 (8), 205/207 (13), 200 (5), 198 (3, M^+ − Br), 176/178 (35), 170 (7), 143 (4), 98 (79), 88 (4). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.31, yield 76%. Anal. Calcd for $C_{11}H_{20}BrNO_2$: C, 47.49; H, 7.25; N, 5.04. Found: C, 47.61; H, 7.37; N, 4.98.

***cis*-1-Allyl-4-[(2-bromo-1,1-dimethyl)ethyl]-3-methoxyazetidin-2-one (8h):** ^{1}H NMR ($CDCl_3$) δ 1.15 and 1.16 (2 × 3H, 2 × s, Me_2C_q), 3.34 (1H, d, J = 9.9 Hz, C*H*(H)Br), 3.58 (3H, s, OMe), 3.60−3.68 (1H, m, NC*H*(H)), 3.66 (1H, d, J = 9.9 Hz, CH(*H*)Br), 3.86 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.16 (1H, d × d, J = 15 Hz, J = 6 Hz, NCH(*H*)), 4.50 (1H, d, J = 5.3 Hz, OCH), 5.19−5.26 (2H, m, $CHCH_2$), 5.68−5.78 (1H, m, $CHCH_2$); ^{13}C NMR ($CDCl_3$) δ 22.61 and 24.15 (Me_2C_q), 37.23 ($C_q(CH_3)_2$), 43.56 (CH_2Br), 44.38 (NCH_2), 59.62 (OMe), 63.75 ($NCHC_q$), 84.40 (OCH), 119.23 (=CH), 131.50 (=CH_2), 168.84 (C=O); IR (NaCl) 1750 cm^{-1} (C=O); MS *m*/*z* 275/277 (0.1, M^+), 191/193 (7), 176/178 (4), 135/137 (1), 99 (100), 98 (5), 86 (2), 83 (3), 81 (2), 67 (3), 55 (7), 49 (2). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.26, yield 90%. Anal. Calcd for $C_{11}H_{18}BrNO_2$: C, 47.84; H, 6.57; N, 5.07. Found: C, 47.75; H, 6.64; N, 4.97.

***cis*-4-[(2-Bromo-1,1-dimethyl)ethyl]-1-ethyl-3-methoxyazetidin-2-one (8i):** ^{1}H NMR ($CDCl_3$) δ 1.16 and 1.18 (2 × 3H, 2 × s, Me_2C_q), 1.19 (3H, t, J = 7.6 Hz, C*H*$_3$CH$_2$), 2.98−3.09 (1H, m, CH$_3$C*H*(H)), 3.34 (1H, d, J = 9.9 Hz, C*H*(H)Br), 3.57 (3H, s, OMe), 3.61−3.70 (1H, m, CH$_3$CH(*H*)), 3.68 (1H, d, J = 9.9 Hz, CH(*H*)Br), 3.87 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.46 (1H, d, J = 5.3 Hz, OCH); ^{13}C NMR ($CDCl_3$) δ 12.67 (*C*H$_3$-CH_2), 22.53 and 24.56 (Me_2C_q), 36.37 (CH_3CH_2), 37.36 (C_q-$(CH_3)_2$), 43.59 (CH_2Br), 59.53 (OMe), 62.87 ($NCHC_q$), 84.33 (OCH), 168.43 (C=O); IR (NaCl) 1753 cm^{-1} (C=O); MS *m*/*z* 263/265 (1, M^+), 221/223 (1), 191/193 (61), 176/178 (30), 113 (3), 100 (66), 99 (100), 98 (44), 97 (13), 83 (35), 82 (16), 81 (24), 79 (9), 72 (20), 71 (16), 70 (11), 69 (20), 68 (16), 67 (37), 59 (20), 57 (13), 56 (61), 55 (65), 53 (29). Flash chromatography petroleum ether/EtOAc 6/4, R_f 0.33, yield 61%. Anal. Calcd for $C_{10}H_{18}BrNO_2$: C, 45.47; H, 6.87; N, 5.30. Found: C, 45.65; H, 6.94; N, 5.41.

***cis*-4-[(2-Bromo-1,1-dimethyl)ethyl]-1-(2-bromoethyl)-3-methoxyazetidin-2-one (8j):** mp 44.7−45.3 °C; ^{1}H NMR ($CDCl_3$) δ 1.17 and 1.19 (2 × 3H, 2 × s, Me_2C_q), 3.33 (1H, d, J = 9.9 Hz, C*H*(H)Br), 3.38−3.62 and 4.03−4.08 (4H, 2 × m, $N(CH_2)_2$), 3.58 (3H, s, OMe), 3.65 (1H, d, J = 9.9 Hz, CH(*H*)-Br), 3.99 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.60 (1H, d, J = 5.3 Hz, OCH); ^{13}C NMR ($CDCl_3$) δ 22.70 and 24.60 (Me_2C_q), 28.32 (NCH_2), 37.48 ($C_q(CH_3)_2$), 43.38 (2 × CH_2Br), 59.75 (OMe), 63.88 ($NCHC_q$), 84.26 (OCH), 169.25 (C=O); IR (KBr) 1740 cm^{-1} (C=O); MS *m*/*z* 341/343/345 (23, M^+), 297/299/301 (9), 269/271/273 (64), 233/235 (18), 191/193 (99), 177/179 (37), 176/178 (60), 112 (27), 106/108 (47), 98 (100), 97 (43), 83 (42), 82 (35), 81 (29), 80 (26), 71 (25), 67 (30), 55 (31), 54 (43). Flash chromatography petroleum ether/EtOAc 6/4, R_f 0.40, yield 77%. Anal. Calcd for $C_{10}H_{17}Br_2NO_2$: C, 35.01; H, 4.99; N, 4.08. Found: C, 35.15; H, 4.87; N, 3.90.

***cis*-1-(2-Benzyloxyethyl)-4-[(2-bromo-1,1-dimethyl)ethyl]-3-methoxyazetidin-2-one (8k):** ^{1}H NMR ($CDCl_3$) δ 1.12 and 1.14 (2 × 3H, 2 × s, Me_2C_q), 3.10−3.19 and 3.59−3.70 (2H, 2 × m, NCH_2), 3.36 (1H, d, J = 9.9 Hz, C*H*(H)Br), 3.59−3.70 and 3.77−3.84 (2H, 2 × m, OCH_2), 3.58 (3H, s, OMe), 3.71 (1H, d, J = 9.9 Hz, CH(*H*)Br), 3.87 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.54 (1H, d, J = 5.3 Hz, OCH), 4.56 (1H, d, J = 11.9 Hz, OC*H*(H)C_6H_5), 4.61 (1H, d, J = 11.9 Hz, OCH(*H*)C_6H_5), 7.25−7.43 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 22.71 and 24.47 (Me_2C_q), 37.45 ($C_q(CH_3)_2$), 41.74 (NCH_2), 43.72 (CH_2Br), 59.59 (OMe), 64.28 ($NCHC_q$), 66.74 (OCH_2), 72.94 ($OCH_2C_6H_5$), 84.40 (OCH), 127.78 and 128.44 (C_o, C_m, C_p), 137.77 (C_q), 169.40 (C=O); IR (NaCl) 1756 cm^{-1} (C=O); MS *m*/*z* 369/371 (0.1, M^+), 192/194 (16), 179 (3), 148 (1), 135 (1), 131 (1), 113 (2), 99 (100), 91 (26), 86 (2), 83 (3), 67 (2), 65 (3), 56 (2), 55 (4). Flash chromatography petroleum ether/EtOAc 6/4, R_f 0.26, yield 85%. Anal. Calcd for $C_{17}H_{24}BrNO_3$: C, 55.14; H, 6.53; N, 3.78. Found: C, 55.30; H, 6.61; N, 3.84.

***cis*-4-[(2-Bromo-1,1-dimethyl)ethyl]-1-cinnamyl-3-methoxyazetidin-2-one (8*l*):** ^{1}H NMR ($CDCl_3$) δ 1.16 and 1.18 (2 × 3H, 2 × s, Me_2C_q), 3.36 (1H, d, J = 9.9 Hz, C*H*(H)Br), 3.58 (OMe), 3.64 (1H, d, J = 9.9 Hz, CH(*H*)Br), 3.78 (1H, d × d, J = 15 Hz, J = 7.3 Hz, NC*H*(H)), 3.90 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.34 (1H, d × d, J = 15 Hz, J = 6 Hz, NCH(*H*)), 4.52 (1H, d, J = 5.3 Hz, OCH), 6.05−6.16 (1H, m, =CH), 6.52−6.58 (1H, m, =CH), 7.24−7.38 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 22.36 and 24.10 (Me_2C_q), 36.95 ($C_q(CH_3)_2$), 43.36 (CH_2Br), 43.52 (NCH_2), 59.21 (OMe), 63.36 ($NCHC_q$), 84.26 (OCH), 122.37 (=CH), 126.15, 127.71 and 128.30 (C_o, C_m, C_p), 133.96 (=CH_2), 135.78 (C_q), 168.30 (C=O); IR (NaCl) 1744 cm^{-1} (C=O); MS *m*/*z* 351/353 (0.2, M^+), 192/194 (54), 159 (25), 130 (24), 117 (66), 116 (18), 115 (53), 100 (46), 99 (100), 91 (31), 86 (24), 84 (42), 83 (13), 67 (13), 57 (10), 56 (12), 55 (38), 51 (12), 49 (22). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.30, yield 63%. Anal. Calcd for $C_{17}H_{22}BrNO_2$: C, 57.96; H, 6.29; N, 3.98. Found: C, 57.75; H, 6.42; N, 3.77.

***cis*-4-[(2-Bromo-1,1-dimethyl)ethyl]-3-methoxy-1-(2-methylallyl)azetidin-2-one (8m):** ^{1}H NMR ($CDCl_3$) δ 1.15 (6H, s, Me_2C_q), 1.70 (3H, s, C_qCH_3), 3.34 (1H, d, J = 9.9 Hz, C*H*(H)Br), 3.54 (1H, d, J = 15.2 Hz, NC*H*(H)), 3.59 (3H, s, OMe), 3.67 (1H, d, J = 9.9 Hz, CH(*H*)Br), 3.79 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.14 (1H, d, J = 15.2 Hz, NCH(*H*)), 4.54 (1H, d, J = 5.3 Hz, OCH), 4.86 and 4.96 (2 × 1H, 2 × s, =CH_2); ^{13}C NMR ($CDCl_3$) δ 20.22, 22.64 and 24.60 (3 × C_qCH_3), 37.12 (C_q-$(CH_3)_2$), 43.59 (CH_2Br), 47.78 (NCH_2), 59.51 (OMe), 63.83 ($NCHC_q$), 84.33 (OCH), 114.52 (=CH_2), 139.23 (=C_q), 169.04 (C=O); IR (NaCl) 1756 cm^{-1} (C=O); MS *m*/*z* no M^+, 192/194 (14), 177/179 (3), 138 (2), 126 (1), 113 (2), 99 (100), 98 (7), 94 (2), 84 (3), 83 (5), 81 (3), 79 (1), 69 (4), 67 (7), 56 (3), 55 (21), 53 (5). Flash chromatography petroleum ether/EtOAc 6/4, R_f

0.45, yield 90%. Anal. Calcd for $C_{12}H_{20}BrNO_2$: C, 49.67; H, 6.95; N, 4.83. Found: C, 49.79; H, 6.91; N, 4.74.

***cis*-4-[(2-Bromo-1,1-dimethyl)ethyl]-3-methoxy-1-(1-vinylcyclopropyl)azetidin-2-one (8n):** ^{1}H NMR ($CDCl_3$) δ 1.02−1.41 (4H, m, $(CH_2)_2$), 1.15 and 1.18 (2 × 3H, 2 × s, Me_2C_q), 3.42 (1H, d, J = 9.9 Hz, C*H*(H)Br), 3.55 (3H, s, OMe), 3.61 (1H, d, J = 9.9 Hz, CH(*H*)Br), 3.80 (1H, d, J = 5.3 Hz, $NCHC_q$), 4.42 (1H, d, J = 5.3 Hz, OCH), 5.05−5.12 (2H, m, $=CH_2$), 5.74−5.87 (1H, m, =CH); ^{13}C NMR ($CDCl_3$) δ 13.39 and 18.15 ($(CH_2)_2$), 22.52 and 23.72 (Me_2C_q), 35.60 and 36.89 (2 × C_q), 44.02 (CH_2Br), 59.55 (OMe), 64.13 (N*C*HC$_q$), 83.75 (OCH), 113.46 ($=CH_2$), 138.63 (=CH), 169.45 (C=O); IR (NaCl) 1755 cm^{-1} (C=O); MS m/z no M$^+$, 166 (1), 138 (1), 123 (1), 121 (3), 119 (3), 99 (3), 88 (15), 86 (76), 84 (100), 70 (1), 69 (1), 55 (1), 51 (35), 49 (91), 48 (8), 47 (32). Flash chromatography petroleum ether/EtOAc 6/4, R_f 0.36, yield 77%. Anal. Calcd for $C_{13}H_{20}BrNO_2$: C, 51.67; H, 6.67; N, 4.63. Found: C, 51.52; H, 6.78; N, 4.52.

***cis*-4-[(2-Bromo-1,1-dimethyl)ethyl]-3-methoxy-1-(1-phenylallyl)azetidin-2-one (8o)** [isolated as a 1/1 mixture of diastereomers]: ^{1}H NMR ($CDCl_3$) δ 1.00, 1.10 and 1.11 (12H, 3 × s, Me_2C_q), 3.13 and 3.24 (2 × 1H, 2 × d, J = 10 Hz, 2 × C*H*(H)Br), 3.45 and 3.57 (2 × 1H, 2 × d, J = 10 Hz, 2 × CH(*H*)Br), 3.54 and 3.56 (2 × 3H, 2 × s, 2 × OMe), 3.79 and 3.96 (2 × 1H, 2 × d, J = 5.3 Hz, 2 × $NCHC_q$), 4.39 and 4.52 (2 × 1H, 2 × d, J = 5.3 Hz, 2 × OCH), 4.77 and 4.97 (2 × 1H, 2 × d, J = 7 Hz, 2 × N*C*H*C*$_6$H$_5$), 5.05−5.33 (4H, m, 2 × CHCH_2), 6.29−6.58 (2H, m, 2 × C*H*CH$_2$), 7.24−7.46 (10H, m, 2 × C_6H_5); ^{13}C NMR ($CDCl_3$) δ 21.58, 22.03, 22.68 and 23.45 (2 × Me_2C_q), 36.35 and 36.57 (2 × $C_q(CH_3)_2$), 43.29 and 43.51 (2 × CH_2Br), 59.73 (2 × OMe), 61.89 and 63.22 (2 × N*C*HC$_6$H$_5$), 62.77 and 64.66 (2 × N*C*HC$_q$), 82.70 and 82.97 (2 × OCH), 116.68 and 117.48 (2 × $=CH_2$), 126.70, 127.04, 127.24, 127.53 and 128.09 (2 × C_o, 2 × C_m, 2 × C_p), 134.25 and 135.36 (2 × =CH), 138.31 and 138.80 (2 × C_q), 167.89 and 168.00 (2 × C=O). Flash chromatography petroleum ether/EtOAc 8/2, R_f 0.34, yield 90%. Anal. Calcd for $C_{17}H_{22}BrNO_2$: C, 57.96; H, 6.29; N, 3.98. Found: C, 57.86; H, 6.38; N, 3.89.

***cis*-4-[(2-Bromo-1,1-dimethyl)ethyl]-1-isopropyl-3-phthalimidoylazetidin-2-one (8p):** mp 120.1−122.0 °C; ^{1}H NMR ($CDCl_3$) δ 1.01 and 1.11 (2 × 3H, 2 × s, Me_2C_q), 1.39 and 1.57 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 3.29 (1H, d, J = 5.6 Hz, C*H*(H)Br), 3.31 (1H, d, J = 5.6 Hz, CH(*H*)Br), 3.61 (1H, septet, J = 6.6 Hz, C*H*Me$_2$), 4.14 (1H, d, J = 5.3 Hz, $NCHC_q$), 5.22 (1H, d, J = 5.3 Hz, OCH), 7.74−7.92 (4H, m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 20.18 and 20.84 (Me_2CH), 23.09 and 23.38 (Me_2C_q), 36.24 ($C_q(CH_3)_2$), 44.35 (CH_2Br), 48.19 (*C*HMe$_2$), 56.26 (N*C*HC$_q$), 63.34 (N*C*HCO), 123.79, 123.92, 134.50 and 134.79 (4 × CH_{ar}), 131.23 and 132.00 (2 × C_q), 163.84, 166.39 and 167.87 (3 × C=O); IR (NaCl) 1746 and 1726 cm^{-1} (C=O); MS m/z no M$^+$, 230 (4), 217 (2), 215 (100), 214 (2), 209 (2), 207 (3), 197 (5), 188 (4), 161 (9), 149 (2), 131 (4), 106 (4), 105 (13), 82 (3), 81 (2), 76 (7), 70 (3), 67 (2), 55 (3). Purified by washing with 2 N hydrochloric acid, followed by recrystallization from methanol, yield 76%. Anal. Calcd for $C_{18}H_{21}BrN_2O_3$: C, 54.97; H, 5.38; N, 7.12. Found: C, 54.83; H, 5.46; N, 6.97.

Reactions of 4-(1-Haloalkyl)-2-azetidinones 4 and 5 and 4-(2-Haloalkyl)-2-azetidinones 7 and 8 with Sodium Methoxide in Methanol. To 10 mmol of the appropriate 2-azetidinone was added 40 mmol of 2 N sodium methoxide in methanol. This mixture was kept at reflux temperature for 4 h. The solvent was subsequently removed by evaporation and the residue was taken up in 20 mL of dichloromethane. The dichloromethane fraction was washed with water and the aqueous phase was again extracted with two times 20 mL of dichloromethane. The combined organic phases were dried (magnesium sulfate) and the crude reaction product was obtained after filtration of the drying agent and evaporation of the solvent. Further purification was performed by flash chromatography.

***Z*-Methyl 2-benzyloxy-4-isopropylamino-4-methylpent-2-enoate (9a):** ^{1}H NMR ($CDCl_3$) δ 1.01 (6H, d, J = 6.60 Hz, Me_2CH), 1.28 (6H, s, $C_q(CH_3)_2$), 1.75 (1H, br s, NH), 2.86 (1H, septet, J = 6.60 Hz, C*H*Me$_2$), 3.80 (3H, s, OMe), 4.88 (2H, s, OCH_2), 6.25 (1H, s, =CH), 7.28−7.44 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 25.82 (CH*Me$_2$*), 28.91 (C_qMe_2), 44.26 (NCH), 52.04 (OMe), 54.12 (C_qMe$_2$), 73.58 (OCH_2), 128.10, 128.17 and 128.46 (C_o, C_m, C_p), 135.52 (=CH), 136.80 (C_q), 143.61 (=C_q), 164.56 (C=O); IR (NaCl) 1720 and 1640 cm^{-1} (C=O and C=C); MS m/z no M$^+$, 248 (9), 216 (18), 200 (63), 174 (8), 126 (25), 113 (8), 105 (6), 100 (8), 99 (8), 98 (23), 92 (20), 91 (83), 88 (32), 86 (80), 84 (100), 83 (18), 71 (12), 65 (17), 59 (11), 58 (19), 55 (13), 51 (79), 49 (95), 48 (30), 47 (57). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.09, yield 45%. Anal. Calcd for $C_{17}H_{25}NO_3$: C, 70.07; H, 8.65; N, 4.81. Found: C, 70.21; H, 8.79; N, 4.74.

***Z*-Methyl 4-allylamino-2-benzyloxy-4-methylpent-2-enoate (9b):** ^{1}H NMR ($CDCl_3$) δ 1.27 (6H, s, $C_q(CH_3)_2$), 1.99 (1H, br s, NH), 3.13 (2H, d, J = 5.93 Hz, NCH_2), 3.79 (3H, s, OMe), 4.87 (2H, s, OCH_2), 5.00−5.09 (2H, m, $=CH_2$), 5.81−5.93 (1H, m, C*H*=CH$_2$), 6.18 (1H, s, =CH), 7.27−7.42 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 28.18 (C_qMe_2), 46.54 (NCH_2), 52.08 (OMe), 53.85 (C_qMe$_2$), 73.53 (OCH_2), 115.47 (CH=*C*H$_2$), 128.19 and 128.50 (C_o, C_m, C_p), 133.85 (=CH), 136.75 (C_q), 137.28 (*C*H=CH$_2$), 144.08 (=C_q), 164.42 (C=O); IR (NaCl) 1720 and 1641 cm^{-1} (C=O and C=C); MS m/z no M$^+$, 274 (67, M$^+$ − Me), 248 (11), 214 (25), 198 (58), 124 (34), 111 (11), 110 (10), 98 (21), 96 (17), 92 (30), 91 (95), 88 (36), 84 (100), 82 (19), 65 (33), 59 (22), 56 (26), 55 (25), 51 (47), 49 (90), 47 (75). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.08, yield 45%. Anal. Calcd for $C_{17}H_{23}NO_3$: C, 70.56; H, 8.01; N, 4.84. Found: C, 70.71; H, 8.14; N, 4.72.

***Z*-Methyl 4-isopropylamino-2-methoxy-4-methylpent-2-enoate (9c):** ^{1}H NMR ($CDCl_3$) δ 1.06 (6H, d, J = 6.27 Hz, Me_2CH), 1.33 (6H, s, $C_q(CH_3)_2$), 1.75 (1H, br s, NH), 2.90 (1H, septet, J = 6.27 Hz, C*H*Me$_2$), 3.68 and 3.78 (2 × 3H, 2 × s, 2 × OMe), 6.20 (1H, s, =CH); ^{13}C NMR ($CDCl_3$) δ 25.88 (CH*Me$_2$*), 28.93 (C_qMe_2), 44.35 (NCH), 51.95 and 59.39 (2 × OMe), 54.03 (C_qMe$_2$), 134.97 (=CH), 144.98 (=C_q), 164.36 (C=O); IR (NaCl) 1725 and 1639 cm^{-1} (C=O and C=C); MS m/z 215 (17, M$^+$), 200 (100, M$^+$ − Me), 172 (19), 158 (31), 157 (39), 141 (27), 140 (17), 126 (75), 125 (78), 105 (47), 100 (19), 98 (21), 97 (43), 84 (25), 83 (25), 75 (28), 68 (31), 57 (48), 55 (29), 53 (12). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.09, yield 46%. Anal. Calcd for $C_{11}H_{21}NO_3$: C, 61.37; H, 9.83; N, 6.51. Found: C, 61.23; H, 9.77; N, 6.62.

***Z*-Methyl 2-benzyloxy-4,4-dimethyl-5-isopropylaminopent-2-enoate (10a):** ^{1}H NMR ($CDCl_3$) δ 1.00 (6H, d, J = 6.27 Hz, Me_2CH), 1.15 (6H, s, $C_q(CH_3)_2$), 1.36 (1H, br s, NH), 2.52 (2H, s, NCH_2), 2.69 (1H, septet, J = 6.27 Hz, C*H*Me$_2$), 3.78 (3H, s, OMe), 4.84 (2H, s, OCH_2), 6.24 (1H, s, =CH), 7.33−7.45 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 22.95 (CH*Me$_2$*), 26.13 (C_qMe_2), 36.71 (C_qMe$_2$), 49.40 (NCH), 51.86 (OMe), 58.44 (NCH_2), 73.60 (OCH_2), 127.92, 128.07 and 128.35 (C_o, C_m, C_p), 135.04 (=CH), 137.02 (C_q), 144.24 (=C_q), 164.71 (C=O); IR (NaCl) 1720 and 1638 cm^{-1} (C=O and C=C); MS m/z 305 (2, M$^+$), 213 (8), 143 (1), 97 (1), 91 (30), 84 (1), 83 (5), 72 (100), 71 (2), 70 (1), 67 (1), 65 (4), 59 (1), 57 (3), 56 (3). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.13, yield 65%. Anal. Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.87; H, 8.99; N, 4.48.

***Z*-Methyl 2-benzyloxy-4,4-dimethyl-5-ethylaminopent-2-enoate (10b):** ^{1}H NMR ($CDCl_3$) δ 1.07 (3H, t, J = 7.26 Hz, CH_2CH_3), 1.17 (6H, s, $C_q(CH_3)_2$), 2.57 (2H, s, NCH_2), 2.62 (2H, q, J = 7.26 Hz, CH_2CH$_3$), 3.79 (3H, s, OMe), 4.85 (2H, s, OCH_2), 6.21 (1H, s, =CH), 7.25−7.47 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 14.91 (CH_2CH_3), 26.29 (C_qMe_2), 36.68 (C_qMe$_2$), 44.87 (CH_2CH_3), 52.02 (OMe), 60.50 (NCH_2), 73.69 (OCH_2), 128.05, 128.17 and 128.43 (C_o, C_m, C_p), 134.71 (=CH), 136.89 (C_q), 144.26 (=C_q), 164.71 (C=O); IR (NaCl) 1721 and 1641 cm^{-1} (C=O and C=C); MS m/z 291 (0.1, M$^+$), 244 (2), 214 (5), 200 (11), 190 (2), 168 (5), 152 (2), 143 (4), 138 (2), 126 (2), 117 (2), 116 (2), 112 (3), 97 (2), 91 (98), 85 (3), 83 (13), 77 (2), 72 (100), 65 (8), 58 (73), 55 (5). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f

0.11, yield 66%. Anal. Calcd for $C_{17}H_{25}NO_3$: C, 70.07; H, 8.65; N, 4.81. Found: C, 70.21; H, 8.74; N, 4.70.

***Z*-Methyl 5-allylamino-2-benzyloxy-4,4-dimethylpent-2-enoate (10c):** ^{1}H NMR ($CDCl_3$) δ 1.16 (6H, s, $C_q(CH_3)_2$), 1.18 (1H, br s, NH), 2.54 (2H, s, NCH_2), 3.20 (2H, d, J = 6.27 Hz, NCH_2), 3.79 (3H, s, OMe), 4.84 (2H, s, OCH_2), 5.03−5.16 (2H, m, $=CH_2$), 5.80−5.89 (1H, m, =CH), 6.22 (1H, s, =CH), 7.26−7.45 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 26.20 (C_qMe_2), 36.82 (C_qMe_2), 51.93 (OMe), 53.12 (NCH_2CH), 60.22 (NCH_2), 73.64 (OCH_2), 115.61 (=CH), 127.98, 128.12 and 128.37 (C_o, C_m, C_p), 134.91 (=CH), 136.96 (C_q), 137.23 ($=CH_2$), 144.20 (=C_q), 164.69 (C=O); IR (NaCl) 1721 and 1643 cm^{-1} (C=O and C=C); MS *m*/*z* 303 (18, M$^+$), 270 (21), 255 (19), 211 (58), 143 (31), 124 (8), 96 (10), 92 (42), 91 (94), 89 (13), 84 (12), 83 (71), 82 (12), 77 (9), 71 (61), 70 (100), 69 (22), 68 (34), 67 (14), 65 (65), 63 (12), 57 (11), 56 (15), 55 (45), 53 (16), 51 (13). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.10, yield 60%. Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62. Found: C, 71.19; H, 8.38; N, 4.52.

***Z*-Methyl 2-benzyloxy-4,4-dimethyl-5-*n*-propylamino-pent-2-enoate (10d):** ^{1}H NMR ($CDCl_3$) δ 0.86 (3H, t, J = 7.26 Hz, CH_2CH_3), 1.17 (6H, s, $C_q(CH_3)_2$), 1.46 (2H, sextet, J = 7.26 Hz, CH_2CH_3), 2.53 (2H, t, J = 7.26 Hz, NCH_2CH_2), 2.56 (2H, s, NCH_2), 2.62 (2H, q, J = 7.26 Hz, CH_2CH_3), 3.79 (3H, s, OMe), 4.84 (2H, s, OCH_2), 6.22 (1H, s, =CH), 7.27−7.45 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 11.54 (CH_2CH_3), 22.61 (CH_2CH_3), 26.17 (C_qMe_2), 36.66 (C_qMe_2), 51.88 (OMe), 52.44 (NCH_2CH_2), 60.47 (NCH_2), 73.60 (OCH_2), 127.92, 128.07 and 128.30 (C_o, C_m, C_p), 134.68 (=CH), 136.80 (C_q), 144.12 (=C_q), 164.60 (C=O); IR (NaCl) 1723 and 1639 cm^{-1} (C=O and C=C); MS *m*/*z* 305 (1, M$^+$), 214 (21), 175 (2), 143 (5), 130 (2), 113 (3), 108 (3), 107 (2), 98 (2), 91 (84), 85 (3), 83 (11), 79 (3), 77 (3), 72 (100), 70 (4), 65 (7), 56 (3), 55 (4). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.09, yield 75%. Anal. Calcd for $C_{18}H_{27}NO_3$: C, 70.79; H, 8.91; N, 4.59. Found: C, 70.67; H, 8.99; N, 4.71.

***Z*-Methyl 4,4-dimethyl-5-isopropylamino-2-methoxy-pent-2-enoate (10e):** ^{1}H NMR ($CDCl_3$) δ 1.04 (6H, d, J = 6.27 Hz, Me_2CH), 1.17 (6H, s, $C_q(CH_3)_2$), 2.55 (2H, s, NCH_2), 2.73 (1H, septet, J = 6.27 Hz, $CHMe_2$), 3.65 and 3.77 (2 × 3H, 2 × s, 2 × OMe), 6.18 (1H, s, =CH); ^{13}C NMR ($CDCl_3$) δ 22.98 ($CHMe_2$), 26.07 (C_qMe_2), 36.66 (C_qMe_2), 49.51 (NCH), 51.86 and 59.59 (2 × OMe), 58.53 (NCH_2), 134.66 (=CH), 145.60 (=C_q), 164.69 (C=O); IR (NaCl) 1726 and 1644 cm^{-1} (C=O and C=C); MS *m*/*z* 229 (4, M$^+$), 214 (3, M$^+$ − Cl), 182 (3), 158 (3), 156 (8), 139 (6), 126 (5), 125 (8), 112 (4), 111 (9), 97 (12), 96 (5), 83 (17), 82 (10), 72 (100), 69 (4), 67 (7), 59 (8), 56 (14), 55 (14), 53 (6). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.12, yield 68%. Anal. Calcd for $C_{12}H_{23}NO_3$: C, 62.85; H, 10.11; N, 6.11. Found: C, 62.71; H, 10.21; N, 6.01.

***Z*-Methyl 5-allylamino-4,4-dimethyl-2-methoxypent-2-enoate (10f):** ^{1}H NMR ($CDCl_3$) δ 1.18 (6H, s, $C_q(CH_3)_2$), 1.25 (1H, br s, NH), 2.56 (2H, s, NCH_2), 3.25 (2H, d, J = 5.94 Hz, NCH_2), 3.65 and 3.77 (2 × 3H, 2 × s, 2 × OMe), 5.06−5.20 (2H, m, $=CH_2$), 5.83−5.93 (1H, m, =CH), 6.17 (1H, s, =CH); ^{13}C NMR ($CDCl_3$) δ 26.11 (C_qMe_2), 36.77 (C_qMe_2), 51.88 and 59.57 (2 × OMe), 53.19 (NCH_2CH), 60.27 (NCH_2), 115.69 (=CH_2), 134.41 (=CH), 137.23 (=CH), 145.98 (=C_q), 164.62 (C=O); IR (NaCl) 1722 and 1643 cm^{-1} (C=O and C=C); MS *m*/*z* 227 (3, M$^+$), 158 (4), 125 (4), 111 (4), 97 (6), 83 (12), 82 (5), 70 (100), 68 (6), 55 (7)53 (3). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.26, yield 60%. Anal. Calcd for $C_{12}H_{21}NO_3$: C, 63.41; H, 9.31; N, 6.16. Found: C, 63.53; H, 9.43; N, 6.01.

***Z*-Methyl 4,4-dimethyl-5-(ethylamino)-2-methoxypent-2-enoate (10g):** ^{1}H NMR ($CDCl_3$) δ 1.10 (3H, t, J = 7.26 Hz, CH_2CH_3), 1.18 (6H, s, $C_q(CH_3)_2$), 2.58 (2H, s, NCH_2), 2.66 (2H, q, J = 7.26 Hz, CH_2CH_3), 3.66 and 3.77 (2 × 3H, 2 × s, 2 × OMe), 6.17 (1H, s, =CH); ^{13}C NMR ($CDCl_3$) δ 15.22 (CH_2CH_3), 26.16 (C_qMe_2), 36.69 (C_qMe_2), 44.96 (CH_2CH_3), 51.89 and 59.57 (2 × OMe), 60.83 (NCH_2), 134.52 (=CH), 145.62 (=C_q), 164.63 (C=O); IR (NaCl) 1721 and 1644 cm^{-1} (C=O and C=C); MS *m*/*z* 215 (3, M$^+$), 184 (4), 158 (5), 143 (4), 125 (6), 111 (5), 99 (4), 97 (8), 83 (21), 67 (6), 58 (100), 55 (16), 53 (6). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.03, yield 50%. Anal. Calcd for $C_{11}H_{21}NO_3$: C, 61.37; H, 9.83; N, 6.51. Found: C, 61.21; H, 9.71; N, 6.40.

***Z*-Methyl 5-cinnamylamino-4,4-dimethyl-2-methoxy-pent-2-enoate (10h):** ^{1}H NMR ($CDCl_3$) δ 1.20 (6H, s, $C_q(CH_3)_2$), 1.54 (1H, br s, NH), 2.62 (2H, s, NCH_2), 3.42 (2H, d, J = 6.26 Hz, NCH_2), 3.65 and 3.76 (2 × 3H, 2 × s, 2 × OMe), 6.19 (1H, s, =CH), 6.28−6.34 and 6.49−6.55 (2 × 1H, 2 × m, 2 × =CH), 7.21−7.39 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 26.16 (C_qMe_2), 36.77 (C_qMe_2), 51.93 and 59.60 (2 × OMe), 52.61 (NCH_2CH), 60.25 (NCH_2), 126.25, 127.29 and 128.52 (C_o, C_m, C_p), 128.70 and 131.21 (2 × =CH), 134.36 (=CH), 137.14 (C_q), 145.60 (=C_q), 164.58 (C=O); IR (NaCl) 1723, 1671 and 1639 cm^{-1} (C=O and C=C); LC-MS *m*/*z* 304 (100, [M + H]$^+$). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.15, yield 68%. Anal. Calcd for $C_{18}H_{25}NO_3$: C, 71.26; H, 8.31; N, 4.62. Found: C, 71.18; H, 8.42; N, 4.78.

***Z*-Methyl 4,4-dimethyl-2-methoxy-5-(2-methylallylamino)pent-2-enoate (10i):** ^{1}H NMR ($CDCl_3$) δ 1.21 (6H, s, $C_q(CH_3)_2$), 1.25 (1H, br s, NH), 1.75 (3H, s, C_qCH_3), 2.56 (2H, s, NCH_2), 3.20 (1H, s, NCH_2C_q=), 3.63 and 3.78 (2 × 3H, 2 × s, 2 × OMe), 4.80−4.88 (2H, m, $=CH_2$), 6.18 (1H, s, =CH); ^{13}C NMR ($CDCl_3$) δ 19.80 (C_qCH_3), 25.81 (C_qMe_2), 36.55 (C_qMe_2), 51.66 and 59.35 (2 × OMe), 56.16 (NCH_2C_q=), 59.75 (NCH_2), 110.53 ($=CH_2$), 134.38 (=CH), 143.95 (=C_q), 145.32 (=C_q), 164.42 (C=O); IR (NaCl) 1725, 1673 and 1636 cm^{-1} (C=O and C=C); MS *m*/*z* 241 (0.1, M$^+$), 158 (1), 126 (1), 125 (3), 113 (1), 111 (1), 97 (3), 84 (100), 83 (3), 82 (8), 80 (1), 79 (1), 70 (1), 69 (1), 68 (2), 67 (4), 59 (2), 57 (3), 55 (27), 53 (2). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.15, yield 45%. Anal. Calcd for $C_{13}H_{23}NO_3$: C, 64.70; H, 9.61; N, 5.80. Found: C, 64.60; H, 9.76; N, 5.71.

***E*-Methyl 4-isopropylamino-4-methyl-2-phenoxypent-2-enoate (16):** ^{1}H NMR ($CDCl_3$) δ 1.09 (6H, d, J = 6.27 Hz, Me_2CH), 1.30 (6H, s, $C_q(CH_3)_2$), 1.73 (1H, br s, NH), 2.66 (1H, septet, J = 6.27 Hz, $CHMe_2$), 3.68 (3H, s, OMe), 6.60 (1H, s, =CH), 6.87−7.32 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 25.86 ($CHMe_2$), 28.64 (C_qMe_2), 44.47 (NCH), 52.31 (OMe), 54.39 (C_qMe_2), 115.11, 122.30 and 129.63 (C_o, C_m, C_p), 138.49 (=CH), 139.48 (=C_q), 157.19 (C_q), 163.88 (C=O); IR (NaCl) 1727 and 1646 cm^{-1} (C=O and C=C); MS *m*/*z* 277 (10, M$^+$), 262 (100, M$^+$ − Me), 234 (29), 220 (21), 219 (39), 187 (19), 160 (38), 159 (27), 131 (15), 126 (28), 125 (44), 100 (21), 91 (39), 84 (19), 83 (21), 82 (10), 77 (51), 59 (31), 58 (53), 55 (25), 51 (25), 49 (15). Flash chromatography CH_2Cl_2/MeOH 95/5, R_f 0.20, yield 78%. Anal. Calcd for $C_{16}H_{23}NO_3$: C, 69.29; H, 8.36; N, 5.05. Found: C, 69.18; H, 8.45; N, 5.14.

1-Allyl-5,5-dimethyl-3-phenoxypyrrolin-2-one (18): ^{1}H NMR ($CDCl_3$) δ 1.29 (6H, s, $C_q(CH_3)_2$), 4.04 (2H, d, J = 5.60 Hz, NCH_2), 5.13−5.30 (2H, m, $=CH_2$), 5.67 (1H, s, =CH), 5.80−5.94 (1H, m, =CH), 7.13−7.39 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 25.16 (C_qMe_2), 41.67 (NCH_2CH), 60.02 (C_qMe_2), 116.89 (=CH_2), 119.89, 124.90 and 129.76 (C_o, C_m, C_p), 121.81 (=CH), 134.12 (=$CHCH_2$), 148.46 (=C_q), 155.29 (C_q), 164.31 (C=O); IR (NaCl) 1854, 1693 and 1640 cm^{-1} (C=O and C=C); MS *m*/*z* 243 (85, M$^+$), 228 (100, M$^+$ − Me), 159 (11), 150 (72), 145 (7), 110 (13), 105 (11), 91 (9), 83 (27), 82 (17), 77 (32), 70 (8), 55 (22), 51 (18). Flash chromatography petroleum ether/EtOAc 75/25, R_f 0.28, yield 70%. Anal. Calcd for $C_{15}H_{17}NO_2$: C, 74.05; H, 7.04; N, 5.76. Found: C, 73.92; H, 7.14; N, 5.70.

Methylation of *cis*-4-[(1-Chloro-1-methyl)ethyl]-1-isopropyl-3-methoxyazetidin-2-one (4h) and *cis*-4-[(2-Bromo-1,1-dimethyl)ethyl]-1-isopropyl-3-methoxyazetidin-2-one (8g). The synthesis of *cis*-4-[(1-chloro-1-methyl)-ethyl]-1-isopropyl-3-methoxy-3-methylazetidin-2-one (**19**) is representative for this alkylation reaction.

β-Lactam **4h** (0.50 g, 2.3 mmol) in 25 mL of tetrahydrofuran was kept at −78 °C under a nitrogen atmosphere. At this temperature, commercially available 0.5 N KHMDS in toluene (17 mL, 8.5 mmol) was added and the resulting mixture was stirred at −78 °C for 1 h. Hereafter, excess iodomethane (2.59 g, 18.2 mmol) was added and the solution was stirred overnight

while warming to room temperature was allowed. The reaction mixture was quenched with saturated ammonium chloride solution (20 mL) and extracted with ethyl acetate (3 × 10 mL). The combined organic layers were dried (magnesium sulfate) and after evaporation of the solvent, purification was performed by flash chromatography, yielding *cis*-4-[(1-chloro-1-methyl)ethyl]-1-isopropyl-3-methoxy-3-methylazetidin-2-one (**19**) (0.32 g, 60%).

***cis*-4-[(1-Chloro-1-methyl)ethyl]-1-isopropyl-3-methoxy-3-methylazetidin-2-one (19):** mp 46.0−46.6 °C; ^{1}H NMR ($CDCl_3$) δ 1.31 and 1.48 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 1.46 (3H, s, C_qCH_3), 1.69 and 1.72 (2 × 3H, 2 × s, Me_2C_q), 3.48 (OMe), 3.71 (1H, s, $NCHC_q$), 3.92 (1H, septet, J = 6.6 Hz, C*H*Me_2); ^{13}C NMR ($CDCl_3$) δ 18.11 (C_qCH_3), 20.23 and 20.32 (Me_2CH), 26.92 and 29.27 (Me_2C_q), 46.23 (CHMe_2), 53.58 (OMe), 72.11 (C_qCl), 73.69 ($NCHC_q$), 86.14 (OC_q), 169.38 (C=O); IR (KBr) 1749 cm^{-1} (C=O); LC-MS m/z 229/231 (100, [M + H]$^+$). Flash chromatography petroleum ether/EtOAC 75/25, R_f 0.42, yield 60%. Anal. Calcd for $C_{11}H_{20}ClNO_2$: C, 56.52; H, 8.62; N, 5.99. Found: C, 56.71; H, 8.73; N, 5.89.

***cis*-4-[(2-Bromo-1,1-dimethyl)ethyl]-1-isopropyl-3-methoxy-3-methylazetidin-2-one (20):** ^{1}H NMR ($CDCl_3$) δ 1.17 and 1.18 (2 × 3H, 2 × s, Me_2C_q), 1.28 and 1.46 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 3.32 (1H, d, J = 9.90 Hz, C*H*(H)Br), 3.46 (1H, s, $NCHC_q$), 3.48 (1H, septet, J = 6.6 Hz, C*H*Me_2), 3.50 (3H, s, OMe), 3.80 (1H, d, J = 9.90 Hz, CH(*H*)Br); ^{13}C NMR ($CDCl_3$) δ 18.20 (C_qCH_3), 20.23 and 20.79 (Me_2CH), 22.37 and 25.28 (Me_2C_q), 37.16 ($C_q(CH_3)_2$), 44.06 (CH_2Br), 47.12 (CHMe_2), 53.40 (OMe), 70.22 (N*C*HC_q), 86.04 (OC_q), 170.10 (C=O); IR (NaCl) 1737 cm^{-1} (C=O); MS m/z 291/293 (0.03, M$^+$), 208 (8), 206 (2), 127 (2), 113 (100), 112 (6), 111 (1), 99 (1), 98 (2), 94 (1), 86 (2), 82 (2), 81 (3), 77 (1), 70 (2), 67 (1), 59 (1), 55 (6). Flash chromatography petroleum ether/EtOAC 6/4, R_f 0.50, yield 52%. Anal. Calcd for $C_{12}H_{22}BrNO_2$: C, 49.32; H, 7.59; N, 4.79. Found: C, 49.21; H, 7.69; N, 4.71.

Ring Opening and Transformation of 2-Azetidinones by Acidic Methanolysis. Acidic methanolysis was performed by bubbling gaseous hydrogen chloride, generated by dropping sulfuric acid to a mixture of sodium chloride and hydrochloric acid (CAUTION), through a 10% solution of the substrate in methanol at 0 °C. This bubbling was maintained for 1 h and the resulting reaction mixture was subsequently kept at room temperature for 24 h, in a closed vessel. Methanol was removed by evaporation and further removal of traces of the solvent was performed by drying on a high-vacuum pump (0.05−0.5 mmHg) for several hours. The residual ring-opened substrate hydrochloric acid salt was taken up in dichloromethane and triethylamine was added. This solution was stirred at room temperature for 4 h, and dichloromethane was subsequently removed in vacuo. Diethyl ether was added and the precipitated triethylammonium chloride was removed by filtration. After drying (magnesium sulfate), filtration, and evaporation, the crude reaction products were obtained.

Methyl (1-isopropyl-3,3-dimethyl-2-aziridinyl)(methoxy)acetate (22): ^{1}H NMR ($CDCl_3$) δ 1.08 and 1.16 (2 × 3H, 2 × d, J = 6.27 Hz, Me_2CH), 1.24 and 1.26 (2 × 3H, 2 × s, Me_2C_q), 1.46 (1H, d, J = 8.9 Hz, NCH), 2.16 (1H, septet, J = 6.27 Hz, C*H*Me_2), 3.44 (3H, s, OMe), 3.48 (1H, d, J = 8.9 Hz, OCH), 3.79 (3H, s, OMe); ^{13}C NMR ($CDCl_3$) δ 17.93 and 23.86 (Me_2C_q), 22.53 and 22.95 (Me_2CH), 40.36 (NC_q), 50.64 (NCH), 51.99 (OMe), 52.74 (C*H*Me_2), 58.63 (OMe), 81.42 (OCH), 171.89 (C=O); IR (NaCl) 1752 cm^{-1} (C=O); MS m/z 215 (2, M$^+$), 200 (5, M$^+$ − Me), 184 (11, M$^+$ − OMe), 172 (36), 156 (100), 144 (20), 142 (12), 126 (4), 114 (27), 112 (28), 110 (11), 99 (10), 98 (11), 84 (7), 75 (2), 70 (2). Yield 75%. Anal. Calcd for $C_{11}H_{21}NO_3$: C, 61.37; H, 9.83; N, 6.51. Found: C, 61.52; H, 9.76; N, 6.56.

Methyl (1-isopropyl-3,3-dimethyl-2-azetidinyl)(methoxy)acetate (23): ^{1}H NMR ($CDCl_3$) δ 0.95 and 1.01 (2 × 3H, 2 × d, J = 6.6 Hz, Me_2CH), 1.03 and 1.26 (2 × 3H, 2 × s, Me_2C_q), 2.75 (1H, septet, J = 6.6 Hz, C*H*Me_2), 2.76 (1H, d, J = 7 Hz, NC*H*(H)), 3.05 (1H, d, J = 7 Hz, NCH(*H*)), 3.18 (1H, d, J = 8.6 Hz, NCH), 3.40 and 3.76 (2 × 3H, 2 × s, 2 × OMe), 3.91 (1H, d, J = 8.6 Hz, OCH); ^{13}C NMR ($CDCl_3$) δ 17.30 and 20.61 (Me_2CH), 22.66 and 27.85 (Me_2C_q), 32.43 (Me_2C_q), 51.73 (OMe), 54.75 (*C*HMe_2), 58.31 (OMe), 60.75 (NCH_2), 71.21 (NCH), 82.55 (OCH), 171.79 (C=O); IR (NaCl) 1741 cm^{-1} (C=O); MS m/z 229 (1, M$^+$), 214 (5, M$^+$ − Me), 170 (5), 126 (100), 106 (2), 104 (8), 99 (10), 96 (4), 84 (31), 82 (3), 72 (4), 70 (5), 67 (3), 59 (3), 56 (8), 55 (5). Yield 73%. Anal. Calcd for $C_{12}H_{23}NO_3$: C, 62.85; H, 10.11; N, 6.11. Found: C, 62.93; H, 9.98; N, 5.97.

Synthesis of Pent-2-enoates 9c and 10e from Aziridine 22 and Azetidine 23. The procedure applied in this transformation is completely analogous to the previously reported one for the ring opening of β-lactams. However, only a small excess of sodium methoxide in methanol (1.1 equiv) was used in this case and reflux was maintained for 2 h. Workup was performed as previously reported. For the spectroscopic data, see above.

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