Rearrangement of 2-Aryl-3,3-dichloroazetidines: Intermediacy of 2-Azetines

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Received September 10, 2001

An easy synthesis of 2-aryl-3,3-dichloroazetidines, a rather unexplored class of azaheterocycles, is described. The title compounds were easily obtained by reduction of the corresponding 4-aryl-3,3-dichloro-2-azetidinones with monochloroalane, which in turn were synthesized by a ketene−imine [2 + 2] cycloaddition. The reactivity of 3,3-dichloroazetidines with bases was investigated, yielding 2-[dimethoxy(aryl)methyl]aziridines by ring contraction when treated with sodium methoxide. Furthermore, reacting the 3,3-dichloroazetidines with sodium hydride in DMSO, followed by aqueous workup, afforded 1-alkyl-2-aroylaziridines, by hydrolysis of the intermediate 2-azetines and ring closure of the transient 3-amino-2-chloro-1-phenyl-1-propanone derivatives. Monitoring this reaction in an NMR tube, using sodium hydride in DMSO-d_6, allowed the characterization of the intermediate strained heterocyclic enamines, i.e., 2-azetines, by ^{1}H and ^{13}C NMR.

Introduction

Azetidines constitute an important class of azaheterocycles, exhibiting a wide range of biological activities.[1−4] However, remarkably little is known about 3,3-dichloroazetidines. In the literature, only a few examples of these functionalized azetidines are reported. The cycloaddition between a 3,3-dichloro-1-azetine and diphenylketene yielded a bicyclic 3,3-dichloroazetidine derivative.[5] A 3,3-dichloroazetidine has also been isolated as a byproduct during α-amino acid synthesis by the reaction of Grignard reagents with ethyl *N*-trichloroethylidenecarbamate.[6] A strained 3,3-dichloro-1-azetine has been reduced to the corresponding azetidine in 37% yield.[7] In fact, until now, only one straightforward synthesis of 3,3-dichloroazetidines has been published.[8] The aldol condensation of 3,3-dichloro-1-azaallylic anions with aldehydes yielded the corresponding α,α-dichloro-*β*-hydroxy ketimines, which, after mesylation and reaction with nucleophiles, afforded the title compounds in moderate to fairly good yields.[8]

Although 3,3-dichloroazetidines are expected to furnish a broad range of reactivities by incorporation of the nitrogen atom and the geminal dichloro unit in the same strained four-membered heterocycle, even less has been reported on the reactivity of these compounds. Only in the latter paper[8] was it described that treatment of 3,3-dichloro-2-methoxy-2,4-diphenylazetidines with lithium aluminum hydride gave rise to the corresponding 3-chloro-2,4-diphenylazetidine in 28% yield.

Many methods for the synthesis of azetidines are known.[1−4] A powerful synthetic method is the reduction of 2-azetidinones to azetidines. This reduction has been performed with a wide variety of reducing agents, including diisobutyl aluminum hydride,[9] monochloroalane and dichloroalane,[10] and lithium aluminum hydride.[11] Although not always unambiguous, the reduction with chloroalanes has already proven to be a powerful method.

In this paper, we wish to present a new entry toward 2-aryl-3,3-dichloroazetidines. The latter compounds can be easily obtained by reduction of the corresponding azetidin-2-ones with monochloroalane, which in turn were generated from a ketene−imine [2 + 2] cycloaddition of dichloroketene and the corresponding aldimine. Furthermore, the reactivity of these functionalized azetidines toward different bases was evaluated because the nature of the title compounds allows both nucleophilic and elimination reactions to take place.

Results and Discussion

The synthesis of 2-aryl-3,3-dichloroazetidines **4** is easily performed by a three-step procedure in moderate to good overall yields. Condensation of the aldehydes **1** with the appropriate amine in dichloromethane in the

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10.1021/jo010914j CCC: $22.00
Published on Web 03/07/2002

Scheme 1

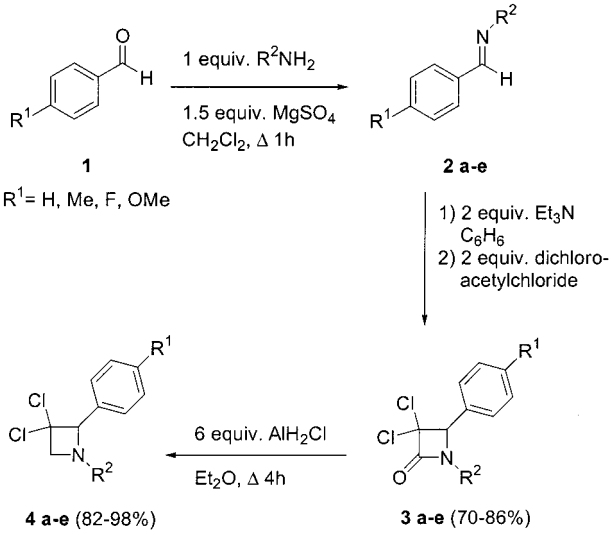


Table 1. Synthesis and Yields of 4-Aryl-3,3-dichloro-2-azetidinones 3 and 2-Aryl-3,3-dichloroazetidines 4

compd	R^1	R^2	yield of **3** (%)	yield of **4** (%)
a	H	^{i}Pr	71	97
b	H	cHex	84	98
c	Me	^{i}Pr	70	82
d	F	^{i}Pr	86	95
e	OMe	^{i}Pr	77	90

presence of magnesium sulfate as drying agent afforded the corresponding aldimines **2**. Subsequently, these imines **2** were used in the cycloaddition reaction with dichloroketene, derived from dichloroacetyl chloride and triethylamine (Scheme 1).[12] Imines **2** and triethylamine were dissolved in benzene, and dichloroacetyl chloride was added dropwise, performing the Staudinger reaction in situ, affording β-lactams **3** in good yields after purification by recrystallization from methanol or flash chromatography (Table 1).

As mentioned in the Introduction, the reduction of 2-azetidinones to the corresponding azetidines has been performed already with different reagents. Although not always unambiguous,[13] the use of chloroalanes has found wide application for this conversion.[9b] Also in the case of 3,3-dichloroazetidin-2-ones, this seemed to be the method of choice. 2-Azetidinones **3** were very cleanly converted to 3,3-dichloroazetidines **4** by reaction with monochloroalane in ether for 4 h at reflux temperature, affording the latter compounds pure after workup of the reaction mixture (Table 1). Trying the same conversion with lithium aluminum hydride in ether at 0 °C for 2 h gave a very complex reaction mixture that was not further analyzed. By comparison of the ^{1}H NMR data, it could be concluded that under the latter reaction conditions no 3,3-dichloroazetidines were formed in this complex reaction mixture.

For investigation of the reactivity of the resulting 3,3-dichloroazetidines, the azetidine **4a** was used as a model substrate. This substrate was subjected to a variety of basic conditions, which are summarized in Table 2.

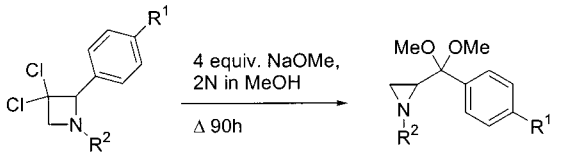
3,3-Dichloroazetidine **4a** proved to be stable in refluxing methanol for 84 h, but especially in the presence of

Table 2. Various Applied Reaction Conditions for the Conversion of 3,3-Dichloro-1-isopropyl-4-phenyl-2-azetidinone 4a to 2-[Dimethoxy(phenyl)methyl]-1-isopropylaziridine 5a

reaction conditions	**4a**[a] (%)	**5a**[a] (%)
MeOH, Δ 84 h	100	0
5 equiv of NaCN, MeOH, Δ 60 h	100	0
3.5 equiv of Ag_2CO_3, MeOH, Δ 20 h	100	0
5 equiv of Et_3N, MeOH, Δ 90 h	100	0
5 equiv of K_2CO_3, MeOH, Δ 90 h	74	26
5 equiv of K_2CO_3, MeOH, Δ 14 days	<4	>96
4 equiv of NaOMe, 0.5 N, MeOH, Δ 90 h	55	45
4 equiv of NaOMe, 0.5 N, MeOH, Δ 14 days	17	83
4 equiv of NaOMe, 2 N, MeOH, Δ 90 h	0	100

[a] Ratios derived from signal integration in ^{1}H NMR.

Scheme 2



a R^1= H, R^2= iPr (92%)
b R^1= H, R^2= cHex (94%)
c R^1= Me, R^2= iPr (84%)
d R^1= F, R^2= iPr (90%)
e R^1= OMe, R^2= iPr (83%)

potassium carbonate and sodium methoxide it was converted rather slowly to 2-[dimethoxy(phenyl)methyl]-aziridine **5a** (Scheme 2). The reaction mechanism is believed to occur via the intermediate 2-azetines **6** (Scheme 3). The conversion of 3,3-dichloroazetidines **4** into aziridines **5** proceeds via elimination of hydrogen chloride, generating the strained heterocyclic enamine **6**. Addition of methanol and expulsion of a chloride anion by the nitrogen lone pair generates the bicyclic aziridinium intermediate **8**, which opens to give the aziridine derivatives **5**. The only products that could be isolated from this reaction were the starting material **4** and the end product **5**. Intermediate workup of the reaction furnished only mixtures of the two latter compounds, e.g. in the presence of potassium carbonate the starting azetidine **4a** and the aziridine **5a** were isolated in a ratio of 74/26 after 90 h and <4/>96 after 14 days (Table 2). The optimal conditions for this reaction were found to be four equivalents of sodium methoxide, 2 N in methanol and reflux for 90 h. These conditions are suitable for the complete conversion of 3,3-dichloroazetidines **4** to the corresponding aziridines **5** (Table 2). The reaction sequence is analogous to the ring contraction of the six-membered enamines **10** to the pyrrolidines **11** (Scheme 4), a reaction which has recently been reviewed and is known as the Duhamel ring contraction of heterocyclic enamines.[14] Previously, these analogous rearrangements of α-halogenated six-membered ring iminium salts with sodium methoxide were reported to be complete after 5 h of reflux.[15] In the present case, the necessary prolonged reaction time probably follows from the difficulty to form the strained 3-chloro-2-azetine intermediate **6**.

To explore further the reactivity of 2-aryl-3,3-dichloroazetidines **4**, reactions with bases in nonnucleophilic

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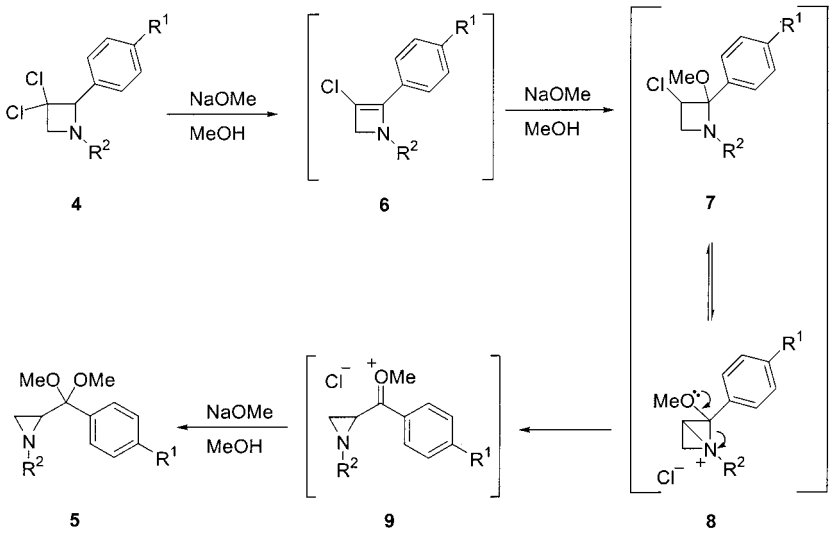
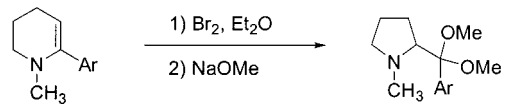
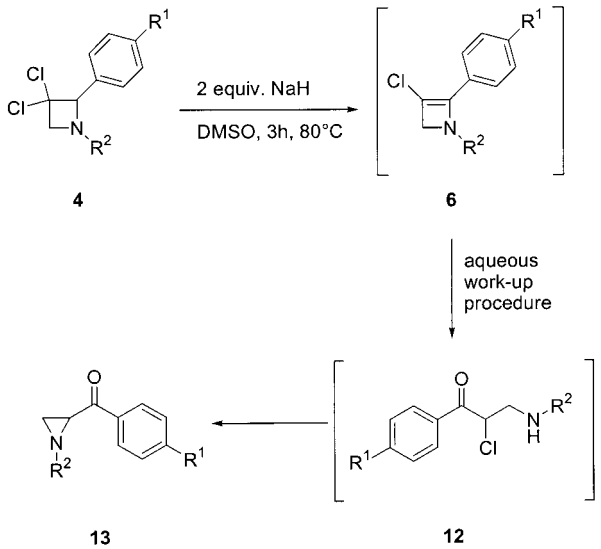
Scheme 3



Scheme 4



Scheme 5



a R^1= H, R^2= iPr (46%)
b R^1= H, R^2= cHex (46%)
c R^1= Me, R^2= iPr (50%)
d R^1= F, R^2= iPr (59%)
e R^1= OMe, R^2= iPr (57%)

solvents were performed. Reacting the azetidines **4** with sodium hydride in tetrahydrofuran at reflux temperature for several hours permitted to recover only the starting products. In contrast, the use of sodium hydride in dimethyl sulfoxide afforded the aziridines **13** (Scheme 5). This reaction gave another indication of the intermediacy of the strained 2-azetines **6**, because the formation of the reaction products **13** can be rationalized by an elimination reaction toward 2-azetines **6**, followed by hydrolysis of this intermediate by the aqueous workup procedure. The 2-chloro-3-(alkylamino)-1-aryl-1-propanone derivatives **12** thus formed cyclized spontaneously to the aziridines **13**. The lower yields of the aziridines are due to purification by flash chromatography. Also, there was one minor component (<10%) present in the reaction mixture, which was always obtained as a mixture with the aziridines **13** and could not be isolated in pure form. Possibly, it concerns the ringopened intermediate **12**, since investigation of the ^{1}H and ^{13}C NMR data of a mixture of the aziridine **13a** (R = ^{i}Pr) and the unknown compound indicates the presence of this acyclic compound. In ^{1}H NMR ($CDCl_3$, 270 MHz), the following characteristic peaks were observed: a doublet at 1.38 ppm (6H, NCH*Me*$_2$), an AB-system and septet between 3.3 and 3.7 ppm (3H, NC*H*Me$_2$ and NCH_2), and a triplet at 6.0 ppm (CHCl). ^{13}C NMR gave the following characteristic peaks: 19.5 and 19.7 (NCH*Me*$_2$), 46.5 (NCH_2), 51.3 or 52.0 (NCH), 77.3 (CHCl), 191.8 (C=O). The aromatic peaks were in the same region as the aromatic signals of the aziridine **13a**. From these data, it is believed that the side product possibly is the intermediate **12a**.

The strained enamine moiety in compounds **6** is responsible for the reactivity of these elusive species. Previously, 2-azetines have only been found to be stable when substituted with an electron-withdrawing group on nitrogen or on the carbon atoms of the four-membered ring.[16] Recently, the formation in low yields of a substituted 1-amino-2-azetine was reported.[17]

Several conditions for the transformation of 2-[dimethoxy(phenyl)methyl]aziridines **5** to aziridines **13** were evaluated (Amberlyst 15,[18a] lithium tetrafluoroborate,[18b] trimethylsilyl iodide,[18c] silica gel,[18d] hydrochloric acid). Only the use of boron trifluoride etherate/iodide ion was successful for this conversion (Scheme 6).[18e] Previously,

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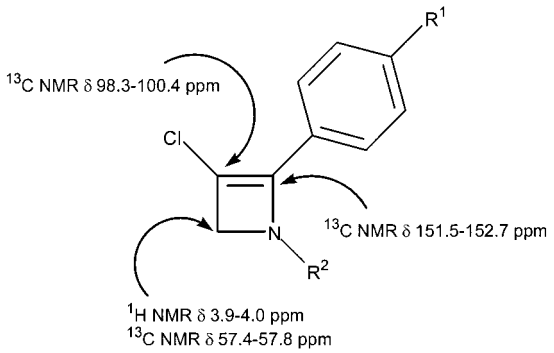
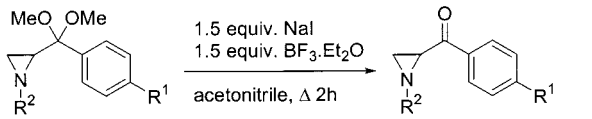


Figure 1. ^{1}H NMR and ^{13}C NMR data of 2-azetines **6** (DMSO-d_6).

Scheme 6



5 **13**

a R^1= H, R^2= iPr (65%)
b R^1= H, R^2= cHex (52%)
c R^1= Me, R^2= iPr (55%)
d R^1= F, R^2= iPr (62%)
e R^1= OMe, R^2= iPr (58%)

this type of aziridines **13**, i.e., 1-alkyl-2-aroylaziridines, has been prepared by addition of phenyllithium to lithium 1-alkyl-2-aziridinecarboxylate[19] or by thermal conversion of 4-isoxazolines and their borane complexes.[20]

The NaH/DMSO-d_6 combination also allowed the reaction to be followed by ^{1}H NMR. Sodium hydride was transferred into an NMR tube, followed by DMSO-d_6. The NMR tube was closed with a septum and flushed with nitrogen. After the evolution of hydrogen ceased, 3,3-dichloroazetidines **4** were introduced through the septum, dissolved in a little amount of DMSO-d_6. Spectra were taken immediately after the introduction of the azetidines and from then on every 30 min. Between the NMR analyses, the NMR tubes were kept in a thermostated water bath at 50 °C. Although some variability occurred, the conversion to 3-chloro-2-azetines **6** was complete after 2−2.5 h, and it was noted that this transformation proceeded quantitatively. 3-Chloro-2-azetines **6** were characterized by ^{1}H and ^{13}C NMR (Figure 1).

The way of formation of these 2-azetines is analogous to previous methods since most of them rely on the elimination of a leaving group at the 3-position of the azaheterocyclic ring.[16a,b,d,e] However, in the latter cases, it concerned reactions with azetidines carrying an electron-withdrawing substituent (e.g., acetyl,[16a,d,e] mesyl,[16b] nitro,[16b] ...) at nitrogen. The present paper is the first report on 2-azetine formation by this method without a pronounced electron-withdrawing substituent at nitrogen.

Until now, all attempts to explore further the reactivity of the intermediate 2-azetines failed. Catalytic hydrogenation, addition of methanol, cycloaddition reactions, etc. all gave very complex reaction mixtures from which no useful compounds could be isolated. This is attributed to the unstability, the reactive properties, and the nonselective reactivity of these 2-azetines.

In conclusion, dimsylsodium in DMSO is a powerful reagent for the generation of 2-azetines from 2-aryl-3,3-dichloroazetidines. The conversion of the latter compounds toward the 2-azetines is apparently much faster than in the case of sodium methoxide in methanol. Current research is pointed toward the further application of this base for the synthesis of more stable 2-azetines.

Experimental Section

^{1}H and ^{13}C NMR spectra were recorded at 270 and 68 MHz, respectively. The type of carbon and hydrogen was determined via DEPT and ^{13}C−^{1}H and ^{1}H−^{1}H COSY techniques. Mass spectra were performed at 70 eV using a GC-MS coupling or a direct inlet system. Ether and THF were freshly distilled from sodium wire and sodium benzophenone ketyl, respectively. Benzene was dried over sodium and distilled. DMSO was distilled and kept over molecular sieves prior to use. Methanol was dried over magnesium and distilled. A stock solution of 2 N sodium methoxide in methanol was prepared. Sodium methoxide solutions (0.5 N) were prepared by dilution of this stock solution. Melting points are uncorrected.

Synthesis of Aldimines 2. A mixture of 0.1 mol of the appropriate aromatic aldehyde **1** in 100 mL of dichloromethane was treated with 0.1 mol of the appropriate amine and 0.15 mol of magnesium sulfate. The mixture was refluxed for 1 h and then filtered. After evaporation of the solvent, aldimines **2** were obtained, and either the solvent was further evaporated under high vacuum (to remove the last traces of solvent) or the aldimines **2** were distilled in vacuo. All aldimines **2** were characterized by ^{1}H NMR affording spectral data in agreement with their structure.

Synthesis of 3,3-Dichloro-*β*-lactams 3. The synthesis of 3,3-dichloro-1-isopropyl-4-phenyl-2-azetidinone (**3a**) is representative. To a solution of *N*-(benzylidene)isopropylamine (**2a**) (3.00 g, 20.5 mmol) in 60 mL of benzene was added triethylamine (4.13 g, 41 mmol), and the mixture was stirred at room temperature. After the dropwise addition of dichloroacetyl chloride (6.00 g, 41 mmol) in 30 mL of benzene, the resulting reaction mixture was stirred for 1 h at room temperature. Triethylamine hydrochloride was filtered off, and the filtrate was washed with saturated sodium bicarbonate solution. After drying over magnesium sulfate, the crude 3,3-dichloro-1-isopropyl-4-phenyl-2-azetidinone (**3a**) was further purified by recrystallization from methanol to afford 3.74 g (71%) of pure compound.

3,3-Dichloro-1-isopropyl-4-phenyl-2-azetidinone (3a): mp 71.5−72.0 °C; ^{1}H NMR ($CDCl_3$) δ 1.18 and 1.40 (2 × 3H, 2 × d, J = 6.93 Hz, Me_2CH), 3.75 (1H, septet, J = 6.93 Hz, C*H*Me$_2$), 5.04 (1H, s, NC*H*C$_6$H$_5$), 7.33−7.53 (5H, m, C$_6$H$_5$); ^{13}C NMR ($CDCl_3$) δ 20.1 and 20.8 (2 × *Me*$_2$CH), 46.5 (*C*HMe$_2$), 73.3 (N*C*HC$_6$H$_5$), 84.1 (CCl_2), 128.3, 128.7 and 129.9 (C_o, C_m, C_p), 133.1 (C_q), 161.5 (C=O); IR (KBr) 1767 cm^{-1} (C=O); MS *m*/*z* 257/259/261 (M^+, 1), 177 (10), 175 (63), 173 (100), 138 (11), 105 (5), 103 (12), 78 (8), 52 (6), 43 (8). Anal. Calcd for $C_{12}H_{13}Cl_2NO$: C, 55.83; H, 5.08; N, 5.43. Found: C, 55.98; H, 5.16; N, 5.32.

1-Cyclohexyl-3,3-dichloro-4-phenyl-2-azetidinone (3b): mp 101.3−101.9 °C; ^{1}H NMR ($CDCl_3$) δ 1.06−1.37, 1.55−1.89, 2.05−2.10 (10H, 3 × m, $(CH_2)_5$), 3.35−3.46 (1H, m, NCH), 5.06 (1H, s, NC*H*C$_6$H$_5$), 7.33−7.46 (5H, m, C$_6$H$_5$); ^{13}C NMR ($CDCl_3$) δ 24.7, 25.0, 30.2 and 30.9 ($(CH_2)_5$), 53.8 (NCH), 73.2 (N*C*HC$_6$H$_5$), 84.1 (CCl_2), 128.3, 128.6 and 129.9 (C_o, C_m, C_p), 133.2 (C_q), 161.5 (C=O); IR (KBr) 1779 cm^{-1} (C=O); MS *m*/*z* 297/299/301 (M^+, 0.21), 175 (47), 172/174/176 (25), 138 (5), 91 (100), 85 (5), 83 (8), 58 (29), 43 (55). Anal. Calcd for $C_{15}H_{17}Cl_2NO$: C, 60.42; H, 5.75; N, 4.70. Found: C, 60.56; H, 5.66; N, 4.62.

3,3-Dichloro-1-isopropyl-4-(4-methylphenyl)-2-azetidinone (3c): mp 84.5−84.9 °C; ^{1}H NMR ($CDCl_3$) δ 1.17 and 1.39

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(2 × 3H, 2 × d, J = 6.60 Hz, Me_2CH), 2.40 (3H, s, C_qCH_3), 3.74 (1H, septet, J = 6.60 Hz, CHMe$_2$), 5.00 (1H, s, NCHC$_6$H$_4$), 7.23−7.28 (4H, m, C$_6$H$_4$); ^{13}C NMR ($CDCl_3$) δ 20.1 and 20.8 (2 × Me_2CH), 21.3 (C_qCH_3), 46.4 (CHMe$_2$), 73.2 (NCHC$_6$H$_4$), 84.2 (CCl_2), 128.3 and 129.4 (C_o, C_m), 130.0 and 140.0 (2 × C_q), 161.5 (C=O); IR (KBr) 1765 cm^{-1} (C=O); MS m/z no M$^+$, 236/238 (M$^+$ − Cl, 4), 188 (61), 186 (100), 153 (8), 151 (23), 118 (8), 116 (12), 115 (38), 91 (8), 65 (5), 43 (6). Anal. Calcd for $C_{13}H_{15}Cl_2NO$: C, 57.37; H, 5.55; N, 5.15. Found: C, 57.50; H, 5.67; N, 5.01.

3,3-Dichloro-1-isopropyl-4-(4-fluorophenyl)-2-azetidinone (3d): mp 66.0−67.0 °C; ^{1}H NMR ($CDCl_3$) δ 1.18 and 1.40 (2 × 3H, 2 × d, J = 6.93 Hz, Me_2CH), 3.76 (1H, septet, J = 6.93 Hz, CHMe$_2$), 5.07 (1H, s, NCHC$_6$H$_4$), 7.15−7.40 (4H, m, C$_6$H$_4$); ^{13}C NMR ($CDCl_3$) δ 20.1 and 20.8 (2 × Me_2CH), 46.5 (CHMe$_2$), 72.5 (NCHC$_6$H$_4$), 84.1 (CCl_2), 115.8 and 130.2 (2 × d, J = 22.0, 8.5 Hz, C_o and C_m), 129.0 (d, J = 2.4 Hz, C_p), 161.3 (C=O), 163.5 (d, J = 249.0 Hz, FC_q); IR (KBr) 1781 cm^{-1} (C=O); MS m/z no M$^+$, 240/242 (M$^+$ − Cl, 1), 221 (1), 190/192/194 (100), 153 (8), 169 (13), 155/7 (9), 120 (6), 73 (2), 43 (2); flash chromatography PE/EtOAc 6/4, R_f = 0.63. Anal. Calcd for $C_{12}H_{12}Cl_2FNO$: C, 52.20; H, 4.38; N, 5.07. Found: C, 52.34; H, 4.49; N, 4.96.

3,3-Dichloro-1-isopropyl-4-(4-methoxyphenyl)-2-azetidinone (3e): mp 106.7−107.4 °C; ^{1}H NMR ($CDCl_3$) δ 1.16 and 1.38 (2 × 3H, 2 × d, J = 6.60 Hz, Me_2CH), 3.74 (1H, septet, J = 6.60 Hz, CHMe$_2$), 3.84 (3H, s, OMe), 4.99 (1H, s, NCHC$_6$H$_4$), 6.96 and 7.28 (2 × 2H, 2 × d, J = 8.91 Hz, C$_6$H$_4$); ^{13}C NMR ($CDCl_3$) δ 20.1 and 20.8 (2 × Me_2CH), 46.3 (CHMe$_2$), 55.3 (OMe), 73.0 (NCHC$_6$H$_4$), 84.4 (CCl_2), 114.0 and 129.7 (C_o, C_m), 124.8 and 160.8 (2 × C_q), 161.5 (C=O); IR (KBr) 1773 cm^{-1} (C=O); MS m/z no M$^+$, 252/254 (M$^+$ − Cl, 11), 205 (24), 203 (39), 89 (12), 86 (69), 84 (100), 51 (32), 49 (88). Anal. Calcd for $C_{13}H_{15}Cl_2NO_2$: C, 54.18; H, 5.25; N, 4.86. Found: C, 54.31; H, 5.16; N, 4.79.

Synthesis of 2-Aryl-3,3-dichloroazetidines 4. The synthesis of 3,3-dichloro-1-isopropyl-2-phenylazetidine (**4a**) is representative. To a solution of aluminum chloride (3.10 g, 23 mmol) in 120 mL of dry ether was added lithium aluminum hydride (0.88 g, 23 mmol) at 0 °C. This reaction mixture was stirred for 10 min at 0 °C and was subsequently refluxed during 30 min. 3,3-Dichloro-1-isopropyl-4-phenylazetidin-2-one (**3a**) (2.00 g, 7.75 mmol) in 10 mL of dry diethyl ether was added dropwise, and after the addition was complete, reflux was maintained during 4 h. The reaction was cooled, and 200 mL of water was carefully added. The water phase was extracted with dichloromethane and dried over magnesium sulfate. After filtration and evaporation of the solvent, 1.84 g (97%) of 3,3-dichloro-1-isopropyl-2-phenylazetidine (**4a**) was obtained in pure form as a lightly yellow colored oil.

3,3-Dichloro-1-isopropyl-2-phenylazetidine (4a): ^{1}H NMR ($CDCl_3$) δ 0.79 and 1.01 (2 × 3H, 2 × d, J = 6.27 Hz, Me_2CH), 2.64 (1H, septet, J = 6.27 Hz, CHMe$_2$), 3.62 (1H, d (broad), J = 8.6 Hz, NCH(H)), 4.06 (1H, d × d, J = 8.6 Hz, J = 1.5 Hz, NCH(H)), 4.61 (1H, s, NCHC$_6$H$_5$), 7.35−7.53 (5H, m, C$_6$H$_5$); ^{13}C NMR ($CDCl_3$) δ 20.0 and 21.0 (2 × Me_2CH), 58.8 (CHMe$_2$), 70.6 (NCH$_2$), 79.8 (CCl_2), 83.2 (NCHC$_6$H$_5$), 127.9 and 128.4 (C_o, C_m, C_p), 137.3 (C_q); IR (NaCl) 2969, 1495, 1453, 1227, 1197 cm^{-1}; MS m/z 173 (M$^+$ − 2 × Cl, 11), 148 (37), 147 (12), 133 (100), 126, (10), 105 (10), 104 (12), 56 (11). Anal. Calcd for $C_{12}H_{15}Cl_2N$: C, 59.03; H, 6.19; N, 5.74. Found: C, 59.17; H, 6.27; N, 5.80.

1-Cyclohexyl-3,3-dichloro-2-phenylazetidine (4b): mp 60.8−61.6 °C; ^{1}H NMR ($CDCl_3$) δ 0.83−1.74 (10H, m, $(CH_2)_5$), 2.26−2.35 (1H, m, NCH), 3.63 (1H, d × d, J = 8.58, 0.66 Hz, NCH(H)), 4.06 (1H, d × d, J = 8.58, 1.65 Hz, NCH(H)), 4.63 (1H, s, NCHC$_6$H$_5$), 7.31−7.55 (5H, m, C$_6$H$_5$); ^{13}C NMR ($CDCl_3$) δ 24.4, 25.7, 30.1 and 31.6 ($(CH_2)_5$), 67.4 (NCH), 70.5 (NCH$_2$), 80.3 (CCl_2), 83.2 (NCHC$_6$H$_5$), 127.9 and 128.5 (C_o, C_m, C_p), 137.5 (C_q); IR (KBr) 2921, 1495, 1450, 1377, 1349, 1284, 1221, 1197, 1175 cm^{-1}; MS m/z 283/285/287 (M$^+$, 60), 248/250 (M$^+$ − Cl, 18), 221 (28), 200/202/204 (M$^+$ − C$_6$H$_{11}$, 41), 188 (40), 187 (99), 158 (100), 144 (59), 115 (53), 104 (35), 83 (33). Anal. Calcd for $C_{15}H_{19}Cl_2N$: C, 63.39; H, 6.74; N, 4.93. Found: C, 63.51; H, 6.81; N, 4.86.

3,3-Dichloro-1-isopropyl-2-(4-methylphenyl)azetidine (4c): ^{1}H NMR (C$_6$D$_6$) δ 0.62 and 0.73 (2 × 3H, 2 × d, J = 6.27 Hz, Me_2CH), 2.11 (3H, s, C_qCH_3), 2.18 (1H, septet, J = 6.27 Hz, CHMe$_2$), 3.25 (1H, d × d, J = 8.58, 0.99 Hz, NCH(H)), 3.80 (1H, d × d, J = 8.58, 1.65 Hz, NCH(H)), 4.44 (1H, s, NCHC$_6$H$_4$), 7.03 and 7.47 (4H, 2 × d, J = 7.59 Hz, C$_6$H$_4$); ^{13}C NMR (C$_6$D$_6$) δ 20.1 and 21.2 (2 × Me_2CH), 41.4 (C_qCH_3), 58.9 (CHMe$_2$), 70.7 (NCH$_2$), 80.6 (CCl_2), 83.6 (NCHC$_6$H$_5$), 127.6 and 127.9 (C_o, C_m, C_p), 134.9 and 138.2 (2 × C_q); IR (NaCl) 2967, 2928, 2845, 1615, 1514, 1456, 1384, 1369, 1331, 1227, 1196 cm^{-1}; MS m/z no M$^+$, 187 (M$^+$ − 2 × Cl, 7), 162 (24), 147 (100), 120 (10), 119 (10), 116 (8), 84 (14). Anal. Calcd for $C_{13}H_{17}Cl_2N$: C, 60.48; H, 6.64; N, 5.42. Found: C, 60.61; H, 6.58; N, 5.34.

3,3-Dichloro-1-isopropyl-2-(4-fluorophenyl)azetidine (4d): ^{1}H NMR ($CDCl_3$) δ 0.75 and 0.98 (2 × 3H, 2 × d, J = 6.27 Hz, Me_2CH), 2.62 (1H, septet, J = 6.27 Hz, CHMe$_2$), 3.59 (1H, d (broad), J = 8.58 Hz, NCH(H)), 4.03 (1H, d × d, J = 8.58, 1.32 Hz, NCH(H)), 4.57 (1H, s, NCHC$_6$H$_4$), 7.03−7.15 and 7.46−7.52 (4H, 2 × m, C$_6$H$_4$); ^{13}C NMR ($CDCl_3$) δ 20.0 and 21.3 (2 × Me_2CH), 58.8 (CHMe$_2$), 70.6 (NCH$_2$), 79.9 (CCl_2), 82.6 (NCHC$_6$H$_5$), 114.9 and 129.7 (C_o, C_m, 2 × d, J = 21.9, 7.3 Hz), 133.2 (C_p, d, J = 3.6 Hz), 162.9 (FC_q, d, J = 246.6 Hz); IR (NaCl) 2970, 2932, 2849, 1607, 1510, 1468, 1457, 1386, 1370, 1226, 1197 cm^{-1}; MS m/z 261/263/265 (M$^+$, 7), 190/192/194 (9), 165 (22), 150 (100), 143 (8), 133 (8), 122 (12), 109 (4), 95 (5), 56 (10). Anal. Calcd for $C_{12}H_{14}Cl_2FN$: C, 54.98; H, 5.38; N, 5.34. Found: C, 55.07; H, 5.48; N, 5.27.

3,3-Dichloro-1-isopropyl-2-(4-methoxyphenyl)azetidine (4e): ^{1}H NMR (C$_6$D$_6$) δ 0.64 and 0.73 (2 × 3H, 2 × d, J = 6.27 Hz, Me_2CH), 2.20 (1H, septet, J = 6.27 Hz, CHMe$_2$), 3.25 (1H, d (broad), J = 8.58 Hz, NCH(H)), 3.28 (3H, s, OMe), 3.80 (1H, d × d, J = 8.58, 1.32 Hz, NCH(H)), 4.42 (1H, s, NCHC$_6$H$_4$), 6.82 and 7.49 (4H, 2 × d, J = 8.58 Hz, C$_6$H$_4$); ^{13}C NMR (C$_6$D$_6$) δ 20.2 and 21.5 (2 × Me_2CH), 54.7 (OMe), 58.9 (CHMe$_2$), 70.7 (NCH$_2$), 81.1 (CCl_2), 83.5 (NCHC$_6$H$_5$), 113.8 and 129.7 (C_o, C_m), 130.0 and 160.5 (2 × C_q); IR (NaCl) 2968, 2932, 2837, 1613, 1585, 1513, 1464, 1385, 1369, 1332, 1303, 1251, 1037 cm^{-1}; MS m/z 273/275/279 (M$^+$, 9), 238/240 (M$^+$ − Cl, 3), 203 (M$^+$ − 2 × Cl, 29), 177 (16), 162 (100), 135 (13), 121 (6), 89 (8), 77 (6), 63 (5), 56 (8). Anal. Calcd for $C_{13}H_{17}Cl_2NO$: C, 56.95; H, 6.25; N, 5.11. Found: C, 57.09; H, 6.38; N, 5.01.

Synthesis of 2-[Dimethoxy(aryl)methyl]-1-alkylaziridines 5. The synthesis of 2-[dimethoxy(phenyl)methyl]-1-isopropylaziridine (**5a**) is representative for the synthesis of these compounds. To 3,3-dichloro-1-isopropyl-2-phenylazetidine (**4a**) (1.00 g, 4.1 mmol) was added 8.2 mL (16.4 mmol) of a 2 N stock solution of sodium methoxide in methanol. The reaction was refluxed for 90 h, and after cooling, the solvent was removed. The residue was taken up in water and extracted three times with dichloromethane. After drying (magnesium sulfate), 0.89 g (92%) of the 2-[dimethoxy(phenyl)methyl]-1-isopropylaziridine (**5a**) was obtained as a yellow oil. Although NMR data revealed only minor impurities (<2%) in the crude reaction products **5**, the latter compounds could be further purified by flash chromatography using dichloromethane/methanol 95/5.

2-[Dimethoxy(phenyl)methyl]-1-isopropylaziridine (5a): ^{1}H NMR ($CDCl_3$) δ 0.53 and 1.05 (2 × 3H, 2 × d, J = 6.27 Hz, Me_2CH), 1.23 (1H, septet, J = 6.27 Hz, CHMe$_2$), 1.28 (1H, d, broad, J = 6.4 Hz, NCH(H)), 1.46 (1H, d × d, J = 6.4, 3 Hz, NCHC$_q$), 2.23 (1H, d, J = 3 Hz, NCH(H)), 3.16 and 3.40 (2 × OMe), 7.30−7.55 (5H, m, C$_6$H$_5$); ^{13}C NMR ($CDCl_3$) δ 21.7 and 21.9 (2 × Me_2CH), 30.9 (NCH$_2$), 45.4 (NCHC$_q$), 49.3 and 49.5 (2 × OMe), 61.7 (CHMe$_2$), 99.9 (C(OMe)$_2$), 127.2 and 127.7 (C_o, C_m), 127.6 (C_p), 140.5 (C_q); IR (NaCl) 2967, 2832, 1450, 1339, 1249, 1196, 1136, 1108 cm^{-1}; MS m/z 235 (M$^+$, 0.63), 220 (M$^+$ − Me, 2), 205 (M$^+$ − 2 × Me, 6), 204 (M$^+$ − OMe, 15), 190 (50), 151 (100), 105 (17), 91 (11), 77 (10), 42 (5). Anal. Calcd for $C_{14}H_{21}NO_2$: C, 71.46; H, 8.99; N, 5.95. Found: C, 71.63; H, 8.79; N, 5.82.

1-Cyclohexyl-2-[dimethoxy(phenyl)methyl]aziridine (5b): ^{1}H NMR ($CDCl_3$) δ 0.86−1.06, 1.28−1.37 and 1.67−1.77 (10H, 3 × m, $(CH_2)_5$), 1.27 (1H, d × d, J = 6.27, 0.66 Hz, NCH(H)), 1.47 (1H, d × d, J = 6.27, 2.97 Hz, NCHC$_q$), 2.19

(1H, d, J = 2.97 Hz, NCH(*H*)), 3.15 and 3.38 (2 × OMe), 7.27−7.37 and 7.50−7.55 (5H, 2 × m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 25.0, 25.1, 25.9 and 32.3 (C_5H_{10}), 30.3 (NCH_2), 44.8 (N*C*HC$_q$), 49.3 and 49.5 (2 × OMe), 70.0 (N*C*H), 99.9 (*C*(OMe)$_2$), 127.2 and 127.7 (C_o, C_m), 127.9 (C_p), 140.5 (C_q); IR (NaCl) 2929, 2854, 1489, 1449, 1369, 1249, 1197, 1175, 1102, 1073, 1051 cm^{-1}; MS *m*/*z* no M$^+$, 245 (4), 230 (55), 162 (4), 151 (8), 147 (16), 105 (16), 91 (11), 86 (35), 84 (54), 49 (10). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.14; H, 9.15; N, 5.09. Found: C, 74.28; H, 9.30; N, 4.94.

2-[Dimethoxy(4-methylphenyl)methyl]-1-isopropylaziridine (5c): ^{1}H NMR ($CDCl_3$) δ 0.59 and 1.06 (2 × 3H, 2 × d, J = 6.27 Hz, *Me*$_2$CH), 1.24 (1H, septet, J = 6.27 Hz, C*H*Me$_2$), 1.28 (1H, d, broad, J = 6.5 Hz, NC*H*(H)), 1.46 (1H, d × d, J = 6.5, 3 Hz, NC*H*C$_q$), 2.20 (1H, d, J = 3 Hz, NCH(*H*)), 2.34 (3H, s, C$_q$C*H*$_3$), 3.15 and 3.37 (2 × OMe), 7.15 and 7.42 (4H, 2 × d, J = 8 Hz, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 21.1 (C$_q$*C*H$_3$), 21.8 and 21.9 (2 × *Me*$_2$CH), 30.8 (NCH_2), 45.5 (N*C*HC$_q$), 49.2 and 49.4 (2 × OMe), 61.8 (*C*HMe$_2$), 99.8 (*C*(OMe)$_2$), 127.1 and 128.4 (C_o, C_m), 137.2 and 137.5 (2 × C_q); IR (NaCl) 2967, 2831, 1511, 1455, 1382, 1367, 1340, 1249, 1196, 1136, 1107 cm^{-1}; MS *m*/*z* 249 (M$^+$, 0.22), 234 (M$^+$ − Me, 0.61), 219 (M$^+$ − 2 × Me, 5), 218 (M$^+$ − OMe, 12), 204 (42), 165 (100), 144 (6), 119 (24), 105 (12), 91 (11). Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.39; H, 9.43; N, 5.50.

2-[Dimethoxy(4-fluorophenyl)methyl]-1-isopropylaziridine (5d): ^{1}H NMR ($CDCl_3$) δ 0.55 and 1.06 (2 × 3H, 2 × d, J = 6.27 Hz, *Me*$_2$CH), 1.24 (1H, septet, J = 6.27 Hz, C*H*Me$_2$), 1.30 (1H, d × d, J = 6.5, 0.7 Hz, NC*H*(H)), 1.45 (1H, d × d, J = 6.5 Hz, J = 3.3 Hz, NC*H*C$_q$), 2.22 (1H, d, J = 3.3 Hz, NCH(*H*)), 3.12 and 3.39 (2 × OMe), 7.03 and 7.51 (4H, 2 × t, J = 8.91 Hz, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 21.8 and 21.9 (2 × *Me*$_2$CH), 31.1 (NCH_2), 45.3 (N*C*HC$_q$), 49.3 and 49.4 (2 × OMe), 61.7 (*C*HMe$_2$), 99.6 (*C*(OMe)$_2$), 114.5 and 129.1 (C_o, C_m, 2 × d, J = 20.7, 8.6 Hz), 136.4 (C_q, d, J = 3.6 Hz), 162.5 (FC$_q$, d, J = 246.6 Hz); IR (NaCl) 3062, 2968, 2833, 1604, 1508, 1455, 1382, 1367, 1340, 1294, 1252, 1223, 1196, 1156, 1137 cm^{-1}; MS *m*/*z* no M$^+$, 234 (2), 222 (5), 209 (20), 208 (30), 169 (100), 123 (38), 109 (13), 95 (15), 42 (13). Anal. Calcd for $C_{14}H_{20}FNO_2$: C, 66.38; H, 7.96; N, 5.53. Found: C, 66.51; H, 8.09; N, 5.40.

2-[Dimethoxy(4-methoxyphenyl)methyl]-1-isopropylaziridine (5e): ^{1}H NMR ($CDCl_3$) δ 0.59 and 1.06 (2 × 3H, 2 × d, J = 6.27 Hz, *Me*$_2$CH), 1.24 (1H, septet, J = 6.27 Hz, C*H*Me$_2$), 1.26 (1H, d, broad, J = 6.27 Hz, NC*H*(H)), 1.46 (1H, d × d, J = 6.27 Hz, J = 3.3 Hz, NC*H*C$_q$), 2.20 (1H, d, J = 3.3 Hz, NCH(*H*)), 3.13, 3.37 and 3.79 (3 × OMe), 6.87 and 7.46 (4H, 2 × d, J = 8.91 Hz, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 21.9 (2 × *Me*$_2$CH), 30.9 (NCH_2), 45.5 (N*C*HC$_q$), 49.2, 49.4 and 55.1 (3 × OMe), 61.8 (*C*HMe$_2$), 99.8 (*C*(OMe)$_2$), 113.0 and 128.4 (C_o, C_m), 132.8 and 159.2 (2 × C_q); IR (NaCl) 2966, 2833, 1612, 1583, 1511, 1464, 1381, 1366, 1340, 1301, 1247, 1196, 1136, 1107, 1042 cm^{-1}; MS *m*/*z* 265 (M$^+$, 2), 250 (M$^+$ − Me, 2), 235 (M$^+$ − 2 × Me, 13), 234 (M$^+$ − OMe, 5), 220 (83), 203 (2), 181 (65), 135 (100), 122 (11), 121 (13), 86 (17), 84 (28), 77 (18), 49 (28), 47 (13). Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.90; H, 8.74; N, 5.28. Found: C, 68.06; H, 8.89; N, 5.11.

Synthesis of 1-Alkyl-2-aroylaziridines 13. The synthesis of 1-isopropyl-2-benzoylaziridine (**13a**) is representative for the synthesis of these compounds. Sodium hydride (0.33 g; 8.25 mmol, 60% dispersion in oil) was washed two times with 5 mL of pentane and evaporated to dryness. Dry DMSO (6 mL) was added, and the mixture was stirred for 15 min at room temperature to generate dimsylsodium. Subsequently, 1.00 g (4.1 mmol) of 3,3-dichloro-1-isopropyl-2-phenylazetidine **4**, dissolved in 6 mL of dry DMSO, was added dropwise at room temperature. After the addition was completed, the mixture was kept at 80 °C for 2 h. After cooling, 20 mL of water was added and the water phase was extracted three times with 10 mL of diethyl ether. The combined organic phases were dried over magnesium sulfate and after filtration and evaporation of the solvent, the crude 1-isopropyl-2-benzoylaziridine (**13a**) was obtained. Further purification was performed by flash chromatography to yield 0.36 g (46%) of the pure compound.

1-Isopropyl-2-benzoylaziridine (13a): ^{1}H NMR ($CDCl_3$) δ 1.18 and 1.21 (2 × 3H, 2 × d, J = 6.27 Hz, *Me*$_2$CH), 1.68 (1H, septet, J = 6.27 Hz, C*H*Me$_2$), 1.79 (1H, d × d, J = 6.6 Hz, J = 2 Hz, NC*H*(H)), 2.29 (1H, d × d, J = 3, 2 Hz, NCH(*H*)), 2.94 (1H, d × d, J = 6.6, 3 Hz, NC*H*C═O), 7.34−7.61 and 8.05−8.09 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 21.8 and 22.2 (2 × *Me*$_2$CH), 36.5 (NCH_2), 40.3 (N*C*HC═O), 61.7 (*C*HMe$_2$), 128.2 and 128.6 (C_o, C_m), 133.2 (C_p), 136.9 (C_q), 196.3 (C═O); IR (NaCl) 1682 cm^{-1} (C═O); MS *m*/*z* 189 (M$^+$, 13), 174 (18), 146 (30), 133 (64), 105 (100), 91 (50), 84 (54), 77 (67), 57 (23), 42 (66). Flash chromatography: CH_2Cl_2/MeOH 98/2, R_f = 0.41. Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 76.25; H, 8.09; N, 7.32.

1-Cyclohexyl-2-benzoylaziridine (13b): ^{1}H NMR ($CDCl_3$) δ 1.01−1.86 (12H, m, C_6H_{11} and NC*H*(H)), 2.29 (1H, d, broad, J = 1.65 Hz, NCH(*H*)), 2.94 (1H, d × d, J = 6, 3 Hz, NC*H*C═O), 7.45−7.61 and 8.05−8.08 (5H, m, C_6H_5); ^{13}C NMR ($CDCl_3$) δ 24.7, 24.8, 25.9, 32.3 and 32.7 (C_5H_{10}), 35.8 (NCH_2), 39.6 (N*C*HC═O), 69.5 (N*C*H), 128.2 and 128.5 (C_o, C_m), 133.0 (C_p), 136.9 (C_q), 196.4 (C═O); IR (NaCl) 1682 cm^{-1} (C═O); MS *m*/*z* 229 (M$^+$, 38), 228 (16), 186 (11), 177 (14), 147 (14), 146 (44), 133 (87), 124 (100), 110 (35), 109 (33), 105 (84), 97 (31), 96 (25), 91 (43), 77 (60), 55 (52), 54 (14), 51 (13). Flash chromatography: CH_2Cl_2/MeOH 98/2, R_f = 0.34. Anal. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.69; H, 8.46; N, 6.03.

1-Isopropyl-2-(4-methylbenzoyl)aziridine (13c): ^{1}H NMR ($CDCl_3$) δ 1.18 and 1.21 (2 × 3H, 2 × d, J = 6.27 Hz, *Me*$_2$CH), 1.67 (1H, septet, J = 6.27 Hz, C*H*Me$_2$), 1.77 (1H, d × d, J = 6.6, 2 Hz, NC*H*(H)), 2.29 (1H, d × d, J = 3, 2 Hz, NCH(*H*)), 2.42 (3H, s, CH_3C_q), 2.92 (1H, d × d, J = 6.6, 3 Hz, NC*H*C═O), 7.28 and 7.97 (4H, 2 × d, J = 7.92 Hz, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 21.7 (CH_3C_q), 21.9 and 22.2 (2 × *Me*$_2$CH), 36.4 (NCH_2), 40.2 (N*C*HC═O), 61.7 (*C*HMe$_2$), 128.4 and 129.3 (C_o, C_m), 134.5 (C_p), 144.1 (C_q), 195.8 (C═O); IR (NaCl) 1679 cm^{-1} (C═O); MS *m*/*z* 203 (M$^+$, 17), 188 (11), 160 (25), 147 (55), 119 (100), 105 (54), 91 (55), 84 (49), 65 (26), 57 (22), 55 (19), 43 (27); flash chromatography CH_2Cl_2/MeOH 98/2, R_f = 0.13. Anal. Calcd for $C_{13}H_{17}NO$: C, 76.81; H, 8.43; N, 6.89. Found: C, 76.89; H, 8.38; N, 6.95.

1-Isopropyl-2-(4-fluorobenzoyl)aziridine (13d): ^{1}H NMR ($CDCl_3$) δ 1.19 and 1.21 (2 × 3H, 2 × d, J = 6.27 Hz, *Me*$_2$CH), 1.68 (1H, septet, J = 6.27 Hz, C*H*Me$_2$), 1.79 (1H, d × d, J = 6, 2 Hz, NC*H*(H)), 2.29 (1H, m, NCH(*H*)), 2.88 (1H, d × d, J = 6, 3 Hz, NC*H*C═O), 7.12−7.28 and 8.05−8.15 (4H, 2 × m, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 21.9 and 22.2 (2 × *Me*$_2$CH), 36.5 (NCH_2), 40.5 (N*C*HC═O), 61.8 (*C*HMe$_2$), 115.8 and 131.0 (C_o, C_m, 2 × d, J = 22.0, 9.8 Hz), 133.3 (C_p, d, J = 2.5 Hz), 165.8 (FC$_q$, d, J = 253.9 Hz), 194.8 (C═O); IR (NaCl) 1683 cm^{-1} (C═O); MS *m*/*z* 207 (M$^+$, 8), 192 (11), 164 (18), 152 (43), 124 (99), 110 (38), 96 (56), 85 (70), 75 (16), 58 (16), 43 (100); flash chromatography CH_2Cl_2/MeOH 98/2, R_f = 0.36. Anal. Calcd for $C_{12}H_{14}FNO$: C, 69.55; H, 6.81; N, 6.76. Found: C, 69.66; H, 6.90; N, 6.70.

1-Isopropyl-2-(4-methoxybenzoyl)aziridine (13e): mp 81.4−82.4 °C; ^{1}H NMR ($CDCl_3$) δ 1.18 and 1.20 (2 × 3H, 2 × d, J = 6.27 Hz, *Me*$_2$CH), 1.66 (1H, septet, J = 6.27 Hz, C*H*Me$_2$), 1.76 (1H, d × d, J = 6.6, 1.65 Hz, NC*H*(H)), 2.27 (1H, d, broad, J = 1.65 Hz, NCH(*H*)), 2.89 (1H, d × d, J = 6.6, 3 Hz, NC*H*C═O), 3.87 (OMe), 6.95 and 8.07 (4H, 2 × d, J = 8.91 Hz, C_6H_4); ^{13}C NMR ($CDCl_3$) δ 21.9 and 22.2 (2 × *Me*$_2$CH), 36.2 (NCH_2), 40.1 (N*C*HC═O), 55.5 (OMe), 61.7 (*C*HMe$_2$), 113.8 and 130.6 (C_o, C_m), 129.8 (C_p), 163.6 (C_q), 194.6 (C═O); IR (KBr) 1672 cm^{-1} (C═O); MS *m*/*z* 219 (M$^+$, 14), 176 (11), 163 (48), 135 (100), 121 (36), 107 (11), 92 (14), 84 (45), 77 (16), 57 (13), 42 (29); flash chromatography CH_2Cl_2/MeOH 98/2, R_f = 0.28. Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.21; H, 7.81; N, 6.39. Found: C, 71.33; H, 7.87; N, 6.29.

Synthesis of 1-Alkyl-2-aroylaziridines 13 by Hydrolysis of Aziridines 5. The synthesis of 1-isopropyl-2-(4-methoxybenzoyl)aziridine (**13e**) is representative for the synthesis of these aziridines **13**. To a solution of 0.11 g (0.4 mmol) of 2-[dimethoxy(4-methoxyphenyl)methyl]-1-isopropylaziridine (**5e**) in 1 mL of acetonitrile was added 0.09 g (0.6 mmol) sodium iodide at room temperature. To this stirred solution was added dropwise 0.08 mL (0.6 mmol) of boron trifluoride etherate. The resulting mixture was kept under reflux for 2 h and subsequently poured into a saturated sodium bicarbonate solution.

The water phase was extracted three times with 10 mL of chloroform, and the combined organic layers were subsequently washed with a 10% sodium thiosulfate solution and brine. After being dried over magnesium sulfate, the crude product **13e** was obtained. Purification by flash chromatography yielded 0.05 g (58%) of pure compound. See the previous section for spectroscopic data.

Characterization of 1-Alkyl-2-aryl-3-chloro-2-azetines 6. The characterization of 3-chloro-1-isopropyl-2-phenyl-2-azetine **6a** is representative for all other 2-azetines **6**. In an NMR tube was weighed 0.0200 g (0.5 mmol, 60% dispersion in oil) of sodium hydride, which was washed two times with pentane. Residual pentane was removed by heating. The NMR tube was closed with a septum and flushed with N_2 gas. Meanwhile, 1 mL of DMSO-d_6 was added. H_2 gas started to evolve. After 10 min, the H_2 evolution stopped, and 0.0610 g (0.25 mmol) of 3,3-dichloro-1-isopropyl-2-phenylazetidine **4a**, dissolved in 1 mL of DMSO-d_6, was introduced in the NMR tube, while also one drop of tetramethylsilane was added. Directly after addition, an ^{1}H NMR spectrum was taken and afterward the NMR tube was kept at 50 °C in a thermostated water bath. From then on, ^{1}H NMR spectra were taken every 30 min. In all cases, 100% conversion was reached after 2−2.5 h, while no side products were observed. The 2-azetine **6a** thus formed was also characterized by ^{13}C NMR.

3-Chloro-1-isopropyl-2-phenyl-2-azetine (6a): ^{1}H NMR (DMSO-d_6) δ 0.94 (6H, d, J = 6.6 Hz, Me_2CH), 3.46 (1H, septet, J = 6.6 Hz, CHMe$_2$), 3.94 (2H, s, NCH$_2$), 7.36−7.51 (5H, m, C_6H_5); ^{13}C NMR (DMSO-d_6) δ 17.6 (Me_2CH), 48.5 (CHMe$_2$), 57.6 (NCH$_2$), 100.4 (ClC$_q$), 125.4 and 128.8 (C$_o$, C$_m$), 129.4 (C$_p$), 152.5 (NC$_q$).

3-Chloro-1-cyclohexyl-2-phenyl-2-azetine (6b): ^{1}H NMR (DMSO-d_6) δ 1.00−1.73 (10H, m, C_5H_{10}), 2.96−3.04 (1H, m, NCH), 4.00 (2H, s, NCH$_2$), 7.35−7.51 (5H, m, C_6H_5); ^{13}C NMR (DMSO-d_6) δ 24.7, 25.2 and 28.3 (C_5H_{10}), 57.4 (NCH$_2$), 59.2 (NCH), 100.1 (ClC$_q$), 125.4 and 128.7 (C$_o$, C$_m$), 129.6 (C$_p$), 152.4 (NC$_q$).

3-Chloro-1-isopropyl-2-(4-methylphenyl)-2-azetine (6c): ^{1}H NMR (DMSO-d_6) δ 0.93 (6H, d, J = 6.6 Hz, Me_2CH), 2.32 (3H, s, C$_q$CH$_3$), 3.45 (1H, septet, J = 6.6 Hz, CHMe$_2$), 3.91 (2H, s, NCH$_2$), 7.25 and 7.39 (4H, 2 × d, J = 7.92 Hz, C_6H_4); ^{13}C NMR (DMSO-d_6) δ 17.6 (Me_2CH), 20.9 (C$_q$CH$_3$), 48.5 (CHMe$_2$), 57.5 (NCH$_2$), 99.3 (ClC$_q$), 125.4 and 129.3 (C$_o$, C$_m$), 126.7 and 138.3 (2 × C$_q$), 152.6 (NC$_q$).

3-Chloro-1-isopropyl-2-(4-fluorophenyl)-2-azetine (6d): ^{1}H NMR (DMSO-d_6) δ 0.84 (6H, d, J = 6.6 Hz, Me_2CH), 3.44 (1H, septet, J = 6.6 Hz, CHMe$_2$), 3.94 (2H, s, NCH$_2$), 7.31 and 7.54 (4H, 2 × m, C_6H_4); ^{13}C NMR (DMSO-d_6) δ 17.6 (Me_2-CH), 48.5 (CHMe$_2$), 57.7 (NCH$_2$), 100.2 (ClC$_q$), 115.9 and 127.7 (C$_o$, C$_m$, 2 × d, J = 21.9, 8.6 Hz), 133.1 (C$_p$, d, J = 2.5 Hz), 151.5 (NC$_q$), 161.9 (FC$_q$, d, J = 251.4 Hz).

3-Chloro-1-isopropyl-2-(4-methoxyphenyl)-2-azetine (6e): ^{1}H NMR (DMSO-D$_6$) δ 1.00 (6H, d, J = 6.27 Hz, Me_2-CH), 3.50 (1H, septet, J = 6.27 Hz, CHMe$_2$), 3.85 (3H, s, OMe), 3.96 (2H, s, NCH$_2$), 7.08 and 7.49 (4H, 2 × d, J = 8.58 Hz, C_6H_4); ^{13}C NMR (DMSO-d_6) δ 17.9 (Me_2CH), 48.8 (CHMe$_2$), 55.5 (OMe), 57.8 (NCH$_2$), 98.3 (ClC$_q$), 114.6 and 127.3 (C$_o$, C$_m$), 122.4 and 159.8 (2 × C$_q$), 152.7 (NC$_q$).

JO010914J