Graphical Abstract

Diels-Alder Cycloaddition of 2-Azadienes to Methyl 2-(2,6-Dichlorophenyl)-2*H*-Azirine-3-Carboxylate in the Synthesis of Methyl 4-Oxo-1,3-Diazabicyclo[4.1.0]heptane-6-Carboxylates

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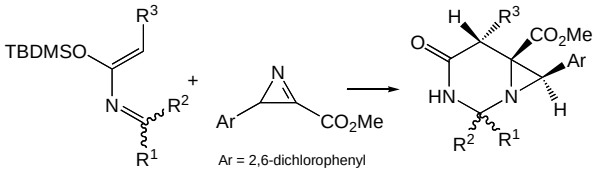
M. José Alves*, M. Miguel Durães, A. Gil Fortes
Departamento de Química, Universidade do Minho, Campus de Gualtar, 4700-320 Braga, Portugal



Diels-Alder Cycloaddition of 2-Azadienes to Methyl 2-(2,6-Dichlorophenyl)-2*H*-Azirine-3-Carboxylate in the Synthesis of Methyl 4-Oxo-1,3-Diazabicyclo[4.1.0]heptane-6-Carboxylates

M. José Alves,*[a] M. Miguel Durães,[a] A. Gil Fortes[a]

[a] Departamento de Química, Universidade do Minho, Campus de Gualtar, 4700-320 Braga, Portugal

Abstract

A number of fused 4-oxo-1,3-diazabicyclo[4.1.0]heptane-6-carboxylates, a new type of compound, have been obtained by Diels-Alder cycloaddition between nucleophilic 2-azadienes and an electrophilic 2*H*-azirine. The reactions are completely *endo*- and *regio*selective, the azirine being added by its less hindered face to the diene. There are two isomers **7** and **8** formed from dienes **1** due either to isomerization of the cycloadducts **7** and **8** or by isomerization of the C=N bond of the diene during the reaction. The isomer **10** is formed from diene **2e**, and a single diastereoisomer structure **4a-i** is formed from dienes **11**. Some pyrimidones **8a**,**7c**/**8c**, **7e**, **10**, **11d** have been hydrolyzed leading to functionalised aziridines **12**, **13** and **15**.

Keywords: 2-azadienes, 2*H*-azirines, Diels-Alder cycloaddition.

Introduction

Methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** has been reacted with dienes **1**, **2**[1] and **4**. It had been obtained before by pyrolysis of the methyl 3-(2,6-dichlorophenyl) α-azidopropenate[2] and used in [4+2] π cycloaddition with commercial dienes. Reactions occur at room temperature with excellent stereoselectivity, being *endo*[3] to carbodienes and *exo*[4] to furan and diphenylisobenzofuran. The 2-azadienes were obtained according to methodology developed by Ghosez[5] from acylimidates and *tert*-butyldimethylsilyl triflates for

[a] Departamento de Química, Universidade do Minho, Campus de Gualtar, 4710-057 Braga, Portugal; Fax nº: 00 351 (2)53 678983
Email: mja@quimica.uminho.pt

compounds **1** and **2**, and from LiHMDS, trimethylsilyl chloride and triethylamine in one pot reaction for compounds **4**.[5] Nucleophilic 2-azadienes of this type had been combined with a range of electron poor dienophiles, such as aldehydes,[6a-b] nitroso compounds,[7,8,9] olefinic compounds,[10] naphthoquinones,[11] quinones,[12] activated acetylenic dienophiles,[12,13] and activated nitriles,[12] in order to obtain the 6 membered ring compounds or their hydrolysis derivatives. A chiral nitroso compound was employed giving cycloadducts with high facial selectivity.[9] Also, activated olefinic dienophiles were used together with nucleophilic 2-azadienes in the presence of a chiral copper(II) complex to give enantiomerically pure piperidones.[14] The results we now report were obtained by Diels-Alder cycloaddition between electrophilic 2*H*-azirine **6** and the nucleophilic 2-azadiens **1**, **2** and **4**. The literature contains examples of the cycloaddition of electron poor 2-azadienes to simple imines and to an azirine [15] but this work represents the first examples of normal electron demanding cycloadditions between 2-azadienes and an azirine.

Results and Discussion

Synthesis of 2-Azadienes

From imidates

The 2-azadienes **1** and **2** were obtained in two steps according to the procedure devised by Ghosez *et al.* for this type of compound. Commercial imidates and acid chlorides were mixed together in dry DCM and over N_2, to form the acylimidates **3** as intermediates. The acylimidates were further silylated in ether in the presence of *tert*-butyldimethylsilyl chloride. Products were obtained in good yields (Scheme 1) contaminated with N-acylimidate, according to ^{1}H NMR spectra, and were used without purification in the synthesis of cycloadducts.

Scheme 1

Compounds **1a** and **1b** have been prepared previously. Compound **1b** was shown to have the *Z* configuration for the C-3 to C-4 bond[5]. Compounds **1c** and **1d** are new compounds and the same configuration is assigned. In solution compounds **1b-d** were found to consist of mixture of stereomers in relation to C-1. The major isomers were deduced to have the *EZ* configuration, based on spectroscopic evidence for

cycloadducts obtained as discussed later. Stereomer **2** is formed in the series **e** together with stereomer **1**. Compounds **1e** and **2e** are formed in 1 : 4 ratio when neat TBDMSOTf is added to the acylimidate solution, and a 1 : 1 ratio of isomers when TBDMSOTf is added dropwise diluted in ether. This result led us to assume the diene **2e** to be the kinetic product of silylation of the acylimidate with TBDMSOTf. Stereomer **2e** was assigned as *EE* configuration on the basis of the spectroscopic data of cycloadduct **10** obtained along with the adduct **7e** in the reaction of **1e**/**2e** to azirine **6**.

From aldehydes

2-Azadienes **4** were obtained in one pot reaction by combination of 4-5 fold excess of LiHMDS, freshly distilled aldehyde and trimethylsilyl chloride to produce the imine **5**, that was further acylated in the presence of an acid chloride and triethylamine, according to scheme 2.

Scheme 2

This is a modified method of one initially used by Ghosez to generate azadienes of type **4**.[5] Excellent yields were obtained in most cases. All 2-azadienes **4** referred to here are new compounds that were shown to be single isomers in solution, with the exception of **4i**, where a second isomer is observed (isomeric ratio 10 : 1). The *EZ* stereochemistry for the compounds is assigned in accordance with a range of analogous compounds obtained before.[5] Three examples are shown below (Fig 1):

Fig 1

The minor compound in series **i** is assumed to have the *EE* configuration according to other cases reported in literature for the same type of dienes.[5] Due to the instability of the 2-azadienes **4**, they were identified by ^{1}H NMR spectroscopy and were used without purification in the cycloadditions.

Cycloadditions of 2-azadienes 1 and 2 to 2*H*-azirine 6

2-Azadienes of type **1a-d** react at room temperature with the azirine **6** to give the cycloadducts **7** and **8** (Scheme 3). Usually the desilylated compound precipitated out of the reaction mixture as a solid that was obtained by filtration. After repeating these

reactions in several conditions we find that the better yields correspond to reactions performed in very small amounts of diethyl ether. As an alternative procedure after the consumption of the azirine the reaction material was redissolved in DCM, stirred with SiO_2 followed by dry flash chromatography. Poorer yields of products **7**/**8** were obtained in all cases. Also treatment of the reaction mixture with tetramethylammonium fluoride gave compound **7b** in a poorer yield (41 %). The primary silyloxy cycloadduct could never be isolated or even observed by ^{1}H NMR analysis.

The solid obtained from reaction of **1a** (one stereomer) with the azirine **6** was a mixture (1 : 1 ratio) of **7a**/**8a** in 53 % yield. Redissolution of the solid in DCM and stirring the solution with SiO_2 for 24 h gave **7a** quantitatively. A single isomer **7b** was obtained from **1b** in 51 % yield after filtration. The starting diene contained only traces of a minor isomer. Reaction of **1c** (4 : 1 mixture of stereomers) produced an oil that was treated with DCM and SiO_2 for 3 days. The crude showed two diastereomers **7c** and **8c** in a 1 : 1 ratio. After flash chromatography the isomer **7c** was partially separated (25 %), together with a fraction containing the mixture of both isomers (33%), in total yield of 58%. Curiously the diastereomeric ratio after chromatography changed to 4.5 (**7c**) : 1 (**8c**). Reaction of **1d** (2 : 1 ratio of stereomers) with the azirine **6** gave an oil which was treated with SiO_2 in DCM for 7 days. ^{1}H NMR spectrum of the reaction mixture showed a 3 : 1 mixture of diastereomers that were fully separated after flash chromatography as two solids, **7d** (27 %) and **8d** (11 %).

Scheme 3

Unexpectedly no relationship is observed between the diastereomeric ratio of the adducts **7**/**8** and the stereomeric ratio of the precursor dienes. In cases where the products were obtained after treatment with SiO_2 a possible explanation is the isomerization of products **8** into **7**. It is also relevant that the diastereomeric ratio difference between a mixture of **7c** and **8c** that was enriched in **7c** after flash chromatography. In series **a** two isomers **7** and **8** (1 : 1 ratio) precipitated out of the reaction mixture before treatment with SiO_2, having started the cycloaddition from **1a** as a single isomer. In this case it is more plausible that the C=N bond rotation between the *EZ* and *ZZ* isomer forms can explain the isomeric ratio of adducts.

Possibly a chemical equilibrium between the *EZ* and *ZZ* forms, that is not observable in $CDCl_3$ solution, occurs during the cycloaddition giving the respective adducts. Another possibility is that a step-wise mechanism rather than a concerted Diels-Alder process could operate in this case. The same could not be said about the cycloaddition of **1b** where a single diene isomer gave a single cycloadduct.

Scheme 4

A crystal structure confirmed the structure of compound **7c**[1] . This shows that the reaction goes through an *endo* approach of the azirine **6** from its less hindered face to *EZ* configuration of the diene **1**. Also, NOESY spectra for **7c** show that the 5-H and 2-Me were on the same side of the molecule. On the other hand the minor isomer **8c** showed 7-H to be on the same side of 2-Me, which would be explained for the same *endo* approach of the less crowded face of the azirine to the minor diene isomer *ZZ* (Fig 2). Further support for the difference between the diastereomers **7** and **8** in 2-C is obtained by hydrolysis of compounds **7c** and **8c** which gave the same product **12** as seen ahead (Scheme 6).

Fig 2.

On reacting a mixture of dienes **1e** and **2e** (1 : 4 ratio) with the azirine **6** a white solid formed after stirring the reaction mixture for 7 days at room temperature. The solid was analysed by ^{1}H NMR showing it to be a mixture of diastereomers identified as **7e** and **10**, in 1.2 (**7e**) : 1 (**10**) ratio. This is another case besides **a** and **b** where a solid is isolated, without previous contact with silica. As in case **a** the isomeric ratio of dienes does not match with the isomeric ratio of cycloadducts. So the observations made for the case **a** can now be used to explain to case **e**. Flash chromatography partially separated **7e** (30%) as a white solid together with a mixture of **7e** and **10** (21 %) also as a solid, total yield 51%. The NOESY spectrum of **7e** showed the methoxy group at 2-C in the proximity of 7-H and the methyl group at 5-C close in space to 7-H. On the other hand the NOESY spectrum of the minor isomer **10** showed proximity between 5-H and 7-H, which would rule out structure **8** and strongly suggests structure **10** instead (Fig 3).

Fig 3.

Structure **10** should be formed from attack of the less hindered face of the azirine on the less stable diene configuration *EE*. The hydrolysis product of compound **10** confirms a different configuration of the stereocentre 5-C of this compound related to structure**s 7** and **8** as seen later. Cycloaddition preparations of series **e** showed that starting with a mixture of dienes **1e** and **2e** (*ca*. 1 : 1 ratio) and with a mixture of dienes **1e** and **2e** (*ca*. 1 : 4 ratio) isomers **7e** and **10** formed in the same isomeric ratio (1 : 1). This leads us to propose that an isomerization takes place about 3-C to 4-C in the diene during the course of the reaction.

^{1}H NMR spectra of compounds **7c** and **8c** showed the influence of the ethoxyl group through space on protons 5-H and 7-H. When this proximity is observed the 5-H and 7-H protons suffer a shift to lower field in the spectra. In compound **7c** 7-H suffer a shift to lower field (+ 0.31 ppm) when compared to 7-H in compound **8c**. On the other hand, 5-H in compound **8c** shows up at lower field (+ 0.35 ppm) compared to 5-H in compound **7c**. Comparison of ^{1}H NMR chemical shifts of 5-H and 7-H obtained to the series **c** apply to the diastereomeric pair in series **d**, but not in series **a** (Table 1).

Cycloadditions of 2-azadienes 4 to 2*H*-azirine 6

2-Azadienes of type **4a-i** react at room temperature with the azirine **6** to give the cycloadducts **11** as single isomers. Products were generally obtained in good yields (Scheme 5). In most cases the desilylated compound precipitated out of the reaction as a solid practically pure (**b**, **d**, **e**, **f** and **g**) that was obtained by filtration. In other cases the product was obtained as an oil (**a**, **c**, **h**, **i**) that was subjected to dry flash chromatography (**a**, **h**, **i**) resulting in a drop in the yield of the reaction. In case **c** a polymer formed together with an oil. The oil crystallized after addition of diethyl ether. The primary silylated cycloadduct could never be observed by ^{1}H NMR analysis of the products. In accordance with results obtained for the cycloaddition of **7** and **8** the approach of reactants is proposed to take place from the less hindered face of the azirine.

Scheme 5

Major features of the ^{1}H NMR spectra for compounds **11** are the 5-H and 7-H chemical shifts, comparable to 5-H and 7-H chemical shifts of compounds **7**. Namely the 5-H in the 2,5-diphenyl disubstituted compounds **11d** and **7d** are respectively 4.63 ppm and 4.41 ppm. Also the two 5-H of the monosubstituted **11c** and **7a** showed similar chemical shift values: 3.57 / 3.16 ppm (**11c**) and 3.40 / 3.16 ppm (**7a**). Compounds **8** showed chemical shifts somewhat further apart: 3.34 / 3.08 (**8a**) and 5.09 (**8d**). 2-H Chemical shifts in structures **11** are all around the same chemical shifts between 5.86 and 6.52 ppm, showing the influence of the nitrogen atoms and an aromatic ring attached to the 2-C.

Hydrolysis of the cycloadducts

Heating an ether solution of **7a** afforded the hydrolysis product in trace amounts. Compound **12a** could be obtained pure in 74 % yield when a solution of **8a** in THF was treated with aq. HCl (1 eq.) diluted in THF. Also, a mixture of **7c** and **8c** was treated the same way to give product **12c** in 87 % yield (Scheme 6). As both diastereomers **7c** and **8c** gave the same hydrolysis product this confirms the stereochemistry of adducts discussed above.

Scheme 6

The hydrolysis of the mixture of **7e**/**10** (1.2 : 1 ratio) produced a different result. In this case two products **12e** and **13** (Fig 4) were obtained (1.2 : 1) that were characterized after separation by dry flash chromatography.

Fig.4

A possible mechanism for the hydrolysis can be envisaged from conversion of compounds **8a** into **7a**, through **9** as the intermediate (Scheme 4). On the other hand, compound **11d** would form the imine **14** in the presence of excess of HCl to generate the final product **15** (Scheme 7).

Scheme 7

Major features for assignment of structures **12**, **13** and **15** are the two doublets due to the NH-CH moiety of the aziridine ring coupling *J ca.* 9 Hz at 2.5 - 3.5 ppm (Table 2). Addition of D_2O exchanged the mobile proton and the CH then shows up as a sharp singlet.

Conclusion

Fused systems containing 2-oxocarbonylaziridines have been obtained with excellent diastereoselectivity by Diels-Alder cycloaddition between an electrophilic 2*H*-azirine and nucleophilic 2-azadienes. The reaction occurs at room temperature in the absence of catalysis producing moderate to good yields of products. Since the purification of the intermediate compounds were avoided in all steps, the yields may be considered good even in compounds **7** and **8** and some **11** where the results are poorer. The pyrimidone compounds **7**, **8** and **11** are by themselves compounds with potential biological interest, but the same could be said about the hydrolysis products **12**, **13** and **15** which are also masked α-aminoesters with functionalised side chains. Specially structure **15**, where a β-amido group makes it a potential interesting compound after some minor manipulations. Introducing chirality both in the azirine and the diene in order to turn the reactions enantioselective are currently underway.

Experimental

General

^{1}H NMR spectra were recorded on a Varian Unity Plus 300 (300MHz) spectrometer. Multiplicities are recorded as broad peaks (br), singlets (s), doublets (d), triplets(t), doublet of doublets (dd) quartets (q) doublet of quartets (dq) and multiplets (m). *J* values are in Hz. Infrared spectra were recorded on a Bomem MB 104 or on a Perkin-Elmer 1600 FT-IR spectrometer. Solid samples were run as nujol mulls, and liquids as thin films. Mass spectra were recorded on a VG Autospec M. spectrometer as electron impact spectra (70 eV). Microanalyses were performed in a LECO-CHNS-932 analyser. Melting points (mp) were determined on a Gallenkamp block and are uncorrected. Dry column flash chromatography was carried out using Kieselgel 60 and water pump vacumm. Thin layer chromatography (TLC) was carried out on 0.25 mm silica gel layer 60DC- Ferigplatter Durasil-25 UV_{254}. Diethyl ether and tetrahydrofuran were dried over sodium using benzophenone as indicator.

Triethylamine and the acid chlorides were freshly distilled prior to use. The aldehydes were purified by crystallization if solids or by distillation if liquids. Dry flash chromatography was performed on silica gel 60 <0.063 mm for columm chromatography. Petroleum ether 40 – 60 ºC was distilled before use.

General Procedure for the Synthesis of the N-Acylimidates

Triethylamine recently dried was added in one portion to a solution of the imidate hydrochloride in dry DCM, stirred at room temperature under nitrogen. The acid chloride was added dropwise to the reaction mixture. Stirring was continued for another 30 min., and dried petroleum ether 40 - 60 ºC (40 mL) was added. The reaction mixture was filtered over celite and the filtrate concentrated to a residual oil that was redissolved in dry petroleum ether 40 - 60 ºC (20 mL) and passed again over a pad of celite. The filtrate was concentrated to give a pale yellow oil that was identified as the respective acylimidate by ^{1}H NMR spectroscopy.

Ethyl *N*-acetylacetimidate 3a

Reaction mixture: ethyl acetimidate hydrochloride (1.00 g, 8.10 mmol, 1 eq.) in DCM (25 mL), triethylamine (2.46 mL, 17.8 mmol, 2.2 eq.), acetyl chloride (0.58 mL, 8.10 mmol, 1 eq.). Yield 0,82 g (84 %). ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.93 (t, *J* = 7.2 Hz, 3 H), 1.68 (s, 3 H), 1.89 (s, 3 H), 3.82 (q, *J* = 7.2 Hz, 2 H) ppm.

Ethyl *N*-propionyl acetimidate 3b

Reaction mixture: ethyl acetimidate hydrochloride (2.00 g, 16.2 mmol., 1 eq.) in DCM (25 mL), triethylamine (5.42 mL, 39.2 mmol, 2.2 eq.), propionyl chloride (1.41 mL, 16.20 mmol, 1 eq.). Yield 1.47 g (66 %). ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.12 (t, *J* = 7.2 Hz, 3 H), 1.27 (t, *J* = 7.5 Hz, 3 H), 1.98 (s, 3 H), 2.41 (q, *J* = 7.5 Hz, 2 H), 4.08 (q, *J* = 7.2 Hz, 2 H) ppm.

Ethyl *N*-phenylacetyl acetimidate 3c

Reaction mixture: ethyl acetimidate hydrochloride (0.58 g, 4.70 mmol, 1 eq.) in DCM (25 mL), triethylamine (1.42 mL, 10.33 mmol, 2.2 eq.), phenylacetyl chloride (0.62 mL, 4.70 mmol, 1 eq.). Yield 0,95 g (98 %). ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.25 (t, *J* = 7.2 Hz, 3 H), 1.77 (s, 3 H), 3.72 (s, 2 H), 4.07 (q, *J* = 7.2 Hz, 2 H), 7.30 - 7.40 (m, 5 H, ArH) ppm.

Methyl *N*-phenylacetyl benzimidate 3d

Reaction mixture: methyl benzimidate hydrochloride (0.70 g, 4.08 mmol, 1 eq.) in DCM (25 mL), triethylamine (1.24 mL, 8.98 mmol, 2.2 eq.), phenylacetyl chloride (0.54 mL, 4.08 mmol, 1 eq.). Yield 0,74 g (55 %), contaminated with methyl benzimidate hydrochloride 23%. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 3.66 (s, 2 H), 3.82 (s, 3 H), 7.04 - 7.04 (m, 10 H, ArH) ppm.

Methyl N-propionyl benzimidate 3e

Reaction mixture: methyl benzimidate hydrochloride (1.00 g, 5.83 mmol, 1 eq.) in DCM (25 mL), triethylamine (1.77 mL, 12.80 mmol, 2.2 eq.), propionyl chloride (0.51 mL, 5.83 mmol, 1 eq.). Yield 0,82 g (74 %). ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.06 (t, *J* = 7,5 Hz, 3 H), 2.34 (q, *J* = 7.5 Hz, 2 H), 3.87 (s, 3 H), 7.24 - 7.62 (m, 5 H, ArH) ppm.

General Procedure for the Synthesis of the 2-Azadienes 1 and 2

Triethylamine recently dried was added in one portion to a solution of the acylimidate in dry ether stirred at room temperature and under N_2. *tert*-Butyldimethylsilyl triflate diluted in dry ether was added dropwise. After the addition was complete the reaction mixture was placed in the freezer for 10 min.. The reaction mixture was allowed to reach room temperature and the ethereal phase was separated and the lower phase washed with dry ether (2 x 25 mL). The organic layers were combined, dried and the ether evaporated. A pale brown oil was obtained that was shown by ^{1}H NMR to be the respective 2-azadienes expected, contaminated with a variable amount of the starting acylimidate.

4-Ethoxy-2-(*tert*-butyldimethylsilyloxy)-3-aza-1,3-pentadiene 1a

Reaction mixture: ethyl *N*-acetyl acetimidate **3a** (0.82 g, 6.82 mmol, 1 eq.), dry diethyl ether (25 mL), triethylamine (1.05 mL, 7.59 mmol, 1.1 eq.), *tert*-butyldimethylsilyl triflate (1.58 mL, 6.90 mmol, 1 eq.), diluted in dry diethyl ether (10 mL). Yield 1.28 g (65%) contaminated with starting imidate (16 %) in accordance with the ^{1}H NMR data. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.16 (s, 6 H), 0.91 (s, 9 H),

1.06 (t, *J* = 7.2 Hz, 3 H), 2.01 (s, 3 H), 3.42 (s, 1 H), 3.70 (s, 1 H), 4.08 (q, *J* = 6.9 Hz, 2 H) ppm.

2-Ethoxy-4-(*tert* -butyldimethylsilyloxy)-3-aza-2,4-hexadiene 1b

Reaction mixture: ethyl *N*-propionyl acetimidate **3b** (1.47 g, 10.30 mmol, 1 eq.), dry diethyl ether (25 mL), triethylamine (1.57 mL, 11.30 mmol, 1.1 eq.), *ter*t-butyldimethylsilyl triflate (2.36 mL, 10.30 mmol, 1 eq.), diluted in dry diethyl ether (10 mL). Yield 2.90 g (87 %), contaminated with starting acylimidate (20 %) in accordance with the ^{1}H NMR data. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.12 (s, 6 H), 0.90 (s, 9 H), 1.26 (t, *J* = 6.9Hz, 3 H), 1.57 (d, *J* = 6.6 Hz, 3 H), 1.98 (s, 3 H), 3.78 (q, *J* = 6.6 Hz, 1 H), 4.10 (q, *J* = 6.9 Hz, 2 H) ppm.

4-Ethoxy-1-phenyl-2-(*tert*-butyldimethylsilyloxy)-3-aza-1,3-pentadiene 1c

Reaction mixture: ethyl *N*-acetylphenyl acetimidate **3c** (0.95 g, 4.63 mmol, 1 eq.), dry diethyl ether (25 mL), triethylamine (0.71 mL, 5.10 mmol, 1.1 eq.), *tert*-butyldimethylsilyl triflate (1.10 mL, 4.63 mmol, 1 eq.), diluted in dry diethyl ether (10 mL). Yield 1.46 g (86 %), contaminated with starting imidate (13 %) in accordance with the ^{1}H NMR data. Mixture of isomers (4 : 1). Major isomer ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.21 (s, 6 H), 1.01 (s, 9 H), 1.33 (t, *J* = 7.2 Hz, 3 H), 2.11 (s, 3 H), 4.18 (q, *J* = 7.2 Hz, 2 H), 4.77 (s, 1 H), 7.20 - 7.30 (m, 3 H), 7.75 (d, *J* = 7.2 Hz, 2 H) ppm. Minor isomer (some peaks) 0.22 (s, 6 H), 0,98 (s, 9 H), 1.91 (s, 3 H), 4.30 (q, *J* = 7,5 Hz, 2 H), 5.26 (s, 1 H) ppm.

1-Methoxy-1,4-diphenyl-3-(*tert*-butyldimethylsilyloxy)-2-aza-1,3-butadiene 1d

Reaction mixture: ethyl *N*-acetylphenyl benzimidate **3d** (0.74 g, 2.93 mmol, 1 eq.), dry diethyl ether (25 mL), triethylamine (0.45 mL, 3.22 mmol, 1.1 eq.), *tert*-butyldimethylsilyl triflate (0.67 mL, 2.93 mmol, 1 eq.), diluted in dry diethyl ether (10 mL). Yield 1.05 g (88 %), contaminated with starting acylimidate (10 %) in accordance with the ^{1}H NMR data. Mixture of isomers (2 : 1). Major isomer (some peaks): ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.27 (s, 6 H), 1.00 (s, 9 H), 3.93 (s, 3 H), 4.63 (s, 1 H). Minor isomer (some peaks), 0.12 (s, 6 H), 0.95 (s, 9 H), 3.73 (s, 3 H), 5.22 (s, 1 H).

(1*E*, 3*Z*) 1-Methoxy-1-phenyl-3-(t-butyldimethylsilyloxy)-2-aza-1,3-pentadiene 1e and (1*E*, 3*E*) 1-methoxy-1-phenyl-3-(t-butyldimethylsilyloxy)-2-aza-1,3-pentadiene 2e

Reaction mixture: methyl *N*-propionyl benzimidate **3e** (0.82 g, 4.29 mmol, 1 eq.), dry diethyl ether (25 mL), triethylamine (0.65 mL, 4.72 mmol, 1.1 eq.), *tert*-butyldimethylsilyl triflate (0.99 mL, 4.29 mmol, 1 eq.), diluted in dry diethyl ether (10 mL). Yield 1.14 g (82 %), contaminated with starting acylimidate (18 %) in accordance with the ^{1}H NMR data. Mixture of isomers (4 : 1). Major isomer (**2e**): ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.20 (s, 6 H), 0.95 (s, 9 H), 1.44 (d, *J* = 6.6 Hz, 3 H), 3.66 (q, *J* = 6.6 Hz, 1 H), 3.86 (s, 3 H), 7.30 - 7.40 (m, 3 H), 7.50 - 7.70 (m, 2 H) ppm. Minor isomer (**1e**) : 0.14 (s, 6 H), 0.88 (s, 9 H), 1.25 (d, *J* = 6.6 Hz, 3 H), 3.88 (s, 3 H), 3.90 (q, *J* = 6.6 Hz, 1 H) ppm.

Synthesis of 2-Azadienes 4

Method A

To 1,1,1,3,3,3-hexamethyldisilazane (1 eq.) was added n-butyllithium (1,6 M in hexanes, 0.9 eq.) over a 5 min. period. The reaction solution was kept under magnetic stirring for 15 min. at room temperature and then cooled in an ice/water bath. Dry THF (the amount needed for 0.6M of LiHMDS) was added and the mixture stirred further for 20 min.. A solution of the aldehyde (1 eq.) freshly distilled in dry THF was added over a 7 min. period and the resulting solution stirred for 30 min.. Trimethylsilyl chloride (0.9 eq.) was added in one portion and the stirring continued for 30 min. Triethylamine (1.1 eq.) was added followed by the acid chloride (1.3 eq.) in dry ether. The cooling bath was removed and the mixture was stirred at room temperature for 2 hours. The inorganic salts were filtrated off over celite and the ether was removed in the rotary evaporator to give the crude product, as a solid or an oil.

Method B

To lithium 1,1,1,3,3,3-hexamethyldisilazanate (4-5 eq.) in dry ether, cooled at 0 ºC and in N_2 atmosphere was added the aldehyde (1 eq.) freshly distilled in dry ether over a 5 min. period. The cooling bath was removed and the reaction mixture was stirred for 3 hours at room temperature. Then the reaction mixture was cooled to 0º C

again and trimethylsilyl chloride (1.3 eq.) added in one portion. After stirring the reaction mixture at 0º C for 5 min., the bath was removed and the mixture stirred at room temperature for 1 h 15 min.. After this time, triethylamine (1.1 eq.) was added in one portion followed by dropwise addition of the acid chloride (1.3 eq.) in dry ether. The reaction mixture was transferred to an water bath at 30º C and the stirring was continued for another 2 h.. The inorganic salts were filtrated off over celite and the ether was removed to give the crude product as a solid or an oil.

1-Phenyl-3-trimethylsilyloxy-2-aza-1,3-pentadiene 4a

Reaction mixture: lithium 1,1,1,3,3,3-hexamethyldisilazanate (3.94 mL, 2.84 g, 16.97 mmol, 4.5 eq.) in dry ether (20 mL), benzaldehyde (0.39 mL, 0.4 g, 3.77 mmol, 1 eq.) dissolved in dry ether (1 mL), trimethylsilyl chloride (2.10 mL, 0.53 g, 16.97 mmol, 4.5 eq.), triethylamine (0.57 mL, 0.42 g, 4.15 mmol, 1.1 eq.), phenylacetyl chloride (0.33 mL, 0.35 g, 3.77 mmol, 1 eq.) in dry ether (4 mL). Yield of a yellow solid 0.73 g (*ca.* 60%), contaminated with the starting aldehyde, in accordance with ^{1}H NMR data. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.28 (s, 9 H, $SiMe_3$), 1.77 (d, *J* = 7.2Hz, 3 H), 5.25 (q, *J* = 7.2Hz, 1 H), 7.25 - 7.35 (m, ArH, 1 H), 7.38 - 7.50 (m, 2 H, ArH), 7.78 - 7.82 (m, 2 H, ArH), 8.35 (s, 1 H, 1-H) ppm.

1-(4-Nitrophenyl)-3-trimethylsilyloxy-2-aza-1,3-pentadiene 4b

Reaction mixture: lithium 1,1,1,3,3,3-hexamethyldisilazanate (3.08 mL, 2.22 g, 13.24 mmol, 5 eq.) in dry ether (13 mL), 4-nitrobenzaldehyde (0.40 g, 2.65 mmol, 1 eq.), trimethylsilyl chloride (0.39 mL, 0.35 g, 3.18 mmol, 1.2 eq.), triethylamine (0.40 mL, 0.29 g, 2.91 mmol, 1.1 eq.), propionyl chloride (0.30 mL, 0.32 g, 3.44 mmol, 1.3 eq.) in dry ether (3 mL). Yield of a yellow solid 0.61 (*ca.* 83%) in accordance with ^{1}H NMR. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.28 (s, 9 H, $SiMe_3$), 1.81 (d, *J* = 7.5 Hz, 3 H), 5.43 (q, *J* = 7.5Hz, 1 H, 4-H), 7.94 (d, *J* = 9.0 Hz, 2 H, ArH), 8.27 (d, *J* = 9.0 Hz, 2 H, ArH), 8.32 (s, 1 H, 1-H) ppm.

1-(4-Fluorophenyl)-3-trimethylsilyloxy-2-aza-1,3-butadiene 4c

Reaction mixture: lithium 1,1,1,3,3,3-hexamethyldisilazanate (3.75 mL, 2.70 g, 16.12 mmol, 5 eq.) in dry ether (16 mL), 4-fluorobenzaldehyde (0.35 mL, 0.40 g, 3.22

mmol, 1 eq.) in dry ether (3 mL), trimethylsilyl chloride (0.60 mL, 0.53 g, 4.84 mmol, 1.5 eq.), triethylamine (0.49 mL, 0.36 g, 3.55 mmol, 1.1 eq.), acetyl chloride (0.30 mL, 0.33 g, 4.19 mmol, 1.3 eq.) in dry ether (4 mL). Yield of a yellow oil 0.64 g (65%), contaminated with the starting aldehyde (25 %) in accordance with ^{1}H NMR data. ^{1}H NMR (300 MHz, $CDCl_3$)[a)], δ = 4.31 (s, 1 H, 4-H), 4.65 (s, 1 H, 4-H), 8.25 (s, 1 H, 1-H) ppm.

a) only some peaks have been observed in the crude oil.

1,4-Diphenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene 4d

Reaction mixture: lithium 1,1,1,3,3,3-hexamethyldisilazanate (4.38 mL, 3.15 g, 18.85 mmol, 5 eq.) in dry ether (19 mL), benzaldehyde (0.38 mL, 0.40 g, 3.77 mmol, 1 eq.) in dry ether (4 mL), trimethylsilyl chloride (0.56 mL, 0.49 g, 4.52 mmol, 1.2 eq.), triethylamine (0.57 mL, 0.42 g, 4.15 mmol, 1.1 eq.), phenylacetyl chloride (0.65 mL, 0.76 g, 4.90 mmol, 1.3 eq.) in dry ether (5 mL). Yield of a orange oil 1.19 g (*c.a.* 100%) in accordance with ^{1}H NMR data. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.24 (s, 9 H, $SiMe_3$), 5.90 (s, 1 H, 4-H), 7.18 (t, *J* = 7.5 Hz, 1 H, ArH), 7.33 (t, *J* = 7.5 Hz, 3 H, ArH), 7.42 - 7.50 (m, 2 H, ArH), 7.63 (d, *J* = 7.5 Hz, 2 H, ArH), 7.82 - 7.85 (m, 2 H, ArH), 8.51 (s, 1 H, 1-H) ppm.

1-(4-Nitrophenyl)-4-phenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene 4e

Reaction mixture: lithium 1,1,1,3,3,3-hexamethyldisilazanate (3.08 mL, 2.22 g, 13.24 mmol, 5 eq.) in dry ether (13 mL), 4-nitrobenzaldehyde (0.40 g, 2.65 mmol, 1 eq.), trimethylsilyl chloride (0.39 mL, 0.35 g, 3.18 mmol, 1.2 eq.), triethylamine (0.40 mL, 0.29 g, 2.91 mmol, 1.1 eq.), phenylacetyl chloride (0.46 mL, 0.53 g, 3.44 mmol, 1.3 eq.) in dry ether (3 mL). Yield of a red solid 0.90 g (*c.a.* 99%) in accordance with ^{1}H NMR data. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.29 (s, 9 H, $SiMe_3$), 6.17 (s, 1 H, 4-H), 7.35 (t, *J* = 7.5 Hz, 2 H, ArH), 7.63 (d, *J* = 7.5 Hz, 2 H, ArH), 8.01 (d, *J* = 8.7 Hz, 2 H, ArH), 8.31 (d, *J* = 8.7 Hz, 2 H, ArH), 8.52 (s, 1 H, 1-H) ppm.

1-(4-Fluorophenyl)-4-phenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene 4f

Reaction mixture: lithium 1,1,1,3,3,3-hexamethyldisilazanate (3.75 mL, 2.7 g, 16.12 mmol, 5 eq.) in dry ether (16 mL), 4-fluorobenzaldehyde (0.35 mL, 0.40 g, 3.22 mmol, 1 eq.) dissolved in dry ether (3 mL), trimethylsilyl chloride (0.6 mL, 0.53 g,

4.84 mmol, 1.5 eq), triethylamine (0.49 mL, 0.36 g, 3.55 mmol, 1.1 eq.), phenylacetyl chloride (0.55mL, 0.65 g, 4.19 mmol, 1.3 eq.) in dry ether (4 mL). Yield of a yellow solid 1.10 g (*ca.* 100 %), in accordance with ^{1}H NMR data. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.25 (s, 9 H, $SiMe_3$), 5.92 (s, 1 H, 4-H), 7.17 (m, 3 H, ArH), 7.35 (t, J = 7.8 Hz, 2 H, ArH), 7.65 (d, J = 7.8 Hz, 2 H, ArH), 7.87 (dd, $J_{2',3'}$ = 8.7 Hz, $J_{F,3'}$ = 5.4 Hz, 2 H), 8.48 (s, 1 H, 1-H) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 0.7 ($SiMe_3$), 105.3 (4-C), 115.9 (d, $J_{F,3'}$ = 21.8 Hz, Ar), 126.0 (Ar), 128.1 (Ar), 128.5 (Ar), 130.8 (d, $J_{F,2'}$ = 8.3 Hz, Ar), 132.2 (d, $J_{F,1'}$ = 3.2 Hz, Ar), 136.3 (Ar), 153.3 (3-C), 154.2 (1-C), 164.6 (d, $J_{F,4'}$ = 252.2 Hz, Ar) ppm.

1-(4-Methoxyphenyl)-4-phenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene 4g

Reaction mixture: lithium 1,1,1,3,3,3-hexamethyldisilazanate (2.73 mL, 1.97 g, 11.75 mmol, 4 eq.) in dry ether (15 mL), 4-methoxybenzaldehyde (0.36 mL, 0.4 g, 2.94 mmol, 1 eq.) dissolved in dry ether (4 mL), trimethylsilyl chloride (1.45 mL, 1.28 g, 11.75 mmol, 4 eq), triethylamine (0.45 mL, 0.33 g, 3.23 mmol, 1.1 eq.), phenylacetyl chloride (0.56 mL, 0.68 g, 4.41 mmol, 1.5 eq.) in dry ether (4 mL). Yield of an orange oil 0.94 g (71 %) contaminated with 28% of the starting aldehyde in accordance with ^{1}H NMR data. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.24 (s, 9 H, $SiMe_3$), 3.88 (s, 3 H), 5.78 (s, 1 H, 4-H), 6.99 (d, J = 9.0 Hz, 2 H, ArH), 7.16 (t, J = 7.5 Hz, 1 H), 7.26 - 8.38 (m, 2 H, ArH), 7.62 (d, J = 7.5 Hz, 2 H), 7.81 (d, J = 9 Hz, 2 H), 8.44 (s, 1 H, 1-H) ppm.

1-(3-Furyl)-4- phenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene 4h

Reaction mixture: hexamethyldisilazane (0.98 mL, 0.75 g, 4.63 mmol, 1 eq.), in dry THF (8 mL), n-butyllithium (1.6M in hexanes, 2.6 mL, 4.16 mmol, 0.9 eq.) in dry tetrahydrofuran (8 mL), 3-furaldehyde (0.35 mL, 0.4 g, 4.16 mmol, 0.9 eq.) dissolved in dry tetrahydrofuran (1 mL), trimethylsilyl chloride (0.51 mL, 0.45 g, 4.16 mmol, 1.9 eq), triethylamine (0.66 mL, 0.46 g, 4.68 mmol, 1.1 eq.), phenylacetyl chloride (0.71 mL, 0.84 g, 5.41 mmol, 1.3 eq.) in dry ether (6 mL). Yield of a yellow solid 1.36 g (*ca.* 100%) in accordance with ^{1}H NMR data.

^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.20 (s, 9 H, $SiMe_3$), 5.83 (s, 1 H, 4-H), 6.89 (br s, 1 H, furyl), 7.16 (t, J = 7.5 Hz, 1 H), 7.31 (t, J = 7.5 Hz, 2 H), 7.48 (s, 1 H, furyl), 7.59 (d, J = 7.2 Hz, 1 H), 7.85 (s, 1 H, furyl), 8.44 (s, 1 H, 1-H) ppm.

1-(4-Fluorophenyl)-3-trimethylsilyloxy-2-aza-1,3-pentadiene 4i

Reaction mixture: lithium 1,1,1,3,3,3-hexamethyldisilazanate (3.75 mL, 2.70 g, 16.12 mmol, 5 eq.) in dry ether (16 mL), 4-fluorobenzaldehyde (0.35 mL, 0.40 g, 3.22 mmol, 1 eq.) dissolved in dry ether (3 mL), trimethylsilyl chloride (0.48 mL, 0.42 g, 3.87 mmol, 1.2 eq), triethylamine (0.49 mL, 0.36 g, 3.55 mmol, 1.1 eq.), propionyl chloride (0.36 mL, 0.39 g, 4.19 mmol, 1.3 eq.) in dry ether (4 mL). Yield of a yellow solid 0.75 g (93 %) in accordance with ^{1}H NMR data. The solid is a mixture of isomers in a ratio 10 : 1 according to ^{1}H NMR data. Major isomer, ^{1}H NMR (300 MHz, $CDCl_3$), δ = 0.27 (s, 9 H, $SiMe_3$), 1.76 (d, *J* = 7.2 Hz, 3 H), 5.23 (q, *J* = 7.2 Hz, 1 H, 4-H), 7.10 (t, *J* = 9.0 Hz, 2 H, ArH), 7.78 (dd, $J_{2',3'}$ = 9.0 Hz, $J_{F,3'}$ = 5.7 Hz, 2 H,), 8.27 (s, 1 H, 1-H) ppm. The ^{1}H NMR of the minor isomer is coincident with the spectrum of the major isomer except for a peak at δ =1.98 (d, *J* = 7.2 Hz, 3 H) ppm.

General Procedure for the Cycloaddition Products 7 and 8

To a solution of the 2-azadiene dissolved in dry ether, methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate was added in one portion. The reaction mixture was stirred at room temperature under N_2 for 3 to 7 days, after which the reaction was complete according to TLC (DCM). In some cases a white solid precipitated out of the reaction mixture and was characterized as the cycloadduct **7** or the cycloadduct **8** or a mixture of **7** and **8**. In other cases no precipitate was formed. The solvent was removed, the residual oil dissolved in DCM and SiO_2 was added. The mixture was stirred for several days at room temperature, SiO_2 was filtered off, the solvent was removed leaving an oil that was subject to dry flash chromatography (SiO_2, diethyl ether / petroleum ether 40 - 60 ºC, polarity gradient) to give the respective cycloadducts **7** and **8**, as a white solids.

Methyl 7-(2,6-dichlorophenyl)-2α-ethoxy-2β-methyl-4-oxo-1,3-diazabicyclo[4.1.0] heptane-6β-carboxylate 7a

4-Ethoxy-2-(*tert*-butyldimethylsilyloxy)-3-aza-1,3-pentadiene **1a** (0.67 g, 2.76 mmol, 1 eq.), methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.61 g, 2.48 mmol, 0.9 eq.), dry diethyl ether (5 mL), 7 days. Yield 0.50 g (53 %).White solid, mixture of two isomers (1 : 1): methyl 7-(2,6-dichlorophenyl)-2β-ethoxy-2α-methyl-4-oxo-1,3-

diaza-bicyclo[4.1.0]heptane-6β-carboxylate **7a** and methyl 7-(2,6-dichlorophenyl)-2α-ethoxy-2β-methyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate **8a**. Treatment of the solid with DCM (20 mL), SiO_2 (1 g), 5 days, formed exclusively methyl 7-(2,6-dichlorophenyl)-2β-ethoxy-2α-methyl-4-oxo-1,3-diazabicyclo[4.1.0]heptan-6β-carboxylate **7a** 0.50 g (53 %). White solid, m.p. 173.5 - 176.0 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.18 (t, *J* = 6.9 Hz, 3 H), 1.85 (s, 2 H), 3.16 (d, *J* = 18.3 Hz, 1 H), 3.32 (s, 1 H, 7-H), 3.40 (d, *J* = 18.3 Hz, 1-H), 3.46 (s, 3 H, OMe), 3.65 (dq, *J* = 9.0 Hz, *J* = 7.2 Hz, 1 H), 3.84 (dq, *J* = 9.0 Hz, *J* = 7.2 Hz, 1 H), 6.42 (br s, 1 H, N H, disappears after D_2O exchange), 7.14 (m, 1 H), 7.28 (dd, *J* = 6.9 Hz, *J* = 0.9 Hz, 2 H) ppm.^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 15.3 (Me), 23.5 (Me), 30.3 (CH_2), 44.2 (CH), 52.4 (OMe)[a)], 58.7 (OCH_2), 97.2 (2-C), 128.4 (Ar), 128.7 (Ar), 130.1 (Ar), 135.3 (Ar), 168.9 (CO), 169.8 (CO). IR (nujol): ν = 1725, 1750, 3101, 3206 cm^{-1}. $C_{16}H_{18}Cl_2N_2O_4$ (373.2): calcd. C 51.45, H 4.82, N 7.51; found C 51.12, H 4.87, N 7.59.

a) 6-C may coincide with OMe at δ 52.4 ppm.

Methyl 7-(2,6-dichlorophenyl)-2β-ethoxy-2α-methyl-4-oxo-1,3-diaza-bicyclo[4.1.0] heptane-6β-carboxylate 8a

4-Ethoxy-2-(*tert*-butyldimethylsilyloxy)-3-aza-1,3-pentadiene **1a** (0.63 g, 2.59 mmol, 1 eq.), methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.57 g, 2.33 mmol, 0.9 eq.), dry diethyl ether (15 mL). Yield 0.22 g (25%). White solid, m.p. 176.0 - 177.5 ºC. ^{1}H NMR, (300 MHz, $CDCl_3$), δ = 1.24 (t, *J* = 7.2 Hz, 3 H), 1.78 (s, 3 H), 3.08 (d, *J* = 18.3 Hz, 1 H, 1-H), 3.34 (d, *J* = 18.3 Hz, 1 H, 1-H), 3.49 (s, 3 H, OMe), 3.58 (s, 1 H, 7-H), 3.82 (dq, *J* = 7.2 Hz, *J* = 9.0 Hz, 1 H), 3.96 (dq, *J* = 9.0 Hz, *J* = 7.2 Hz, 1 H), 5.84 (br s, 1 H, N H, disappears after D_2O exchange), 7.14 (m, 1 H), 7.28 (dd, *J* = 9.0 Hz, *J* = 6.9 Hz, 2 H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 15.4 (Me), 23.9 (Me), 30.5 (CH_2), 44.3 (CH), 52.5 (OMe)[a)], 58.9 (OCH_2), 97.2 (2-C), 128.9 (Ar), 129.5 (Ar), 130.1 (Ar), 135.4 (Ar), 168.7 (CO), 168.9 (CO). IR (nujol): ν = 1737, 3182, 3269, 3301 cm^{-1}. $C_{16}H_{18}Cl_2N_2O_4$ (373.2): calcd. C 51.44, H 4.82, N 7.51; found C 51.27, H 4.66, N 7.33.

a) 6-C may coincide with OMe at δ 52.5 ppm.

Methyl 7-(2,6-dichlorophenyl)-2α-ethoxy-2β,5α-dimethyl-4-oxo-1,3-diazabicyclo[4.1.0] heptane-6β-carboxylate 7b

Method A

2-Ethoxy-4-(*tert*-butyldimethylsilyloxy)-3-aza-2,4-hexadiene **1b** (0.65 g, 2.52 mmol, 1 eq.), methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.55 g, 2.23 mmol, 0.9 eq.), dry diethyl ether (15 mL), 5 days. Yield 0.44 g (51%). White solid, m.p. 140.5 - 146.5 ºC.[a)] ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.18 (t, *J* = 7.2 Hz, 3 H), 1.56 (d, *J* = 7.2 Hz, 3 H), 1.77 (s, 3 H), 3.19 (q, *J* = 7.2 Hz, 1 H, 5-H), 3.56 (s, 3 H, OMe), 3.59 (s, 1 H, 7-H), 3,76 (dq, *J* = 8.4 Hz, *J* = 7.2 Hz, 1 H), 3.91 (dq, *J* = 7.2 Hz, *J* = 8.4 Hz, 1 H), 5.88 (br s, 1 H, N H, disappears after D_2O exchange), 7.12 (m, 1 H), 7.30 (d, *J* = 6.9 Hz, 2 H) ppm.^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 13.0 (Me), 15.1 (Me), 27.9 (Me), 34.4 (CH), 41.1 (CH), 47.6 (6-C), 52.5 (OMe), 59.2 (OCH_2), 95.8 (2-C), 128.4 (Ar), 129.0 (Ar), 129.9 (Ar), 135.4 (Ar), 169.0 (CO), 169.6 (CO) ppm. IR (nujol): ν = 1667, 1723, 3164 cm $^{-1}$ $C_{17}H_{20}Cl_2N_2O_4$ (387.3): calcd. C 52.73, H 5.21, N 7.23; found C 52.59, H 5.19, N 7.26.

a) Traces of a second isomer evidence for which are signals at δ 1.80 ppm (s, 3 H) and 6.04 (br s, 1 H, N H).

Method B

To a solution of the 2-ethoxy-4-(*tert*-butyldimethylsilyloxy)-3-aza-2,4-hexadiene **1b** (0.68 g, 2.64 mmol, 1 eq.) dissolved in dry ether (15 mL) methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.58 g, 2.37 mmol, 0.9 eq.) was added in one portion. The reaction mixture was stirred at room temperature under N_2 for 5 days, until complete according to TLC (DCM). The reaction mixture was evaporated and the residual oil was dissolved in DCM (10 mL). Tetrabutylammonium fluoride (1.37 mL, 4.74 mmol, 1.8 eq.) was added. The mixture was stirred for 45 min. at room temperature and then washed with water (2 x 15 mL). The organic layer was dried over $MgSO_4$ and the solvent removed giving an oil that was kept in the freezer for 48 h. A white solid was formed and washed with diethyl ether (0.38 g, 42%), that proved to be the title compound as shown by a comparison (NMR, TLC) with the specimen obtained previously.

Methyl 7-(2,6-dichlorophenyl)-2α-ethoxy-5α-phenyl-2β-methyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 7c and methyl 7-(2,6-dichlorophenyl)-2β-ethoxy-5α-phenyl-2α-methyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 8c

4-Ethoxy-1-phenyl-2-(*tert*-butyldimethylsilyloxy)-3-aza-1,3-pentadiene **1c**, (1.94 g, 6.05 mmol, 1 eq.), methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (1.18 g, 4.84 mmol, 0.8 eq.), dry diethyl ether (15 mL), 6 days. An oil was formed which is a mixture of two diastereomers 1 (**7c**) : 1 (**8c**) ratio. Flash chromatography (SiO_2, diethyl ether / petroleum ether 40 - 60 ºC, polarity gradient) gave two fractions: i) mixture of a major and a minor isomers 2 (**7c**) : 1 (**8c**), 0.72 g (33 %), further separated by recrystallization DCM / petroleum ether giving a major isomer 0.45 g (21 %) and a minor isomer 0.24 g (11 %); ii) **7c**, major isomer 0.55 g (25%). Total yield of isomer **4c** 1.0 g (46 %), white solid, m.p. 181.2 – 183.2 ºC. ^{1}H NMR (300 MHz; $CDCl_3$), δ = 1.13 (t, *J* = 7.2 Hz, 3 H), 1.91 (s, 3 H), 3.40 (s, 3 H), 3.75 (dq, *J* = 9.0 Hz, *J* = 7.2 Hz, 1 H), 3.94 (dq, *J* = 9.0 Hz, *J* = 7.2 Hz, 1 H), 4.13 (s, 1 H, H-7), 4.40 (s, 1 H, H-5), 6.03 (br s, 1 H, N H, disappears after D_2O exchange), 7.06 - 7.13 (m, 1 H), 7.23 - 7.28 (m, 2 H), 7.28 - 7.37 (m, 3 H), 7.41 - 7.46 (m, 2 H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 15.3 (Me), 27.5 (Me), 40.7 (CH), 46.9 (CH), 49.7 (6-C), 52.4 (OMe), 59.2 (OCH_2), 96.0 (2-C), 127.9 (Ar), 128.2 (Ar), 128.5 (Ar), 129.4 (Ar), 129.5 (Ar), 130.3 (Ar), 133.3 (Ar), 135.7 (Ar), 167.4 (CO), 168.7 (CO) ppm. IR (nujol): ν = 1750, 3062, 3167 cm^{-1}. $C_{22}H_{22}Cl_2N_2O_4$ (449.3): calcd. C 58.76, H 4.89, N 6.23; found C 58.84, H 4.96, N 6.24. Minor isomer **8c** 0.24 g (11 %), white solid, m.p. 134.5 - 137.5 ºC. ^{1}H NMR, (400 MHz, $CDCl_3$), δ = 1.29 (t, *J* = 7.2 Hz, 3 H), 1.80 (s, 3 H), 3.39 (s, 3 H), 3.73 (dq, *J* = 9.0 Hz, *J* = 7.2 Hz, 1 H), 3.82 (s, 1 H, 7-H), 4.03 (dq, *J* = 7.2 Hz, *J* = 9.0 Hz, 1 H), 4.75 (s, 1 H, 5-H), 6.29 (br s, N H, disappears after D_2O exchange, 1 H), 7.07 - 7.11 (m, 1 H), 7.29 - 7.32 (m, 3 H), 7.46 (d, *J* = 6.9 Hz, 2 H) ppm. ^{13}C NMR (75,7 MHz, $CDCl_3$), δ =15.3 (Me), 23.8 (Me), 42.9 (CH), 46.8 (CH), 49.3 (6-C), 52.0 (OMe), 59.1 (OCH_2), 97.7 (2-C), 127.7 (Ar), 127.8 (Ar), 128.6 (Ar), 129.0 (Ar), 130.1 (Ar), 131.2 (Ar), 133.9 (Ar), 135.5 (Ar), 168.4 (CO), 169.5 (CO) ppm. IR (nujol): ν = 1742, 1757, 3094, 3203 cm^{-1}. $C_{22}H_{22}Cl_2N_2O_4$ (449.3): calcd. C 58.76, H 4.89, N 6.23; found C 58.69, H 5.22, N 6.14.

Methyl 7-(2,6-dichlorophenyl)-2β,5α-diphenyl-2α-methoxy-4-oxo-1,3-diazabicyclo [4.1.0]heptane-6β-carboxylate 7d and methyl 7-(2,6-dichlorophenyl)-2α,5β-diphenyl-2β-methoxy-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 8d

1-Methoxy-1,4-diphenyl-3-(*tert*-butyldimethylsilyloxy)-2-aza-1,3-butadiene **1d** (1.75 g, 4.76 mmol, 1 eq.), methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (1.04 g, 4.28 mmol, 0.9 eq.), dry diethyl ether (15 mL), 6 days. Total yield 0.81 g (38%). White solid, mixture of the two isomers 3 (**7d**) : 1 (**8d**). The major isomer **7d**, white solid, m.p. 175.5 - 177.5 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 3.22 (s, 3 H, OMe), 3.35 (s, 3 H, OMe), 3.80 (s, 1 H, 7-H), 4.41 (s, 1 H, 5-H), 6.59 (br s, 1 H, N H, disappears after D_2O exchange), 7.10 - 7.18 (m, 1 H), 7.24 - 7.38 (m, 7 H), 7.48 - 7.56 (m, 3 H), 7.88 - 7.93 (m, 2 H) ppm. ^{13}C NMR (75,7 MHz, $CDCl_3$), δ = 39.7 (CH), 47.9 (CH), 50.1 (6-C), 52.0 (OMe), 52.2 (OMe), 98.2 (2-C), 127.6 (Ar), 128.0 (Ar), 128.2 (Ar), 128.5 (Ar), 128.6 (Ar), 129.57 (Ar), 129.6 (Ar), 130.4 (Ar), 132.6 135.8 (Ar), 138.8 (Ar), 167.0 (CO), 168.0 (CO) ppm. IR (nujol): ν = 1673, 1735, 3064, 3187, 3278 cm^{-1}. HR MS (EI): calcd. for $C_{26}H_{22}Cl_2N_2O_4$ 496.0956 [$M^{+\cdot}$], found 496.0960. The minor isomer **8d**, white solid, m.p. 189.1 – 190.1 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 3.13 (s, 3 H, OMe), 3.15 (s, 3 H, OMe), 3.66 (s, 1 H, 7-H), 5.09 (s, 1 H, 5-H), 6.37 (br s, NH, disappears after D_2O exchange, 1 H), 7.03 (m, 1 H), 7.13 (m, 2 H), 7.24 - 7.38 (m, 3 H), 7.44 - 7.51 (m, 3 H), 7.68 - 7.74 (m, 2 H), 7.78 - 7.84 (m, 2 H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 43.6 (CH), 47.2 (CH), 50.7 (Me), 51.2 (6-C), 52.0 (OMe), 99.2 (2-C), 127.3 (Ar), 127.4 (Ar), 128.3 (Ar), 128.5 (Ar), 128.8 (Ar), 128.91(Ar), 128.94 (Ar), 130.0 (Ar), 135.5 (Ar), 135.8 (Ar), 136.8 (Ar), 167.0 (CO), 169.2 (CO) ppm. IR (nujol): ν = 1674, 1750, 3069, 3177 cm^{-1}. HR MS (EI): *m/z* (%) = (43) [M^{+} - CH_3O]; calcd. for $C_{25}H_{19}Cl_2N_2O_4$ 465.0772 [$M^{+\cdot}$], found 465.0767.

Methyl 7-(2,6-dichlorophenyl)-2β-phenyl-5α-methyl-2α-methoxy-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 7e and methyl 7-(2,6-dichlorophenyl)-2α-phenyl-5α-methyl-2β-methoxy-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 10

1-Methoxy-1-phenyl-3-(*tert*-butyldimethylsilyloxy)-2-aza-1,3-pentadiene 4 (**1e**) : 1 (**2e**) ratio (0.59 g, 1.93 mmol, 1 eq.), methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-

carboxylate **6** (0.42 g, 1.74 mmol, 0.9 eq.), dry diethyl ether (15 mL), 7 days. Total yield 0.39 g (51%) as a mixture of the two diastereomers 1.2 (**7e**) : 1 (**10**). Flash chromatography gave the major product **7e** 0.23 g (30%), and a mixture of **7e** and **10** (21 %) also as a solid. Compound **7e** is a white solid, m.p. 212.0 - 214.0 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.48 (d, *J* = 6.9 Hz, 3 H), 2.59 (q, *J* = 6.9 Hz, 1 H, 5-H), 3.22 (s, 3 H, OMe), 3.56 (s, 3 H, OMe), 3.77 (s, 1 H, 7-H), 6.62 (br s, 1 H , N H, disappears after D_2O exchange), 7.18 (t, *J* = 7.8 Hz, 1 H), 7.32 (d, *J* = 7.8 Hz, 2 H), 7.38 - 7.44 (m, 3 H), 7.72 - 7.75 (m, 2 H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 12.5 (Me), 35.5 (CH), 40.7 (CH), 47.8 (6-C), 52.3 (OMe), 52.8 (OMe), 98.1 (2-C), 127.3 (Ar), 128.4 (Ar), 128.6 (Ar), 129.0 (Ar), 129.6 (Ar), 130.2 (Ar), 135.5 (Ar), 139.1 (Ar), 168.8 (CO), 169.5 (CO) ppm. IR (nujol): ν = 1673, 1731, 1746, 3067, 3176, 3276 cm^{-1}. $C_{21}H_{20}Cl_2N_2O_4$ (435.3): calcd. C 57.89, H 4.59, N 6.43; found C 57.70, H 4.70, N 6.50. The sample containing the mixture of two isomers was subjected again to flash chromatography (SiO_2, diethyl ether / petroleum ether, polarity gradient) giving a small amount of the minor isomer **10** as a white solid, m.p. 187.0 - 188.4 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.65 (d, *J* = 7.2 Hz, 3 H), 3.32 (s, 3 H, OMe), 3.36 (s, 3 H, OMe), 3.48 (s, 1 H, 7-H), 3.82 (q, *J* = 7.2 Hz, 1 H, 5-H), 6.37 (br s, 1 H , N H, disappears after D_2O exchange), 7.00 - 7.06 (m, 1 H), 7.13 (d, *J* = 7.5 Hz, 2 H), 7.42 - 7.50 (m, 3H), 7.60 - 7.68 (m, 2 H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 16.1 (Me), 36.1 (CH), 44.1 (CH), 51.0 (OMe), 51.3 (6-C), 52.0 (OMe), 99.0 (2-C), 127.0 (Ar), 128.5 (Ar), 128.7 (Ar), 128.8 (Ar), 129.9 (Ar), 135.6 (Ar), 136.6 (Ar), 167.5 (CO), 172.7 (CO) ppm. IR (nujol): ν = 1680, 1751, 3063, 3179 cm^{-1}. $C_{21}H_{20}Cl_2N_2O_4$ (435.3) : calcd. C 57.89, H 4.59, N 6.43; found C 57.63, H 4.55, N 6.51.

General Procedure for the Cycloaddition Products 11

To the crude 2-azadiene in ether was added the methyl 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.9 eq.) at room temperature. The progress of the reaction was followed by TLC until disappearance of the starting azirine. In most cases products precipitated pure (**11b**, **11c**, **11d**, **11e**, **11f**, **11g**) and were washed with cold ether. In cases **11a**, **11h** and **11i** the reaction mixture gave an oil or a mixture of an oil and a solid that were combined and subjected to dry flash chromatography.

Methyl 7-(2,6-dichlorophenyl)-2α-phenyl-5α-methyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 11a

1-Phenyl-3-trimethylsilyloxy-2-aza-1,3-pentadiene **4a** (0.37 g, 1.57 mmol, 1 eq.) in ether (10 mL) and 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.35 g, 1.41 mmol, 0.9 eq.); reaction was complete in 6 days. Yield 0.13 g (28 %) after flash chromatography (SiO_2, diethyl ether / petroleum ether, gradient polarity). White solid, m.p. 166.6 - 169.7 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.70 (d, *J* = 7.2 Hz, 3 H), 3.40 (q, *J* = 6.9 Hz, 1 H, 5-H), 3.51 (s, 3 H, OMe), 3.74 (s, 1 H, 7-H), 5.86 (s, 1 H, 2-H), 5.96 (br s, 1 H, NH), 7.02 - 7.20 (m, 3 H, ArH), 7.38 - 7.52 (m, 5 H, ArH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$), 13.0 (Me), 35.8 (CH), 37.4 (CH), 48.3 (6-C), 52.4 (OMe), 70.1 (CH), 127.4 (Ar), 128.3 (Ar), 128.5 (Ar), 128.8 (Ar), 129.6 (Ar), 130.4 (Ar), 135.2 (Ar), 136.7 (Ar), 169.1 (CO), 171.5 (CO). IR (nujol), ν = 1724, 1738, 3083, 3216 cm^{-1}. $C_{20}H_{18}Cl_2N_2O_3$ (405.3): calcd. C 59.26, H 4.49, N 6.91; found C 59.12, H 4.64, N 6.93.

Methyl 7-(2,6-dichlorophenyl)-2α-[4-(nitrophenyl)]-5α-methyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 11b

1-(4-Nitrophenyl)-3-trimethylsilyloxy-2-aza-1,3-pentadiene **4b** (0.17 g, 0.61 mmol, 1 eq.) in ether (10 mL) and 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.14 g, 0.55 mmol, 0.9 eq.). The reaction was complete in 1 day. Yield 0.39 g (71 %), white solid m.p. 168.6 - 171.1 ºC . ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.58 (d, *J* = 6.9 Hz, 3 H), 3.42 (q, *J* = 6.9 Hz, 1 H, 5-H), 3.53 (s, 3 H, OMe), 3.76 (s, 1 H, 7-H), 5.98 (s, 2 H, 2-H + N H), 7.09 (dd, *J* = 6.9 Hz, *J* = 9 Hz, 1 H, ArH), 7.17 (d, *J* = 6.9 Hz, 2 H, ArH), 7.70 (d, *J* = 9 Hz, 2 H, ArH), 8.31 (d, *J* = 9 Hz, 2 H, ArH,) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 13.0 (Me), 35.9 (CH), 37.4 (CH), 48.4 (6-C), 52.6 (OMe), 69.3 (CH), 124.0 (Ar), 128.7 (Ar), 128.8 (Ar), 129.8 (Ar), 135.0 (Ar), 143.1 (Ar), 148.5 (Ar), 168.7 (CO), 171.8 (CO) ppm. IR (nujol), ν = 1674, 1749, 3223 cm^{-1}. $C_{20}H_{17}Cl_2N_3O_5$ (450.3): calcd. C 53.34, H 3.80, N 9.33; found C 53.36, H 4.13, N 9.19.

Methyl 7-(2,6-dichlorophenyl)-2α-4-fluorophenyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 11c

1-(4-Fluorophenyl)-3-trimethylsilyloxy-2-aza-1,3-butadiene **4c** (0.50 g, 2.09 mmol, 1 eq.) in ether (15 mL) and 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.41 g, 1.67 mmol, 0.8 eq.). The reaction was complete in 6 days. Yield 0.11 g (16 %), white solid after washings with ether, m.p. 189.6 - 191.2 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 3.16 (d, *J* = 18.3 Hz, 1 H , 5-H), 3.48 (s, 3 H, OMe), 3.57 (d, *J* =18.3 Hz, 1 H, 5-H), 3.75 (s, 1 H, 7-H), 5.87 (br s, 1 H, N H), 5.89 (s, 1 H, 2-H), 7.04 - 7.19 (m, 5 H, ArH), 7.48 – 7.54 (m, 2H, ArH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 30.8 (CH_2), 39.4 (CH), 45.1 (6-C), 52.7 (OMe), 70.3 (CH), 115.9 (d, $J_{F, 3'}$ = 22.0 Hz, Ar), 128.4 (Ar), 128.8 (Ar), 129.5 (d, $J_{F, 2'}$ = 8.4 Hz, Ar), 129.7 (Ar), 132.5 (d, $J_{F, 1'}$ = 3.2 Hz, Ar), 135.4 (Ar), 163.4 (d, $J_{F, 4'}$ = 249.3 Hz, Ar), 168.8 (CO), 168.9 (CO) ppm. IR (nujol), ν = 1686, 1748, 3098, 3257 cm^{-1}. $C_{19}H_{15}Cl_2F N_2O_3$ (409.3): calcd. C 55.76, H 3.70, N 6.85; found C 55.73, H 4.12, N 6.77.

Methyl 7-(2,6-dichlorophenyl)-2α,5α-diphenyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 11d

1,4-Diphenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene **4d** (0.62 g, 2.11 mmol, 1 eq.) in ether (15 mL) and 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.41 g, 1.69 mmol, 0.8 eq.). The reaction was complete in 4 days. Yield 0.59 g (75 %), white solid, m.p. 210.2 - 213.6 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 3.38 (s, 3 H, OMe), 4.24 (s, 1 H, 7-H), 4.63 (s, 1 H, 5-H), 6.04 (s, 1 H, 2-H), 6.06 (br s, 1 H, N H), 7.05 (dd, *J* = 6.9 Hz, *J* = 9 Hz, 1 H, ArH), 7.15 (d, *J* = 6.9 Hz, 2 H, ArH), 7.32 - 7.38 (m, 3H, ArH) 7.42 - 7.44 (m, 3 H, ArH), 7.46 - 7.60 (m, 4 H, ArH) ppm.^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 37.4 (CH), 48.2 (CH), 49.2 (6-C), 52.3 (OMe), 70.2 (CH), 127.0 (Ar), 127.90 (Ar), 127.94 (Ar), 128.5 (Ar), 128.9 (Ar), 129.0 (Ar), 129.6 (Ar), 129.8 (Ar), 131.1 (Ar), 133.1 (Ar), 135.7 (Ar), 136.6 (Ar), 168.4 (CO), 169.4 (CO) ppm. IR (nujol), ν = 1680, 1735, 3147, 3235 cm^{-1}. $C_{25}H_{20}Cl_2N_2O_3$ (467.4): calcd. C 64.24, H 4.74, N 5.99; found C 64.22, H 4.62, N 6.07.

Methyl 7-(2,6-dichlorophenyl)-2α-4-(nitrophenyl)-5α-phenyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 11e

1-(4-Nitrophenyl)-4-phenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene **4e** (0.20 g, 0.59 mmol, 1 eq.) in ether (10 mL) and 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.13 g, 0.53 mmol, 0.9 eq.). The reaction was complete in 2 days. Yield 0.17 g

(61%). White solid, m.p. 195.1 - 196.8 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 3.86 (s, 3 H, OMe), 4.26 (s, 1 H, 7-H), 4.63 (s, 1 H, 5-H), 6.15 (s, 1 H, 2-H), 6.25 (br s, 1 H, N H), 7.04 - 7.10 (m, 1 H, ArH), 7.14 - 7.20 (m, 2 H, ArH), 7.32 - 7.42 (m, 3 H, ArH) 7.50 - 7.58 (m, 2 H, ArH), 7.74 (d, *J* = 9 Hz, 2 H, ArH), 8.30 (d, *J* = 9 Hz, 2 H, ArH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 37.8 (CH), 48.8 (CH), 49.6 (6-C), 52.8 (OMe), 69.9 (CH), 124.5 (Ar), 128.0 (Ar), 128.4 (Ar), 128.7 (Ar), 129.2 (Ar), 129.4 (Ar), 129.6 (Ar), 131.3 (Ar), 133.1 (Ar), 136.0 (Ar), 143.4 (Ar),148.8 (Ar), 168.5 (CO), 170.5 (CO) ppm. IR (nujol), ν = 1681, 1748, 3092, 3194 cm^{-1}. $C_{25}H_{19}Cl_2N_3O_5$ (512.4): calcd. C 58.60, H 3.75, N 8.20; found C 58.61, H 4.01, N 8.24.

Methyl 7-(2,6-dichlorophenyl)-2α-4-fluorophenyl-5α-phenyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 11f

1-(4-Fluorophenyl)-4-phenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene **4f** (0.59 g, 1.97 mmol, 1 eq.) in ether (15 mL) and 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.43 g, 1.78 mmol, 0.9 eq.). The reaction was complete in 2 days. Yield 0.60 g (70 %). White solid, m.p. 152.4 - 153.3 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 3.38 (s, 3 H, OMe), 4.22 (s, 1 H, 7-H), 4.61 (s, 1 H, 5-H), 6.03 (s, 1 H, 2-H), 6.09 (br s, 1 H, NH), 7.02-7.19 (m, 5 H, ArH), 7.32 - 7.40 (m, 3 H, ArH), 7.44 - 7.48 (m, 4 H, ArH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 37.8 (CH), 48.6 (CH), 49.6 (6-C), 52.7 (OMe), 116.3 (d, $J_{F, 3'}$ = 22.0 Hz), 128.28 (Ar), 128.30 (Ar), 129.0 (Ar), 129.4 (Ar), 129.5 (d, $J_{F, 2'}$ = 6.8 Hz), 130.2 (Ar), 131.5 (Ar), 132.0 (d, $J_{F, 1'}$ = 3.0 Hz), 133.5 (Ar), 136.1 (Ar), 163.5 (d, $J_{F, 4'}$ = 249.0 Hz), 168.8 (CO), 170.3 (CO). IR (nujol), ν = 1688, 1743, 3187 cm^{-1}. $C_{25}H_{19}FCl_2N_2O_3$ (485.4): calcd. C 61.86, H 3.95, N 5.77; found C 61.53, H 4.67, N 5.54.

Methyl 7-(2,6-dichlorophenyl)-2α-4-(methoxyphenyl)-5α-phenyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 11g

1-(4-Methoxyphenyl)-4-phenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene **4g** (0.68 g, 2.07 mmol, 1 eq.) in ether (10 mL) and 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.40 g, 1.66 mmol, 0.8 eq.). The reaction was complete in 2.5 days. Yield 0.49 g (60%). White solid, m.p. 208.1 - 210.3 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 3.37 (s, 3 H, OMe), 3.84 (s, 3 H, OMe), 4.22 (s, 1 H, 7-H), 4.61 (s, 1 H, 5-H), 5.99 (s, 1 H, 2-H), 6.02 (br s, 1 H, N H), 6.94 (d, *J* = 8.7 Hz, 2 H, ArH), 7.04 (dd, *J* =

9 Hz, *J* = 6.9 Hz, 1 H, ArH), 7.14 (d, *J* = 6.9 Hz, 2 H, ArH), 7.30-7.37 (m, 3 H, ArH), 7.43 (d, *J* = 8.7 Hz, 2 H, ArH), 8.30 (dd, *J* = 8.1 Hz, *J* = 6.3 Hz, 2 H, ArH,) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 37.4 (CH), 48.1 (CH), 49.2 (6-C), 52.3 (OMe), 55.3 (OMe), 69.8 (CH), 114.2 (Ar), 127.85 (Ar), 127.88 (Ar), 128.3 (Ar), 128.5 (Ar), 128.86 (Ar), 128.88 (Ar), 129.9 (Ar), 131.1 (Ar), 133.2 (Ar), 135.7 (Ar), 160.3 (Ar), 168.5 (CO), 169.5 (CO). IR (nujol), ν = 1675, 1727, 3168 cm^{-1}. $C_{26}H_{22}Cl_2N_2O_4$ (497.4): calcd. C 62.78, H 4.47, N 5.63; found C 62.54, H 4.77, N 5.47.

Methyl 7-(2,6-dichlorophenyl)-2α-3-furyl-5α-phenyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 11h

1-(3-Furyl)-4-phenyl-3-trimethylsilyloxy-2-aza-1,3-butadiene **4h** (0.65 g, 2.27 mmol, 1 eq.) in ether (15 mL) and 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.44 g, 0.82 mmol, 0.8 eq.). The reaction was complete in 7 days. Yield 0.23 g (28 %) after flash chromatography (SiO_2, diethyl ether / petroleum ether, polarity gradient). White solid, m.p. 173.5 - 173.9 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 3.36 (s, 3H, OMe), 4.16 (s, 1H, 7-H), 4.50 (s, 1H, 5-H), 6.01 (br s, 1 H, N H), 6.52 (s, 1 H, 2-H), 7.06 (dd, *J* = 6,9 Hz, *J* = 9.0 Hz, 1 H, ArH), 7.21 (d, *J* = 6.9 Hz, 2 H, ArH), 7.31 - 7.39 (m, 4 H, ArH) 7.43 - 7.44 (m, 1 H, ArH), 7.47 - 7.50 (m, 2 H, ArH), 7.63 (s, 1 H, ArH) ppm. ^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 37.6 (CH), 48.8 (CH), 49.9 (6-C), 52.7 (OMe), 64.5 (CH), 109.3 (furyl), 123.0 (Ar), 128.5 (Ar), 129.0 (Ar), 129.6 (Ar), 130.0 (Ar), 131.2 (Ar), 133.3 (Ar), 136.2 (Ar), 141.1 (Ar), 144.3 (furyl), 168.7 (CO), 169.8 (CO) ppm. IR (nujol), ν = 1736, 1753, 3213 cm^{-1}. $C_{23}H_{18}Cl_2N_2O_4$ (457.3): calcd. C 60.40, H 3.98, N 6.13; found C 60.42, H 4.22, N 6.06.

Methyl 7-(2,6-dichlorophenyl)-2α-4-(fluorophenyl)-5α-methyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate 11i

1-(4-Fluorophenyl)-3-trimethylsilyloxy-2-aza-1,3-pentadiene **4i** (0.29 g, 1.16 mmol, 1 eq.) in ether (10 mL) and 2-(2,6-dichlorophenyl)-2*H*-azirine-3-carboxylate **6** (0.26 g, 1.05 mmol, 0.9 eq.). The reaction was complete in 1 day. Yield 0.15 g (96 %), brownish oil (very impure). After dry flash chromatography (diethyl ether/ petroleum ether, polarity gradient) gave a white solid (33 %), m.p. 213.4 - 215.0 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.70 (d, *J* = 6.9 Hz, 3 H), 3.39 (q, *J* = 6.9 Hz, 1 H, 5-H), 3.51 (s, 3 H), 3.72 (s, 1 H, 7-H), 5.86 (s, 2 H, 2-H + N H), 7.04 - 7.19 (m, 5 H, ArH), 7.44 -

7.50 (m, 2 H, ArH) ppm.^{13}C NMR (75.5 MHz, $CDCl_3$), δ = 13.5 (Me), 36.3 (CH), 37.9 (CH), 48.8 (6-C), 52.9 (OMe), 69.9 (CH), 116.3 (d, $J_{F,3'}$ = 22.0 Hz), 128.9 (Ar), 129.1 (Ar), 129.8 (d, $J_{F,2'}$ = 8.3 Hz), 130.7 (Ar), 133.2 (d, $J_{F,1'}$ = 3.0 Hz), 135.7 (Ar), 163.7 (d, $J_{F,4'}$ = 249.0 Hz), 169.4 (CO), 171.9 (CO) ppm. IR (nujol), ν = 1674, 1751, 3088, 3193 cm^{-1}. $C_{20}H_{17}Cl_2FN_2O_3$ (423.3): calcd. C 56.74, H 4.06, N 6.62; found C 56.60, H 4.16, N 6.63.

General Procedure for the Hydrolysis Products 12, 13 and 15

To a solution of the pyrimidone or of the mixture of diastereomeric pyrimidones in THF was added dropwise HCl diluted in THF, in an ice/water bath. After the addition was complete the mixture was stirred at room temperature for 1 h. THF was partially removed to a 1/3 of the original volume and aq. $NaHCO_3$ (20 mL) was added. The mixture was vigorously stirred for 15 min. The organic phase was separated and the aq. phase was washed with DCM (3 x 25 mL). The organic phases were combined, washed with water (25 mL), and dried over $MgSO_4$. The solvent was removed giving a pale yellow oil that crystallized in the fridge. The solid was recrystallized from DCM/ petroleum ether 40 - 60 ºC giving the product as a white solid. In one case (**e**) the hydrolysis compounds **12** and **13** were shown to be a mixture of two isomers that were separated by flash chromatography (SiO_2, diethyl ether / petroleum ether, gradient polarity).

Methyl 2-[(2-acetylamino)-2-oxoethyl]-3-(2,6-dichlorophenyl)aziridine-2-carboxylate 12a

Methyl 7-(2,6-dichlorophenyl)-2β-ethoxy-2α-methyl-4-oxo-1,3-diaza-bicyclo[4.1.0] heptan-6β-carboxylate **8a** (0.21 g, 0.56 mmol), THF (10 mL) and conc. HCl (46 μl) in THF (5 mL). Yield 0.14 g (74 %). White solid, m.p. 164.3 -165.1 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 2.35 (s, 3H, Me), 2.67 (d, *J* = 17.1 Hz, 1 H), 2.87 (br d, *J* = 8.4 Hz,1 H, N H aziridine, disappears after D_2O exchange), 3.21 (d, *J* = 8.4 Hz, 1 H, 3-H), 3.57 (s, 3 H, OMe), 3.83 (d, *J* = 17.1 Hz, 1 H), 7.18 (t, *J* = 7.5 Hz, 1 H), 7.27 (d, *J* = 7.5 Hz, 2 H), 8.82 (br s, 1 H, N H) ppm. ^{13}C NMR, (75.7 MHz, $CDCl_3$) δ = 25.0 (Me), 41.0 (CH_2), 42.6 (2-C), 45.5 (CH), 53.0 (OMe), 127.8 (Ar) 128.9 (Ar), 129.5 (Ar), 130.9 (Ar), 135.7 (Ar), 170.5 (CO), 171.0 (CO), 171.3 (CO) ppm. IR (nujol), ν = 1725, 1745, 3205, 3255 cm^{-1}. $C_{14}H_{14}Cl_2N_2O_4$ (345.0) : calcd. C 48.71, H 4.06, N

8.12; found C 48.26, H 4.16, N 8.07. HR MS (EI): *m/z* (%) = (0.1) [M^+], calcd. for $C_{14}H_{14}O_4N_2Cl_2$ 344.0331, found 344.0325.

Methyl 2-[(2-acetylamino)-2-oxoethyl]-1-methyl-3-(2,6-dichlorophenyl)aziridine-2-carboxylate 12b

Methyl 7-(2,6-dichlorophenyl)-2α-ethoxy-2β,5α-dimethyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate **7b** (0.60 g, 2.46 mmol), THF (15 mL) and conc. HCl (200 μl) in THF (10 mL). Yield 0.37 g (42 %). White solid, m.p. 116.3 - 117.4 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.30 (d, *J* = 7.2 Hz, 3 H), 2.43 (s, 3 H, Me), 2.85 (br d, *J* = 9.0 Hz, 1 H, N H aziridine, disappears after D_2O exchange), 3.37 (d, *J* = 9.0 Hz, 1 H, 3-H), 3.56 (s, 3 H, OMe), 3.75 (q, *J* = 7.2 Hz, 1 H), 7.18 (t, *J* = 8.4 Hz, 1 H), 7.28 (d, *J* = 8.4 Hz, 2 H), 8.71 (br s, 1 H, N H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 12.9 (Me), 25.5 (Me), 41.2 (CH), 41.8 (CH), 45.8 (2-C), 53.2 (OMe), 127.9 (Ar) 129.1 (Ar), 129.4 (Ar), 130.9 (Ar), 135.5 (Ar), 170.4 (CO), 172.1 (CO), 173.1 (CO) ppm. IR (nujol), ν = 1724, 1741, 3067, 3157, 3211 cm^{-1}. $C_{15}H_{16}O_4N_2Cl_2$ (359.2): calcd. C 50.15, H 4.45, N 7.80; found C 50.24, H 4.68, N 7.80.

Methyl 2-[(2-acetylamino)-2-oxoethyl]-1-phenyl-3-(2,6-dichlorophenyl)aziridine-2-carboxylate 12c

Methyl 7-(2,6-dichlorophenyl)-2α-ethoxy-5α-phenyl-2β-methyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate **7c** and methyl 7-(2,6-dichlorophenyl)-2β-ethoxy-5α-phenyl-2α-methyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate **8c** (0.21 g, 0.46 mmol), THF (10 mL) and conc. HCl (38 μl) in THF (5 mL). Yield 0.17 g (87 %). White solid, m.p. 191.1 - 191.6 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 2.40 (d, *J* = 9.9 Hz, 1 H, 3-H), 2.43 (s, 3 H, Me), 3.08 (br d, *J* = 9.9 Hz, 1 H, N H aziridine, disappears after D_2O exchange), 3.56 (s, 3 H, OMe), 5.02 (s, 1 H, 1-H), 7.12 (t, *J* = 7.5 Hz, 1 H), 7.28 (d, *J* = 7.5 Hz, 2 H), 7.36 - 7.45 (m, 5 H), 7.88 (br s, 1 H, N H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 25.3(Me), 41.5 (CH), 45.5 (2-C), 53.0 (CH), 53.3 (OMe), 127.7 (Ar) 128.9 (Ar), 129.0 (Ar), 129.9 (Ar), 130.5 (Ar), 131.1 (Ar), 131.7 (Ar), 135.5 (Ar), 170.7 (CO), 171.0 (CO), 171.9 (CO) ppm. IR (nujol), ν

= 1735, 3168, 3242 cm^{-1}. $C_{20}H_{18}Cl_2N_2O_4$. 1/2 H_2O (430.3): calcd. C 55.82, H 4.23, N 6.51; found C 55.87, H 4.43, N 6.47.

Methyl 2-[(2-benzoylamino)-2-oxoethyl]-1-phenyl-3-(2,6-dichlorophenyl)aziridine-2-carboxylate 12d

Methyl 7-(2,6-dichlorophenyl)-2β,5α-diphenyl-2α-methoxy-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate **7d** (0.22 g, 0.44 mmol), THF (10 mL) and conc. HCl (37 μl) in THF (5 mL). Yield 0.15 g (68%). White solid, m.p. 180.2 - 181.2 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 2.51 (d, *J* = 9.9 Hz, 1 H, 3-H), 3.02 (br d, *J* = 9.9 Hz,1 H, N H aziridine, disappears after D_2O exchange), 3.55 (s, 3 H, OMe), 5.93 (s, 1 H, 1-H), 7.09 - 7.15 (m, 1 H), 7.22 - 7.62 (m, 10 H), 7.75 (d, *J* = 7.2 Hz, 2 H), 8.66 (br s, 1 H, N H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 40.8 (CH), 46.0 (2-C), 52.5 (CH), 53.0 (OMe), 127.7 (Ar) 128.3 (Ar), 128.9 (Ar), 129.0 (Ar), 131.1 (Ar), 131.5 (Ar), 131.7 (Ar), 131.8 (Ar), 132.6 (Ar), 133.2 (Ar), 135.7 (Ar), 164.6 (CO), 171.1 (CO), 173.6 (CO) ppm. IR (nujol), ν = 1714, 1731, 3168, 3263 cm^{-1}. HR MS (FAB): calcd. 483.0878 [M+1], found 483.0876.

Methyl 2-[(2-benzoylamino)-2-oxoethyl]-1-methyl-3-(2,6-dichlorophenyl)aziridine-2-carboxylate 12e and 13

Methyl 7-(2,6-dichlorophenyl)-2β-phenyl-5α-methyl-2α-methoxy-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate **7e** and methyl 7-(2,6-dichlorophenyl)-2α-phenyl-5α-methyl-2β-methoxy-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate **10**, mixture 1.2 (**7e**) : 1 (**10**), (0.37 g, 0.85 mmol), THF (10 mL), conc. HCl (71 μl) in THF (5 mL). Total yield 0.27 g (75%) : two isomers 1.2 (**12e**) : 1 (**13**). The isomers were partially isolated after flash chromatography (SiO_2, diethyl ether / petroleum ether 40 - 60 ºC, polarity gradient). Compound **12e** (0.1 g, 29 %), white solid, m.p. 189.3 ºC - 190.0 ºC. ^{1}H NMR, (300 MHz, $CDCl_3$), δ = 1.41 (d, *J* = 7.2 Hz, 3 H), 2.38 (d, *J* = 9.3 Hz, 1 H), 3.39 (d, *J* = 9.3 Hz, 1 H, 3-H), 3.58 (s, 3 H, OMe), 4.44 (q, *J* = 7.2 Hz, 1 H, 1-H), 7.18 (t, *J* = 8.1 Hz, 1 H), 7.30 (br d, *J* = 7.5 Hz, 2 H), 7.54 (m, 2 H), 7.63 (m, 1 H), 7.92 (dd, *J* = 8.4 Hz, *J* = 1.2 Hz, 2 H), 9.25 (br s, 1 H, N H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 12.8 (Me), 41.0 (CH), 46.1 (2-C), 51.1 (OMe), 127.7 (Ar) 128.9 (Ar), 129.3 (Ar), 131.3 (Ar), 132.8 (Ar), 133.2 (Ar), 135.6 (Ar), 165.1 (CO), 171.0 (CO), 175.3 (CO) ppm. IR (nujol), ν = 1712, 1735, 3071, 3279 cm

$^{-1}$. $C_{20}H_{18}Cl_2N_2O_4$. 1/2 H_2O (421.3): calcd. C 55.82, H 4.23, N 6.51; found C 55.99, H 4.31, N 6.54.

Compound **13**, white solid, m.p. 139.5 - 139.9 º C. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 1.58 (d, *J* = 7.5 Hz, 3 H), 2.97 (d, 9.0 Hz, 1 H, NH aziridine), 3.38 (d, *J* = 9 Hz,1 H, 3-H), 3.42 (q, *J* = 7.5 Hz, 1 H, 1-H), 3.64 (s, 3 H, OMe), 7.20 (t, *J* = 7.8 Hz, 1 H), 7.31 (d, *J* = 7.8 Hz, 1 H), 7.40 - 7.55 (m, 2 H), 7.55 - 7.70 (m, 1 H), 7.98 (dd, *J* = 6.9 Hz, *J* = 1.5 Hz , 2 H), 10.4 (br s, 1 H, N H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 14.6 (Me), 44.4 (CH), 44.7 (CH), 46.6 (2-C), 53.3 (OMe), 127.0 (Ar) 127.8 (Ar), 128.5 (Ar), 128.9 (Ar), 129.9 (Ar), 130.4 (Ar), 133.0 (Ar), 135.5 (Ar), 164.9 (CO), 169.9 (CO), 170.8 (CO) ppm. IR (nujol), ν = 1725, 1735, 3070, 3295 cm^{-1}. HR MS (FAB): calcd. 421.0722 [M+1], found 421.0703.

Methyl 2-[carbamoyl(phenyl)methyl]-3-(2,6-dichlorophenyl)aziridine-2-carboxylate 15

Methyl-7-(2,6-dichlorophenyl)-2α,5α-diphenyl-4-oxo-1,3-diazabicyclo[4.1.0]heptane-6β-carboxylate **11d** (0.32 g, 0.68 mmol, 1 eq.), THF (15 mL), containing conc. HCl (2.44 mL). Yellow solid 0.17 g (67 %), m.p. 167.5 - 167.7 ºC. ^{1}H NMR (300 MHz, $CDCl_3$), δ = 2.42 (d, *J* = 8.7 Hz, 1 H, 3-H), 3.04 (d, 8.7 Hz, 1 H, NH aziridine), 3.58 (s, 3 H, OMe), 4.88 (s, 1 H, 1' H), 5.77 (s,2 H, NH_2), 7.10 (t, *J* = 7.2 Hz, 1 H), 7.22 (d, *J* = 7.5 Hz, 2 H), 7.33 - 7.40 (m, 3 H), 7.48 (d, *J* = 7.8 Hz, 2 H) ppm. ^{13}C NMR (75.7 MHz, $CDCl_3$), δ = 42.0 (CH), 46.1 (2-C), 51.9 (CH), 53.0 (OMe), 127.6 (Ar) 128.3 (Ar), 128.7 (Ar), 129.0 (Ar), 130.2 (Ar), 131.2 (Ar), 133.7 (Ar), 135.5 (Ar), 171.0 (CO), 173.7 (CO). IR (nujol), ν = 1685, 1740, 3171, 3290 cm^{-1}. $C_{18}H_{16}Cl_2N_2O_3$ (379.3): calcd. C 57.00, H 4.26, N 7.39; found C 56.99, H 4.48, N 7.20.

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Table 1. Some data for pyrimidones **7**, **8** and **11**.

compound	Mp (ºC)	^{1}H NMR a), δ_H in p.p.m., *J* in Hz
7a	173.5-176.0	5-H 3.16 (d, *J* 18.3, 1 H), 3.40 (d, *J* 18.3, 1 H); 7-H 3.32 (s, 1 H)
8a	176.0-177.5	5-H 3.08 (d, *J* 18.3, 1 H), 3.34 (d, *J* 18.3, 1 H); 7-H 3.58 (s, 1 H)
7b	140.5-146.5	5-H 3.19 (q, *J* 7.2, 1 H); 7-H 3.59 (s, 1 H)
7c	181.2-183.2	5-H 4.40 (s, 1 H,); 7-H 4.13 (s, 1 H)
8c	134.5-137.5	5-H 4.75 (s, 1 H); 7-H 3.82 (s, 1 H)
7d	175.5-177.5	5-H 4.41 (s, 1 H); 7-H 3.80 (s, 1 H)
8d	189.1-190.1	5-H 5.09 (s, 1 H); 7-H 3.66 (s, 1 H)
7e	212.0-214.0	5-H 2.59 (q, *J* 6.9, 1 H); 7-H 3.77 (s, 1 H)
10	187.0-188.4	5-H 3.82 (q, *J* 7.2, 1 H); 7-H 3.48 (s, 1 H)
11a	166.6-169.7	5-H 3.40 (q, *J* 6.9, 1 H); 7-H 3.74 (s, 1 H)
11b	168.6-171.1	5-H 3.42 (q, *J* 6.9, 1 H); 7-H 3.76 (s, 1 H)
11c	189.6-191.2	5-H 3.57 (d, *J* 18.3, 1 H), 3.16 (d, *J* 18.3, 1 H); 7-H 3.75 (s, 1H)
11d	210.2-213.6	5-H 4.63 (s, 1 H); 7-H 4.24 (s, 1 H)
11e	195.1-196.8	5-H 4.63 (s, 1 H); 7-H 4.26 (s, 1 H)
11f	152.4-153.3	5-H 4.61 (s, 1 H); 7-H 4.22 (s, 1 H)
11g	208.1-210.3	5-H 4.61 (s, 1 H); 7-H 4.22 (s, 1 H)
11h	173.5-173.9	5-H 4.50 (s, 1 H); 7-H 4.16 (s, 1 H)
11i	213.4-215.0	5-H 3.39 (q, *J* 6.9, 1 H); 7-H 3.72 (s, 1 H)

a) selected peaks

Table 2. Some data for aziridines **12**, **13** and **15**.

compound	Mp (ºC)	yield (%)	^{1}H NMR (CH and NH of the aziridine ring), δ_H in p.p.m., *J* in Hz
12a[a)]	164.3-165.1	74	CH 3.21 (d, *J* 8.4, 1 H); NH 2.87 (br d, *J* 8.4, 1 H)
12b[b)]	116.3-117.4	42	CH 3.37 (d, *J* 9, 1 H); NH 2.85 (d, *J* 9, 1 H)
12c[c)]	191.1-191.6	87	CH 2.40 (d, *J* 9.9, 1 H); NH 3.08 (d, *J* 9.9, 1 H)
12d[d)]	180.2-181.2	68	CH 2.51 (d, *J* 9.9, 1 H); NH 3.02 (d, *J* 9.9, 1 H)
12e[e)]	189.3-190.0	29[f)]	CH 3.39 (d, *J* 9.3, 1 H); NH 2.83 (d, *J* 9.3, 1 H)
13[e)]	139.5-139.9	25[f)]	CH 3.38 (d, *J* 9.0, 1 H), NH 2.97 (d, *J* 9.0, 1 H)
15	167.5-167.7	67	CH 2.42 (d, *J* 8.7, 1 H), NH 3.04 (d, *J* 8.7, 1H)

a) obtained from hydrolysis of compound **8a**; b) obtained from hydrolysis of compound **7b**; c) obtained from hydrolysis of an isomeric mixture (1:1) of compounds **7c** and **8c**; d) obtained from hydrolysis of compound **7d**; e) **12e** and **13** were obtained from hydrolysis of a mixture of compound **7e** and **10**; f) partially separated after flash chromatography; total yield of **12e** and **13** is 75%.

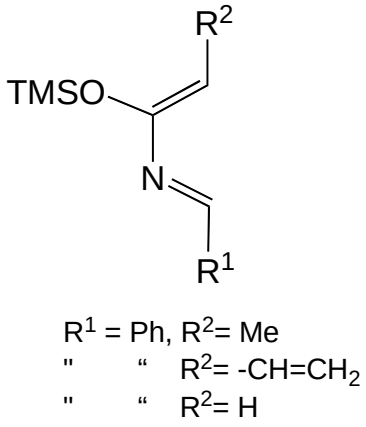


Fig 1. Some examples of *EZ* configuration of 2-azadienes reported in the literature.

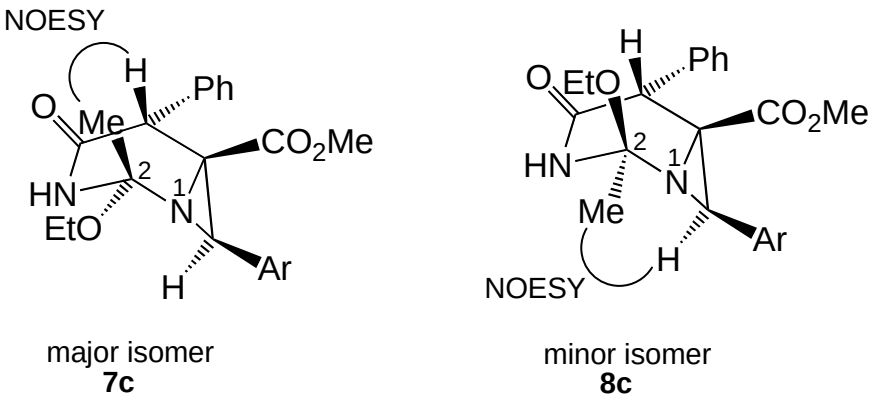
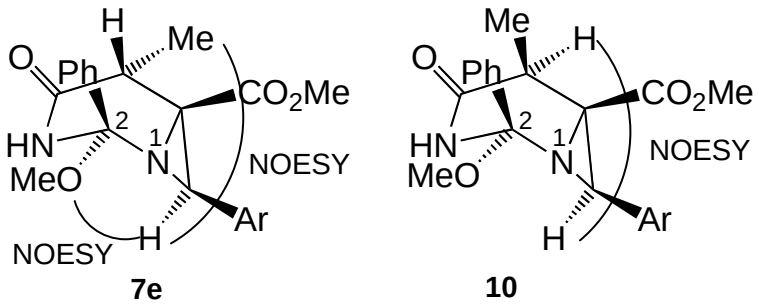
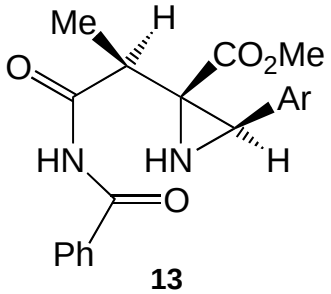


Fig 2. Compounds **7c** and **8c** showing the interaction through space (NOESY).



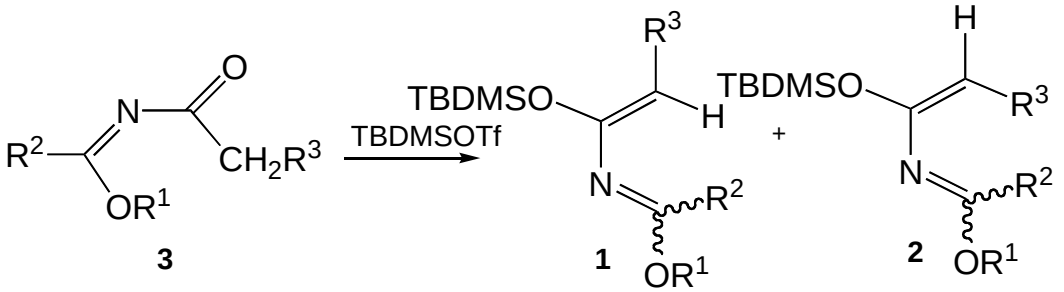
7e **10**

Fig 3. Compounds **7e** and **10** showing the interaction through space (NOESY).



13

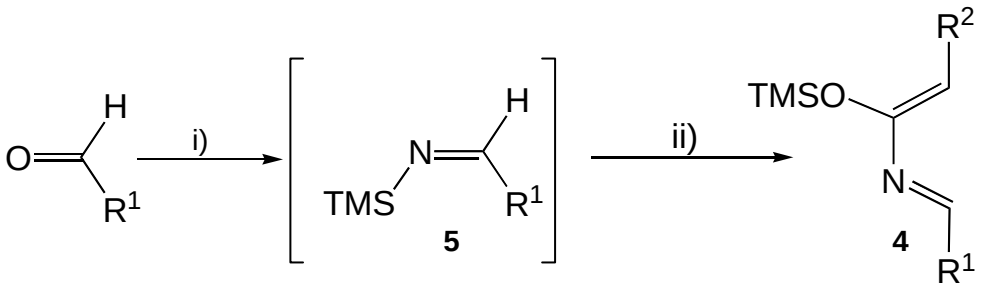
Fig 4. Structure of compound **13**.



3 **1** **2**

	R^1	R^2	R^3	Yield (%)	ratio 1: 2
a	Et	Me	H	65	100 : 0
b	Et	Me	Me	87	100 : 0
c	Et	Me	Ph	86	100 : 0
d	Me	Ph	Ph	88	100 : 0
e	Me	Ph	Me	82	20 : 80

Scheme 1. Preparation of 2-azadienes **1** and **2**

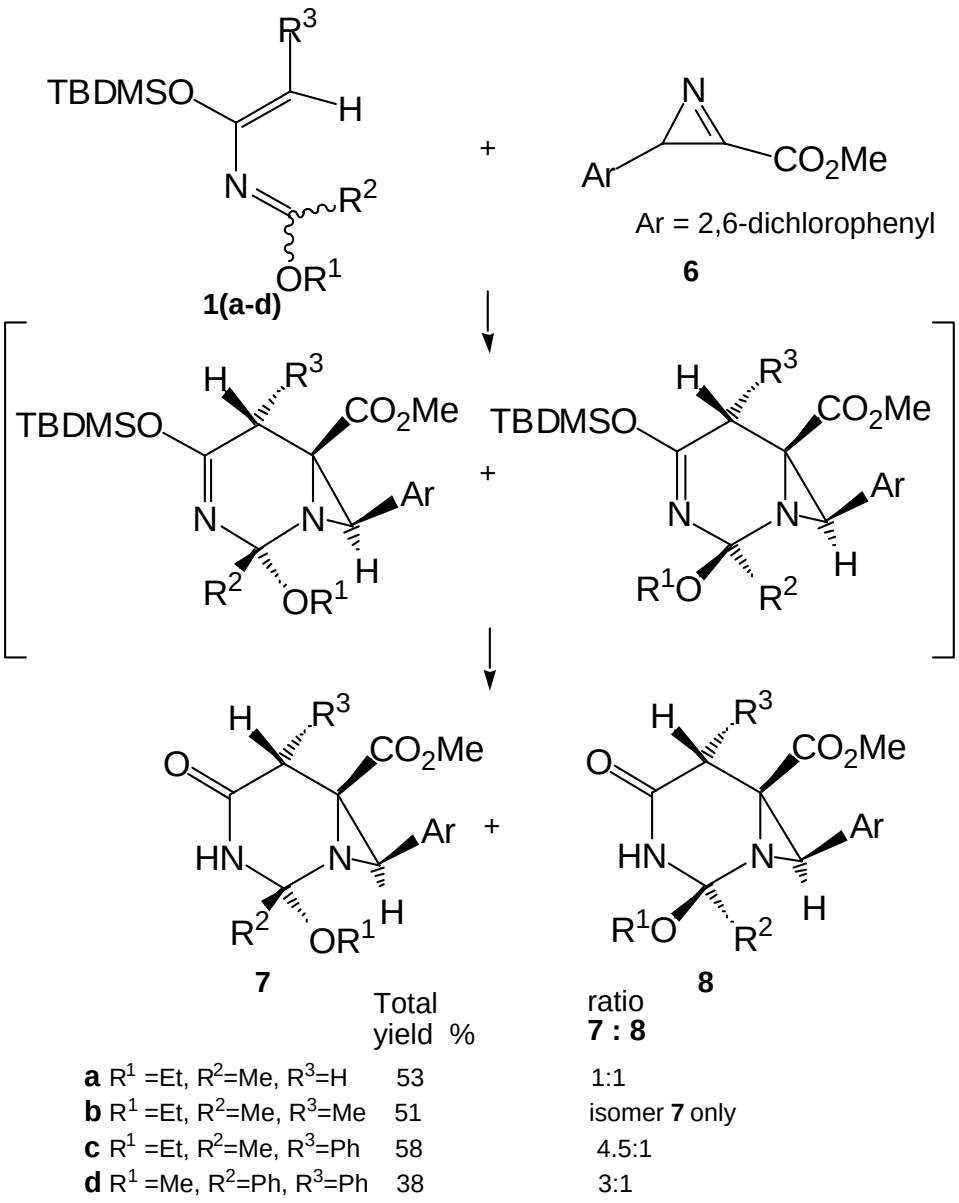


Compound		Yield
4a	R^1 = Ph, R^2 =H	60
b	R^1= 4-$NO_2C_6H_4$, R^2 =H	83
c	R^1= 4-FC_6H_4, R^2 =H	65
d	R^1= Ph, R^2 =Ph	100
e	R^1= 4-$NO_2C_6H_4$, R^2 =Ph	99
f	R^1= 4-FC_6H_4, R^2 =Ph	100
g	R^1= 4-$MeOC_6H_4$, R^2 =Ph	71
h	R^1= 3-furyl, R^2 =Ph	100
i	R^1= 4-FC_6H_4, R^2 =Me	100[a)]

[a)] **4i** showed to be a mixture of isomers 10 (*EZ*) : 1 (*EE*) ratio

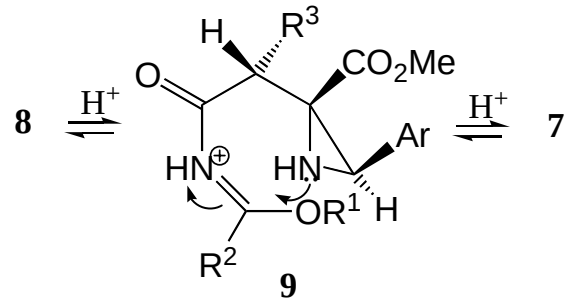
Method A: i) HMDS (1 eq.), BuLi (0.9 eq.), TMSCl (0.9 eq.); ii) Et_3N (1.1 eq.), R^2CH_2COCl (1.3 eq.);
Method B: i) LiHMDS (4 - 5 eq.), TMSCl (1.3 eq.); ii) Et_3N (1.1 eq.), R^2CH_2COCl (1.3 eq.);

Scheme 2. Preparation of 2-azadienes **4**.

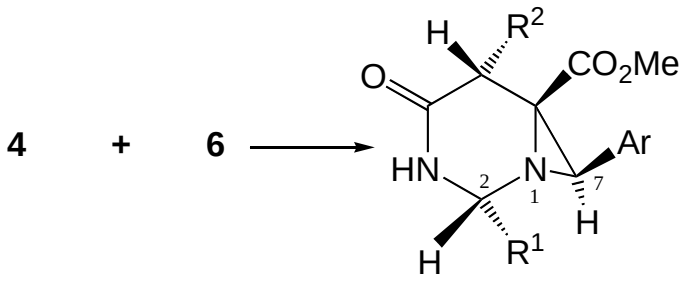


	Total yield %	ratio **7 : 8**
a R^1 =Et, R^2=Me, R^3=H	53	1:1
b R^1 =Et, R^2=Me, R^3=Me	51	isomer **7** only
c R^1 =Et, R^2=Me, R^3=Ph	58	4.5:1
d R^1 =Me, R^2=Ph, R^3=Ph	38	3:1

Scheme 3. Preparation of the pyrimidinones **7** and **8**.

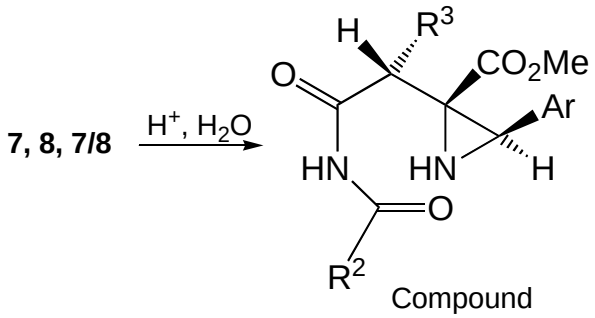


Scheme 4. Possible isomerization mechanism between compounds **8** and **7**.



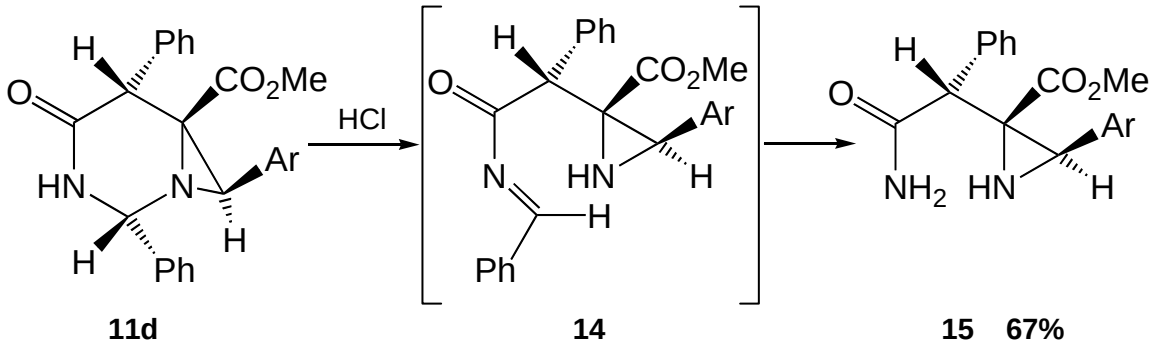
Compound	Yield (%)
11a	28
b	71
c	16
d	75
e	61
f	70
g	60
h	28
i	33

Scheme 5. Preparation of pyrimidones **11**.



Compound	Yield (%)
12a, R^2= Me, R^3= H	74
b, R^2= Me, R^3= Me	42
c, R^2= Me, R^3= Ph	87
d, R^2= Ph, R^3= Ph	68
e, R^2= Ph, R^3= Me	75

Scheme 6. Hydrolysis of compounds **7**, **8** or mixture of **7/8**.



Scheme 7. Hydrolysis of compound **11d**.