Synthesis of monocyclic diaziridines and their fused derivatives

Nina N. Makhova,* Vera Yu. Petukhova, and Vladimir V. Kuznetsov

N.D. Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences,
47, Leninsky prosp., 119991 Moscow, Russian Federation
E-mail: mnn@ioc.ac.ru

Abstract

Diaziridines and their fused analogues have a wide-range potential as a test subjects for theoretical and practical application. This review covers our investigations focused on the development of optimal methods for the synthesis of monocyclic and fused diaziridine derivatives. Several approaches to the preparation of monocyclic diaziridine derivatives were developed: (1) a synthesis of 3,3-di- and 1,3,3-trialkylmono- and α,ω-bis(diaziridin-1-yl)alkanes from ketoxime *O*-sulfonates and ammonia, and primary aliphatic amines, respectively, as well as of practically previously inaccessible 3-monoalkyldiaziridines from ammonium salts of aldoxime *O*-sulfonic acids and ammonia (2) a synthesis of diaziridines from carbonyl compounds, primary aliphatic amines, and aminating reagents in water (or a water–MeOH mixture) at controlled pH of the medium, as well as from carbonyl compounds, amines and *N*-chloroalkylamines in aprotic solvents in the presence of K_2CO_3, and (3) a synthesis of 1,2,3-trialkyldiaziridines from *N*-chloroalkylamines without carbonyl compounds in the presence of primary aliphatic amines at high pressure. As regards fused diaziridine derivatives, general and simple methods were developed to prepare four types of these structures: 1,5-diazabicyclo[3.1.0]hexanes, 1,6-diazabicyclo[4.1.0]heptanes, 1,3,5-triazabicyclo[3.1.0] hexanes, including the parent compound and 2,4-nonsubstituted structures, and 1,3,6-triazabicyclo[3.1.0]hexanes, the latter being previously unknown. The diastereomers have been isolated for 3,3′-bi- and 1,1′-alkylenebisdiaziridines. As a whole the investigations performed in our laboratory have resulted in the simple and general methods for preparing any kind of monocyclic and fused diaziridine derivatives that give high opportunities in the study of their chemical and stereochemical properties, and applications.

Keywords: Monocyclic diaziridines, bi(bis)diaziridines, fused diaziridines, general methods for the synthesis, mechanism, pH_{opt}, diastereomers, racemate, *meso* form

Contents

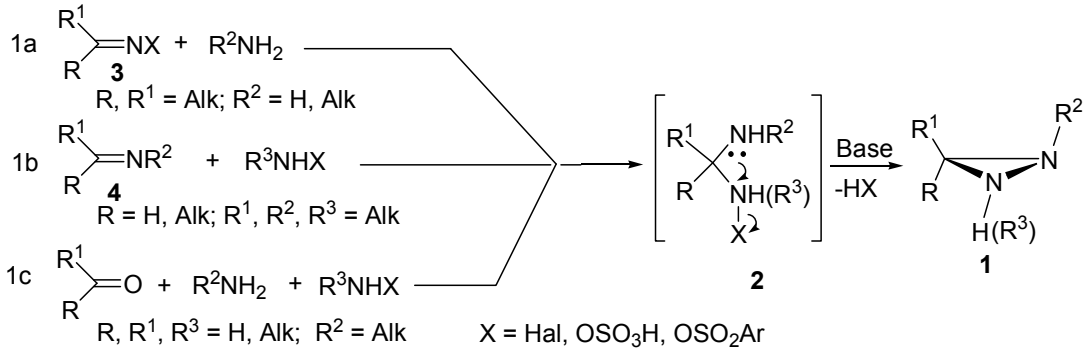
1. Introduction

Diaziridines (1,2-diazacyclopropanes) were first synthesized in 1959 by three groups of investigators who employed analogous methods.[1-3] During the first 20 years the most essential contribution to this chemistry was made by Prof. E. Schmitz.[4-6] Since that time several reviews on the synthesis and chemical properties of diaziridines have been published.[4-9] Diaziridines proved to be unique chemical objects. First of all, diaziridines are among a few matters that contain nitrogen atoms which are configuration-stable under trivial conditions (inversion barriers 20-27 kcal/mol), and, consequently, these compounds have been extensively used to investigate stereochemistry of nitrogen.[10,11] This side of diaziridine chemistry was studied basically by Prof. R. G. Kostyanovsky.[9,11] Secondly, diaziridine derivatives are of interest as neurotropically active compounds.[12-15] Furthermore, diaziridines are prone to ring expansion reactions with electrophilic reagents (ketenes, isocyanates, isothiocyanates, and acylating reagents), which led to the development of new simple methods for the preparation of both known and previously unknown heterocyclic systems.[8,16-20] And, finally, diaziridines have a high formation enthalpy as a result of the input both of the hydrazine fragment and three-member strained cycle and of low toxicity, which can be potentially useful for replacing hydrazine derivatives in rocket propellants. However some diaziridines had been absolutely or almost inaccessible (e.g. 3-monoalkyldiaziridines, diaziridines with functional groups incorporated in the substituents, and

some fused diaziridine-containing systems). Moreover, most of the methods for the diaziridine preparation had not been optimized. Over the last years we have studied in detail the known approaches to the synthesis of monocyclic diaziridines as well as to their different fused derivatives and developed convenient and optimal methods (including previously unknown) to prepare any of these structures. These results have been provided in this review that comprises the Introduction (Section 1), two main issues – synthesis of monocyclic diaziridines (Section 2) and synthesis of fused diaziridines (Section 3), and references.

2. Synthesis of Monocyclic Diaziridine

The formation of the diaziridine ring resulting in monocyclic diaziridines **1** is based on intramolecular S_N^i cyclization of *N*-X-aminal **2** that theoretically can be obtained through any of three ways: (1) an interaction of primary aliphatic amines or ammonia with the condensation product **3** of carbonyl compounds and aminating reagents (*N*-galogenamines, hydroxylamine-*O*-sulfonic acid (HASA) or hydroxylamine *O*-esters) (Scheme 1a), (2) an interaction of imines **4** (the condensation products of carbonyl compounds and primary aliphatic amines) with aminating reagents, (Scheme 1b) and (3) mixing of the three components (carbonyl compounds, primary aliphatic amines or ammonia, and aminating reagents) (Scheme 1c).



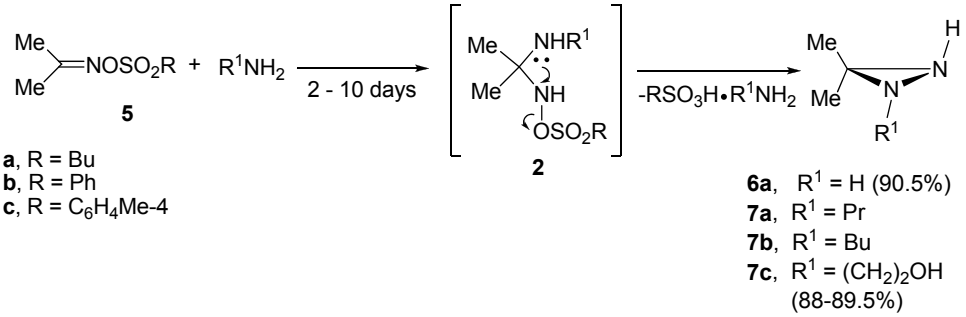
Scheme 1. The most general approaches to the synthesis of monocyclic diaziridines **1**.

According to literature data available prior to our researches, not all of the above substrates could enter these three reactions. Our results regarding the study of each of the three approaches to the synthesis of monocyclic diaziridines as well as regarding the development of a new method based on an interaction of *N*-chloroalkylamines and primary aliphatic amines at high pressure are discussed in this Section.

2.1. Monocyclic diaziridines and α,ω-bis(diaziridin-1-yl)alkanes from oxime *O*-esters and primary aliphatic amines or ammonia

A synthesis of 3,3-di- and 1,3,3-trisubstituted diaziridines from ketoxime *O*-sulfonates **5** and ammonia and primary aliphatic amines, respectively, had been described only for ketones with electron-withdrawing substituents – hexafluoroacetone[21] and dimethylmesoxalate[22] (Scheme 1a, R = R′ = CF_3, CO_2Me; X = $OSO_2C_6H_4Me$-4). The use of ketoxime *O*-sulfonates **5** obtained from aliphatic ketones raised doubts in view of their higher inclination to Beckman rearrangement.[23] We studied the possibility of preparing 3,3-di- and 1,3,3-trialkyldiaziridines using as a model 3,3-dimethyl- **6a** and 1-alkyl-3,3-dimethyldiaziridines **7a-f** from acetonoxime *O*-sulfonates **5a-c** and from other acetonoxime *O*-esters (acyloximes **8**, phosphates **9**, sulfinates **10**, and picrate **11**) and ammonia or primary aliphatic amines, respectively, in aprotic organic solvents (ether, dioxane, $CHCl_3$, and CH_2Cl_2).[24,25]

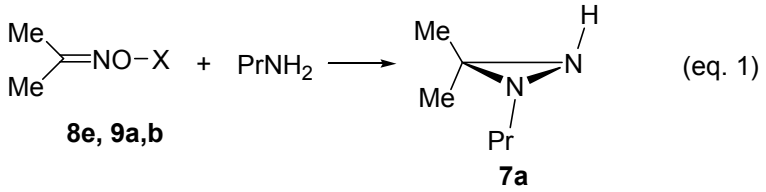
There are at least two electrophilic centers in oxime *O*-esters **5** and **8-11,** to which a nucleophilic attack can be applied – the oxime carbon atom and central atom of the acidic fragment. The amine attack at the central atom of the acidic fragment in acetonoxime *O*-sulfonates **5** is sterically hindered. So 1-alkyl-3,3-dimethyldiaziridines **7a-c** were successfully synthesized from all oxime *O*-esters **5a-c** and primary aliphatic amines at room temperature (Scheme 2). As the temperature increased, the yields of **7** reduced given Beckman rearrangement of initial esters **5**. 3,3-Dimethyldiaziridine **6a** was prepared in an autoclave at 9 MPa.



Scheme 2. Synthesis of 3,3-dimethyl-**(6a)** and 1-alkyl-3,3-dimethyldiaziridines **7** from acetonoxime *O*-sulfonates **5**.

A synthesis of diaziridines from other acetonoxime *O*-esters **8-11** was carried out on example of their reaction with propylamine. It was found that only phosphates **9a,b** were capable to form 1-propyl-3,3-dimethyldiaziridines **7a** in moderate yields (52-67%). Not very high yields in this case were probably associated with side alkylation or phosphorylation reactions where to these esters had a tendency. In acyloximes **8a-d** the carbon atom of the acyl fragment appeared to be the strongest electrophilic centre, and thus corresponding amides were obtained. 1-Propyl-3,3-dimethyldiaziridine **7a** in the yield 82% was achieved only when sterically hindered

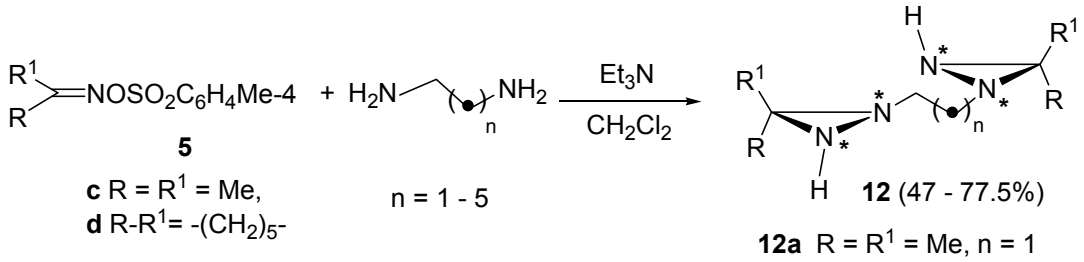
O-mesitylcarbonyl acetonoxime **8e** was used. Sulfinates **10a,b** and picrate **11** did not form diaziridine **7a** similarly to *O*-esters **8a-d** (equation 1).



8e, 9a,b **7a**

8 X = COR
a R = Me, **b** R = Ph, **c** R = CH_2Cl, **d** R = CCl_3
e R = $C_6H_2Me_3$-2,4,6
9 X = $P(O)R_2$
a R = OPh, **b** R = OPr^i
10 X = S(O)R
a R = OMe, **b** R = OC_6H_4Me-4
11 X = $C_6H_2(NO_2)_3$-2,4,6

A reaction of ketoxime *O*-*p*-toluenesulfonates **5c,d** with 1,ω-diaminoalkanes was utilized for the synthesis of α,ω-bis(3,3-dialkyldiaziridin-1-yl)alkanes **12**. The diastereomeric racemate 1*S*,*2*S*,*1′*S*,*2′*S** and *meso*-1*S*,*2*S*,*1′*R*,*2′*R** were isolated for α,ω-bis(3,3-dimethyldiaziridin-1-yl)ethane **12a** by fractional crystallization and the *meso* structure confirmed by X-ray diffraction analysis (Scheme 3).[26]



5
c R = R^1 = Me,
d R-R^1= -$(CH_2)_5$-

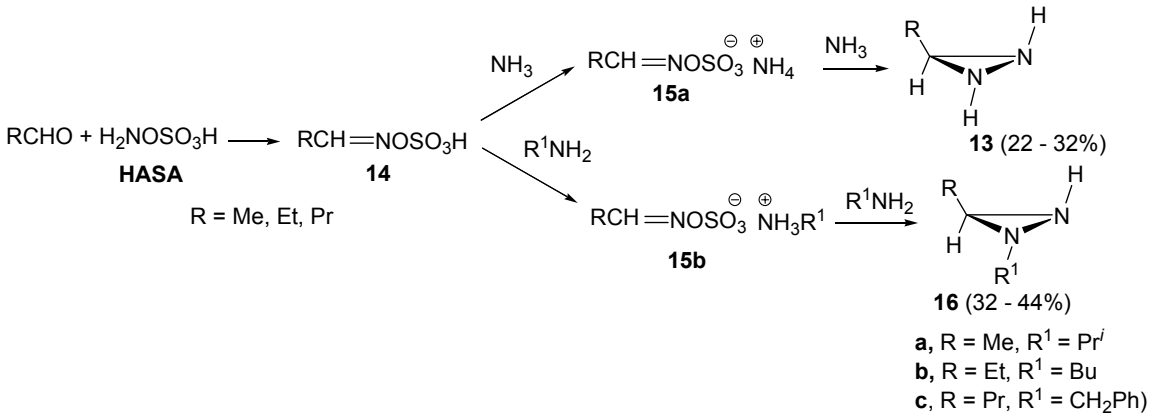
n = 1 - 5

12 (47 - 77.5%)
12a R = R^1 = Me, n = 1

Scheme 3. Synthesis of α,ω-bis(3,3-dialkyldiaziridin-1-yl)alkanes **12**.

The developed method for the synthesis of 3,3-dimethyldiaziridine **6a** from acetonoxime *O*-sulfonates **5** according to Scheme 2 was considered unsuitable for preparing, practically, previously inaccessible 3-monoalkyldiaziridines **13** from analogous derivatives of aldehydes. This is because aldoxime *O*-sulfonates as well as aldoxime *O*-sulfonic acids **14** decompose immediately after formation to give corresponding nitriles and sulfonic or sulfuric acids, respectively. We showed for the first time that aliphatic aldoxime *O*-sulfonic acids **14** could be stabilized as ammonium or alkylammonium salts **15a,b.** It was found that alkylammonium salts **15b** were stable at room temperature but that ammonium salts **15a** only survived in saturated aqueous solution of NH_3 (> 40%) at a lower temperature. To prepare **15a**, aqueous NH_3 was saturated with gaseous NH_3 under cooling, and then a freshly prepared cold solution of **14** was

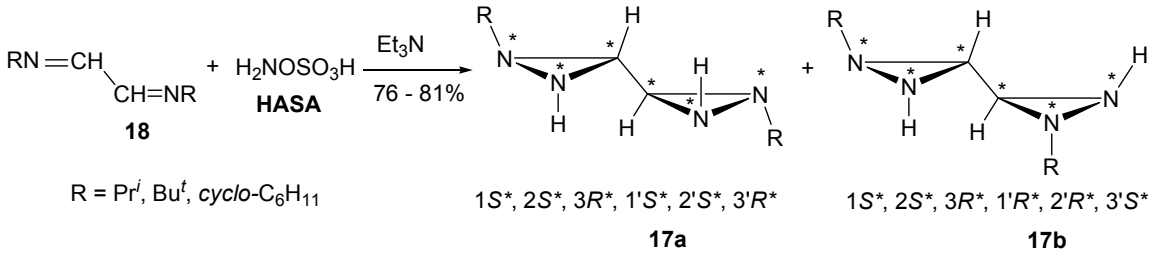
added. A flow of gaseous NH_3 passing through solution of **15a** at a lower temperature resulted in 3-alkyldiaziridines **13** in moderate yields. 1,3-Dialkyldiaziridines **16a-c** were prepared by the interaction of primary aliphatic amines with salts **15b** in H_2O or in MeOH–H_2O mixture[27] (Scheme 4).



Scheme 4. Synthesis of 3-mono-(**13**) and 1,3-disubstituted diaziridines **16** from aldoxime *O*-sulfonic acids salts **15a,b**.

2.2. 3,3′-Bidiaziridines from diimines of glyoxal and 1,2-bis(methylamino)ethane-1,2-diol dihydrochloride

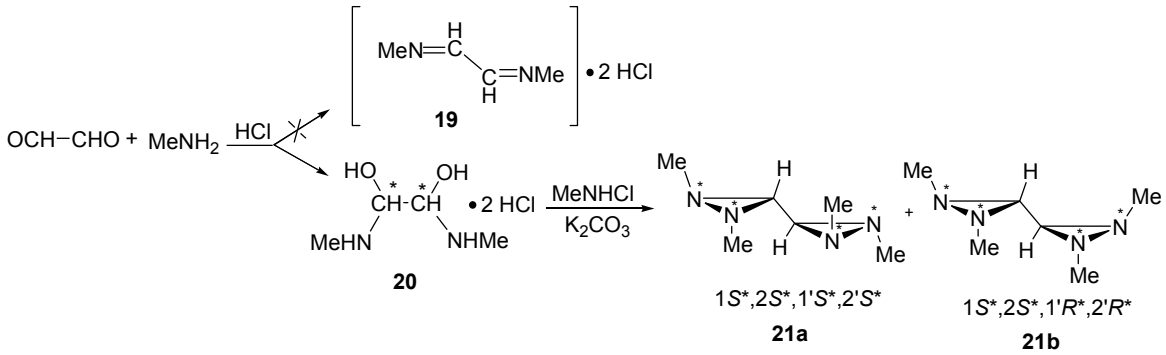
The second approach to the synthesis of monocyclic diaziridines (Scheme 1b) had been rather well developed by E. Schmitz.[5,6] Using this approach we managed to synthesize the first representatives of 3,3′-bidiaziridines **17** from diimines **18** of glyoxal.[28] It was found that this approach could be used only for diimines **18** with branched alkyl substituents. Reactions of glyoxal with primary aliphatic amines containing normal aliphatic radicals did not terminate at the stage of diimines as they underwent further condensation or polymerization.[29] Reactions of diimines **18** with HASA in the presence of TEA in MeOH at -5 → 20 ^oC afforded 1,1′-dialkyl-3,3′-bidiaziridines **17** in high yields. These compounds were generated as a mixture of several diastereomeres as evidenced by the ^1H NMR spectra of the crude products because 1,1′-dialkyl-3,3′-bidiaziridines **17** contained besides nitrogen atoms one more chiral centre, *viz.* the carbon atom of the diaziridine ring. However, isolation of the final products by vacuum distillation or sublimation always afforded a mixture of only the two most thermodynamically favorable diastereomers in a ratio from 2:1 to 9:1. The NOE experiments and X-ray diffraction analysis of one of the synthesized diaziridines demonstrated that the isolated diastereomers were the (1*S**,2*S**,3*R**,1'*S**,2'*S**,3'*R**) racemate **17a** and the (1*S**,2*S**,3*R**,1'*R**,2'*R**,3'*S**) *meso* form **17b** (Scheme 5)



Scheme 5. Synthesis of 1,1′-dialkyl-3,3′-bidiaziridines 1**7** with branched alkyl substituents.

To prepare bidiaziridines with normal aliphatic radicals at nitrogen atoms an attempt was made to stabilize the diimine of glyoxal and methylamine at the instant of its formation as the dihydrochloride salt **19**. Thus, treatment of the organic layer formed after mixing of aqueous solutions of reagents with conc. HCl followed by twofold treatment with K_2CO_3 led only to bis(methylamino)ethane-1,2-diol dihydrochloride **20** whose structure was established as a mixture of two diastereomers by ^{1}H NMR with use 2D COSY-LR experiment, ^{13}C NMR and MS (Scheme 6). This showed for the first time that aliphatic α-aminocarbinoles can be stabilized as hydrochlorides.[30]

To synthesize 1,1′,2,2′-tetramethyl-3,3′-bidiaziridine **21** dihydrochloride **20** was added to a solution of *N*-chloromethylamine in an aprotic organic solvent ($CHCl_3$ or CH_2Cl_2) in the presence of different bases (TEA, diethylamine or K_2CO_3). In the presence of organic bases, dihydrochloride **20** liberates free bis(methylamino)ethane-1,2-diol**,** which at once enters a self-condensation reaction that results in olygomers. The synthesis of bidiaziridine **21** was successful only in heterogeneous media in the presence of K_2CO_3 as base. According to the NMR spectroscopic data, compound **22** was a mixture of two diastereomers - racemate **21a** and *meso*-**21b** in a ratio ≈ 3:2 (Scheme 6), from which **21b** was isolated in the individual state and its structure was established by X-ray diffraction analysis. The kinetics of inversion of diastereomers **21a** and **21b** was studied by ^{1}H NMR spectroscopy at heating in $CHCl_3$.[30] Each of the individual diastereomers formed an initial mixture of racemate **21a** and *meso*-**21b** (ca. 3:2) in ~ 5 h.

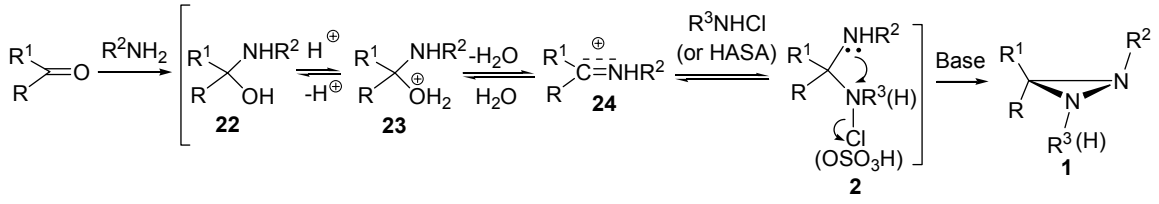


Scheme 6. Synthesis of 1,1′,2,2′-tetramethyl-3,3′-bidiaziridine **21.**

The mixtures of diastereomers of 3,3′-bidiaziridines **17a,b** (R = *t*-Bu) and **21a,b** were resolved into three stereoisomers - *meso* and two enantiomers by the gas-chromatography using the chiral stationary phase – Chirasil-β-Dex, where permethylated β-dextrin was linked to polyoxymethylene through an undecamethylene 11C-spacer.[31]

2.3. Monocyclic diaziridines by mixing carbonyl compounds, primary aliphatic amines and aminating reagents

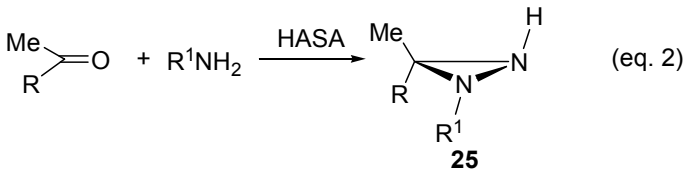
2.3.1. In water at controlled pH of the medium. Among the three approaches to diaziridine ring formation the simplest is based on an interaction of the carbonyl compound, primary aliphatic amine (or ammonia), and an aminating reagent (HASA or *N*-halogenamines) (Scheme 1c). However, yields of diaziridines **1** in these reactions were often not quantitative. We have examined the proposed mechanism of the diaziridine ring formation to identify those factors that most likely influence the reaction.[32-34] We found that yields of monocyclic diaziridines **1** synthesized by mixing the three components in water depended on pH of the reaction medium. To explain this effect we assumed that *N*-X-aminal **2**, in this case, was generated through α-aminomethylation, the result of which depended on the acid-base properties of the reaction medium and electronic effects of substituents in the initial components.[32,33] If so, the first step of the diaziridine synthesis is an interaction of the carbonyl compound with primary aliphatic amine (or ammonia) leading to α-aminocarbinol **22**. The transformation of this then occurs via protonation with formation of oxonium ion **23** followed by its dehydration into carbenium-iminium cation **24**, and should depend upon pH of the medium by analogy with the other α-aminomethylation reactions. Further interaction between cation **24** and the aminating reagent results in *N*-X-aminal **2** that rapidly cyclizes into product diaziridine **1** (Scheme 7). In order to check this hypothesis, we looked at the synthesis of diaziridines **1** from carbonyl compounds and amines that contained substituents with different *I*-effects, and aminating reagents (HASA or *N*-chloroalkylamines) at different fixed pH values. The effect of the substituents in amines was evaluated relative to their pK_{BH+} values, whereas the effect of the carbonyl compounds was evaluated relative to the sum of Taft induction constants ∑σ* of the substituents at the carbonyl groups.



Scheme 7. Possible scheme for diaziridine ring formation from carbonyl compounds, primary aliphatic amines, and aminating reagents in water.

Indeed, it was found that the highest yield of diaziridines **1** in water was achieved at an optimum pH (pH_{opt}) that shifts to a less alkaline region as the ─*I*-effect of the substituents in the carbonyl compound increased and the pK_{BH+} value of amine decreases.[32,33] The dependence of the 1,3,3-trialkyldiaziridines **25** and 1,2,3-trialkyldiaziridines **26** yields upon the pH of the reaction medium is presented in Figs. 1 and 2 according to equations 2 and 3, respectively.

As seen from Figures 1 and 2, diaziridine ring formation from amines with electron-withdrawing substituents in the side chain is less sensitive to pH than from the amines with simple alkyl substituents. The formation of the 1,5-diazabicyclo[3.1.0]hexanes **29** is practically insensitive to pH over the 6.5 – 13.0 pH range.



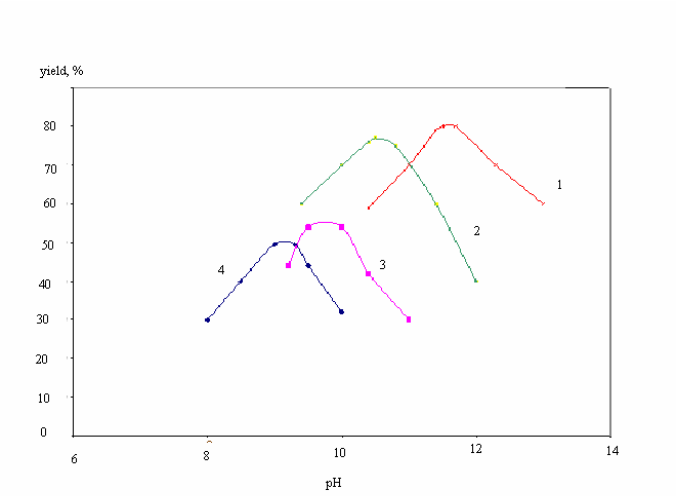
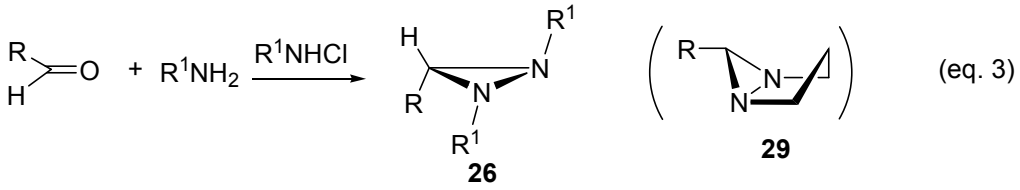


Figure 1. The yields of the 1,3,3-trialkyldiaziridines **25** at pH_{opt} according to equation 2: (1) R = R^1 = Me; (2) R = Me, R^1 = $(CH_2)_2NHAc$; (3) R = CH_2NHAc, R^1 = $(CH_2)_2OH$; (4) R = CH_2NHAc, R^1 = $(CH_2)_2NHAc$.



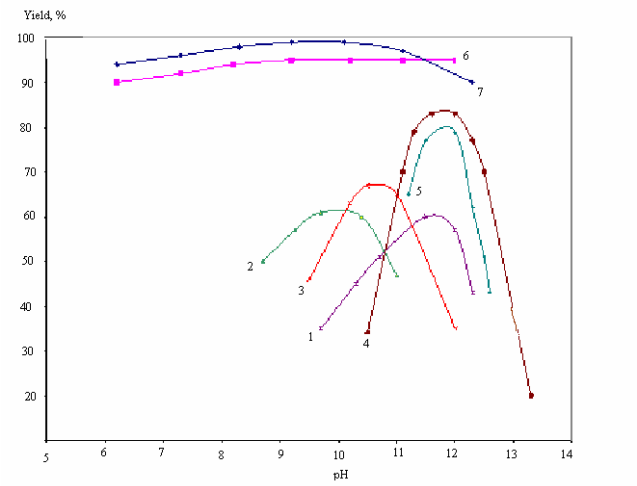
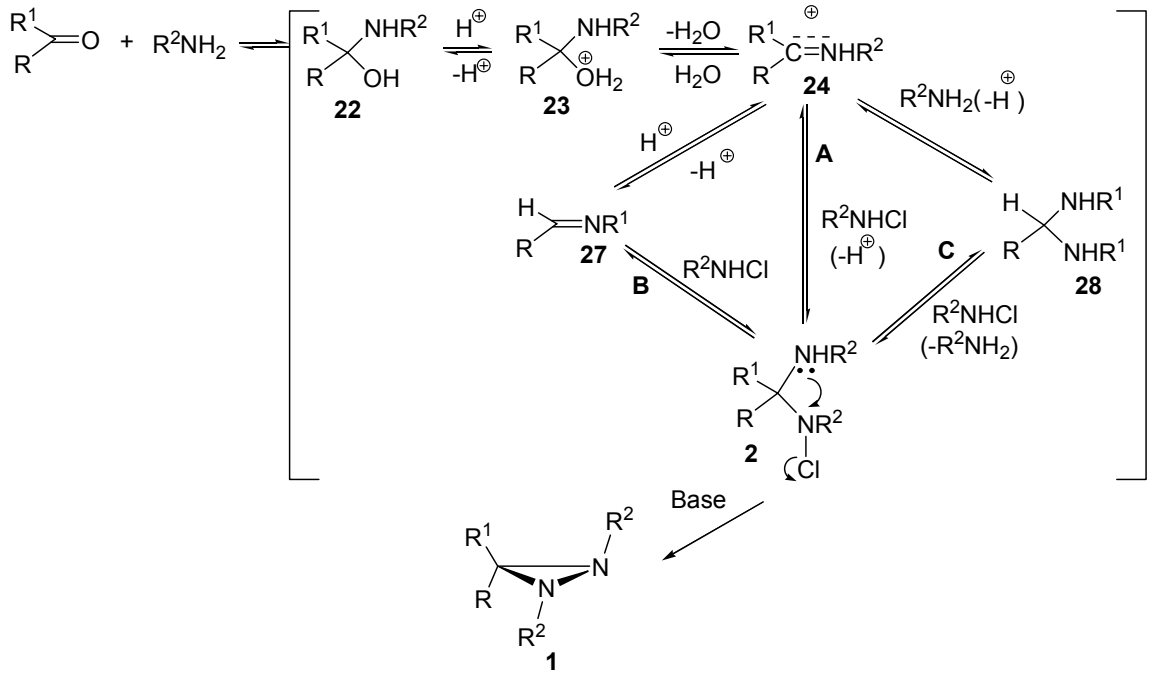


Figure 2. The yields of the 1,2,3-trialkyldiaziridines **26** and 1,5-diazabicyclo[3.1.0]hexanes **29** at pH_{opt} according to equation 3: (1) R = R^1= Me; (2) R = Me, R^1 = Et; (3) R= Me, R^1 = $(CH_2)_2NHAc$; (4) R = H, R^1 = Me, (5) R = H, R^1 = $(CH_2)_2NHAc$,: (6) R = H, R^1-R^1 = $(CH_2)_3$; (7) R = Me, R^1-R^1 = $(CH_2)_3$.

These differences may be explained by different competing pathways leading to the key intermediate, *N*-X-aminal **2** (Scheme 8) (this Scheme is for *N*-chloroalkylamine R^2NHCl as an aminating reagent): the aforesaid Path A through iminium cation **24,** the formation of imine **27** followed by its reaction with *N*-chloroalkylamine (Path B), and the preliminary formation of aminal **28** followed by its exchange chlorination in the reaction with *N*-chloroalkylamine (Path C). The formation of diaziridines **1** follows from a loss of HCl.

To identify the optimal pathway of the transformation of iminium cation **24** quantum chemical calculations for the synthesis of the simplest product **1a** (R = R^1 = H, R^2 = Me) were performed. The calculations were carried out on a basis of the density functional theory (B3LYP) with account for solvent effect using the PCM model.[35] The calculated potential energy surface with stationary points corresponding **22a, 23a, 24a, 27a, 28a, 2a** and **1a** is shown in Fig. 3.

The stationary point corresponding to the protonation product of intermediate **22a**, *viz* cation **23a** was not found because the geometry optimization led to the elimination of the water molecule giving rise to structure **24a**. The estimated energy for **23a** was obtained by the geometry optimization with the fixed C-O bond length of 1.4 Å. Since the formation of cationoid species **24a** is accompanied by a substantial gain in energy (9.02 kcal/mol), dehydration of compound **23a** is presumably barrierless. The calculations showed that Path A was the most energetically favorable pathway for the transformation of cation **24a** in aqueous solution. The reaction can also follows by paths B or C though these are less probable. The formation of reaction product **1a** is accompanied by a larger energy gain (35.67 kcal/mol) that provides the driving force needed for the overall transformation. Path C is evidently most favorable for the synthesis of bicyclic products **29.**



Scheme 8. The possible pathways for the key intermediate **2** formation in reaction of carbonyl compound, primary aliphatic amine and *N*-chloroalkylamine in water.

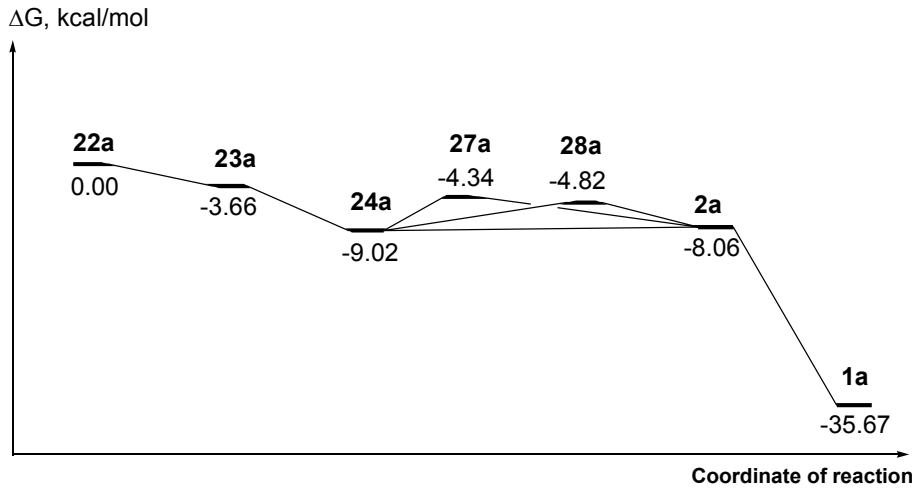
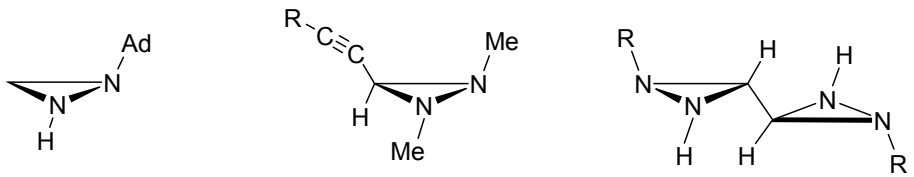


Figure 3. Potential energy surface calculated for the transformation of α-aminocarbinol **22a** into 1,2-dimethyldiaziridine **1a** calculated at the PCM-B3LYP/6-31G* level.

The medium pH-dependent approach to diaziridine synthesis from amines, carbonyl compounds and aminating reagents in water (or the water–MeOH mixture) allowed to prepare a lot of diaziridines **1** with different kinds of substituents in both carbonyl compounds and amines, including reagents with electron-withdrawing substituents,[32-34] sterically hindered

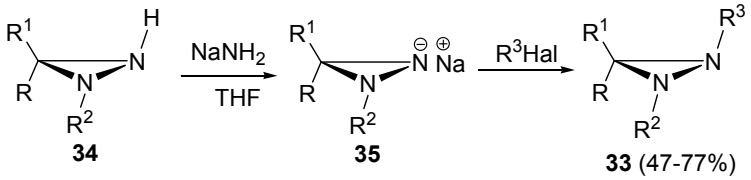
1-aminoadamantane,[36] α-acethylenic aldehydes,[37] and to synthesize derivatives previously inaccessible, e.g. **30-32.**



30 **31** R = $(EtO)_2CH$, $Me_2(CH_2OH)C$ **32** R = Me, Et

As the final result of this part researches, we developed a new and simpler approach to the synthesis of 1,2-di- and 1,2,3,-trialkyldiaziridines based on direct chlorination of a mixture of a carbonyl compound with an excess of primary aliphatic amine in water.[35] In this case the optimum pH was determined by the carbonyl compound to amine molar ratio (~ 1:8-10). This approach was used to develop a method for the preparation of 1,2-dialkyldiaziridines suitable for technological application.

2.3.2. In aprotic organic solvents in the presence of K_2CO_3. Unfortunately, the methods based on reactions in aqueous media cannot be extended to the synthesis of diaziridines from water-insoluble reagents. One of the approaches to the synthesis of 1,2-disubstituted diaziridines **33** from such reagents was alkylation of *N*-monoalkyldiaziridines **34** after preparation of their sodium salts **35** under the action of $NaNH_2$.[38] However this method demands the use of strictly anhydrous dipolar aprotic solvents and strong bases (Scheme 9).



34 **35** **33** (47-77%)

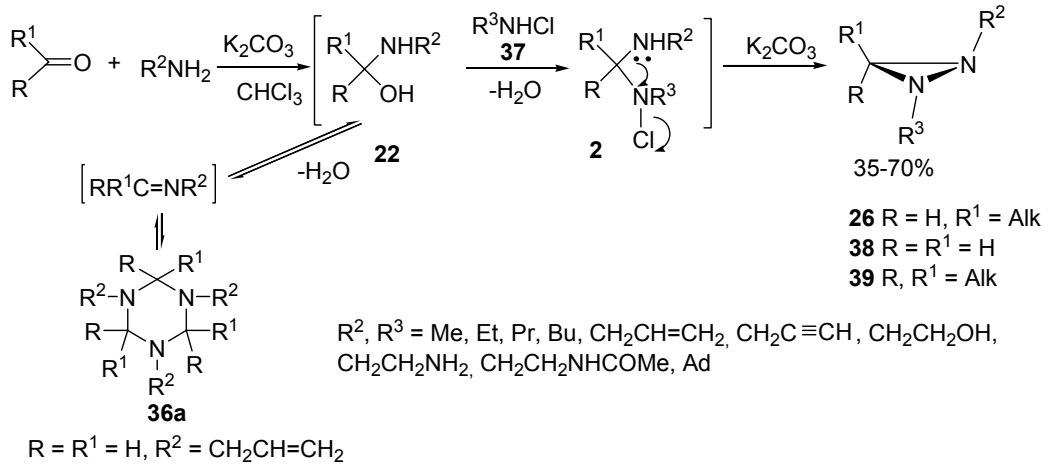
R = H, R^1 = Me; R = R^1 = Me; R-R^1 = $(CH_2)_5$;
R^2 = Me, Et, $CH_2CH{=}CH_2$, $CH_2C{\equiv}CH$; R^3 = Bu, $PhCH_2$; Hal = Cl, Br

Scheme 9. Synthesis of 1,2-disubstituted diaziridines **33** by *N*-alkylation of 1-monoalkyl diaziridines sodium salts **35**.

To synthesize diaziridines from water-insoluble reagents a new approach based on the interaction of carbonyl compounds, primary aliphatic amines and *N*-chloroalkylamines in aprotic organic solvents in the presence of K_2CO_3 was offered.[39] A preliminary ^1H NMR study of a model interaction between allylamine and formaldehyde showed that α-aminicarbinol **22b** (R = R^1 = H, R^2 = $CH_2CH{=}CH_2$) could survive in the aprotic organic solvent containing K_2CO_3 for a reasonably long time without conversion to hexahydro-1,3,5-triazine **36a** (R = R^1 = H)

(Scheme 10). K_2CO_3, which exhibits both basic and dehydration properties, is likely to result in stabilization of α-aminocarbinol **22.** However, in order to perform the reaction successfully the reaction mixture needs to be continuously and efficiently stirred for contact with K_2CO_3. In our test, when stirring stopped, a water layer appeared within a few minutes, and hexahydro-1,3,5-triazine **36a** was formed. Based on these results, we explored the synthesis of 1,2-disubstituted diaziridines by adding an *N*-chloroalkylamine **37** to the mixture of carbonyl compound and primary aliphatic amine in the presence of K_2CO_3 (in $CHCl_3$ or CH_2Cl_2 under intensive stirring). *N*-Chloroalkylamines **37** were generated by the reaction of corresponding amines with NaOCl followed by extraction with $CHCl_3$ or CH_2Cl_2 used as reaction solvents. In the case of amine and *N*-chloroalkylamine **37** with identical alkyl groups, 1 mol *t*-BuOCl was added to 2 moles of amine in the same solvents.

This approach proved to be very fruitful.[39] Carbonyl compounds and primary aliphatic amines with different substituents, including functional and sterically hindered amines, were introduced to this reaction and a variety of 1,2-di-(**38**), 1,2,3-tri-(**26**) and 1,2,3,3-tetraalkyldiaziridines **39** was synthesized in 35-70% yields.[39,40] Evidently, under these conditions, the interaction of α-aminicarbinols **22** and *N*-chloroalkylamines **37** resulted in *N*-chloroaminals **2** that further cyclized to the diaziridine products (Scheme 10).

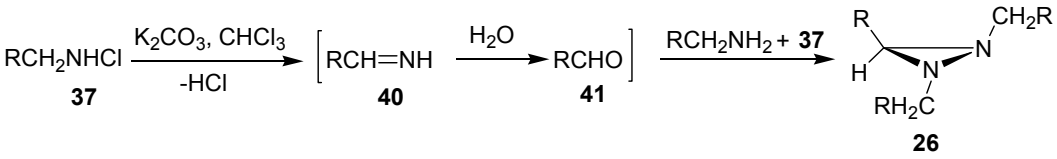


Scheme 10. Synthesis of monocyclic diaziridines **26**, **38 and 39** from carbonyl compounds, primary aliphatic amines and *N*-chloroalkylamines **37** in aprotic organic solvents in the presence of K_2CO_3.

2.4. 1,2,3-Trialkyldiaziridines from N-chloroalkylamines and primary aliphatic amines at high pressure

During the optimization of the above method for the synthesis of 1,2-di-, 1,2,3-tri- and 1,2,3,3-tetraalkyldiaziridines **38**, **26** and **39**, we studied the behavior of *N*-chloroalkylamines **37** in the presence of an excess of corresponding amine in chloroorganic solvents. It was found that such reactions with an amine carrying the same alkyl fragment, in the presence of K_2CO_3 and

a small amount of water at room temperature resulted in 1,2,3-trialkyldiaziridines **26** where the 3-alkyl fragment contains one CH_2 group less than the alkyl fragment of the initial compounds as it becomes the carbon centre of the three-membered ring. Given the structure of the products, we assumed that the first step of this reaction is the conversion of *N*-chloroalkylamines **37** into aldimines **40** by E_2-loss of HCl in the presence of amine. Hydrolysis of **40** by the water would then give aldehydes **41,** which can enter into reaction with amines and *N*-chloroalkylamines **37** leading to 1,2,3-trialkyldiaziridines **26** by analogy with the method described above (Scheme 11).[34]



Scheme 11. Synthesis of 1,2,3-trisubstituted diaziridines **26** from *N*-chloroalkylamines **37** and primary aliphatic amines in aprotic solvents in the presence of K_2CO_3.

However, the slow rate of this reaction impedes its application. For aliphatic *N*-chloroalkylamines **37**, the reaction requires several days, and for those synthesized from amines with lower basicity it takes several weeks. Anyhow, this variant of the synthesis of diaziridines **26** could be useful in those cases where carbonyl compounds are less accessible than the corresponding amines. In light of these findings, we used high pressure to accelerate this reaction. The reactions were carried out in a Teflon ampoule placed in a special reaction block at 300, 500, and 700 MPa. The reaction kinetics were examined for the interaction of *N*-chloroethylamine **37a** (R = Me) and ethylamine and revealed that these reactions were the second order at all the pressures (Figure 4).

Thus, the limiting step of the process is the bimolecular interaction of *N*-chloroethylamine **37a** with ethylamine followed by elimination of the HCl molecule. It was found that the optimal conditions for this reaction resulting 1,2-diethyl-3-methyldiaziridine **26a** in yield 95% are a molar ratio of *N*-chloroethylamine **37a** to ethylamine of 1:2.5 with 0.5 mol of K_2CO_3, 1-2% of water (by volume) and 500 MPa pressure at 15 ^oC. A several other *N*-chloroalkylamines **37b-f** were used in the analogous reaction under the identified conditions. In all cases the taget 1,2,3-trialkyldiaziridines **26b-f** were prepared in high yields (Scheme 12).[41]

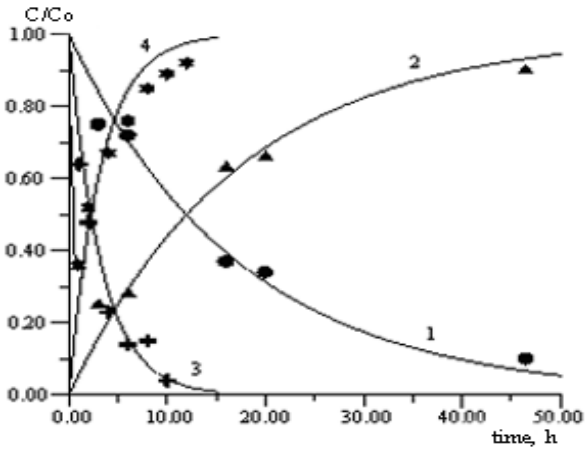
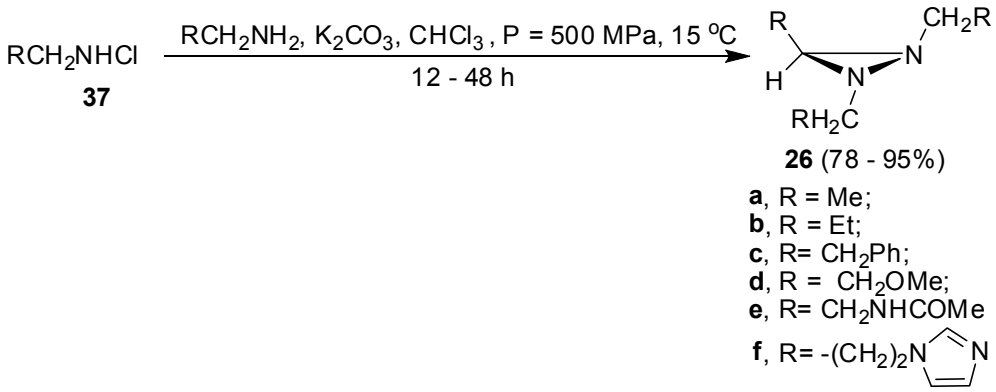


Figure 4. Kinetic curves for the formation of 1,2-diethyl-3-methyldiaziridine **26a** (R = Me) from *N*-chloroethylamine **37a** and $EtNH_2$ at high pressure. Curves 1 and 3 correspond to consumption of *N*-chloroethylamine **37a** while curves 2 and 4 correspond to accumulation of diaziridine **26a**. Curves 1 and 2 were recorded at 300 MPa and curves 3 and 4 were recorded at 500 MPa.

So, a new method for preparing 1,2,3-trialkyldiaziridines **26** in high yields based on the transformation of *N*-chloroalkylamines **37** without using carbonyl compounds, but in the presence of primary aliphatic amines with the same alkyl fragment, potassium carbonate and a small amount of water at high pressure was developed.



Scheme 12. Synthesis of 1,2,3-trialkyldiaziridines **26a-f** from *N*-chloroalkylamines **37a-f** and corresponding alkylamines at high pressure.

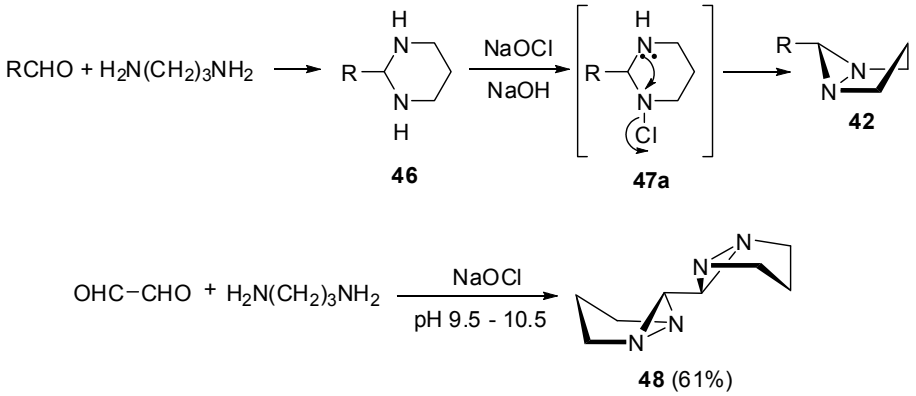
3. Synthesis of Fused Diaziridine Derivatives

In addition to the methods for the synthesis of monocyclic diaziridines we have also developed methods for the preparation of four types of fused derivatives of monocyclic diaziridines:

1,5-diazabicyclo[3.1.0]hexanes **42**, 1,6-diazabicyclo[4.1.0]heptanes **43**, 1,3,5-triazabicyclo[3.1.0]-hexanes **44,** and 1,3,6-triazabicyclo[3.1.0]hexanes **45.** Compounds **42**[42-44] and **44**[47,48] had been described in literature, and we elaborated new and simpler approaches to their preparation and synthesized the parent and 2,4-unsubstituted structures **44**. Only one example of bicycle **43** had been described,[43] and we proposed a general method for the synthesis of a range of derivatives. Bicyclic compounds **45** were hitherto unknown.

3.1. 1,5-Diazabicyclo[3.1.0]hexanes and 1,6-diazabicyclo[4.1.0]heptanes

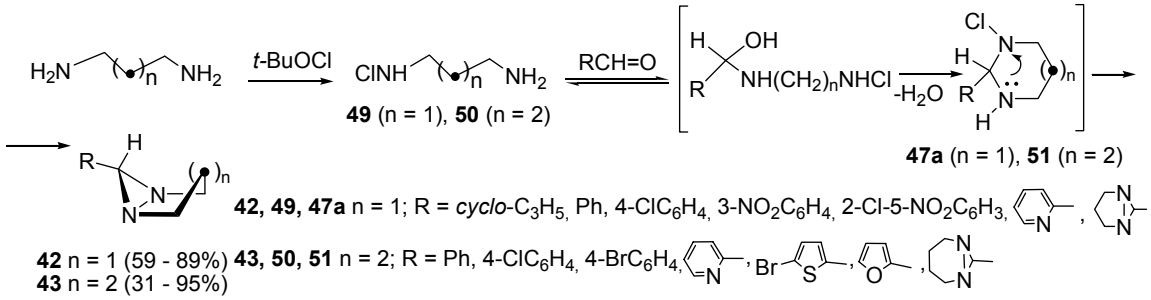
Earlier,[42-44] 1,5-diazabicyclo[3.1.0]hexanes **42** had been synthesized by halogenation of 1,3-diazacyclohexanes **46**, formed from aldehydes and 1,3-diaminopropane with NaOCl in water, followed by intramolecular cyclization of ensuing cyclic *N*-Cl-aminal **47a**. We used this variant of the synthesis of bicycles **42** in a combination with controlled pH of the medium (9.5-10.5) to prepare the first representative of 6,6′-bis(1,5-diazabicyclo[3.1.0]hexanes) **48** from glyoxal and 1,3-diaminopropane. According to X-ray diffraction data both bicyclic fragments in compound **48** exist in boat conformation[45] (Scheme 13).



Scheme 13. The known method for the preparation of 1,5-diazabicyclo[3,1,0]hexanes **42** and synthesis of 6,6′-bis(1,5-diazabicyclo[3,1,0]hexanes) **48.**

The procedure to give monocyclic diaziridines in aprotic solvents[39] was extended to the synthesis of 1,5-diazabicyclo[3.1.0]hexanes **42** and 1,6-diazabicyclo[4.1.0]heptanes **43** (an interaction of equimolar amounts of carbonyl compounds, 1,3-diaminopropane or 1,4-diamino-butane, respectively, and *t*-BuOCl in the presence of K_2CO_3 in $CHCl_3$).[46] This variant allowed bicycles **42** and **43** to be more easily isolated and in increased yields (50-52%). However, this procedure appeared unsuitable for reactions with carbonyl compounds carrying substituents sensitive to strong halogenating reagents such as NaOCl or *t*-BuOCl. To overcome this limitation

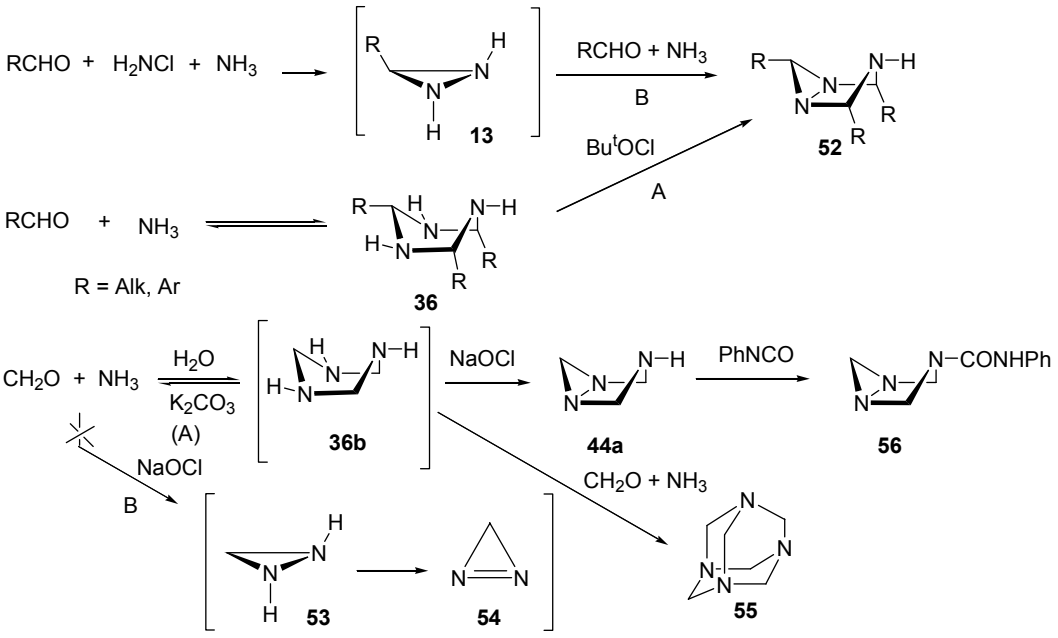
1,3-diaminopropane or 1,4-diaminobutane were first halogenated to their monochloro derivatives **49** and **50**, respectively, and the condensation with carbonyl compounds then followed. This gave 1,3-diaza- or 1,4-diaza-1-chlorocycloalkanes **47a** and **51** subsequently transformed to 6-substituted 1,5-diazabicyclo[3.1.0]hexanes **42** and 7-substituted 1,6-diaza-bicyclo[4.1.0]heptanes **43** under the action of bases. The study of the base nature's effect indicated that the best results were obtained where starting diamines were used in an equimolar excess (Scheme 14)[46].



Scheme 14. Synthesis of 1,5-diazabicyclo[3.1.0]hexanes **42** and 1,6-diazabicyclo[4.1.0]heptanes **43** from *N*-monochloroalkylenediamines.

3.2. Parent and 2,4-unsubstituted 1,3,5-triazabicyclo[3.1.0]hexanes

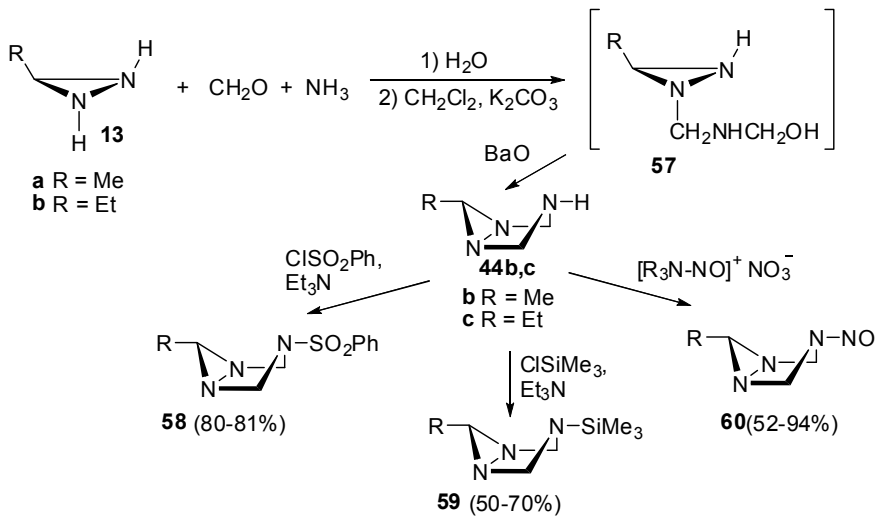
The known synthesis of 2,4,6-trisubstituted 1,3,5-triazabicyclo[3.1.0]hexanes **52** is based on two reactions: cyclization of the corresponding 2,4,6-trialkyl(aryl)hexahydro-1,3,5-triazines **36** with *t*-BuOCl[47] (path A, Scheme 15) or interaction of aldehydes, *N*-chloroamine and ammonia at low temperature[48] (path B, Scheme 15). Path B evidently includes the formation of 3-monosubstituted diaziridines **13** followed by their condensation with two moles of aldehyde and one mole of ammonia. We used pathway A to synthesize parent 1,3,5-triazabicyclo[3.1.0]hexane **44a** from the equilibrium mixture of CH_2O and NH_3 condensation products in water (after its treatment with K_2CO_3 - "Henry solution") with NaOCl at low temperature (-20 ^oC).[49] As shown in that work,[49] this solution contained a small amount of unsubstituted hexahydro-1,3,5-triazine **36b**. Path B in this reaction should be excluded because the parent unsubstituted diaziridine **53** (if it would be formed) in these conditions must be oxidized to parent diazirine **54.** The yield of **44** (b.p. = 74 ^oC/1 Torr) was only 5% and urotropin **55** was the main reaction product. The structure of compound **44a** was based upon by ^1H, ^{13}C and ^{15}N NMR data, and on the basis of conversion into phenylisocyanate derivative **56** (Scheme 15).[50]



Scheme 15. Synthesis of parent 1,3,5-triazabicyclo[3.1.0]hexane **44a** and its phenylisocyanate derivative **56**.

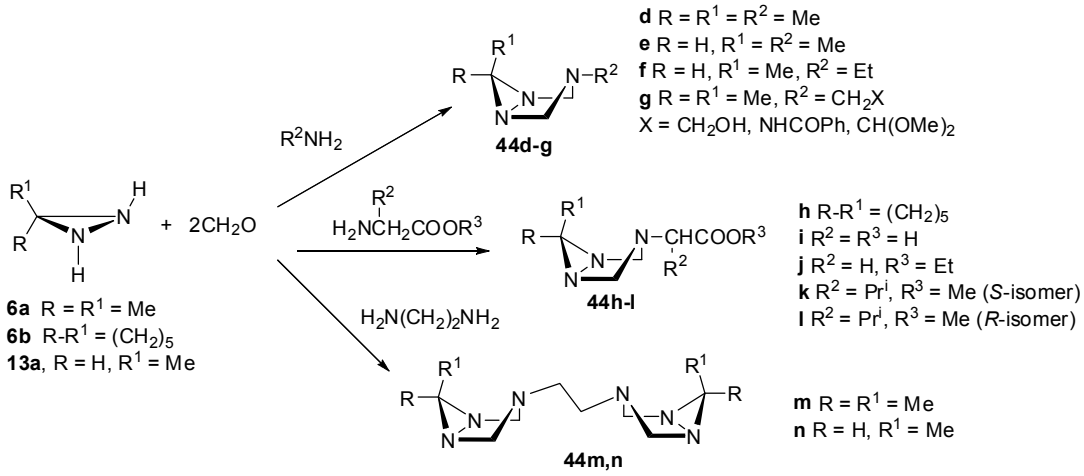
It had been earlier shown[12,51] that diaziridines containing one or two unsubstituted nitrogen atoms behaved as NH acids in the Mannich reaction and only underwent α-aminomethylation. The absence of the α-aminomethylation ability in aziridines[24-54] and oxaziridines[55]is a generic property of these three-membered nitrogen-containing heterocycles. Therefore, in order to use path B of Scheme 15 to prepare 2,4-unsubstituted 1,3,5-triazabicyclo[3.1.0]hexanes **44**, it is necessary to carry out Mannich condensation of 1,2-unsubstituted diaziridines with ammonia which is more basic. Attempts to implement Mannich condensation of 3-monoalkyldiaziridines **13a,b** or 3,3-dimethyldiaziridine **6a** with NH_3 and CH_2O in both aqueous and methanolic media, and in an aprotic organic solvent failed – in all the cases urotropin **55** was produced. The best conditions for the synthesis of compounds **44b,c** proved to be condensation of diaziridines **13a,b** with NH_3 and CH_2O in water with subsequent twofold treatment with K_2CO_3, extraction of the resulting organic layer into the aprotic organic solvent, and exposure to a basic dehydrating reagent such as K_2CO_3 or BaO (Scheme 16).[56,57] The yields of compounds **44b,c** under these conditions were 85-91%, and the yield of by- **55** did not exceed 5%.

Presumably, the first step of this reaction in water is kinetically controlled α-aminomethylation of diaziridines **13a,b** to give an intermediate of type **57**, which unless it is diverted, is in the equilibrium with the starting materials and gradually decomposes giving **55** as thermodynamic the product of reaction. However, removal of intermediate **57** into an aprotic phase that contains dehydrating reagents facilitates its condensation into bicycles **44b,c**. The synthesized compounds were readily derivatized at N(3) to give phenylsulfonamides **58**, trimethylsilylanes **59,** and nitroso **60** (Scheme 16).[57]



Scheme 16. Synthesis of 2,4-unsubstituted 1,3,5-triazabicyclo[3.1.0]hexanes **44b,c** and their derivatives **58-60**.

Condensation of 3,3-dialkyldiaziridines **6a** and **6b** with NH_3 and CH_2O under these latter conditions gave a complex mixture of products. However when NH_3 was replaced by primary aliphatic amines or amino acids the reaction was unambiguously in giving 3-substituted 1,3,5-triazabicyclo[3.1.0]hexanes **44d-n.** 3-Methyldiaziridine **13a** also was entered this reaction successfully (Scheme 17).[57,58].

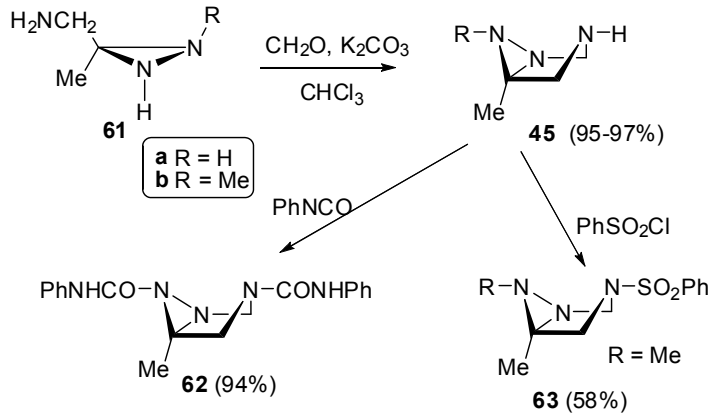


Scheme 17. Synthesis of 3-substituted 1,3,5-triazabicyclo[3.1.0]hexanes **44d-n**.

3.3. 1,3,6-Triazabicyclo[3.1.0]hexanes

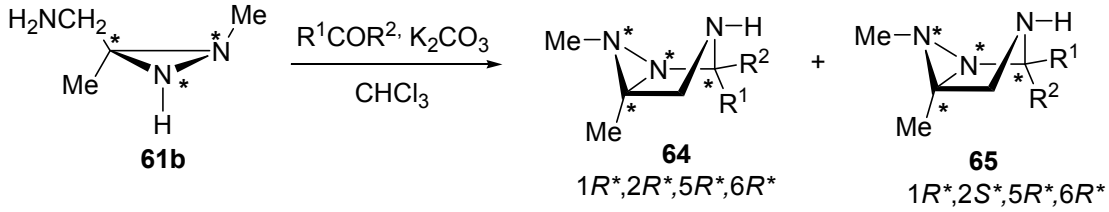
The regularity of the diaziridine behaviour that we observed in the Mannich reaction indicates that intramolecular α-aminomethylation of the diaziridine nitrogen atoms could be possible if an amino group, more basic than diaziridine was introduced into the ring as a *C*-substituent. Indeed,

the interaction of 3-aminomethyldiaziridines **61a,b** with CH_2O in $CHCl_3$ in the presence of K_2CO_3 under heat led to the formation of the first representatives of the new 1,3,6-triazabicyclo[3.1.0]hexane heterocyclic system **45,** which were characterized as phenylisocyanate and phenylsulfonate derivatives **62** and **63** (Scheme 18).[56]



Scheme 18. Synthesis of the first examples of 1,3,6-triazabicyclo[3.1.0]hexanes **45**.

The reaction of diaziridine **61b** with aromatic and heteroaromatic aldehydes proceeded diastereoselectively to form a mixture of two racemates 1*R**,2*R**,5*R**,6*R** **64a-d** and 1*R**,2*S**,5R*,6*R** **65a-d** in a ratio of (3-20) : 1. The predominant diastereomers was isolated in all the cases[59] and X-ray diffraction showed that 1*R**,2*R**,5*R**,6*R**-2-(2-bromothien-5-yl)-1,3,6-triazabicyclo[3.1.0]hexane **64d** crystallized as a conglomerate. The reaction with symmetric ketones ($R^1 = R^2 =$ Me) gave rise exclusively to the (1*R**,5*R**,6*R**) racemate **64e** (Scheme 19).



a R^1 = H, R^2 = 2-OHC_6H_4, **b** R^1 = H, R^2 = 2,4-$(OH)_2C_6H_3$, **c** R^1 = H, R^2 = 4-$MeOC_6H_4$, **d** R^1 = H, R^2 = 2-Br-thiophene, **e** $R^1 = R^2$ = Me

Scheme 19. Synthesis of 2-substituted 1,3,6-triazabicyclo[3.1.0]hexanes diastereomers **64** and **65**.

The methods so developed allowed the synthesis of both monocyclic and fused diaziridine derivatives with any kinds of substituents and in high yields, provided excellent opportunities for their applications in organic and pharmaceutical chemistry as well as their stereochemistry to be explored.

Acknowledgements

The authors are grateful to Dr. Yu. A. Strelenko and Dr. M. I. Struchkova for recording the NMR spectra and Dr. K. A. Lyssenko for X-ray diffraction studies. These investigations were partially supported by INTAS (grant 99-0157), RFFI (grants 97-03-33021, 04-03-32799) and Russian Presidium of the Ruassian Academy of Sciences, the programme "Development of Methods for the Synthesising Chemical Compounds and Creating New Materials". Authors express special thanks to the Referee for his huge both scientific and technical input.

4. References

1. Abendroth, H. J.; Henrich, G. *Angew. Chem*. **1959**, *71*, 283; *Ger. Pat*. 1082889 (1960), *Chem. Abstr*. **1961**, *55*, 16930b.
2. Paulsen, S. R. *Belg. Pat*. 1959, 588352.
3. Schmitz, E. *Angew. Chem*. **1959**, *71*, 127.
4. Schmitz, E. *Dreiringe mit zwei Heteroatomen,* Sringer-Verlag: Berlin-Heidelberg-New York, 1967.
5. Schmitz, E. *Advances in Heterocyclic Chemistry,* 1979, Vol. 24, pp 63-107.
6. Schmitz, E. In *Comprehensive Heterocyclic Chemistry*, *1-st Edn*., Lwowski, W., Ed., Pergamon: Oxford, 1984, *7*, Part 5.08, 195-236.
7. S. Hai, S. M.; Qureshi, A. W.; Begum, A. *Pakistan J. Sci. and Ind. Res.* **1975**, *18*, 116.
8. Heine, H. W. In *The Chemistry of Heterocyclic Compounds*, Hassner, A., Ed., Wiley-Interscience Publication, **1983**, *42*, 547-629.
9. Kostyanovsky, R. G.; Murugan, R.; Sutharchanadevi, M. In *Comprehensive Heterocyclic Chemistry II*, Katritzky, A. R.; Rees, C. W.; Scriven, E. F. V., Eds., Pergamon Press, 1996, *1A*, pp 347-364.
10. Mannschreck, A.; Radeglia, R.; Grundemann, E.; Ohme, R. *Chem. Ber*. **1967**, *100*, 1778.
11. Shustov, G. V.; Zolotoi, A. B.; Zaichenko, N. L.; Dyachenko, O. A.; Atovmyan, L. O.; Kostyanovsky, R. G. *Tetrahedron* **1984**, *40*, 2151.
12. Paget, Ch. J.; Davis, Ch. S. *J. Med. Chem*. **1964**, *7*, 626.
13. Kostyanovsky, R. G.; Shustov, G. V.; Nabiev, O. L. *Khim.-farm. Zh*. **1986**, *20*, 671 (*Pharm. Chem. J*. **1986**, *20*, 385 (Engl. Transl).
14. Khmel'nitskii, L. I.; Makhova, N. N.; Lebedev, O. V.; Epishina, L. V.; Suvorova, L. I. *Tez. Dokl. II s"ezda farmatsevtov of Latv. SSR* [*Abstr. of Papers, II Meeting of Pharmacists of Latv. SSR*, Riga, 1984 (in Russian)].
15. Prokopov, A. A.; Kotlova, L. I.; Berlyand, A. S. *Khim.-farm. Zh*. **2005**, *39*, 8 (in Russian). (*Pharm.l Chem. J.* **2005**, *39*, 345 (Engl. Transl.)).
16. Shevtsov, A. V.; Petukhova, V. Yu.; Strelenko, Yu. A.; Lyssenko, K. A.; Fedyanin, I. V.; Makhova, N. N. *Mendeleev Commun.* **2003**, 221.

17. Shevtsov, A. V.; Petukhova, V. Yu.; Strelenko, Yu. A.; Makhova, N. N. *Mendeleev Commun.* **2005**, 29.
18. Shevtsov, A. V.; Petukhova, V. Yu.; Strelenko, Yu. A.; Lyssenko, K. A.; Makhova, N. N.; Tartakovsky, V. A. *Izv. Akad. Nauk., Ser. Khim*. **2005**, 997 (*Russ. Chem. Bull. Int. Ed.* **2005**, *54*, 1021)
19. Shevtsov, A. V.; Kuznetsov, V. V.; Kislukhin, A. A.; Petukhova, V. Yu.; Strelenko, Yu. A.; Makhova, N. N. *J. Het. Chem.* **2006,** *43*, 881.
20. Shevtsov, A. V.; Kuznetsov, V. V.; Molotov, S. I.; Lyssenko, K. A.; Makhova, N. N. *Izv. Akad. Nauk., Ser. Khim*. **2006**, 534 (*Russ. Chem. Bull. Int. Ed.* **2006**, *55*, 554).
21. Zeifman, Yu. V.; Abduganiev, E. G.; Rokhlin, E. M.; Knunaynz, I. L. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1972**, 2737 [*Bull. Acad. Sci. USSR, Div. Chem. Sci*., **1972**, *21*, 2667 (Engl. Transl)].
22. Kostyanovsky, R. G.; Shustov, G. V.; Markov, V. I. *Izv. Aksd. Nauk SSSR, Ser. Khim.* **1974**, 2823 [*Bull. Acad. Sci. USSR, Div. Chem. Sci*. **1974**, *23*, 2725 (Engl. Transl)].
23. L. G. Donaruma, W. Z. Heldt, In *Organic Reactions,* Cope, A. C., Ed., Wiley & Sons, Inc., New York - London, 1960, *11*, p 1.
24. Mikhailyuk, A. N.; Makhova, N. N.; Bova, A. E.; Khmel'nitskii, L. I.; Novikov, S. S. *Izv. AN SSSR, Ser. Khim.* **1978**, 1566 [*Bull. Acad. Sci. USSR, Div. Chem. Sci*. **1978**, *27*, 1367 (Engl. Transl.)].
25. Makhova, N. N.; Petukhova, V. Yu.; Khmel'nitskii, L. I. *Izv. AN SSSR, Ser. Khim.* **1982**, 2107 [*Bull. Acad. Sci. USSR, Div. Chem. Sci*. **1982**, *31*,1858 (Engl. Transl)].
26. Petukhova V. Yu.; Strelenko Yu. A.; Lyssenko K. A.; Makhova N. N.; *Izv. Acad. Nauk, Ser. Khim.* **2007,** 1491 (*Russ. Chem. Bull., Int. Ed*. **2007**, *56*, 1550).
27. Mikhailyuk, A. N.; Petukhova, V. Yu.; Makhova, N. N. *Mendeleev. Commun*. **1997**, 60.
28. Petukhova, V. Yu.; Kuznetsov, V. V.; Shevtsov, A. V.; Strelenko, Yu. A.; Makhova, N. N.; Lyssenko, K. A.; Antipin, M. Yu. *Izv. Acad. Nauk, Ser. Khim.* **2001**, 421 (*Russ. Chem. Bull., Int. Ed*. **2001**, *50*, 440).
29. Carson, J. *J. Am. Chem. Soc*. **1953**, *75*, 4337.
30. Petukhova, V. Yu.; Makhova, N. N.; Ananikov, V. P.; Strelenko, Yu. A.; Fedyanin, I. V. *Izv. Acad. Nauk, Ser. Khim.* **2004**, 612 (*Russ. Chem. Bull., Int. Ed*. **2004**, *53*, 641).
31. Shevtsov, A. V.; Schurig, V.; Petukhova, V. Yu.; Makhova, N. N. *Proceeding of the Russian Symposium* "Chromatography and Chromatographic Equipment", Moscow, **2004**, 279.
32. Kuznetsov, V. V.; Makhova, N. N.; Strelenko, Yu. A.; Khmel'nitskii, L. I. *Izv. Acad. Nauk SSSR, Ser. Khim.* **1991**, 2861 [Bull. Acad. Sci. USSR*, Div. Chem. Sci.* **1991**, *40*, 2496 (Engl. Transl.)].
33. Kuznetsov, V. V.; Makhova, N. N.; Khmel'nitskii, L. I. *Izv. Acad. Nauk, Ser. Khim.* **1997**, 1410 [*Russ. Chem. Bull.* **1997**, *46*, 1354 (Engl. Transl.)].
34. Kuznetsov, V. V.; Makhova, N. N.; Dmitriev, D. E.; Seregin, V. V. *Mendeleev Commun.* **2005**, 116.

35. Kuznetsov, V. V.; Ovchinnikova, V. B.; Ananikov, V. P.; Makhova, N. N. *Izv. Acad. Nauk, Ser. Khim.* **2006**, 1978 (*Russ. Chem. Bull., Int. Ed*. **2006**, *55*, 2056).
36. Kuznetsov, V. V.; Makhova, N. N;. Chervin, I. I.; Kostyanovsky, P. G. *Izv. Acad. Nauk, Ser. Khim.* **1997**, 861 [*Russ. Chem. Bull.* **1997**, *46*, 828 (Engl. Transl.)].
37. Makhova, N. N.; Kamalova, N. G.; Strelenko, Yu. A. *Mendeleev Commun*. **2001**, 227.
38. Makhova, N. N.; Karpov, G. A.; Mikhailyuk, A. N.; Khmel'nitskii, L. I. *Mendeleev Commun.* **1999**, 112.
39. Makhova, N. N.; Mikhailyuk, A. N.; Kuznetsov, V. V.; Kutepov, S. A.; Belyakov, P. A. *Mendeleev Commun*. **2000**, 182.
40. Makhova, N. N.; Kuznetsov, V. V.; Kostyanovsky, R. G. *Izv. Acad. Nauk, Ser. Khim.* **1996**, 1869 [*Russ. Chem. Bull.* **1997**, *45*, 1780 (Engl. Transl.)].
41. Kuznetsov, V. V.; Syroeshkina, Yu. S.; Moskvin, D. I.; Struchkova, M. I.; Makhova, N. N.; Zharov, A. A. *J. Heterocycl. Chem.* **2008,** *45*, 497.
42. Ohme, R.; Schmitz, E.; Dolge, P. *Chem. Ber*. **1966**, *99*, 2104.
43. Shustov, G. V.; Denisenko, S. N.; Chervin, I. I.; Asfandiarov, N. L.; Kostianovsky, R. G. *Tetrahedron* **1985**, *41*, 5719.
44. Bronstert K., *Ger. Pat*. 3607993, **1987**, *Chem. Abstr*. **1987**, *107*, 236687h.
45. Kuznetsov, V. V.; Makhova, N. N.; Dekaprilevich, M. O. *Izv. Acad. Nauk, Ser. Khim.* **1999**, 623 [*Russ. Chem. Bull.* **1999**, *48*, 617 (Engl. Transl.)].
46. Kuznetsov V. V.; Kutepov S. A.; Makhova N. N.; Lyssenko K. A.; Dmitriev D. E. *Izv. Acad. Nauk, Ser. Khim.* **2003**, 638 (*Russ. Chem. Bull., Int. Ed*. **2003**, *52*, 665).
47. Nilsen A. T.; Atkins R. L.; Moore D. W.; La Berge J. M. *Tetrahedron Lett*. **1973**, 1167.
48. Schmitz E. *Chem Ber*. **1962**, *95*, 688.
49. Richmond H. H.; Myers G. S.; Wright G. F. *J. Am. Chem. Soc.* 1948, 70, 3659.
50. Makhova N. N.; Petukhova V. Yu.; Chabina T. V.; Khmel'nitskii L. I. *Izv. Acad. Nauk, Ser. Khim.* **1993**, 1665 [*Russ. Chem. Bull.* **1993**, *42*, 1602 (Engl. Transl.)].
51. Nabiev O. G.; Shakhgel'diev M. A.; Chervin I. I.; Kostyanovsky R. G. *Dokl. Akad. Nauk SSSR* 1**985**, *284*, 872 [*Dokl. Chem*. **1985**, *284*, 307 (Engl. Transl.)].
52. Bistrov V. F.; Yuzhakova O. A.; Kostyanovsky R. G. *Dokl. Akad. Nauk SSSR* 1**962**, *147*, 843 (in Russian).
53. Kostyanovsky R. G.; Pan'shin O. A.; Papoyan T. E.; *Dokl. Akad. Nauk SSSR* 1**967**, *177*, 1099 (in Russian).
54. Kostyanovsky R. G.; Alekperov R. G.; Kadorkina G. K.; Chervin I. I.; *Izv. Acad. Nauk SSSR, Ser. Khim.* **1987**, 2523 [*Bull. Acad. Sci. USSR, Div. Chem. Sci.* **1987**, *36*, 2343 (Engl. Transl.)].
55. Varlamov S. V.; Kadorkina G. K.; Kostyanovsky R. G. *Khim. Heterotsikl. Soedin*. **1988**, 396 [*Chem. Heterocycl. Compd*. **1988,** *24*, 320 (Engl. Transl.)].
56. Makhova N. N.; Mikhailyuk A. N.; Bova A. E.; Petukhova V. Yu.; Chabina T. V.; Khmel'nitskii L. I. *Mendeleev Commun*. **1992**, 146.

57. Makhova N. N.; Mikhailyuk A. N.; Bova A. E.; Chabina T. V.; Khmel'nitskii L. I. *Izv. Acad. Nauk, Ser. Khim.* **1993**, 2091 [*Russ. Chem. Bull.* **1993**, *42*, 2004 (Engl. Transl.)].
58. Shevtsov A. V.; Petukhova V. Yu.' Makhova N. N. *Izv. Acad. Nauk, Ser. Khim.,* **2003**, 2160 (*Russ. Chem. Bull. Int. Ed*. **2003**, *52*, 2282).
59. Shevtsov A. V.; Petukhova V. Yu.' Makhova N. N.; Lyssenko K. A. *Izv. Acad. Nauk, Ser. Khim.* **2002**, 1381 (*Russ. Chem. Bull. Int. Ed*. **2002**, *51*, 1497).

Authors' biographical data

Nina N. Makhova was born in 1938 in the city Chita (USSR). She graduated from Mendeleev Chemical Technology University (Moscow, USSR) in 1960. She received a Ph.D. degree in organic chemistry at Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences (ZIOC RAS), in 1971, Dr. Sc. in organic chemistry at ZIOC RAS in 1989 and professor – in 1994. From 1995 until now she is a head of Laboratory of Nitrogen-Containing Compounds at ZIOC RAS. Her scientific interests have been focused on the chemistry of nitrogen–oxygen compounds, in the first place, three–five-membered heterocycles (1,2,5-oxadiazoles, diaziridines, azetidines, imidazoles, triazoles, tetrazoles), a search for physiologically active and high-energy structures in these classes of compounds and the stereochemistry. She is a member of several scientific councils in Russia.

Vera Yu. Petukhova was born in the Moscow (USSR). She graduated from Mendeleev Chemical Technology University (Moscow, USSR) in 1979. She received a Ph.D. degree in organic chemistry at Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences (ZIOC RAS), in 1992. From 1992 until now she is the senior scientific researcher in Laboratory of Nitrogen-Containing Compounds at ZIOC RAS. Her scientific interests have been focused on the chemistry of three-membered nitrogen-containing heterocycles – diaziridines, mainly on the synthesis and reactivity of different bicyclic and fused derivatives and the study of their physiological activity and stereochemistry.

Vladimir V. Kuznetsov was born in 1956 in the settlement Gasoprovodsk of Moscow region (USSR). He graduated from Mendeleev Chemical Technology University (Moscow, USSR) in 1979. He received a Ph.D. degree in organic chemistry at Zelinsky Institute of Organic Chemistry, Russian Academy of Sciences (ZIOC RAS), in 1992. From 1992 until now he is a senior scientific researcher in Laboratory of Nitrogen-Containing Compounds at ZIOC RAS. His scientific interests have been connected with the search of optimal methods for the synthesis and the study of structure, reactivity and application of small nitrogen-containing heterocycles, in the first place, diaziridines and their fused derivatives.