Study of ring cleavage in quaternary ammonium salts of 1,3-diazaadamantane*

S. Z. Vatsadze, V. S. Semashko, M. A. Manaenkova, and N. V. Zyk*

Department of Chemistry , Moscow State University,
1 Leninskie Gory, 119992 Moscow, Russian Federation.
Fax: +7 (495) 932 8846. E-mail: szv@org.chem.msu.ru

A series of quaternary ammonium salts of 5,7-dimethyl-1,3-diazaadamantan-6-one bearing aryl and alkyl substituents was synthesized. On treatment with aqueous KOH, these compounds undergo ring cleavage to give 3,7-diazabicyclo[3.3.1]nonane derivatives. The product structure was confirmed by ^{1}H and ^{13}C NMR and IR spectroscopy.

Key words: quaternary ammonium salts, 5,7-dimethyl-1,3-diazaadamantan-6-one, ring cleavage.

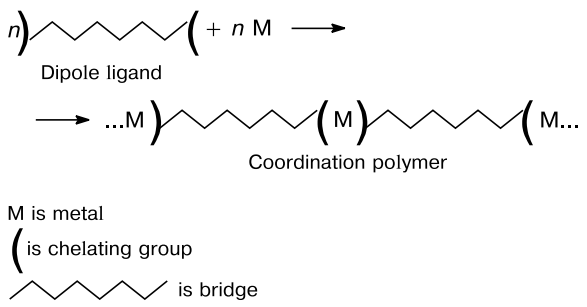
The design and synthesis of molecules capable of self-assembly is an important trend in modern chemistry. The self-assembly principle underlies many biological processes, giving rise to nanosystems of a definite structure (the best known self-assembling system is DNA).[1,2] From the standpoint of organic chemistry, self-assembly is based on noncovalent (secondary) interactions[2] (hydrogen bonds, π-stacking, charge transfer complexes, hydrophobic interactions, coordination bonds, and van der Waals interactions).

The use of self-assembly principle opens up broad prospects for the preparation of nanostructures with unique properties. Apart from simulation of biological processes, this allows one to obtain molecular devices, sensor materials, which change their properties depending on the external action (photo, chemical, electrical, and mechanical),[3] liquid crystals, polymer and gel solutions used in modern optics, electronics, and so on.[4,5]

In our opinion, of most interest is the preparation of coordination polymers based on self-assembly where binding of a metal to a polydentate ligand is the driving force of the process (Scheme 1). These supramolecular structures combine the properties introduced by both the metal ion and the organic ligand. Depending on the ligand denticity and the metal coordination number and coordination environment, this may give diverse supramolecular assemblies (linear chains, branched two-dimensional networks, three-dimensional frameworks, *etc.*)[3,4].

The studies dealing with preparation of phases with reversible solution—gel (or sol—gel) transition are of interest in this field. For example, the reversible solution—gel transition in the metal—ligand systems containing two different metals (lanthanum or europium + cobalt or zinc as metals and 2,6-bis(benzimidazolyl)pyridine derivatives as ligands) has been studied.[6] This furnished thermally and mechanically sensitive gels.

Scheme 1



3,7-Diazabicyclo[3.3.1]nonanes (bispidines) are biologically active compounds.[7] For example, 9-oxo derivatives exhibit analgesic activity,[8] and unsymmetrical *N*-substituted diazabicyclononanes are used as antiarrhythmic drugs.[9]

The 3,7-diazabicyclo[3.3.1]nonane system is also of interest for coordination chemistry, as this ligand can form stable chelates with metals.[10]

By connecting two bispidine fragments by a bridge, one can obtain a ligand able to form coordination polymers of diverse geometry depending on the linker type and the mode of connection of chelating groups to each other. This brings about the task of synthesizing various substituted 3,7-diazabicyclo[3.3.1]nonanes, including unsymmetrical *N*,*N*′-disubstituted derivatives. For the preparation of ditopic ligands (see Scheme 1) bridging of positions 9 of two bicyclononane cages appears most effi-

* Dedicated to Academician V. A. Tartakovsky on occasion of his 75th birthday.

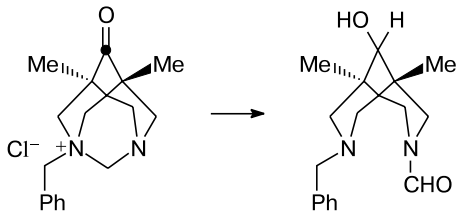
Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 8, pp. 1496—1501, August, 2007.

1066-5285/07/5608-1555

cient. Hence, convenient methods for 9-functionalization of 3,7-diazabicyclo[3.3.1]nonane are required.

This study starts a series of works on the use of 3,7-diazabicyclo[3.3.1]nonane systems as new ligands for the preparation of metal gels. Previously,[11] we discovered a new method for the synthesis of unsymmetrical *N*,*N*-disubstituted 3,7-diazabicyclo[3.3.1]nonane derivatives bearing the 9-hydroxy group. The ring cleavage reaction of 1-benzyl-5,7-dimethyl-6-oxo-1-azonia-3-azaadamantane chloride (**1a**) induced by aqueous alkali results in the stereoselective formation of *anti*-7-benzyl-3-formyl-1,5-dimethyl-3,7-diazabicyclo[3.3.1]nonan-9-ol (**2a**) (Scheme 2).

Scheme 2



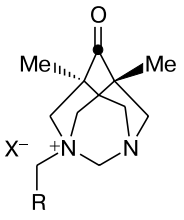
1a **2a**

Reagents and conditions: 5 KOH, H_2O, 12 h.

Salt **1a** and its analogs are promising as the initial compounds for the synthesis of various unsymmetrically substituted 3,7-diazabicyclo[3.3.1]nonanes. Here we studied substrates that can be involved in such processes and specific features of this reaction for each of the substrates.

Results and Discussion

As a continuation of previous work,[11] we prepared a number of salts of 5,7-dimethyl-1,3-diazaadamantan-6-one with various substituents at the quaternary nitrogen atom (aromatic or aliphatic). These were 5,7-dimethyl-1-(2-nitrobenzyl)-6-oxo-3-aza-1-azoniaadamantane bromide (**1b**), 5,7-trimethyl-6-oxo-3-aza-1-azoniaadamantane iodide (**1c**), and 5,7-dimethyl-1-propyl-6-oxo-3-aza-1-azoniaadamantane iodide (**1d**).



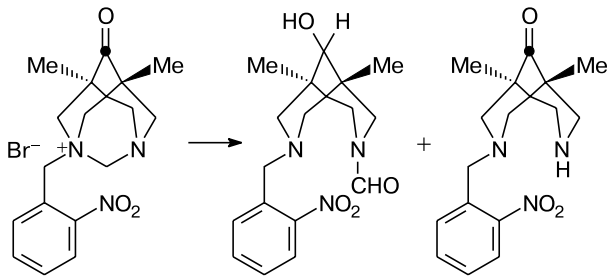
1b—d

1	R	X
b	*o*-NO_2Ph	Br
c	H	I
d	CH_2Me	I

This selection of salts with various groups at the quaternary nitrogen atom provides the possibility of elucidating the substituent effect on the reaction and obtaining various diazabicyclononanes with aromatic and aliphatic substituents at nitrogen atoms.

On treatment with a fivefold excess of KOH in water for 12 h, all salts **1b—d** underwent ring cleavage to give unsymmetrically *N*-substituted 3,7-diazabicyclo[3.3.1]nonanes; however, the product composition and yields were different. Thus the transformation of compound **1a** gave a precipitate of only *N*-formyl derivative **2a** in 72% yield; in the case of compound **1b**, the precipitate was a mixture of *N*-formyl- (**2b**) and *N*-unsubstituted product (**3b**) in 2 : 1 molar ratio (Scheme 3) (yields 40% and 16%, respectively, calculated relative to the pure product).

Scheme 3



1b **2b** **3b**

2 : 1

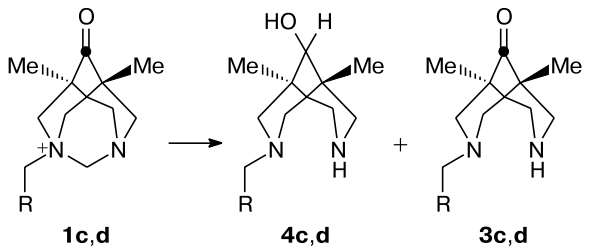
Reagents and conditions: 5 KOH, H_2O, 12 h.

In both cases, the mother liquors contained two products (*N*-formyl-substituted derivative **2a** or **2b** and *N*-unsubstituted derivative **3a** or **3b**); in the case of salt **1a**, the former compound predominated, while for salt **1b**, the latter one was predominant.

The ring cleavage in salt **1b** carried out in the presence of 5 equivalents of formaldehyde resulted in precipitation of only *N*-formyl derivative **2b**, the product yield being increased to 95%.

In the case of alkyl salts **1c** and **1d**, cleavage (Scheme 4) did not give *N*-formyl derivatives at all. Probably, the intermediate hemiaminal was rapidly hydrolyzed under these conditions (the presumptive reaction mechanism is

Scheme 4



1c,d **4c,d** **3c,d**

Reagents and conditions: 5 KOH, H_2O, 12 h.

R = H (**1c**, **3c**, **4c**), CH_2Me (**1d**, **3d**, **4d**)

shown in Scheme 5) and, hence, the reduction of the carbonyl group in position 9 became impossible.

In both cases, the reaction products did not precipitate but remained in solution as a finely dispersed suspension and could be isolated by chloroform extraction. The formation of these products was confirmed by ^{1}H and ^{13}C NMR and IR spectroscopy data.

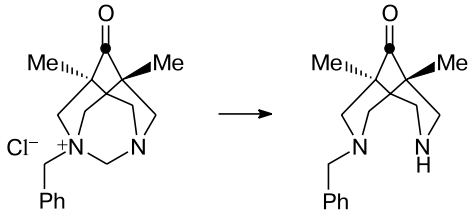
Compound **3c** or **3d** containing a 9-oxo group predominated in both cases. The rate of ring cleavage reaction was lower for alkyl salts than for benzyl salts. In the order of decreasing reaction rate, these salts can be arranged in the sequence: **1b** > **1a** > **1c** > **1d**. In the last-mentioned case, the reaction was not completed even in several days, and the aqueous phase after extraction contained a considerable amount of the unreacted salt.

In all cases of ring cleavage reactions, the replacement of KOH by NaOH did not cause any changes, although it has been reported[12] that the rates of anionic rearrangements with hydride transfer depend on the cation.

Previously, we determined[11] the structure of compound **2a** by NMR and X-ray diffraction analysis. The ^{1}H NMR spectra of compounds **2b** and **2a** are similar.

When the reaction of **1a** with 1 equiv. of KOH was carried out in a two-phase H_2O—$CHCl_3$ system (2 : 3 v/v), product **3a** containing no alcohol or formyl group was isolated from the organic phase in 48% yield[11] (Scheme 6).

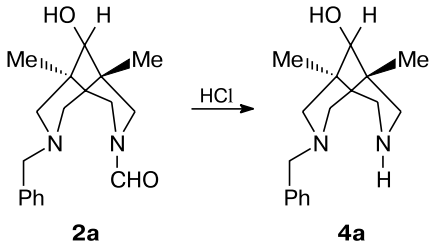
Scheme 6



Reagents and conditions: 1 KOH, $H_2O/CHCl_3$, 1 h.

In addition, treatment with concentrated HCl afforded the product of hydrolysis of compound **2a**, 1,5-dimethyl-3-benzyl-3,7-diazabicyclo[3.3.1]nonan-9-ol (**4a**), in 73% yield (Scheme 7).[11]

Scheme 7



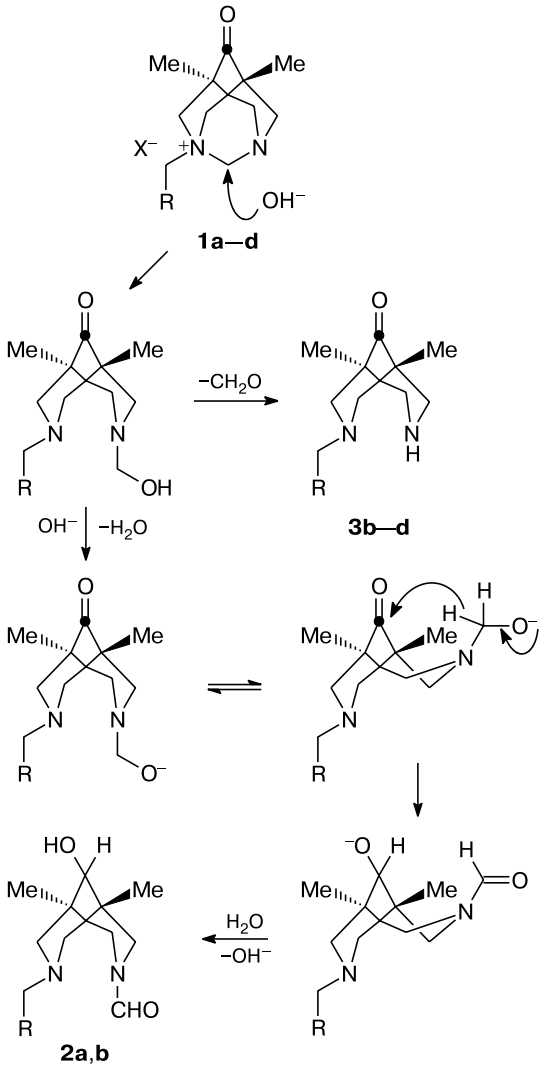
The product mixtures obtained in the reactions according to Schemes 3 and 4 were identified by comparison with the spectra of benzyl derivatives (see Scheme 2).

Figure 1 shows the ^{1}H NMR spectra (in $CDCl_3$) for the product mixture formed according to Scheme 3 and product **2a** (see Scheme 2).

The NMR spectra of the reaction products formed according to Scheme 4 exhibit two sets of signals. The pattern of signals (multiplicity and chemical shifts) observed for the bicyclic cage resembles that observed in the spectra of known benzyl analogs (**2a**,**b**, **3b**,**a**, **4a**). For illustration, Fig. 2 shows the ^{13}C NMR spectrum of a product mixture formed from diazaadamantane salt **1c** (in DMSO-d_6).

Thus, we found that ring cleavage in quaternary diazaadamantane salts having a benzyl substituent af-

Scheme 5



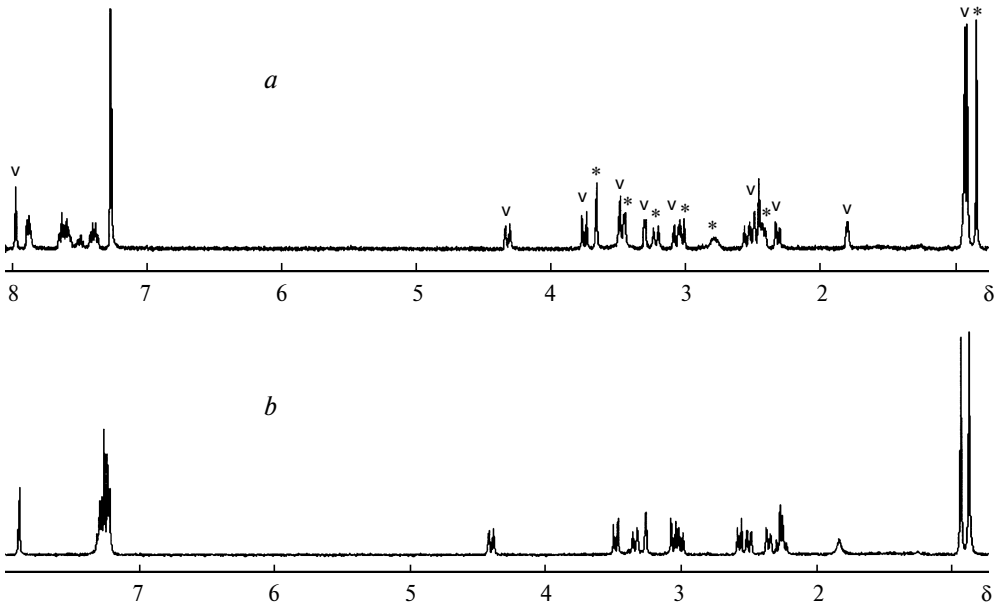


Fig. 1. (a) ^{1}H NMR spectrum of a mixture of **2b** and **3b** (the signals of **2b** are ticked and the signals for **3b** are asterisked, the signals for aromatic protons are omitted); (*b*) spectrum of compound **2a**. In both cases, $CDCl_3$ served as the solvent. Detailed signal assignment is given in the Experimental.

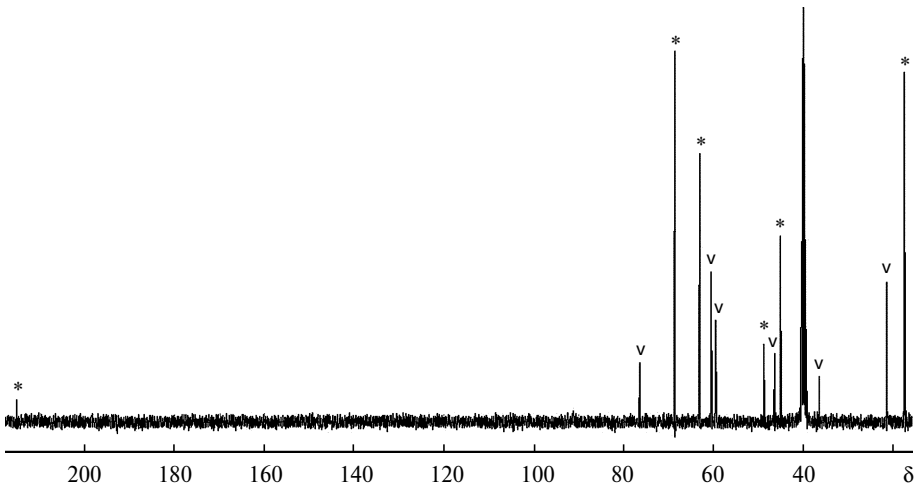


Fig. 2. ^{13}C NMR spectrum of a mixture of products **3c** and **4c** (in DMSO-d_6). The signals of compound **3c** are asterisked and the signals of compound **4c** are ticked. Detailed signal assignment is given in the Experimental.

fords mainly *N*-formyl-substituted bispidines with the 9-hydroxy group, whereas in the presence of an alkyl substituent, bispidine with the 9-oxo group is formed as the major product.

The results of further studies on the dependence of the reactivity of substrates and reaction pathways on the substituent at the quaternary nitrogen atom will be published elsewhere.

Experimental

The reagents and solvents were purified by standard procedures.[13] ^{1}H NMR spectra were recorded on a Bruker Avance-400 spectrometer operating at 400 MHz at 28 °C. The chemical shifts are referred to internal HMDS. IR spectra were measured on UR-20 (in thin film or Nujol) and Specord 75 IR instruments (Nujol). The melting points were determined in block in an open capillary and were not corrected. Elemental analysis of the compounds was carried out on a Carlo-Erba CPT analyzer.

Preparation of quaternary ammonium salts of 5,7-dimethyl-1,3-diazaadamantane

1-Benzyl-5,7-dimethyl-6-oxo-3-aza-1-azoniaadamantane chloride (1a). Benzyl chloride (2.11 g, 0.016 mol) was added to a solution of 5,7-dimethyl-1,3-diazaadamantan-6-one (3 g,

0.016 mol) in benzene (25 mL) and the mixture was refluxed for 4 h. After cooling, the precipitate was filtered off, washed with benzene, and recrystallized from chloroform to give 3.55 g (70 %) of compound **1a**, m.p. 239—242 °C (Ref. 14: m.p. 242—247 °C). The spectral characteristics were reported previously.[11]

5,7-Dimethyl-1-(*o*-nitrobenzyl)-6-oxo-1-aza-1-azoniaadamantane bromide (1b). The procedure was similar to that described above except that benzyl chloride was replaced by *o*-nitrobenzyl bromide (3.6 g, 0.016 mol). Yield 3.96 g (60%), m.p. 240—242 °C. ^{1}H NMR (DMSO-d_6), δ: 0.85 (s, 6 H, 2 Me); 3.0 (d, 2 H, H_{ax}(4), H_{ax}(8), J = 12.3 Hz); 3.45 (d, 2 H, H_{eq}(4), H_{eq}(8), J = 12.5 Hz); 3.73 (d, 2 H, H_{ax}(9), H_{ax}(10), J = 11.0 Hz); 3.82 (d, 2 H, H_{eq}(9), H_{eq}(10), J = 11.0 Hz); 4.77 (s, 2 H, C$\underline{H}_2$Ar); 4.90 (s, 2 H, NC$\underline{H}_2$N); 7.79 (d, 1 H, CH(6)(Ar), J = 7.2 Hz); 7.80—7.91 (m, 2 H, CH(4), CH(5), Ar); 8.19 (d, 1 H, CH(3), Ar, J = 7.8 Hz). ^{13}C NMR (DMSO-d_6), δ: 15.5 (Me); 45.5 (C$\underline{\text{Me}}$); 60.0 (C$\underline{H}_2$Ar); 61.5 (C(4), C(8)); 64.5 (C(9), C(10)); 79.0 (N$\underline{\text{C}}H_2$N); 120.0 (C1(Ar)); 126.5 (C3(Ar)); 133.0, 134.5 (C4(Ar), C6(Ar)); 137.0 (C5(Ar)); 151.0 (C2(Ar)); 206.0 (C=O). Found (%): C, 51.33; H, 5.62; N, 10.66. $C_{17}H_{22}BrN_3O_3$. Calculated (%): C, 51.52; H, 5.56; N, 10.61.

1,5,7-Trimethyl-6-oxo-1-aza-1-azoniaadamantane iodide (1c). Methyl iodide 8 g (0.056 mol) was added to a solution of 5,7-dimethyl-1,3-diazaadamantan-6-one (10.15 g, 0.056 mol) in dry EtOH (30 mL), and the flask was gently heated with stirring for 15 min. Then EtOH (20 mL) was added and the mixture was stirred for additional 15 min. The precipitate thus formed was filtered off and recrystallized from alcohol. Cooling of the mother liquor gave an additional product. The total yield was 15.1 g (81%), m.p. 241—242 °C (Ref. 15: m.p. 240—241 °C). ^{1}H NMR (DMSO-d_6), δ: 0.9 (s, 6 H, 2 Me); 2.95 (s, 3 H, $N^+C\underline{H}_3$); 3.08, 3.38 (both d, 2 H each, H(9), H(10), J = 2.35 Hz); 3.82 (br.s, 4 H, H(4), H(8)); 4.78 (br.s, 2 H, NC$\underline{H}_2$N). ^{13}C NMR (DMSO-d_6), δ: 15.3 (C$\underline{\text{C}}H_3$); 45.1 (C$\underline{\text{Me}}$); 48.8 (C$\underline{H}_3N^+$); 61.4 (C(4), C(8)); 67.4 (C(9), C(10)); 79.1 (N$\underline{\text{C}}H_2$N); 206.9 (C=O). IR (Nijol), ν/cm^{-1}: 1730 (C=O). Found (%): C, 41.00; H, 5.93; N, 8.70. $C_{11}H_{29}IN_2O$. Calculated (%): C, 40.99; H, 5.90; N, 8.70.

5,7-Dimethyl-6-oxo-1-propyl-1-aza-1-azoniaadamantane iodide (1d). Propyl iodide (8.5 g, 0.05 mol) was added to a solution of 5,7-dimethyl-1,3-diazaadamantan-6-one (9 g, 0.05 mol) in dry benzene (150 mL). The mixture was refluxed for ~5 h; after cooling, the precipitate was filtered off, washed with benzene, and dried. Yield 9.9 g (57%) (from $CHCl_3$), m.p. 184—185 °C (dec.). ^{1}H NMR ($CDCl_3$), δ: 1.00—1.12 (m, 9 H, 3 Me); 1.75—1.85 (m, 2 H, MeC$\underline{H}_2$CH$_2$); 2.98 (d, 2 H, H_{ax}(4), H_{ax}(8), J = 14.6 Hz); 3.57 (d, 2 H, H_{ax}(9), H_{ax}(10), J = 11.5 Hz); 3.65—3.73 (m, 2 H, MeCH$_2$C$\underline{H}_2$); 3.90 (d, 2 H, H_{eq}(4), H_{eq}(8), J = 12.7 Hz); 4.45 (d, 2 H, H_{eq}(9), H_{eq}(10), J = 12.0 Hz); 5.48 (s, 2 H, NC$\underline{H}_2$N). Found (%): C, 44.48; H, 6.64; N, 8.18. $C_{13}H_{23}N_2OI$. Calculated (%): C, 44.57; H, 6.57; N, 8.00.

Ring cleavage reactions of the salts

Ring cleavage of salt 1a by 5 equiv. KOH in water. Compound **1a** (1.2 g, 0.0039 mol) was added to a solution of KOH (1 g, 0.020 mol) in H_2O (20 mL) and the mixture was stirred for 12 h. Then the mixture was diluted with water (100 mL) and kept for 16 h at 4 °C. The precipitate was filtered off, washed with water, and recrystallized from EtOH to give 0.46 g (64%) of product **2a**. The spectral characteristics were reported previously.[11]

Ring cleavage of salt 1b by 5 equiv. KOH in water. Salt **1b** (1 g, 0.0025 mol) was placed in a solution of KOH (0.69 g, 0.012 mol) in H_2O (12 mL). A yellow precipitate was formed immediately. Water (12 mL) was added to the solution and the mixture was stirred for 4 h. Then the mixture was additionally diluted with water (70 mL) and kept for 16 h at 4 °C. The yellowish precipitate was filtered off, washed with water and ethanol, and dried. The precipitate (0.48 g) was a mixture of products **2b** and **3b** (molar ratio 2 : 1; yields 40 and 16%, respectively). ^{1}H NMR ($CDCl_3$), δ: 0.85 (s, 3 H, 2 CH$_3$ (**3b**)); 0.91, 0.93 (both s, 3 H each, 2 Me (**2b**)); 1.80 (d, 1 H, OH (**2b**), J = 4.7 Hz); 2.32 (dd, 1 H, H_{ax}(6)/H_{ax}(8) (**2b**), J = 11.2 Hz, J = 2.2 Hz); 2.38—2.60 (m, 5 H, CH$_2$ (**3b**), (**2b**)); 2.80 (br.s, 1 H, NH (**3b**)); 3.02 (d, 1 H, CH$_2$ (**3b**), J = 11.9 Hz); 3.07 (d, 1 H, H_{ax}(2) (**2b**), J = 13.5 Hz); 3.22 (d, 1 H, CH$_2$ (**3b**), J = 14.1 Hz); 3.30 (d, 1 H, H(9) (**2b**), J = 3.7 Hz); 3.43—3.55 (m, 3 H, H(10), H_{eq}(2) (**2b**), CH$_2$ (**3b**)); 3.67 (s, 1H, CH$_2$Ar (**3b**)); 3.75 (d, 1 H, H(10) (**2b**), J = 14.9 Hz); 4.32 (d, 1 H, H_{eq}(4) (**2b**), J = 13.5 Hz); 7.34—7.44, 7.46—7.53, 7.55—7.66, 7.83—7.91 (all m, 6 H each, CH, Ar (**2b**, **3b**)); 7.97 (s, 1 H, CHO (**2b**)).

Ring cleavage of salt 1b by 5 equiv. KOH in water in the presence of formaldehyde. A solution (2.0 g, 0.005 mol) of salt **1b** in water (70 mL) was added to a solution of KOH (1.4 g, 0.025 mol) and formaldehyde (0.76 g, 0.025 mol) in water (30 mL), and the mixture was stirred for 7 h at room temperature. The yellowish precipitate was filtered off, washed with water and ether, and dried to give 1.6 g (95%) of compound **2b**, m.p. 235—240 °C. Found (%): C, 61.36; H, 7.05; N, 12.34. $C_{17}H_{23}N_3O_4$. Calculated (%): C, 61.25; H, 6.95; N, 12.60. ^{1}H NMR (DMSO-d_6), δ: 0.76, 0.77 (both s, 3 H each, 2 Me); 2.18—2.37 (m, 4 H, H(6), H(8)); 2.50 (d, 1 H, H_{ax}(4), J = 13.8 Hz); 3.02 (d, 1 H, H_{ax}(2), J = 13.5 Hz); 3.15 (d, 1 H, H(9), J = 5.1 Hz); 3.39 (d, 1 H, C$\underline{H}_2$Ar, J = 14.9 Hz); 3.54 (d, 1 H, H_{eq}(2), J = 11.7 Hz); 3.60 (d, 1 H, C$\underline{H}_2$Ar, J = 15.2 Hz); 4.09 (d, 1 H, H_{eq}(4), J = 13.9 Hz); 4.98 (d, 1 H, OH, J = 5.1 Hz); 7.46—7.56 (m, 1 H, H(Ar)); 7.65—7.70 (m, 2 H, H(Ar)); 7.85—7.95 (m, 2 H, H(Ar), CHO).

Ring cleavage of salts 1c, 1d by 5 equiv. KOH in water (general procedure). A solution of the salt (0.005 mol) and KOH (1.5 g, 0.0025 mol) in water (35 mL) was stirred for ~35 h. The reaction mixture was extracted with chloroform, and the extract was dried over anhydrous Na_2SO_4 and concentrated to dryness. The yellowish oil thus formed was analyzed.

Ring cleavage of salt 1c. Mixture of products **3c** and **4c** (0.48 g, molar ratio 3 : 1, yields 40 and 13%, respectively). IR (film), ν/cm^{-1}: 1715 (C=O (**3c**)). ^{1}H NMR (DMSO-d_6), δ: 0.66 (s, 2 H, 2 Me (**4c**)); 0.75 (s, 6 H, 2 Me (**3c**)); 2.03 (s, 1 H, NC$\underline{H}_3$ (**4c**)); 2.11 (s, 3 H, NC$\underline{H}_3$ (**3c**)); 2.19—2.25 (m, 2.66 H, H_{ax}(2), H_{ax}(4) (**3c**), H_{ax}(2), H_{ax}(4) (**4c**)); 2.32 (d, 0.66 H, H_{eq}(2), H_{eq}(4) (**4c**), J = 10.8 Hz); 2.36 (dd, 0.66 H, H_{ax}(6), H_{ax}(8) (**4c**), J = 13.7 Hz, J = 2.7 Hz); 2.57 (dd, 2 H, H_{ax}(6), H_{ax}(8) (**3c**), J = 13.9 Hz, J = 2.7 Hz); 2.77 (d, 0.66 H, H_{eq}(6), H_{eq}(8) (**4c**), J = 13.9 Hz); 2.97 (br.s, 0.33 H, H(9) (**4c**)); 3.11 (d, 2 H, H_{eq}(2), H_{eq}(4) (**3c**), J = 11.7 Hz); 3.24 (d, 2 H, H_{eq}(6), H_{eq}(8) (**3c**), J = 13.7 Hz); 4.70 (br.s, 0.33 H, NH (**4c**)). ^{13}C NMR (DMSO-d_6), δ: 17.5 (C$\underline{\text{H}}_3$C (**3c**)); 21.5 (C$\underline{\text{H}}_3$C (**4c**)); 36.5 (MeC$\underline{\text{}}$ (**4c**)); 45.1 (MeC$\underline{\text{}}$ (**3c**)); 46.5 (NC$\underline{\text{H}}_3$ (**4c**)); 49.0 (NC$\underline{\text{H}}_3$ (**3c**)); 59.5, 60.5 (CH$_2$ (**4c**)); 63.2, 68.8 (CH$_2$ (**3c**)); 76.5 (C$\underline{\text{O}}$H, (**4c**)); 210.5 (C$\underline{\text{}}$=O (**3c**)).

Ring cleavage of salt 1d. Mixture of products **3c** and **4c** (0.01 g, molar ratio 10 : 1). ^{1}H NMR ($CDCl_3$), δ: 0.74 (s, 0.6 H, 2 Me (**4d**)); 0.80—0.86 (m, 6.3 H, 2 Me (**3d**), $C\underline{H}_3CH_2$ (**4d**)); 0.89 (t, 3 H, $C\underline{H}_3CH_2$ (**3d**), J = 7.3 Hz); 1.18—1.27 (m, 0.2 H, $CH_2C\underline{H}_2Me$ (**4d**)); 1.40—1.53 (m, 2 H, $CH_2C\underline{H}_2Me$ (**3d**)); 2.00 (t, 0.2 H, $NC\underline{H}_2CH_2Me$ (**4d**), J = 7.1 Hz); 2.08—2.16 (m, 2.2 H, $NC\underline{H}_2CH_2Me$ (**3d**), CH_2 (**4d**)); 2.27 (dd, 2 H, CH_2 (**3d**), J = 11.5 Hz, J = 1.8 Hz); 2.43 (d, 0.2 H, CH_2 (**4d**), J = 11.3 Hz); 2.52 (d, 0.2 H, CH_2 (**4d**), J = 12.7 Hz); 2.77 (d, 2 H, CH_2 (**3d**), J = 12.7); 2.86 (d, 0.2 H, CH_2 (**4d**), J = 13.9 Hz); 3.03—3.17 (m, 2.1 H, CH_2 (**3d**), H(9) (**4d**)); 3.23 (d, 2 H, CH_2 (**3d**), J = 13.7 Hz).

This work was supported by the Russian Foundation for Basic Research (Project No. 06-03-33077).

References

1. J.-M. Lehn, *Supramolecular Chemmistry. Concepts and Perspectives*, VCH, Weinheim—New York—Basel—Cambridge—Tokyo, 1995.
2. H.-J. Schneider and A.K. Yatsimirsky, *Principles and Methods in Supramolecular Chemistry*, John Wiley and Sons Ltd, Chichester, England, 2000, 349 pp.
3. C. Janiak, *J. Chem. Soc.*, *Dalton Trans.*, 2003, 2871.
4. S. Kitagawa, R. Kitaura, and S. Noro, *Angew. Chem. Int. Ed. Engl.*, 2004, **43**, 2334.
5. J. B. Beck and S. J. Rowan, *Polymer Preprints*, 2004, **45**, 79.
6. J. B. Beck and S. J. Rowan, *J. Am. Chem. Soc.*, 2003, **125**, 13922.
7. S. Weidmann, *Annual Review of Physiology*, 1993, **55**, 1.
8. A. Samhammer, U. Holzgrabe, and R. Haller, *Arch. Pharm. (Weinheim, Ger.)*, 1989, **322**, 551.
9. (a) G. L. Garrison, K. D. Berlin, B. J. Scherlag, R. Lazzara, E. Patterson, T. Fazekas, S. Sangiah, C. L. Chen, F. D. Schubot, and D. van der Helm, *J. Med. Chem.*, 1996, **39**, 2559; (b) M. Paroczai and E. Karpati, *Pharmacol. Res.*, 1991, **24**, 149.
10. (a) P. Comba, B. Martin, A. Prikhod´ko, H. Pritzkow, and H. Rohwer, *Comptes Rendus Chimie*, 2005, **6**, 1506; (b) P. Comba, M. Kerscher, *Cryst. Eng. Comm.*, 2004, **6**, 197; (c) S. Z. Vatsadze, V. S. Tyurin, N. V. Zyk, A. V. Churakov, L. G. Kuz´mina, E. V. Avtomonov, R. D. Rakhimov, and K. P. Butin, *Izv. Akad. Nauk. Ser. Khim.*, 2005, 1773 [*Russ. Chem. Bull., Int. Ed.*, 2005, **54**, 1825].
11. S. Z. Vatsadze, V. S. Tyurin, A. I. Zatsman, M. A. Manaenkova, V. S. Semashko, D. P. Krut´ko, N. V. Zyk, A. V. Churakov, and L. G. Kuz´mina, *Zh. Org. Khim.*, 2006, **42**, 1225 [*Russ. J. Org. Chem.*, 2006, **55** (Engl. Transl.)].
12. I. Watt, S. N. Whittleton, and S. M. Whitworth, *Tetrahedron*, 1986, **42**, 1047.
13. a) L. F. Tietze, T. Eicher, *Reaktionen und Synthesen im organisch-chemischen Praktikum und Forschungslaboratorium*, Georg Thieme Verlag, Stuttgard—New York, 1991; b) *Organikum*, *Organisch-chemisches Grundpraktikum*, VEB Deutscher Verlag Der Wissenschaften, Berlin, 1990.
14. G. G. Minasyan, M. B. Mkrtchyan, and Ts. E. Agadzhanyan, *Armyanskii khim. Zh.* [*Armenian Chem. J.*], 1986, **39**, 44.
15. G. G. Minyasyan, A. D. Arutyunyan, G. G. Adamyan, and Ts. E. Agadzhanyan, *Khim. Geterotsikl. Soedinen.* [*Chem. Heterocycl. Comp.*], 1994, **3**, 401.

Received May 30, 2007