ISSN 1070-3632, Russian Journal of General Chemistry, 2008, Vol. 78, No. 4, pp. 614–622. © Pleiades Publishing, Ltd., 2008.
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[1+1]-Cyclization of 4-(1-Adamantyl)-2,6-diformylphenol with 1,3-Bis(aminoalkyl)adamantanes

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Received July 20, 2007

Abstract—Selective [1+1]-cyclization of 4-(1-adamantyl)-2,6-diformylphenol with 1,3-bis(aminoalkyl)-adamantane under high dilution conditions in methanol was used to synthesize a new type of adamantine araliphanes, macrocyclic nitrogen-containing compounds with phenolic and adamantane fragments incorporated in the macroring. The [1+1]-cyclization reaction proceeds unusually to form, along with macrocyclic Schiff bases, methanol addition products at one of the N=CH groups of these compounds. The [1+1]-cyclization pattern is shown to depend on the reaction conditions and the structure of the starting diamine.

DOI: 10.1134/S1070363208040178

Macrocyclic polyimines (Schiff bases) attract enduring and widesperead researcher's attention, primarily due to their complex-forming properties. The possibility of widely varying dialdehydes and diamines used as starting materials allows synthesis of various-size macrocycles incorporating fragments of various nature: aliphatic, carbocyclic, and heteroaromatic [1–3]. The presence of diverse fragments with diverse functional substituents endows such macrocycles with the ability for selective molecular recognition of guests of various nature.

Azomethines and their reduction products and complexes exhibit a broad spectrum of properties that deserve steadfast attention. These are catalytic activity [4], luminescent [5], electrochemical [6], and magnetic [7] properties, as well as biologic activity [8]. Macrocyclic Schiff bases and their complexes are considered as a new class of stable materials for non-linear optical studies [9] and potential contrast compounds for medical diagnostics and biomedical studies [10].

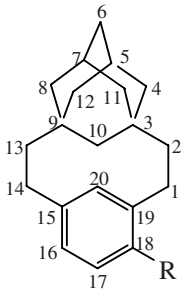
The synthesis of macrocycles by the Schiff reaction is facile but nonselective: As a result, complex mixtures of products including various-size macrocycles formed by [1+1]-, [2+2]-, [3+3]-, and other cyclocondensations and intermolecular acyclic condensations are obtained [3]. Therefore, individual reaction products are too difficult and often impossible to isolate. By this reason, thorough choice of reaction conditions in each specific case is needed. Nowadays the most popular synthetic approaches to macrocyclic Schiff bases make use of templates of different nature and high-dilution reaction conditions [3, 11].

In the present work we have synthesized a new type of adamantane araliphanes, macro-cylic nitrogen-containing compounds having phenolic and adamantly fragments incorporated in the macroring. The term "araliphane" was introduced in the chemistry of cyclic compounds in 1990s to define cyclophanes in which the aromatic fragment is replaced by aliphatic or alicyclic.

The first representatives of this type of compounds, [2.2](1,3)-adamantano- and dithia[3.3](1,3)-adamantana–araliphanes **A, B** and some of their analogs and derivatives, were synthesized [12–14].

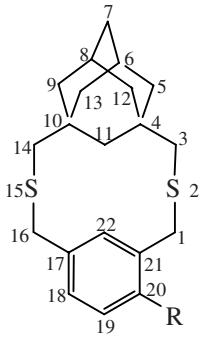
Dithiaadamantana-araliphanes **B** were prepared by cyclization of 1,3-bis(sulfanylmethyl)adamantanes with the corresponding bis(bromomethyl)benzenes. Oxidation of thio derivatives **B** to sulfones, followed by pyrolysis gave araliphanes **A**.

In the present work we started from 4-(1-adamantyl)-2,6-diformyl-phenol (**I**). It was prepared



A

[2.2](1,3)-Adamantana-methacyclophane-18-R



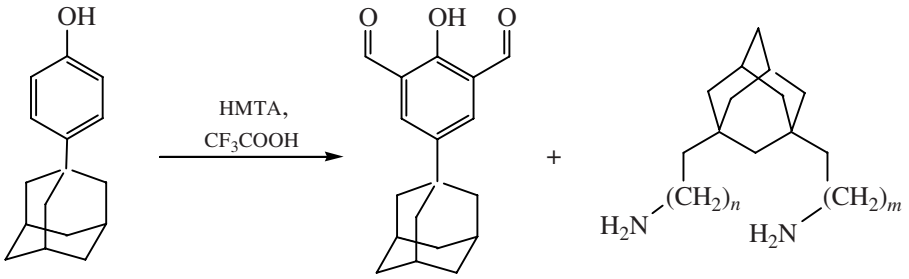
B

2,15-Dithia-[3.3]-(1,3)-Adamantana-methacyclophane-20-R

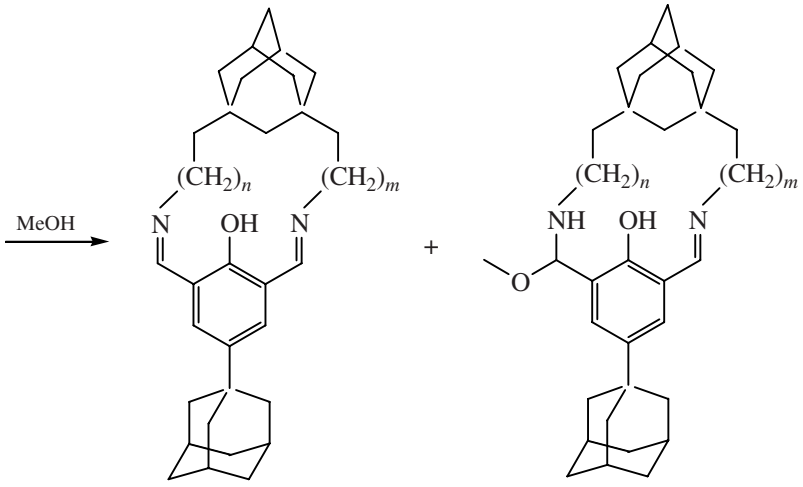
by the reaction of 4-(1-adamantyl) phenol with hexamethylenetetramine in a trifluoroacetic acid medium (yield 96%) by a specially developed procedure. Dialdehyde **I** was reacted with 1,3-di(aminoalkyl)adamantanes **II–IV** under high-dilution conditions in a methanol–chloroform medium. It was found that the reaction proceeds selectively at room temperature to give nitrogen-containing adamantanophanes via [1+1]-cyclization exclusively. The yields are close to quantitative. Along with expected macrocyclic Schiff bases **V–VII**, methanol addition products at one of the N=CH bonds of these compounds, i.e. methoxy derivatives **VIII–XI**, are formed (see table).

Let us dwell specially on the nomenclature of the compounds obtained. It is based on that accepted for adamantyl–araliphanes **A, B** [13], and the only difference is in macroring atom numbering.

Vogtle and co-workers [12–14] prepared only symmetrical macrorings, while we have both symmetrical and unsymmetrical compounds. Therefore, to preserve a constant numbering of the 1,3-adamantane fragment, we suggest to start numbering from this fragment, rather than from $ArCH_2$, like was the case of compounds **A, B**.



I **II–IV**



V–VII **VIII–XI**

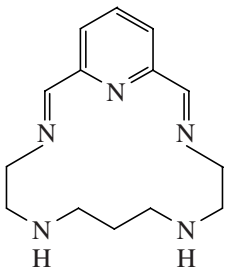
II, V, VIII, $n = m = 0$; **III, VI, IX**, $n = 0$, $m = 1$; **IV, VII, XI**, $n = m = 1$; **X**, $n = 1$, $m = 0$.

Reaction conditions and yields of reaction products

Starting diamine, no. (amount)	Reaction time, h (room temperature)	Reaction product			
		Schiff base		methoxy derivative	
		comp. no.	yield	comp. no.	yield
II, (0.5 mmol, 0.1 g)	120	**V**	0.24 g, 100%		
II, (0.75 mmol, 0.15 g)	24			**VIII**	0.29 g, 78%
III, (0.5 mmol, 0.104 g)	120	**VI**	0.21 g, 92%	–	
III, (0.75 mmol, 0.156 g)	12	**VI**	0.05 g, 15%	**IX + X**	0.28 g, 78%
IV, (0. 5 mmol, 0.11 g)	12	**VII**	0.07 g, 29%	**XI**	0.19 g, 76%
IV, (0. 75 mmol, 0.165 g)	96	**VII**	0.12 g, 34%	**XI**	0.24 g, 63%
IV, (0. 25 mmol, 0.055 g)[a]	12 + 1 h under reflux	**VII**	0.11 g, 70%		

[a] The reaction was carried out in ethanol.

Both specific features of the reaction of dialdehyde **I** with 1,3-di(aminoalkyl)adamantanes **II–IV** are nontrivial. As known, there are only a few examples of [1+1]-cyclocondensations leading to macrocyclic Schiff bases, and they usually relate to fairly large cycles: from 17- to 27-membered and larger [3, 15–17]. In our case, small and sufficiently rigid cycles, i.e. 12-, 13-, and 14-membered cycles with 10 cycle-forming atoms incorporated in rigid fragments, are formed in high yields. The formation of cyclic monoimines like **VIII–XI** in reactions of dialdehydes with diamines has, to our knowledge, never been reported. The only exception is a complex with the ligand formed by methanol addition at one of the CH=N bonds of ligand L (see below), whose formation was observed by Nelson [2] in the course of transmetalation of Ag^+ with Ni^{2+} in the silver complex $[AgL]_2[ClO_4]_2$ in anhydrous methanol. The motive force of this process is considered to be the coordination demand of the nickel ion: The silver complex has a pentagonal coordination, while the nickel complex is octahedral.

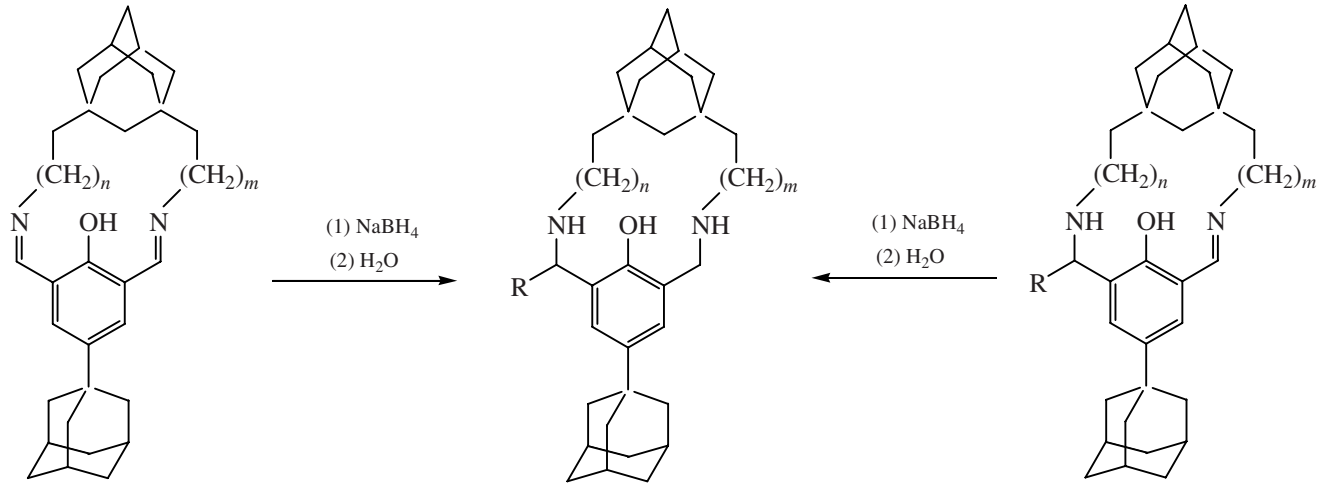


L

Our results show that the chosen reagents complement each other exceptionally well, which is the main structural condition for successful cyclization. The possibility of formation of Schiff bases **V–VII** and methoxy derivatives **VIII–XI** is, in our opinion, determined by two factors: size of the macrocycle formed and stability of compounds **V–VII** and **VIII–XI**. As the CH–N and CH(OMe)NH fragments play an important role in imparting rigidity to the ring, the probability of formation of a "pure" Schiff base should decrease with decreasing ring size. In their turn, rigid reaction conditions (temperature, time) should prevent formation of methoxy derivatives **VIII–XI**.

The experimental results provide evidence for the above suggestions. When the reaction mixture formed by mixing the reagents, aldehyde **I** and amine **II** or **III**, was left for 3–5 days, the only products were Schiff bases **V** and **VI**, respectively. If the mixture was kept for only one day before workup, methoxy derivatives **VIII–X** were isolated exclusively. In the case of the largest macroring, if the reaction mixture was left for a night before treatment, a 1 : 4 mixture of Schiff base **VII** and methoxy derivative **XI** was formed, while if the reaction mixture was left for 24 h, a 1 : 2 mixture of same products was formed. The reaction of dialdehyde **I** with diamine **II** in ethanol for 1 h under reflux lead exclusively to the Schiff base in ~70% yield.

Note that the Schiff bases and corresponding methoxy derivatrives obtained have different solubilities in methanol, what favors their separation. The Schiff bases usually form precipitates and can be filtered off.



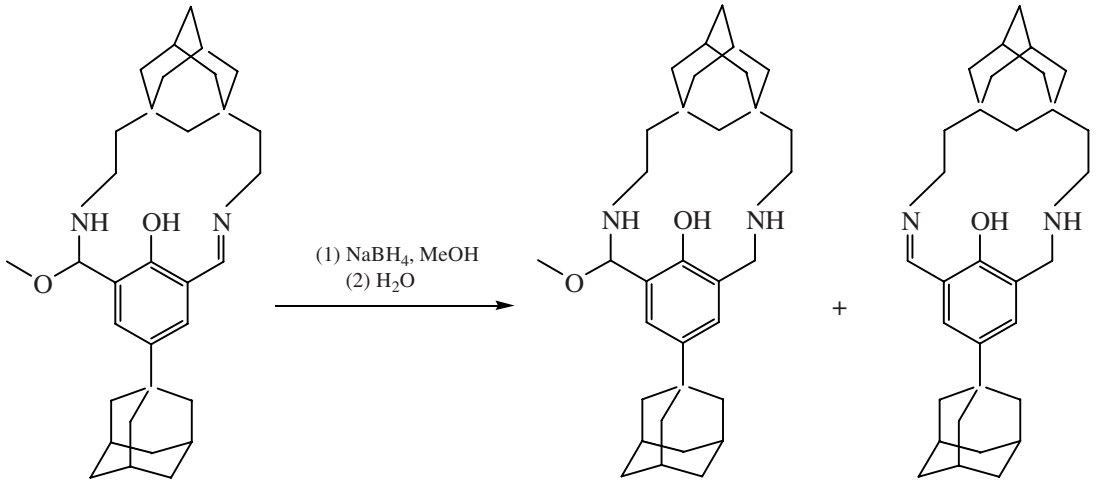
V, VI **XII–XVI** **VIII–X**

XII, $n = m = 0$, R = H; **XIII**, $n = 0$, $m = 1$, R = H; **XIV**, $n = m = 0$; R = OMe; **XV**, $n = 0$, $m = 1$, R = OMe; **XVI**, $n = 1$, $m = 0$, R = OMe.

Reduction of Schiff bases **V, VI** and methoxy derivatives **VIII–X** with sodium borohydride in chloroform–methanol, toluene-methanol, or dioxane-toluene-methanol mixtures leads to corresponding saturated reaction products **XII–XVI**.

The behavior of methoxy derivative **XI** containing the largest 14-membered ring is slightly different. In this case, its reduction gives a mixture of two compounds, saturated **XVII** and unsaturated **XVIII**. The latter product can be called "semi-Schiff" base.

The experimental data show that macrocycle **XVIII** is a secondary reaction product. Derivatives **V–XI** all are yellow powders which decolorize immediately upon reduction. The same picture is also observed also with methoxy derivative **XI**.



XI **XVII** **XVIII**

However, if the reaction mixture just after reduction is diluted with water and methylene chloride and left to stand for some time at room temperature, the solution becomes yellow, and macrocycle **XVIII** is found among the reaction products. Such a facile elimination of methanol from compound **XVII** can be explained by the fact that its macroring size is sufficiently large to withstand additional strain created by the CH=N fragment.

The structure of the compound obtained was studied by means of ^{1}H and ^{13}C NMR spectroscopy and ESI mass spectrometry. It was found that molecular ions are present in the mass spectra, except for that of methoxy derivative **XVII** containing the largest macroring (reduction product of compound **XI**). In the latter case, no molecular ion is observed, but an intense $[M - \mathrm{MeOH}]^+$ ion peak is present.

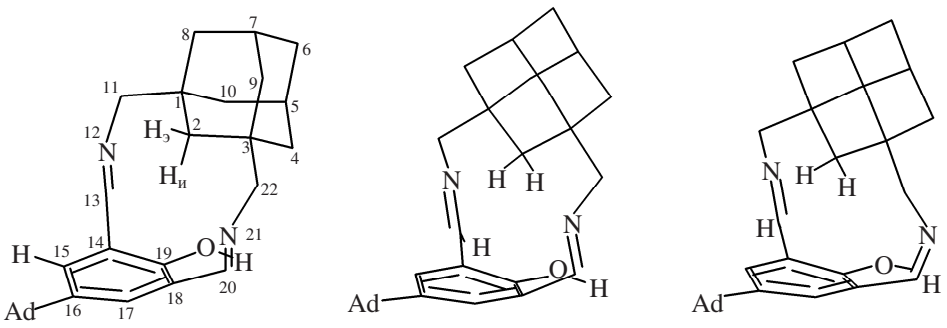
The mass spectra of methoxy derivatives **VIII–XI** and their reduction products **XIV–XVII** all contain $[M + 40]^+$ ion peaks. These ions may arise from capture of K^+ under conditions of mass spectral analysis.

The ^{1}H NMR spectra of Schiff bases **V–VII** show broad singlets of methine (CH=N fragments) and aromatic protons at 8.50–8.90 and 7.30–7.60 ppm, respectively. Protons of the methylene groups bound with nitrogen in the AdCH_2N= and AdCH_2CH_2N= fragments give signals at 3.35 and 3.70 ppm, respectively. Overlapping multiplets of the adamantane protons and α-methylene protons belonging to the AdCH_2CH_2N= fragments are observed in the range 2.20–1.20 ppm. Note that the spectrum of compound **V** having the smallest macroring displays a broadened singlet at 2.35 ppm. We assigned this signal to the intra-annular proton of the methylene group belonging to the adamantane fragment and incorporated in the macroring (see figure). The downfield shift of this proton is evidently associated with the deshielding effect of the benzene ring. As the macroring size increases, this signal disappears. The strong anisotropic effect of the benzene ring on intra-annular hydrogen atoms of the cycle-forming methylene group of the adamantane nucleus in adamantana–araliphanes [12–14, 18].

In the case of monomethoxy derivatives **VIII–XI**, proton signals of the methine (~5.70 ppm) and methoxy (~3.40 ppm) groups belonging to the CH(OCH_3)NH fragment appear. The CH_2NH methylene proton signals are observed at ~3.30 and 2.70 ppm. The spectra of the condensation products of compound **I** with unsymmetrical amine **III** (compounds **IX, X** show double sets of all characteristic signals, implying formation of two isomers with different location of the double bond in the macroring.

In the spectra of the reduction products of Schiff bases **V–VII** and methoxy derivatives **VIII, XI**, that is compounds **XII–XVII**, the signals of the ArCH=N methine protons disappear, and signals of the ArCH_2NH methylene protons appear at ~3.90 ppm. The spectra of the compounds with the smallest-size macrorings all show a signal of the adamantane methylene group incorporated in the macroring at 2.35–2.39 ppm.

The ^{13}C NMR spectra of Schiff bases **V–VII** contain signals of the AdCH=N carbon at ~165 ppm and that of the AdCH_2N= and AdCH_2CH_2N= methylene carbons at ~54 and ~48 ppm, respectively. In the case of monomethoxy derivatives **VIII–XI**, signals of the tertiary and primary carbon atoms of the CH(OCH_3)NH fragment are observed at ~99–100 and ~53–54 ppm, respectively. The spectra of reduction



MM2 molecular structrures and atom numbering in the isomers of compound **V**.

products **XII–XVII** no longer show azomethine carbon signals, and $ArCH_2NH$ methylene carbon signals appear in the range 61–62 ppm. Note that all the spectra show well-defined signals of carbon atoms of the monosubstituted adamantane in the phenolic fragment of the macroring. At the same time, the carbon signals of the adamantanaphane fragment are fairly difficult to assign. This is explained by the fact that the adamantanaphane fragment is incorporated in a sufficiently rigid macroring having no symmetry plane characteristic of 1,3-disubstituted adamantanes. In this case, all the ten carbon atoms of the adamantane fragment may be nonequivalent (see figure). Evidence for this suggestion is provided by the observation in almost all spectra of two signals from tertiary carbon atoms ($C^{Ad}_{5\,7}$), while usually these atoms in 1,3-disubstituted adamantanes have the same chemical shifts [19]. As to the geometric configuration of –CH=N– double bonds in macrorings **V–XI** (see figure), this issue is hardly worth consideration, since we failed to obtain single crystals of the synthesized compounds, appropriate for X-ray diffraction analysis.

Hence, it was shown that the reaction of 4-(1-adamantyl)-2,6-diformylphenol with 1,3-di(aminoalkyl)adamantanes under high dilution involves [1+1]-cyclization to form selectively azaadamantanaaraliphanes in high yields. The specific feature of this reaction is the formation, along with Schiff bases, of less strained monomethoxy derivatives via methanol (solvent) addition at one of two CH=N bonds.

EXPERIMENTAL

The ^1H and ^{13}C NMR spectra were taken on a Bruker Avance 400 spectrometer (400 MHz) in $CDCl_3$, working frequencies 400 and 100 MHz, respectively. The ^1H and ^{13}C chemical shifts were measured against residual $CHCl_2$ (7.25 ppm) and $CDCl_3$ (76.92 ppm) respectively. The numbering of carbon atoms in the ^{13}C NMR spectra is presented in the figure. The ^1H and ^{13}C NMR spectra of the [1+1]-cyclization products was performed in the following terms: $\delta(H_i–C^{Ad}_2)$ is the chemical shift of the intra-annular hydrogen atom of the methylene group belonging to the adamantane fragment included in the macroring; $\delta(C_{1\text{-}Ad})$ and $\delta(C_{1,3\text{-}Ad})$ are the ^{13}C chemical shifts of the 1-adamantyl and 1,3-adamantylidene fragments, respectively.

The ESI mass spectra were obtained on an Agilent 1100 LC/MS device. TLC was carried out on DC Alufolien Kieselgel 60 F_{254} plates (Merck), development in UV light. All solvents used were purified and dehydrated by standard procedures. The elemental analysis data (C, H, N) for all new compounds agree with empirical formula.

4-(1-Adamantyl)-2,6-diformylphenol (I) was obtained from 4-(1-adamantyl)phenol [20] and hexamethylenetetramine in trifluoroacetic acid analogously to 4-*p-tert*-butyl-2,6-diformylphenol [21]. Yield 96%, mp 193-195°C. ^1H NMR spectrum, δ, ppm: 11.43 s (1H, OH), 10.23 s (2H, CH=O), 7.95 s (2H, ArH), 2.12 s (3H, CH^{Ad}), 1.90 s (6H, CH^{Ad}), 1.80–1.60 m (6H, CH^{Ad}). ^{13}C NMR spectrum, δ_C, ppm: 192.46 (CHO), 161.77, 143.45, 134.45, 134.44, 122.80 (C^{Ar}), 43.00, 36.44, 35.76, 28.72 (C^{Ad}).

1,3-Bis(aminomethyl)adamantane (II), 3-(2-aminoethyl)-1-(aminomethyl)adamantane (III), and 1,3-bis(2-aminoethyl)adamantane (IV) were obtained by reported procedures [22].

Synthesis of derivatives (**V–XI**) *(general procedure).* Methanol, 10 ml, was placed in a three-necked flask equipped with a magnetic stirrer, two dropping funnels, reflux condenser, and gas-inlet tube, and diluted solvents of equimolar amounts of dialdehyde and diamine in methanol were simultaneously added dropwise under argon. Dial-dehyde was preliminary dissolved in chloroform and then diluted with methanol. To dissolve 0.5 mmol of compounds, 3–4 ml of $CHCl_3$ and 45 ml of MeOH were used for dialdehyde and 45 ml of MeOH for diamine. The addition of the reaction components was carried out for 4–5 h, after which the reaction mixture was kept for a given time at room temperature (see table). If the resulting Schiff base precipitated, tt was filtered off and washed with methanol. The mother liquor was evaporated on a rotary evaporator at a temperature of no higher than 25°C. If no precipitate formed, the reaction mixture was evaporated to dryness. The residue was triturated with water, filtered, and dried in air. The reaction products are friable yellow powders. Melting points could be measured only for **IX** + **X** and **XI**, 130–132 and 128–130°C, respectively. The other compounds did not melt up to 300°C.

Reduction of macrocyclic compounds V–XI *(general procedure).* The reaction was carried out at room temperature under argon. Sodium borohydride was added in portions to a stirred solution of the macrocycle. Compound **V** was dissolved in a 1:2 methanol–toluene mixture, compound **VI**, in a 1:1:0.5

toluene–dioxane–methanol mixture, and compounds **VIII, IX + X,** and **XI**, in an 0.5–1.1 chloroform–methanol mixture. To reduce 0.25 mmol of macrocyclic compound, 3.5–7.5 mmol of $NaBH_4$ was used. The reaction mixture was decomposed with water and extracted with toluene or chloroform. The organic extracts were washed with water until neutral pH and evaporated on a rotary evaporator. The following products and yields, %, were obtained: **XII**, 100 (from **V**); **XIII** 94 (from **VII**); **XIV**, 100 (from **VIII**); **XV + XVI**, 92 (from **IX + X**), and **XVII + XVIII**, 83 (from **XI**). The products all do not melt below 300°C.

16-(1-Adamantyl)-12,21-diaza-[3.3](1,3)-adamantanametacyclophane-12,20-dien-19-ol (V). ^{1}H NMR spectrum, δ, ppm: 8.52 br.s (2H, ArCH=N), 7.65 br.s (2H, ArH), 3.35 s (4H, $AdCH_2N$=), 2.39 br.s (1H, H_i–C_2^{Ad}), 2.12–1.31 m (28H, AdH). ^{13}C NMR spectrum, δ_C, ppm: 165.42 (ArCH=N), 159.65, 141.19 (ArC), 54.54 ($AdCH_2N$=), δ ($C_{1\text{-}Ad}$): 43.19, 36.73, 35.56, 28.94; δ ($C_{1,3\text{-}Ad}$): 44.80 (C^2), 40.66, 40.48 ($C^{4,10}$)[1], 39.67, 39.56 ($C^{8,9}$)[1], 36.40 (C^6), 35.10, 34.63 ($C^{1,3}$), 28.72, 28.65 ($C^{5,7}$). Mass spectrum, *m/z* (I_{rel}, %): 443.4 (M^+, 100). $C_{30}H_{38}NO_2$. Calculated *M* 442.65.

16-(1-Adamantyl)-12,21-diaza-[3.4](1,3)-adamantanametacyclophane-12,20-dien-19-ol (VI). ^{1}H NMR spectrum, δ, ppm: 8.90 s, 8.75 br.s, 8.60 br.s (2H, ArCH=N), 8.34 s, 7.95 br.s, 7.35 br.s (2H, ArH), 3.72 m (2H, $AdCH_2CH_2N$=), 3.34 s (2H, $AdCH_2N$=), 2.17–1.30 m (31H, AdH + $AdCH_2CH_2N$=). Mass spectrum, *m/z* (I_{rel}, %): 457.3 (M^+,100). $C_{31}H_{40}NO_2$. Calculated *M* 456.68.

17-(1-Adamantyl)-12,22-diaza-[4.4](1,3)-adamantanametacyclophane-13,21-diene-20-ol (VII). ^{1}H NMR spectrum, δ, ppm: 14.17 br.s (1H, OH), 8.57 br.s (2H, ArCH=N), 7.64 br.s (2H, ArH), 3.63 br.s (4H, $AdCH_2CH_2N$=), 2.10-1.30 m (33H, AdH + $AdCH_2CH_2N$=). ^{13}C NMR spectrum, δ_C, ppm: 166.09 (ArCH=N), 159.37, 141.21, 134.19, 128.18 (ArC), 47.85 ($AdCH_2CH_2N$=), 36.50 ($AdCH_2CH_2N$=); δ ($C_{1\text{-}Ad}$): 43.20, 36.70, 35.55, 28.93; δ ($C_{1,3\text{-}Ad}$): 45.37 (C^2), 42.11 ($C^{4,10,8,9}$), 36.59 (C^6), 32.91 ($C^{1,3}$), 28.83 ($C^{5,7}$). Mass spectrum, *m/z* (I_{rel}, %): 471.5 (M^+, 100). $C_{32}H_{42}NO_2$. Calculated *M* 470.70.

16-(1-Adamantyl)-13-methoxy-12,21-diaza-[3.3]–(1,3)-adamantanametacyclophan-20-ene-19-ol (VIII). ^{1}H NMR spectrum, δ, ppm: 8.26 s (1H, ArCH=N), 7.57 s (1H, Ar–H), 7.19 br.s (1H, ArH), 5.74 s (1H, C*H*OMe), 3.40 s (3H, OCH_3), 3.40–3.26 m (4H, $AdCH_2N$= + $AdCH_2NH$), 2.35 br.s (1H, H_i–C_2^{Ad}), 2.06–1.24 m (28H, AdH). ^{13}C NMR spectrum, δ_C, ppm: 165.49, 165.39 (Ar–CH=N), 157.31, 140.75, 127.82, 126.77, 124.81, 117.95 (ArC), 99.35 (ArC*H*OMe), 53.82 ($AdCH_2N$=), 53.79 (OCH_3), 39.36 ($AdCH_2NH$); δ ($C_{1\text{-}Ad}$): 43.21, 36.67, 35.45, 28.88; δ ($C_{1,3\text{-}Ad}$): 43.10 (C^2), 40.15 ($C^{4,10}$, $C^{8,9}$), 36.15 (C^6), 34.75 ($C^{1,3}$), 28.46, 28.43 ($C^{5,7}$). Mass spectrum, *m/z* (I_{rel}, %): 515.1 [*M* + K]$^+$ (82), 475.1 (M^+, 100). $C_{31}H_{42}N_2O_2$. Calculated, %: *M* 474.69.

16-(1-Adamantyl)-13-methoxy-12,21-diaza-[3.4]–(1,3)-adamantanametacyclophan-20-en-19-ol (IX) and 17-(1-adamantyl)-14-methoxy-13,21-diaza-[4.3]–(1,3)-adamantanametacyclophan-21-en-20-ol (X). ^{1}H NMR spectrum, δ, ppm: 8.33 s, 8.26 s, 8.24 s, (1H, ArCH=N), 7.57 s, 7.55 s (1H, ArH), 7.17 br.s, 7.15 s (1H, Ar–H), 5.73 br.s, 5.71 s (1H, C*H*OMe), 3.55 m (2H, $AdCH_2N$= + $AdCH_2CH_2N$=), 3.39 s (3H, OCH_3), 3.38 s, 3.37 s, 3.24 br.s, 3.22 br.s, 2.68 m (2H, $AdCH_2NH$ + $AdCH_2CH_2NH$), 2.34 br.s, 2.32 br.s (1H, H_i–C_2^{Ad}), 2.06-1.26 m (30H, AdH + $AdCH_2CH_2$. ^{13}C NMR spectrum, δ_C, ppm: 165.42, 165.32, 164.77 (Ar–CH=N), 157.39, 157.34, 157.24, 140.68, 127.73, 127.55, 126.76, 126.54, 124.87, 118.01, 117.94 (Ar–C), 99.49, 99.37 (Ar*C*HOMe), 54.60 ($AdCH_2N$=), 53.91, 53.82 (OCH_3), 48.16 ($AdCH_2CCH_2N$=), 39.44 (CH_2CH_2NH), 34.80, 34.75 ($AdCH_2CH_2N$=); δ ($C_{1\text{-}Ad}$): 43.21, 36.67, 35.43, 28.88; δ ($C_{1,3\text{-}Ad}$): 45.85, 45.05 (C^2), 41.90, 41.83 ($C^{4,10}$)[1], 40.29, 40.23 ($C^{8,9}$)[1], 36.49, 36.33 (C^6), 32.71, 32.58 ($C^{1,3}$), 28.68 ($C^{5,7}$). Mass spectrum, *m/z* (I_{rel}, %): 529.1 [*M* + K]$^+$, (100), 489.1 (M^+, 90). $C_{32}H_{44}N_2O_2$. Calculated *M* 488.72.

17-(1-Adamantyl)-14-methoxy-13,22-diaza-[4.4]–(1,3)-adamantanametacyclophan-21-ene-20-ol (XI). ^{1}H NMR spectrum, δ, ppm: 8.33 s (1H, ArCH=N), 7.55 s (1H, Ar–H), 7.16 br.s (1H, ArH), 5.71 s (1H, CHOMe), 3.56 m (2H, $AdCH_2CH_2N$=), 3.39 s (3H, OCH_3), 3.38 m, 2.68 m (2H, $AdCH_2CH_2N$=), 2.07–1.20 m (33H, Ad-H + $AdCH_2CH_2$). ^{13}C NMR spectrum, δ_C, ppm: 164.76 (ArCH=N), 157.32, 140.70, 127.56, 126.58, 124.88, 118.02 (ArC), 99.49 (Ar*C*HOMe), 53.92 (OCH_3), 48.36, 47.77, 47.52 ($AdCH_2CH_2N$= + $AdCH_2CH_2NH$), 36.45 ($AdCH_2$ · CH_2N); δ ($C_{1\text{-}Ad}$): 43.22, 36.68, 35.44, 28.89; δ ($C_{1,3\text{-}Ad}$): 45.16 (C^2), 41.96 ($C^{4,10}$, $C^{8,9}$), 36.52 (C^6), 32.83 ($C^{1,3}$), 28.89 ($C^{5,7}$). Mass spectrum, *m/z* (I_{rel}, %): 543.1 [*M* +

[1] The assignment is not inambiguously.

K] (66), 503.1 (M^+, 61), 471.1 [M – MeOH]$^+$ (100). $C_{33}H_{46}N_2O_2$. Calculated, %: M 502.75.

16-(1-Adamantyl)-12,21-diaza-[3,3] (1,3)-adamantanametacyclophan-19-ol (XII). ^{1}H NMR spectrum, δ, ppm: 6.93 br.s (2H, ArH), 3.82 br.s (4H, ArCH_2N), 2.39-2.29 m (5H, H_i–C_2^{Ad} + AdCH_2NH), 2.10–1.30 m (28H, AdH). ^{13}C NMR spectrum, δ_C, ppm: 154.34, 141.54, 124.90, 123.96 (ArC), 61.72 (ArCH$_2$NH), 53.22 (AdCH$_2$NH); δ ($C_{1\text{-}Ad}$): 43.49, 36.88, 35.37, 29.06; δ ($C_{1,3\text{-}Ad}$): 44.01 (C^2), 43.43 ($C^{4,10}$)m 40.55 ($C^{8,9}$), 36.78 (C^6), 33.77 ($C^{1,3}$), 28.73, 28.53 ($C^{5,7}$). Mass spectrum, *m/z* (I_{rel}, %): 447.3 (M^+, 100). $C_{30}H_{42}NO_2$. Calculated M 446.68.

16-(1-Adamantyl)-12,21-diaza-[3,4] (1,3)-adamanttanametacyclophan-19-ol (XIII). ^{1}H NMR spec-trum, δ, ppm: 8.93 br.s (1H, NH), 8.55 br.s (1H, NH), 7.47 s (1H, ArH), 4.20 m (4H, ArCH_2NH), 2.96 br.s (2H, AdCH$_2$CH_2NH), 2.55 br.s (2H, AdCH_2NH), 2.10–1.30 m (31H, AdH + AdCH_2CH$_2$). ^{13}C NMR spectrum, δ_C, ppm: 152.89, 143.52, 130.08, 120.36 (ArC), 66.81 (ArCH$_2$NH), 47.86 (AdCH$_2$*C*H$_2$NH), 32.98 (Ad*C*H$_2$CH$_2$NH); δ ($C_{1\text{-}Ad}$): 43.11, 36.63, 35.67, 28.76, δ ($C_{1,3\text{-}Ad}$): 45.96 (C^2), 41.08 ($C^{4,10}$), 38.52 ($C^{8,9}$), 36.63 (C^6), 32.08 ($C^{1,3}$), 28.16 ($C^{5,7}$). Mass spectrum, *m/z* (I_{rel}, %): 461.4 (M^+, 100). $C_{31}H_{44}NO_2$. Calculated, %: M 460.71.

16-(1-adamantanyl)-13-methoxy-12,21-diaza-[3.3](1,3)-adamantanametacyclophan-19-ol (XIV). ^{1}H NMR spectrum, δ, ppm: 7.36 s (1H, ArH), 6.94 br.s (1H, ArH), 5.67 s (1H, CHOMe), 3.91 br.s (2H, ArCH$_2$NH), 3.37 br.s (4H, AdCH$_2$NH), 2.35 br.s (1H, H_i–C_2^{Ad}), 2.05–1.24 m (28H, Ad–H). ^{13}C NMR spectrum, δ_C, ppm: 153.54, 141.43, 124.95, 123.83, 122.56, 122.09 (Ar–C), 99.86 (Ar*C*HOMe), 61.52 (Ar CH$_2$NH), 53.91, 53.70 (AdCH$_2$NH), 53.67 (OCH$_3$); δ ($C_{1\text{-}Ad}$): 43.35, 36.67, 35.47, 28.97; δ ($C_{1,3\text{-}Ad}$): 48.40 (C^2), 40.31, 40.11 ($C^{4,10}$, $C^{8,9}$), 36.70 (C^6), 33.69 ($C^{1,3}$), 28.41, 28.31 ($C^{5,7}$). Mass spectrum, *m/z* (I_{rel}, %): 517.3 [M + K]$^+$ (37), 477.3 (M^+, 100). $C_{31}H_{44}N_2O_2$. Calculated, %: M 476.1.

16-(1-Adamantyl)-13-methoxy-12,21-diaza-[3.4]–(1,3)-adamantanametacyclophan-19-ol (XV) and 17-(1-adamantyl)-14-methoxy-13,21-diaza-[4.3]–(1,3)-adamantanametacyclophan-20-ol (XVI). ^{1}H NMR spectrum, δ, ppm: 7.39 s, 7.38 s, 7.37 s (1H, ArH), 6.96 br.s (1H, ArH), 5.70 s, 5.67 s (1H, C*H*OMe), 3.96 s, 3.93 s (2H, ArCH_2NH), 3.41 s (3H, OCH$_3$), 3.40 s, 2.68 m (2H, AdCH$_2$CH_2NH + AdCH_2NH), 2.35 br.s (1H, H_i-C_2^{Ad}), 2.07–1.27 m (30H, AdH + AdCH_2CH$_2$). ^{13}C NMR spectrum, δ_C, ppm: 153.68, 141.46, 124.95, 123.94, 122.51, 122.20 (Ar–C), 100.28 + 99.97 (Ar*C*HOMe), 61.77, 61.69 (ArCH$_2$NH), 53.97, 53.84 (OCH$_3$), 53.17, 48.44 (Ad*C*H$_2$NH + AdCH$_2$*C*H$_2$NH), 32.58, 32.48 (Ad*C*H$_2$CH$_2$NH); δ ($C_{1\text{-}Ad}$): 43.42, 36.83, 35.53 29.04, δ ($C_{1,3\text{-}Ad}$): 45.92 (C^2), 42.08, 41.98 ($C^{4,10}$)^1, 40.26, 40.16 ($C^{8,9}$)^1, 36.49, 36.41 (C^6), 33.88 ($C^{1,3}$), 28.69, 28.63 ($C^{5,7}$). Mass spectrum, *m/z* (I_{rel}, %): 531.3 [M + K], (100), 491.3 (M^+, 90). $C_{32}H_{46}N_2O_2$. Calculated: M 490.70.

17-(1-Adamantyl)-14-methoxy-13,22-diaza-[4.4]–(1,3)-adamantanametacyclophan-20-ol (XVII) and 17-(1-adamantyl)-13,22-diaza-[4.4](1,3)-adamantanametacyclophan-13-en-20-ol (XVIII). ^{1}H NMR spectrum, δ, ppm: 7.35 br.s (1H, ArH), 6.94 br.s (1H, ArH), 5.65 s (1H, C*H*OMe), 3.94 br.s (2H, ArCH$_2$NH), 3.39 s (3H, OCH$_3$), 3.39, 2.65 m (4H, AdCH$_2$CH$_2$NH), 2.06–1.24 m (33H, AdH + AdCH_2CH$_2$). ^{13}C NMR spectrum, δ_C, ppm: 153.71, 141.43, 124.95, 123.82, 122.51, 122.16 (ArC), 100.28 (Ar*C*HOMe), 53.83 (OCH$_3$), 47.69 (AdCH$_2$*C*H$_2$NH), 32.61 (Ad*C*H$_2$CH$_2$. NH); δ ($C_{1\text{-}Ad}$): 43.42, 36.83, 35.53, 29.04; δ ($C_{1,3\text{-}Ad}$): 43.95 (C^2), 42.04 ($C^{4,10}$, $C^{8,9}$), 36.51 (C^6), 35.42 ($C^{1,3}$), 29.70, 28.98 ($C^{5,7}$). Mass spectrum, *m/z* (I_{rel}, %): 543.1 [M + K]$^+$ (66), 503.1 (M^+, 61), 471.1 [M – MeOH]$^+$ (100). $C_{33}H_{46}N_2O_2$. Calculated, %: M 502.75.

ACKNOWLEDGMENTS

The work was financially supported by the Russian Foundation for Basic Research (project no. 05-03-32845).

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