Synthesis of 5-methylidenehexahydropyrrolo[1,2-*a*]imidazoles and 6-methylideneoctahydropyrrolo[1,2-*a*]pyrimidines by the reaction of 1-alkynyl-1-chlorocyclopropanes with lithium derivatives of 1,2- and 1,3-diaminoalkanes*

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A reaction of 1-alkynyl-1-chlorocyclopropanes with excess of lithium derivative of 1,2-diaminoethane leads to 5-methylidenehexahydropyrrolo[1,2-*a*]imidazoles in 35—72% yields, whereas analogous reaction with lithium derivative of 1,3-diaminopropane gives 6-methylideneoctahydropyrrolo[1,2-*a*]pyrimidine in up to 50% yield. A mechanism of these unusual multi-step processes includes dehydrochlorination of 1-alkynyl-1-chlorocyclopropanes to form conjugated alkynylcyclopropenes capable of addition of monoalkylamide ions at the double bond, leading to the corresponding secondary cyclopropylamines; the latter under the reaction conditions isomerize to the linear imines, which further undergo a cascade cyclization with sequential involvement of the C=N and C≡C bonds.

Key words: alkynylchlorocyclopropanes, 1,2-diaminoethane, 1,3-diaminopropane, hexahydropyrrolo[1,2-*a*]imidazoles, octahydropyrrolo[1,2-*a*]pyrimidines, hexahydropyrimidines, elimination, nucleophilic addition, cyclopropane ring opening, cascade cyclization.

Recently, we have shown[2] that the action of sterically hindered lithium dialkylamides on 1-(alk-1-ynyl)-1-chlorocyclopropanes **1** *in situ* generates conjugated alkynylcyclopropenes. The latter readily add nucleophiles of various nature at the double bond of the cyclopropene ring, such as dialkylamide ions,[2,3] diazoles,[3] alcohols,[4] phenols,[4] thiophenols, and alkanethiols,[5] forming the corresponding functionalized alkynylcyclopropanes in up to 80% yields. Analogous reactions with lithium monoalkylamides,[6] depending on the nature of substituent at the triple bond, lead either to 1,2-dienes, having in the molecule one carbon atom less than in the starting compound, or conjugated iminoalkylcyclopropenes. When monolithium derivatives of 1,2- and 1,3-diaminoalkanes are used in these reactions, carbon skeleton of the starting compounds undergoes complete transformation to form the earlier unknown 5-methylidenehexahydropyrrolo[1,2-*a*]-imidazoles and 6-methylideneoctahydropyrrolo[1,2-*a*]-pyrimidines.[1] Compounds of these series exhibit a wide range of biological activity,[7—10] as well as are convenient precursors for obtaining chiral pyrrolidines.[11] The present work is devoted to the detailed study of these new unusual reactions.

The reaction of 1-chloro-2,2-dimethyl-1-phenylethynylcyclopropane (**1a**) and 1-chloro-1-phenylethynylspiro[2.5]octane (**1b**) with a four-fold excess of lithium 2-aminoethylamide** in THF at 20 °C with subsequent aqueous quenching the reaction mixture leads to 5-benzylidenehexahydropyrrolo[1,2-*a*]imidazoles **3a,b** in 65 and 72% yields, respectively (Scheme 1). In both cases, the formation of mixtures of *Z*- and *E*-isomers was observed with predominance of the latter (1 : 4 for **3a** and 1 : 4.2 for **3b**). Their identification was accomplished based on the NOESY-2D proton spectra having correlations between the methine protons at the double bond and the protons of the methylidene fragment at position 6. In the case of the starting cyclopropane **1c**, having a bulky *tert*-butyl substituent at the triple bond, an exclusive formation of the *E*-isomer of the corresponding bicyclic derivative **3c** in lower (~35%) yield took place. The latter was isolated from the reaction mixture in the individual state by chromatography on Al_2O_3.

The use of lithium derivative of 1,3-diaminopropane in these reactions changes their stereo- and regioselectivity. For instance, the reaction of cyclopropanes **1a** and **1b** with a four-fold excess of this compound leads to 6-benzylideneoctahydropyrrolo[1,2-*a*]pyrimidines **4a** and **4b** as ex-

* For preliminary communication, see Ref. 1.

** In all the cases, the required lithium derivatives of α,ω-diaminoalkanes were obtained by addition of a solution of BuLi in hexane to a small excess of the corresponding diamine in THF.

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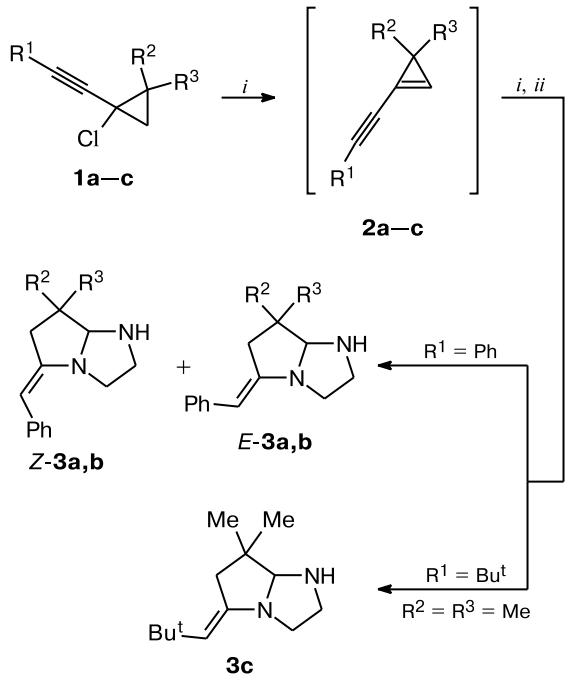
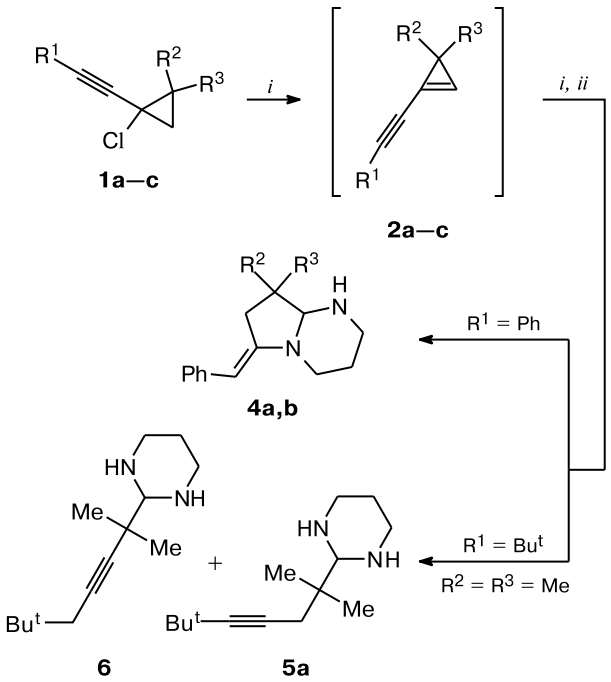
Scheme 1



1, 2	R^1	R^2	R^3	3	R^2	R^3
a	Ph	Me	Me	**a**	Me	Me
b	Ph	$(CH_2)_5$		**b**	$(CH_2)_5$	
c	Bu^t	Me	Me			

Reagents and conditions: *i*. $NH_2(CH_2)_2NH_2$—BuLi, THF, 20 °C; *ii*. H_2O.

Scheme 2



4a: $R^2 = R^3 = Me$; **4b:** $R^2 + R^3 = (CH_2)_5$

Reagents and conditions: *i*. $NH_2(CH_2)_3NH_2$—BuLi, THF, 20 °C; *ii*. H_2O.

clusive *E*-isomers in 50 and 27% yields, respectively (Scheme 2). In contrast to compounds **3**, which are liquids, these both products are crystalline substances, that allowed us to isolate them in the individual state by recrystallization from hexane.

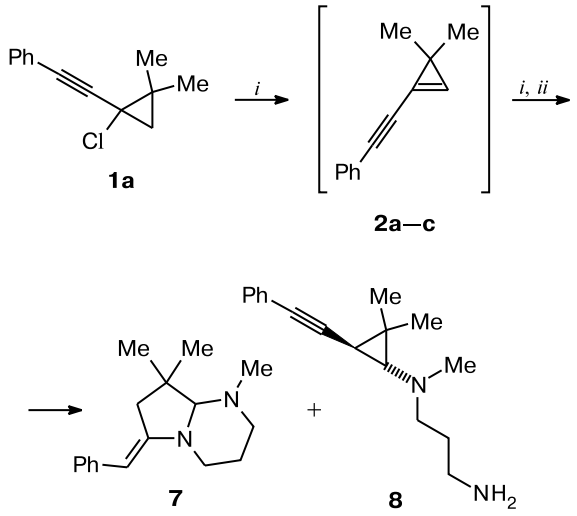
At the same time, the reaction of chlorocyclopropane **1c** with the same reagent, independent on the reaction time, gives no expected bicyclic compounds, rather formation of two similar in the structure products in the ratio 1 : 1.35 in 72% total yield was observed. Comparison of the integral intensities of the signals for the protons of the *tert*-butyl and methyl groups, as well as methylene fragments at the nitrogen atoms (δ 2.6—3.5) reveals that the molecules of these both compounds contain a *tert*-butylethynyl, propane-2,2-diyl, and propylene-1,3-diamine fragments in the ratio 1 : 1 : 1, whereas the number of the signals for the CH_2 groups in their ^{13}C NMR spectra indicates the symmetry of the structure with respect to the central carbon atom of the trimethylene bridge. Proceeding from these data, the minor component of the mixture obtained was identified as aminal **5a**, whereas a predominant one, as its isomer **6**, differing in position of the triple bond (see Scheme 2) and arising, obviously, due to the migration of the latter under the strongly basic conditions.

The structure of the minor product **5a** was also confirmed by alternative synthesis.

As it could have been supposed, the lithium derivative of *N*-methyl-1,3-diaminopropane reacts with chlorocyclopropane **1a** nonselectively. Competition of the primary and secondary amino groups results in the formation of a mixture of the corresponding *E*-isomer of *N*-methyl-substituted pyrimidine **7** and *trans*-isomer of aminocyclopropane **8** in the ratio 1.5 : 1 in 68% total yield (Scheme 3). Compound **7** was successfully isolated by crystallization from hexane in >90% purity and 37% yield, whereas the structure of product **8** was confirmed by comparison of the ^1H and ^{13}C NMR spectra of the reaction mixture with the spectral data for other analogous aminocyclopropanes obtained earlier.[3]

Proceeding from the available data published earlier[3,12—14] and the data obtained in this work, the formation of products **3**, **4**, and **7** can be described as follows (Scheme 4). In the first step, the starting chlorocyclopropanes **1** upon the action of lithium monoalkylamides present in the reaction medium undergo elimination of HCl to generate conjugated alkynylcyclopropenes **2**, which under conditions used add monoalkylamide ions to form cyclopropylamines **9** (see Ref. 3). The latter undergo the ring opening to form linear imines **10**,[12] which due to the presence of the amino group give intramolecular cascade cyclization with sequen-

Scheme 3



Reagents and conditions: *i*. $MeNH(CH_2)_3NH_2$—BuLi, THF, 20 °C; *ii*. H_2O.

tial involvement of the C=N (see Ref. 13) and C≡C bonds (see Ref. 14) through the intermediate formation of the nitrogen-containing cyclic structures **11**.

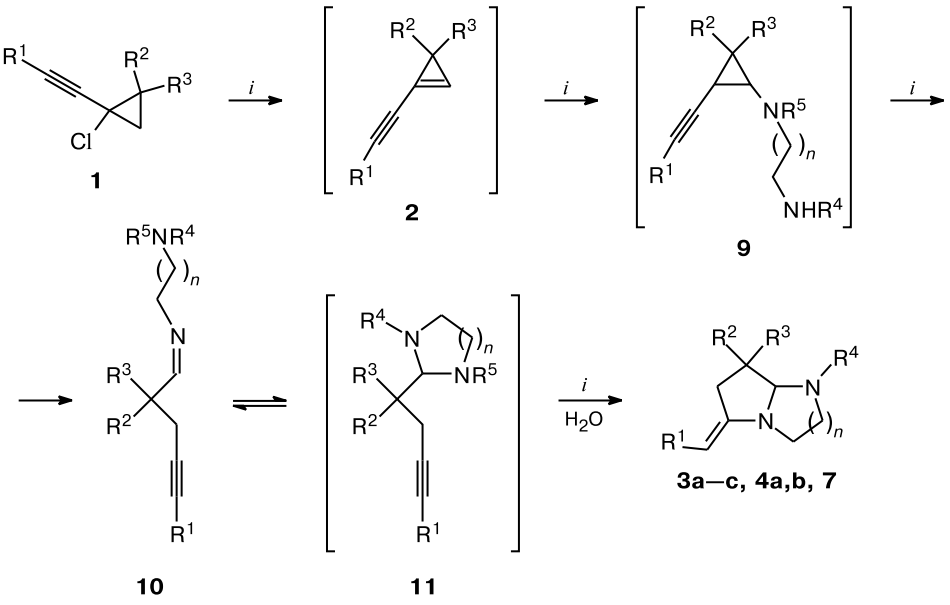
The following data confirm the scheme suggested. Earlier,[3] it has been shown that alkynylchlorocyclopropanes **1** react with lithium dialkylamides by the addition—elimination mechanism to form the corresponding dialkylamino(alkynyl)cyclopropanes. Therefore, it could be expected that lithium monoalkylamides would behave similarly, giving the corresponding secondary cyclopropylamines **9**.

A possibility of the key step of the mechanism suggested, *i.e.*, isomerization of cyclopropylamines **9** to imines **10**, was confirmed by the data,[12] from which it follows that the lithiation of *N*-alkyl-*N*-cyclopropylamines results in the three-membered ring opening to form the corresponding linear imines. Formation of hexahydropyrimidine **5a** by the reaction of chlorocyclopropane **1c** with lithium derivative of 1,3-diaminopropane is an evidence of the analogous process followed by the intramolecular cyclization at the C=N bond (see Scheme 2).

The outcome of the reactions of arylchlorocyclopropanes **12a,b**, containing no triple bond with lithium monoalkyl- and aminoalkylamides confirms a generality of similar transformations. It turned out that heating compounds **12a,b** with a four-fold excess of lithium propylamide in THF at 60 °C for 4—5 h leads to the corresponding imines **15a,b** in 50—55% yield. The latter, obviously, are formed due to the three-membered ring opening in the *N*-lithium derivatives of aminocyclopropanes **14**, which result from the addition of lithium propylamide at the double bond of the *in situ* generated conjugated arylcyclopropenes **13** (Scheme 5).

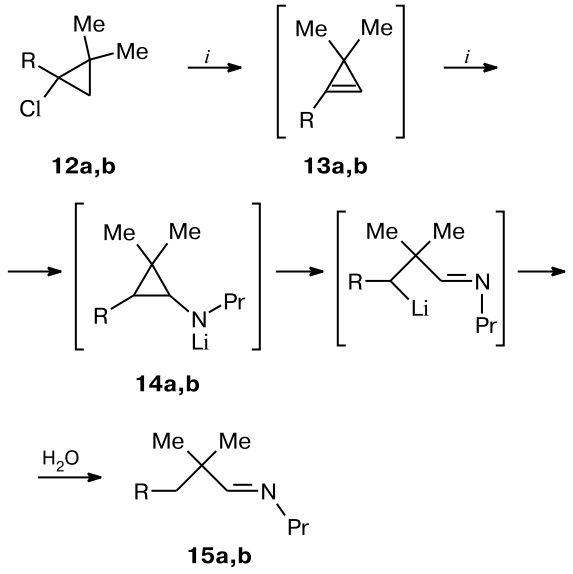
When lithium derivative of 1,3-diaminopropane is used in these reactions, further cyclization of the arising linear imine **16** occurs, consisting in the addition of the primary amino group to the C=N bond and leading to hexahydropyrimidine **17** in 63% yield (Scheme 6).

Scheme 4



Reagents and conditions: *i*. $R^4NH(CH_2)_{n+1}NH_2$—BuLi (n = 1, 2, R^4 = H, Me; R^5 = H, Li), THF, 20 °C.

Scheme 5



14a—17a: R = Ph; **14b—17b**: R = 4-MeOC$_6$H$_4$

Reagents and conditions: *i*. PrNHLi, THF, 20 °C.

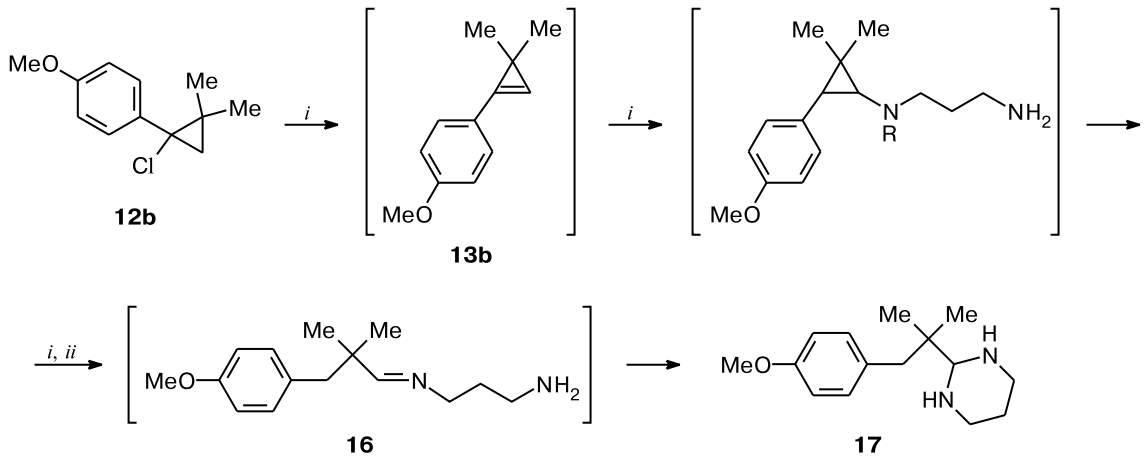
A separate experiment showed that the ring opening also takes place during lithiation of unsubstituted cyclopropylamine **18**. When 0.5 equiv. of Bu^{t}Li was added to its solution in THF-d$_8$ at −90 °C with subsequent heating to −20 °C and quenching with water, the NMR spectroscopic data indicated a complete conversion of the starting compound and formation of 2,4,6-triethylhexahydro-1,3,5-triazine **19**, whose yield determined from the spectral data was 49%. This product, obviously, results from the trimerization of propanaldimine described in the literature,[15] the latter is formed due to the three-membered ring opening in the unstable intermediate lithium cyclopropylamide (Scheme 7).

To confirm possible involvement of aminals **11** in the last step of the mechanism suggested (see Scheme 4), we accomplished an independent synthesis of two representatives of this class of compounds. In the first step, the starting acetylenic chlorides **20** reacted with isobutyraldehyde in the two-phase system toluene—50% aqueous KOH in the presence of tetrabutylammonium iodide.[16] The thus obtained aldehydes **21** (the yields were 58 and 53% for **21a** and **21b**, respectively) further reacted with a three-fold excess of 1,3-diaminopropane in CH_2Cl_2 at room temperature in the presence of anhydrous Na_2SO_4, that led to the target hexahydropyrimidine derivatives **5a,b** in 78—85% yields (Scheme 8).

Addition of compound **5b** to equimolar amount of lithium derivative of 1,3-diaminopropane in THF at room temperature gives exclusively 6-benzylideneoctahydropyrrolo[1,2-*a*]pyrimidine (**4a**), which was isolated in the individual state by recrystallization from hexane in 72% yield (Scheme 9). Compound **5a**, similarly treated, does not undergo the intramolecular cyclization, only being isomerized to aminal **6** by ~50% and forming a mixture of substances analogous to that obtained in the reaction of chlorocyclopropane **1c** with lithium derivative of 1,3-diaminopropane (see Scheme 2).

Formation of isomer **6**, obviously, results from the triple bond migration upon the action of the strongly basic lithium derivative of 1,3-diaminopropane present in the reaction mixture. Significant difference in the behavior of compounds **5a** and **5b** under conditions used, by all accounts, is due to the considerably lower polari-

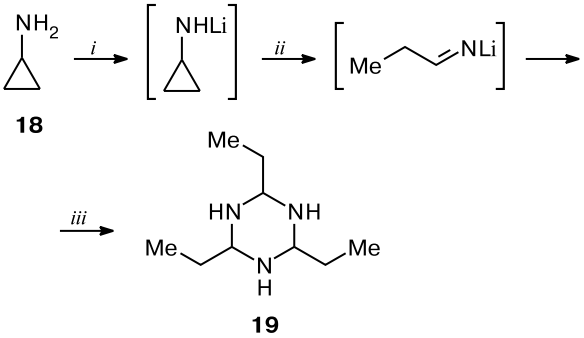
Scheme 6



R = H, Li

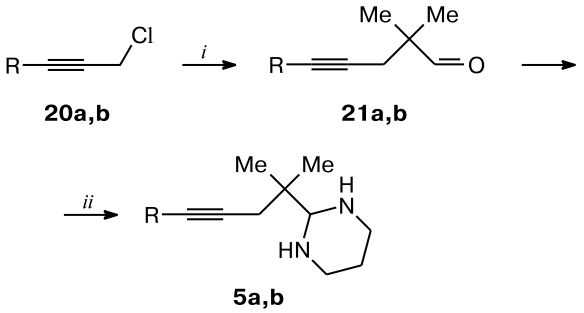
Reagents and conditions: *i*. $NH_2(CH_2)_3NH_2$—BuLi, THF, 50—60 °C; *ii*. H_2O.

Scheme 7



Reagents and conditions: *i*. Bu^{t}Li, THF-d_8, –90 °C; *ii*. THF, –20 °C; *iii*. H_2O.

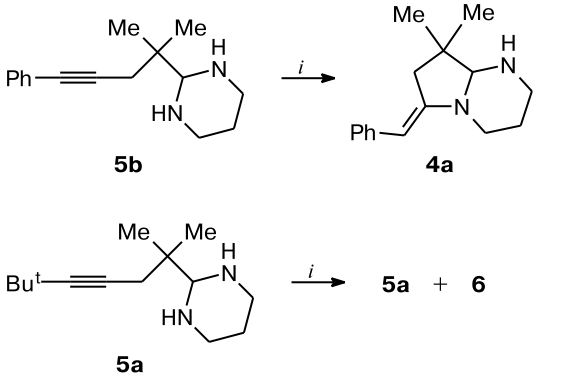
Scheme 8



R = Bu^t (**5a**, **20a**, **21a**), Ph (**5b**, **20b**, **21b**)

Reagents and conditions: *i*. Me_2CHCHO, KOH/H_2O/PhMe, Bu_4NI, 50 °C; *ii*. $H_2N(CH_2)_3NH_2$, CH_2Cl_2, Na_2SO_4.

Scheme 9



Reagents and conditions: *i*. 1) $NH_2(CH_2)_3NH_2$—BuLi, THF, 20 °C; 2) H_2O.

zation of the triple bond in the first compound than in the second, that sharply decreases its reactivity toward nucleophiles.

In conclusion, we have suggested an original approach to the synthesis of 5-methylidenepyrrolo[1,2-*a*]imidazoles and 6-methylideneoctahydropyrrolo[1,2-*a*]pyrimidines based on the reaction of 1-alkynyl-1-chlorocyclopropanes with lithium derivatives of 1,2- and 1,3-diaminoalkanes. A mechanism of these unusual multi-step reactions has been established with identification of the intermediates.

Experimental

GLC-analysis of the starting substances and products obtained was carried out on a Hewlett-Packard 5890 Series II instrument with a HP-1 (30 m×0.153 mm) capillary column and a Hewlett-Packard 3396A automatic integrator. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-200p spectrometer for $CDCl_3$ solutions, using $SiMe_4$ as an internal standard. Mass spectra were recorded on a Finningan MAT INCOS-50 and Finningan DSQ II GLC-MS spectrometers.

The starting 1-alkynyl-1-chlorocyclopropanes **1a—c** were synthesized according to the procedure suggested by us earlier,[17] acetylenic aldehydes **21a,b** were obtained from the corresponding chlorides **20a,b** and freshly distilled isobutyraldehyde.[16]

Reaction of 1-(alk-1-ynyl)-1-chlorocyclopropanes 1a—c with diaminoalkane lithium derivatives (general procedure). A solution of BuLi in hexane (1.6 *M*, 5 mL, 8 mmol) was added to a solution of the corresponding α,ω-diaminoalkane (10 mmol) in anhydrous THF (15 mL) at 0 °C. The starting alkynylchlorocyclopropane **1a—c** (2 mmol) was added to the mixture obtained and this was stirred for 2 h at room temperature. Then the reaction mixture was treated with water, extracted with diethyl ether, the organic layer was 3 times washed with water and dried with anhydrous Na_2SO_4. The solvent was evaporated, and the residue obtained was subjected to chromatography or recrystallization to isolate products **3a—c**, **4a—b**, or a mixture of compounds **5** and **6**.

5-Benzylidene-7,7-dimethylhexahydro-1*H*-pyrrolo[1,2-*a*]-imidazole (3a) was obtained from chlorocyclopropane **1a** and 1,2-diaminoethane in 65% yield as a mixture of *E*- and *Z*-isomers (the ratio was 4 : 1) and isolated by chromatography on neutral Al_2O_3 (hexane—diethyl ether, 10 : 1). Found (%): C, 78.56; H, 8.96; N, 12.13. $C_{15}H_{20}N_2$. Calculated (%): C, 78.90; H, 8.83; N, 12.27.

E-Isomer. ^{1}H NMR, δ: 0.92 (s, 3 H, Me); 1.20 (s, 3 H, Me); 1.35 (br.s, 1 H, NH); 2.76 (dd, 1 H, CHHC=, J = 15 Hz, J = 1.3 Hz); 2.81 (dd, 1 H, CHHC=, J = 15 Hz, J = 1.9 Hz); 3.10—3.22 (m, 4 H, NCH_2CH_2N); 4.29 (s, 1 H, CH); 5.36 (dd, 1 H, PhCH=, J = 1.9 Hz, J = 1.3 Hz); 7.02 (br.t, 1 H, *p*-H, J = 7 Hz); 7.14 (br.d, 2 H, *o*-H, J = 7 Hz); 7.25 (br.t, 2 H, *m*-H, J = 7 Hz). ^{13}C NMR, δ: 21.5 (Me); 26.4 (Me); 39.5 (CMe_2); 46.3, 47.9, 48.7 (3 CH_2); 87.8 (NCHN); 96.7 (PhCH=); 122.9, 126.4, 128.0 (Ph); 139.5 (C(1), Ph); 149.8 (PhCH=C). MS, *m/z*: 229 $[M^+]$, 228 $[M - H]^+$.

Z-Isomer. ^{1}H NMR, δ: 0.99 (s, 3 H, Me); 1.17 (s, 3 H, Me); 1.35 (br.s, 1 H, NH); 2.46 (dd, 1 H, CHHC=, J = 15.1 Hz, J = 1.5 Hz); 2.52 (dd, 1 H, CHHC=, J = 15.1 Hz, J = 1.4 Hz); 3.1—3.3 (m, 4 H, NCH_2CH_2N); 4.29 (s, 1 H, CH); 5.25 (dd, 1 H, PhCH=, J = 1.5 Hz, J = 1.4 Hz); 7.00—7.35 (m, 5 H, Ph). ^{13}C NMR, δ: 21.3 (Me); 26.2 (Me); 38.4 (CMe_2); 46.6, 47.6, 52.2 (3 CH_2); 90.3 (NCHN); 96.7 (PhCH=); 123.2, 127.3, 127.6 (Ph); 138.5 (C(1), Ph); 149.7 (PhCH=C). MS, *m/z*: 229 $[M^+]$, 228 $[M - H]^+$.

5´-Benzylidenehexahydrospiro[cyclohexane-1,7´-pyrrolo-[1,2-*a*]imidazole] (3b) was obtained from chlorocyclopropane **1b** and 1,2-diaminoethane in 72% yield as a mixture of *E*- and *Z*-isomers (the ratio was 4.2 : 1) and isolated by chromatography on neutral Al_2O_3 (hexane—diethyl ether, 10 : 1). Found (%): C, 80.67; H, 8.79; N, 9.97. $C_{18}H_{24}N_2$. Calculated (%): C, 80.55; H, 9.01; N, 10.44.

E-Isomer. ^{1}H NMR, δ: 1.20—1.85 (m, 11 H, 5 CH_2 + NH); 2.72 (dd, 1 H, CHHC=, J = 15.6 Hz, J = 1.7 Hz); 2.81 (dd, 1 H, CHHC=, J = 15.6 Hz, J = 1.1 Hz); 3.05—3.30 (m, 4 H, NCH_2CH_2N); 4.17 (s, 1 H, CH); 5.39 (dd, 1 H, PhCH=, J = 1.7 Hz, J = 1.1 Hz); 7.01 (br.t, 1 H, *p*-H, J = 7 Hz); 7.20—7.45 (m, 4 H, *o*-, *m*-H). ^{13}C NMR, δ: 22.9, 23.3, 25.2, 30.3, 36.5 (5 CH_2); 41.8, 47.3, 49.7 (CH_2C=, NCH_2CH_2N); 42.3 (C_{quat}); 88.1 (NCHN); 97.9 (PhCH=); 123.1, 126.5, 128.1 (Ph); 139.6 (C(1), Ph); 150.9 (PhCH=C). MS, *m/z*: 268 [M^+], 267 [M – H]$^+$.

Z-Isomer. ^{1}H NMR, δ: 1.20—1.85 (m, 11 H, 5 CH_2 + NH); 2.48 (dd, 1 H, CHHC=, J = 15.8 Hz, J = 1.3 Hz); 2.73 (dd, 1 H, CHHC=, J = 15.8 Hz, J = 1.3 Hz); 2.90—3.15 (m, 4 H, NCH_2CH_2N); 4.23 (s, 1 H, CH); 5.26 (dd, 1 H, PhCH=, J = 1.3 Hz, J = 1.3 Hz); 7.0—7.48 (m, 5 H, Ph). ^{13}C NMR, δ: 22.7, 25.2, 26.0, 29.9, 35.6 (5 CH_2); 37.6 (C_{quat}); 43.4, 46.6, 52.6 (CH_2C=, NCH_2CH_2N); 90.2 (NCHN); 97.4 (PhCH=); 123.3, 127.3, 127.7 (Ph); 138.7 (C(1), Ph); 150.5 (PhCH=C). MS, *m/z*: 268 [M^+], 267 [M – H]$^+$.

(*E*)-5-(2,2-Dimethylpropylidene)-7,7-dimethylhexahydro-1*H*-pyrrolo[1,2-*a*]imidazole (3c) was obtained from chlorocyclopropane **1c** and 1,2-diaminoethane in 35% yield and isolated by chromatography on neutral Al_2O_3 (hexane—diethyl ether, 20 : 1). Found (%): C, 75.05; H, 11.41; N, 13.23. $C_{13}H_{24}N_2$. Calculated (%): C, 74.94; H, 11.61; N, 13.45. ^{1}H NMR, δ: 0.91 (s, 9 H, Bu^t); 1.05 (s, 3 H, Me); 1.11 (s, 3 H, Me); 1.82 (s, 2 H, CH_2C=); 2.75—3.10 (m, 4 H, NCH_2CH_2N); 3.89 (s, 1 H, CH); 4.31 (Bu^{t}CH=). ^{13}C NMR, δ: 19.7 (Me); 29.6 (Me); 29.9 (3 Me); 32.2 (CMe_3); 41.5, 45.9, 48.1 (3 CH_2); 42.1 (CMe_2); 90.2 (NCHN); 112.9 (Bu^{t}CH=); 127.1 (Bu^{t}CH=C). MS, *m/z*: 208 [M^+].

(*E*)-6-Benzylidene-8,8-dimethyloctahydropyrrolo[1,2-*a*]-pyrimidine (4a) was obtained from chlorocyclopropane **1a** and 1,3-diaminopropane in 50% yield and isolated from the reaction mixture by recrystallization from hexane. Found (%): C, 79.37; H, 9.02; N, 11.39. $C_{16}H_{22}N_2$. Calculated (%): C, 79.29; H, 9.15; N, 11.56. ^{1}H NMR, δ: 1.02 (s, 3 H, Me); 1.19 (s, 3 H, Me); 1.40 (br.s, 1 H, NH); 1.60—1.72 (m, 2 H, $NCH_2CH_2CH_2NH$); 2.55 (dd, 1 H, CHHC=, J = 16.3 Hz, J = 2.0 Hz); 2.65—2.90 (m, 2 H, CHHN, CHHNH); 2.73 (dd, 1 H, CHHC=, J = 16.3 Hz, J = 1.6 Hz); 3.21—3.35 (m, 1 H, CHHNH); 3.50 (s, 1 H, CH); 3.65—3.78 (m, 1 H, CHHN); 5.21 (dd, 1 H, PhCH=, J = 2.0 Hz, J = 1.6 Hz); 6.99 (br.t, 1 H, *p*-H, J = 7 Hz); 7.19 (br.d, 2 H, *o*-H, J = 7 Hz); 7.25 (br.t, 2 H, *m*-H, J = 7 Hz). ^{13}C NMR, δ: 21.8 (Me); 25.2 ($CH_2CH_2CH_2$); 25.8 (Me); 36.7 (CMe_2); 43.9, 44.0, 45.0 (3 CH_2); 82.4 (NCHN); 93.7 (PhCH=); 122.8, 126.1, 128.1 (Ph); 139.7 (C(1), Ph); 146.6 (PhCH=C). MS, *m/z*: 242 [M^+], 241 [M – H]$^+$.

(*E*)-6´-Benzylidenehexahydro-1´*H*-spiro[cyclohexane-1,8´-pyrrolo[1,2-*a*]pyrimidine] (4b) was obtained from chlorocyclopropane **1a** and 1,3-diaminopropane in 27% yield and isolated from the reaction mixture by recrystallization from hexane. Found (%): C, 80.56; H, 9.09; N, 10.06. $C_{19}H_{26}N_2$. Calculated (%): C, 80.80; H, 9.28; N, 9.92. ^{1}H NMR, δ: 1.18—1.85 (m, 13 H, 6 CH_2 + NH); 2.47 (dd, 1 H, CHHC=, J = 16.3 Hz, J = 1.4 Hz); 2.60—2.84 (m, 2 H, CHHN, CHHNH); 2.92 (dd, 1 H, CHHC=, J = 16.3 Hz, J = 1.3 Hz); 3.20—3.35 (m, 1 H, CHHNH); 3.46 (s, 1 H, NCHN); 3.60—3.74 (m, 1 H, CHHN); 5.19 (br.s, 1 H, PhCH=); 7.00 (br.t, 1 H, *p*-H, J = 7 Hz); 7.15—7.35 (m, 4 H, *o*-, *m*-H). ^{13}C NMR, δ: 22.5, 23.5, 25.4, 26.3, 29.4, 35.9 (6 CH_2); 39.2, 44.3, 45.4 (CH_2C=, $NCH_2CH_2CH_2N$); 40.7 (C_{quat}); 83.3 (NCHN); 94.0 (PhCH=); 123.0, 126.3, 128.4 (Ph); 139.9 (C(1), Ph); 147.1 (PhCH=C). MS, *m/z*: 282 [M^+], 281 [M – H]$^+$.

Compounds 5a and 6. The reaction of chlorocyclopropane **1c** with 1,3-diaminopropane lithium derivative according to the general procedure gives a mixture of aminals **5a** and **6** in the ratio 1 : 1.35 in 72% total yield, which was purified from high-molecular-weight products by passing through a short layer of neutral Al_2O_3 and characterized without separation.

2-(2,6,6-Trimethylhept-4-yn-2-yl)hexahydropyrimidine (5a). ^{1}H NMR, δ: 0.91 (s, 6 H, 2 Me); 1.15 (s, 9 H, 3 Me); 1.30—1.52 (m, 4 H, $NCH_2CH_2CH_2N$, 2 NH); 2.06 (s, 2 H, $CH_2C{\equiv}C$); 2.62—2.71 and 3.08—3.21 (both m, 4 H, $NCH_2CH_2CH_2N$); 3.24 (s, 1 H, NCHN). ^{13}C NMR, δ: 23.3 (CMe_2); 27.4 (CMe_3); 27.8, 29.2 ($C{\equiv}CCH_2$, $NCH_2CH_2CH_2N$); 31.3 (CMe_3); 37.2 (CMe_2); 46.6 ($NCH_2CH_2CH_2N$); 75.9, 91.1 (C≡C); 78.2 (NCHN). MS, *m/z*: 222 [M^+], 221 [M – H]$^+$.

2-(2,6,6-Trimethylhept-3-yn-2-yl)hexahydropyrimidine (6). ^{1}H NMR, δ: 0.95 (s, 9 H, 3 Me); 1.22 (s, 6 H, 2 Me); 1.28—1.50 (m, 4 H, $NCH_2CH_2CH_2N$, 2 NH); 2.12 (s, 2 H, $CH_2C{\equiv}C$); 2.72—2.85 and 3.20—3.30 (both m, 4 H, $NCH_2CH_2CH_2N$); 3.15 (s, 1 H, NCHN). ^{13}C NMR, δ: 26.6 (CMe_2); 28.1, 33.7 ($NCH_2CH_2CH_2N$, $C{\equiv}CCH_2$); 29.0 (CMe_3); 31.1, 36.3 (CMe_3, CMe_2); 46.1 ($NCH_2CH_2CH_2N$); 78.0 (NCHN); 80.8, 86.1 (C≡C). MS, *m/z*: 223.2169 [M + H]$^+$ (calculated: 223.2174).

Compounds 7 and 8. The reaction of chlorocyclopropane **1a** with *N*-methyl-1,3-diaminopropane lithium derivative according to the general procedure after passing through a short layer of neutral Al_2O_3 in a mixture hexane and dichloromethane (2 : 1) gave a mixture of products **7** and **8** in the ratio 1.5 : 1 in 68% total yield, from which compound **7** was isolated in the individual state by recrystallization from hexane in 37% yield.

(*E*)-6-Benzylidene-1,8,8-trimethyloctahydropyrrolo[1,2-*a*]-pyrimidine (7). Found (%): C, 79.62; H, 10.12; N, 10.05. $C_{18}H_{28}N_2$. Calculated (%): C, 79.36; H, 10.36; N, 10.28. ^{1}H NMR, δ: 1.11 (s, 3 H, Me); 1.27 (s, 3 H, Me); 1.6—2.15 (m, 3 H, $NCH_2CH_2CH_2NMe$, $NCH_2CH_2CHHNMe$); 2.29 (s, 3 H, NMe); 2.53 (dd, 1 H, CHHC=, J = 16.3 Hz, J = 2.1 Hz); 2.50—2.62 (m, 1 H, $NCH_2CH_2CH_2NMe$); 2.72 (dd, 1 H, CHHC=, J = 16.3 Hz, J = 1.6 Hz); 2.75 (s, 1 H, CH); 2.87—2.99 (m, 1 H, $NCH_2CH_2CHHNMe$); 3.52—3.64 (m, 1 H, $NCHHCH_2CH_2NMe$); 5.19 (dd, 1 H, PhCH=, J = 2.1 Hz, J = 1.6 Hz); 6.98 (br.t, 1 H, *p*-H, J = 7 Hz); 7.19 (br.d, 2 H, *o*-H, J = 7 Hz); 7.24 (br.t, 2 H, *m*-H, J = 7 Hz). ^{13}C NMR, δ: 22.4 (Me); 24.0 ($CH_2CH_2CH_2$); 27.9 (Me); 38.2 (CMe_2); 42.2 (NMe); 42.8, 45.9, 56.2 (3 CH_2); 89.8, 93.0 (NCHN, PhCH=); 122.7, 126.2, 128.1 (Ph); 139.9 (C(1), Ph); 146.5 (PhCH=C). MS, *m/z*: 256 [M^+], 255 [M – H]$^+$.

***trans*-1-[*N*-(3-Aminopropyl)-*N*-methylamino]-2,2-dimethyl-3-phenylethynylcyclopropane (8).** ^{1}H NMR, δ: 1.09 (d, 1 H, CCH, *cyclo*-C_3H_2, J = 3.8 Hz); 1.21 (s, 3 H, Me); 1.22 (s, 3 H, Me); 1.35 (br.s, 2 H, NH_2); 1.60—1.72 (m, 1 H, $NCH_2CH_2CH_2NH_2$); 1.67 (d, 1 H, NCH, *cyclo*-C_3H_2, J = 3.8 Hz); 1.75—2.15 (m, 4 H, $NCH_2CH_2CH_2N$); 2.25 (s, 3 H, NMe); 7.1—7.4 (m, 5 H, Ph). ^{13}C NMR, δ: 19.3, 21.5, 22.0 (2 Me,

C≡C<u>C</u>H); 26.8 (<u>C</u>Me$_2$); 31.1 (NCH$_2$<u>C</u>H$_2$CH$_2$N); 40.6 (NCH$_2$CH$_2$<u>C</u>H$_2$NH$_2$); 41.8 (NMe); 55.6 (MeN<u>C</u>H$_2$); 59.9 (<u>C</u>HN); 78.8, 90.1 (C≡C); 124.2 (C(1), Ph); 127.2, 128.1, 131.4 (Ph).

Reaction of chlorocyclopropanes 12a,b with lithium propylamide (general procedure). A solution of BuLi in hexane (1.6 *M*, 5 mL, 8 mmol) was added to a solution of 1-aminopropane (590 mg, 10 mmol) in anhydrous THF (10 mL) at 0 °C, followed by addition of the starting chlorocyclopropane **12** (2 mmol) to the mixture obtained, the reaction mixture was heated to 60 °C and stirred at this temperature for 5 h. Then the reaction mixture was treated with water, 2 times extracted with diethyl ether, the organic layer was washed with water and dried with anhydrous Na_2SO_4. Then, the solvent was evaporated, and the residue obtained was subjected to microdistillation *in vacuo* (a bath temperature was 120—140 °C, 1 Torr) to isolate products **15a,b**.

***N*-(2,2-Dimethyl-3-phenylpropylidene)-*N*-propylamine (15a)** was obtained from chlorocyclopropane **12a** in 55% yield. Found (%): C, 82.52; H, 10.33; N, 7.05. $C_{14}H_{21}N$. Calculated (%): C, 82.70; H, 10.41; N, 6.89. ^{1}H NMR, δ: 0.84 (t, 3 H, <u>Me</u>CH$_2$, *J* = 7.4 Hz); 1.03 (s, 6 H, 2 Me); 1.50—1.71 (m, 2 H, MeC<u>H</u>$_2$); 2.70 (s, 2 H, PhC<u>H</u>$_2$); 3.32 (br.t, 2 H, NCH$_2$, *J* = 6.9 Hz); 7.05—7.30 (m, 5 H, Ph); 7.54 (br.s, 1 H, C<u>H</u>=NPr). ^{13}C NMR, δ: 11.6 (<u>Me</u>CH$_2$); 23.9 (Me<u>C</u>H$_2$); 24.7 (2 Me); 39.9 (<u>C</u>Me$_2$); 46.4 (<u>C</u>H$_2$Ph); 63.2 (N<u>C</u>H$_2$); 126.0, 127.4, 130.5 (Ph); 138.1 (C(1), Ph); 171.2 (<u>C</u>H=NPr).

***N*-[2,2-Dimethyl-3-(4-methoxyphenyl)propylidene]-*N*-propylamine (15b)** was obtained from chlorocyclopropane **12b** in 51% yield. Found (%): C, 77.35; H, 9.72; N, 5.88. $C_{15}H_{23}NO$. Calculated (%): C, 77.21; H, 9.93; N, 6.00. ^{1}H NMR, δ: 0.85 (t, 3 H, <u>Me</u>CH$_2$, *J* = 7.4 Hz); 1.02 (s, 6 H, 2 Me); 1.51—1.72 (m, 2 H, MeC<u>H</u>$_2$); 2.65 (s, 2 H, PhC<u>H</u>$_2$); 3.32 (br.t, 2 H, NCH$_2$, *J* = 6.9 Hz); 3.77 (s, 3 H, OMe); 6.75—6.83 (m, 2 H, *m*-H); 6.95—7.05 (m, 2 H, *o*-H); 7.52 (br.s, 1 H, C<u>H</u>=NPr). ^{13}C NMR, δ: 11.6 (<u>Me</u>CH$_2$); 23.8 (Me<u>C</u>H$_2$); 24.5 (2 Me); 39.9 (<u>C</u>Me$_2$); 46.5 (<u>C</u>H$_2$Ph); 55.0 (OMe); 63.2 (N<u>C</u>H$_2$); 113.1, 131.3 (Ph); 130.3 (C(1), Ph); 157.9 (<u>C</u>OMe); 171.3 (<u>C</u>H=NPr).

Reaction of chlorocyclopropane 12b with lithium derivative of 1,3-diaminopropane. A solution of BuLi in hexane (1.6 *M*, 5 mL, 8 mmol) was added to a solution of 1,3-diaminopropane (740 mg, 10 mmol) in anhydrous THF (15 mL) at 0 °C, followed by addition of chlorocyclopropane **12b** (420 mg, 2 mmol), the reaction mixture was heated to 60 °C and stirred at this temperature for 5—6 h until the starting substance completely converted (GLC monitoring). Then the reaction mixture was worked-up with water, extracted with diethyl ether, the organic layer was 3 times washed with water and dried with anhydrous Na_2SO_4. The solvent was evaporated *in vacuo*, the residue obtained was dissolved in the hexane—diethyl ether (2 : 1) mixture, passed through a short layer of neutral Al_2O_3, a viscous substance obtained after repeated concentration (312 mg, 63%) according to the NMR spectroscopic data contained ~90% of 2-[1-(4-methoxyphenyl)-2-methylprop-2-yl]hexahydropyrimidine (**17**). ^{1}H NMR, δ: 0.89 (s, 6 H, 2 Me); 1.35—1.54 (m, 2 H); 2.08 (br.s, 2 H, 2 NH); 2.62 (s, 2 H, C<u>H</u>$_2$CMe$_2$); 2.72—2.86 (m, 2 H, NC<u>H</u>$_2$CH$_2$C<u>H</u>$_2$N); 3.14 (s, 1 H, NCHN); 3.17—3.26 (m, 2 H, NC<u>H</u>$_2$CH$_2$C<u>H</u>$_2$N); 3.81 (s, 3 H, OMe); 6.82—6.89 (m, 2 H, *m*-H); 7.09—7.16 (m, 2 H, *p*-H). ^{13}C NMR, δ: 23.2 (C<u>Me</u>$_2$); 27.6 (NCH$_2$<u>C</u>H$_2$CH$_2$N); 37.8 (<u>C</u>Me$_2$); 46.4 (<u>C</u>H$_2$); 46.7 (N<u>C</u>H$_2$CH$_2$<u>C</u>H$_2$N); 54.8 (OMe); 80.5 (N<u>C</u>HN); 111.6, 130.8 (Ph); 133.2 (C(1), Ph); 158.3 (<u>C</u>OMe).

Reaction of cyclopropylamine with *tert*-butyllithium. Tetrahydrofuran-d$_8$ (0.4 mL) and cyclopropylamine (45 mg, 0.78 mmol) were placed into an NMR tube thoroughly purged with dry argon, a ^{1}H NMR spectrum was recorded, then, the solution was cooled to −90 °C, followed by injection of a solution of *tert*-butyllithium in pentane (1.5 *M*, 0.26 mL, 0.39 mmol). The temperature of the tube was slowly raised to −20 °C, 1 drop of water was added, and ^{1}H and ^{13}C NMR spectra were recorded, which showed a complete absence of the starting cyclopropylamine and the formation of 2,4,6-triethyl-1,3,5-triazine **19** as a major product, which was identified based on the comparison of chemical shifts in the ^{13}C NMR spectrum with the literature data.[18] The yield of compound **19** was 49%, which was determined from the spectrum by comparison of the integral intensities of the methine proton signal (δ = 3.42) and the residual protons of the solvent (δ = 3.68) used as an internal standard.

Condensation of acetylenic aldehydes 21a,b with 1,3-diaminopropane. Synthesis of hexahydropyrimidines 5a,b (general procedure). Anhydrous Na_2SO_4 (5 g) was added to a solution of 1,3-diaminopropane (1480 mg, 20 mmol) in dichloromethane (20 mL), then, a solution of the corresponding aldehyde **21** (10 mmol) in dichloromethane (5 mL) was poured in over 5 min. The mixture obtained was kept at room temperature for 1 day, then 3 times washed with water, dried with anhydrous Na_2SO_4. The solvent was evaporated *in vacuo*, a residual viscous oily substance obtained, according to the NMR spectroscopic data, was hexahydropyrimidine derivatives **5a**,**b** in >90% purity.

2-(2,6,6-Trimethylhept-4-yn-2-yl)hexahydropyrimidine (5a) was obtained in 85% yield from aldehyde **21a.** Its spectra were completely identical to the spectra of the minor product of the reaction of cyclopropane **1c** with lithium derivatives of 1,3-diaminopropane.

2-(2-Methyl-5-phenylpent-4-yn-2-yl)hexahydropyrimidine (5b) was obtained in 78% yield from aldehyde **21b**. ^{1}H NMR, δ: 1.08 (s, 6 H, 2 Me); 1.25—1.60 (m, 4 H, NCH$_2$C<u>H</u>$_2$CH$_2$N, 2 NH); 2.46 (s, 2 H, CH$_2$C≡C); 2.71—2.90 and 3.15—3.29 (both m, 4 H, NC<u>H</u>$_2$CH$_2$C<u>H</u>$_2$N); 3.38 (s, 1 H, NCHN). ^{13}C NMR, δ: 22.8 (C<u>Me</u>$_2$); 27.5, 29.6 (C≡C<u>C</u>H$_2$, NCH$_2$<u>C</u>H$_2$CH$_2$N); 37.3 (<u>C</u>Me$_2$); 46.3 (N<u>C</u>H$_2$CH$_2$<u>C</u>H$_2$N); 77.9 (NCHN); 82.3, 87.7 (C≡C); 123.7 (C(1), Ph); 127.2, 127.9, 131.2 (Ph).

Cyclization of compound 5b upon the action of lithium derivative of 1,3-diaminopropane. A solution of BuLi in hexane (1.6 *M*, 0.6 mL, 1 mmol) was added to a solution of 1,3-diaminopropane (74 mg, 1 mmol) in anhydrous THF (5 mL) at 0 °C, followed by addition of compound **5b** (242 mg, 1 mmol), and the mixture obtained was stirred at room temperature for 30 min. Then, the reaction mixture was treated with water, extracted with diethyl ether, the organic layer was 3 times washed with water and dried with anhydrous Na_2SO_4. The solvent was evaporated *in vacuo*. A residue obtained was recrystallized from hexane to obtain compound **4a** (175 mg, 72%), whose spectra were identical to the product obtained by the reaction of lithium derivative of 1,3-diaminopropane with chlorocyclopropane **1a**.

Under analogous conditions, aminal **5a** after aqueous treatment of the reaction mixture and evaporation of the solvent gives a mixture of the starting compound and its isomer **6** in the molar ratio 1 : 1 in 76% total yield, which were characterized without separation.

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