Available online at www.sciencedirect.com
SCIENCE DIRECT®
Tetrahedron 60 (2004) 2137–2145
Tetrahedron

Mechanism of the heterocyclization of *vic*-alkynylanthra- and *vic*-alkynylnaphthoquinone diazonium salts

Lidiya G. Fedenok,* Igor I. Barabanov, Valentina S. Bashurova and George A. Bogdanchikov

Institute of Chemical Kinetics and Combustion, Siberian Branch of Russian Academy of Sciences, Novosibirsk 630090, Russian Federation

Received 28 August 2003; revised 25 November 2003; accepted 18 December 2003

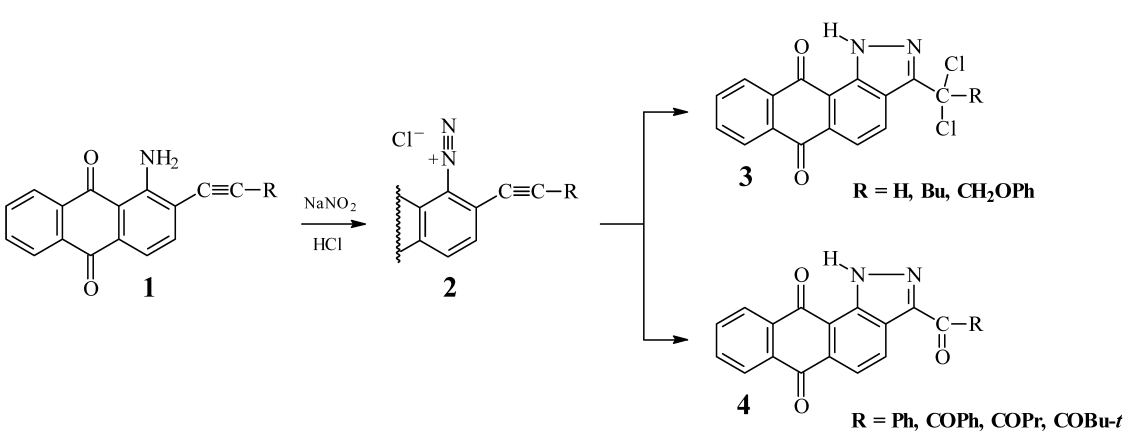
Abstract—On the basis of experimental data and of quantum-chemical calculations, a principal scheme for the mechanism of cyclization of *vic*-alkynylanthra- and *vic*-alkynylnaphthoquinone diazonium salts resulting in the formation of 5- and 6-membered heterocycles is proposed. Within the framework of the new notions of the reaction mechanism, a possibility of controlling the formation of condensed pyrazole or pyridazine rings is demonstrated.
© 2004 Elsevier Ltd. All rights reserved.

1. Introduction

Cyclization of *ortho*-alkynylbenzene diazonium salts, discovered by Richter more than a century ago,[1] has been used in organic synthesis as a method for preparation of cinnolines.[2,3] At the same time, recently, when studying diazotization and cyclization of 2-alkynyl-1-amino-9,10-anthraquinones **1**, it was demonstrated that cyclization of diazonium salts **2** (Scheme 1) went with closure not of the 6-membered pyridazine ring, but of a 5-membered pyrazole ring.[4–6] Depending on the structure of the acetylenic substituent, formation of derivatives of either 3-(1,1-dichloroalkyl)-1*H*-naphtho[2,3-*g*]indazole-6,11-dione **3**,[5] or of 3-acyl-1*H*-naphtho[2,3-*g*]indazole-6,11-dione **4**[6] is observed (Scheme 1).

The results obtained did not fit into the framework of the generally assumed one-stage mechanism of cyclization of *ortho*-alkynylbenzene diazonium salts proposed by Schofield and Simpson (Scheme 2).[7–9]

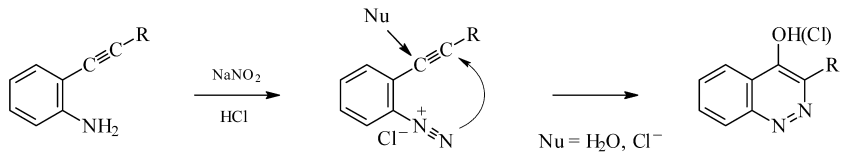
This has served as a serious motive for studying the causes of the 'abnormal' behaviour of *vic*-aminoalkynylanthraquinones **1** in the cyclization reaction that goes via a diazonium salt. For this purpose, we studied the behaviour of 5-amino-3-diethylamino-6-(heptyn-1-yl)-1,4-naphthoquinone **5** in diazotization and cyclization reactions (preliminary communication[10]). The choice of compound **5** was not random. Here, the presence of the electron-donating diethylamino group in the quinone ring considerably quenches the acceptor influence of the carbonyl groups. We supposed



Scheme 1.

Keywords: *vic*-Alkynylanthraquinone and *vic*-alkynylnaphthoquinone diazonium salts; Heterocyclization; Mechanisms; Benzoindazolediones; Benzocinnolinetriones.
* Corresponding author. Tel.: +7-3832-333349; fax: +7-3832-342350; e-mail address: fedenok@kinetics.nsc.ru

0040–4020/$ - see front matter © 2004 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2003.12.058



Scheme 2.

that if the change in the cyclization direction of **2** was determined by electronic factors, then, in the cyclization of naphthoquinone **5**, one could expect formation of reaction products with both 5- and 6-membered heterocycles.

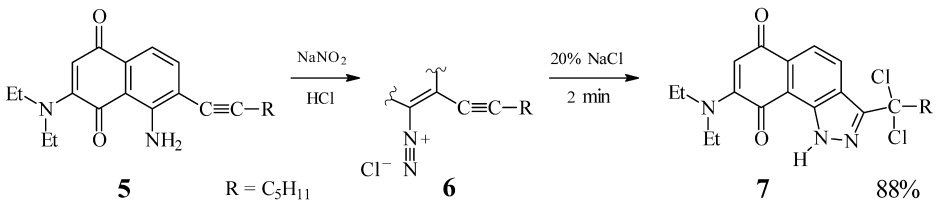
The method of running cyclization of *vic*-aminoalkynylarenes developed many decades ago (via diazotization) was extremely simple. Diazotization and cyclization reactions were run in one flask with heating at the second stage. The combination of a high acidity required at the stage of diazotization, and of a heightened temperature at the cyclization stage was a considerable limitation for introducing into this reaction aminoalkynylarenes, which were sensitive to these rather harsh reaction conditions. So, all the attempts to accomplish cyclization of **5** by this method failed due to the many side reactions, which gave a mixture of reaction products. These circumstances made us develop a new method for this reaction, which would make it possible to remove these limitations. The novelty of the experimental technique consisted in separating the diazotization and cyclization stages. We succeeded in this by creating conditions under which the diazotization rate considerably exceeded that of cyclization. For this, diazotization of **5** was run at room temperature in a water–acetone HCl solution using an excess of $NaNO_2$ (up to 3-fold). Under such conditions, diazotization was complete within about 1 min. The moment of completion was controlled visually by the change of the characteristic color from dark-violet (the solution of the hydrochloride of amine **5**) to light-brown (the solution of the 3-diethylamino-6-(heptyn-1-yl)-1,4-naphthoquinone-5-diazonium chloride **6**). After this, the reaction mixture was rapidly diluted with a 10–30-fold amount of either water or NaCl solution etc. In this way, the cyclization of **6** was carried out under rather mild conditions different from those of diazotization. The possibility of independent variation of the very cyclization conditions made the study of its mechanisms comfortable. The transformations of **6** were observed visually by the change of the solution color and with the help of thin-layer chromatography (TLC). In all the experiments using HCl, the two reactions (diazotization and cyclization) were run at room temperature.

2. Results and discussion

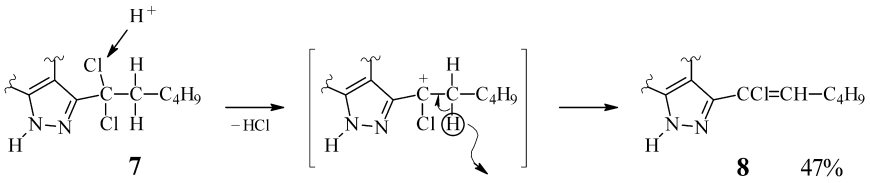
In the course of our studies, it was established that at a 10-fold dilution of the diazonium salt **6** solution with a 20% solution of NaCl, its transformation was completed rapidly, within less than 2 min. The process went with formation of only one reaction product **7** (Scheme 3).

The structure of compound **7** was identified with the help of analytical, spectral and chemical methods. Its IR spectrum dos not contain vibrations of NH_2 and C≡C groups, but has vibrations of the N–H link of the heterocycle. In the ^1H NMR spectrum there are signals of all the aliphatic protons (21H, 0.8–3.8 ppm), of protons of the quinoid (1H, 5.88 ppm) and benzoid (2H, 7.8–8.7 ppm) rings, and a characteristic signal (1H, 11.47 ppm) of the NH link of the heterocycle. The cyclization product **7** is a rather unstable compound with an increased tendency to elimination of HCl. In this connection, in the results of element analysis there was a great dispersion in estimation of chlorine atoms in the molecule >1, but <2. The same peculiarity of **7** was manifested also in its mass spectrum. The extreme right-hand doublet of peaks with *m/z* 385 and 387 corresponds, with respect to the intensity ratio of 3:1, unequivocally to the molecular formula $C_{21}H_{24}ClN_3O_2$ (M^+). The maximal intensity in the spectrum belongs to the peak with *m/z* 356 $(M-C_2H_5)^+$ accompanied, also in accordance with the natural isotope composition (Cl^{35} and Cl^{37}) by a peak with *m/z* 358. The presence of characteristic peak with *m/z* 268 $(M-ClC{=}CHC_4H_9)^+$ without the concomitant peak of 270 indicates that the remaining chlorine atom is in the lateral chain of the pyrazole ring. Therein, elimination of HCl from **7** takes place during heating of the sample in the letting-in chamber.

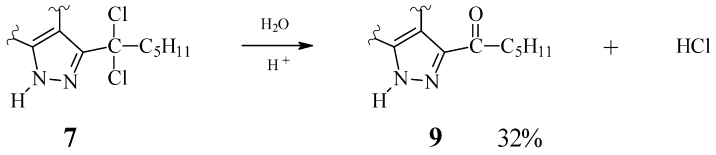
The high lability of **7** was also apparent during chromatography on silica gel in $CHCl_3$. Here, it is completely transformed mainly into two products **8** and **9** in a ratio 3:2. According to the spectral data, one may unequivocally attribute to the compound **8** which has the molecular formula $C_{21}H_{24}ClN_3O_2$, the structure of 3-(1-chlorohexen-1-yl)-8-diethylamino-1*H*-benzo[*g*]indazole-6,9-dione. Indeed, in its ^1H NMR spectrum there are very characteristic chemical shifts of the vinyl proton in the form of a triplet



Scheme 3.



Scheme 4.

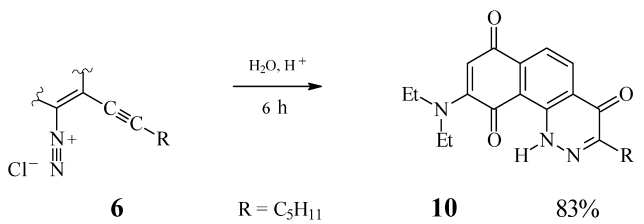


Scheme 5.

(6.55 ppm) and of two protons in the α-carbon atom of the lateral chain in the form of a quartet (2.50 ppm). Most probably, the transformation of the dichloride **7** into **8** goes according to Scheme 4.

Compound **9** with the molecular formula $C_{21}H_{25}N_3O_3$, according to IR and ^{1}H NMR spectra, represents a ketone. It was logical to hypothesize that this ketone was a product of usual hydrolysis of **7**, and the heterocycle in it had the same 5-membered structure (Scheme 5). This hypothesis is confirmed by the proximity of the positions of the vibrations of the N–H bond (IR spectra) and of the NH proton signals (^{1}H NMR spectra) in the spectra of compounds **7**, **8** and **9** (see Section 4).

It turned out that if the obtained solution of the diazonium salt **6** were diluted with a multiple volume of water, the cyclization would go much more slowly. Therein, irrespective of the degree of dilution (10, 15, 20 or 30-fold), the time of transformation of the diazonium salt was equal and amounted to about 6 h. The absence of dependence on the concentration of chloride anions in diluted solutions makes one think that the role of nucleophile here is played by the water molecule. In all cases, the same reaction product **10** is formed (Scheme 6). According to analytical data, this compound has the same molecular formula as **9**, but its melting point is 149–151 °C, which is 4 °C lower than that of the ketone **9** (153–155 °C). The spectral characteristics of these compounds are also different. The greatest difference is in the positions of extinction bands of vibrations of the N–H bond and of the signal of this proton in the ^{1}H NMR spectrum. The shift of this absorption band to the low-frequency field, and that of the proton NH signal to the low field in spectra of **10** as compared to those of **7**, **8**, and **9** suggests a stronger intramolecular hydrogen bond. This fact may be regarded as a corroboration of the 6-membered structure of the heterocycle in **10**. Here, the spatial position of groups (N–H and C=O) is favorable for the formation of a stronger intramolecular hydrogen bond.



Scheme 6.

The final determination of structures of **9** and **10** was made with the help of the mass spectra of these compounds. So, in the mass spectrum of **9** there are peaks corresponding to cations C_5H_{11} (71), COC_5H_{11} (99), (M-COC_5H_{11}) (268) and (M-C_5H_{11}) (296), which unequivocally indicates the presence of a carbonyl group in the side chain. At the same time, the absence of these characteristic peaks in the mass spectrum of **10** suggests that the carbonyl group of this ketone is included in the heterocycle. One has to add that the same ketone **10** is formed in insignificant amounts as a result of transformation of the dichloride **7** during chromatography in $CHCl_3$ on silica gel.

In this way, the experimental data obtained indicate that cyclization of the diazonium salt **6** goes with formation of both a 5-membered ring in the benzo[*g*]indazoledione **7** and a 6-membered one in the benzo[*h*]cinnolinetrione **10**. Naturally, the question arose whether the formation of reaction products with the 5- or 6-membered heterocycle went by two independent mechanisms, or they had common initial stages. Thus, quantum-chemical studies of possible pathways of cyclization of the diazonium salt **6** were carried out. Calculations of standard enthalpies of formation of compounds from simple substances at 298 K (H_f) were carried out by a semi-empiric method AM1.[11] In Figure 1,

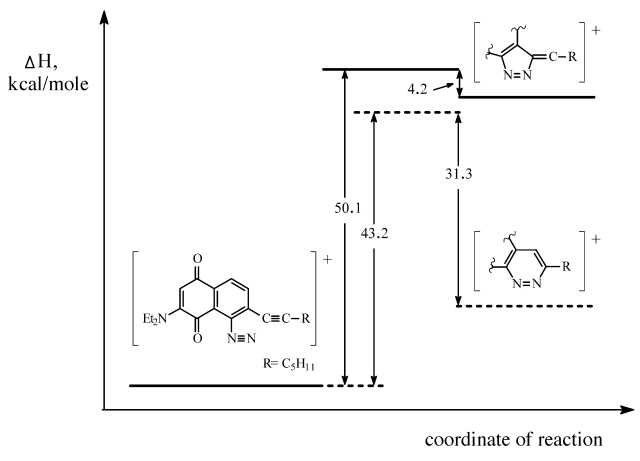


Figure 1. Thermodynamic characteristics for cyclization of the diazonium cation of salt **6**.

changes of cyclization enthalpy are presented depending on the coordinate of cyclization reaction of cation of the diazonium salt **6** with formation of cations with 5- and 6-membered rings are presented. One can see that these are energetically extremely unfavorable processes with activation energies of >43 kcal/mol. The calculation results, in our opinion, are not unexpected. Indeed, all the atoms included in the functional groups (–C≡CR and $-^{+}N{\equiv}N$) have the sp-hybridization, which determines their linear structure. Such geometry is not favorable for intramolecular interaction of functional groups despite their high reaction capacity. The facility of realization of cyclization even at room temperature suggests that the reaction goes in a different way. It is logical to hypothesize that the cyclization process takes place after the interaction of the diazonium salt with the nucleophile. The most likely for such an interaction is the triple bond whose electrophilicity is considerably higher due to the powerful influence of the diazonium group possessing negative inductive and mesomeric effects. As a result, the β-carbon atom of the triple bond acquires a certain positive charge (+0.05), and the α-carbon atom, a negative one (−0.29). Such a distribution of charges ensures quite a definite direction of the nucleophile attack on the β-carbon atom. In model calculations, we used chloride as the nucleophile. A comparison of the calculated heat of the reaction of addition of the anion to the α- and β-carbon atoms of the triple bond shows a greater energy advantage of addition to the latter by 11 kcal/mol. In Figure 2, the dependence of enthalpy of cyclization of a hypothetical neutral molecule ***X*** (chlorine atom at the β-carbon atom of the multiple bond) on the reaction coordinate is presented. One can see that the process of intramolecular cyclization of the neutral molecule already becomes exothermal with an energy gain of 15.6 kcal/mol and activation energy of 24.1 kcal/mol. It is reasonable to hypothesize that in reality the nucleophile addition and cyclization go in a coordinated manner. So, as the C^{β}–Cl bond is formed, the pair of bonding-electrons of the triple bond go to the atom C^{α}. This results in a change of hybridization of carbon atoms, and therefore, to a linear geometry of the multiple bonds, which does not contribute to the convergence of the reaction centers and to their interaction with closure of the ring at the C^{α} atom. As a result, at the first stage of ring formation, according to calculations, a 5-membered 3*H*-pyrazole heterocycle with an *exo*-cyclic double bond in position 3 (structure ***I*** in Fig. 2) must be formed. It is quite obvious that a compound of such structure must be very labile and easily transformed into more stable cyclic products. Thus, transformation of ***I*** into the dichloride **7** can be easily imagined as a result of secondary nucleophilic attack on the same carbon atom by Cl^{-}.

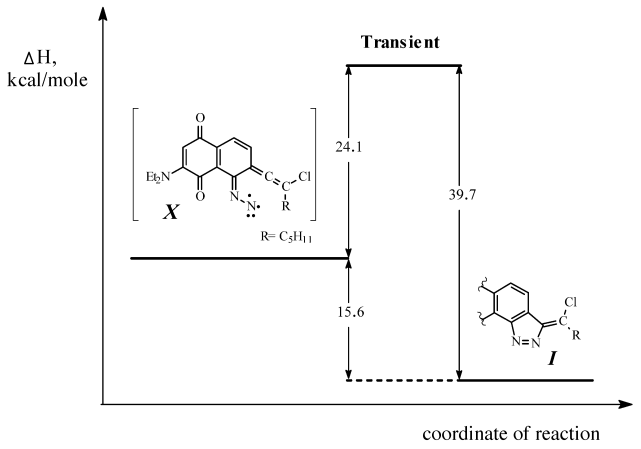
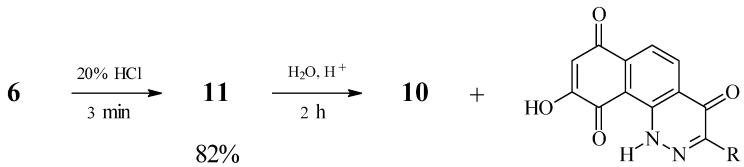


Figure 2. The dependence of enthalpy for cyclization of a hypothetical neutral molecule ***X*** on the reaction coordinate.

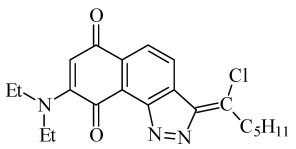
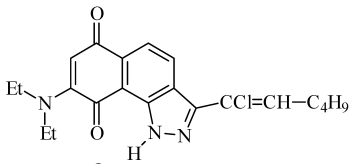
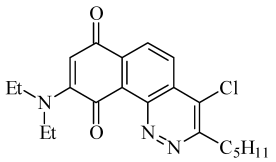
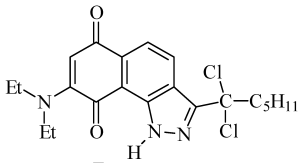
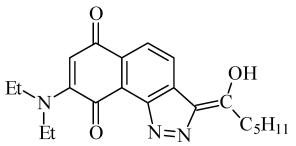
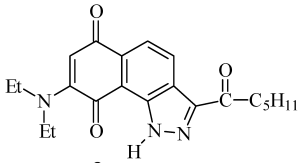
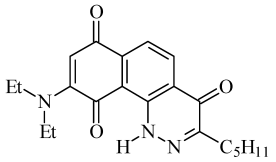
Trying to detect the intermediate in the course of the reaction, we diminished the nucleophilic properties of the medium in order to decrease the probability of attack on the *exo*-cyclic double bond by the nucleophile. For this purpose, the diazonium salt **6** was diluted by 18% HCl, neglecting possible complications caused by side processes. Indeed, under these conditions we observed a change of color of the reaction solution twice: a quick change of the brown color to a red-violet one, and then its gradual conversion to a red-brown one (within about 2 h). With the help of TLC, we also noted the appearance of an unknown reaction product **11** and its subsequent transformation into **10** accompanied by a partial hydrolysis of the diethylamino group (Scheme 7).

Interruption of the reaction after 3 min made it possible to isolate and characterize compound **11**. It was established that it had the same molecular formula as the chlorovinyl derivative **8** ($C_{21}H_{24}ClN_3O_2$), but quite different spectral characteristics. The absence of vibrations of C≡C and N–H bonds in the IR spectrum of **11** indicated that this was a cyclization product. In its ^{1}H NMR spectrum there are signals of all the aliphatic protons, including $N(C_2H_5)_2$, and of three protons of the benzoid and quinoid rings. A distinctive feature of this spectrum is the absence of the N–H signal. It was possible to ascribe to the compound **11**, according to analytical and spectral data, equally the structure of the intermediate ***I***, and the structure of the 4-chloro-9-diethylamino-3-pentylbenzo[*h*]cinnoline-7,10-dione ***Z*** (Table 1). In this connection, it was especially important to study the chemical behaviour of the isolated compound **11**. In the first place, it was necessary to clear up whether it was capable of being transformed into those cyclization products which had been isolated and characterized by us earlier when we carried it out in a slightly acid medium. So, firstly, it was established that an intense stirring of the chloroform solution of **11** with an equal volume of a 20% NaCl solution resulted rapidly and with a



Scheme 7.

Table 1. Enthalpies of formation of intermediates and final products of cyclization of the diazonium salts **6**

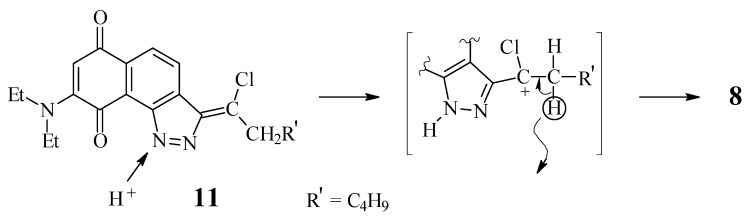
Compound	H_f (kcal/mol)
 **11*(I)***	27.53
 **8**	20.91
 ***Z***	−1.32
 **7**	−3.02
 **11a**	−10.29
 **9**	−22.59
 **10**	−38.40

high yield in the formation of dichloride **7**. Secondly, if in this case one takes, instead of NaCl solution, a 18% HCl, then cyclization goes, although rapidly, but with formation of a mixture of reaction products: **7** (60%), **8** (15%) and **10** (25%) (the total yield of 90%). Further on, during the chromatography on silica gel in $CHCl_3$, **11** is also transformed into a mixture of the compounds **8**, **9**, and **10** in an approximate ratio of 2:2:1 (the total yield of 80%). One can see that the experimental data obtained are in a rather good accordance with the structure ***I*** for the intermediate compound **11**. It was a quantum-chemical calculation of energies of formation of possible intermediate and final reaction products that permitted us making a final choice between structures ***I*** and ***Z*** (Table 1). Demonstrative in this aspect is the comparison of the values H_f for isomer compounds **11**, **8** and ***Z***. Whereas, the transformation of ***Z*** into **8** is an endothermic process, (reaction enthalpy is +22.2 kcal/mol), the transformation of **11** into **8**, on the contrary, is an exothermic process with an energy gain of 6.6 kcal/mol. The facility of transformation of **11** into **8** at room temperature is serious evidence in favor of structure ***I***. Most probably, this transformation can be imagined as a prototropic isomerization catalyzed by hydrogen ions (Scheme 8).

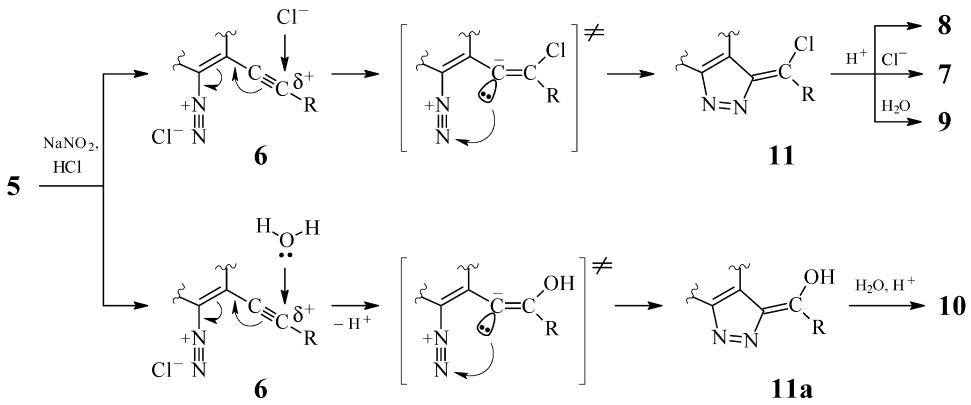
As a result, on the basis of a thorough analysis of experimental and calculated data, we have proposed a principal scheme of the mechanism of cyclization of the *vic*-alkynylquinone diazonium salt **6** (Scheme 9) which is radically different from the commonly accepted mechanism of cyclization of *ortho*-alkynylbenzene diazonium salts.

This is a multistage process which is initiated by the nucleophile (Cl^-, H_2O) attack on the β-carbon atom of the triple bond carrying a positive charge. Formation of the bond with the nucleophile is accompanied by a change of hybridization of carbon atoms of the multiple bonds (sp on sp^2) and, as a consequence thereof, by a change of its linear geometry. All this contributes to an intramolecular convergence of reaction groups, their interaction with formation of the 5-membered 3*H*-pyrazole ring with an *exo*-cyclic double bond. The formed cyclization product **11** (intermediate), possessing the maximum energy among the possible cyclic products (Table 1), strives to become stabilized with a lowering of energy. Depending on the reaction conditions, its transformations take place either with conservation of the size of the heterocycle and its transformation into a 1*H*-pyrazole ring, or with its extension to a 6-membered pyridazine ring. The question of how such extension of a heterocycle occurs remains open and makes the subject of separate study.

A heightened reaction capacity is characteristic, first of all, of the *exo*-cyclic double bond of the intermediate. Under the general electron acceptor influence of the N=N-fragment of the heterocycle and of the quinoid nucleus, although weakened by the donor diethylamino group, this bond is polarized. According to calculations, the carbon atom incorporated into the ring has a charge of −0.14, and the external carbon atom bound to the chlorine atom has a charge of +0.04. Such a distribution of charges under the conditions of increased nucleophilicity of the medium (dilution of **6** with a 20% NaCl solution) contributes to a repeated attack of chloride anion with formation of dichloride **7**. In this way, the formation of a less stable reaction product **7** takes place under the conditions of kinetic control. As for the formation of the most stable reaction product **10**, it is observed under thermodynamic control when the reaction goes slowly during 6 h (Scheme 6) and 2 h (Scheme 7). The driving force of transformation of **11** and **11a** into **10** going with extension of the heterocycle is its exothermicity. A condensed heterocyclic system with a 6-membered pyridazine ring is more stable than that with a 5-membered pyrazole one (Table 1). It is just by this that one can explain the partial transformation of dichloride **7**



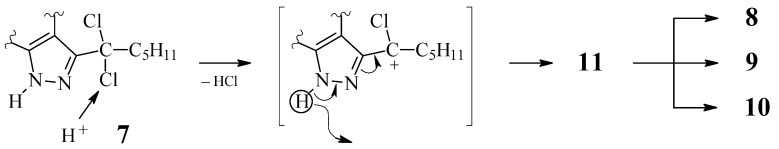
Scheme 8.



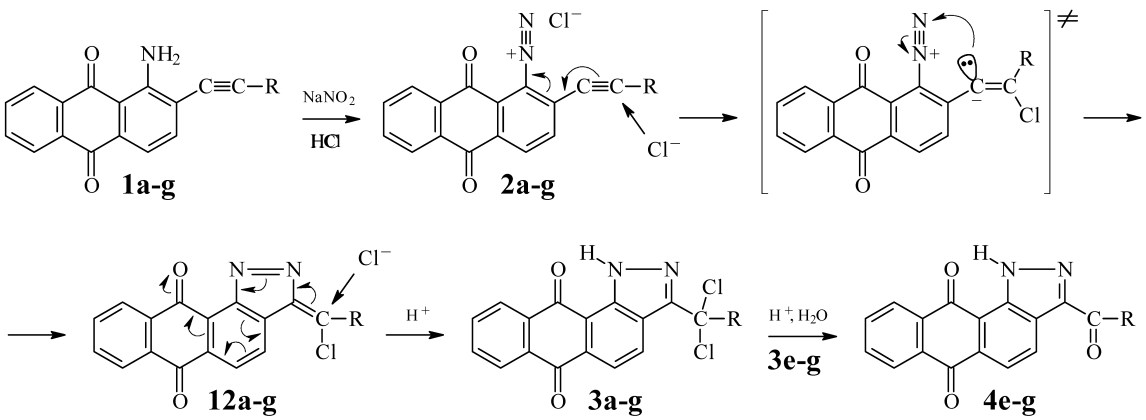
Scheme 9.

into ketone **10** during the chromatography in $CHCl_3$ on silica gel. Proceeding from general reasoning, we believe that its formation goes via the same intermediate **11**. It seems that the initial stage of formation of carbonium ion is the same as that in Scheme 4. However, thereafter the proton goes not from the carbon atom, but from the nitrogen atom (Scheme 10). The probability of the latter event seems to be lower, because the thermodynamic characteristics of **11** are higher than those of vinylchloride **8** (Table 1). Further on, the intermediate, as already noted above, is transformed under these conditions into three products: **8**, **9** and **10**.

The high reaction capacity of the intermediate determines its low stationary concentration. The unique opportunity of observing, in the course of reaction, the formation of intermediate cyclization product (Scheme 7) was a result of a lucky choice of the substrate and of its cyclization conditions. The presence of a strong donor substituent of +C character in the quinoid nucleus lowered the activity of

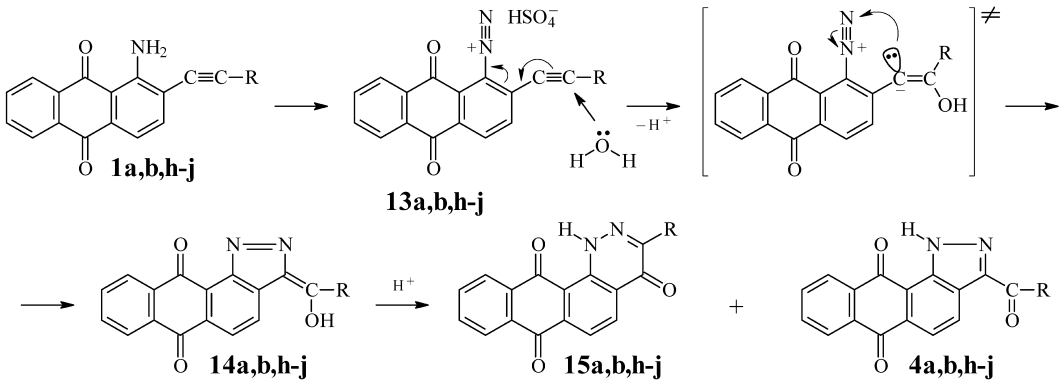


Scheme 10.



a: R = H; **b:** R = Bu; **c:** R = CH_2OPh; **d:** R = 1-HO-*cyclo*-C_6H_{10}; **e:** R = COPh; **f:** R = COBu-*t*; **g:** R = COPr.

Scheme 11.



a: R = H; **b:** R = Bu; **h:** R = C(OH)Me$_2$; **i:** R = CH(OH)Pr; **j:** R = CH(OH)Pr-*i*.

Scheme 12.

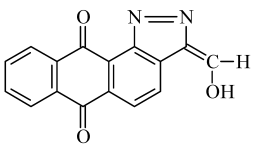
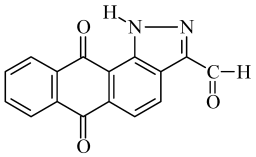
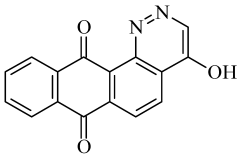
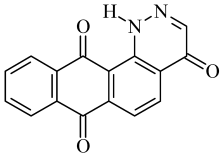
the *exo*-cyclic double bond so much that under certain conditions it became possible to obtain its measurable concentration.

Essential is the fact that under similar conditions, when studying the cyclization of the 2-alkynyl-9,10-anthraquinone-1-diazonium chlorides **2**, we failed to detect the intermediate directly. However, this fact does not disprove but only substantiates the generality of the new notions of the mechanism of cyclization of *vic*-alkynylarene diazonium salts in a series of quinones. In this case, the intermediate (Scheme 11) must have the structure **12**. One can see that here the *exo*-cyclic double bond has to be polarized to a higher degree than in **11** which has a strong donor substituent. This contributes to the fact that even under the conditions of a lowered nucleophilicity of the medium, a rapid interaction with the nucleophile and formation of respective dichlorides **3** takes place. Previously,[12] we showed that the formation of the ketones **4** also goes through dichloride **3** which, due to peculiarities of their structure are prone to a rapid hydrolysis (Scheme 11).

The complete removal of the strong nucleophile (Cl^-) from the reaction mass has permitted us to change the course of reaction.[12] This variant has been used by us when running the diazotization and cyclization reaction in diluted H_2SO_4 (Scheme 12). Under these conditions, the role of the nucleophile is played by the molecule of H_2O. As one could expect from the point of view of the new notions of the cyclization mechanism, the reaction rate slowed down, but apart from the acyl derivatives of naphthoindazole **4**, we also observed the formation of derivatives of naphthocinnolinetriones **15** (Scheme 12). In this case, too, we failed to detect the intermediate **14**, which is also quite natural. In Table 2, calculated data on the energy of formation of the intermediate and of possible final products of cyclization of **13a** are presented. One can see that the maximal value of energy corresponds to the intermediate **14a** which under the reaction conditions tends to become stabilized with a loss of energy. One of the pathways is that of transition to a stable tautomeric form of the ketone **4**. As it is known, it does not require large energy expenditures. Another pathway is isomerization with an extension of the ring and formation of the most stable naphthocinnolines **15** (the enthalpy of this process for **14a** amounts to 25.7 kcal/mol). The mechanism of such ring transformation is very interesting and will be the subject of a further investigation.

We established[12] that the direction of the reaction with an extension of the heterocycle was promoted by an increase of acidity of the medium. An increase of the sulfuric acid concentration at the cyclization stage to 38% purposely permits formation of naphthocinnolinetriones **15** with a high yield. It is of paramount importance that the change of

Table 2. Enthalpies of formation of intermediate and final products of cyclization of the diazonium salts **13a**

Compound	H_f (kcal/mol)
 **14a**	32.31
 **4a**	22.29
 **15a**(tautomer)	8.67
 **15a**	6.61

medium acidity influences only the proportion of reaction products, but not the reaction rate. This fact shows once again that the rate-determining stage is the intermediate formation. All its subsequent transformations are exothermic and go at a high rate. Such a typical situation is the cause of the low stationary concentrations of intermediates, which makes their detection very problematic.

3. Conclusion

In conclusion, the study of cyclization of 3-diethylamino-6-(heptyn-1-yl)-1,4-naphthoquinone-5-diazonium chloride has demonstrated that this is a multistage process. It has been established that the intermediate cyclization product has a 5-membered structure of the 3*H*-pyrazole ring with an *exo*-cyclic double bond. A principal scheme of the mechanism of cyclization of *vic*-alkynylanthra- and *vic*-alkynylnaphthoquinone diazonium salts, which is radically different from that commonly accepted for cyclization of *ortho*-alkynylbenzene diazonium salts is proposed. It has been demonstrated that the direction of further transformations of the intermediate with conservation of the size of the heterocycle or with its extension can be predicted and changed by means of varying the reaction conditions. This has made it possible to obtain from the same *vic*-alkynylamino-9,10-anthraquinones, with a good yield, derivatives of either naphthoindazolediones or naphthocinnolinetriones. The two classes of these compounds are interesting as potential biologically active substances.

4. Experimental

4.1. General

^{1}H NMR spectra were recorded on a Bruker AM-250 spectrometer in $CDCl_3$, internal standard $SiMe_4$, IR spectra were so on a UR-20 spectrophotometer in $CHCl_3$. Mass spectra were obtained on a Finnigan MAT instrument. The control of the course of reaction and of the individual identity of substances was performed with the help of TLC on Silufol UV-254 plates ($CHCl_3$ or benzene–ether).

4.1.1. 5-Amino-3-diethylamino-6-(heptyn-1-yl)-1,4-naphthoquinone (5). 5-Amino-3-diethylamino-6-iodo-1,4-naphthoquinone (1.57 g, 4.2 mmol) was condensed with heptyne-1 (1 mL, 0.74 g, 7.7 mmol) in the presence of $Pd(PPh_3)_2Cl_2$ (0.12 g) and CuI (0.12 g) in Et_3N (106 mL) in an inert atmosphere at 50 °C for 7 h, 120 mL of toluene was added, and the obtained solution was decanted. The residue formed after the removal of toluene and Et_3N in vacuum was dissolved in $CHCl_3$ (150 mL), washed with water (600 mL) and $CHCl_3$ was distilled off. The non-purified product was dried in vacuum and chromatographed on silica gel; the admixtures were eluted with toluene, and **5** was so with a mixture of toluene and ether (1:1). Having distilled off the solvent, the substance was recrystallized from hexane (60 mL): 1.28 g (90%) of **5** was obtained as red-orange crystals, mp 72–73 °C (hexane); [Found: C, 74.92; H, 7.73; N, 8.32. $C_{21}H_{26}N_2O_2$ requires C, 74.52; H, 7.74; N, 8.28%]; $\nu_{max}(CHCl_3)$ 3490, 3360 (NH_2), 2230 (C≡C), 1655, 1620 cm^{-1} (C═O); δ_H (250 MHz, $CDCl_3$) 7.45 (1H, d, *J*=7.7 Hz, H-8(7)), 7.29 (1H, d, *J*=7.7 Hz, H-7(8)), 5.77 (1H, s, H-2), 3.47 (4H, q, *J*=7.4 Hz, CH_2N), 2.47 (2H, t, *J*=7.0 Hz, ≡C–CH_2), 1.70–1.55 (2H, m, ≡C–CH_2–CH_2), 1.55–1.15 (4H, m, C(CH_2)$_2CH_3$), 1.25 (6H, t, *J*=7.4 Hz, CH_3CH_2N), 0.90 (3H, t, *J*=6.9 Hz, CH_3).

4.1.2. 3-(1,1-Dichlorohexyl)-8-diethylamino-1*H*-benzo[*g*]indazole-6,9-dione (7). To solution of quinone **5** (0.10 g, 0.3 mmol) in acetone (5 mL) at 20 °C with a strong stirring were successively added: 18% HCl (5 mL), $NaNO_2$ (0.07 g, 1.0 mmol) in water (1 mL), and mixed for 1 min. The solution of the obtained 3-diethylamino-6-(heptyn-1-yl)-1,4-naphthoquinone-5-diazonium chloride (**6**) was immediately poured out into 20% aqueous solution of NaCl (100 mL), stirred for 2 min and extracted with $CHCl_3$. After drying the extract, distilling off the solvent in vacuum and recrystallization from a mixture of toluene and hexane, 0.11 g (88%) of cyclization product **7** was obtained as light-brown crystals; δ_H (250 MHz, $CDCl_3$) 11.47 (1H, br s, NH), 8.50 (1H, d, H-5(4)), 7.92 (1H, d, H-4(5)), 5.88 (1H, s, H-7), 3.60 (4H, q, CH_2N), 2.90 (2H, t, $CClCH_2$), 2.00–1.20 (12H, m, C(CH_2)$_3CH_3$, CH_3CH_2N), 0.95 (3H, t, CH_3); *m*/*z* (EI) 387 (M^+, 24), 385 (M^+, 71), 372 (12), 370 (39), 358 (38), 356 (100), 268 (17%).

4.1.3. 9-Diethylamino-3-pentyl-1*H*-benzo[*h*]cinnoline-4,7,10-trione (10). To solution of **5** (0.10 g, 0.3 mmol) in acetone (5 mL) at 20 °C, with energetic stirring, 18% HCl (5 mL) and $NaNO_2$ (0.07 g, 1.0 mmol) in water (1 mL) were successively added and stirred for 1 min. The solution of the diazonium salt **6** formed was immediately poured out into water (250 mL) and kept at 20 °C for 5 h. The product was extracted with $CHCl_3$, the extract was run through a thin layer of silica gel, and the solvent was distilled off in vacuum; 0.086 g (83%) of chromatographically pure product **10** was obtained as brown crystals, mp 149–151 °C ($CHCl_3$–hexane); [Found: C, 68.44; H, 6.61; N, 11.08. $C_{21}H_{25}N_3O_3$ requires C, 68.64; H, 6.86; N, 11.44%]; $\nu_{max}(CHCl_3)$ 3355 (NH), 1655, 1620 cm^{-1} (C═O); δ_H (250 MHz, $CDCl_3$) 12.95 (1H, br s, NH), 8.60 (1H, d, *J*=7.8 Hz, H-6(5)), 7.97 (1H, d, *J*=7.8 Hz, H-5(6)), 5.90 (1H, s, H-8), 3.55 (4H, q, *J*=7.0 Hz, CH_2N), 2.85 (2H, t, *J*=8.2 Hz, ═CCH_2), 1.85–1.00 (12H, m, C(CH_2)$_3CH_3$, CH_3CH_2N), 0.88 (3H, t, CH_3); *m*/*z* (EI) 367 (M^+, 34), 338 (46), 242 (100%).

4.1.4. Transformations of 3-(1,1-dichlorohexyl)-8-diethylamino-1*H*-benzo[*g*]indazole-6,9-dione 7 on silica gel in $CHCl_3$. 0.150 g of **7** in $CHCl_3$ was placed onto a plate with silica gel and eluted thrice with $CHCl_3$. After separation of stained silica gel bands, and washing-off the substances from them, obtained were:

1. 0.065 g (47%) of 3-(1-chlorohexen-1-yl)-8-diethylamino-1*H*-benzo[*g*]indazole-6,9-dione (**8**) as light-brown crystals, mp 114–115 °C ($CHCl_3$–hexane); [Found: C, 65.37; H, 6.23; Cl, 9.49. $C_{21}H_{24}ClN_3O_2$ requires C, 65.36; H, 6.27; Cl, 9.19%]; $\nu_{max}(CHCl_3)$ 3465 (NH), 1670, 1625 cm^{-1} (C═O); δ_H (250 MHz, $CDCl_3$) 11.55 (1H, br s, NH), 8.30 (1H, d, *J*=8.7 Hz, H-5(4)), 7.85 (1H, d, *J*=8.7 Hz, H-4(5)), 6.55 (1H, t, *J*=6.9 Hz, ═CH), 5.85 (1H, s, H-7), 3.60 (4H, q, *J*=7.0 Hz, CH_2N), 2.50 (2H, q, *J*=6.9 Hz, ═CCH_2),

1.70–1.20 (10H, m, $C(CH_2)_2CH_3$, CH_3CH_2N), 0.95 (3H, t, CH_3).

2. 0.038 g (32%) of 8-diethylamino-3-hexanoyl-1*H*-benzo[*g*]indazole-6,9-dione (**9**) as dark-violet crystals, mp 153–155 °C (toluene); [Found: C, 68.66; H, 6.80; N, 11.65. $C_{21}H_{25}N_3O_3$ requires C, 68.64; H, 6.86; N, 11.44%; $\nu_{max}(CHCl_3)$ 3450 (NH), 1690, 1670, 1625 cm^{-1} (C=O); δ_H (250 MHz, $CDCl_3$) 11.75 (1H, br s, NH), 8.58 (1H, d, J=8.2 Hz, H-5(4)), 8.00 (1H, d, J=8.2 Hz, H-4(5)), 5.88 (1H, s, H-7), 3.60 (4H, q, J=7.0 Hz, CH_2N), 3.20 (2H, t, J=7.2 Hz, $COCH_2$), 1.80 (2H, m, $COCH_2CH_2$), 1.60–1.00 (10H, m, $C(CH_2)_2CH_3$, CH_3CH_2N), 0.90 (3H, t, CH_3); *m*/*z* (EI) 367 (M^+, 99), 352 (54), 338 (100), 296 (8), 268 (45), 99 (6), 71 (24%).
3. 0.015 g (13%) of 9-diethylamino-3-pentyl-1*H*-benzo[*h*]-cinnoline-4,7,10-trione **10**.

4.1.5. 3-(1-Chlorohexylidene)-8-diethylamino-3*H*-benzo[*g*]indazole-6,9-dione (11). To solution of **5** (0.14 g, 0.4 mmol) in acetone (7.9 mL) were added successively 18% HCl (7.9 mL) and $NaNO_2$ (0.10 g, 1.5 mmol) in water (2.3 mL) under continuous stirring. The stirring was continued thereupon for another 1 min. The obtained solution of diazo salt **6** was immediately poured into 18% HCl (131 mL) and immediately extracted with stirring with toluene (160 mL). The organic layer was separated, washed with low concentrated aqueous $NaHCO_3$ (~1%) solution and water to neutral reaction. After removal of the solvent in vacuum, the residue was chromatographed on silica gel in a mixture of $CHCl_3$ and ether (10:1). The yield of **11** was 0.13 g (82%): dark-violet crystals, mp 124–125 °C ($CHCl_3$–hexane); [Found: C, 65.55; H, 5.99; Cl, 9.02. $C_{21}H_{24}ClN_3O_2$ requires C, 65.36; H, 6.27; Cl, 9.19%]; $\nu_{max}(CHCl_3)$ 1695, 1625 cm^{-1} (C=O); δ_H (250 MHz, $CDCl_3$) 8.45 (2H, s, H-4,5), 5.85 (1H, s, H-7), 3.56 (4H, q, J=7.0 Hz, CH_2N), 3.38 (2H, t, J=7.7 Hz, $=CCH_2$), 1.94 (2H, m, $=CCH_2CH_2$), 1.35 (6H, t, J=7.0 Hz, CH_3CH_2N), 1.25 (4H, s, $C(CH_2)_2CH_3$), 0.90 (3H, t, CH_3).

Acknowledgements

We would like to thank Professors V. G. Kostrovsky and M. S. Shvartsberg for helpful discussion. This work was supported by the Russian Foundation for Basic Research (Grant No 01-03-32455a).

References and notes

1. Von Richter, V. *Ber. Dtsch. Chem. Ges.* **1883**, *16*, 677.
2. Porter, A. E. A. In *Comprehensive organic chemistry. Diazines and benzodiazines*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon: Oxford, 1979; Vol. 4, pp 122–124.
3. Singerman, G. M. *Heterocyclic compounds. Condensed pyridazines including cinnolines phthalazines*; Wiley: New York, 1973; Vol. 27. pp 62–63.
4. Shvartsberg, M. S.; Ivanchikova, I. D.; Fedenok, L. G. *Tetrahedron Lett.* **1994**, *35*, 6749–6752.
5. Shvartsberg, M. S.; Ivanchikova, I. D.; Fedenok, L. G. *Izv. Akad. Nauk, Ser. Khim.* **1996**, 1803–1807.
6. Ivanchikova, I. D.; Fedenok, L. G.; Shvartsberg, M. S. *Izv. Akad. Nauk, Ser. Khim.* **1997**, 110–114.
7. Schofield, K.; Simpson, J. C. E. *J. Chem. Soc.* **1945**, 520.
8. Schofield, K.; Swain, T. *J. Chem. Soc.* **1949**, 2393–2399.
9. Vasilevsky, S. F.; Tretyakov, E. V. *Liebigs Ann.* **1995**, 775–779.
10. Fedenok, L. G.; Barabanov, I. I.; Ivanchikova, I. D. *Tetrahedron Lett.* **1999**, *40*, 805–808.
11. Dewar, M. J. S.; Zoebisch, E. G.; Mealy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* **1985**, *107*, 3902–3909.
12. Fedenok, L. G.; Barabanov, I. I.; Ivanchikova, I. D. *Tetrahedron* **2001**, *57*, 1331–1334.