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HETEROCYCLIZATION OF COMPOUNDS CONTAINING DIAZO AND CYANO GROUPS. 6.* THEORETICAL AND EXPERIMENTAL INVESTIGATIONS OF CYCLIZATION OF 2-CYANO-2-DIAZOACETAMIDES TO 5-HYDROXY-1,2,3-TRIAZOLE-4-CARBONITRILES

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A series of N-alkyl- and N-aryl-2-cyano-2-diazoacetamides was synthesized by the reaction of 2-amino-2-cyanoacetamides with sodium nitrite in hydrochloric acid. The mechanism of their heteroelectrocyclization to 5-hydroxy-1,2,3-triazoles was investigated kinetically and theoretically by the B3LYP/6-31 + G method. The conclusion was made on the basis of the determined activation energy of the cyclization process, reaction parameters ρ, and kinetic isotope effects, that there is a difference between the mechanisms of cyclization of the N-alkyl and N-aryl derivatives of 2-cyano-2-diazoacetamide: cyclization of the N-alkyl derivatives takes place by a monorotatory mechanism, while cyclization of the N-aryl derivatives takes place by a mechanism where one of the stages is heteroelectrocyclization of 2-diazoacetimidates.*

Keywords: diazo compounds, 1,2,3-triazoles, heteroelectrocyclization, kinetic isotope effect, quantum-chemical calculations.

The cyclization of diazo compounds containing amide, amidine, imidate, and vinyl groups at the α-position to the diazo group is a preparatively convenient method for the production of various derivatives of 1,2,3-triazole and pyrazole. Together with the significance of these compounds for the synthesis of heterocycles polyfunctional diazo compounds are suitable models for investigation of the mechanisms of the electrocyclization of heteroatomic π-conjugated compounds [2]. On the basis of theoretical and kinetic investigations of the cyclization of vinyldiazomethanes to 3H-pyrazolines [3] and 2-diazoethanimine to 1,2,3-triazoles [4] the special features of the electrocyclization of the heteroatomic compounds were revealed, and a new type of electrocyclic process (heteroelectrocyclic reactions) was identified [5-7]. A knowledge of the relationships governing the cyclization reactions in turn made it possible to predict the direction of the previously uninvestigated reactions and to plan the synthesis of new heterocyclic compounds based on them [8]. At the same time very few thorough investigations on the heterocyclization of polyfunctional diazo compounds have been described in the literature.

The present work was devoted to kinetic and theoretical study of the mechanisms of heterocyclization of the derivatives of 2-cyano-2-diazoacetamide (**1**) to 4-cyano-5-hydroxy-1,2,3-triazoles (**2**).

* For Communication 5, see [1].

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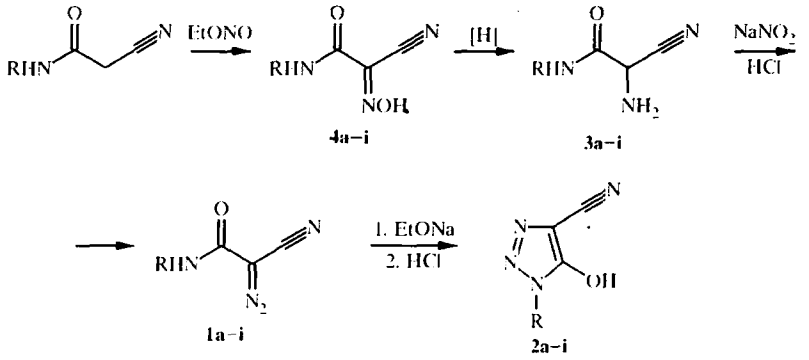
The diazoacetamides **1a-i** were synthesized by diazotization of the respective amines **3a-i**, obtained according to the following scheme:



1-3 **a** R = C_6H_4OMe, **b** C_6H_4Me-4, **c** Ph, **d** C_6H_4Br-4, **e** C_6H_4COOEt-4, **f** H, **g** Me, **h** C_6H_{11}, **i** $PhCH_2$

The triazoles **2a-i** were isolated as a result of the treatment of compounds **1a-i** with solution of sodium ethoxide and then with 0.1 N hydrochloric acid. The cyclic products **2a-f** were also obtained *via* recrystallization of the diazo compounds **1a-f** from water.

When heated, diazomalonamide slowly undergoes cyclization to 5-hydroxy-1,2,3-triazole [9]. The equilibrium between the two compounds, established after boiling for several days in ethanol, is shifted toward the chain form.

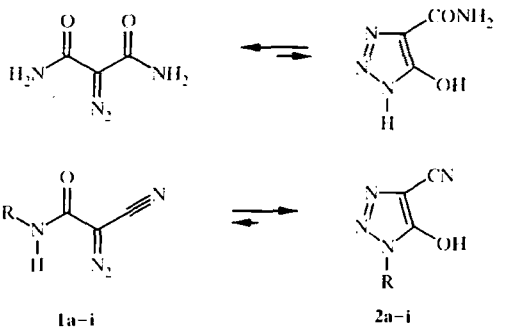


TABLE 1. The Constants of Equilibrium between Diazo Compounds **1a-i** and Triazoles **2a-i** in Ethanol (according to UV Spectroscopy)

R	$K = [2]/[1]$				
	306 K	314 K	321 K	326 K	331 K
C_6H_4OMe-4 (**a**)	21.2±1.3	19.8±1.2	18.8 ± 1.3	—	—
C_6H_4Me-4 (**b**)	20.1±1.2	19.2±1.1	18.1 ± 1.1	—	—
Ph (**c**)	19.3±1.1	18.3±1.9	18.0± 1.0	—	—
C_6H_4Br-4 (**d**)	17.0±1.0	15.2±1.2	15.0+1.1	—	—
C_6H_4COOEt-4 (**e**)	16.5±1.6	14.3±1.1	13.3±1.3	—	—
H (**f**)		-	10.2±0.5	9.4±0.3	8.8±0.2
Me (**g**)	—	—	12.7±0.3	11.0±0.2	9.9±0.3
C_6H_{11} (**h**)	—	—	13.1±0.4	11.2±0.3	9.3±0.3
$PhCH_2$ (**i**)	-	-	10.0±0.3	9.3±0.3	8.1±0.3

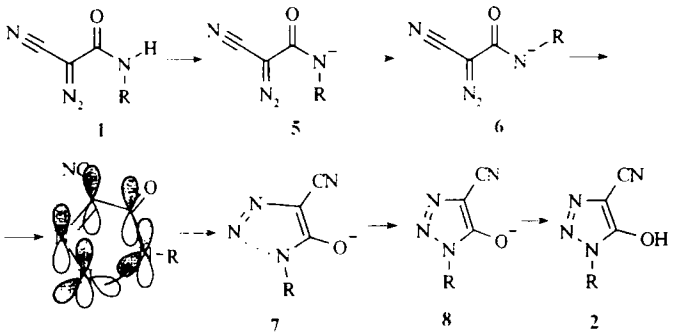
TABLE 2. The Constants of Equilibrium between Diazo Compounds **1a,f,i** and the Triazoles **2a, f, i** (according to PMR Spectroscopy)

R	$K = [2]/[1]$ at 35°C in solvents					
	D_2O	CD_3CN	DMSO-d_6	Acetone-d_6	C_6D_6	C_2D_5OD
C_6H_4OMe-4 (**a**)	~100		21±3	16±1	0.7±0.1	16±2
Me (**f**)	45.4±2.1	27±2	3.2±0.8	1.2±0.2	0.30±0.02	11±1
$PhCH_2$ (**i**)	60±9		6.2±0.2	1.5±0.2	0.24±0.03	19.0±0.8

By UV, IR, and PMR spectroscopy we found that unlike diazomalonamide under similar conditions α-cyano-α-diazoacetamides **1a-i** reach an equilibrium with the cyclic isomers **2a-i**, which is shifted toward the cyclic form (Tables 1 and 2). The position of equilibrium is greatly affected by the properties of the solvent. The equilibrium is shifted toward the cyclic structure **2** in polar solvents (water, DMSO, alcohol, acetone, acetonitrile) and toward the diazo compounds **1** in aprotic solvents (benzene). The position of equilibrium depends slightly on the electronic and steric characteristics of the substituent at the nitrogen atom of the carboxamide function (position 1 of the triazole ring). Here electron-withdrawing substituents destabilize the cyclic structure to some extent.

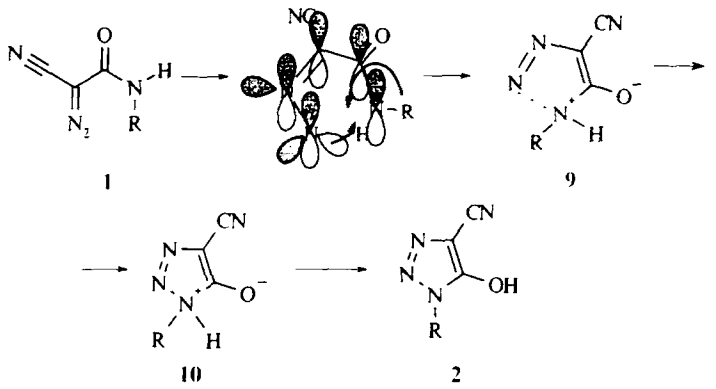
The cyclization of diazo compounds **1** can be supposed to take place in the following way.

A. Initially, a proton in structure **1** is detached with the formation of the imidolate anion **5**. The next stage of the process is *E–Z* isomerization of structure **5** to **6**. The *Z*-configuration of diazo compounds **6** is favorable for cyclization to the triazolate anion **8** and presumably takes place by a heteroelectrocyclic mechanism [5-7]. At the final stage the triazolate anion **8** is protonated, and the final product **2** is formed.



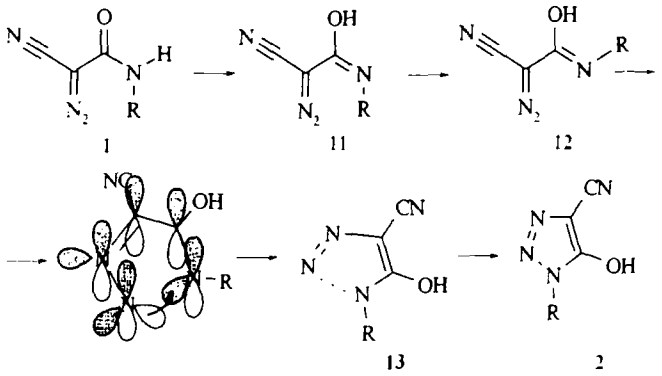
The sufficiently high energy barrier for deprotonation of diazo compounds **1** (in the order of 550-620 kJ/mole) is probably explained by low acidity of amides (p*K*a ~ 15-28) [10-12] and also by the high (positive) value of the reaction entropy change. The *Z–E* isomerization of imidolates (the second stage of the process) is characterized by a lower reaction barrier (65-80 kJ/mole) and by the reaction parameter ρ = 2.1 [13]. The third stage (heteroelectrocyclization) must have an even lower reaction barrier (about 60 kJ/mole) [14]. The profile of the energy change for the proposed mechanism A and also for mechanisms B and C is shown in Fig. 1.

B. The cyclization of diazo compound **1** to triazole **2** consists of two stages, i.e., the actual cyclization to the zwitterionic compound **10**, accompanied by rotation about the imide C–N bond (a monorotatory mechanism), and subsequent 1,3-proton shift in compound **10**.



In contrast to mechanism A, mechanism B must be characterized by low values for the reaction parameter ρ, typical of electrocyclic reactions [15], and negative values for the activation entropy. The 1,3-sigmatropic shift must take place with a low barrier on account of the instability of structure **10** [16]. Mechanism B can therefore be regarded as a single-stage process.

C. Migration of a proton in the amide **1** takes place initially with the formation of hydroxyimine **11**. The second stage of the process is *E*–*Z*-isomerization to the compound **12**. At the final stage cyclization of compound **12** takes place according to heteroelectrocyclic mechanism without rotation about the C–N bond [5-7].



In the case of intramolecular proton transfer, by analogy with [17], the first stage of the mechanism must have a barrier of 240-310 kJ/mole. The participation of the protic solvent lowers the barrier of proton transfer to 100-125 kJ/mole [17]. It is also known that proton transfer in aryl-substituted amidines takes place with lower activation energy (53-56 kJ/mole) [18]. The *Z*–*E*-isomerization of hydroxyimines and the cyclization of diazoimines have approximately equal reaction barriers (60-80 kJ/mole) [4, 5, 13, 14].

The formation of a new N–N bond is common to all three mechanisms (Fig. 1). In order to compare the energy barriers of the electrocyclic and heteroelectrocyclic reactions of diazoacetamides we performed the *ab initio* B3LYP/6-31 + G* calculations of the transition states for the monorotatory cyclization of diazoamide **1** to triazole **10** (course B) and the two nonrotatory cyclizations of diazoimines **6** to **8** (course A) and **12** to **2** (course C) [19, 20].

TABLE 3. The Relative Energies of the Cyclization Stage by the *ab initio* B3LYP/6-31 + G* Method

Mechanism	Relative energies, kJ/mole (structure)		
A	0 (**6**)	55.8 (**7**)	-63.6 (**8**)
B	0 (**1**)	131.8 (**9**)	133.6 (**10**)
B	0 (**12**)	67.0 (**13**)	-30.2 (**1**)

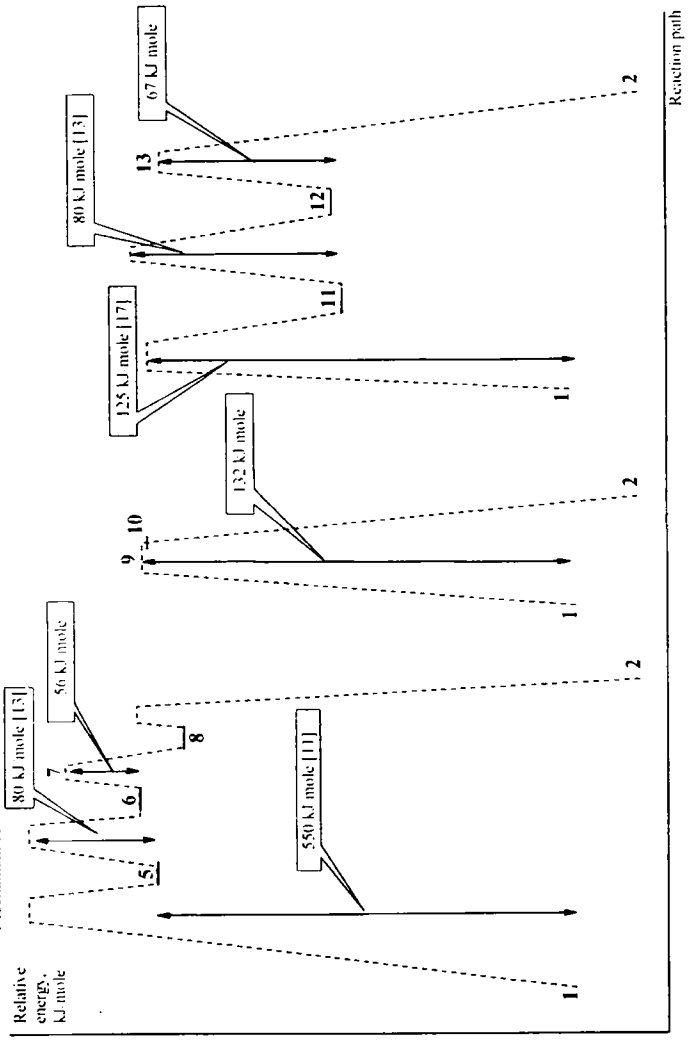


Fig. 1. The energy profile of cyclization of diazoamides **1** to triazoles **2**.

TABLE 4. The Kinetic Data of Cyclization of Diazo Compounds **1** to Isomeric Triazoles **2**

Compound	Observed reaction rate constants $k_{obs} \cdot 10^4$, sec^{-1}									
	306 K		314 K		321 K		326 K		331 K	
	initial	final	initial	final	initial	final	initial	final	initial	final
a	4.95±0.05	3.54±0.09	11.3±0.1	10.5±0.2	22.5±0.3	20.1 ±0.5				
b	5.58±0.09	3.60±0.08	11.3±0.2	9.6±0.2	22.4±0.4	19.8±0.5				
c	7.02±0.08	4.64±0.09	14.5±0.1	12.8±0.2	26.2±0.3	25.8±0.3				
d	10.62±0.09	7.34±0.05	21.3±0.2	16.7±0.3	38.3±0.3	37.8±0.3				
e	11.91 ±0.09	8.64±0.02	26.0±0.3	25.0±0.3	46.5±0.3	45.5±0.5				
f					0.600±0.003	0.602±0.003	1.14±0.011	1.1310.012	1.77±0.02	1.78+0.02
g					0.520±0.005	0.525±0.005	0.888±0.007	0.890±0.007	1.37±0.02	1.38±0.03
h					0.472±0.003	0.470±0.003	0.808±0.008	0.810±0.008	1.17±0.03	1.16±0.03
i					0.577±0.003	0.579±0.004	0.992±0.007	0.990±0.007	1.53±0.02	1.54±0.03

As seen from Table 3, the barrier of the monorotatory cyclization [**1** to **10**, course B] is higher than the barriers of the nonrotatory cyclization [**6** and **8** to **12** and **2**, courses A and C respectively]. This can easily be explained by the need to expend energy on rotation about the C–N bond of amides for the first process. In contrast to amide **1** the unshared electron pair in the molecules of diazoimines **6** and **12** is localized in the plane of the molecule, and rotation about the C–N bond is not therefore required for the formation of the N–N bond. These data agree well with the results of calculations [4, 7] for the cyclization of 2-diazoethanimine to 1H-1,2,3-triazole. By comparison of the barriers to cyclization of imines **6** and **12** it is possible to see that the cyclization takes place more readily in the π-conjugated anion than in the neutral molecule. This relation becomes understandable if the mechanism of the formation of the new σ-bond from the unshared electron pair of the heteroatom in the electrocyclic reaction is considered in detail. In the transition from the neutral iminol **12** to imidate **6** the energy of the orbital corresponding to the unshared electron pair of the nitrogen atom of the imidate group is increased, and this makes it more accessible for electrophilic attack by the diazo group. The energy of activation of imidate **6** to triazolate **7** agrees well with the kinetic data (k = 0.06 sec^{-1} at 188 K) obtained on investigation of the cyclization of 2-diazomalonamides by the action of bases [14]. The high energy of deprotonation of amides (550 kJ/mole) [11] makes it impossible to realize mechanism A in a neutral medium.

The activation energy of the cyclization of iminol **12** is about 65 kJ/mole lower than that of amide **1**, but according to the calculated data the energy of iminol **12** is by 80 kJ/mole higher than that of amide **1**. Determination of the exact magnitude of the barrier of transition between the tautomeric forms and the effect of the solvents on this barrier is an extremely difficult task for the given level of theoretical calculations. The choice between mechanisms B and C therefore requires either more accurate calculations or experimental kinetic investigations.

The kinetic investigations of the cyclization of 2-diazoacetamides **1** to 5-hydroxy-1,2,3-triazoles **2** were carried out by UV spectroscopy. Calculation of the kinetics of cyclization of diazo compounds to triazoles has shown that the degree of transformation was not less than 90% (Table 1). The reaction is described by a first order kinetic equation; the rate constants were obtained as the mean values from three parallel experiments. The relative error with a confidence level of 0.98 and 0.95 (for the determination of the rate constants and activation parameters respectively) was not greater than 5%. The observed rate constants are given in Table 4.

As seen from the data in Table 4, the rate constant of the cyclization of aromatic derivatives **1a-e** is an order of magnitude higher than the rate constant of cyclization of aliphatic amides **1f-i**. In the case of compounds **1a-e** a difference is observed in the rate constants determined from the rates of consumption and formation of compounds **1a-e** and **2a-e**; an isobestic point is not strictly observed at the intersections of the family of spectral

TABLE 5. The Rate Constants of the Individual Stages of Cyclization of Diazoanilides **1a-i**

Compound	Rate constants of individual stages $k_i \cdot 10^4$ at											
	306 K				314 K				321 K			
	k_1	k_{-1}	k_2	k_{-2}	k_1	k_{-1}	k_2	k_{-2}	k_1	k_{-1}	k_2	k_{-2}
a	69	101	9	0.28	342	1160	44	0.65	1162	7110	147	1.28
b	75	136	11	0.29	539	3040	67	0.62	1387	10600	180	1.31
c	98	192	14	0.38	897	6760	115	0.84	5750	147000	713	1.55
d	154	344	25	0.66	1031	7400	163	1.49	9300	317000	1404	2.74
e	204	538	33	0.77	1524	12800	235	1.82	11300	397000	1750	3.40

	321 K		326 K		331 K	
	k_1	k_{-1}	k_1	k_{-1}	k_1	k_{-1}
f	0.546	0.0536	1.030	0.110	1.589	0.181
g	0.482	0.0380	0.814	0.074	1.244	0.126
h	0.439	0.0335	0.742	0.060	1.044	0.126
i	0.524	0.0524	0.896	0.096	1.371	0.169

TABLE 6. The Activation Energy of the Cyclization of Compounds **1** and the Opening of the Ring **2**

Compound	Activation parameters for the rate constants											
	k_1			k_{-1}			k_2			k_{-2}		
	$\Delta_H^{\neq}$, kJ/mole	$\Delta_S^{\neq}$, J/mole·K	$\Delta_G^{\neq}$, kJ/mole	$\Delta_H^{\neq}$, kJ/mole	$\Delta_S^{\neq}$, J/mole·K	$\Delta_G^{\neq}$, kJ/mole	$\Delta_H^{\neq}$, kJ/mole	$\Delta_S^{\neq}$, J/mole·K	$\Delta_G^{\neq}$, kJ/mole	$\Delta_H^{\neq}$, kJ/mole	$\Delta_S^{\neq}$, J/mole·K	$\Delta_G^{\neq}$, kJ/mole
a	151600	209	89320	229500	470	89400	148900	183	94366	80850	-68	101100
b	157600	230	89060	236800	495	89290	160900	224	94148	78850	-74	100900
c	218900	432	90160	358700	894	92290	209700	386	94672	73800	-89	100300
d	219700	437	89470	367000	924	91650	215300	408	93716	75000	-80	98800
e	215600	427	88350	355500	891	89980	212300	401	92802	78750	-66	98400
f	91700	-41.6	105100	104930	-20	111350						
g	81100	-75.9	105430	103260	-28	112250						
h	73900	-08.9	105640	105920	-25	113950						
i	82300	-71.4	105220	100750	-33	111350						

TABLE 7. The Values of the Reaction Parameter ρ of the Hammett and Taft Equation

The value of ρ for the cyclization of compounds **1a-e**				
T, K	k_1	k_{-1}	k_2	k_{-2}
306	0.79±0.07	1.2±0.2	0.94±0.10	0.79±0.29
314	0.51±0.15	1.0±0.4	0.71±0.15	0.48±0.19
321	0.43±0.05	1.4±0.5	0.61±0.09	0.51±0.19

The values of ρ and *S* for the cyclization of compounds **1f-i**				
T, K	k_1		k_{-1}	
	ρ	*S*	ρ	*S*
321	0.01	0.1	0.02	0.12
326	0.01	0.1	0.01	0.12
331	0.01	0.1	0.01	0.10

curves with time. Since the cyclization of diazoanilides **1a-e** to triazoles **2a-e** takes place with a yield close to quantitative, these data indicate the formation of an intermediate product. Moreover, on investigation of the given equilibrium reaction by PMR spectroscopy the appearance of third signal for the methoxy group at 3.99 (acetone-d_6) or 3.93 ppm (ethanol-d_6) was observed. Its integral intensity did not exceed 2% of the total integral of the signal of the methoxy groups in compounds **1a** and **2a**. The other signals of the intermediate compound (the aromatic ring) could not be detected on account of their superimposition on the signals of the initial and final compounds. Differences in the rate constants are not observed for the alkyl derivatives **1f-i**, and the family of spectral curves has an isobestic point. It can consequently be concluded that in this case there is no accumulation of the intermediate product.

Thus, for the aliphatic derivatives **1f-i** the cyclization reaction is reversible, and the observed rate constants are equal to the sum of the forward and reverse reactions (Table 5). For the aromatic derivatives **1a-e** the reaction can be represented in the following form:

$$A \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} B \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} C$$

Since according to the PMR spectroscopic data the intermediate product accumulates to the extent of not more than 2%, it is possible to use the method of stationary states [22] and reduce the kinetic equations to the following:

$$\frac{dA}{dt} = \frac{k_{-1}k_{-2} + k_1k_2 + k_1k_{-2}}{k_{-1} + k_{-2} + k_2}(A - A\infty) \; ; \quad \frac{dC}{dt} = \frac{k_{-1}k_{-2} + k_1k_2 + k_1k_{-2}}{k_{-1} + k_{-2} + k_1}(C - C\infty)$$

In view of the fact that $k_1 >> k_2$ and $k_1 >> k_{-2}$ (Table 1) the expressions for the observed rate constants can be simplified, and the rate constants of the individual reactions can be determined approximately (Table 5):

$$k_{-2} = \frac{k_{in} \cdot (K+1)}{K^2} \; ; \quad k_2 \approx \frac{k_{in} \cdot k_{fin} \cdot (K+1)}{(k_{in} - k_{fin}) \cdot K} \; ;$$

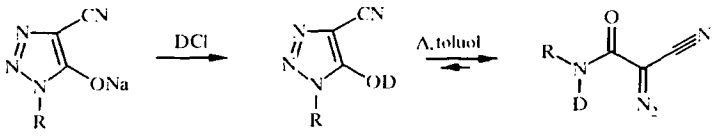
$$k_1 = \frac{X \cdot Y \cdot k_{in} - k_{fin} \cdot k_{-2}}{X - X \cdot Y - k_{fin}} \; ; \quad k-1 = \frac{k_1 \cdot k_2}{k_{-2} \cdot K} \; ,$$

where k_{in} is the decrease rate constant of the initial compound, and k_{fin} is the formation rate constant of the final compound:

$$X = k_2 + k_{-2} \; ; \quad Y = \frac{k_{-2} - k_{fin}}{k_{-2} - k_{in}} \; ; \quad K = \frac{k_1 \cdot k_2}{k_{-1} \cdot k_{-2}} = \frac{C\infty}{A\infty}.$$

The activation parameters (Table 6) and the Hammett and Taft reaction constants ρ (Table 7) were determined for each elementary stage. As seen from the tables, all stages of the process (both forward and reverse) have low positive value for the reaction constant ρ, while the cyclization of the aliphatic diazoamides **1f-i** depends almost entirely on the steric effect of the substituent. The forward and reverse stages for the cyclization of amides **1f-i** are characterized by a negative value for the entropy of reaction, whereas a high positive value is observed for the diazoanilides **1a-e**.

We determined the kinetic isotope effect for the cyclization of the aryl and alkyl derivatives of diazoacetamides **1**. For this purpose we synthesized 2-cyano-2-diazoacetodeuteroamides **14c,d,h,i** according to the following scheme:



15c.d.h.i **16c.d.h.i** **14c.d.h.i**

14–16 c R = Ph, d R = C_6H_4Br-4, h R = C_6H_{11}, i R = $PhCH_2$

The fraction of the labelled product, calculated on the basis of the data from the mass spectra (from the intensity ratios of M^+ for the deuterated and undeuterated compounds), amounted to 92% for the compound **14c**, 99% for **14d**, 84% for **14h**, and 94% for **14i**.

As follows from Table 8, anilides **1c,d** are characterized by a primary kinetic isotope effect, while alkylamides **1h,i** give a secondary effect. Moreover, for aromatic derivatives **1c,d** no differences were observed in the rate constants determined from the disappearance of the initial and appearance of the final product. Thus, it can be supposed that for the aliphatic derivatives there is a change in the hybridization of the N–D nitrogen atom at the rate-determining stage, while the cyclization of the aromatic derivatives is realized as a two-stage process with approximately equal activation barriers, at one of which the N–D bond is broken.

The primary kinetic isotope effect, the positive value of ρ, and the positive value of the entropy change for the reverse process make it possible to reject the course B for the cyclization of N-aryl derivatives **1a-e**. The nature of the effect of substituents (electron-withdrawing substituents accelerate the reaction [14]) and also the values of the activation parameters (a positive change of entropy for the forward reaction and a negative value for the reverse reaction) for the cyclization of N-aryl derivatives **1a-e** agree well with mechanism C.

TABLE 8. The Kinetic Isotope Effect for the Cyclization of Diazoamides **1c,d,g,i** to Triazoles **2c,d,g,i**

Compound	Rate constant of cyclization of compounds (**14c,d,g,i**), $k_D \cdot 10^4$ sec^{-1}, at 321 K	KIE, k_H/k_D
c	4.0±0.1	6.41
d	6.7±0.2	5.6
g	0.42±0.01	1.12
i	0.41±0.01	1.11

TABLE 9. The Characteristics of the Synthesized Compounds

Compound	Empirical formula	Found, % / Calculated, %				mp, °C	Yield, %
		C	H	Br	N		
1a	$C_{10}H_8N_4O_2$	55.7 / 55.6	3.8 / 3.7		26.2 / 25.9	136-139	79
1b	$C_{10}H_8N_4O$	59.4 / 60.0	4.2 / 4.0		28.3 / 28.0	123-125	85
1c	$C_9H_6N_4O$	56.9 / 58.1	3.1 / 3.3		29.8 / 30.1	64-68	82
1d	$C_9H_5BrN_4O$	41.1 / 40.8	2.1 / 1.9	30.3 / 30.2	21.4 / 21.1	153-154	87
1e	$C_{12}H_{10}N_4O_3$	55.6 / 55.8	3.9 / 3.9		21.5 / 21.7	173-174	86
1h	$C_9H_{12}N_4O$	56.5 / 56.2	6.6 / 6.3		28.9 / 29.2	101-102	74
1i	$C_{10}H_8N_4O$	59.8 / 60.0	3.9 / 4.0		28.2 / 28.0	63-65	80
2a	$C_{10}H_8N_4O_2$	55.3 / 55.6	3.9 / 3.7		25.8 / 25.9	136-138	99
2b	$C_{10}H_8N_4O$	59.9 / 60.0	3.9 / 4.0		25.8 / 28.0	127-128	99
2c	$C_9H_6N_4O$	57.8 / 58.1	3.6 / 3.3		30.2 / 30.1	83-85	99
2d	$C_9H_5BrN_4O$	40.3 / 40.8	1.9 / 1.9	30.1 / 30.2	21.4 / 21.1	154-156	99
2e	$C_{12}H_{10}N_4O_3$	55.9 / 55.8	4.1 / 3.9		21.4 / 21.7	165-166	99
2h	$C_9H_{12}N_4O$	56.4 / 56.2	6.4 / 6.3		29.1 / 29.2	170-172	99
2i	$C_{10}H_8N_4O$	60.3 / 60.0	4.2 / 4.0		28.1 / 28.0	97-98	99
3a	$C_{10}H_{11}N_3O_2$	58.9 / 58.5	5.6 / 5.4		20.5 / 20.5	127-129	42
3b	$C_{10}H_{11}N_3O$	63.6 / 63.5	5.9 / 5.9		22.1 / 22.2	129-131	46
3c	$C_9H_9N_3O$	61.6 / 61.7	5.4 / 5.2		24.1 / 24.0	115-117	46
3d	$C_9H_8BrN_3O$	42.5 / 42.5	3.2 / 3.2	31.6 / 31.5	16.3 / 16.5	142-143	40
3e	$C_{12}H_{13}N_3O_3$	58.3 / 58.3	5.5 / 5.3		17.0 / 17.0	145-147	41
3h	$C_9H_{15}N_3O$	59.4 / 59.6	8.4 / 8.3		23.2 / 23.2	91-93	48
3i	$C_{10}H_{11}N_3O$	63.2 / 63.5	5.7 / 5.9		22.0 / 22.2	103-104	40
4a	$C_{10}H_9N_3O_3$	54.5 / 54.8	4.2 / 4.1		19.0 / 19.1	216-218	73
4b	$C_{10}H_9N_3O_2$	59.4 / 59.1	4.5 / 4.5		21.0 / 20.7	242-244	77
4c	$C_9H_7N_3O_2$	57.2 / 57.1	3.8 / 3.7		22.4 / 22.2	229-230	81
4d	$C_{10}H_6BrN_3O_2$	40.4 / 40.3	2.3 / 2.3	29.9 / 29.8	16.6 / 15.7	243-245	71
4e	$C_{12}H_{11}N_3O_4$	55.0 / 55.2	4.2 / 4.2		16.1 / 16.1	261-263	86
4h	$C_9H_{13}N_3O_2$	55.4 / 55.4	6.7 / 6.7		21.5 / 21.5	209-210	78
4i	$C_{10}H_9N_3O_2$	59.3 / 59.1	4.8 / 4.5		21.0 / 20.7	212-213	83
14c	$C_9H_7DN_4O$				29.7 / 29.9	Oil	26
14d	$C_9H_7DBrN_4O$				20.7 / 21.1	Oil	32
14h	$C_9H_{11}DN_4O$				29.2 / 29.1	Oil	12

TABLE 10. The Spectral Characteristics of Compounds **1-4**

Compound	IR spectrum (KBr), ν, cm^{-1}	UV spectrum (ethanol), λ_{max}, nm, (log ε)	Mass spectrum, *m/z* (%)
1a	3350, 2932, 2880, 2235 (CN), 2132 (N_3), 1685 (CO)	227 (4.18), 270 (4.15)	216 (71), 173 (100), 160 (69), 145 (69), 133 (90)
1b	3350, 2932, 2880, 2235 (CN), 2145 (N_3), 1670 (CO)	227 (4.25), 267 (4.10)	200 (100), 157 (48), 144 (79), 143 (44), 117 (88)
1c	3275, 3070, 3035, 2332 (CN), 2150 (N_3), 1660 (CO)	227 (4.13), 267 (4.04)	186 (43), 130 (40), 129 (33), 104 (33), 103 (100)
1d	3330, 3190, 3150, 3110, 2225 (CN), 2130 (N_3), 1680 (CO)	227 (4.20), 268 (4.12)	266 (64), 264 (54), 184 (24), 183 (52), 182 (18)
1e	3333, 3000, 2940, 2210 (CN), 2115 (N_3), 1700, 1680 (CO)	227 (4.22), 270 (4.05)	
1h	3290, 3070, 2940, 2870, 2238 (CN), 2160 (N_3), 1640 (CO)	245 (4.11)	192 (39), 111 (44), 83 (83), 82 (69), 67 (50), 55 (100)
1i	3275, 3070, 3035, 2940, 2230 (CN), 2145 (N_3), 1660 (CO)	244 (4.10)	
2a	3085, 2830, 2270 (CN)	255 (4.30)	
2b	3120, 3060, 3030, 2810, 2270 (CN)	256 (4.24)	
2c	3082, 3000, 2270 (CN)	255 (4.25)	
2d	3190, 2970, 2780, 2265 (CN)	256 (4.20)	
2e	3200, 2950, 2810, 2265 (CN), 1700 (CO)	255 (4.23)	
2h	2955, 2876, 2244 (CN)	272 (4.20)	
2i	3090, 2950, 2870, 2250 (CN)	273 (4.25)	
3a	3410, 3315, 3025, 2945, 2850, 2260 (CN), 1700 (CO)	253 (4.20)	
3b	3428, 3242, 2940, 2890, 2252 (CN), 1700 (CO)	246 (4.21)	
3c	3410, 3323, 3073, 2942, 2260 (CN), 1707 (CO)	239 (4.09)	
3d	3405, 3335, 3050, 2910, 2240 (CN), 1685 (CO)	250 (4.20)	
3e	3410, 3320, 3080, 2930, 2225 (CN), 1710, 1690 (CO)	252 (4.10)	
3h	3365, 3320, 3190, 2951, 2882, 2255 (CN), 1665 (CO)		
3i	3287, 3320, 3190, 2950, 2250 (CN), 1670 (CO)		
4a	3350, 3140, 2980, 2860, 2240 (CN), 1680 (CO)	334 (4.23), 285 (3.55), 317 (3.51)	
4b	3335, 3140, 2980, 2860, 2240 (CN), 1680 (CO)	332 (4.38), 307 (3.69)	
4c	3340, 3232, 3027, 2865, 2250 (CN), 1680 (CO)	324 (4.40) 290 (3.72)	
4d	3300, 3210, 3155, 3005, 2840, 2235 (CN), 1650 (CO)	336 (4.28), 295 (3.30)	
4e	3340, 3220, 3030, 2866, 2245 (CN), 1710, 1640 (CO)		
4h	3350, 2960, 2870, 2225 (CN), 1664 (CO)	228 (4.02), 265 (3.44)	
4i	3120, 2970, 2835, 2870, 2252 (CN), 1635 (CO)	223 (3.88), 270 (3.57)	

TABLE 11. The Chemical Shifts, Multiplicity, and Spin–Spin Coupling Constants in the PMR Spectra of the Synthesized Compounds

Compound	PMR spectra (DMSO-d_6), δ, ppm
1a	9.95 (1H, s, NH); 7.51 (2H, d, J = 9 Hz, ArH); 6.80 (2H, d, J = 9 Hz, ArH); 3.70 (3H, s, OMe)
1b	9.90 (1H, s, NH); 7.40 (2H, d, J = 9 Hz, ArH); 7.08 (2H, d, J = 9 Hz, ArH); 2.25 (3H, s, Me)
1c	9.93 (1H, s, NH); 8.0-6.7 (5H, m, Ph)
1d	10.3 (1H, s, NH); 7.77 (4H, s, ArH)
1e	10.35 (1H, s, NH); 8.11 (2H, d, J = 8 Hz, ArH); 7.74 (2H, d, J = 8 Hz, ArH); 4.39 (2H, q, J = 7.2 Hz, OCH_2); 1.38 (3H, t, J = 7.2 Hz, Me)
1h	9.95 (1H, d, J = 8 Hz, NH); 2.7-3.2 (1H, m, CH); 0.5-2.2 (10H, m, C_5H_{10})
1i	9.90 (1H, t, NH); 7.0 (5H, s, Ph); 5.20 (2H, d, CH_2)
2a	7.64 (2H, d, J = 9 Hz, ArH); 7.10 (2H, d, J = 9 Hz, ArH); 3.88 (3H, s, OMe)
2b	7.63 (2H, d, J = 9 Hz, ArH); 7.36 (2H, d, J = 9 Hz, ArH); 2.42 (3H, s, Me)
2c	8.2-6.8 (5H, m, Ph)
2d	7.78 (4H, s, ArH)
2e	8.12 (2H, d, J = 8 Hz, ArH); 7.82 (2H, d, J = 8 Hz, ArH); 4.43 (2H, q, J = 7.2 Hz, OCH_2); 1.40 (3H, t, J = 7.2 Hz, Me)
2h	3.8 (1H, septet, J = 8 Hz, CH); 0.8-2.2 (10H, m, C_5H_{10})
2i	7.3 (5H, s, Ph); 5.72 (2H, d, CH_2)
3a	9.40 (1H, s, NH); 7.56 (2H, d, J = 9 Hz, ArH); 6.85 (2H, d, J = 9 Hz, ArH); 4.65 (1H, s, CH); 3.75 (3H, s, OMe)
3b	9.90 (1H, s, NH); 7.48 (2H, Hz, J = 8 Hz, ArH); 7.10 (2H, d, J = 8 Hz, ArH); 4.67 (1H, s, CH); 2.25 (3H, s, Me)
3c	9.92 (1H, s, NH); 8.1-6.7 (5H, m, Ph); 4.67 (1H, s, CH)
3d	10.40 (1H, s, NH); 7.78-7.36 (4H, m, C_6H_4); 4.72 (1H, s, CH)
3e	10.3 (1H, br. s, NH); 8.00 (2H, d, J = 8.5 Hz, ArH); 7.65 (2H, d, J = 8.5 Hz, ArH); 4.70 (1H, s, CH); 4.35 (2H, q, J = 7.2 Hz, OCH_2); 1.36 (3H, t, J = 7.2 Hz, Me)
3h	7.87 (1H, d, J = 8 Hz, NH); 4.39 (1H, s, CH); 2.7-3.2 (1H, m, CH); 0.5-2.2 (10H, m, C_5H_{10})
3i	9.92 (1H, t, NH); 6.95 (5H, s, Ph); 5.13 (2H, d, CH_2); 4.49 (1H, s, CH)
4a	9.40 (1H, s, NH); 7.61 (2H, d, J = 9 Hz, ArH); 6.88 (2H, d, J = 9 Hz, ArH); 3.77 (3H, s, OMe)
4b	10.26 (1H, s, NH); 7.55 (2H, d, J = 8 Hz, ArH); 7.12 (2H, d, J = 8 Hz, ArH); 2.26 (3H, s, Me)
4c	9.98 (1H, s, NH); 8.1-6.8 (5H, m, Ph)
4d	10.51 (1H, s, NH); 7.85-7.40 (4H, m, C_6H_4)
4e	14.0 (1H, br. s, OH); 10.8 (1H, br. s, NH); 8.10 (2H, d, J = 8.5 Hz, ArH); 7.85 (2H, d, J = 8.5 Hz, ArH); 4.36 (2H, q, J = 7.2 Hz, OCH_2); 1.36 (3H, t, J = 7.2 Hz, Me)
4h	8.21 (1H, br. s, NH); 2.55-3.1 (1H, m, CH); 0.7-2.0 (10H, m, C_5H_{10})

On the other hand, the negative value of the activation entropy and also the slight dependence of the reaction rate for the transformation of diazo compounds **1f-i** to 1-alkyl-1,2,3-triazoles **2f-i** on the electronic characteristics of the substituent agree with mechanism B. The secondary kinetic isotope effect for this process also agrees with this mechanism, since there is a change in the hybridization of the nitrogen atom of the carboxamide function [21]. Mechanism C is not realized for the alkyl derivatives **1f-i** on account of the high activation energy of the transition from the carboxamide form to the hydroxyimine form.

The introduction of a substituent capable of π-conjugation (in this case an aryl residue) to the nitrogen atom of the carbamoyl group probably reduces the activation energy of the transition. Dimroth [10], who studied the kinetics of ring opening of 4-carbamoyl-5-hydroxy-1,2,3-triazoles to diazo compounds, also noticed the considerably higher rate of ring opening for the aryl derivatives than for the alkyl derivatives.

Thus, we have demonstrated that the cyclization of the N-alkyl and N-aryl derivatives of 2-cyano-2-diazoacetamide takes place by different mechanisms; the cyclization of N-alkyl derivatives proceeds by a monorotatory mechanism, while that of aryl derivatives takes place by a mechanism where one of the stages is heteroelectrocyclization of 2-diazoacetimidates.

TABLE 12. The Spectral Characteristics of the Deuterium Derivatives of Diazo Compounds **14c,d,h,i**

Compound	IR spectrum (KBr), ν, cm^{-1}	Mass spectrum, *m/z*, (%)
14c	2860, 2830 (ND), 2220 (CN), 2115 (N_2), 1670 (CO)	187 (55), 186 (4.7)
14d	2960, 2850 (ND), 2220 (CN), 2125 (N_2), 1670 (CO)	267 (87), 266 (0.8), 265 (79)
14h	2855, 2830 (ND), 2210 (CN), 2116 (N_2), 1620 (CO)	193 (45), 192 (8.5)
14i	2960, 2850 (ND), 2220 (CN), 2115 (N_2), 1640 (CO)	201 (64), 200 (4)

EXPERIMENTAL

The thermodynamics and kinetics of cyclization were studied by UV spectroscopy on a Beckmann M-26 spectrometer in a thermostated cuvette from the variation of the optical density of the solution obtained adding 100 μl of a solution of the investigated substance (concentration ~$1 \cdot 10^{-4}$ M) in ethanol to a cuvette with 2.00 ml of ethanol at 227 and 268 nm, corresponding to the absorption maxima of the initial and final substances. The PMR spectra were recorded on a Bruker 400 instrument at 400 MHz. The IR spectra were obtained on a UR-20 spectrometer in KBr tablets.

Compounds **1,2f,g** were synthesized by the method [23]. The physico-chemical and spectral characteristics are given in Tables 9-12.

2-Cyano-2-diazoacetamides (1f-e,h,i) (General Procedure). To solution of aminonitrile **3a-e,h,i** (40 mmol) in 1N hydrochloric acid (120 ml) solution of sodium nitrite (2.8 g, 41 mmol) in water (15 ml) was added dropwise at 0°C. The precipitate was filtered off, washed with water, and dried over phosphorus pentoxide in a vacuum desiccator. The product formed yellow crystals.

5-Hydroxy-1,2,3-triazole-4-carbonitriles (2a-e,h,i) (General Procedure). A. To solution of sodium ethylate (0.68 g, 10 mmol) in ethanol (50 ml) the respective compound **1a-e,h,i** (10 ml) was added with stirring. After 30 min the precipitate was filtered off and washed with ethanol and with ether. The colorless fine crystals of 1-substituted sodium 4-cyano-1,2,3-triazol-5-olate were dissolved in 50 ml of water and acidified to pH 2 with 1N hydrochloric acid at 0°C. The precipitate was filtered off, washed with water, and dried over phosphorus pentoxide in a vacuum desiccator.

B. Solution of diazo compound **1a-e,h,i** (10 mmol) was boiled in ethanol. The reaction was monitored by TLC. Ethanol was removed under vacuum, and the residue was crystallized from aqueous ethanol. The product formed colorless crystals.

2-Amino-2-cyanoacetamides (3a-e,h,i) (General Procedure). To aluminum amalgam, prepared from aluminum foil (3.51 g, 0.13 mol), saturated solution of the oxime **4a-e,h,i** in ethanol was added dropwise with stirring at 0°C in such a way that the temperature of the reaction mixture did not exceed 25°C. The mixture was stirred for 4 h, water (8 ml) was added, and the mixture was stirred for further 4 h. The precipitated aluminum hydroxide was filtered off and washed on the filter with 300 ml of hot ethanol. The filtrate was concentrated at reduced pressure. The precipitate was filtered off and crystallized from ethanol. The product formed colorless or light-yellow crystals.

2-Cyano-2-hydroxyiminoacetamides (4a-e,h,i) (General Procedure). To suspension of the respective N-substituted 2-cyanoacetamide (0.1 mol) in ethanol (150 ml) solution of sodium ethoxide (0.68 g, 0.1 mol) in ethanol (100 ml) was added. The mixture was stirred for 30 min, the obtained solution was cooled to 0°C, ethyl nitrite (10 ml, 0.012 mol) was added, and the mixture was kept for 1 h. The reaction mass was neutralized with concentrated hydrochloric acid (10 ml), and the precipitate was filtered off and washed with hot ethanol. The filtrate was concentrated at reduced pressure until precipitate began to separate and was then cooled. The precipitate was filtered off and crystallized from ethanol. The product formed light-yellow crystals.

N-Deutero Derivatives of 2-Cyano-2-diazoacetamide (14c,d,h,i). The respective 1-substituted sodium 4-cyano-1,2,3-triazol-5-olate **15c,d,h,i** (0.2 g) was dissolved in D_2O (5 ml). DCl was added to pH 5. The precipitated compound **16c,d,h,i** was filtered off and dried under vacuum. It was then dissolved in 10 ml of absolute toluene and boiled for 5-6 h. The solution was evaporated to dryness at reduced pressure, and diazo compound was isolated on a column with silica gel 40/100 μ as sorbent and chloroform as eluent.

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