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CONDENSED ISOQUINOLINES. 20*. CHARACTERISTIC FEATURES OF THERMAL REARRANGEMENT OF 7,12-DIHYDRO-5H-ISOQUINO[2,3-*a*]QUINAZOLIN-5-ONE TO FORM 6,11-DIHYDRO-13H-ISOQUINO[3,2-*b*]QUINAZOLIN-13-ONE

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We studied the dependence of the direction of conversions for salts of angular 7,12-dihydro-5H-isoquino[2,3-a]quinazolin-5-one on temperature and the nature of the anion: heating in high-boiling solvents leads either to aromatization of the heterosystem or to the rearrangement product, the linear 6,11-dihydro-13H-isoquino[3,2-b]quinazolin-13-one. When its hydrobromide is heated in high-boiling solvents, along with dimerization of the linear isomers, processes of oxidation at the positions 6 and 11 of the heterosystem occur. The dimer obtained in the reaction with morpholine is readily cleaved, with formation of a 6-(4-morpholyl)-substituted linear compound.

Keywords: 6,11-dihydro-13H-isoquino[3,2-*b*]quinazolin-13-one, 11H-isoquino[3,2-*b*]-quinazoline-6,13-dione, oxidation, rearrangement.

The structure of the heterocyclic system of isoquino[3,2-*b*]quinazoline combines two heterocycles of practical importance: isoquinoline and quinazoline, derivatives of which are widely distributed in nature; and among the derivatives of both synthetic and natural origin, a large number are used as drugs. However, because of their relative inaccessibility, the properties of the derivatives of isoquino[3,2-*b*]quinazoline has been practically unstudied so far. Only a few reactions of its 11-oxo derivative are known [2]. The biological activity has been studied only in the case of 6,11-dihydro-13H-isoquino[3,2-*b*]quinazolin-13-one (**1**), for which a rather high level of antifungal and antimicrobial activity has been observed [3]. Earlier [4, 5], a relatively simple method was developed to obtain quinazolinone **1** and its 6-alkyl derivatives, including rearrangement of the corresponding isomeric derivatives with an angular structure: 7,12-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-ones (**2**). In this paper, we consider some features of this process and also the reaction of oxidation of compound **1**.

Isomerization of compound **2** to form quinazolinone **1** occurs at temperatures above 140°C. With the aim of optimizing the process conditions, we tested different high-boiling solvents: N-methyl-2-pyrrolidone [4], dimethylaminoacetonitrile, benzonitrile, dichlorobenzene. In this case, the reaction was accompanied by formation of byproducts, the amount of which increased in proportion to the time the salt of the angular

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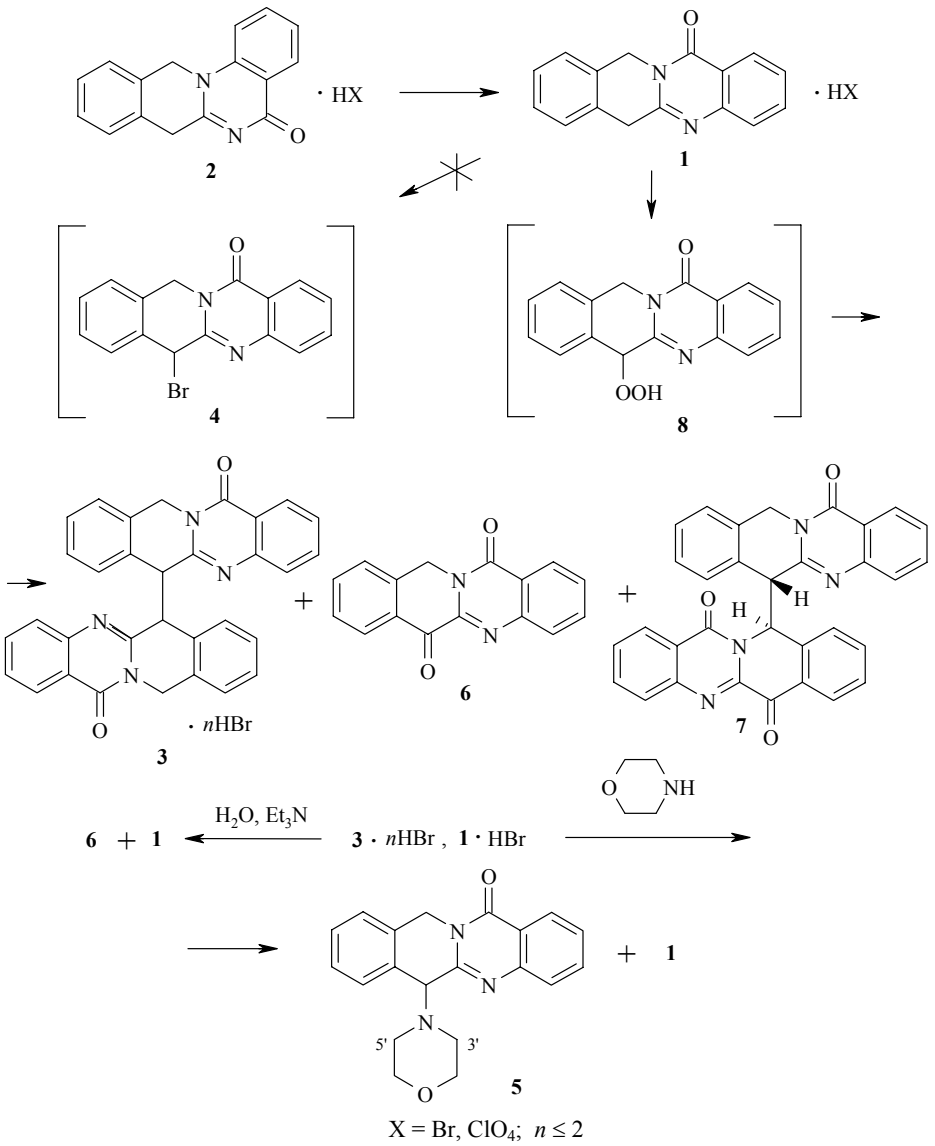
isoquinoquinazolone was heated. Thus heating the hydrobromide of compound **2** in N-methyl-2-pyrrolidone for 6 h (or in benzonitrile for 3 h) led to formation of a mixture of products containing (according to TLC data) only traces of compound **1**. For a longer heating time (~8 h), a complex mixture of compounds was formed which could not be separated. Most likely in this case further conversions of compound **1** occur, evidence for which is the identical result in the experiment with its hydrobromide.



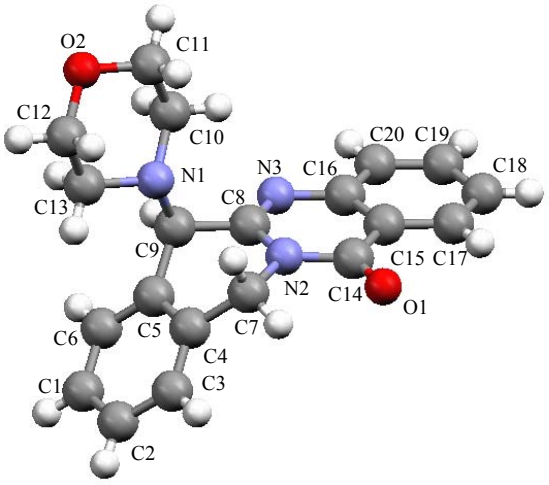
We could isolate several substances from the reaction mixture. After it was cooled, a precipitate formed which after recrystallization from acetic acid contained ~15% hydrobromide of compound **1**. Attempts at repeated recrystallization of the mixture led only to an increase in the content of this compound. In the ^{1}H NMR spectrum of the mixture, signals from eight aromatic and three aliphatic protons corresponded to the unknown product: 6.51 ppm (s), 5.87 ppm (d), and 4.68 ppm (d) with ^2J = 16.8 Hz (Table 1). Previously in 6-benzylisoquino[3,2-*b*]quinazoline, we observed a similar set of signals and a similar type of splitting of the signals from protons of the methylene group $C_{(11)}H_2$ [5]. This allowed us to assume that during rearrangement of compound **2** to form quinazolinone **1**, substitution at one of the methylene groups occurs in structure **1**, leading

TABLE 1. ^{1}H NMR and ^{13}C Spectra of compounds **1**, **3**, **5-7**, **11**

Com-pound	^{1}H NMR spectrum, δ, ppm (*J*, Hz)				^{13}C NMR spectrum, δ, ppm. (*J*, Hz)	
	ArH	$C_{(11)}H_2$	$C_{(6)}H$	Other signals	C (sp^2)	C (sp^3)
1	8.15 (1H, d, ^{o}J = 8.0, H-1), 7.73 (1H, t, ^{o}J = 8.0, H-3), 7.57 (1H, d, ^{o}J = 8.0, H-4), 7.45 (3H, m, H-2,7,10), 7.30 (2H, m, H-8,9)	5.23 (2H, s)	4.15 (2H, s)	—	—	—
3	8.19 (2H, d, ^{o}J = 8.0, H-1,1'), 7.78 (2H, t, ^{o}J = 8.0, H-3,3'), 7.69 (2H, m, H-7,7'), 7.65 (2H, d, ^{o}J = 8.0, H-4,4'), 7.57 (2H, m, H-10,10'), 7.52 (2H, t, ^{o}J = 8.0, H-2,2'), 7.42 (4H, m, H-8,9,8',9')	5.87 (2H, d, ^{2}J = 17.6, $C_{(11)}\underline{H}_AH_B$, $C_{(11')}\underline{H}_AH_B$), 4.68 (2H, d, ^{2}J = 17.6, $C_{(11)}H_A\underline{H}_B$, $C_{(11')}H_A\underline{H}_B$)	6.51 (2H, s)	—	159.73 ($C_{(13)}$), 157.75 ($C_{(5a)}$), 136.28, 131.46 ($C_{(4a)}$), 130.92, 128.90, 128.37, 127.69, 127.58, 127.46, 126.89, 122.94 (br.), 119.30	45.18 $C_{(11)}$), 36.05 ($C_{(6)}$)
5	8.16 (1H, dd, ^{m}J = 1.2, ^{o}J = 8.0, H-1), 7.76 (1H, td, ^{m}J = 1.2, ^{o}J = 8.0, H-3), 7.63 (1H, d, ^{o}J = 8.0, H-4), 7.48 (3H, m, H-2,7,10), 7.36 (2H, m, H-8,9)	5.70 (1H, d, ^{2}J = 15.2, $C_{(11)}\underline{H}_AH_B$), 4.99 (1H, d, ^{2}J = 15.2, $C_{(11)}H_A\underline{H}_B$)	4.36 (1H, s)	3.47 (4H, m, $C_{(2')}H_2$, $C_{(6')}H_2$), 2.44 (2H, m, $C_{(3')}\underline{H}_AH_B$, $C_{(5')}\underline{H}_AH_B$), 2.33 (2H, m, $C_{(3')}H_A\underline{H}_B$, $C_{(5')}H_A\underline{H}_B$)	—	—
6	8.29 (1H, d, ^{o}J = 8.0, H-7), 8.14 (1H, d, ^{o}J = 8.0, H-1), 7.94 (1H, d, ^{o}J = 8.0, H-4), 7.90 (1H, t, ^{o}J = 8.0, H-9), 7.79 (1H, t, ^{o}J = 8.0, H-3), 7.71 (1H, d, ^{o}J = 7.6, H-10), 7.65 (1H, td, ^{m}J = 1.6, ^{o}J = 7.2, H-8), 7.58 (1H, t, ^{o}J = 8.0, H-2)	5.39 (2H, s)	—	—	177.42 (C-6), 161.20 (C-13), 147.12 (C-5a), 145.29 (C-4a), 137.82, 135.27, 135.24, 129.97, 129.32, 129.06, 128.71, 127.67, 127.36, 126.67, 121.78	44.87 (C-11)
7	8.11 (1H, d, ^{o}J = 8.0, H-7'), 7.91 (4H, m, Ar-H), 7.67-7.45 (5H, m, Ar-H), 7.38-7.28 (3H, m, Ar-H), 7.01 (1H, t, ^{o}J = 8.0, H-8), 6.78 (1H, d, ^{o}J = 8.0, H-10'), 6.28 (1H, d, ^{o}J = 8.0, H-**7**)	5.34 (1H, d, ^{3}J = 17.6, $C_{(11)}\underline{H}_AH_B$, 3.47 (1H, br., $C_{(11)}H_A\underline{H}_B$), 6.73 (1H, d, ^{3}J = 6.8, H-11')	4.65 (1H, d, ^{3}J = 6.8)	—	176.53 ($C_{(6')}$), 160.80 ($C_{(5a)}$), 160.41 ($C_{(13)}$), 152.12 ($C_{(13')}$), 147.34 ($C_{(5a')}$), 146.47 ($C_{(4a)}$), 145.35 ($C_{(4a')}$), 136.13, 135.70, 134.84, 134.28, 133.16, 131.56,130.50, 129.88, 129.55, 129.47, 129.31, 128.81, 128.18 (br., 2C), 127.60, 127.43, 127.00 (2C), 126.90, 126.60, 121.54, 119.98	56.28 ($C_{(11')}$), 54.90 ($C_{(6)}$), 44.33 ($C_{(11)}$)
11	8.26 (1H, d, ^{o}J = 8.0, H-7), 8.02 (1H, d, ^{o}J = 7.6, H-10), 7.92 (2H, m, H-3,4), 7.82 (1H, t, ^{o}J = 7.2, H-2), 7.78 (1H, d, ^{o}J = 7.2, H-1), 7.68 (2H, m, H-8, 9)	7.15 (1H, br. s)	—	7.37 (1H, br. s, OH)	178.25 ($C_{(6)}$), 160.53 ($C_{(13)}$), 146.71 ($C_{(3)}$), 144.89 ($C_{(5a)}$), 140.13 ($C_{(4a)}$), 135.89, 135.84, 130.30, 129.97, 129.83, 129.70, 129.18, 127.39, 127.18, 122.49	73.26 (d, J_{CH} = 162, $C_{(11)}$)

to the appearance of a chiral center and consequently to the appearance of diastereotopicity. In the ^{13}C NMR spectrum of the mixture obtained, we also observe signals from 16 carbon atoms of the heteroaromatic system of isoquino[3,2-*b*]quinazolin-13-one and among them, 2 signals at 45.18 ppm (CH_2) and 36.05 ppm (CH). Considering the known fact that the methylene group in benzyl-substituted derivatives is quite sensitive to oxidation by oxygen in the air [6] and based on the spectral data obtained for the unknown compound, we hypothesized the structure of a polyhydrobromide dimer: 6,11,6′,11′-tetrahydro[6,6′]bi[isoquino[3,2-*b*]-quinazolin]-13,13′-dione (**3**) (Scheme 1). The basis for this hypothesis was also the previously described example [7] of oxidative dimerization of benzimidazo[1,2-*b*]isoquinolin-11(5H)-one, leading to a dimer with a symmetric structure. The half set of signals in the NMR spectra of structure **3** is due to the high symmetry of its molecule. Moreover, we also did not rule out the possibility for formation of 6-bromo-6,11-dihydro-13H-isoquino[3,2-*b*]quinazolin-13-one (**4**), as the result of oxidative bromination [8]. However, a serious argument in favor of structure **3** was obtained in analysis of the chromatomass spectrometry data for the mixture: peaks corresponding to its major component were for ions with *m*/*z* (I_{rel}, %): 495 $[M+1]^+$ (90), 249 $[M/2+2]^+$ (80), and 247 $[M/2]^+$ (100).

Additional confirmation of the structure for dimer **3** was obtained in an attempt to recrystallize the mixture of hydrobromides of compounds **1** and **3** from morpholine. In this case, even after boiling a solution of the components for just 5 min, we obtained in 38% yield (Scheme 1) 6-morpholino-6,11-dihydro-13H-isoquino[3,2-*b*]quinazolin-13-one (**5**), the structure of which was established based on X-ray diffraction data as well as by spectral methods (Fig. 1, Tables 2 and 3). The isoquinoline and quinazoline moieties of the molecule do not lie in the same plane, but rather are at a small angle due to the conformation of the pyridine ring of the isoquinoline moiety: the *boat* conformation, which is the most characteristic conformation for 1,4-hexadienes [9]. The morpholine ring is located in a pseudoaxial position, which is quite explainable by the interaction between the dipolar bonds $C_{(9)}$–$N_{(1)}$ and $C_{(8)}$–$N_{(3)}$. As we know [9], an anticlinal position of the polar substituent on the atom adjacent to the carbonyl group is most favorable; in this case, the $C_{(8)}$–$N_{(3)}$ multiple bond, the length of which (1.294 Å) proved to be intermediate between the lengths of the standard double bonds C=N (1.339 Å in pyridine) and C=O (1.235 Å in amides) [10].



Structure of compound **5**

In the ^1H NMR spectrum of 6-morpholino-substituted **5**, there are signals from the eight protons of the morpholine moiety. In this case, the protons of the methylene groups bonded to the nitrogen atom proved to be nonequivalent, and are observed as two multiplets with chemical shift difference $\Delta\delta$ = 0.11 ppm (Table 1),

which suggests conformational anchoring of the position of the morpholine ring. The protons of the methylene group $C_{(11)}H_2$, as would be expected [5], are also magnetically nonequivalent and give two doublets with $\Delta\delta = 0.71$ ppm and $^2J = 15.5$ Hz.

Dimer **3** proved to be unstable relative to treatment with not only morpholine but also relatively weaker bases. Thus even when the mixture of hydrobromides of compounds **1** (~15%) and **3** were reacted with water in the presence of Et_3N, nucleophilic substitution of the isoquinoquinazoline moiety occurred at the 6 position as well as further oxidation of the reaction product, which led to a mixture of 11H-isoquino[3,2-*b*]quinazoline-6,13-dione (**6**) and compound **1** (~60%, according to ^{1}H NMR data). We should note that formation of compound **6** was also detected spectrally (^{1}H NMR) in the reaction mixture when carrying out the rearrangement, but in amounts insufficient for identification. In its ^{1}H NMR spectrum, two doublets are found downfield from the eight aromatic protons at 8.29 ppm (H-8), 8.14 ppm (H-1), but in the region of absorption by the aliphatic protons we only see one signal at 5.39 ppm (2H, s) of the methylene group $C_{(11)}H_2$, corresponding to the signal at 44.87 ppm in the ^{13}C NMR. The carbon atoms of the carbonyl groups resonate in the 177.42 ppm region ($C_{(6)}$, in the region characteristic for carbon atoms of the ketone carbonyl groups) and the 161.20 ppm region ($C_{(13)}$). In the IR spectrum, we find two bands for stretching vibrations of the carbonyl groups in the 1690 and 1670 cm^{-1} region.

In addition to compounds **3** and **6** (the formation of which during rearrangement of the salt of compound **2** was detected by spectral methods), we isolated from the reaction mixture in pure form and characterized one more product (scheme 1): 6,11-dihydro-11′H-[6,11′]bi[isoquino[3,2-*b*]quinazolinyl]-13,6′,13′-trione (**7**). This compound, in contrast to dimer **3**, proved to be stable to treatment with nucleophiles and is not cleaved when treated with morpholine. In the ^{1}H NMR spectrum of dimer **7**, we observed a very complicated pattern for

TABLE 2 Some Bond Angles (ω) in the Molecule of Compound **5**

Angle	ω, deg	Angle	ω, deg
$C_{(3)}C_{(4)}C_{(7)}$	121.99(12)	$C_{(16)}C_{(15)}C_{(14)}$	119.78(12)
$C_{(5)}C_{(4)}C_{(7)}$	117.97(11)	$N_{(2)}C_{(14)}C_{(15)}$	113.70(11)
$C_{(6)}C_{(5)}C_{(9)}$	122.97(12)	$N_{(3)}C_{(16)}C_{(15)}$	122.38(12)
$C_{(4)}C_{(5)}C_{(9)}$	116.73(11)	$N_{(3)}C_{(16)}C_{(20)}$	118.57(12)
$N_{(2)}C_{(7)}C_{(4)}$	110.02(10)	$C_{(10)}N_{(1)}C_{(13)}$	108.71(10)
$N_{(3)}C_{(8)}N_{(2)}$	125.05(12)	$C_{(10)}N_{(1)}C_{(9)}$	110.68(10)
$N_{(3)}C_{(8)}C_{(9)}$	119.28(11)	$C_{(13)}N_{(1)}C_{(9)}$	111.56(10)
$N_{(2)}C_{(8)}C_{(9)}$	115.67(11)	$C_{(8)}N_{(2)}C_{(14)}$	122.23(11)
$N_{(1)}C_{(9)}C_{(5)}$	110.66(10)	$C_{(8)}N_{(2)}C_{(7)}$	120.02(11)
$N_{(1)}C_{(9)}C_{(8)}$	108.42(10)	$C_{(14)}N_{(2)}C_{(7)}$	117.65(10)
$C_{(5)}C_{(9)}C_{(8)}$	108.70(10)	$C_{(8)}N_{(3)}C_{(16)}$	116.85(11)

TABLE 3 Bond Lengths (*l*) in the Molecule of Compound **5**

Bond	*l*, nm	Bond	*l*, nm
$C_{(4)}$–$C_{(5)}$	1.3965(18)	$C_{(11)}$–$O_{(2)}$	1.4286(18)
$C_{(4)}$–$C_{(7)}$	1.5040(18)	$C_{(12)}$–$O_{(2)}$	1.4297(18)
$C_{(5)}$–$C_{(9)}$	1.5131(18)	$C_{(12)}$–$C_{(13)}$	1.514(2)
$C_{(7)}$–$N_{(2)}$	1.4817(16)	$C_{(13)}$–$N_{(1)}$	1.4702(17)
$C_{(8)}$–$N_{(3)}$	1.2938(17)	$C_{(14)}$–$O_{(1)}$	1.2239(16)
$C_{(8)}$–$N_{(2)}$	1.3833(17)	$C_{(14)}$–$N_{(2)}$	1.4002(16)
$C_{(8)}$–$C_{(9)}$	1.5150(17)	$C_{(14)}$–$C_{(15)}$	1.4614(18)
$C_{(9)}$–$N_{(1)}$	1.4811(17)	$C_{(15)}$–$C_{(16)}$	1.4012(19)
$C_{(10)}$–$N_{(1)}$	1.4686(17)	$C_{(16)}$–$N_{(3)}$	1.3955(17)
$C_{(10)}$–$C_{(11)}$	1.510(2)		

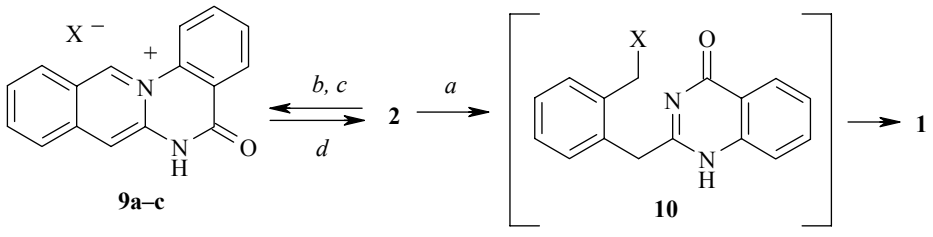
absorption in the aromatic region (overall integrated intensity 17H). The protons of the methylene group $C_{(11)}H_2$ are not equivalent, and form an AB spin system with chemical shift differences $\Delta\delta$ = 1.9 ppm. In this case, the signal from one of the protons is observed as a doublet with ^2J = 17.6 Hz (5.34 ppm), while the second is observed as a broadened multiplet at 3.47 ppm, which is transformed to a doublet (3.52 ppm) with ^2J = 17.6 Hz at 80°C. The temperature dependence of the shape of the signal from only one proton of the pair for $C_{(11)}H_2$ is explained by conformational changes in the pyridine ring of the isoquinoline moiety. The position of the signals from the methine protons, one of which falls within the absorption region for aromatic protons, is established based on COSY HH data: two doublets with $\Delta\delta$ = 2.15 ppm and ^3J = 6.8 Hz. Both the *cis* and *trans* arrangement of the protons could correspond to this vicinal spin–spin coupling constant [11]. Based on analysis of spatial models, realization of specifically the structure of the *trans* isomer seems most likely to us. Indirect evidence for this comes from the position of the two doublets of the aromatic protons upfield (6.76 ppm, H-10′ and 6.27 ppm, H-7) compared with the rest of the aromatic protons and the corresponding signals in the starting compound **1**: only in the *trans* isomer do these protons fall within the region of shielding of the multiple bonds $N_{(5)}$=$C_{(5a)}$ and $C_{(13')}$=O respectively. In the ^{13}C NMR spectrum, we find the signals from 32 carbon atoms. These include a signal in the 176.53 ppm region ($C_{(6')}$), characteristic for absorption by the carbon atoms of ketone carbonyl groups, and three signals in the aliphatic region: 56.28 ppm ($C_{11'}$), 54.90 ppm ($C_{(6)}$), 44.33 ppm ($C_{(11)}$). Comparative analysis of the electronic spectra of 6,13-dioxoisoquinoquinazoline **6** and the dimer **7** also showed a high degree of similarity between them.

We should point out that in addition to compounds **3**, **6**, and **7**, in the reaction mixture we spectrally detected the presence of other compounds, most likely having a dimer structure (~6:1:3), but in amounts an order of magnitude smaller than for compounds **3**, **6**, and **7**.

With the aim of determining the characteristic features of the mechanism for the formation of oxidation products **3**, **6**, and **7**, we studied the effect of protonation and the nature of the anion in salts of compound **1** on the outcome of the oxidation reaction. Prolonged heating of the perchlorate of compound **1** in benzonitrile also led to a mixture of oxidation products, the major component of which was the dimer **3**. This suggests that the probability of formation of 6-bromoisoquinoquinazoline **4** as an intermediate in synthesis of compounds **3**, **6**, and **7** is low, while the most likely mechanism obviously includes a step of formation of the 6-peroxide **8** when exposed to oxygen in the air [6]. Confirmation of this hypothesis also comes from the fact that we also obtained compound **6** with prolonged passage of air through the solution of the base **1** in benzonitrile with heating. Thus the primary conditions for oxidation of compound **1** are high temperature (>180°C) and access to oxygen in the air.

Back in [4] it was noted that the perchlorate of compound **2** is also easily rearranged to form the linear isomer when heated in N-methyl-2-pyrrolidone. It was found that carrying out this reaction at a higher temperature (in benzonitrile) leads to a different result: the hydroiodide and the perchlorate of compound **2** are readily oxidized to form the corresponding 5-oxo-5H,6H-isoquino[2,3-*a*]quinazolin-13-ium salts **9a,b** (Scheme 2). We should note that we previously attempted to accomplish aromatization of the isoquino[2,3-*a*]quinazoline system [13]. A positive result was obtained only in the case when the perchlorate of 6-methyl-7,12-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-one was heated in nitrobenzene, while the hydrobromide and the perchlorate of compound **2** under these conditions were converted to complicated mixtures of products. Obviously using benzonitrile ensures gentler oxidation (by oxygen in the air), in contrast to nitrobenzene, which is an oxidizing agent itself. Oxidation of the above-indicated salts in benzonitrile, rather than rearrangement as in the case of the hydrobromide, can be explained by the appearance of steric hindrances to formation of the intermediate compound **10** [4] (Scheme 2) for attack by bulkier anions at the 12 position of compound **2**. The bromide **9c** was obtained when we attempted to acylate the base **2** at 150°C with *o*-bromomethylbenzoic acid chloride. The salts **9a-c** are easily reduced by $NaBH_4$ in ethanol to form the base **2**, which proves that the angular structure is preserved in the oxidation products. The ^{1}H NMR spectra of salts **9a-c** are characterized by the presence

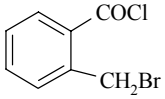
Scheme 2



9 a X = I, **b** X = ClO_4, **c** X = Br;

a: HBr, PhCN; *b*: HI, PhCN (**9a**); $HClO_4$, PhCN (**9b**); *c* (**9c**)

d: $NaBH_4$, EtOH



downfield of an NH signal at 13.66 ppm (broad s) and an H-12 signal in the 10.90-11.31 ppm region (s), characteristic for the H-12 proton of the heteroaromatic 18 π-electron system of isoquino[2,3-*a*]quinazoline [12]. The position of the signals from the H-1 and H-11 protons proved to be sensitive to the nature of the anion: for the bromide **9c**, they are observed further downfield than for the iodide and the perchlorate (see Experimental) due to the different degrees of interaction between ions of different volume in solution.

EXPERIMENTAL

The melting points were determined on a Boetius heating stage and uncorrected. The IR spectra of the compounds in KBr disks were recorded on a Pye Unicam SP3-300. The ^1H and ^{13}C spectra were obtained on a Varian Mercury 400 (400 MHz and 100 MHz respectively) in DMSO-d_6, internal standard TMS; the UV spectra were recorded on a Specord M-400 spectrophotometer. The mass spectra were obtained on an AGILENT/100 Series HPLC/mass spectrometer (chemical ionization (CI), acetonitrile containing 0.05% formic acid). X-ray diffraction analysis was carried out on a Bruker CCD Detector (MoKα, graphite monochromator, θ/2θ scanning, $2\theta_{max}$ = 60°) with measurement of the intensities of 3397 independent reflections (R_{all} = 0.049). The spectral characteristics of compounds **1**, **3**, **5-7**, **11** are shown in Table 1.

7,12-Dihydro-5H-isoquino[2,3-*a*]quinazolin-5-one Hydroiodide (2·HI). HI (3 ml) was added to a solution of isoquinoquinazoline **2** (1 g, 4.03 mmol) in acetic acid (10 ml). The precipitate that formed after 30 min was filtered out and washed with acetone. Yield 1.29 g (85%), mp 335-338°C (AcOH). IR spectrum (thin film), ν, cm^{-1}: 3450 (NH), 3040, 1725 (C=O, C=N), 760. ^1H NMR spectrum, δ, ppm (*J*, Hz): 8.39 (1H, d, ^oJ = 8.8, H-4); 8.34 (1H, dd, ^oJ = 7.8, ^mJ = 0.8, H-1); 8.17 (1H, td, ^oJ = 7.8, ^mJ = 0.8, H-2); 7.85 (1H, t, ^oJ = 7.8, H-3); 7.60 (1H, m, H-11); 7.46-7.41 (3H, m, H-8 to H-10); 5.68 (2H, s, $C_{(12)}H_2$); 4.50 (2H, s, $C_{(7)}H_2$). Found, %: C 50.96; H 3.30; N 7.47. $C_{16}H_{13}IN_2O$. Calculated, %: C 51.08; H 3.48; N 7.45.

6,11-Dihydro-11′H-6,11′-bi(isoquino[3,2-*b*]quinazoline)-13,6′,13′-trione (7). A solution of the hydrobromide **2.** HBr (1 g, 3.04 mmol) in benzonitrile (15 ml) was boiled for 1 h and then cooled; then acetone (30 ml) was added. The precipitate formed by the next day was filtered out and washed with acetone. The solid material, which was a mixture of the hydrobromides of compounds **1** and **3**, was recrystallized from acetic acid, and 0.5 g was obtained of a mixture containing ~15% hydrobromides of compounds **1** and **3**. The acetone filtrate was evaporated down under vacuum and 2-propanol was added to the residue. The colorless precipitate formed was filtered out and recrystallized from DMF; dimer **7** was obtained. Yield 0.3 g (35%), mp 279 -281°C

(DMF). IR spectrum (thin film), ν, cm^{-1}: 1670 (broad, C=O), 1590 (broad, C=N), 1470, 1310, 768, 750. UV spectrum (MeOH), λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 276 (248.18), 284 (244.09), 309 (142.39), 320 (128.40), 355 (71.19). Found, %: C 75.12; H 3.80; N 11.03. $C_{32}H_{20}N_4O_3$.Calculated, %: C 75.58; H 3.96; N 11.02.

6-Morpholino-6,11-dihydro-13H-isoquino[3,2-*b*]quinazolin-13-one (5). A mixture of hydrobromides of compounds **1** (15%) and **3** (2 g, 6.08 mmol, calculated on the basis of **2**·HBr), was dissolved with heating in morpholine (12 ml, 14.0 mol) and boiled for 5 min. The solvent was evaporated under vacuum, water (20 ml) was added to the residue; the solid material (containing isoquinoquinazoline **1** and compound **5**) was filtered out, washed with water and 2-propanol and recrystallized from DMF. The mixture obtained was boiled in Ac_2O (10 ml) for 5 h. The mixture was cooled; the precipitate formed was filtered out, washed with acetone, and recrystallized from DMF, and compound **5** was obtained. Yield 0.7 g (35%), mp 248-250°C (DMF). IR spectrum (thin film), ν, cm^{-1}: 1678 (C=O), 1603 (C=N), 1110 (C–O), 870, 775, 755. Mass spectrum, *m*/*z* (I_{rel}, %): 334 $[M+1]^+$ (98), 247 $[M+1-C_4H_9NO]^+$ (100). Found, %: N 12.61. $C_{20}H_{19}N_3O_2$. Calculated, %: N 12.60.

Crystallographic Data. Crystals of compound **5** ($C_{20}H_{19}N_3O_2$), grown from $CHCl_3$, were colorless and monoclinic. At 133 K: a = 9.9221(7), b = 14.800(1), c = 12.0369(9) Å, β = 110.739(1)°, V = 1653.0(2) $Å^3$, d_{calc} = 1.340 g/cm^3, space group $P2(1)/n$, Z = 4, $F(000)$ = 704, μ = 0.088 mm^{-1}. The structure was deciphered by the direct method using the SHELXL-97 software package [13]. The values of 226 parameters were corrected on F^2 by the least squares method [14]. R_1 = 0.0489, wR_2 = 0.1007.

11H-Isoquino[3,2-*b*]quinazoline-6,13-dione (6). A mixture of hydrobromides of compounds **1** (15%) and **3** (2 g, 6.08 mmol) was suspended in 2-propanol (aq.) (30 ml); Et_3N (5 ml) was added, and the mixture was boiled for 15 min. The precipitate formed after cooling was filtered out and washed with 2-propanol. The solid material was carefully washed with water and after recrystallization from DMF, 0.75 g (50%) pure isoquino[3,2-*b*]quinazolinone **1** was obtained. After 2 days, a crystalline, a dark-pink precipitate of compound **6** fell out of the filtrate. The precipitate was filtered out, washed with a small amount of 2-propanol, and recrystallized from dioxane. Yield 0.6 g (38%), mp 209 -210°C (dioxane). IR spectrum (thin film), ν, cm^{-1}: 1690 (C=O), 1670 (broad, C=O, C=N), 1305, 775, 750. UV spectrum (MeOH), λ_{max}, nm ($\varepsilon \cdot 10^{-3}$): 214 (29.97), 268 (10.62), 302 (8.12), 316 (8.43), 340 (7.80). Mass spectrum, *m*/*z* (I_{rel}, %): 263 $[M+1]^+$ (100). Found, %: C 73.13; H 3.78; N 10.70. $C_{16}H_{10}N_2O_2$. Calculated, %: C 73.27; H 3.84; N 10.68.

5-Oxo-5H,6H-isoquino[2,3-*a*]quinazolin-13-ium Iodide (9a). Isoquino[2,3-*a*]quinazoline hydroiodide **2** (1 g, 2.66 mmol) was boiled in benzonitrile (15 ml) for 40 min. The precipitate formed after cooling was filtered out and washed with acetone. Yield 0.61 g (61%), mp 260-261°C (AcOH). IR spectrum (thin film), ν, cm^{-1}: 3450 (NH), 3040, 1690 (broad, C=O), 1645 (broad, C=N), 1330, 1135, 875, 755. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 13.67 (1H, br. s, NH); 10.94 (1H, s, H-12); 8.97 (1H, d, ^oJ = 8.8, H-1); 8.47 (2H, m, H-4,11); 8.22 (2H, m, H-3,8); 8.09 (2H, m, H-2,7); 7.99 (1H, t, ^oJ = 7.6, H-9); 7.83 (1H, t, ^oJ = 7.6, H-10). Found, %: C 51.27; H 2.90; N 7.47. $C_{16}H_{11}IN_2O$. Calculated, %: C 51.36; H 2.96; N 7.49.

5-Oxo-5H,6H-isoquino[2,3-*a*]quinazolin-13-ium Perchlorate (9b) was obtained similarly from) of the perchlorate of compound **2** (1 g, 2.87 mmol). Yield 0.68 g (68%), mp 311-312°C (AcOH). IR spectrum (thin film), ν, cm^{-1}: 3450 (NH), 3040, 1700 (broad, C=O), 1648 (broad, C=N), 1233, 1080 (ClO_4^-), 890, 764, 615. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 13.66 (1H, br. s, NH); 10.91 (1H, s, H-12); 8.95 (1H, d, ^oJ = 8.8, H-1); 8.46 (2H, m, H-4,11); 8.22 (2H, m, H-3,8); 8.09 (2H, m, H-2,7); 7.99 (1H, t, ^oJ = 7.6, H-9); 7.82 (1H, t, ^oJ = 7.6, H-10). Found, %: C 55.35; H 3.11; Cl 10.24; N 8.10. $C_{16}H_{11}ClN_2O_5$. Calculated, %: C 55.43; H 3.20; Cl 10.23; N 8.08.

5-Oxo-5H,6H-isoquino[2,3-*a*]quinazolin-13-ium Bromide (9c). A mixture of isoquinoquinazoline **2** (1 g, 4.03 mmol) and 2-bromomethylbenzoic acid chloride (1.17 g, 5.0 mmol) was interfused on an oil bath at 130--150°C for 2 h. After cooling, the melt was triturated with acetone (10 ml.) The solid material was filtered out and washed with acetone. Yield 0.55 g (42%), mp 307-309°C (AcOH). IR spectrum (thin film), ν, cm^{-1}: 3450 (NH), 3040, 1700 (broad, C=O), 1640 (broad, C=N), 1352, 1325, 890, 758. ^{1}H NMR spectrum,

δ, ppm (*J*, Hz): 13.66 (1H, br. s, NH); 11.32 (1H, s, H-12); 9.27 (1H, d, ^{o}J = 8.8, H-1); 8.73 (1H, d, ^{o}J = 8.0, H-11); 8.45 (1H, d, ^{o}J = 7.6, H-4); 8.24-8.18 (2H, m, H-3,8); 8.10 (1H, s, H-7); 8.08 (1H, m, H-2); 7.97 (1H, t, ^{o}J = 7.6, H-9); 7.82 (1H, t, ^{o}J = 7.6, H-10). Found, %: C 58.67; H 3.29; Cl 24.43; N 8.60. $C_{16}H_{11}BrN_2O$. Calculated, %: C 58.74; H 3.39; Br 24.42; N 8.56.

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