

## CONDENSED ISOQUINOLINES.

### 10\*. BOROHYDRIDE REDUCTION

#### IN THE 5H-ISOQUINO[2,3-*a*]-

#### QUINAZOLIN-5-ONE SERIES

V. M. Kisel, L. M. Potikha, A. V. Turov, and V. A. Kovtunenکو

*Borohydride reduction in a series of 7-benzyl- and newly synthesized 7-arylmethylene-7,12-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-ones leads stereoselectively to erythro-7-benzyl-6,6a,7,12-tetrahydro-5H-isoquino[2,3-*a*]quinazolin-5-ones. 7,7-Disubstituted 7,12-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-ones are inert to the action of sodium borohydride, but spiro[5H-isoquino[2,3-*a*]quinazolin-7(12H),2'-indane]-5-one is reduced under rigid conditions to 6,6a-dihydrospiro[5H-isoquino[2,3-*a*]quinazolin-7(12H),2'-indan]-5-one. 7-Acetyl- and 7-benzoyl-6,11-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-ones are converted in an aqueous alcoholic solution of sodium borohydride to the previously described 6,6a,7,12-tetrahydro-5H-isoquino[2,3-*a*]quinazolin-5-one. The structure and special features of the conformational behavior of the reduction products obtained were demonstrated by <sup>1</sup>H NMR spectroscopy.*

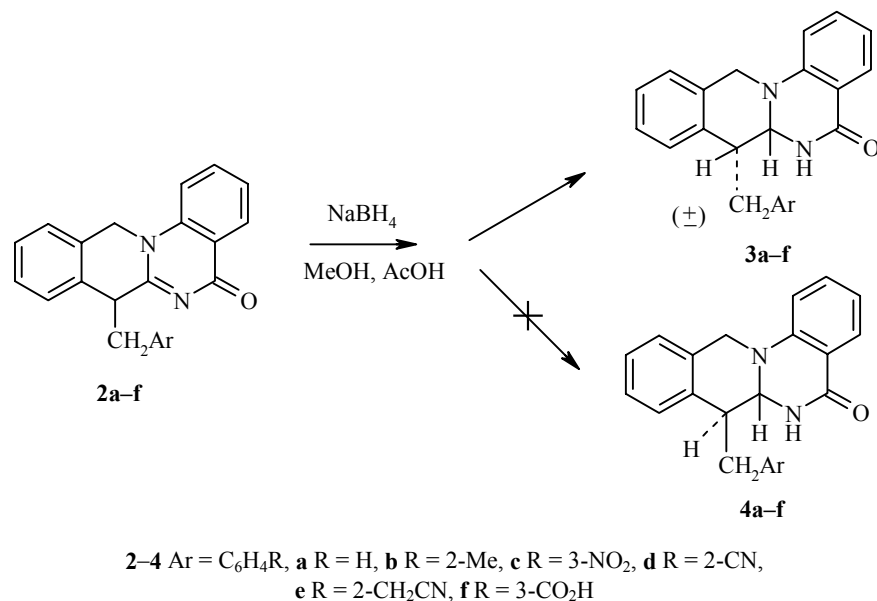
**Keywords:** condensed isoquinolines, condensed quinazolines, borohydride reduction.

We showed previously [2] that reduction of 7,12-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-one (**1**) and its N<sub>(6)</sub> quaternary salt leads to 6,6a,7,12-tetrahydro-5H-isoquino[2,3-*a*]quinazolin-5-ones, the methylation of which occurs at the N<sub>(13)</sub> nodal nitrogen atom with the formation of tetrahydroisoquinoquinazolinium salts of various stereochemical structure depending on the substituent at N<sub>(6)</sub>. In view of the promise of searching for biologically active substances among isoquinolines and quinazolines, the azine fragments of which are partially or completely hydrogenated, investigations have been continued in the present work in the 6,6a,7,12-tetrahydro-5H-isoquino[2,3-*a*]quinazolin-5-one series. For this purpose we have studied the reduction of 7-benzyl-7,12-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-ones (**2**), synthesized previously [1,3] by the alkylation of isoquinoquinazolone **1** with benzyl halides.

As might have been expected [4], sodium borohydride in boiling methanol readily reduces the C<sub>(6a)</sub>=N<sub>(6)</sub> double bond in the hydrohalides of dihydroisoquinoquinazolones **2**·HX. The free bases **2** may also be subjected to reduction, however their reactivity and the yields of the reduction products were significantly less. The conduct of the reaction requires the use of more rigid conditions, *viz.* 1.5 h boiling in methanol with a sevenfold excess of sodium borohydride in the presence of acetic acid. The resulting compounds **3a-f** (for confirmation of

\* For Part 9 see [1].

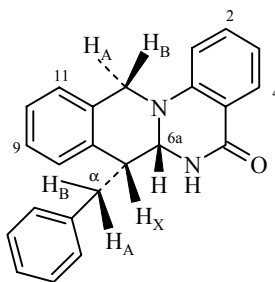
their structure see below) were identical to samples obtained from the protonated salts, i.e. the possible reduction of the amide group under these conditions does not take place [5]. The presence of a C=O band in the IR spectra of the reduction products (Table 1) indicates the retention of the carbonyl group in the course of the reaction, for which the regular [6] high frequency displacement (by 25-30  $\text{cm}^{-1}$ ) compared with the dihydro derivatives **2** was noted. The band for the stretching vibrations of the C=N bond was absent, but there was a band for an N-H bond at 3050  $\text{cm}^{-1}$ .



Theoretically the formation of two diastereomeric reduction products is possible, in which the hydrogen atoms of the C<sub>(6a)</sub>-C<sub>(7)</sub> fragment are disposed on one (*erythro*) or different (*threo* isomer) sides of the tetrahydroisoquinoline ring. However in all cases one set of signals was observed in the <sup>1</sup>H NMR spectra of the unpurified products isolated in yields close to quantitative. This indicates the high degree of stereoselectivity of the reduction reaction. It is evident that attack of the compound **2** molecule by borohydride anion at the C<sub>(6a)</sub> atom from the side screened by the benzyl substituent is unlikely. On the other hand the alternative direction of attack from the opposite side is sterically more preferred and must lead to the *erythro* products. The <sup>1</sup>H NMR spectral data of reduction products **3a-f** are given in Table 2. The presence in these spectra of a doublet with coupling constant 3.4 Hz at 5.22-5.41 ppm, belonging to the signal of the 6a-H proton attracts attention. The size of the observed vicinal coupling constant is more characteristic [7] for a cisoid orientation of protons. We have carried out a series of experiments using the nuclear Overhauser effect (NOE), with compound **3a** as example (spectrum in Fig. 1), with the aim of establishing unequivocally the structure of the reduction products and the features of their conformational behavior. Saturation was carried out sequentially at the resonance frequency of each of the aliphatic protons and also of the aromatic proton giving a signal at high field (6.36 ppm), which stands separately from the signals of the remaining aromatic protons. The results of these experiments are summarized in Table 3. The high mutual values of the NOE in the experiments for {6a-H}\* and {7-H}, of 8 and 13% respectively confirm the structure of the reduction products as *erythro*-7-benzyl-6,6a,7,12-tetrahydro-5H-isoquino[2,3-*a*]quinazolin-5-ones **3a-f**.

\* Braces denote protons at the resonance frequency of which saturation was carried out in the NOE experiment.

TABLE 1. Characteristics of 6,6a,7,12-Tetrahydro-5H-isoquino[2,3-*a*]-quinazolin-5-ones



Compound	Empirical formula	Found, %			mp, °C	IR spectrum, $\nu$ , $\text{cm}^{-1}$			Yield, %
		Calculated, %				C=O	N-H	other signals	
		C	H	N					
<b>3a</b>	C <sub>23</sub> H <sub>20</sub> N <sub>2</sub> O	81.23	6.02	8.22	200	1665	3040		75
		81.15	5.92	8.23					
<b>3b</b>	C <sub>24</sub> H <sub>22</sub> N <sub>2</sub> O	81.43	6.35	8.05	217	1660	3040		74
		81.38	6.26	7.90					
<b>3c</b>	C <sub>23</sub> H <sub>19</sub> N <sub>3</sub> O <sub>3</sub>	71.72	5.01	11.27	210	1660	3060	1345, 1520 (NO <sub>2</sub> )	79
		71.68	4.97	10.90					
<b>3d</b>	C <sub>24</sub> H <sub>19</sub> N <sub>3</sub> O	78.90	5.32	11.57	227	1663	3040	2220 (CN)	62
		78.88	5.24	11.50					
<b>3e</b>	C <sub>25</sub> H <sub>21</sub> N <sub>3</sub> O	79.21	6.03	10.99	207	1660	3060	2239 (CN)	61
		79.13	5.98	11.07					
<b>3f</b>	C <sub>24</sub> H <sub>20</sub> N <sub>2</sub> O <sub>3</sub>	75.00	5.30	7.40	219	1675, 1660	3060	2900 (OH)	52
		74.98	5.24	7.39					
<b>3g</b>	C <sub>24</sub> H <sub>22</sub> N <sub>2</sub> O <sub>2</sub>	77.89	6.09	7.59	216	1665	3060		77
		77.81	5.99	7.56					
<b>3h</b>	C <sub>23</sub> H <sub>19</sub> BrN <sub>2</sub> O* <sup>2</sup>	65.93	4.62	6.78	238	1675	3040		69
		65.88	4.57	6.68					
<b>3i</b>	C <sub>27</sub> H <sub>29</sub> N <sub>3</sub> O	78.72	7.23	10.40	168	1660	3040		71
		78.80	7.10	10.21					
<b>3j</b>	C <sub>23</sub> H <sub>20</sub> N <sub>2</sub> O <sub>2</sub>	77.56	5.70	7.72	217	1630	3040	2900 (OH)	67
		77.51	5.66	7.86					
<b>3k</b>	C <sub>23</sub> H <sub>19</sub> BrN <sub>2</sub> O <sub>2</sub> * <sup>3</sup>	63.40	4.52	6.55	223	1650	3050		65
		63.46	4.40	6.44					
<b>3l</b>	C <sub>23</sub> H <sub>20</sub> N <sub>2</sub> O <sub>3</sub>	73.83	5.40	7.47	200	1645	3000		66
		74.18	5.41	7.52					
<b>3m</b>	C <sub>25</sub> H <sub>24</sub> N <sub>2</sub> O <sub>3</sub>	75.03	6.11	7.01	205	1660	3060		76
		74.98	6.04	7.00					

\* From phenylmethylene derivative **5a**.

\*<sup>2</sup> Found, %: Br 18.95. Calculated, %: Br 19.06.

\*<sup>3</sup> Found, %: Br 18.49. Calculated, %: Br 18.36.

The size of the dihedral angle H-C<sub>(6a)</sub>-C<sub>(7)</sub>-H was determined to be about 50° with the aid of a modified Karplus equation from the size of the observed coupling constant allowing for the electronegativity of substituents and their orientation relative to the interacting protons [8].

As analysis of a molecular model showed the size of the angle found corresponds to a "distorted half-chair" conformation for the tetrahydroisoquinoline ring (Fig. 2, a) in which the C<sub>(6a)</sub> carbon atom is separated from the plane of the remaining atoms of the bicycle. This conclusion is in agreement with the results of the NOE experiment for {7-H}, indicating the steric proximity of this proton to the proton at N<sub>(6)</sub>.

TABLE 2. <sup>1</sup>H NMR Spectra of the Compounds Synthesized,  $\delta$ , ppm, Coupling Constants ( $J$ ), Hz

Compound	N <sub>(6)</sub> -H	H <sub>arom</sub> , m*	8-H, d, $J = 8$	6a-H, d, ${}^3J = 3.4$	12-H <sub>A</sub> , d, ${}^2J = 16$	12-H <sub>B</sub> , d, ${}^2J = 16$	7-H, t, ${}^3J = 6$	$\alpha$ -H <sub>A</sub> , dd, ${}^2J = 12.7$ , ${}^3J = 3.4$	$\alpha$ -H <sub>B</sub> , dd, ${}^2J = 12.7$ , ${}^3J = 10.3$	Other signals
<b>3a</b>	8.87	8.21-6.82 (12H)	6.36	5.39	4.74	4.31	3.28	3.56	2.62	
<b>3b</b>	8.61	8.20-6.85 (11H)	6.23	5.41	4.86	4.36	3.27	3.44	2.80	1.74 (3H, s, CH <sub>3</sub> )
<b>3c</b>	8.60	8.00-6.75 (11H)	6.18	5.22	4.83	4.24	3.22	3.51	2.70, m	
<b>3d</b>	8.52	8.20-6.78 (11H)	6.03	5.26	4.87	4.26	3.25	3.50	2.90	
<b>3e</b>	8.61	7.90-6.80 (11H)	6.05	5.27	5.00	4.30	3.10-3.70, m		2.60, m (3H)* <sup>2</sup>	
<b>3f</b>	8.72	7.82-6.75 (11H)	6.13	5.21	4.91	4.27	3.20-3.60, m		2.60, m	
<b>3g</b>	8.32	8.13-6.65 (11H)	6.45	5.39	4.74	4.29	3.20	3.50	2.59	3.75 (3H, s, OCH <sub>3</sub> )
<b>3h</b>	8.42	7.80-6.75 (11H)	6.25	5.23	4.82	4.26	3.20	3.45	2.60, m	
<b>3i</b>	8.43	8.17-6.42 (12H)		5.35	4.71	4.29	3.27, m* <sup>3</sup> (6H)		2.50	1.11 (6H, t, $J = 7$ , CH <sub>3</sub> )
<b>3j</b>	8.18	7.82-6.55 (11H)	6.33	5.22	4.88	4.26	3.19, m	3.33, m	2.74	9.00 (1H, s, OH)
<b>3k</b>	8.40	7.81-6.60 (10H)	6.36	5.20	4.88	4.24	3.16	3.26	2.80	
<b>3l</b>	8.47	8.00-6.18 (11H)		5.18	4.84	4.23	3.19, m		2.50, m	8.54 (2H, s, OH)
<b>3m</b>	8.82	8.12-6.40 (11H)		5.38	4.68	4.28	3.28	3.50	2.60	3.80 (3H, s, 3'-OCH <sub>3</sub> ) 3.62 (3H, s, 4'-OCH <sub>3</sub> )

\* The signal of the 4-H proton was identified in several cases as dd ( ${}^oJ = 8$ ,  ${}^mJ = 1.5$ ) at 8.15 (for compounds **3a,b,d,i**), 8.09 (**3g,m**), 7.86 (**3e**), 7.78 (**3j-l**), and 7.76 ppm (**3h**).

\*<sup>2</sup> Overlapped with the signal (2H, s, CH<sub>2</sub>CN).

\*<sup>3</sup> Overlap of signals for 7-H, H<sub>A</sub>, -N(CH<sub>2</sub>)-

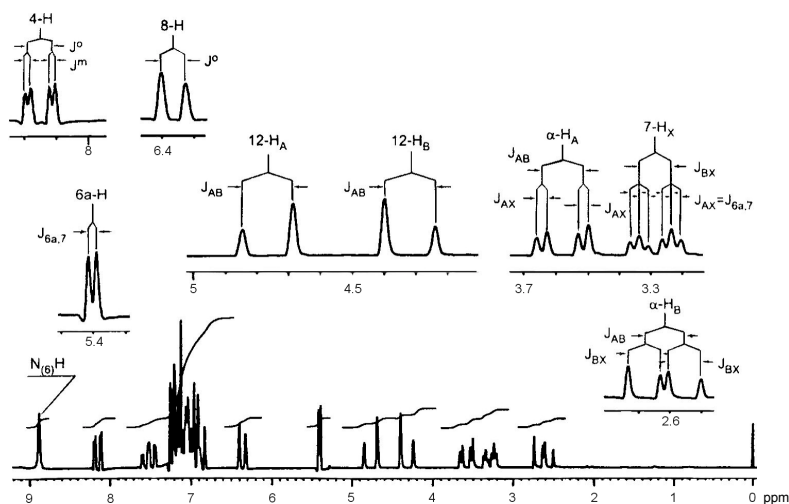


Fig. 1.  $^1\text{H}$  NMR spectrum of tetrahydroisoquinoquinazolinone **3a** in  $\text{CDCl}_3$ .

The  $^1\text{H}$  NMR spectra also permit establishment of the conformational fixing of the 7-benzyl group indicated by the significant size of the NOE for the N–H signal in the experiment with irradiation of the  $\{\alpha\text{-H}_A\}^*$  proton and the absence of such in the case of  $\{\alpha\text{-H}_B\}$ . As analysis of the molecular model showed, the spatial proximity of the N–H and  $\alpha\text{-H}_A$  protons combined with the markedly higher spatial proximity of the 7-H and N–H protons detected in the  $\{7\text{-H}\}$  experiment is permitted only for two hindered conformations of the benzyl radical. From the size of the coupling constants (10.3 Hz) between the 7-H and  $\alpha\text{-H}_B$  protons and also the value for the dihedral angle  $\text{H-C}_{(7)}\text{-C}_{(a)}\text{-H}_B$  calculated on it of  $150^\circ$ , it follows that the conformation with the transoid orientation of these protons is preferred (Fig. 2, b). The significant diamagnetic displacement of the 8-H proton signal at 6.36 ppm is also readily explained (assignment of the signal was based on the results of the NOE experiments for  $\{7\text{-H}\}$  and  $\{8\text{-H}\}$ ), since in the most occupied conformation the proton is in the magnetic shielding zone of the benzene ring of the 7-benzyl substituent.

TABLE 3. Results of NOE Experiments on the  $^1\text{H}$  NMR Spectrum of Isoquinoquinazolinone **3a**

Irradiated proton		Observations		Irradiated proton		Observations	
$\delta$ , ppm	assignment	NOE, %	assignment	$\delta$ , ppm.	assignment	NOE, %	assignment
6.36	8-H	10	7-H	3.56	$\alpha\text{-H}_A$	31	$\alpha\text{-H}_B$
						5	$\text{N}_{(6)}\text{-H}$
5.39	6a-H	2	12-H <sub>B</sub>	3.28	7-H	13	8-H
			7-H			13	6a-H
4.74	12-H <sub>A</sub>	20	12-H <sub>B</sub>			6	$\text{N}_{(6)}\text{-H}$
			1-H	2.62	$\alpha\text{-H}_B$	26	$\alpha\text{-H}_A$
			11-H			7	1-H
						7	11-H
4.31	12-H <sub>B</sub>	2	6a-H				
		14	12-H <sub>A</sub>				

\* The symbol  $\alpha$  denotes the carbon atom of the methylene group of the benzyl substituent at  $\text{C}_{(7)}$ ; in accordance with the generally accepted designation in AB spin systems of interacting geminal protons the symbol A is conferred on the more low field of them.

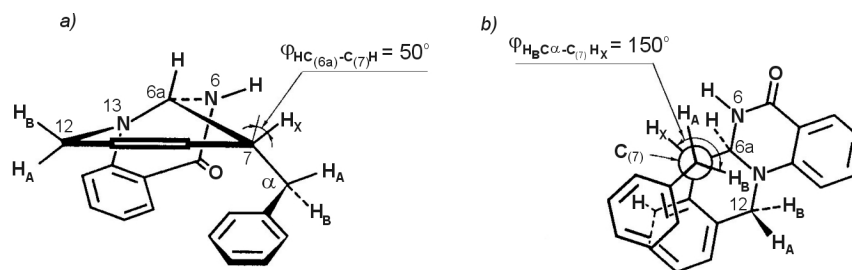
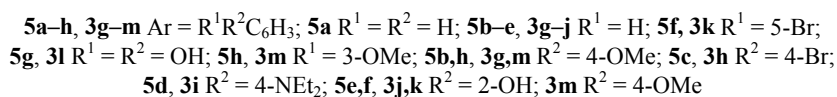
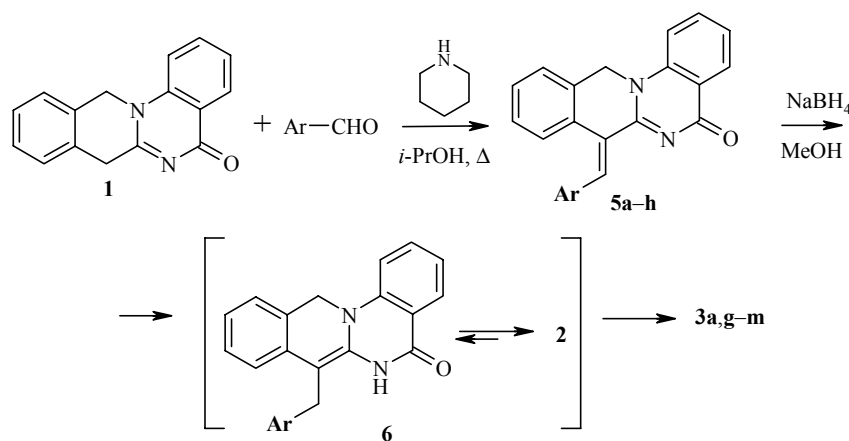


Fig. 2. Preferred conformation for isoquinoquinazoline **3a**:  
 a) view from the side of the benzene ring of the isoquinoline fragment; b) view along the  $C_{\alpha}-C_{(7)}$  bond.

The method given for obtaining 7-benzyl substituted tetrahydroquino-quinazolines is evidently limited by the availability of the corresponding benzyl halides. Consequently it seemed of interest to develop alternative routes for their synthesis. In view of the previously discovered [9] reactivity of the 7-methylene group in isoquinoquinazoline **1** in reactions with carbonyl compounds, we carried out condensation of it with substituted benzaldehydes by heating in 2-propanol in the presence of piperidine. 7-(1-Arylmethylene)-7,12-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-ones **5a-h** were obtained for the first time in this way (Table 4).



It should be mentioned that only one of the two possible isomers is formed, as indicated by the single set of signals in the  $^1H$  NMR spectra of the unpurified reaction products. However we did not carry out assignment of *E*- or *Z*-configurations for the compounds synthesized. It turned out that sodium borohydride also reduces both  $C_{(6a)}=N_{(6)}$  and  $C_{(7)}=C_{\alpha}$  double bonds in the arylmethylene derivatives **5**. In view of the inertness of sodium borohydride towards isolated double bonds it may be suggested that in the first stage the reaction occurs as a 1,4-addition to the vinylimino fragment with the formation of 7-benzyl-6,12-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-ones of the type of **6**. Subsequently they underwent a tautomeric conversion into the more preferred form **2** [8], the subsequent reduction of which is completed by the formation of the tetrahydro derivatives **3** with the *erythro* configuration. In favor of the proposed sequence of conversions is the stereoselectivity of the whole process, established by the absence of significant quantities of side products from the  $^1H$  NMR spectra of the unpurified reaction products.

TABLE 4. Characteristics of 7-Arylidene-7,12-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-ones

Compound	Empirical formula	Found, %			mp, °C	IR spectrum, $\nu$ , $\text{cm}^{-1}$			$^1\text{H}$ NMR spectrum, $\delta$ , ppm, coupling constant ( $J$ ), Hz				Yield, %
		Calculated, %				C=O	C=N	other bands	C-H, 1H, s	H <sub>arom</sub> , m*	C <sub>(12)</sub> H <sub>2</sub> , s	other signals	
<b>5a</b>	C <sub>23</sub> H <sub>16</sub> N <sub>2</sub> O	82.20 82.12	4.83 4.79	8.39 8.33	259	1635	1605			8.22-7.15 (14H)	5.47		90
<b>5b</b>	C <sub>24</sub> H <sub>18</sub> N <sub>2</sub> O <sub>2</sub>	78.52 78.67	5.00 4.95	7.89 7.65	220	1629	1598		8.15	8.41-6.81 (12H)	5.22	3.82 (3H, s, OCH <sub>3</sub> )	98
<b>5c</b>	C <sub>23</sub> H <sub>15</sub> BrN <sub>2</sub> O* <sup>2</sup>	66.48 66.52	3.50 3.64	7.09 6.75	251	1640	1605		8.03	8.30-7.15 (12H)	5.23		95
<b>5d</b>	C <sub>27</sub> H <sub>25</sub> N <sub>3</sub> O	79.62 79.58	6.30 6.18	10.29 10.31	205	1650	1595		8.20-6.60 (13H)		5.39	3.37 (4H, q, $J = 7$ , NCH <sub>2</sub> ); 1.10 (6H, t, $J = 7$ , CH <sub>3</sub> )	87
<b>5e</b>	C <sub>23</sub> H <sub>16</sub> N <sub>2</sub> O <sub>2</sub>	78.43 78.39	4.60 4.58	8.02 7.95	293	1600-1580		3060 (OH)	8.23-6.60 (13H)		5.45	10.02 (1H, s, OH)	83
<b>5f</b>	C <sub>23</sub> H <sub>15</sub> BrN <sub>2</sub> O <sub>2</sub> * <sup>3</sup>	64.00 64.05	3.41 3.51	6.62 6.50	287	1600	1580	3040 (OH)	8.02	8.27-6.88 (11H)	5.50	10.50 (1H, s, OH)	80
<b>5g</b>	C <sub>23</sub> H <sub>16</sub> N <sub>2</sub> O <sub>3</sub>	75.01 74.99	4.42 4.38	7.47 7.60	>300, dec.	1670	1595	3080 (OH)		8.20-6.70 (12H)	5.44	9.50(1H, s, OH); 9.15(1H, s, OH)	75
<b>5h</b>	C <sub>25</sub> H <sub>20</sub> N <sub>2</sub> O <sub>3</sub>	75.71 75.74	5.01 5.08	7.10 7.07	245	1629	1600		8.09	8.33-6.77 (11H)	5.22	3.89 (3H, s, OCH <sub>3</sub> ); 3.70 (3H, s, OCH <sub>3</sub> )	96

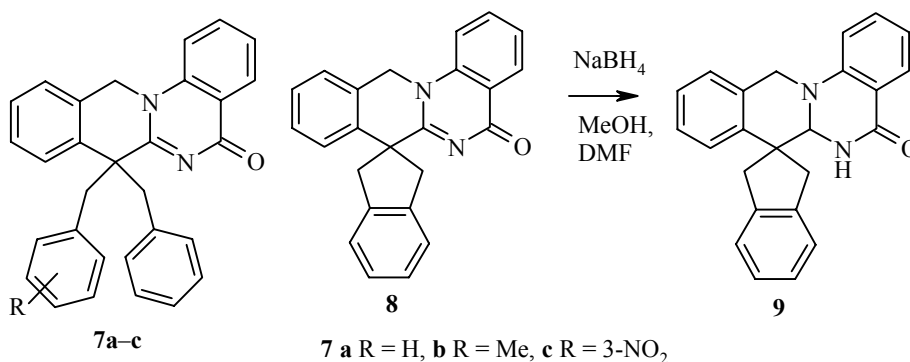
\* The signal for the 4-H aromatic proton is observed as dd ( $^oJ = 8$ ,  $^mJ = 1.5$ ) at 8.37 ppm for **5b**; 8.26 for **5c**; 8.23 for **5f**; 8.15 for **5g**; 8.29 for **5h**. The signal for the aromatic 3'-H and 5'-H protons in the spectrum of compound **5d** was in the form of d ( $J = 8$ ) at 6.64 ppm.

\*<sup>2</sup> Found, %: Br 19.37. Calculated, %: Br 19.24.

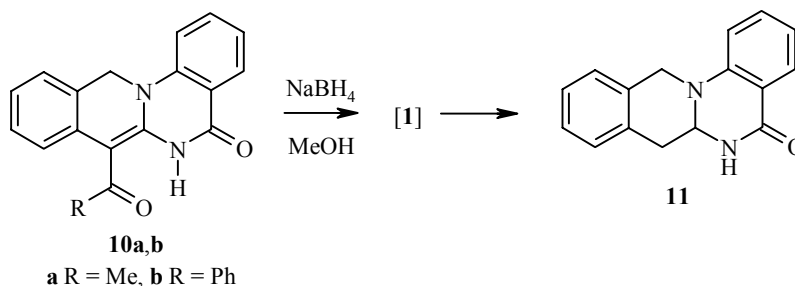
\*<sup>3</sup> Found, %: Br 18.71. Calculated, %: Br 18.53.

The means of obtaining compounds **3** from isoquinoquinazolinone **1** through arylmethylene derivatives is profitably different from the route through benzyl derivatives **2** by the higher overall yields (which was shown in the example of the synthesis of the Ar-unsubstituted compound **3a**) and, which is more important, it opens the possibility of obtaining benzyl derivatives **3** with functional groups inclined towards alkylation in the aryl radical (phenolic hydroxyls, dialkylamino groups), unavailable by alternative methods.

We also attempted to carry out the reduction of the dibenzyl substituted isoquinoquinazolines **7a-c** synthesized previously. It is evident that by virtue of the steric screening of the  $C_{(6a)}=N_{(6)}$  bond in these compounds noted in the same work, they proved to be inert towards the action of sodium borohydride even under rigid conditions (extended boiling in DMF, dioxane, methanol, alcohol-acetic acid mixtures). Only in the case of spiro[5H-isoquino[2,3-*a*]quinazolin-7(12H),2'-indane]-5-one (**8**) (in which the steric shielding of the bond being reduced is reduced to a minimum) by heating of a solution in an alcohol-DMF mixture with a fivefold excess of  $\text{NaBH}_4$  for 1 h was a reduction product successfully obtained, *viz.* 6,6a-dihydrospiro[5H-isoquino[2,3-*a*]quinazolin-7(12H),2'-indan]-5-one (**9**). As a consequence of the asymmetry of this compound, all the protons of the methylene groups proved to be magnetically nonequivalent and in the  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ ) were observed as three AB spin systems. The significant paramagnetic displacement (in comparison with benzyl derivatives **3**) of the N-H group proton, the broadened singlet of which was observed at 6.01 ppm, is evidently a consequence of the influence of the benzene ring of the indane fragment. The proton under consideration falls in the zone of its magnetic shielding.



In view of the literature data on the possibility of borohydride reduction of enaminocarbonyl compounds [10] we also studied the behavior of 7-acetyl- and 7-benzoyl-6,11-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-ones **10** under the conditions described above [9]. However it turned out that in both cases the reaction proceeded to the known 6,6a,7,12-tetrahydro-5H-isoquino[2,3-*a*]quinazolin-5-one (**11**) [2].



Evidently the acyl derivatives **10** are subject to base catalyzed (by sodium borohydride) deacylation in alcoholic medium with the intermediate formation of isoquinoquinazoline **1**, which is then reduced to the tetrahydro derivative **11**. However attempts to confirm such a sequence of conversions by TLC (using compound **1** as a reference standard) were unsuccessful, which is linked rather with the high rate of the reduction compared with the fission reaction.



## EXPERIMENTAL

The IR spectra of compounds in KBr disks were recorded on a Pye Unicam SP3-300 instrument. The  $^1\text{H}$  NMR spectra of the substances synthesized, **3b-f**, **5**, **6c-f**, and **8d-g** in  $\text{DMSO-d}_6$  and **3a**, **6a,b,g**, and **8a-c** in  $\text{CDCl}_3$  were obtained on a Bruker WP 100 SY (100 MHz), internal standard was TMS.

**General Procedure for the Reduction of Isoquinoquinazolones 2, 5, and 10. erythro-7-Benzyl-6,6a,7,12-tetrahydro-5H-isoquino[2,3-a]quinazolin-5-ones (3) and 6,6a,7,12-Tetrahydro-5H-isoquino[2,3-a]quinazolin-5-one (11).** Sodium borohydride (1.9 g, 50 mmol) was added in small portions to a suspension of **2** hydrohalide (10 mmol) in methanol (50 ml). At the end of the vigorous reaction, during which the starting material dissolved, the mixture was boiled for 30 min. The solvent was distilled off at reduced pressure, the residue treated with 10% NaOH solution (20 ml), the product was filtered off, and washed with water. Reduction of the free bases **2** and acyl derivatives **10a,b** was carried out analogously using a sevenfold excess of  $\text{NaBH}_4$ . Boiling time was increased to 1.5 h. Compounds **3a-g** and **11** were obtained. The tetrahydro derivatives **3h-j** were synthesized analogously from arylmethylidene derivatives **5**, using a fivefold excess of  $\text{NaBH}_4$ , boiling time was 1 h.

**7-(1-Arylmethylene)-7,13-dihydro-5H-isoquino[2,3-a]quinazolin-5-ones (5a-h).** A mixture of isoquinoquinazoline **1** (1 g, 4.03 mmol), piperidine (0.8 ml, 8.06 mmol), and benzaldehyde (4.8 mmol) in 2-propanol (20 ml) was boiled for 3 h. The starting material **1** passed into solution as the reaction took place. The solvent was evaporated on a rotary evaporator, the residue was rubbed under water, the product was filtered off, washed with water, and with dioxane.

**6,6a-Dihydrospiro[5H-isoquino[2,3-a]quinazolin-7(12H),2'-indan]-5-one (9).** Spiroindane **8** (1.15 g, 5 mmol) was dissolved with heating in a mixture of DMF (10 ml) and methanol (20 ml), and  $\text{NaBH}_4$  (0.95 g, 25 mmol) was added in small portions to the solution obtained. At the end of the vigorous reaction the mixture was boiled for 1 h. The solvent was distilled off under reduced pressure, the residue was treated with 10% NaOH solution (20 ml), the product was filtered off, washed with water, and with alcohol. Yield 73%; mp  $210^\circ\text{C}$  (acetonitrile).  $^1\text{H}$  NMR spectrum ( $\text{CDCl}_3$ ),  $\delta$ , ppm,  $J$  (Hz): 7.20-8.45 (12H, m,  $H_{\text{arom}}$ ); 5.92 (1H, s, 7-H); 5.14 (1H, s, 6a-H); 4.71 (1H,  $^2J = 16$ , 12- $H_A$ ); 4.32 (1H, d,  $^2J = 16$ , 12- $H_B$ ); 3.93 (1H, d,  $^2J = 17$ , 1'(3')- $H_A$ ); 3.61 (1H,  $^2J = 17$ , 3'(1')- $H_A$ ); 3.30 (1H,  $^2J = 17$ , 3'(1')- $H_B$ ); 2.96 (1H,  $^2J = 17$ , 1'(3')- $H_B$ ). IR spectrum (KBr),  $\nu$ ,  $\text{cm}^{-1}$ : 1655 (C=O), 3050 (N-H). Found, %: C 81.63; H 5.70; N 7.99.  $\text{C}_{24}\text{H}_{20}\text{N}_2\text{O}$ . Calculated, %: C 81.79; H 5.66; N 7.95.

## REFERENCES

1. V. M. Kisel, L. M. Potikha, and V. A. Kovtunenکو, *Khim. Geterotsikl. Soedin.*, 643 (2000).
2. V. M. Kisel, V. A. Kovtunenکو, A. V. Turov, A. K. Tyltin, and F. S. Babichev, *Khim. Geterotsikl. Soedin.*, 389 (1991).
3. V. M. Kisel, L. M. Potikha, and V. A. Kovtunenکو, *Khim. Geterotsikl. Soedin.*, 423 (1995).
4. A. Khaioش, *Complex Hydrides in Organic Chemistry* [in Russian], Khimiya, Leningrad (1971), p. 315.
5. N. Umino, N. Iwakuma, and N. Itoh, *Tetrahedron Lett.*, 763 (1976).
6. A. J. Gordon and R. A. Ford, *A Chemist's Companion*, Wiley-Interscience, New York (1972), 560 pp., [Russian translation] Mir, Moscow (1976), p. 213.
7. V. F. Bystrov, *Usp. Khim.*, **41**, 512 (1972).
8. C. A. G. Haasnoot, F. A. A. M. Leeuw, and C. Altona, *Tetrahedron*, **36**, 2783 (1980).
9. V. M. Kisel, V. A. Kovtunenکو, L. M. Potikha, A. K. Tyltin, V. S. Nikitchenko, and F. S. Babichev, *Ukr. Khim. Zh.*, **58**, 790 (1992).
10. Ya. F. Freimanis, *Chemistry of Enamino Ketones, Enamino Imines, and Enamino Thiones* [in Russian], Zinatne, Riga (1974).