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CONDENSED ISOQUINOLINES 29*. OXIDATION REACTIONS OF 5-ARYL-7,12-DIHYDROISOQUINO[2,3-*a*]QUINAZOLINIUM SALTS

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5-Aryl-7,12-dihydroisoquino[2,3-a]quinazolinium perchlorates are readily oxidized by atmospheric oxygen to form the products of oxidative coupling 5,5'-bis(aryl)-3,3'-dihalo[7,7']bi[isoquino-[2,3-a]quinazoline-13,13'-diylium perchlorates. Heating 3-chloro-5-phenyl-7,12-dihydroisoquino-[2,3-a]quinazolinium perchlorate in nitrobenzene gives the 3-chloro-5-phenylisoquino[2,3-a]quinazolin-13-ium perchlorate. The aromatic 5-arylisoquino[2,3-a]quinazoline derivatives obtained react with nucleophilic reagents to form addition products at the C-12 atom.

Keywords: 5-arylisoquino[2,3-*a*]quinazoline, isoquinolines, condensed quinazolines, borohydride reduction, oxidation, oxidative coupling.

The first representatives of the isoquino[2,3-*a*]quinazoline system were obtained quite recently [2, 3] and they included 5-aryl-substituted derivatives [2, 4]. However, by contrast to 5-oxoisoquino[2,3-*a*]quinazolines, the properties of the latter were not studied. The already existing data for the biological activity of isoquinoquinazolines [5, 6] and 4-arylquinazolines condensed along the *a* edge [7-9] points to the potential of such an investigation.

We have previously proposed [4] a method for the synthesis of the 5-aryl-7,12-dihydroisoquino-[2,3-*a*]quinazolinium salts **1a-c** consisting of reaction of *o*-(bromomethyl)phenylacetonitrile with *o*-amino-benzophenones **2a-c** and subsequent cyclization of the initially formed 2-aryl-3-imino-1,4-dihydroisoquinoline hydrobromides **3a-c** in the presence of perchloric acid. In this work the reaction was subjected to closer study with the aim of optimizing the method of synthesizing the isoquinoquinazolinium salts **1** and to study the spectroscopic and chemical properties of the products.

We have found that the outcome of the reaction of o-(bromomethyl)phenylacetonitrile with benzophenones **2** depends markedly on both the reaction conditions and on the nature of the substituent in reagent **2**. Hence heating in acetonitrile, in some examples (**2b,c**) gave a mixture of the isoquinolineimine bromides **3** together with an unknown product. Addition of catalytic amounts of acetic acid to the reaction mixture virtually suppresses the formation of the side product. When the reaction is carried out in 2-propanol the unknown material is the sole product. And in the case of the benzophenone **2d** gives the unknown material

* For Communication 28 see [1].

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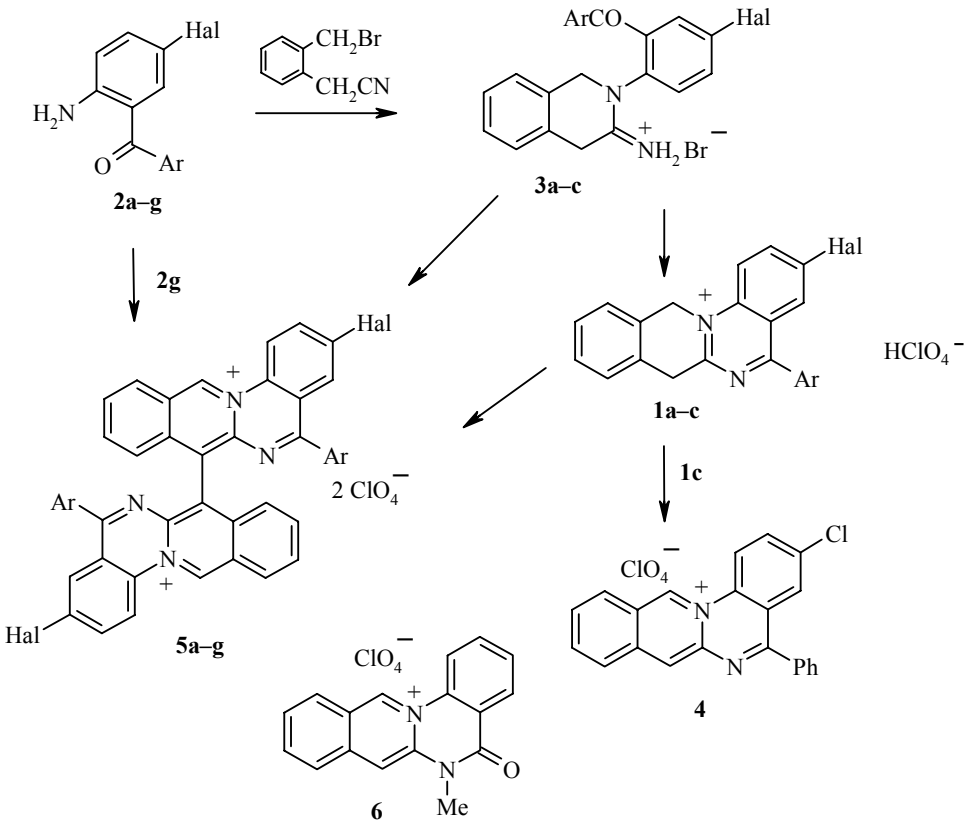


1a–c – **5a–g** Ar, Hal; **a** 4-$O_2NC_6H_4$, Br; **b** 4-BrC_6H_4, Br; **c** Ph, Cl; **d** 4-MeC_6H_4, Br

as the sole product independently of the conditions. the benzophenone **2d** the unknown material is the sole product independently of the conditions. A similar result was obtained upon prolonged heating (6-30 h) the iminoisoquinoline hydrobromides **3a-c** with the 5-arylisoquinoquinazolium **1a-c** in acetonitrile and in other solvents (benzonitrile, DMSO). On the basis of this data and also the tendency of condensed 1,4-dihydro-isoquinolines towards oxidation discovered by us earlier [10-12] we propose that the products are due to oxidation by atmospheric oxygen in this case. It would be logical to suggest that such a reaction can also occur in the presence of other oxidants, e.g. in nitrobenzene since the aromatic derivatives isoquino[2,3-*a*]quinazolin-5(6H)-one [10] and 13-oxo-5H,13H-isoquino[3,2-*b*]quinazolin-13(5H)-one [12] were previously obtained under these conditions. Heating the 5-aryl-7,12-dihydroisoquino[2,3-*a*]quinazolinium perchlorates **1a-c** in nitrobenzene also readily formed the oxidation products, the result of this reaction depending on the nature of the substituent in the 5-aryl group. Hence the 5-(4-nitro-phenyl)- and 5-(4-bromophenyl) derivatives **1a,b** gave products identical to those obtained before by heating the starting salts in benzonitrile or acetonitrile and the 5-(4-tolyl) derivative **1c** gave a compound close in spectroscopic parameters to the products of oxidation of salts **1a,b** but differing in the presence of an additional proton signal in the aromatic region.

The IR spectra of all of the oxidation products show the absence of carbonyl and hydroxyl stretching bands in the characteristic regions and the ^{1}H NMR spectra show only signals in the aromatic proton region. On the basis of the IR and NMR spectroscopic data and elemental analysis the synthesized compound can be assigned the structure of the aromatic salt 3-chloro-5-phenylisoquino[2,3-*a*]quinazolin-13-ium perchlorate (**4**) for the product of oxidation of salt **1c** in nitrobenzene and the products of oxidative coupling as the 5,5'-bis(aryl)-3,3'-dihalo[7,7']bi[isoquino[2,3-*a*][quinazoline]-13,13'-diylium perchlorates **5a-d** in the remaining

TABLE 1. Spectroscopic Characteristics of the 5-Arylisoquino-[2,3-*a*]quinazoline derivatives **4**, **5a-d**, **7a,b**

Compound	IR spectrum, ν, cm^{-1}	^{1}H NMR spectrum, δ, ppm (*J*, Hz)		
		ArH	1H, s, H-12	1H, s, H-7
4	1615 (C=N), 1555, 1500, 1440, 1420, 1355, 1090, 760, 625	9.36 (1H, d, ^3J = 9.0, H-1); 8.75 (1H, d, ^3J = 8.4, H-11); 8.69 (1H, dd, ^3J = 9.0, ^4J = 1.2, H-2); 8.54 (1H, d, ^3J = 8.0, H-8); 8.33 (1H, t, ^3J = 8.0, H-9); 8.19 (1H, d, ^4J = 1.2, H-4); 8.17 (1H, t, ^3J = 8.0, H-10); 7.93 (2H, m, H-2',6'); 7.75 (3H, m, H-4',3',5')	11.41	9.28
5a	1615 (C=N), 1595, 1550, 1400, 1350 (NO_2), 1100, 660	9.45 (1H, d, ^3J = 9.0, H-1); 8.99 (1H, d, ^3J = 8.4, H-11); 8.70 (1H, dd, ^3J = 9.0, ^4J = 2.0, H-2); 8.24 (2H, m, H-4,10); 8.16 (3H, m, H-9,3',5'); 8.00 (1H, d, ^3J = 8.0, H-8); 7.56 (2H, d, ^3J = 8.8, H-2',6')	11.80	—
5b	1600 (C=N), 1585, 1540, 1500, 1420, 1395, 1350, 1090, 620	9.37 (1H, d, ^3J = 9.0, H-1); 8.96 (1H, d, ^3J = 8.4, H-11); 8.76 (1H, dd, ^3J = 9.0, ^4J = 2.0, H-2); 8.30 (1H, d, ^4J = 2.0, H-4); 8.26 (1H, t, ^3J = 8.0, H-10); 8.18 (1H, t, ^3J = 8.0, H-9); 8.00 (1H, d, ^3J = 8.0, H-8); 7.56 (2H, t, ^3J = 8.8, H-3',5'); 7.18 (2H, d, ^3J = 8.8, H-2',6')	11.73	—
5c	1615 (C=N), 1595, 1550, 1500, 1395, 1350, 1090, 620	9.49 (1H, d, ^3J = 9.0, H-1); 8.98 (1H, d, ^3J = 8.4, H-11); 8.56 (1H, dd, ^3J = 9.0, ^4J = 2.0, H-2); 8.26 (1H, t, ^3J = 8.0, H-10); 8.17 (1H, t, ^3J = 8.0, H-9); 8.14 (1H, d, ^4J = 2.0, H-4); 8.06 (1H, d, ^3J = 8.0, H-8); 7.48 (1H, t, ^3J = 7.6, H-4'); 7.35 (2H, t, ^3J = 7.6, H-3',5'); 7.22 (2H, d, ^3J = 7.6, H-2',6')	11.73	—
5d*	1610 (C=N), 1595, 1545, 1500, 1425, 1390, 1345, 1090, 620	9.44 (1H, d, ^3J = 9.0, H-1); 8.99 (1H, d, ^3J = 8.4, H-11); 8.78 (1H, dd, ^3J = 9.0, ^4J = 2.0, H-2); 8.31 (1H, d, ^4J = 2.0, H-4); 8.25 (1H, t, ^3J = 8.0, H-10); 8.16 (1H, t, ^3J = 8.0, H-9); 8.04 (1H, d, ^3J = 8.0, H-8); 7.14 (2H, t, ^3J = 8.8, H-2',6'); 7.12 (2H, d, ^3J = 8.8, H-3',5')	11.73	—
7a	1665 (C=N), 1595, 1540, 1485, 770	7.69 (1H, d, ^3J = 7.8, H-2); 7.66 (2H, d, ^3J = 9.0, H-2',6'); 7.50 (4H, m, H-1, H-1,3'–5'); 7.04-6.96 (4H, m, H-1,8,10,11); 6.89 (1H, t, ^3J = H-9)	5.08, 2H	5.5
7b	1660 (C=N), 1590, 1535, 1485, 770	7.71 (1H, d, ^3J = 7.8, H-2); 7.64 (2H, d, ^3J = 9.0, H-2',6'); 7.48 (3H, m, H-1,3',5'); 7.14 (1H, s, H-4); 7.09-6.96 (3H, m, H-8,10,11); 6.90 (1H, t, ^3J = H-9)	5.02, 2H	5.5

* A signal is observed at 2.28 ppm (3H, s, CH_3) in the ^{1}H NMR spectrum.

cases. We have carried out a detailed comparative analysis of the spectroscopic characteristics of these compounds and the model compound 6-methyl-5-oxo-5,6-dihydroisoquino[2,3-*a*]quinazolin-13-ium perchlorate (**6**) (the structure of which has been established before [13]) in order to confirm the structures of the oxidation products.

With this in mind we measured their ^{1}H and ^{13}C NMR spectra (Table 1) and also used homonuclear (COSY) and heteronuclear (HMBC and HMQC) 2D correlation spectroscopy. In addition, we have recorded their NOESY 1D and NOESY spectra to measure the steric proximity of individual protons. The data for the heteronuclear correlation for the aryl derivatives **4, 5c,d** and the simpler compound **6** are given in Table 2. The available data allows us to perform a full assignment of signals in the proton and carbon spectra and to draw conclusions regarding the structure of the compound studied. Figure 1 shows the assignments of signals and the arrows depict the structurally significant HMBC correlations. Hence for compound **6** the proton with a chemical

shift of 8.63 ppm has a correlation with two quaternary carbon atoms absorbing at 140.6 and 141.4 ppm which correspond to the nodal C(7a) and C(6a) atoms. The latter atoms also correlates with the signals for the protons of the 6-methyl group and H-12 which are 3 chemical bonds distant. Assignment of the carbonyl carbon atom signal was made on the basis of its correlation on the one hand with the methyl group signal at N-6 and on the other hand with the H-4 proton signal. It was interesting that the carbonyl atom C-5 has a strong correlation with the signal for atom H-1 which is 4 chemical bonds distant from it. We consider this correlation as due to a W type interaction. There is also a 4 bond correlation between the signals for the methyl group protons and the C-7 atom signal.

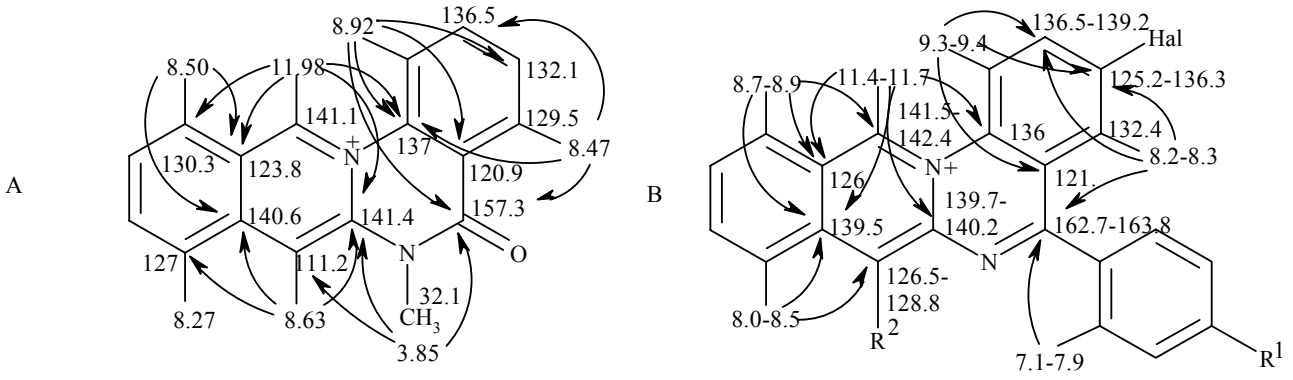


Figure 1. Structurally significant HMBC correlations for compound **6** (A) and **4, 5b,d** (B).

A similar study was made for compounds **4** and **5a-d**. For the various spectra we have found a whole series of analogies with the corresponding spectra of compound **6**. Hence a singlet is found to lowest field with a chemical shift of 11.4-11.8 ppm. In addition there are found several aromatic proton signals to unusually low field. The single marked difference in the ^{1}H NMR spectra of compound **4** and the salts **5a-d** is the presence of the H-7 one-proton singlet at 9.28 ppm with a small shift of the signals of the 5-phenyl protons to low field. Assignment of the protons signals was made using 2D COSY spectroscopy. The spin multiplets agree with the proposed structure and the positions of the cross peaks permit a full assignment of the proton spectra. The low field shift of a series of signals in the spectrum points to the presence of a delocalized positive charge in the heterocyclic fragment. Nonbonded interactions also make a contribution to the deshielding of protons located closely in space due to the angular structure of the molecule. The presence of such an interaction is proved by a study of NOE correlations. Using the NOESY-1D method with saturation of the H-12 proton signal at 11.7 ppm for both compounds **5c,d** a change in intensity of the H-1 signal of about 30% was found. The H-11 proton signal changes in intensity by 10-11%. A close value of the NOE was also found for the H-12 proton upon saturation of the H-1 proton. An interesting feature of the NOE experiments for these compounds is that the observed effects are negative rather than positive as is usually the case. Stationary NOE experiments also give very similar results. The only possible explanation for this effect is that the correlation time for the molecule is too small. This is a feature of molecules with a high molecular weight. Hence this experiment is an indirect confirmation of the dimer structure of the salt **5a-d** molecules. In this case the molecular weight is close to 1000 and negative NOE values are possible. The structure of the carbon skeleton of the molecules of compounds **4** and **5c,d** were proved using ^{13}C NMR measurements. The number of signals in the carbon spectra agreed with the number of non-equivalent carbon atoms present in the molecule. Editing of the spectra according to spin multiplicities was carried out using the DEPT method. Here, as expected (Table 2), there were located the signal for the methyl group (for **5d**) and 10 CH signals (for **5c,d** two were of double intensity) or 11 CH signals in the case of compound **4**. Assignment of the carbon signals of the methine groups were made using the heteronuclear HMQC spectra. The carbon-proton correlations found are given in Table 2 and the most structurally significant

values displayed in Figure 1. The most interesting result is the correlation of the carbon atom signal with a chemical shift of 141.5-142.4 with the proton signal at 11.4-11.8 ppm. In addition to a secure assignment of the corresponding carbon signal it confirmed that the signal at 11.4-11.8 ppm in the ^{1}H NMR spectrum is, in fact, the deshielded H-12 proton. The correlation of the low field signal for H-1 at 9.33-9.37 ppm with the high field carbon signal at 122 ppm was slightly unexpected. This suggests that a non-bonded interaction rather than electronic factors made a basic contribution to the deshielding of the H-1 signal.

Further confirmation of the structure of molecules came from proton-carbon correlation using the gradient HMBC method and led to a full assignment of the signals in the ^{13}C NMR spectra. The chemical shift of the C-5 atom proved to be unexpected. As a signal occurs in the spectrum at 162.7-163.8 ppm it would be

TABLE 2. Proton-Carbon Correlations for compounds **4, 5b,d, 6**

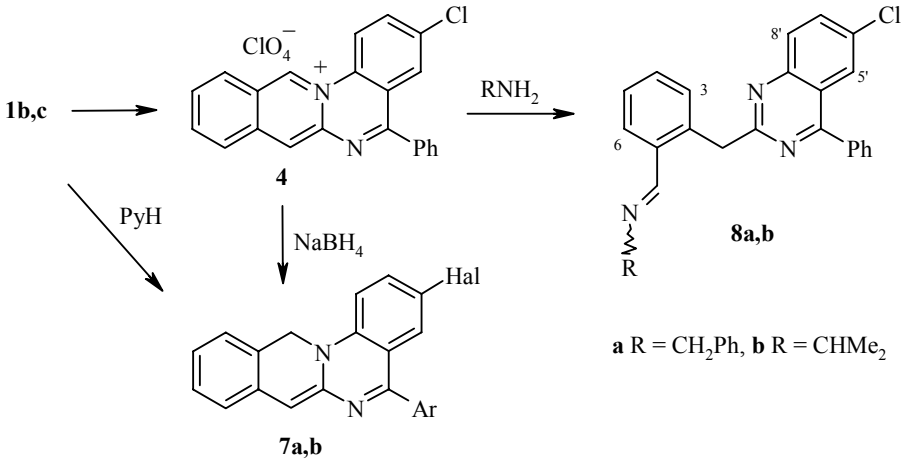
Atom number	^{13}C NMR spectrum, δ, ppm	^{1}H NMR spectrum, δ, ppm; HMQC correlation	Chemical shifts of protons for which HMBC correlations exist, δ, ppm
1	2	3	4
		Compound **4**	
1	122.0	9.33	—
2	136.5	8.69	8.19, 9.33
3	136.3	—	8.19
4	132.3	8.19	8.69
4a	121.6	—	9.33
5	163.8	—	7.93, 8.19
6a	140.2	—	11.41
7	126.5	9.28	8.55, 8.17
7a	139.5	—	11.41, 8.75, 8.56, 8.33
8	128.3	8.56	—
9	137.6	8.33	8.75
10	129.4	8.17	—
11	130.8	8.75	11.41, 8.33
11a	126.2	—	9.28, 8.17
12	141.5	11.41	—
13a	135.8	—	11.41, 8.69, 8.19
1'	135.6	—	7.75
2'	130.5	7.93	7.75
3'	129.8	7.75	7.93
4'	132.1	7.75	7.93
		Compound **6**	
1	119.1	8.92	7.99
2	136.5	8.26	8.47, 7.99
3	132.1	7.99	8.92
4	129.5	8.47	8.26, 7.99
4a	120.9	—	8.92, 7.99
5	157.3	—	8.92, 8.47, 3.85
6a	141.4	—	10.98, 3.85
7	111.2	8.63	10.98, 8.27, 3.85
7a	140.6	—	8.63, 8.50, 8.27
8	127.0	8.27	8.63, 7.92
9	138.6	8.19	8.50, 7.92
10	130.3	7.92	—
11	130.6	8.50	10.98, 8.19
11a	123.8	—	10.98, 8.63, 8.50, 8.27, 7.92
12	141.1	10.98	—
13a	137.0	—	10.98, 8.92, 8.47, 8.26
CH_3	32.1	3.85	—

TABLE 2. (continued)

1	2	3	4
		Compound **5b**	
1	121.8	9.37	—
2	139.6	8.76	8.30
3	125.5	—	9.37, 8.76, 8.30
4	132.4	8.30	8.76
4a	121.7	—	9.37
5	162.7	—	9.37, 8.30, 7.18
6a	139.7	—	11.73
7	128.8	—	8.00
7a	139.6	—	11.73, 8.96, 8.18
8	126.9	8.00	—
9	138.5	8.18	8.96
10	132.5	8.26	8.18, 8.00
11	131.8	8.96	11.73
11a	126.2	—	8.26, 8.00
12	142.2	11.73	8.96
13a	136.6	—	11.73, 9.37, 8.76, 8.30
1'	134.4	—	7.56
2'	132.3	7.18	7.56
3'	132.6	7.56	7.18
4'	126.0	—	7.56, 7.18
		Compound **5d**	
1	122	9.44	—
2	139.2	8.78	8.31
3	125.2	—	9.44, 8.78, 8.31
4	132.4	8.31	8.78
4a	121.8	—	9.44
5	163.4	—	9.44, 8.31, 7.14
6a	139.7	—	11.74
7	128.5	—	8.04, 11.74
7a	139.6	—	8.99, 8.16, 8.04
8	126.9	8.04	—
9	138.2	8.16	8.99
10	132.1	8.25	—
11	131.6	8.99	11.74, 8.16, 8.04
11a	126	—	11.74, 8.99, 8.04
12	142.4	11.73	8.99
13a	136.6	—	11.74, 9.44, 8.78, 8.31
1'	132.4	—	7.12
2'	130.2	7.14	7.12, 2.28
3'	130	7.12	—
4'	142.4	—	7.14, 2.28
CH_3	21.4	2.28	7.14

logical to assign it to the C-6a atom since it is located between two heterocyclic nitrogen atoms. However, this signal has correlations with the H-4 and H-2' protons. Hence the C-5 atom is not more than three chemical bonds distant from the given protons and this is only possible in the case that the signal at 162.7-163.8 ppm corresponds to the C-5 atom. This correlation is very strong and occurs in all three compounds studied. It also occurs when the spectra are measured in trifluoroacetic acid. The signal for the C-7 atom (through which the dimerization of the molecules **5c,d** occurs) is basically identified by its correlation with the H-8 proton. A similar correlation is also observed in the case of salt **4**.

An additional confirmation that the compounds **5a-d** are the products of oxidative coupling of the 5-arylisoquinazolinium salts **4** is the high similarity of their UV spectra indicating that they are isoelectronic. In addition the result obtained points to the absence of an interaction between the conjugated systems of the two fragments of the molecule in the compounds **5** which can be fully understood in view of the steric hindrance to their coplanarity.



a R = CH_2Ph, **b** R = $CHMe_2$

a Ar = Ph, Hal = Cl; **b** Ar = 4-BrC_6H_4, Hal = Br

We were unable to record the mass spectra of the 5-arylisoquinoquinazolinium salts **4** and **5a-d** because, on the one hand, of the limits of many methods of molecular weight investigation of the studied compounds (close to 1000 for the dimers **5a-d**) and, on the other, to their lability in the presence of nucleophiles including the traces of water contained in the solvents used. None the less such a result was quite expected. It had been found previously [10] that the 6-methyl-5-oxo-5,6-dihydroisoquino[2,3-*a*]quinazolin-13-ium perchlorate **6**, which is closely related structurally to the salts **4** and **5a-d**, readily reacts with nucleophilic reagents. The reaction occurs at position 12 of the heterosystem and gives products of nucleophilic addition with subsequent fission of the isoquinoline ring at the C(12)–N(13) bond. In the case of compound **4** it was found that the 5-aryl-isoquino[2,3-*a*]quinazolinium perchlorates react by the same scheme. Hence reaction of salt **4** with sodium borohydride in alcohol gives 3-chloro-5-phenyl-12H-isoquino[2,3-*a*]quinazoline (**7a**) which was also obtained by treating the 3-chloro-5-phenyl-7,12-dihydroisoquino[2,3-*a*]quinazolinium perchlorate **1c** with pyridine. It was found that the yield of compound **7a** was not high both in the reduction of salt **4** and in the deprotonation of salt **1c**. The 3-bromo-5-(4-bromophenyl)-12H-isoquinoquinazoline **7b** was also obtained in low yield from the salt **1b**. This is evidently connected with the high susceptibility of compounds **7a,b** towards oxidation and this explains the difficulties in isolation and purification. The ^{1}H NMR spectra of freshly prepared solutions of compounds **7a,b** in DMSO-d_6 confirm their structure as products of the deprotonation of the 7,12-dihydroisoquino-[2,3-*a*]quinazoline system at position 7 or addition of hydride anion to atom C-12 in salt **1c**: the signal for the C(12)H_2 methylene group is observed at 5.1 and 5.02 ppm (2H, s) and the C-7 methine proton signal at 5.5 ppm.

The reaction of 3-chloro-5-phenylisoquino[2,3-*a*]quinazolin-13-ium perchlorate **4** with amines conforms to the pattern found for 5-oxoisoquinoquinazolinium salts **6** [10]. Hence treatment with primary amines gives 2-(2-iminomethyl)benzyl-substituted 6-chloro-4-phenylquinazolines **8a,b** as shown by the spectroscopic data for the products obtained. Features of their ^{1}H NMR spectra are the presence of the imino group proton at 9.04 and 8.90 ppm and aromatic protons occurring as nonoverlapping groups of signals with different spin systems

allowing their exact assignment. The reaction of the salt **4** with secondary amines also occurs readily. However, the separation and characterization of the corresponding adducts of structure **7** could not be achieved because of their high susceptibility to oxidation.

EXPERIMENTAL

The melting points of the synthesized compounds were determined on a Boetius type heating apparatus and are not corrected. IR spectra for the compounds as KBr tablets were recorded on a Pye-Unicam SP3-300 instrument. ^{1}H and ^{13}C NMR spectra were taken on a Varian Mercury 400 (400 and 100 MHz) spectrometer using DMSO-d_6 and with TMS as internal standard and UV spectra on a Specord M400 spectrophotometer. Monitoring of the reaction course and purity of the compounds obtained was carried out by TLC on Silufol UV-254 plates.

3-Chloro-5-phenylisoquino[2,3-*a*]quinazolin-13-ium Perchlorate (4). A solution of the 3-chloro-5-phenylisoquinoquinazolinium salt **1c** (2.21 g, 5 mmol) in nitrobenzene (10 ml) was refluxed for 30 min. After cooling, acetone (30 ml) was added. The yellow precipitate formed was filtered off and washed with acetone. Yield 0.88 g (40%); mp > 300ºC ($MeCO_2H$). UV spectrum (MeOH), λ_{max}, nm ($\varepsilon\times10^{-3}$): 209 (22.1), 224 (26.8), 316 (29.4), 358 (11.0), 515 (4.4). Found, %: C 59.82; H 2.99; Cl 16.10; N 6.37. $C_{22}H_{14}Cl_2N_2O_4$. Calculated, %: C 59.88; H 3.10; Cl 16.07; N 6.35.

5,5-Bis(aryl)-3,3'-dihalo[7,7']bi[isoquino[2,3-*a*]quinazoline]-13,13'-diylium perchlorates 5a-c. A solution of the 5-arylisoquinoquinazolinium salt **1a-c** (10 mmol) in benzonitrile (20 ml) was refluxed for 30 min. Solvent was removed *in vacuo* and 2-propanol (20 ml) was added to the residual oil. The yellow precipitate formed was filtered off and washed with 2-propanol. Recrystallization from acetic acid gave the dimer perchlorates **5a-c** as a yellow crystalline material.

Compound 5a. Yield 2.13 g (40%); mp > 300ºC ($MeCO_2H$). Found, %: C 49.75; H 2.13, Br 15.10; Cl 6.70; N 7.97. $C_{44}H_{24}Br_2Cl_2N_6O_{12}$. Calculated, %: C 49.88; H 2.28; Br 15.08; Cl 6.69; N 7.93.

Compound 5b. Yield 4.24 g (75%); mp > 300ºC ($MeCO_2H$). Found, %: C 46.71; H 2.01; Br 28.36; Cl 6.30; N 5.00. $C_{44}H_{24}Br_4Cl_2N_4O_8$. Calculated, %: C 46.88; H 2.15; Br 28.35; Cl 6.29; N 4.97.

Compound 5c. Yield 2.6 g (60%); mp > 300ºC ($MeCO_2H$). Found, %: C 59.92; H 2.75; Cl 16.12; N 6.40. $C_{44}H_{26}Cl_4N_4O_8$. Calculated, %: C 60.02; H 2.98; Cl 16.11; N 6.36.

3,3'-Dibromo-5,5'-bis(4-methylphenyl)-[7,7']bi[isoquino[2,3-*a*]quinazoline]-13,13'-diylium Perchlorate (5d). *o*-Bromomethylacetophenone (1.26 g, 6 mmol) was added to a solution of (2-amino-5-bromophenyl)-(4-methylphenyl)methanone **2d** (1.45 g, 5 mmol) in acetonitrile (20 ml). The mixture was refluxed for 18 h. The precipitate formed on cooling the mixture was filtered off. The solid material was dissolved in acetic acid and a 70% solution of perchloric acid (3 ml) was added to the warm solution and heated for 3 min. The precipitate formed on cooling was filtered off and washed with acetic acid and acetone. Yield 3.39 g (68%); mp > 300ºC ($MeCO_2H$). UV spectrum (MeOH), λ_{max}, nm ($\varepsilon\times10^{-3}$): 208 (49.9), 232 (62.3), 318 (59.2), 540 (10.9). Found, %: C 55.27; H 2.91; Br 16.05; Cl 7.20; N 5.65. $C_{46}H_{30}Br_2Cl_2N_4O_8$. Calculated, %: C 55.39; H 3.03; Br 16.02; Cl 7.11; N 5.62.

3-Chloro-5-phenyl-12H-isoquino[2,3-*a*]quinazoline (7a). A. $NaBH_4$ (10 mmol) was added portionwise to a suspension of the 3-chloro-5-phenylisoquinoquinazolinium salt **4** (2.2 g, 5 mmol) in methanol (20 ml) and heated for 1 h. After cooling a dark-blue precipitate of compound **7a** was formed. It was filtered off, carefully washed with sodium carbonate solution (15%) and water, and recrystallized from 2-propanol. Yield 0.43 g (25%); mp 136-138ºC (2-propanol). Found, %: C 76.88; H 4.35; Cl 10.37; N 8.25. $C_{22}H_{15}ClN_2$. Calculated, %: C 77.08; H 4.41; Cl 10.34; N 8.17.

B. The 3-chloro-5-phenylisoquinoquinazolinium perchlorate **1c** (2.21 g, 5 mmol) was dissolved with heating in pyridine (10 ml). Water (50 ml) was added to the solution and the precipitate was filtered off and washed with water and alcohol. Yield 0.34 g (20%).

3-Bromo-(4-bromophenyl)-12H-isoquino[2,3-*a*]quinazoline (7b) was prepared by the method B reported above for compound **7a** using 3-bromo-5-(4-bromophenyl)isoquinoquinazolinium perchlorate **1b** (2.83 g, 5 mmol). Yield 0.51 g (22%); mp 168-170ºC (2-propanol). Found, %: C 56.36; H 2.83; Br 34.31; N 6.15. $C_{22}H_{14}Br_2N_2$. Calculated, %: C 56.68; H 3.03; Br 34.28; N 6.01.

N-({2-[(6-Chloro-4-phenyl-2-quinazolinyl)methyl]phenyl}methylidene)(phenyl)methanamine (8a). The 3-chloro-5-phenylisoquinoquinazolinium perchlorate **4** (0.44 g, 1 mmol) was dissolved with heating in benzylamine (4 ml), heated for a further 3 min, and left overnight. Water (50 ml) was added to the solution and the precipitate was filtered off and washed with water and alcohol. Yield 0.28 g (63%); mp 122-124ºC (2-propanol). IR spectrum, ν, cm^{-1}: 1630 (C=N), 1550, 1490, 1390, 700. UV spectrum (MeOH), λ_{max}, nm ($\varepsilon\times10^{-3}$): 206 (132.3), 232 (133.3), 320 (23.5), 520 (1.6). ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 9.04 (1H, s, –N=CH–); 7.96 (1H, d, ^4J = 2.4, H-5'); 7.93 (2H, m, H-6,8'); 7.87 (1H, dd, ^3J = 8.8, ^4J = 2.4, H-7'); 7.65 (2H, m, H-2",6"); 7.55 (3H, m, H-3"-5"); 7.41 (1H, d, ^3J =8.0, H-3); 7.36 (1H, t, ^3J = 8.0, H-4); 7.28 (1H, t, ^3J = 8.0, H-5); 7.15 (5H, s, NCH_2–$C_6\underline{H}_5$); 4.72 (2H, s, –$NC\underline{H}_2$–Ph); 4.71 (2H, s, CH_2). Found, %: C 77.66; H 4.83; Cl 7.93; N 9.40. $C_{29}H_{22}ClN_3$. Calculated, %: C 77.76; H 4.95; Cl 7.91; N 9.38.

N-({2-[(6-Chloro-4-phenyl-2-quinazolinyl)methyl]phenyl}methylidene)-2-propanamine (8b) was prepared by the method reported for compound **8a** using 2-propylamine (4 ml). Yield 0.2 g (51%); mp 130-132ºC (2-propanol). IR spectrum, ν, cm^{-1}: 1625 (C=N), 1550, 1490, 695. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 8.89 (1H, s, –N=CH–); 7.98 (1H, d, ^4J = 2.4, H-5'); 7.95 (1H, d, ^3J = 8.8, H-8'); 7.88 (1H, dd, ^3J = 8.8, ^4J = 2.4, H-7'); 7.86 (1H, dd, ^3J = 8.0, ^4J = 1.6, H-6); 7.68 (2H, m, H-2",6"); 7.59 (3H, m, H-3"-5"); 7.38 (1H, d, ^3J = 8.0, H-3); 7.32 (1H, td, ^3J = 8.0, ^4J = 1.6, H-4); 7.25 (1H, t, ^3J = 8.0, H-5); 4.66 (2H, s, CH_2); 3.47 (1H, m, $\underline{C}H(CH_3)_2$); 1.07 (6H, d, ^3J = 6.4, $CH(C\underline{H}_3)_2$). Found, %: C 74.89; H 5.32; Cl 8.88; N 10.59. $C_{25}H_{22}ClN_3$. Calculated, %: C 75.08; H 5.54; Cl 8.87; N 10.51.

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