

## CONDENSED ISOQUINOLINES

### 31\*. REACTION OF 5-ARYL-3-HALO- 12H-ISOQUINO[2,3-*a*]QUINAZOLINES WITH ELECTROPHILIC REAGENTS

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*Treatment of 5-aryl-3-halo-12H-isoquino[2,3-*a*]quinazolines with electrophilic reagents readily forms their oxidation products. Acylation of the 3-chloro-5-phenyl-7,12-dihydroisoquino[2,3-*a*]quinazolinium perchlorate with Ac<sub>2</sub>O in the presence of pyridine gave the product of electrophilic substitution at the C-7 atom 1-(3-chloro-5-phenyl-12H-isoquino[2,3-*a*]quinazolin-7-yl)-1-ethanone. By the same route phenacyl bromides react with the anhydro base **1** to give 5-aryl-7-(2-aryl-2-oxoethyl)-3-halo-isoquino[2,3-*a*]quinazolin-13-ium bromides. These salts readily react with nucleophilic reagents to form the products of addition at the C-12 atom.*

**Keywords:** 5-aryl-12H-isoquino[2,3-*a*]quinazoline, 5-arylisoquino[2,3-*a*]quinazolin-13-ium bromides, acylation, borohydride reduction, oxidation.

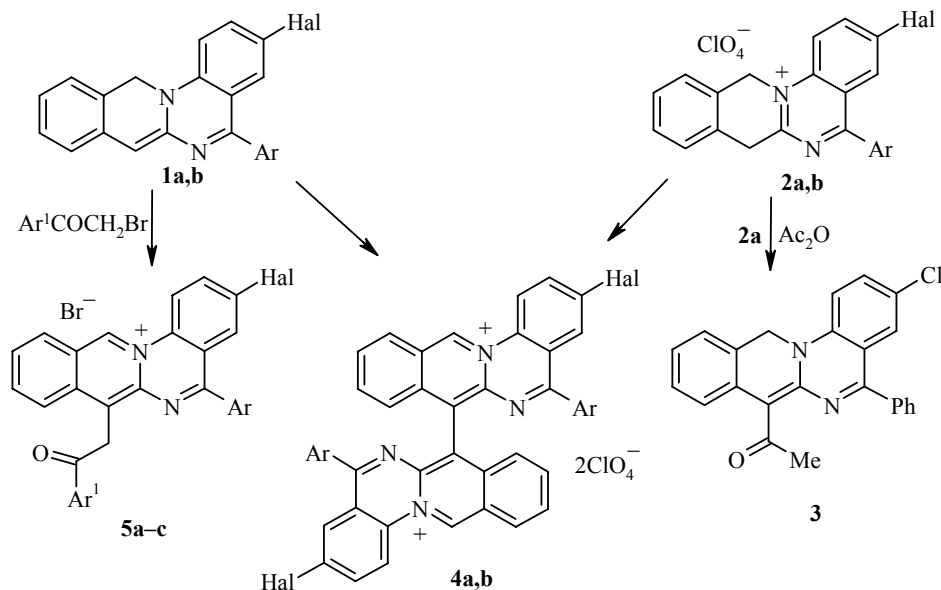
Secondary enamines are characterized by their high reactivity towards electrophilic reagents [2, 3]. We have studied such reactions in a series of condensed isoquinolines in cases where the compounds have both a secondary enamine fragment in the structure (benzimidazo[1,2-*b*]isoquinolin-11(5H)-one) and a methyleneimine fragment (7,12-dihydro-5H-isoquino[2,3-*a*]quinazolin-5-one and 6,11-dihydro-13H-isoquino[3,2-*b*]quinazolin-13-one). It was also of interest to study the features of these reactions in a series of 5-aryl-12H-isoquino[2,3-*a*]quinazolines **1a,b** whose structures also have two potentially reactive nucleophilic centers, i.e. the C-7 atom (the β-carbon of the enamine fragment C(7)=C(6a)–N(13) and the N-6 atom (of the C(5)=N(6) imino group). We have previously [4] found a number of similarities in the behavior of 5-arylisoquinoquinazolines **1a,b** and their protonated 5-aryl-7,12-dihydroisoquino[2,3-*a*]quinazolinium perchlorate salts with the behavior of other condensed isoquinolines [5-8] in oxidation reactions, i.e. a tendency for dehydrogenation at the benzyl position (7 and 12) to form aromatic derivatives including those with a dimeric structure. It would be logical to suggest a similar behavior dependence in electrophilic substitution reactions. However, the resolution of this question proved difficult because of the extreme susceptibility of compounds **1a,b** and **2a,b** to oxidation. In the presence of even weak bases (traces of water and alcohol) products of oxidation and their subsequent reaction with bases are readily formed.

\* For Communication 30 see [1].

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None the less, in some cases we have obtained and reliably established the structure of the products of electrophilic substitution of 5-arylisoino[2,3-*a*]quinazolines.



**1, 2, 4 a** Ar = Ph, Hal = Cl, **b** Ar = 4-BrC<sub>6</sub>H<sub>4</sub>, Hal = Br; **5 a** Ar = Ph, Ar<sup>1</sup> = 4-BrC<sub>6</sub>H<sub>4</sub>, Hal = Cl, **b** Ar = 4-BrC<sub>6</sub>H<sub>4</sub>, Ar<sup>1</sup> = Ph, Hal = Br; **c** Ar = Ar<sup>1</sup> = 4-BrC<sub>6</sub>H<sub>4</sub>, Hal = Br

Heating a mixture of the isoquinolizinium salts **1a,b** with acid chlorides in pyridine or dioxane gives complex mixtures of oxidation and acylation products according to <sup>1</sup>H NMR spectroscopic data. Acylation of salt **2a** with acetic anhydride in the presence of pyridine proved more successful and the reaction mixture gave a modest yield of 1-(3-chloro-5-phenyl-12H-isoquinolizino[2,3-*a*]quinazolin-7-yl)-1-ethanone (**3**). Spectroscopic data identified the reaction product as the 7-acetyl derivatives. The <sup>1</sup>H NMR spectrum of compound **3** showed a three-proton singlet for the introduced acetyl group (2.55 ppm), the absence of a signal for the methine H-7 proton, and the aromatic proton signals shifted to low field of those in the unsubstituted isoquinolizinium salt **1a** [4] (see Table 1, mean  $\Delta\delta \sim 0.2$  ppm). The greatest low field shift was observed for the H-8 proton at 8.07 ppm ( $\Delta\delta = 1.0$  ppm) which falls in the deshielding region of the 7-acetyl substituent carbonyl group. The presence of a carbonyl stretching vibration in the IR spectrum at low frequency (1630 cm<sup>-1</sup>) is due to donor effect of the conjugated system of the 5-arylisoino[2,3-*a*]quinazolines.

The reaction of the 5-arylisoino[2,3-*a*]quinazolines **1a,b** and their salts **2a,b** with isocyanates and aldehydes also leads to the formation of oxidation products according to <sup>1</sup>H NMR spectroscopic data, mainly the dimeric 3,3'-dihalo-5,5'-bis(aryl)[7,7']bi[isoquinolizinium]-13,13'-dium salts **4a,b**. The same result was obtained when attempting to alkylate compounds **1a,b** with benzyl halides. Fusing compound **1a** with methyltosylate gave the 3,3'-dichloro-5,5'-biphenyl[7,7']bi[isoquinolizinium]-13,13'-dium perchlorate **4a** in high yield (65%). The formation of alkylation products of the isoquinolizinium salts **1a,b** with phenacyl bromides upon heating a mixture of the reagents in acetonitrile was unexpectedly successful. It should be noted that an oxidation and not alkylation frequently occurs in this reaction in the case of condensed isoquinolines [6, 9]. Oxidation also occurs in the reaction with 5-arylisoino[2,3-*a*]quinazolines but gives the 5-aryl-7-(2-aryl-2-oxoethyl)-3-haloisoquinolizinium bromides **5a-c**.

TABLE 1. Spectroscopic Characteristics of the 5-Arylisoquinoquinazolines **3**, **5-7**

Compound	IR spectrum, $\nu$ , $\text{cm}^{-1}$	$^1\text{H}$ NMR spectrum, $\delta$ , ppm ( $J$ , Hz)		
		ArH	H-12	Other signals
<b>3</b>	1630 (C=O), 1605 (C=N), 1520, 1375, 1325, 1285, 1000, 760, 690	8.07 (1H, dd, $^{\circ}J = 8.0$ , $^mJ = 1.6$ , H-8); 7.86 (1H, d, $^{\circ}J = 8.5$ , H-1); 7.68 (2H, m, H-2',6'); 7.65 (1H, dd, $^{\circ}J = 8.5$ , $^mJ = 2.4$ , H-2); 7.57 (3H, m, H-3'-H-5'); 7.43 (1H, d, $^mJ = 2.4$ , H-4); 7.31 (1H, d, $^{\circ}J = 8.0$ ); 7.17 (1H, td, $^{\circ}J = 8.0$ , $^mJ = 1.6$ , H-9); 7.10 (1H, td, $^{\circ}J = 8.0$ , $^mJ = 1.6$ , H-10)	5.10 (2H, s)	2.55 (3H, s, CH <sub>3</sub> )
<b>5a</b>	1685 (C=O), 1590 (C=N), 1545, 1350, 1210, 980, 760, 700	9.64 (1H, d, $^{\circ}J = 9.5$ , H-1); 8.98 (1H, d, $^{\circ}J = 8.0$ , H-11); 8.63 (1H, d, $^{\circ}J = 8.5$ , H-8); 8.47 (1H, dd, $^{\circ}J = 9.5$ , $^mJ = 2.4$ , H-2); 8.30 (1H, t, $^{\circ}J = 8.0$ , H-9); 8.21 (1H, d, $^mJ = 2.4$ , H-4); 8.16 (1H, t, $^{\circ}J = 8.0$ , H-10); 8.14 (2H, d, $^{\circ}J = 8.0$ , H-2'',6''); 7.76 (4H, m, H-2',6',3'',5''); 7.66 (1H, t, $^{\circ}J = 8.0$ , H-4'); 7.57 (2H, t, $^{\circ}J = 8.0$ , H-3',5')	11.73 (1H, s)	5.68 (2H, s, CH <sub>2</sub> )
<b>5b</b>	1670 (C=O), 1590 (C=N), 1380, 1345, 1220, 990, 835, 760	9.65 (1H, d, $^{\circ}J = 9.5$ , H-1); 8.95 (1H, d, $^{\circ}J = 8.0$ , H-11); 8.60 (1H, d, $^{\circ}J = 8.0$ , H-8); 8.58 (1H, dd, $^{\circ}J = 9.5$ , $^mJ = 2.4$ , H-2); 8.32 (1H, d, $^mJ = 2.4$ , H-4); 8.30 (1H, t, $^{\circ}J = 8.0$ , H-9); 8.21 (2H, d, $^{\circ}J = 7.5$ , H-2'',6''); 8.14 (1H, t, $^{\circ}J = 8.0$ , H-10); 7.73 (5H, m, H-2',3',5',6',4''); 7.59 (2H, t, $^{\circ}J = 7.5$ , H-3'',5'')	11.73 (1H, s)	5.71 (2H, s, CH <sub>2</sub> )
<b>5c</b>	1680 (C=O), 1580 (C=N), 1390, 1340, 1060, 990, 825, 745	9.57 (1H, d, $^{\circ}J = 9.5$ , H-1); 9.00 (1H, d, $^{\circ}J = 8.0$ , H-11); 8.63 (1H, d, $^{\circ}J = 8.0$ , H-8); 8.59 (1H, dd, $^{\circ}J = 9.5$ , $^mJ = 2.0$ , H-2); 8.34 (1H, d, $^mJ = 2.0$ , H-4); 8.31 (1H, t, $^{\circ}J = 8.0$ , H-9); 8.18 (1H, t, $^{\circ}J = 8.0$ , H-10); 8.14 (2H, d, $^{\circ}J = 8.0$ , H-2'',6''); 7.77 (2H, d, $^{\circ}J = 8.0$ , H-3'',5''); 7.75 (4H, m, H-2',3',5',6')	11.75 (1H, s)	5.69 (2H, s, CH <sub>2</sub> )
<b>6</b>	1677 (C=O), 1590 (C=N), 1545, 1505, 1410, 1280, 1205, 990, 795, 750	7.93 (2H, d, $^{\circ}J = 8.0$ , H-2'',6''); 7.60 (4H, m, H-2',6',3'',5''); 7.51 (1H, dd, $^{\circ}J = 8.5$ , $^mJ = 2.0$ , H-2); 7.41 (2H, d, $^{\circ}J = 8.0$ , H-3',5'); 7.24 (1H, d, $^{\circ}J = 8.5$ , H-1); 7.20 (1H, d, $^mJ = 2.0$ , H-4); 7.18 (1H, d, $^{\circ}J = 7.5$ , H-11); 7.12 (1H, t, $^{\circ}J = 8.0$ , H-9); 7.06 (1H, t, $^{\circ}J = 8.0$ , H-10); 6.97 (1H, d, $^{\circ}J = 8.0$ , H-8)	5.00 (2H, s)	4.35 (2H, s, CH <sub>2</sub> )
<b>7</b>	1690 (C=O), 1593 (C=N), 1550, 1490, 1420, 1390, 1120 (C-O), 1005, 730	7.89 (2H, d, $^{\circ}J = 8.0$ , H-2'',6''); 7.66 (2H, d, $^{\circ}J = 8.0$ , H-2',6'); 7.60 (1H, d, $^{\circ}J = 9.0$ , H-1); 7.56 (4H, m, H-3',5',3'',5''); 7.52 (1H, dd, $^{\circ}J = 9.0$ , $^mJ = 2.4$ , H-2); 7.31 (2H, m, H-4,11); 7.26 (1H, d, $^{\circ}J = 8.0$ , H-8); 7.20 (2H, m, H-9,10)	6.49 (1H, s)	4.73 (1H, d, $^2J = 16.8$ , 7-CH <sub>A</sub> H <sub>B</sub> ); 4.16 (1H, d, $^2J = 16.8$ , 7-CH <sub>A</sub> H <sub>B</sub> ); 3.29 (4H, m, O-CH <sub>2</sub> ); 2.38 (2H, m, N-CH <sub>A</sub> H <sub>B</sub> ); 2.24 (2H, m, N-CH <sub>A</sub> H <sub>B</sub> )

The structure of the alkylation products which is rather complex and not only possible was established by a comparison of their spectroscopic data with the data of the more simple 3-chloroisoquino-5-phenyl-[2,3-*c*]quinazolin-13-ium perchlorate [4] and dimer salts **4a,b** [4]. The IR spectra of the compounds **5a-c** showed carbonyl group stretching vibrations in the range 1670-1685  $\text{cm}^{-1}$ , characteristic of an Ar-C=O system which points to the presence of an acetophenone fragment in the molecule. Hence  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were measured with the use of homonuclear (COSY) and heteronuclear (HMBC and HMQC) 2D correlation spectroscopy. In addition, for an evaluation of the steric proximity of the individual protons NOESY-1D and NOESY spectra were used. For various spectra of compound **5b** a whole series of analogies was found with the corresponding spectra of compounds **4a,b** and the 3-chloro-5-phenylisoquino[2,3-*a*]quinazolin-13-ium perchlorate [4]. Hence in the proton spectrum a singlet with an unusually low field chemical shift of 11.73 ppm was found. This signal has a correlation in the NOESY-1D spectrum with the signals at 9.65 and 8.95 ppm. This points to the proximity of the protons in the molecule in agreement with its angular structure. Hence the unusual chemical shift of the signal is explained on the one hand by the presence of the neighboring quaternary nitrogen atom and on the other with a nonbonding interaction with the proton of the angularly annelated benzene ring. This signal corresponds to the H-12 proton of the isoquinoquinazoline system and is observed in the region characteristic of the isoquino[2,3-*a*]quinazoline aromatic system [4, 5, 7]. A positive assignment of the signals in the proton spectrum can be made from the COSY spectrum. Here, clear correlations can be traced in three spin systems, *viz.* the ABCD of the isoquinoline fragment, the ABC of the 3-bromoquinazoline fragment, and the AA'BB' of the acetophenone fragment. The structure of the carbon skeleton of the molecule follows from its 2D HMBC and HMQC spectra. In the HMQC spectrum there are correlations of all of the proton-bearing carbon atoms in the molecule. Using the previously made assignment of signals in the  $^1\text{H}$  NMR spectra all of the proton-bearing carbon atoms are readily located (see Table 2). A secure assignment of the majority of the quaternary carbon atoms can be made on the basis of the correlations in the HMBC spectrum. Figure 1 shows these signal assignments and the most significant correlations in the HMBC spectrum upon which they are based.

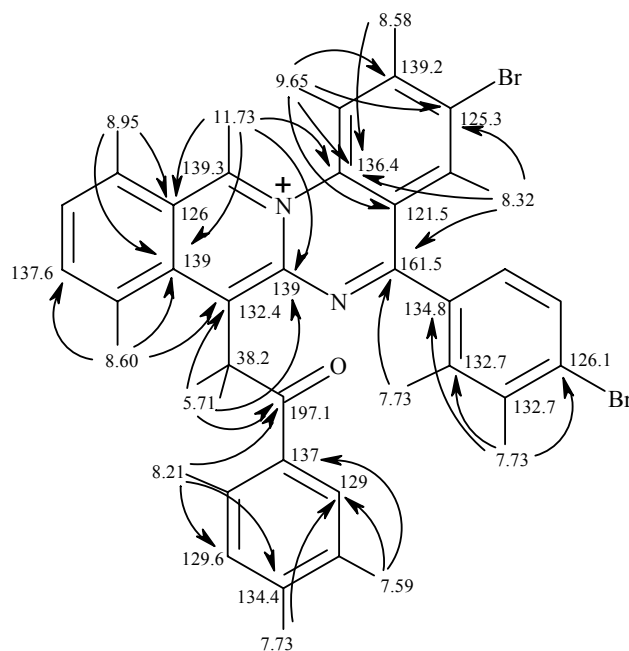


Fig. 1. Structurally important HMBC correlations for compound **5b**.

From the point of view of structure the most important correlation is that of the methylene group protons with the carbonyl group carbon at  $\delta = 197.1$  and the two heterocyclic system carbon atoms at 132.4 and 139 ppm. This confirms the presence of the acetophenone fragment bonded at C-7. In full agreement with this deduction is the observation of the marked homonuclear Overhauser effect for the methylene group protons with the H-8 (4%) and H-2'',6'' protons in the experiment carried out on compound **5a**.

The fact that the *p*-bromophenyl substituent in compound **5b** is bonded to C-5 is confirmed by the presence of the corresponding correlation of C-5 (161.5 ppm) with the *o*-protons at 7.73 ppm. There are also correlations of this carbon with proton H-4 and with H-1 (*via* a W type interaction) completely analogous to that in the spectra of compound **4** [4].

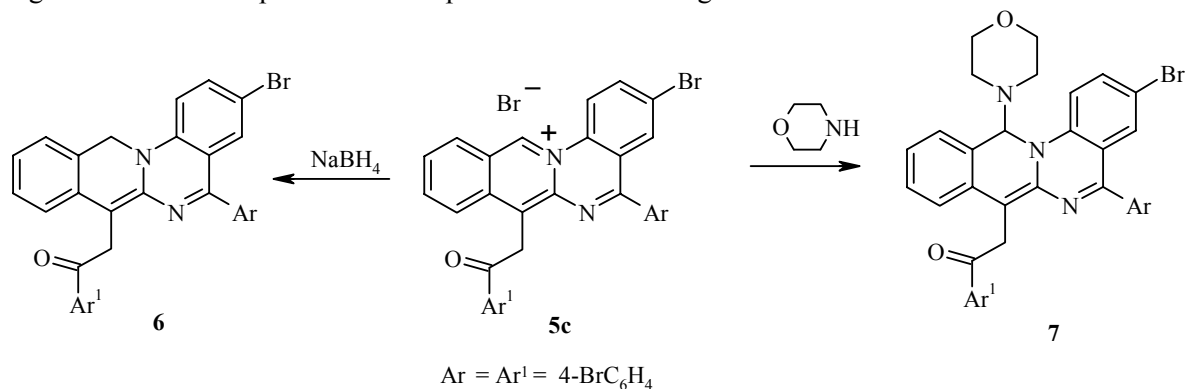
Additional evidence supporting the proposed structure for compounds **5a-c** comes from the overall similarity in the UV spectra of the dimer salts **4**, 3-chloro-5-phenylisoquino[2,3-*a*]quinazolin-13-ium perchlorate [4], and 7-[2-(4-bromophenyl)-2-oxoethyl]isoquinoquinazolinium bromide **5a** which points to their isoelectronicity. The spectrum of compound **5a** differs from the rest only by the presence of a characteristic  $\pi \rightarrow \pi^*$  ketonic band at 255 nm ( $\epsilon \cdot 10^{-3} = 44.5$ ).

The mass spectra of salts **5a,b** were obtained by the HPLC-MS method (CI, acetonitrile, 0.05% formic acid) and showed weak intensity peaks for the 7-[2-(aryl)-2-oxoethyl]-5-aryl-3-haloisoquino[2,3-*a*]quinazolin-13-ium cations (35-40%) and stronger peaks corresponding to the products of the interaction of these cations with water and their subsequent oxidation and decomposition. Such a result is fully in agreement, bearing in mind the ready reaction of aromatic isoquino[2,3-*a*]quinazoline derivatives with nucleophiles seen before [4, 5] in other examples. In fact, the reaction of salt **5c** with sodium borohydride in alcohol readily gives the nucleophilic addition product at the 12 position, i.e. 2-[3-bromo-5-(4-bromophenyl)-12H-isoquino[2,3-*a*]quinazolin-7-yl]-1-(4-bromophenyl)-1-ethanone (**6**). The  $^1\text{H}$  NMR spectrum (Table 1) shows a two-proton methylene group singlet

TABLE 2. Proton-Carbon and Proton-Proton Correlations for Compound **5b**

Atom number	$^1\text{H}$ NMR spectrum, $\delta$ , ppm	COSY correlations, $\delta$ , ppm	HMBC correlations, $\delta$ , ppm	$^{13}\text{C}$ NMR spectrum, $\delta$ , ppm; HMQC correlations
1	9.65	8.65	161.5, 136.4, 125.3, 121.5, 139.2	122.2
2	8.58	9.65	136.4	139.2
3	—	—	—	125.3
4	8.32	—	139.2, 136.4, 125.3, 161.5	131.9
4a	—	—	—	121.5
5	—	—	—	161.5
6a	—	—	—	139
7	—	—	—	132.4
7a	—	—	—	139
8	8.60	8.28	137.6, 132.4, 126	126.1
9	8.30	8.14	139, 131.4	137.6
10	8.14	8.30	126	131.4
11	8.95	8.14	139, 137.6, 126	131.6
11a	—	—	—	126
12	11.73	—	139, 136.4, 131.6, 126	139.3
13a	—	—	—	136.4
1'	—	—	—	134.8
2',3'	7.73	—	134.8, 132.7, 129, 126.1, 161.5	132.7
4''	—	—	—	126.1
4'	—	—	—	134.4
1''	—	—	—	137
2''	8.21	7.59	134.4, 129.6, 197.1	129
3''	7.59	8.21	137, 129	129.6
C=O	—	—	—	197.1
CH <sub>2</sub>	5.71	—	197.1, 139, 132.4	38.2

for H-12 at 5.00 ppm and the aromatic protons of the isoquino[2,3-*a*]quinazoline system shifted to high field, being seen in the same region as the unsubstituted derivative **1b** [4]. This also agrees fully with the observed change in the UV spectrum of a bathochromic shift by an average 5-10 nm and of 60 nm for the long wavelength band when compared with the spectrum of the starting salt **5c**.



The 7-(2-aryl-2-oxoethyl)isoquinoquinazolinium bromides **5a-c**, like other aromatic isoquino[2,3-*a*]quinazoline aromatic derivatives [4, 5], react readily with amines. We have characterized the reaction product of salt **5c** with morpholine as 2-[3-bromo-5-(4-bromophenyl)-12-(4-morpholino)-12H-isoquino[2,3-*a*]quinazolin-7-yl]-1-(4-bromophenyl)-1-ethanone (**7**). A feature of the <sup>1</sup>H NMR spectrum of compound **7** (Table 1) is the presence of the 7-CH<sub>2</sub> methylene group as two AB type doublets with <sup>2</sup>*J* = 16.8 Hz. The N-CH<sub>2</sub> methylene group protons of the morpholine fragment are also non-equivalent and appear as two multiplets with Δδ = 0.14 ppm. This data and the low field positioning of the H-12 proton signal as a singlet at 6.49 ppm identify the structure as the product of addition of the amine at position 12.

## EXPERIMENTAL

Melting points for the compounds synthesized were determined on a Boetius type heating block and are not corrected. IR spectra (KBr tablets) were recorded on a Pye-Unicam SP3-300 instrument and <sup>1</sup>H and <sup>13</sup>C NMR spectra on a Varian Mercury 400 instrument (400 and 100 MHz respectively) using DMSO-*d*<sub>6</sub> and with TMS as internal standard. UV spectra were taken on a Specord M-400 instrument.

The mass spectra of compounds **5a,b** were obtained on an Agilent/100 Series HPLC-MS instrument (CI, acetonitrile, 0.05% formic acid) and are given as the cations of these salts [M-Br]<sup>+</sup>. Because of the instability of the latter only the polyisotopic fragment ions [M-2Br]<sup>+</sup> were recorded. Salts **5a,b** were extremely unstable, particularly in the presence of nucleophiles including water. As a result of the absence of reliable data for the reaction of salts **5** under conditions to those used for recording the mass spectra some of the peaks, particularly those of low intensity are not considered. Monitoring of the reaction course and the purity of the products obtained was carried out by TLC on Silufol UV-254 plates.

**1-(3-Chloro-5-phenyl-12H-isoquino[2,3-*a*]quinazolin-7-yl)-1-ethanone (3)**. A mixture of the isoquinoquinazoline **2a** (4.43 g, 10 mmol) and acetic anhydride (5 ml) was heated to reflux and pyridine (10 ml) was added. After cooling it was diluted with water (60 ml). The precipitate was filtered off, washed with water and then alcohol. Yield 1.19 g (31%); mp 175-177°C (acetone). UV spectrum (MeOH), λ<sub>max</sub>, nm (ε·10<sup>-3</sup>): 207 (83.6), 229 (74.0), 265 (51.1), 285 (51.8), 350 (54.0), 515 (17.8). Found, %: C 74.83; H 4.33; Cl 9.21; N 7.30. C<sub>24</sub>H<sub>17</sub>ClN<sub>2</sub>O. Calculated, %: C 74.90; H 4.45; Cl 9.21; N 7.28.

**5-Aryl-7-(2-aryl-2-oxoethyl)-3-haloisoquino[2,3-*a*]quinazolin-13-ium Bromides (5a-c)**. The phenacyl bromide (20 mmol) was added to a solution of the 5-aryliisoquinoquinazoline **1a,b** (10 mmol) in

acetonitrile (30ml) and refluxed for 3-5 h. After this time the solution had changed color from blue to yellow and a yellow precipitate formed. The product was cooled, the precipitate filtered off, washed with acetone, and recrystallized from acetic acid.

**Compound 5a.** Yield 3.28 g (53%); mp 278-280°C (AcOH). UV spectrum (MeOH),  $\lambda_{\max}$ , nm ( $\epsilon \cdot 10^{-3}$ ): 208 (61.9), 228 (54.1), 255 (44.5), 317 (44.5), 520 (7.7). Mass spectrum (CI),  $m/z$  ( $I_{\text{rel}}$ , %): 542.0 [M-2Br]<sup>+</sup> (31), 539.2 [M-2Br]<sup>+</sup> (40), 536.8 [M-2Br]<sup>+</sup> (60), 98.4 (100). Found, %: C 58.15; H 3.00; Br 25.84; Cl 5.71; N 4.56. C<sub>30</sub>H<sub>19</sub>Br<sub>2</sub>ClN<sub>2</sub>O. Calculated, %: C 58.23; H 3.10; Br 25.83; Cl 5.73; N 4.53.

**Compound 5b.** Yield 3.38 g (51%). Mp 195-198°C (AcOH). Mass spectrum (CI),  $m/z$  ( $I_{\text{rel}}$ , %): 601.0 [M-2Br+H<sub>2</sub>O]<sup>+</sup> (100), 585.2 [M-2Br]<sup>+</sup> (15), 582.6 [M-2Br]<sup>+</sup> (35), 581.3 [M-2Br]<sup>+</sup> (17), 99.2 (50), 99 (50), 583 [M-Br]<sup>+</sup> (35), 601 [M-Br+H<sub>2</sub>O]<sup>+</sup> (100). Found, %: C 54.25; H 2.80; Br 36.14; N 4.25. C<sub>30</sub>H<sub>19</sub>Br<sub>3</sub>N<sub>2</sub>O. Calculated, %: C 54.33; H 2.89; Br 36.14; N 4.22.

**Compound 5c.** Yield 4.6 g (62%). Mp 298-300°C (AcOH). Found, %: C 48.45; H 2.37; Br 43.09; N 3.80. C<sub>30</sub>H<sub>18</sub>Br<sub>4</sub>N<sub>2</sub>O. Calculated, %: C 48.55; H 2.44; Br 43.07; N 3.77.

**2-[3-Bromo-5-(4-bromophenyl)-12H-isoquino[2,3-*a*]quinazolin-7-yl]-1-(4-bromophenyl)-1-ethanone (6).** NaBH<sub>4</sub> (0.38 g, 10 mmol) was added portionwise to a suspension of the 5-(4-bromophenyl)isoquinoquinazolinium salt **5c** (2.2 g, 5 mmol) in methanol (20 ml) and heated for 1 h. After cooling the solution formed a dark-blue precipitate of compound **6**. The precipitate was filtered off, thoroughly washed with a 15% solution of sodium carbonate and water, and recrystallized from 2-propanol. Yield 1.13 g (34%); mp 183-184°C (2-propanol). UV spectrum (MeOH),  $\lambda_{\max}$ , nm ( $\epsilon \cdot 10^{-3}$ ): 210 (163.3), 232 (185.5), 256 (163.3), 322 (126.2), 360 (81.6), 600 (26.0). Found, %: C 54.25; H 2.80; Br 36.14; N 4.25. C<sub>30</sub>H<sub>19</sub>Br<sub>3</sub>N<sub>2</sub>O. Calculated, %: C 54.33; H 2.89; Br 36.14; N 4.22.

**2-[3-Bromo-5-(4-bromophenyl)-12-(4-morpholino)-12H-isoquino[2,3-*a*]quinazolin-7-yl]-1-(4-bromophenyl)-1-ethanone (7).** The 5-(4-bromophenyl)isoquinoquinazolinium salt **5c** (2.2 g, 5 mmol) was dissolved with heating in morpholine (10 ml). Heating was continued for a further 3 min and then left overnight. The solution was diluted with water (100 ml) and the precipitate was filtered off, washed with water, and then alcohol. Yield 0.75 g (20%); mp 175-177°C (2-propanol). Found, %: C 54.43; H 3.45; Br 32.02; N 5.67. C<sub>34</sub>H<sub>26</sub>Br<sub>3</sub>N<sub>3</sub>O<sub>2</sub>. Calculated, %: C 54.57; H 3.50; Br 32.03; N 5.62.

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