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CONDENSED ISOQUINOLINES. 38*. AZOLO[*b*]ISOQUINOLINES FROM 2-(HALOMETHYL)BENZOIC ACID DERIVATIVES

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On interacting 2-(chloromethyl)-, 2-(bromomethyl)benzonitrile or methyl 2-(bromomethyl)benzoate with 1-R-1H-imidazoles and 1-R-1H-benzimidazoles quaternary diazolium salts are formed, the heating of which with bases (K_2CO_3, Et_3N) led to the intramolecular acylation products, 1-alkyl-10-amino-1H-imidazo[1,2-b]isoquinolin-4-ium halides, 5-alkyl-6-amino-5H-benzimidazo[1,2-b]isoquinolin-12-ium halides, or 1-alkyl-1H-imidazo[1,2-b]isoquinolin-4-ium-10-olate halides.

Keywords: benzimidazo[1,2-*b*]isoquinoline, 2-(bromomethyl)benzoate, 2-(bromomethyl)benzonitrile, imidazo[1,2-*b*]isoquinoline, cyclization.

Construction of an isoquinoline fragment for the synthesis of condensed derivatives of 3-amino-isoquinoline as a method of forming the tricyclic azolo[*b*]isoquinoline system is rarely used [2, 3]. Among the known methods of constructing these heterosystems in only two variants the key stage of cyclization is the formation of the C(3)–C(4) bond of the isoquinoline ring. One of them consists of the condensation of phthaloyl dichloride with benzimidazole in the presence of base [4], and the second, a more general method developed by us, is based on the cyclization of quaternary azolium salts formed on interacting *o*-bromomethyl-benzophenones with 1,3-diazoles [5]. The present work, in the indicated scheme of synthesis of azolo-[*b*]isoquinolines, uses derivatives of *o*-toluic acid, *viz*. 2-(chloromethyl)benzonitrile (**1b**), 2-(bromomethyl)-benzonitrile (**1a**), and methyl 2-(bromomethyl)benzoate (**8**). The latter is frequently used in various hetero-cyclizations, including those for obtaining isoquinoline derivatives [6-9], while nitriles **1a,b** are rarely used for this purpose and the schemes for converting them are more complex [10-13]. The relatively simple method of synthesis of azolo[*b*]isoquinolines proposed by us enables the preparation of their previously unavailable amino and hydroxy derivatives.

On interacting halo nitriles **1a,b** with 1-alkyl-1*H*-imidazoles, 1-alkyl-1*H*-benzimidazoles, or 1-methyl-1*H*-1,2,4-triazole, quaternary azolium salts **2a-e, 3a,b**, and **4** were formed respectively. Salts **2a-c** were obtained in high yield (Table 1) on moderate heating (to 50°C) of the reactants in acetonitrile.

*For Communication 37, see [1].

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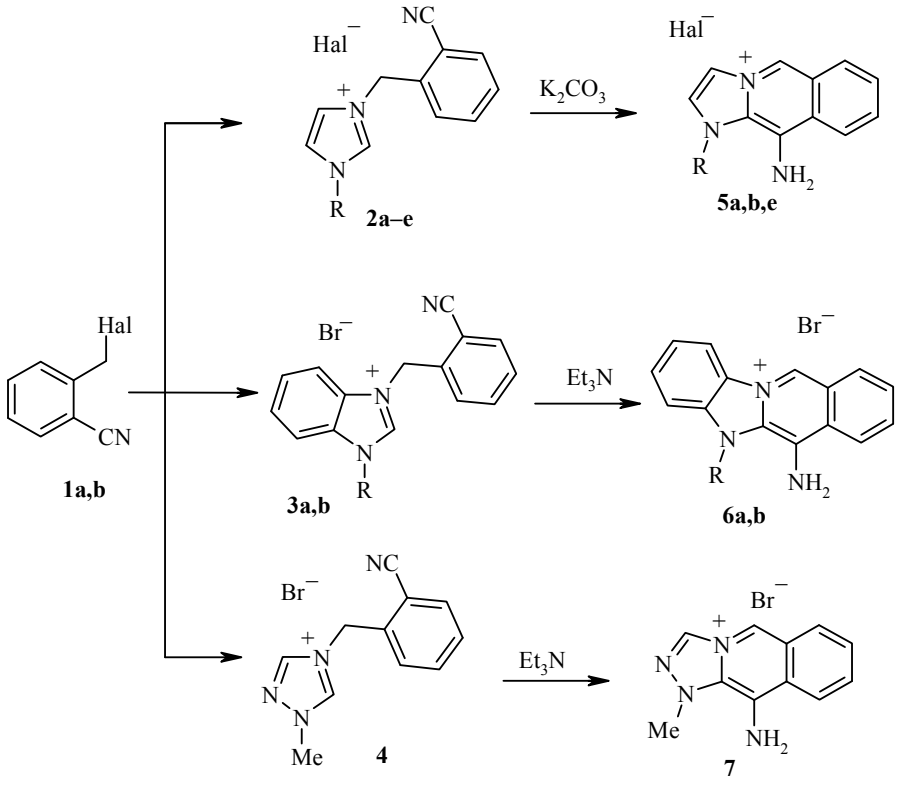


1 a Hal = Br, **b** Hal = Cl; **2a–c**, **5a**,**b** Hal = Br, **2d**,**e**, **5e** Hal = Cl;
2, **5 a**,**d** R = Me, **b**,**e** R = Et, **c** = Bn; **3**,**6 a** R = Me, **b** R = Et

With benzimidazole derivatives and 1,2,4-triazole under these conditions, the reaction proceeded more slowly and led to products **3a,b** and **4** in lower yield, increasing which may be achieved by fusing the reactants (110°C, 5-10 min). The nature of the halogen in the starting halo nitrile did not prove to have a significant effect on the rate and yield of alkylation product, but in difference to bromides **2a-c**, chlorides **2d,e** proved to be hygroscopic compounds, which complicated both the preparation of analytical samples of them and further conversion into cyclic products. The nature of the anion affected the spectral properties of imidazolium salts **2a,d** and **2b,e** insignificantly. The greatest marked changes in the spectral picture of chlorides **2d,e**, in comparison with bromides **2a,b** were the shift of 0.25-0.27 ppm of the H-2 proton signal in the ^{1}H NMR spectra towards low field (Table 2), and the high-frequency shift of the band of the stretching vibrations ν_{CN} by 5 cm^{-1} in the IR spectra (Table 3). This is caused by the changes in the spatial localization of the anion and the degree of bonding of it with the cation.

Examples are known of intramolecular cyclization of quaternary salts of 1,3-diazoles at position 2 with the participation of nitrile [14, 15] or ester [16] groups, such as the intramolecular acylation of derivatives of α-methylsulfonylacetonitrile or malononitrile on heating in DMF in the absence of a basic catalyst. Conversion of diazolium salts **2-4** under such conditions does not occur, although cyclization does take place, but only on heating in the presence of base (K_2CO_3 or Et_3N). We note that a significant role is played by the quality of the solvent, cyclization products are formed in good yield and with a high degree of purity only on using anhydrous DMF. 1-Alkyl-10-amino-1*H*-imidazo[1,2-*b*]isoquinolin-4-ium bromides **5a,b** are obtained on using potassium carbonate. On heating 1-benzylimidazolium bromide **2c** with base a complex mixture of reaction products is formed which we link with the effect of the substituent at the N(1) atom. The cyclization product of chlorides **2d,e** was isolated under the same conditions in only one case. 1-Ethyl-1*H*-imidazo[1,2-*b*]isoquinolinium chloride (**5e**) was obtained on using salt **2e**, which is less hygroscopic than **2d**. The use of Et_3N on cyclizing imidazolium salts **2** leads to a significant increase in reaction time, a reduction in the yield of the desired

TABLE 1. Physicochemical Characteristics of Compounds **2-6, 9**, and **10**

Compound	Empirical formula	Found, % / Calculated, %				mp, °C*	Yield, %
		C	H	Hal	N		
2a	$C_{12}H_{12}BrN_3$	51.78 / 51.82	4.30 / 4.35	28.76 / 28.73	15.14 / 15.11	183-185	89
2b	$C_{13}H_{14}BrN_3$	53.37 / 53.44	4.86 / 4.83	27.38 / 27.35	14.35 / 14.38	78-80	82
2c	$C_{18}H_{16}BrN_3$	61.09 / 61.03	4.50 / 4.55	22.53 / 22.56	11.87 / 11.86	186-187	78
3a	$C_{16}H_{14}BrN_3$	58.60 / 58.55	4.32 / 4.30	24.31 / 24.35	12.78 / 12.80	251-252	80
3b	$C_{17}H_{16}BrN_3$	59.70 / 59.66	4.69 / 4.71	23.37 / 23.35	12.30 / 12.28	223-224	76
4	$C_{11}H_{11}BrN_4$	47.38 / 47.33	4.00 / 3.97	28.62 / 28.63	20.06 / 20.07	129-130	70
5a	$C_{12}H_{12}BrN_3$	51.80 / 51.82	4.37 / 4.35	28.75 / 28.73	15.09 / 15.11	270-273 (decomp.)	51
5b	$C_{13}H_{14}BrN_3$	53.49 / 53.44	4.86 / 4.83	27.31 / 27.35	14.39 / 14.38	145-148 (decomp.)	49
5e	$C_{13}H_{14}ClN_3$	62.99 / 63.03	5.72 / 5.70	14.30 / 14.31	16.98 / 16.96	251-254 (decomp.)	25*[2]
6a	$C_{16}H_{14}BrN_3$	58.60 / 58.55	4.31 / 4.30	24.38 / 24.35	12.79 / 12.80	312-315 (decomp.)	53
6b	$C_{17}H_{16}BrN_3$	59.70 / 59.66	4.74 / 4.71	23.32 / 23.35	12.30 / 12.28	309-311 (decomp.)	50
9a	$C_{13}H_{15}BrN_2O_2$	50.21 / 50.18	4.85 / 4.86	25.69 / 25.68	9.01 / 9.00	150-152	92
10a	$C_{12}H_{10}N_2O$	72.66 / 72.71	5.10 / 5.08	—	14.17 / 14.13	> 300 (decomp.)	32
10b	$C_{18}H_{14}N_2O$	79.00 / 78.81	5.12 / 5.14	—	10.27 / 10.21	> 250 (decomp.)	35

*Solvents: MeCN (compounds **2a-c, 3a,b, 4, 9a**) and DMF (compounds **5a,b,e, 6a,b,** and **10b**).

*[2]Yield is given from calculation on the starting chloro nitrile **1b**.

products, and accumulation of side products in the reaction mixture. At the same time in the case of benzimidazolium salts **3a,b** the use of the indicated base was preferred, the yields of 5-alkyl-6-amino-5*H*-benzimidazo[1,2-*b*]isoquinolin-12-ium bromides **6a,b** were greater when using Et_3N than with potassium carbonate. Cyclization of 1,2,4-triazolium salt **4** was accompanied by the formation of a large quantity of side products. The presence of 10-amino-1-methyl-1*H*-[1,2,4]triazolo[4,3-*b*]isoquinolin-4-ium bromide (**7**) in the reaction mixture was successfully recorded by ^{1}H NMR on brief heating of salt **4** in the presence of Et_3N. The structures of the amino derivatives of azolo[*b*]isoquinolines **5-7** were established on the basis of their spectral data. The signal of the primary amino group in the ^{1}H NMR spectra of salts **5-7** was observed at 6.7-7.3 ppm as a two-proton singlet exchanging with D_2O, and in the IR spectra two stretching vibrational absorption bands at 3354-3307 ($^{as}\nu$) and 3307-3209 ($^{s}\nu$) cm^{-1} correspond to this group. The formation of the aromatic system of azolo[*b*]isoquinoline is shown by the presence in their ^{1}H NMR spectra of a one-proton singlet at 10.5-9.1 ppm at low field, assigned to the H-5 proton signal (for salts **5** and **7**) or H-11 (for salts **6**) on the basis of the data of the NOESY experiment carried out for compound **5a** (Fig. 1).

The structure of the azolo[*b*]isoquinolinium salts **5b** and **6a,b** was confirmed by data of UV spectra. The shape of the absorption curve in the long-wave region corresponded to their 10-aryl- and 6-aryl-substituted analogs obtained previously [5] (Fig. 2), and the observed bathochromic shift of the absorption maxima (by ~10-20 nm) into the long-wave region agreed with the presence of a more donating NH_2 group in the chromophor.

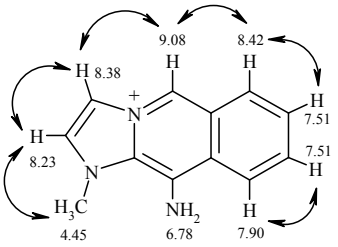


Fig. 1. Structurally important NOESY correlations for compound **5a** cation.

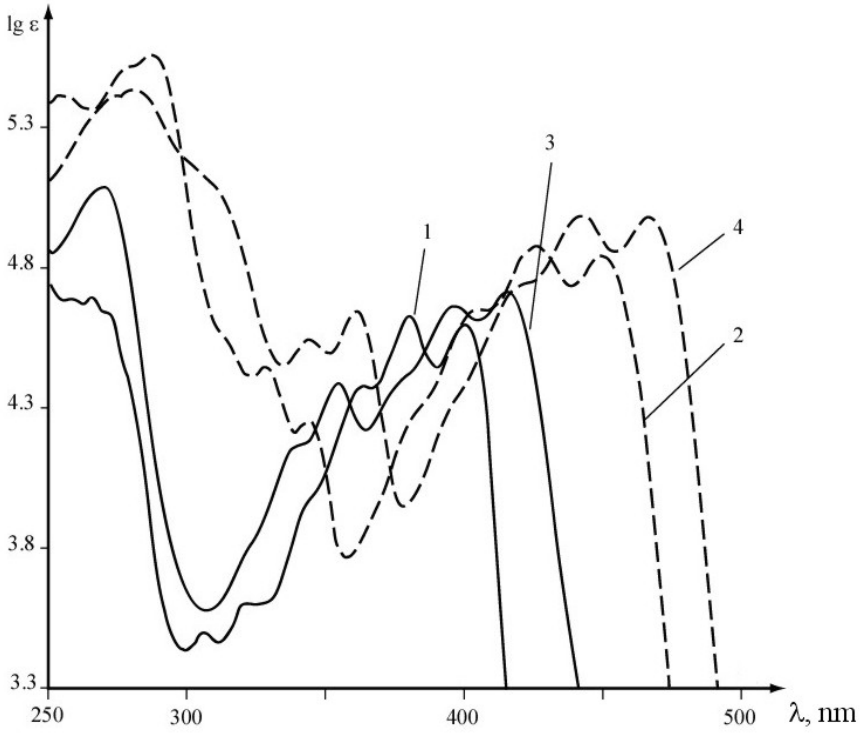
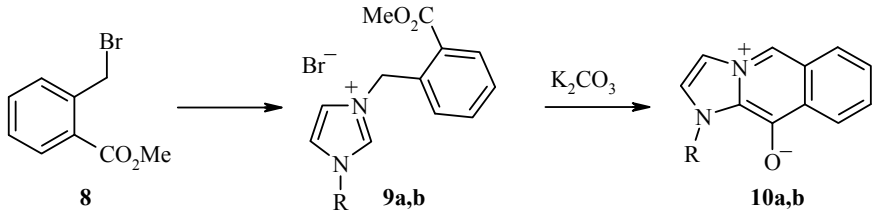


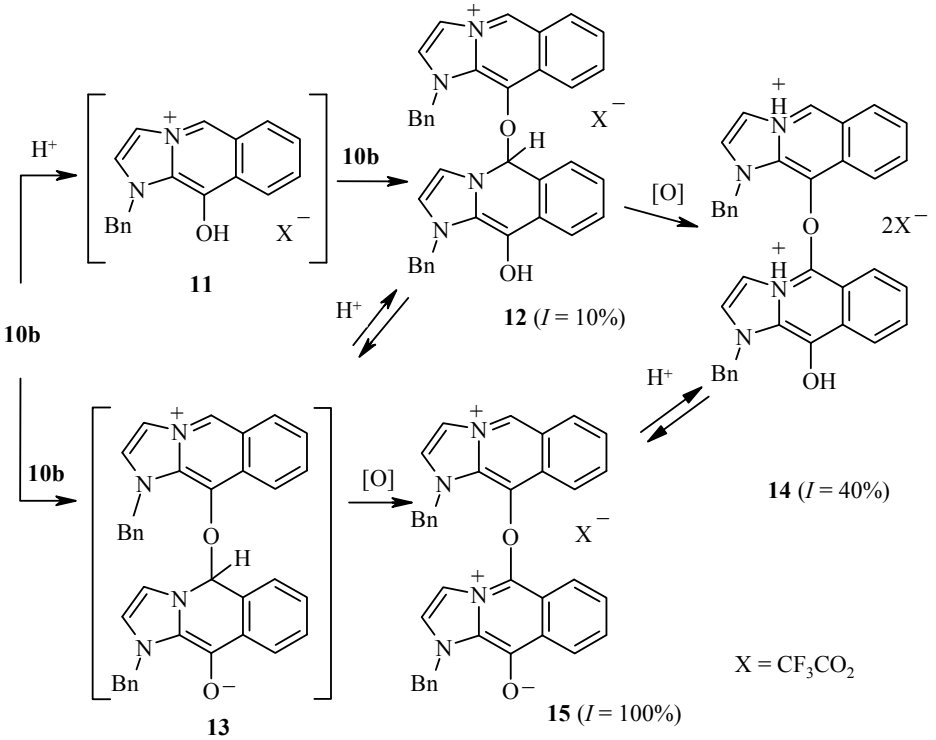
Fig. 2. Absorption spectra (in MeOH) of 10-(4-chlorophenyl)-1-methyl-1*H*-imidazo[1,2-*b*]isoquinolin-4-ium bromide [5] (*1*), 6-(4-chlorophenyl)-5-methyl-5*H*-[3,1]benzimidazo[1,2-*b*]isoquinolin-12-ium bromide [5] (*2*), 10-amino-1-ethyl-1*H*-imidazo[1,2-*b*]isoquinolin-4-ium bromide (**5b**) (*3*), and 6-amino-5-methyl-5*H*-[3,1]benz-imidazo[1,2-*b*]isoquinolin-12-ium bromide (**6a**) (*4*).

The sequence of conversions which leads to azolo[*b*]isoquinoline derivatives may also be carried out using *o*-bromomethylbenzoic acid ester **8**. On interacting ester **8** with 1-alkylimidazoles in MeCN at room temperature the corresponding 1-alkyl-3-[2-(methoxycarbonyl)benzyl]-1*H*-imidazol-3-ium bromides **9a,b** were formed. Compound **9** was isolated in a pure state but salt **9b** contained a mixture of products of further conversions.



a R = Me, **b** R = Bn

On heating imidazolium bromides **9a,b** with bases an intramolecular cyclization occurred with the formation of derivatives of imidazo[1,2-*b*]isoquinoline, the structure of which depended on the reaction conditions. Boiling the reaction mixture for 3 h in ethanol in the presence of potassium carbonate led to 1-alkyl-1*H*-imidazo[1,2-*b*]isoquinolin-4-ium-10-olates **10a,b**, difficultly soluble compounds having a deeper color (orange) than the corresponding amino derivatives **5-7** (yellow). The betaine structure of the cyclization products **10a,b** was established on the basis of data of elemental analysis and spectral characteristics. In particular, in the ^{1}H NMR spectra all the signals of the aromatic protons of the imidazo[1,2-*b*]isoquinoline tricycle were shifted towards high field, and in the IR spectra there were no bands at $\nu > 3100$ cm^{-1}. However a strong band was observed at 1477 cm^{-1}, characteristic of the vibrations of a carboxyl group anion (Table 3). The structure of compound **10b** was also confirmed by UV spectral data, taken in methanol in the presence of NaOH and HCl. An increase of base did not affect the position of maxima and the shape of the absorption curve, while in the presence of acid (HCl) a hypsochromic shift of 35 nm was observed for the long-wave maximum ($\lambda = 445$ nm), which is the result of forming a protonated form of type **11**. It is known that isoquinolinium salts readily add nucleophiles at position 1 [17]. Since in the case of azolo[*b*]isoquinolinium salts the C(5) atom is in such a position [18], the formation of a protonated form of type **11** assists the progress of such a reaction.



This was confirmed by the mass spectral data of compound **10b**, recorded by the GLC method (the low solubility of methyl derivative **10a** did not enable its qualitative mass spectrum to be obtained) on introducing the sample in CF_3CO_2H solution. In its spectrum signals were observed for cations with an *m/z* value

TABLE 2. Data of ^{1}H NMR Spectra of Compounds **2-7, 9, 10**

Compound	Chemical shifts (DMCO-d_6), δ, ppm (*J*, Hz)		
	Protons at C-sp^2	Protons at C-sp^3	NH_2
1	2	3	4
2a	9.51 (1H, s, H-2); 7.90 (1H, d, ^3J = 7.8, H-3'); 7.87 (1H, s, H-4); 7.79 (1H, s, H-5); 7.75 (1H, t, ^3J = 8.0, H-5'); 7.65 (1H, d, ^3J = 8.0, H-6'); 7.60 (1H, t, ^3J = 8.0, H-4')	5.76 (2H, s, 3-CH_2); 3.97 (3H, s, 1-CH_3)	—
2b	9.61 (1H, s, H-2); 7.96 (1H, s, H-4); 7.86 (1H, d, ^3J = 7.8, H-3'); 7.77 (1H, s, H-5); 7.75 (1H, t, ^3J = 8.0, H-5'); 7. 66 (1H, d, ^3J = 8.0, H-6'); 7.60 (1H, t, ^3J = 8.0, H-4')	5.75 (2H, s, 3-CH_2) ; 4.31 (2H, q, ^3J = 7.2, 1-CH_2); 1.50 (3H, t, ^3J = 7.2, CH_3)	—
2c	9.75 (1H, s, H-2); 7.94 (1H, s, H-4); 7.86 (1H, d, ^3J = 8.0, H-3'); 7.81 (1H, s, H-5); 7.76 (1H, t, ^3J = 8.0, H-5'); 7. 69 (1H, d, ^3J = 8.0, H-6'); 7.61 (1H, t, ^3J = 8.0, H-4'); 7.52 (2H, d, ^3J = 7.0, H-2",6"); 7.38 (3H, m, H-3"–H-5")	5.77 (2H, s, 3-CH_2); 5.55 (2H, s, 1-CH_2)	—
2d*	9.78 (1H, s, H-2); 7.87 (1H, s, H-4); 7.83 (1H, d, ^3J = 7.8, H-3'); .76 (3H, m, H-5,5',6'); 7.58 (1H, m, H-4')	5.80 (2H, s, 3-CH_2); 3.99 (3H, s, 1-CH_3)	—
2e*	9.86 (1H, s, H-2); 7.97 (1H, s, H-4); 7.86 (1H, d, ^3J = 7.8, H-3'); 7.78 (1H, s, H-5); 7.75 (1H, t, ^3J = 8.0, H-5'); 7. 70 (1H, d, ^3J = 8.0, H-6'); 7.60 (1H, t, ^3J = 8.0, H-4')	5.78 (2H, s, 3-CH_2); 4.32 (2H, q, ^3J = 7.2, 1-CH_2); 1.51 (3H, t, ^3J = 7.2, CH_3)	—
3a	10.09 (1H, s, H-2); 8.08 (1H, d, ^3J = 8.0, H-4); 7.89 (1H, d, ^3J = 8.0, H-7); 7.86 (1H, d, ^3J = 7.8, H-3'); 7.73–7.57 (5H, m, H-5,6, H-4'–H-6')	6.07 (2H, s, 3-CH_2); 4.20 (3H, s, 1-CH_3)	—
3b	10.34 (1H, s, H-2); 8.14 (1H, d, ^3J = 8.0, H-4); 7.86 (1H, d, ^3J = 7.8, H-3'); 7.82 (1H, d, ^3J = 8.0, H-7); 7.72–7.57 (5H, m, H-5,6, H-4'–H-6')	6.10 (2H, s, 3-CH_2); 4.66 (2H, q, ^3J = 7.2, 1-CH_2); 1.64 (3H, t, ^3J = 7.2, CH_3)	—
4	10.42 (1H, s, H-5); 9.36 (1H, s, H-3); 7.88 (1H, d, ^3J = 7.8, H-3'); 7.77 (1H, t, ^3J = 8.0, H-5'); 7.72 (1H, d, ^3J = 8.0, H-6'); 7.62 (1H, t, ^3J = 8.0, H-4')	5.86 (2H, s, 4-CH_2); 4.13 (3H, s, 1-CH_3)	—
5a	9.08 (1H, s, H-5), 8.42 (1H, m, H-6); 8.38 (1H, d, ^3J = 1.6, H-3); 8.23 (1H, d, ^3J = 1.6, H-2);	4.45 (3H, s, 1-CH_3)	6.78 (2H, s)
5b	9.20 (1H, s, H-5); 8.48 (2H, m, H-3,6); 8.36 (1H, s, H-2); 7.91 (1H, m, H-9); 7.52 (2H, m, H-7,8)	4.89 (2H, q, ^3J = 7.0, 1-CH_2); 1.47 (3H, t, ^3J = 7.0, CH_3)	6.81 (2H, s)
5e	9.15 (1H, s, H-5); 8.52 (1H, m, H-6); 8.45 (1H, br. s, H-3); 8.32 (1H, br. s, H-2); 7.92 (1H, m, H-9); 7.53 (2H, m, H-7,8)	4.89 (2H, q, ^3J = 7.0, 1-CH_2); 1.47 (3H, t, ^3J = 7.0, CH_3)	6.91 (2H, s)

TABLE 2 (continued)

1	2	3	4
6a	10.54 (1H, s, H-11); 8.76 (1H, m, H-1); 8.58 (1H, m, H-10); 8.18 (1H, m, H-7); 8.06 (1H, m, H-4); 7.90 (1H, t, ^3J = 8.0, H-3); 7.73 (1H, t, ^3J = 8.0, H-2); 7.67 (2H, m, H-8,9)	4.54 (3H, s, CH_3)	6.98 (2H, s)
6b	10.12 (1H, s, H-11); 8.77 (1H, m, H-1); 8.61 (1H, m, H-10); 8.18 (1H, m, H-7); 8.06 (1H, m, H-4); 7.85 (1H, t, ^3J = 8.0, H-3); 7.72–7.69 (3H, m, H-2,8,9)	5.07 (2H, q, ^3J = 7.0, CH_2); 1.45 (3H, t, ^3J = 7.0, CH_3)	6.86 (2H, s)
7*[2]	9.91 (1H, s, H-5); 9.21 (1H, s, H-3); 8.52 (1H, d, ^3J = 8.0, H-6); 8.02 (1H, d, ^3J = 8.0, H-9); 7.57 (2H, m, H-7,8)	4.62 (3H, s, CH_3)	7.23 (2H, s)
9a	9.23 (1H, s, H-2); 8.02 (1H, d, ^3J = 8.0, H-3'); 7.80 (1H, s, H-4); 7.78 (1H, s, H-5); 7.70 (1H, t, ^3J = 8.0, H-5'); 7.58 (1H, t, ^3J = 8.0, H-4'); 7.41 (1H, d, ^3J = 8.0, H-6')	5.76 (2H, s, 3-CH_2); 3.90 (3H, s, 1-CH_3); 3.88 (3H, s, OCH_3)	—
9b*[3]	9.54 (1H, s, H-2); 8.00 (1H, br. d, ^3J = 7.8, H-3'); 7.96 (1H, s, H-4); 7.80 (1H, s, H-5); 7.70 (1H, t, ^3J = 8.0, H-5'); 7.59 (1H, t, J = 8.0, H-4'); 7.49-7.36 (6H, m, H-6', H-2''–H-6'')	5.79 (2H, s, 3-CH_2); 5.55 (2H, s, 1-CH_2); 3.84 (3H, s, OCH_3)	—
10a	8.31 (1H, d, ^3J = 8.0, H-6); 7.95 (1H, s, H-5); 7.16-7.03 (4H, m, H-2,3,8,7); 6.74 (1H, d, ^3J = 8.0, H-9)	4.45 (3H, s, CH_3)	—
10b	8.36 (1H, d, ^3J = 8.0, H-6); 7.93 (1H, s, H-5); '); 7.37 (3H, m, H-3,3',5'); 7.30 (1H, m, H-4'); 7.25 (1H, s, H-2); 7.18 (1H, t, ^3J = 8.0, H-8); 7.09 (1H, t, ^3J = 8.0, H-7); 6.76 (1H, d, ^3J = 8.0, H-9)	6.23 (2H, s, 1-CH_2)	—

*Spectra of hydrates of **2d** and **2e** are given.

*[2]Mixture of compounds **4** and **7**, 18% content of salt **7**.

*[3]Spectrum of a mixture containing 85% salt **9b**.

corresponding to the dimerization product, but the signal for the protonated form of the starting compound **11** was absent. Dimerization may be effected in two ways, with the participation of the protonated form of **11** and the formation of compound **12**, to which the low intensity signal (10%) in the spectrum corresponds, or without its participation with the formation of dimer **13**. Oxidation of compound **12** leads to salt **14**, to which the signal with I_{rel} = 40% corresponds, and oxidation of compound **13** leads to salt **15** with a signal of intensity 100%. Further conversions of salts **12** and **14** may also lead to the most stable product **15**. In the spectrum of compound **10b** low intensity signals are observed for the products of cleavage of substituents at atoms N(1) and N(1') in a type **15** dimer.

TABLE 3. Data of IR Spectra of Compounds **2-6, 9, 10**

Com-pound	ν, cm^{-1}
2a	3087, 2992, 2224 (CN), 1575, 1161, 778, 766, 755, 621
2b	3054, 3013, 2956, 2222 (CN), 1561, 1450, 1163, 765
2c	3075, 2227 (CN), 1566, 1556, 1455, 1359, 1212, 1150, 765, 713
2d*	3410 (H_2O), 3137, 3075, 2227 (CN), 1633, 1563, 1450, 1161, 765
2e*	3410 (H_2O), 3147, 3090, 2227 (CN), 1633, 1569, 1454, 1161, 765
3a	3008, 2222 (CN), 1571, 1486, 1445, 1367, 1347, 1217, 1130, 776, 758, 747
3b	3018, 2977, 2956, 2222 (CN), 1569, 1483, 1444, 1427, 1269, 1210, 778, 765, 755
4	3106, 3023, 2972, 2222 (CN), 1574, 1437, 1163, 985, 768, 626
5a	3322($^{as}NH_2$), 3221($^{s}NH_2$), 3081, 1636 ($C=N^+$), 1611, 1497, 1463, 1432, 1337, 797
5b	3307 (NH_2), 3209 (NH_2), 3054, 1636 ($C=N^+$), 1605, 1421, 1331, 1321, 1243, 820, 737
5e	3312 (NH_2), 3209 (NH_2), 3065, 1644 ($C=N^+$), 1604, 1494, 1421, 1334, 1323, 1243, 822, 737
6a	3354 (NH_2), 3307 (NH_2), 3173, 3018, 1638 ($C=N^+$), 1605, 1507, 1481, 1419, 323, 737
6b	3328 (NH_2), 3271 (NH_2), 3178, 2980, 1638 ($C=N^+$), 1605, 1501, 1481, 1419, 1331, 1241, 758, 747
9a	3090, 3034, 1706 (C=O), 1429, 1269 (^{as}COC), 1197, 1166, 1080 (^{s}COC), 745, 625
9b*[2]	3059, 2951, 1713 (C=O), 1558, 1455, 1437, 1272 (^{as}COC), 1148, 1083 (^{s}COC), 729, 716
10a	3086, 1569, 1545, 1504, 1477 ($C–O^-$), 1312, 754
10b	3064, 1566, 1543, 1509, 1477 ($C–O^-$), 1416, 1310, 760, 706

*Spectra of the hydrates of **2d** and **2e** are given.
*[2]Spectrum of a mixture containing 85% salt **9b**.

EXPERIMENTAL

The IR spectra were recorded on a Perkin–Elmer Spectrum BX instrument in KBr disks. The ^{1}H NMR spectra were recorded on a Bruker Avance DRX 500 instrument (at 500 MHz) with TMS as internal standard. The NOESY experiment was carried out on a Varian Mercury 400 instrument (at 400 MHz), internal standard was TMS. The UV spectra were obtained on a Perkin–Elmer Lambda 20 UV-vis spectrometer in methanol.
Melting points were determined on a Tile heating instrument. A check on the purity of the obtained compounds was effected by the GLC mass spectrometric method on an Agilent 1100 Series instrument, with an Agilent LC/MSD SL selective detector (samples were introduced in a matrix of CF_3CO_2H, ionization by EI).

3-(2-Cyanobenzyl)-1-R-1*H*-imidazolium Bromides 2a-c (General Method). 1-R-1*H*-imidazole (2.55 mmol) was added to a solution of 2-(bromomethyl)benzonitrile (**1a**) (0.5 g, 2.55 mmol) in MeCN (10 ml). The mixture was heated on a water bath at 50°C for 10 h. The solvent was evaporated in vacuum, and diethyl ether (10 ml) was added to the residue. The solid was filtered off and washed with ether.

3-(2-Cyanobenzyl)-1-R-1*H*-imidazol-3-ium chlorides 2d,e were obtained by the method of synthesis of products **2a-c** using 2-(chloromethyl)benzonitrile **1b**. Oily products were obtained (**2d,e**·n**H$_2$O**) rapidly deliquescing in the air, which were dried and stored without access to air.

3-(2-Cyanobenzyl)-1-R-1*H*-benzimidazol-3-ium Bromides 3a,b and 4-(2-Cyanobenzyl)-1-methyl-1*H*-1,2,4-triazol-4-ium Bromide (4) (General Method). A mixture of benzonitrile **1a** (0.5 g, 2.55 mmol) and 1-R-1*H*-benzimidazole or 1-methyl-1*H*-1,2,4-triazole (2.55 mmol) was heated on an oil bath for 5-10 min at 110°C. Acetone (10 ml) was added to the melt, which was triturated, and the crystalline solid was filtered off and washed with acetone.

1-Alkyl-10-amino-1*H*-imidazo[1,2-*b*]isoquinolin-4-ium Bromides 5a,b (General Method). Potassium carbonate (0.3 g, 2.17 mmol) was added to a solution of salt **2a,b** (2.16 mmol) in anhydrous DMF (10 ml). The mixture was stirred for 1 h at room temperature, then heated for 30 min gradually raising the temperature to 100°C. After cooling, the solid was filtered off, washed with acetone and with water, and then recrystallized from DMF.

Compound 5b. UV spectrum, λ_{max}, nm (log ε): 242 (5.02), 270 (5.08), 341* (4.17), 354 (4.39), 378* (4.41), 396 (4.67), 415 (4.71).

10-Amino-1-ethyl-1*H*-imidazo[1,2-*b*]isoquinolin-4-ium chloride (5e) was obtained by the method of synthesis of products **5a,b**, using the hydrate of chloride **2e**.

5-Alkyl-6-amino-5*H*-benzimidazo[1,2-*b*]isoquinolin-12-ium bromides 6a,b were obtained by the method of synthesis of products **5a,b**, using Et_3N (0.5 ml, 3.6 mmol) in place of K_2CO_3.

Compound 6a. UV spectrum, λ_{max}, nm (log ε): 282 (5.44), 344 (4.55), 361 (4.65), 423* (4.76), 442 (4.99), 467 (4.99).

Compound 6b. UV spectrum, λ_{max}, nm (log ε): 280 (5.46), 342 (4.56), 359 (4.65), 422* (4.80), 440 (5.03), 465 (5.03).

3-[2-(Methoxycarbonyl)benzyl]-1-methyl-1*H*-imidazol-3-ium Bromide (9a). 1-Methyl-1*H*-imidazole (1 ml, 12.2 mmol) was added to a solution of 2-(bromomethyl)benzoic acid ester **8** (2.79 g, 12.2 mmol) in acetonitrile (25 ml) and the mixture was maintained at room temperature for 2 day. The precipitated solid was filtered off, washed with a small volume of acetonitrile, and recrystallized from acetonitrile.

1-Methyl-1*H*-imidazo[1,2-*b*]isoquinolin-4-ium-10-olate (10a). Salt **9a** (3 g, 9.64 mmol) was dissolved by heating in ethanol (50 ml) and K_2CO_3 (2.66 g, 19.30 mmol) was added. The mixture was boiled for 3.5 h, cooled, and the solid filtered off. The filtrate was evaporated, acetonitrile (10 ml) was added to the residue, and triturated. The solid was filtered off, thoroughly washed with hot water, and with hot DMF.

1-Benzyl-1*H*-imidazo[1,2-*b*]isoquinolin-4-ium-10-olate (10b). 1-Benzyl-1*H*-imidazole (1 g, 6.32 mmol) was added to a solution of 2-(bromomethyl)benzoic acid ester **8** (1.45 g, 6.32 mmol) in acetonitrile (25 ml). The solution was maintained at room temperature for 2 day and 50% solvent evaporated. Diethyl ether (20 ml) was added, the solution was separated from the oily residue containing imidazolium salt **9b** (85%). The residue was dissolved in ethanol (30 ml) and K_2CO_3 (1.74 g, 12.64 mmol) was added. The mixture was boiled for 3 h, and after cooling, the solid was filtered off. The filtrate was evaporated, acetonitrile (10 ml) was added to the residue, and triturated. The solid was filtered off, thoroughly washed with hot water, and crystallized from DMF.

UV spectrum, λ_{max}, nm (log ε): 262 (5.23), 340* (4.82), 353 (5.00), 407* (4.91), 445 (5.06). Mass spectrum, *m/z* (I_{rel}, %): 549 (10), 548 (40), 547 $[M]^+$ (100), 456 (10), 365 (15), 199 (11).

REFERENCES

1. L. M. Potikha, R. M. Gutsul, A. S. Plaskon, V. A. Kovtunenko, and A. A. Tolmachev, *Khim. Geterotsikl. Soedin.*, 417 (2011). [*Chem. Heterocycl. Comp.*, **47**, 342 (2011)].
2. A. G. Nemazanyi, Yu. M. Volovenko, T. A. Silaeva, M. Yu. Kornilov, and F. S. Babichev, *Khim. Geterotsikl. Soedin.*, 1104 (1991). [*Chem. Heterocycl. Comp.*, **27**, 886 (1991)].

*Points of inflexion are shown here and subsequently in the paper.

3. F. Tegtmeier, F. E. Janssens, J. E. Leenaerts, K. A. van Rossem, M. J. Alcazar-Vaca, P. Martinez-Jimenez, J. M. Bartolome-Nebreda, A. Gomez-Sanchez, F. J. Fernandez-Gadea, and J. L. H. van Reempts, WO Pat. Appl. 2003044023; *Chem. Abs.*, **139**, 6872 (2003).
4. A. Johnson, *J. Org. Chem.*, **41**, 836 (1976).
5. L. M. Potikha, V. V. Sypchenko, and V. A. Kovtunenko, *Khim. Geterotsikl. Soedin.*, 1360 (2010). [*Chem. Heterocycl. Comp.*, **46**, 1096 (2010)].
6. M. S. Allen, P. Skolnick, and J. M. Cook, *J. Med. Chem.*, **35**, 368 (1992).
7. E. Reimann and F. Grasberger, *Monatsh. Chem.*, **136**, 193 (2005).
8. W.-D. Z. Li and H. Yang, *Tetrahedron*, **61**, 5037 (2005).
9. T. Shono, H. Hamaguchi, M. Sasaki, S. Fujita, and K. Nagami, *J. Org. Chem.*, **48**, 1621 (1983).
10. K. Ando, T. Tokoroyama, and T. Kubota, *Bull. Chem. Soc. Jpn.*, **53**, 2885 (1980).
11. E. Reimann and A. Hoeglmueller, *Arch. Pharm.*, **318**, 487 (1985).
12. K. Van Rompaey, I. Van den Eynde, N. De Kimpe, and D. Tourwe, *Tetrahedron*, **59**, 4421 (2003).
13. P. G. Jagtap, E. Baloglu, G. Southan, W. Williams, A. Roy, A. Nivorozhkin, N. Landrau, K. Desisto, A. L. Salzman, and C. Szabo, *Org. Lett.*, **7**, 1753 (2005).
14. S. V. Litvinenko, Yu. M. Volovenko, and F. S. Babichev, *Khim. Geterotsikl. Soedin.*, 1698 (1990). [*Chem. Heterocycl. Comp.*, **26**, 1415 (1990)].
15. S. V. Litvinenko, Yu. M. Volovenko, and F. S. Babichev, *Khim. Geterotsikl. Soedin.*, 224 (1993). [*Chem. Heterocycl. Comp.*, **29**, 194 (1993)].
16. S. V. Litvinenko, Yu. M. Volovenko, and F. S. Babichev, *Khim. Geterotsikl. Soedin.*, 1528 (1992). [*Chem. Heterocycl. Comp.*, **28**, 1307 (1992)].
17. R. F. Cookson, D. P. Nowotnik, R. T. Parfitt, J. E. Airey, and A. S. Kende, *J. Chem. Soc., Perkin Trans. 1*, 201 (1976).
18. A. Messmer, G. Hajos, A. Gelléri, and L. Radics, *Tetrahedron*, **42**, 5415 (1986).