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# 1-Acylmethylbenzimidazole-2-sulfonic Acids and Their Cyclization by *N*-Nucleophiles

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**Abstract**—New preparation method was developed for derivatives of 1,4-dihydro-1,2,4-triazino[4,3-*a*]-, 2-aryl-1(9)*H*-, and 1-R-imidazo[1,2-*a*]benzimidazole underlain by newly synthesized 1-acylmethylbenzimidazole-2-sulfonic acids. The latter react with 2-aminoethanol affording along with the previously described compounds of the 1-(2-hydroxyethyl)imidazobenzimidazole series also compounds of formerly unknown polycyclic system, 2,3,11,12-tetrahydro-1,3-oxazolo[2,3-*a*]imidazo[1,2-*a*]benzimidazole.

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One method of the synthesis of compounds of imidazo[1,2-*a*]benzimidazole series whose derivatives are recommended for application in medicine as drugs [1] is based on the intramolecular cyclization of 1-acylmethyl-2-chlorobenzimidazoles under the action of ammonia or primary amines [2]. The same procedure but using hydrazine and its derivatives provides substituted 1,4-dihydro-1,2,4-triazino[4,3-*a*]benzimidazoles [3]. Compared with 2-chlorobenzimidazole the benzimidazole-2-sulfonic acids readily exchanging the sulfo group with nucleophiles are easier available [4, 5]. Their direct *N*-alkylation is an efficient way to simple and functionalized 1-alkyl-substituted derivatives [6].

In this study the synthesis of previously unknown bielectrophilic 1-acylmethylbenzimidazole-2-sulfonic acids **I** is described and their heterocyclization under the action of *N*-nucleophiles is examined. In aqueous alcohol in the presence of 2 equiv of KOH [6] the benzimidazole-2-sulfonic acid practically does not undergo alkylation with phenacyl bromide, apparently because of the competing decomposition of the initial bromoketone. 1-Acylmethyl derivatives **Ia–Ig** form in 70–80% yields in anhydrous DMF from the preliminary prepared dipotassium salt of benzimidazole-2-sulfonic acid (**II**).

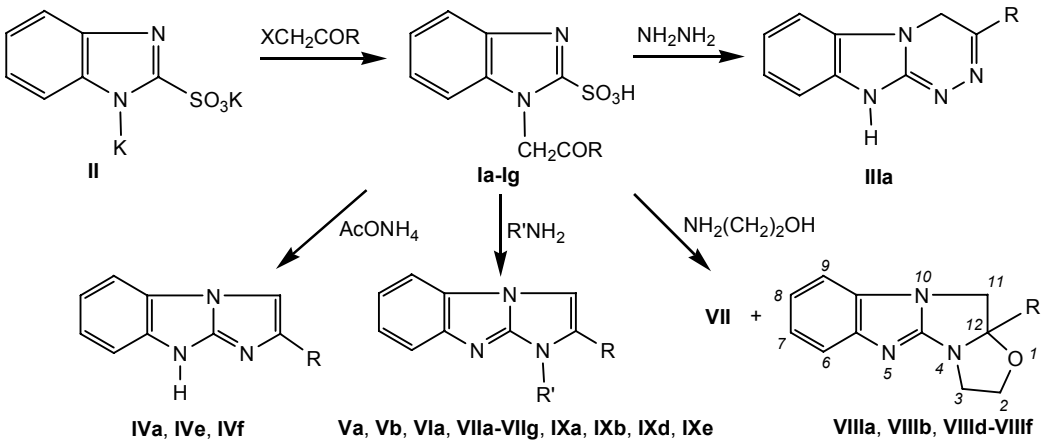
Compound **Ia** successfully underwent cyclization with hydrazine hydrate giving 3-phenyltriazinobenzimidazole (**IIIa**) (Scheme 1).

The cyclization of 1-acylmethyl-2-chlorobenzimidazoles with ammonia and low boiling primary amines into the corresponding derivatives of imidazo[1,2-*a*]-benzimidazole occurs at heating under pressure [2]. We found that N-unsubstituted compounds **IV** are easier obtained from sulfonic acid **I** by melting with ammonium acetate at 130–140°C.

Compounds **Ia** and **Ib** like their 2-chloro-substituted analogs cleanly reacted with aniline providing 1-phenyl-2-R-imidazobenzimidazoles **Va** and **Vb**. In the $^1$H NMR spectra (DMSO-$d_6$) of compounds **IV** that according to [7] exist in 9*H*-tautomeric form and of 1-substituted derivatives **V** the most downfield signal is unexpectedly the proton $H^3$ (8.0–8.1 ppm), in contrast to the pronounced π-excess in the imidazobenzimidazole system and to the occurrence of the electrophilic substitution commonly at the position *3*. This fact is obviously due to the formation of the electrostatically stabilized complexes of compounds **IV** and **V** with DMSO, since in $CDCl_3$ the signal of the $H^3$ proton shifts to the region 7.0 ppm. According to the data of quantum-chemical calculations on the potential energy surface (PES) of each among model

† Deceased.

**Scheme 1.**




R = Ph (**a**), 4-$CH_3C_6H_4$ (**b**), 4-$OMeC_6H_4$ (**c**), 4-$BrC_6H_4$ (**d**), 4-$ClC_6H_4$ (**e**), 4-$FC_6H_4$ (**f**), $CH_3$ (**g**); R' = Ph (**V**), $CH_2CH_2$-N$(CH_2)_5$ (**VI**), $(CH_2)_2OH$ (**VII**), $(CH_2)_3OH$ (**IX**).

systems 1*H*- and 9*H*-imidazo[1,2-*a*]benzimidazole–DMSO a couple of minima exists with close values of energy with the maximum stabilization energies $\Delta E_{stab}$ –7.0 and –6.6 kcal mol$^{-1}$ respectively,* where just the proton $H^3$ suffers the strongest deshielding effect from the oxygen atom of DMSO. The calculation by GIAO method [8] also confirms that the complex formation with DMSO should result in the increase in the chemical shift of the $H^3$ proton in both tautomers by 1.0–1.5 ppm. It concerns the atom $H^5$ to a lesser extent, and the signals of the other protons remain practically unchanged (see the table).

A special preparative importance have the reactions of acids **I** with dialkylaminoalkylamines which provide a possibility as shown by an example of compound **VIa** to obtain in high yield in one stage 1-dialkylaminoalkyl derivatives of imidazo[1,2-*a*]benzimidazole possessing a versatile pharmacologic action [9, 10].

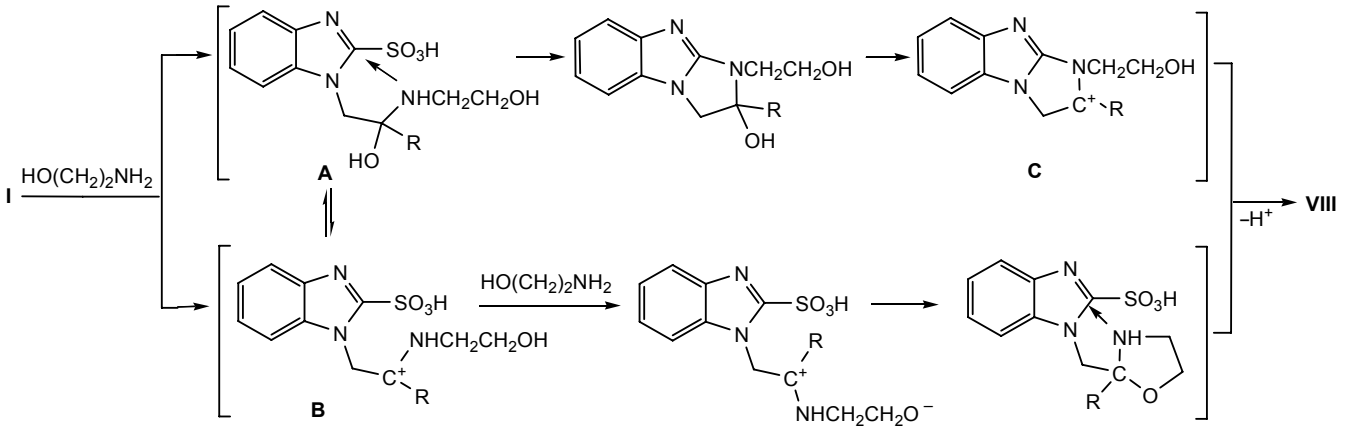
Sulfonic acids **Ia**, **Ib** and **Id–If** enter peculiarly in reaction with 2-aminoethanol. In these reactions with an overall yield of 85–90% along with the expected derivatives of (2-hydroxyethyl)imidazobenzimidazole **VII** formed previously unknown tetracyclic compounds **VIII**. The products ratio essentially depends on the electronic nature of the acyl substituent. 1-Phenacyl-substituted sulfonic acid **Ia** underwent cyclization giving an oxazolidine ring (yield of compound **VIIIa** 38%), and its bromo- and chloroderivatives converted into heterocycles **VIIId** and **VIIIe** in 49 and 61% yields respectively. Sulfonic acids **Ic** and **Ig**

Calculated chemical shifts (δ, ppm) of protons in 1*H*- and 9*H*-tautomers of imidazo[1,2-*a*]benzimidazole and their complexes (1 : 1) with DMSO differing by stabilization energy $\Delta E_{stab}$

| Proton no. | 1*H*-tautomer | Complexes of 1*H*-tautomer | | 9*H*-tautomer | Complexes of 9*H*-tautomer | |
|---|---|---|---|---|---|---|
| | | $\Delta E_{stab}$ –7.0 kcal mol$^{-1}$ | $\Delta E_{stab}$ –6.5 kcal mol$^{-1}$ | | $\Delta E_{stab}$ –6.6 kcal mol$^{-1}$ | $\Delta E_{stab}$ –6.4 kcal mol$^{-1}$ |
| *1* | 6.54 | 6.35 | 6.32 | – | – | – |
| *2* | 6.62 | 6.55 | 6.49 | 7.15 | 7.11 | 7.06 |
| *3* | 7.26 | 8.90 | 8.70 | 7.32 | 8.64 | 8.26 |
| *5* | 7.52 | 8.20 | 8.10 | 7.51 | 8.53 | 8.82 |
| *6* | 7.13 | 7.09 | 7.07 | 7.20 | 7.18 | 7.21 |
| *7* | 7.36 | 7.29 | 7.28 | 7.27 | 7.20 | 7.23 |
| *8* | 7.66 | 7.59 | 7.59 | 7.10 | 7.03 | 7.04 |
| *9* | – | – | – | 6.59 | 6.50 | 6.49 |

* Calculated by the density functional method B3LYP/6-31G**.

**Scheme 2.**




formed only alcohol **VIIc** and **VIIg** in good yields. In the $^1$H NMR spectrum of 2-methylimidazobenzimidazole **VIIg** the observed spin-spin coupling between the protons $H^3$ and 2-$CH_3$ ($^3J$ 1.2 Hz) was uncommonly strong for methylarenes(hetarenes).

The structure of tetracyclic scaffolds **VIII** was confirmed by $^1$H NMR and mass spectra. Their $^1$H NMR spectra are characterized by four incompletely resolved signals (d.d.d) of nonequivalent protons of the $CH_2CH_2$ fragment of the oxazolidine ring in the region 3.3–4.2 ppm and by two doublets of the imidazoline methylene group at 4.1–4.6 ppm. The experimental chemical shifts are in a good agreement with the calculated values (Fig. 1).

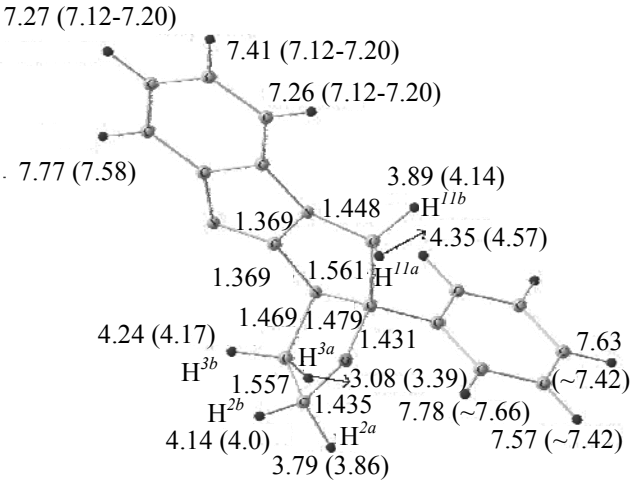



**Fig. 1.** The structure of the molecule of 12-phenyl-2,3,11,12-tetrahydro-1,3-oxazolo[2,3-*a*]imidazo[1,2-*a*]benzimidazole (**VIIIa**) (B3LYP/6-31$^{**}$), bond lengths (Å), calculated and experimental (in parentheses) chemical shifts of protons (ppm).

Taking into account that the authentic 1-acylmethyl-2-(2-hydroxyethylamino)benzimidazoles at heating in 2-aminoethanol are converted exclusively into alcohols **VII** [11, 12], it is presumable that the reaction of bielectrophilic sulfonic acids **I** with this reagent starts by an attack on a carbonyl and not on the sulfo group giving hemiaminals **A** and carbocations **B**. Then follows a cascade cyclization along a single or simultaneously along two routes distinguished by the sequence of stages. In one variant first an oxazolidine ring is closed in cations **B**, and afterwards the intramolecular substitution of the sulfo group provides the imidazoline ring. In the alternative route in hemiaminal **A** the sulfo group is attacked by the aminoethanol residue, and first the imidazoline ring closes, and thereafter through the heterocyclic carbocation **C** the oxazolidine fragment is built up (Scheme 2).

Quantum-chemical calculations show that the weakly nucleophilic OH groups of aminoethanol moieties in carbocations **B** and **C** cannot by themselves attack the insufficiently electrophilic carbocation centers (cf. [13]). The products of such attack with oxonium oxygen atom have not even minima on PES. However the cyclization becomes virtually a barrierless process if the OH group is preliminary ionized by excess aminoethanol.

The absence of oxazolidine derivatives at the cyclization of sulfonic acids **Ic** and **Ig** is due either to the difficulty of the formation of insufficiently stabilized carbocations **B** and **C** (at R = Me), or by their relatively low electrophilicity (at R = *p*-$MeOC_6H_4$).

The molecules of compounds **VIII** have a virtually flat imidazobenzimidazole scaffold with the oxazolidine ring located nearly orthogonally (Fig. 1).

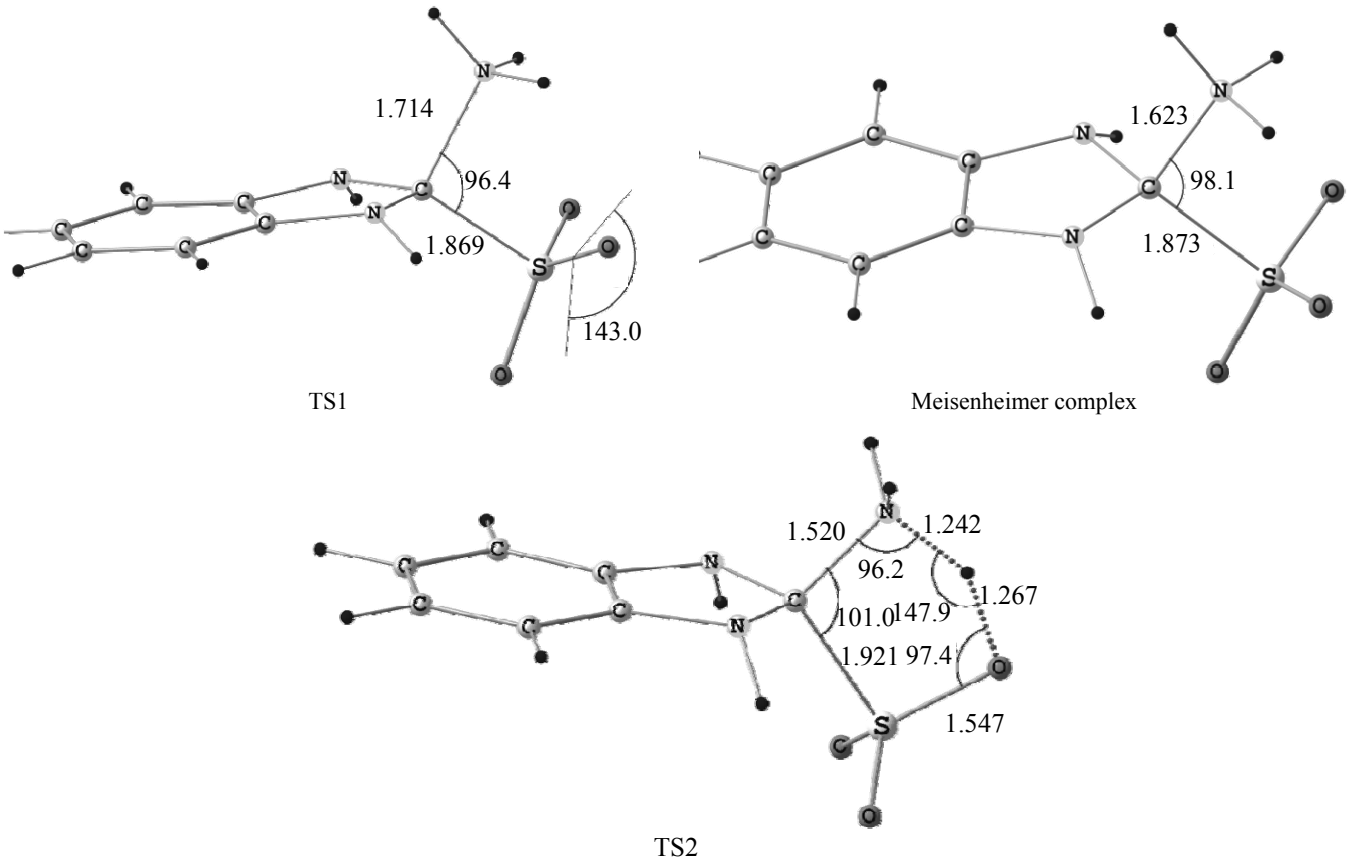



**Fig. 2.** Transition states TS1, TS2 and Meisenheimer complex in the reaction of benzimidazole-2-sulfonic acid with ammonia.

The reaction of sulfonic acids **I** with 3-amino-propan-1-ol is accompanied with strong tarring and results in 2-aryl derivatives of 1-(3-hydroxypropyl)-imidazobenzimidazole **IX** in an yield not exceeding 20%. We did not find tetracyclic structures like compounds **VIII** with an oxazine ring that might form as those obtained in [14].

The course of *N*-substitution of the sulfo group in the benzimidazole-2-sulfonic acid was not formerly discussed. Quantum-chemical calculations performed for a model system benzimidazole-2-sulfonic acid–ammonia has shown that this multistage process starts with the formation of a π-complex of ammonia possessing a $C_s$-symmetry with a polar betaine form of the sulfonic acid ($\mu_{calc}$ 11.2 D) which is of enhanced electrophilicity. The distance between the reacting sites in the π-complex is 2.976 Å. Then through a less polar tetrahedral transition state of relatively low energy TS1 ($\mu_{calc}$ 8.6 D) a transformation into Meisenheimer complex occurs ($\Delta G^{\neq}_{calc}$ 18.0, $\Delta H^{\neq}_{calc}$ 5.4 kcal mol$^{-1}$ with respect to reagents in the gas phase) (Fig. 2). The latter in geometric and energy characteristics nearly does not differ from TS1. Both structures have the same symmetry $C_s$ and the energy difference less than 0.1 kcal mol$^{-1}$.

The transformation of this complex in 2-amino-benzimidazole occurs by two easily proceeding proton transfers involving the ammonia (TS2, $\Delta E^{\neq}_{calc}$ ~0.7 kcal mol$^{-1}$, Fig. 2) and the proton of the NH group of benzimidazole. Both protons move to the oxygen atoms of the sulfo group; therewith the C–S bond is totally destabilized, and the desulfuration completes by the elimination of the sulfurous acid molecule.

## EXPERIMENTAL

IR spectra were recorded on a spectrophotometer Specord 75IR. $^1$H NMR spectra were registered on a spectrometer Varian Unity-300 (300 MHz). Chemical shifts of protons are given with respect to the residual protons of deuterated solvent. Mass spectrum of electron impact (70 eV) was obtained on an instrument Finnigan MAT INCOS 50 with the direct admission of the sample into the ion source.

The reaction progress was monitored and the homogeneity of compounds was checked by TLC on plates with $Al_2O_3$ of III activity grade, eluent $CHCl_3$, development in iodine vapor in a humid chamber.

The optimization of geometry of molecules, complexes, and transition states **TS2** was carried out using the program Firefly 8.0 [15], partially based on the code of the program GAMESS [16]. The calculation of the energy of the found structures was performed with accounting for the correction for the oscillation energy of the zero level applying the scaling factor 0.961 [17]. The calculation of the chemical shifts of protons of imidazo[1,2-*a*]benzimidazole and its complexes with DMSO by GIAO method was carried out using program GAUSSIAN 03 with functional B3LYP, basis 6-31G** [18]. In event of compound **VIIIa** the method SOS DFPT [19] was applied in program version DeMon [20] (theory level B3LYP/6-31G**//PW91-PW91/IGLOII).

Benzimidazole-2-sulfonic acid was synthesized by procedure [21].

**1-Acylmethylbenzimidazole-2-sulfonic acids Ia–Ig**. To a solution of 13.4 g (0.2 mol) of KOH (recalculated to 85% concn.) in 40 mL of water was added by portions 19.8 g (0.1 mol) of benzimidazole-2-sulfonic acid maintaining the mixture temperature no higher than 45–50°C. On cooling the dipotassium salt of benzimidazole-2-sulfonic acid (**II**) was precipitated by adding 100 mL of acetone, the precipitate was filtered off, washed with acetone, dried at 50–60°C. Yield 26 g (95%).

Slurry of 15 mmol of dipotassium salt **II** and 15 mmol of an appropriate haloketone in 10 mL of DMF was stirred for 2 h at 80–85°C. On cooling the reaction mixture was diluted with 20 mL of water, acidified with conc. HCl till pH 1, the separated precipitate was filtered off, washed with water and acetone.

**1-(2-Oxo-2-phenylethyl)benzimidazole-2-sulfonic acid (Ia)**. Yield 71%, mp 307–309°C (DMF–$H_2O$, 9 : 1). IR spectrum, ν, $cm^{-1}$: 3477 (OH), 1688 (C=O). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 6.12 s (2H, $CH_2$), 7.20–7.24 m (2H, $H^{5,6}$), 7.42–7.46 m (1H, $H^{4\text{ or }7}$), 7.57–7.71 m (4H, $H^{7\text{ or }4,3'-5'}$), 8.01–8.04 d (2H, $H^{2',6'}$, *J* 7.1 Hz). Found, %: C 57.10; H 3.74; N 9.10; S 9.96. $C_{15}H_{12}N_2O_4S$. Calculated, %: C 56.95; H 3.82; N 8.86; S 10.14.

**1-[2-(4-Methylphenyl)-2-oxoethyl]benzimidazole-2-sulfonic acid (Ib)**. Yield 72%, mp 302–304°C (DMF–$H_2O$, 9 : 1). IR spectrum, ν, $cm^{-1}$: 3113–3456 (OH), 1692 (C=O). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 2.43 s (3H, Me), 6.35 s (2H, $CH_2$), 7.44 d (2H, $H^{3',5'}$, *J* 8.1 Hz), 7.58–7.63 m (2H, $H^{5,6}$), 7.75–7.85 m (1H, $H^{4\text{ or }7}$), 7.95–8.045 m (3H, $H^{7\text{ or }4,2',6'}$, *J* 7.1 Hz). Found, %: C 58.26; H 4.14; N 8.61; S 9.57. $C_{16}H_{14}N_2O_4S$. Calculated, %: C 58.17; H 4.27; N 8.48; S 9.71.

**1-[2-(4-Methoxyphenyl)-2-oxoethyl]benzimidazole-2-sulfonic acid (Ic)**. Yield 80%, mp 328–330°C (DMF). IR spectrum, ν, $cm^{-1}$: 3354 (OH), 1687 (C=O). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 3.88 s (3H, OMe), 6.33 s (2H, $CH_2$), 7.15 d (2H, $H^{3',5'}$, *J* 6.9 Hz), 7.58–7.64 m (2H, $H^{5,6}$), 7.79–7.82 m (1H, $H^{4\text{ or }7}$), 7.90–7.97 m (1H, $H^{7\text{ or }4}$), 8.05 d (2H, $H^{2',6'}$, *J* 6.9 Hz). Found, %: C 55.31; H 4.18; N 8.19; S 9.13. $C_{16}H_{14}N_2O_5S$. Calculated, %: C 55.48; H 4.07; N 8.09; S 9.26.

**1-[2-(4-Bromophenyl)-2-oxoethyl]benzimidazole-2-sulfonic acida (Id)**. Yield 88%, mp 264–266°C (DMF–$H_2O$, 9 : 1). IR spectrum, ν, $cm^{-1}$: 3398 (OH), 1696 (C=O). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 6.35 s (2H, $CH_2$), 7.58–7.66 m (2H, $H^{5,6}$), 7.72–7.875 m (1H, $H^{4\text{ or }7}$), 7.85 d (2H, $H^{3',5'}$, *J* 8.6 Hz), 7.96–8.05 m (1H, $H^{7\text{ or }4}$), 8.20–8.46 m (2H, $H^{2',6'}$). Found, %: C 45.43; H 2.94; Br 20.11; N 7.14; S 8.11. $C_{15}H_{11}BrN_2O_4S$. Calculated, %: C 45.58; H 2.81; Br 20.22; N 7.09; S 8.11.

**1-[2-Oxo-2-(4-chlorophenyl)ethyl]benzimidazole-2-sulfonic acid (Ie)**. Yield 85%, mp 282–283°C (DMF–$H_2O$, 9 : 1). IR spectrum, ν, $cm^{-1}$: 3455–3172 (OH), 1684 (C=O). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 6.36 s (2H, $CH_2$), 7.58–7.66 m (2H, $H^{5,6}$), 7.71 d (2H, $H^{3',5'}$, *J* 8.6 Hz), 7.77–7.82 m (1H, $H^{4\text{ or }7}$), 7.97–8.02 m (1H, $H^{7\text{ or }4}$), 8.09 d (2H, $H^{2',6'}$, *J* 8.7 Hz). Found, %: C 51.49; H 2.98; Cl 10.27; N 8.12; S 9.14. $C_{15}H_{11}ClN_2O_4S$. Calculated, %: C 51.36; H 3.16; Cl 10.11; N 7.99; S 9.14.

**1-[2-Oxo-2-(4-fluorophenyl)ethyl]benzimidazole-2-sulfonic acid (If)**. Yield 88%, mp 303–307°C (DMF). $^1H$ NMR spectrum (DMSO-$d_6$), δ, ppm: 6.35 s (2H, $CH_2$), 7.31–7.37 m (2H, $H^{5,6}$), 7.56–7.60 m (2H, $H^{3',5'}$), 7.80 d (1H, $H^{4\text{ or }7}$, *J* 7.7 Hz), 7.91 d (1H, $H^{7\text{ or }4}$, *J* 7.8 Hz), 8.16–8.21 m (2H, $H^{2',6'}$, *J* 8.6 Hz). Found, %: N 8.12. $C_{15}H_{11}FN_2O_4S$. Calculated, %: N 8.38.

**1-(2-Oxopropyl)benzimidazole-2-sulfonic acid (Ig)**. Yield 81%, mp 316–317°C ($H_2O$). IR spectrum, ν, $cm^{-1}$: 3445–3186 (OH), 1713 (C=O). $^1H$ NMR

spectrum (DMSO-$d_6$), δ, ppm: 2.28 s (3H, Me), 5.67 s (2H, $CH_2$), 7.58–7.66 m (2H, $H^{5,6}$), 7.72–7.78 m (1H, $H^{4\text{ or }7}$), 7.86–7.93 m (1H, $H^{7\text{ or }4}$). Found, %: C 47.08; H 4.12; N 10.94; S 12.71. $C_{10}H_{10}N_2O_4S$. Calculated, %: C 47.24; H 3.96; N 11.02; S 12.61.

**3-Phenyl-1,4-dihydro-1,2,4-triazino[4,3-*a*]benzimidazole (IIIa)**. A solution of 0.32 g (1 mmol) of sulfonic acid **Ia** in 3 mL of hydrazine hydrate was bolied for 2h. The reaction mixture was cooled, the separated precipitate was filtered off and washed with water. Yield 0.21 g (86%), mp 305–306°C (DMF) (305–308°C [3]). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 5.28 s (2H, $CH_2$), 7.06–7.15 m (2H, $H^{7,8}$), 7.35–7.51 m (5H, $H^{6,9,3'-5'}$), 7.81–7.84 m (2H, $H^{2',6'}$), 11.50 s (1H, NH).

**2-Aryl-1(9)*H*-imidazo[1,2-*a*]benzimidazoles IVa**, **IVe** and **IVf**. A melt of 1 mmol of sulfonic acid **I** in 3 g of ammonium acetate was heated at 135–145°C for 1 h. On cooling the melt was treated with 10 mL of water, the precipitate was filtered off and washed with water and acetone.

**2-Phenyl-1(9)*H*-imidazo[1,2-*a*]benzimidazole (IVa)**. Yield 72%, mp 305–306°C (DMF) (285–287°C [2], 310°C [22]).

**2-(4-Chlorophenyl)-1(9)*H*-imidazo[1,2-*a*]benzimidazole (IVe)**. Yield 75%, mp 316–317°C (DMF). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 7.15 t (1H, $H^{6\text{ or }7}$, $J$ 7.8 Hz), 7.25 t (1H, $H^{7\text{ or }6}$, $J$ 7.8 Hz), 7.37–7.44 m (3H, $H^{5\text{ or }8,3',5'}$), 7.70 d (1H, $H^{8\text{ or }5}$, $J$ 7.8 Hz), 7.83 d (2H, $H^{2',6'}$, $J$ 8.4 Hz), 8.17 s (1H, $H^3$), 11.65 s (1H, NH). Found, %: C 67.34; H 3.85; Cl 13.34; N 15.58. $C_{15}H_{10}ClN_3$. Calculated, %: C 67.30; H 3.77; Cl 13.24; N 15.70.

**2-(4-Fluorophenyl)-1(9)*H*-imidazo[1,2-*a*]benzimidazole (IVf)**. Yield 75%, mp 325–327°C (DMF). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 7.13–7.27 m (4H, $H^{6,7,3',5'}$), 7.38 d (1H, $H^{5\text{ or }8}$, $J$ 7.5 Hz), 7.70 d (1H, $H^{8\text{ or }5}$, $J$ 7.8 Hz), 7.82–7.87 m (2H, $H^{2',6'}$), 8.13 s (1H, $H^3$), 11.70 s (1H, NH). Found, %: N 16.62. $C_{15}H_{10}FN_3$. Calculated, %: N 16.72.

**1,2-Diphenylimidazo[1,2-*a*]benzimidazole (Va)**. A solution of 0.63 g (2 mmol) of sulfonic acid **Ia** in 2 mL of aniline was boiled for 2h, cooled, and diluted with 5 mL of ethyl ether. The formed precipitate was filtered off. Yield 0.4 g (54%), mp 209–210°C (EtOH) (204–206°C [2]). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 7.13 t (1H, $H^{6\text{ or }7}$), 7.23 t (1H, $H^{7\text{ or }6}$), 7.29–7.53 m (11H, $10H_{Ph}$ + $H^{5\text{ or }8}$), 7.83 d (1H, $H^{8\text{ or }5}$, $J$ 7.8 Hz), 8.21 s (1H, $H^3$).

**2-(4-Methylphenyl)-1-phenylimidazo[1,2-*a*]benzimidazole (Vb)** was prepared similarly to compound **Va** from sulfonic acid **Ib**. Yield 62%, mp 200–201°C (EtOH). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 2.34 s (3H, Me), 7.13–7.18 m (5H, $H^{3',5',3''-5''}$), 7.25–7.31 m (2H, $H^{3,6\text{ or }7}$), 7.40–7.42 m (5H, $H^{7\text{ or }6,2',6',2'',6''}$), 7.61 d (1H, $H^{5\text{ or }8}$, $J$ 8.1 Hz), 7.72 d (1H, $H^{8\text{ or }5}$, $J$ 8.1 Hz). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 2.34 s (3H, $CH_3$), 7.04–7.20 m (6H, $H^{6\text{ or }7,3',5',3''-5''}$), 7.33–7.47 m (6H, $H^{7\text{ or }6,5\text{ or }8,2',6',2'',6''}$), 7.73 d (1H, $H^{8\text{ or }5}$, $J$ 8.1 Hz), 7.96 s (1H, $H^3$). Found, %: C 81.63; H 5.37; N 13.10. $C_{22}H_{17}N_3$. Calculated, %: C 81.71; H 5.30; N 13.00.

**1-[2-(Piperidin-1-yl)ethyl]-2-phenylimidazo-[1,2-*a*]benzimidazole dihydrochloride (VIa)**. A mixture of 0.95 g (3 mmol) of sulfonic acid **Ia** and 0.9 mL (6 mmol) of 2-(piperidin-1-yl)ethanamine was heated at 140–150°C for 1 h. On cooling the reaction mixture was treated with 15 mL of water, insoluble oily residue was dissolved in chloroform and subjected to chromatography on a column packed with $Al_2O_3$ (2 × 5 cm), eluent chloroform, collecting the fraction with compound of $R_f$ 0.3. The residue obtained by evaporating chloroform was dissolved in acetone and treated with HCl solution in ethyl ether till pH 1. Yield 0.9 g (72%), mp 223–224°C (223–224°C [23]).

**Reaction of sulfonic acid I with 2-aminoethanol**. A mixture of 2 mmol of 1-acylmethylsulfonic acid **I** and 8 mmol (0.5 mL) of 2-aminoethanol was heated at 150–160°C for 1 h, cooled, treated with 10–15 mL of water, the precipitate was filtered off, dissolved in chloroform, and chromatographed on a column packed with $Al_2O_3$ (2 × 20 cm), eluent chloroform. First compound **VIII** was isolated, $R_f$ 0.8, then derivatives of 2-(1*H*-imidazo[1,2-*a*]benzimidazol-1-yl)ethanol **VII**, $R_f$ 0.2.) Compounds **VIII** did not form from acids **Ic** and **Ig**.

**2-(2-Phenyl-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl)ethanol (VIIa)**. Yield 47%, mp 167–168°C (EtOH) (166–168°C [2], 168–169°C [12]). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 3.75–3.85 m (2H, $NCH_2$), 4.05–4.10 m (2H, $OCH_2$), 5.11 br.s (1H, OH), 7.07 t (1H, $H^{6\text{ or }7}$), 7.22 t (1H, $H^{7\text{ or }6}$), 7.48–7.56 m (4H, $H^{5\text{ or }8,3'-5'}$), 7.68 d (2H, $H^{2',6'}$), 7.78 d (1H, $H^{8\text{ or }5}$), 7.89 s (1H, $H^3$).

**2-{2-(4-Methylphenyl)-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl}ethanol (VIIb)**. Yield 48%, mp 174–175°C ($C_6H_6$) (168–170°C [23]). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 2.44 s (3H, Me), 4.03–4.07 m (2H, $NCH_2$), 4.21–4.26 m (2H, $OCH_2$), 4.85 br.s (1H, OH), 7.19 t (1H, $H^{6\text{ or }7}$, $J$ 7.7 Hz), 7.30–7.38 m (6H,

$H^{3,7\text{ or }6,2',3',5',6'}$), 7.59 d (1H, $H^{5\text{ or }8}$, *J* 8.0 Hz), 7.68 d (1H, $H^{8\text{ or }5}$, *J* 8.1 Hz).

**2-{2-(4-Methoxyphenyl)-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl}ethanol (VIIc)**. Yield 81%, mp 189–190°C (EtOH) (188–190°C [2], 187–188°C [11]). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 3.88 s (3H, OMe), 4.09–4.12 m (4H, $CH_2CH_2$), 5.95 br.s (1H, OH), 7.02 d (2H, $H^{3',5'}$, *J* 8.8 Hz), 7.13 t (1H, $H^{6\text{ or }7}$, *J* 7.8 Hz), 7.17 c (1H, $H^3$), 7.28 t (1H, $H^{7\text{ or }6}$, *J* 8.0 Hz), 7.40 d (2H, $H^{2',6'}$, *J* 8.8 Hz), 7.55 d (1H, $H^{5\text{ or }8}$, *J* 7.8 Hz), 7.65 d (1H, $H^{8\text{ or }5}$, *J* 8.1 Hz).

**2-{2-(4-Bromophenyl)-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl}ethanol (VIId)**. Yield 28%, mp 197–198°C (EtOH) (184–185°C [2], 197–198°C [12]). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 4.07–4.15 m [4H, $(CH_2)_2$], 5.69 br.s (1H, OH), 7.15 t (1H, $H^{6\text{ or }7}$, *J* 7.7 Hz), 7.25 s (1H, $H^3$), 7.80 t (1H, $H^{7\text{ or }6}$, *J* 7.7 Hz), 7.37 d (2H, $H^{3',5'}$), 7.56 d (1H, $H^{5\text{ or }8}$, *J* 7.9 Hz), 7.64 d (2H, $H^{2',6'}$, *J* 8.5 Hz), 7.66 d (1H, $H^{8\text{ or }5}$, *J* 7.6 Hz).

**2-{2-(4-Chlorophenyl)-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl}ethanol (VIIe)**. Yield 23%, mp 196–197°C (EtOH) (194°C [9]). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 4.05–4.08 m [4H, $(CH_2)_2$], 5.87 br.s (1H, OH), 7.14 t (1H, $H^{6\text{ or }7}$, *J* 8.0 Hz), 7.22 s (1H, $H^3$), 7.29 t (1H, $H^{7\text{ or }6}$, *J* 7.4 Hz), 7.43 d (2H, $H^{3',5'}$, *J* 8.4 Hz), 7.49 d (2H, $H^{2',6'}$, *J* 8.7 Hz), 7.55 d (1H, $H^{5\text{ or }8}$, *J* 7.9 Hz), 7.65 d (1H, $H^{8\text{ or }5}$, *J* 8.0 Hz).

**2-{2-(4-Fluorophenyl)-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl}ethanol (VIIf)**. Yield 39%, mp 194–195°C (*i*-PrOH). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 4.06–4.11 m [4H, $(CH_2)_2$], 6.00 br.s (1H, OH), 7.11 t (1H, $H^{6\text{ or }7}$, *J* 7.6 Hz), 7.17 s (1H, $H^3$), 7.18 t (2H, $H^{3',5'}$, *J* 8.5, 8.5 Hz), 7.26 t (1H, $H^{7\text{ or }6}$, *J* 7.9 Hz), 7.48 d.d (2H, $H^{2',6'}$, *J* 8.7, 5.3 Hz), 7.52 d (1H, $H^{5\text{ or }8}$, *J* 7.6 Hz), 7.61 d (1H, $H^{8\text{ or }5}$, *J* 8.2 Hz). Found, %: N 14.08. $C_{17}H_{14}FN_3O$. Calculated, %: N 14.23.

**2-(2-Methyl-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl}ethanol (VIIg)**. Yield 81%, mp 168–169°C (toluene) (167–169°C [2], 162–163°C [12]). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 2.33 d (3H, Me, *J* 1.2 Hz), 4.10–4.15 m [4H, $(CH_2)_2$], 5.85 br.s (1H, OH), 6.98 q (1H, $H^3$, *J* 1.3 Hz), 7.11 t (1H, $H^{6\text{ or }7}$, *J* 7.7 Hz), 7.26 t (1H, $H^{7\text{ or }6}$, *J* 8.3 Hz), 7.48 d (1H, $H^{5\text{ or }8}$, *J* 8.0 Hz), 7.61 d (1H, $H^{8\text{ or }5}$, *J* 7.6 Hz).

**12-Phenyl-2,3,11,12-tetrahydro-1,3-oxazolo-[2,3-*a*]imidazo[1,2-*a*]benzimidazole (VIIIa)**. Yield 38%, mp 157–157°C (benzene–octane, 2 : 1). IR spectrum, ν, $cm^{-1}$: 1630, 1590, 1546. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 3.39 d.d.d (1H, $H^{3A}$, $^2J$ 10.0, $^3J$ 8.2, $^3J$ 6.5 Hz), 3.86 d.d.d (1H, $H^{2A}$, $^2J$ 8.0, $^3J$ 8.1, $^3J$ 4.9 Hz), 4.00 d.d.d (1H, $H^{2B}$, $^2J$ 7.8, $^3J$ 7.8, $^3J$ 6.5 Hz), 4.14 d (1H, $H^{11B}$, *J* 10.9 Hz), 4.17 d.d.d (1H, $H^{3B}$, $^2J$ 10.1, $^3J$ 7.8, $^3J$ 4.9 Hz), 4.57 d (1H, $H^{11A}$, *J* 11.0 Hz), 7.12–7.20 m (3H, $H^{7–9}$), 7.38–7.46 m (3H, $H^{3'–5'}$), 7.58 d (1H, $H^6$, *J* 7.3 Hz), 7.62–7.70 m (2H, $H^{2',6'}$). Mass spectrum, *m/z* ($I_{rel}$, %): 277 (60.8) $[M]^+$, 246 (8.3), 172 (8.3), 117 (10.0), 105 (98.0), 90 (10.0), 77 (54.6), 51 (16.6). Found, %: C 73.49; H 5.60; N 15.03. $C_{17}H_{15}N_3O$. Calculated, %: C 73.63; H 5.45; N 15.15.

**12-(4-Methylphenyl)-2,3,11,12-tetrahydro-1,3-oxazolo[2,3-*a*]imidazo[1,2-*a*]benzimidazole (VIIIb)**. Yield 38%, mp 176–178°C (benzene–octane, 2 : 1). IR spectrum, ν, $cm^{-1}$: 1629, 1590, 1547. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 2.39 s (3H, Me), 3.40 d.d.d (1H, $H^{3A}$, $^2J$ 11.3, $^3J$ 8.3, $^3J$ 6.6 Hz), 3.85 d.d.d (1H, $H^{2A}$, $^2J$ 8.1, $^3J$ 8.1, $^3J$ 5.0 Hz), 4.01 d.d.d (1H, $H^{2B}$, $^2J$ 7.9, $^3J$ 7.9, $^3J$ 6.6 Hz), 4.15 d (1H, $H^{11B}$, *J* 11.1 Hz), 4.18 d.d.d (1H, $H^{3B}$, $^2J$ 11.3, $^3J$ 7.9, $^3J$ 5.0 Hz), 4.57 d (1H, $H^{11A}$, *J* 11.0 Hz), 7.13–7.21 m (3H, $H^{7–9}$), 7.24 d (2H, $H^{3',5'}$, *J* 7.8 Hz), 7.51 d (2H, $H^{2',6'}$, *J* 7.9 Hz), 7.60 d (1H, $H^6$, *J* 7.9 Hz). Found, %: C 74.32; H 6.03; N 14.31. $C_{18}H_{17}N_3O$. Calculated, %: C 74.21; H 5.88; N 14.42.

**12-(4-Bromophenyl)-2,3,11,12-tetrahydro-1,3-oxazolo[2,3-*a*]imidazo[1,2-*a*]benzimidazole (VIIId)**. Yield 49%, mp 190–191°C (EtOH). IR spectrum, ν, $cm^{-1}$: 1628, 1590, 1553. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 3.36 d.d.d (1H, $H^{3A}$, $^2J$ 11.1, $^3J$ 8,2, $^3J$ 6.8 Hz), 3.83 d.d.d (1H, $H^{2A}$, $^2J$ 8.1, $^3J$ 8.0, $^3J$ 4.8 Hz), 4.00 d.d.d (1H, $H^{2B}$, $^2J$ 7.9, $^3J$ 7.8, $^3J$ 6.8 Hz), 4.10 d (1H, $H^{11B}$, *J* 10.9 Hz), 4.22 d.d.d (1H, $H^{3B}$, $^2J$ 11.1, $^3J$ 8.2, $^3J$ 4.8 Hz), 4.55 d (1H, $H^{11A}$, *J* 11.0 Hz), 7.12–7.20 m (3H, $H^{7–9}$), 7.51 d (2H, $H^{2',6'}$, *J* 8.7 Hz), 7.55 d (1H, $H^6$, *J* 7.5 Hz), 7.56 d (2H, $H^{3',5'}$, *J* 8.8 Hz). Found, %: C 57.43; H 4.11; Br 22.30; N 11.97. $C_{17}H_{14}BrN_3O$. Calculated, %: C 57.32; H 3.96; Br 22.43; N 11.80.

**12-(4-Chlorophenyl)-2,3,11,12-tetrahydro-1,3-oxazolo[2,3-*a*]imidazo[1,2-*a*]benzimidazole (VIIIe)**. Yield 61%, mp 181–182°C (EtOH). IR spectrum, ν, $cm^{-1}$: 1636, 1590, 1556. $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 3.37 d.d.d (1H, $H^{3A}$, $^2J$ 11.4, $^3J$ 8.2, $^3J$ 6.7 Hz), 3.84 d.d.d (1H, $H^{2A}$, $^2J$ 8.1, $^3J$ 8.0, $^3J$ 4.9 Hz), 4.02 d.d.d (1H, $H^{2B}$, $^2J$ 7.8, $^3J$ 7.8, $^3J$ 6.7 Hz), 4.10 d (1H, $H^{11B}$, *J* 11.0 Hz), 4.23 d.d.d (1H, $H^{3B}$, $^2J$ 11.5, $^3J$ 7.8, $^3J$ 4.9 Hz), 4.56 d (1H, $H^{11A}$, *J* 10.1 Hz), 7.12–7.20 m (3H, $H^{7–9}$), 7.41 d (2H, $H^{2',6'}$, *J* 8.6 Hz), 7.57 d (1H, $H^6$, *J* 6.7 Hz), 7.59 d (2H, $H^{3',5'}$, *J* 8.6 Hz). Found, %: C

65.57; H 4.42; Cl 11.25; N 13.60. $C_{17}H_{14}ClN_3O$. Calculated, %: C 65.49; H 4.53; Cl 11.37; N 13.48.

**12-(4-Fluorophenyl)-2,3,11,12-tetrahydro-1,3-oxazolo[2,3-*a*]imidazo[1,2-*a*]benzimidazole (VIIIf)**. Yield 34%, mp 153–154°C (toluene). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 3.34 d.d.d (1H, $H^{3A}$, $^2J$ 11.5, $^3J$ 8.3, $^3J$ 6.7 Hz), 3.83 d.d.d (1H, $H^{2A}$, $^2J$ 8.1, $^3J$ 8.0, $^3J$ 4.9 Hz), 4.00 d.d.d (1H, $H^{2B}$, $^2J$ 7.9, $^3J$ 7.8, $^3J$ 6.7 Hz), 4.07 d (1H, $H^{11B}$, $J$ 11.0 Hz), 4.11 d.d.d (1H, $H^{3B}$, $^2J$ 11.5, $^3J$ 8.1, $^3J$ 4.9 Hz), 4.53 d (1H, $H^{11A}$, $J$ 11.1 Hz), 7.09–7.11 m (3H, $H^{7–9}$), 7.19 d (2H, $H^{2',6'}$, $J$ 8.6 Hz), 7.54 d (1H, $H^6$, $J$ 6.7 Hz), 7.61 d (2H, $H^{3',5'}$, $J$ 8.6 Hz). Found, %: N 14.37. $C_{17}H_{14}FN_3O$. Calculated, %: N 14.23.

**2-Aryl-substituted 1-(3-hydroxypropyl)imidazo-[1,2-*a*]benzimidazoles (IX)**. A mixture of 2 mmol of sulfonic acid **I** and 8 mmol (0.6 mL) of 3-aminopropan-1-ol was heated at 160–165°C for 1 h. The cooled mixture was treated with 5–10 mL of water, the obtained precipitate was dissolved in chloroform and chromatographed on a column with $Al_2O_3$ (2 × 20 cm), eluent chloroform, collecting the fraction with $R_f$ 0.2.

**3-(2-Phenyl-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl)propan-1-ol (IXa)**. Yield 48%, mp 158–159°C (EtOAc) (155–156°C [12]).

**3-{2-(4-Methylphenyl)-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl}propan-1-ol (IXb)**. Yield 26%, mp 176–177°C (EtOAc) (170–171°C [23]). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 1.88 t (2H, $CH_2\underline{CH_2}CH_2$, $J$ 6.0 Hz), 2.42 s (3H, Me), 3.57 t (2H, $NCH_2$, $J$ 7.5 Hz), 4.20 t (2H, $OCH_2$, $J$ 6.0 Hz), 5.82 br.s (1H, OH), 7.12 t (1H, $H^{6\text{ or }7}$, $J$ 7.7 Hz), 7.22–7.37 m (6H, $H^{3,7\text{ or }6,2',3',5',6'}$), 7.55 d (1H, $H^{5\text{ or }8}$, $J$ 8.1 Hz), 7.65 d (1H, $H^{8\text{ or }5}$, $J$ 8.1 Hz).

**3-{2-(4-Bromophenyl)-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl}propan-1-ol (IXc)**. Yield 23%, mp 204–205°C (EtOH) (199–200°C [9]). $^1$H NMR spectrum (DMSO-$d_6$), δ, ppm: 1.88 t (2H, $CH_2\underline{CH_2}CH_2$, $J$ 6.6 Hz), 4.11 t (2H, $NCH_2$, $J$ 7.2 Hz), 4.69 t (2H, $OCH_2$, $J$ 5.1 Hz), 7.07 t (1H, $H^{6\text{ or }7}$, $J$ 7.5 Hz), 7.21 t (1H, $H^{7\text{ or }6}$, $J$ 7.5 Hz), 7.51–7.59 m (3H, $H^{5\text{ or }8,2',6'}$), 7.73–7.77 m (3H, $H^{8\text{ or }5,3',5'}$), 7.97 c (1H, $H^3$).

**3-{2-(4-Chlorophenyl)-1*H*-imidazo[1,2-*a*]benzimidazol-1-yl}propan-1-ol (IXd)**. Yield 14%, mp 192–193°C (EtOH) (187–188°C [9]). $^1$H NMR spectrum ($CDCl_3$), δ, ppm: 1.89 t (2H, $CH_2\underline{CH_2}CH_2$, $J$ 5.8 Hz), 3.58 t (2H, $NCH_2$, $J$ 5.7 Hz), 4.20 t (2H, $OCH_2$, $J$ 6.0 Hz), 5.73 br.s (1H, OH), 7.14 t (1H, $H^{6\text{ or }7}$, $J$ 7.2 Hz), 7.24 s (1H, $H^3$), 7.31 t (1H, $H^{7\text{ or }6}$, $J$ 7.5 Hz), 7.40–7.48 m (4H, $H^{2',3',5',6'}$),7.56 d (1H, $H^{5\text{ or }8}$, $J$ 7.8 Hz), 7.65 c (1H, $H^{8\text{ or }5}$, $J$ 8.1 Hz).

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