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Imidazo[1,2-*a*]benzimidazole Derivatives: XXVIII.* Syntheses and Heterocyclizations on the Basis of 1-Allyl-2-aminobenzimidazole

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Abstract—Addition of hydrogen bromide at the double bond of 1-allyl-2-amino-1*H*-benzimidazole and 3-alkyl-(benzyl)-1-allyl-2-amino-1*H*-benzimidazolium halides was studied. The resulting 1-(2-bromopropyl) derivatives were subjected to thermolysis under different conditions, and the structure of dehydrobromination products was determined and proved by independent synthesis via prototropic isomerization of the allyl group by the action of bases.

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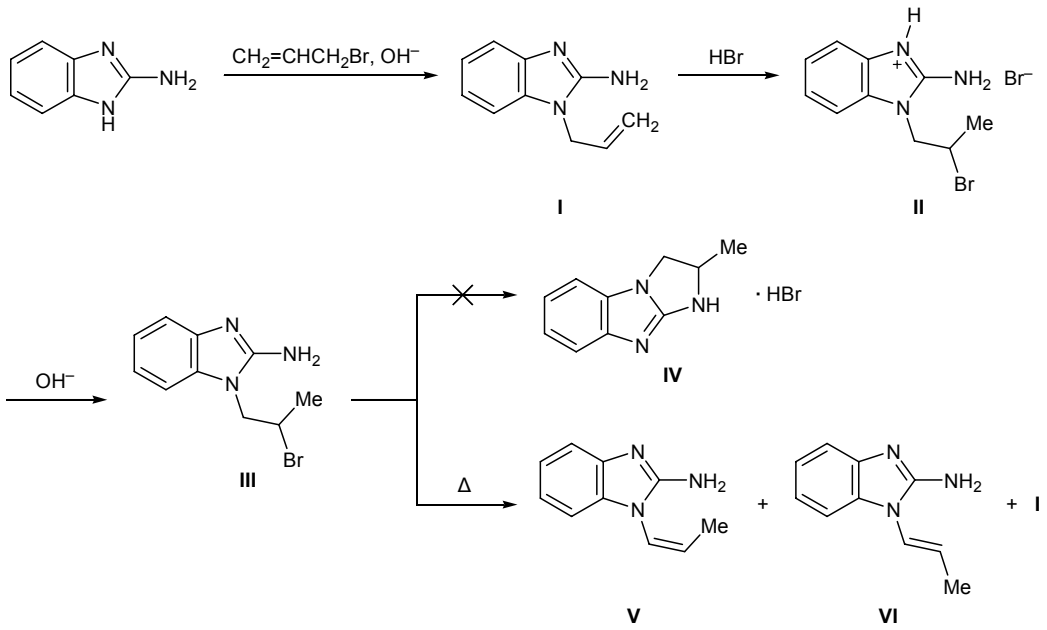
Allyl-substituted aromatic and heterocyclic compounds attract researchers' attention due to their high reactivity and the possibility for synthesizing fused heterocyclic systems on their basis. Intramolecular cyclizations of α-allyl-substituted hetarenethiones [2–4] and hetarenamines [5, 6] were reported in a number of publications. Development of new methods for the synthesis of imidazo[1,2-*a*]benzimidazole derivatives from 1-allyl-2-aminobenzimidazole (**I**) is promising, taking into account broad spectrum of biological activity intrinsic to that tricyclic system [7–11].

First of all, the procedure for the synthesis of amine **I** was optimized. N-Substituted 2-aminobenzimidazoles were commonly prepared by amination of

Scheme 1.



* For communication XXVII, see [1].

N-substituted benzimidazoles according to Chichibabin [12]. However, treatment of 1-allylbenzimidazole with sodium amide resulted in formation of only polymerization products [13]. Later on [14] we examined alkylation of 2-aminobenzimidazole with allyl bromide under different conditions and found that this reaction in the two-phase system acetone–40–50% NaOH or KOH selectively yields 1-allyl-2-aminobenzimidazole (96–97%; cf. [15]). Presumably, the nucleophilicity of nitrogen-centered anion in acetone sharply increases [16], so that no side reactions occur. The allylation of 2-aminobenzimidazole in alcoholic alkali was accompanied by formation of small amounts of 1,3-diallyl- and 1,2,3-triallyl-substituted derivatives.

By heating 1-allyl-2-aminobenzimidazole (**I**) in 48% hydrobromic acid we obtained stable 2-amino-1-(2-bromopropyl)-1*H*-benzimidazole hydrobromide (**II**). The addition of HBr followed the Markovnikov pattern. The ^{1}H NMR spectrum of the product lacked signals assignable to vinyl fragment, while a signal from methyl protons appeared as a doublet at δ 1.75 ppm (J_{HH} = 7.1Hz). Unlike 1-alkyl-3-(2-chloroethyl)-2,3-dihydro-1*H*-benzimidazol-2-imines [17] and 1-alkyl-2-(ω-chloroalkylamino)-1*H*-bezimidazoles [18] which were reported previously to readily undergo intramolecular cyclization on heating, free base **III** obtained by treatment of hydrobromide **II** with aqueous ammonia turned out to be thermally stable; no cyclization was observed when compound **III** was heated to the melting point (mp 126–127°C) or 15–20°C above, whereas further rise in temperature led to tarring.

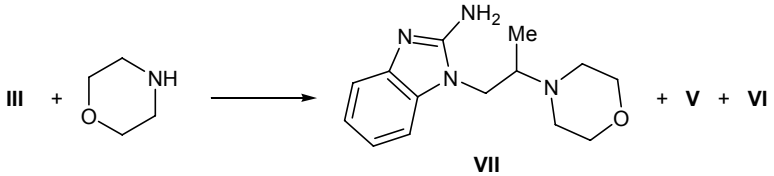
When amine **III** was heated in xylene over a period of 1 h, an oily material separated from the reaction mixture and crystallized on further heating under reflux. According to the TLC data, the product was a mixture of several compounds which we failed to separate by column chromatography (further decomposition occurred during chromatography on aluminum oxide). With a view to identify the components, the product mixture was treated with picric acid. According to the ^{1}H NMR data, the resulting mixture contained amine **I**, *cis*- and *trans*-isomeric 2-amino-1-(prop-2-en-1-yl)-1*H*-benzimidazoles **V** and **VI**, and initial amine **III**. Some signals in the spectrum were not identified. Presumably, compounds **V** and **VI** are formed due to strong basicity of amine **III**, which is also typical of other 1-substituted 2-aminobenzimidazoles [16]; compound **III** acts as hydrogen bromide acceptor, leading to dehydrobromination products. Migration of the double bond is accompanied by appearance in the ^{1}H NMR spectra of signals from protons in the CH_3 and NCH= groups as doublets of doublets with coupling constants characteristic of each isomer ($^3J_{HH}$ = 7.8 and 14.0 Hz for *cis* and *trans* isomers, respectively).

In order to exclude dehydrobromination by the action of amine **III**, its thermolysis was performed in the presence of excess triethylamine. Nevertheless, in this case a mixture of several compounds was formed as well, whereas no cyclic system **IV** was obtained. Amine **III** also failed to undergo cyclization in acetic acid.

It is known that 2-amino-1-(ω-dialkylaminoalkyl)-benzimidazoles are not only pharmacologically active compounds [19] but also potential intermediate products for their synthesis [20–22]. To obtain new derivatives of this series we examined nucleophilic replacement of bromine in compound **III** by morpholine. The reaction was not selective, and, apart from the desired 2-amino-1-(2-morpholinopropyl)-1*H*-benzimidazole (**VII**), *cis*- and *trans*-isomeric 2-amino-1-(prop-2-en-1-yl)-1*H*-benzimidazoles **V** and **VI** were formed (Scheme 2). According to the ^{1}H NMR data, the product ratio was 9:2:9.

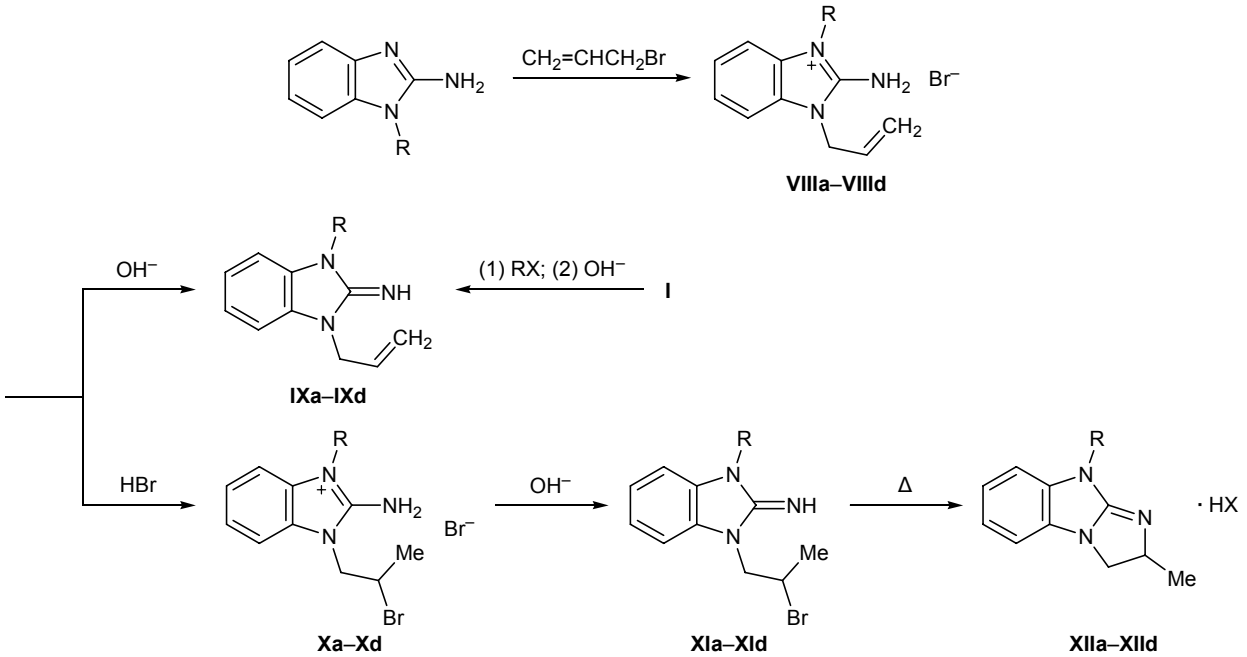
The formation of *cis*- and *trans*-2-amino-1-(prop-2-en-1-yl)benzimidazoles **V** and **VI** was confirmed by studying prototropic isomerization of 1-allyl-2-aminobenzimidazole by the action of potassium hydroxide in dimethyl sulfoxide. When the reaction mixture was kept for 20 h at room temperature, the conversion was only 30% with formation of *cis* isomer **V**. Subsequent keeping at room temperature over a period of 30 day resulted in complete migration of the double bond with formation of a 1:1 mixture of *cis* and *trans* isomers. At elevated temperature, 75–80°C, the migration of the

Scheme 2.



VII

Scheme 3.



R = Me (**a**), $PhCH_2$ (**b**), $Et_2NCH_2CH_2$ (**c**), 2-morpholinoethyl (**d**); **XII**, HX = HBr (**a**, **b**), 2HCl (**c**, **d**).

double bond was complete in 4 h, and the ratio of *cis* and *trans* isomers **V** and **VI** was 6:5. The isomerization of 1-allyl-2-aminobenzimidazole by the action of potassium hydroxide in DMSO at 100°C required 15 min, the *cis*/*trans* isomer ratio being 1:1.

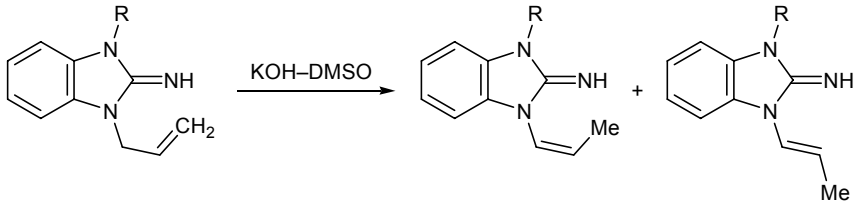
Quaternization of initial amine **I** with alkyl (benzyl) halides or the reaction of 1-substituted 2-aminobenzimidazoles with allyl bromide gave the corresponding 3-substituted 1-allyl-2-aminobenzimidazolium halides **VIIIa**–**VIIIf**. Like compound **I**, quaternary salts **VIIIa**–**VIIIf** readily took up hydrogen bromide at the double bond in the allyl substituent to produce 3-R-2-amino-1-(2-brompropyl)-1*H*-benzimidazolium halides **Xa**–**Xd**, and treatment of the latter with basic reagents (NH_4OH, Na_2CO_3, etc.) afforded benzimidazol-2-imines **XIa**–**XId** (Scheme 3).

Unlike 1-(2-bromopropyl) derivative **III**, heating of 3-substituted 1-(2-bromopropyl)-2,3-dihydro-1*H*-benzimidazol-2-imines **XIa**–**XId** in boiling toluene or without a solvent at a temperature exceeding their melting points by 15–20°C led to intramolecular cyclization with participation of the bromoalkyl fragment and imino group with formation of 9-R-2-methyl-2,3-dihydroimidazo[1,2-*a*]benzimidazoles which were isolated as hydrohalides **XIIa**–**XIId**. The cyclization was accompanied by upfield shift of signals from protons formerly belonging to the 2-bromopropyl substituent. The rigid structure of the terminal dihydroimidazole ring (due to the presence of methyl group in the 2-position) and appearance of a chiral center at C^2 makes protons in the endocyclic methylene group (C^3H_2) nonequivalent, and they resonate in the ^1H NMR spectra of **XIIa**–**XIId** (free bases) as two triplets at δ 3.32–3.35 (H_{ax}, J_{HH} = 6.5–7.5 Hz) and 3.95–3.98 ppm (H_{eq}, J_{HH} = 8.1–8.6 Hz).

When the reaction was performed in a solvent in the presence of a base (e.g., triethylamine), the cyclization was accompanied by dehydrobromination to give *cis*/*trans*-isomeric 1-(prop-2-en-1-yl)-substituted benzimidazole derivatives **XIII** and **XIV** (Scheme 4). Migration of the exocyclic double bond in 1-allyl-3-methyl- and 1-allyl-3-benzyl-2,3-dihydro-1*H*-benzimidazol-2-imines **IXa** and **IXb** by the action of KOH in DMSO confirmed the structure of the dehydrobromination products. In both cases, the isomerization on short heating (15 min, 100°C) was selective and, unlike the transformation of compound **I** under analogous conditions, the products were the corresponding *trans* isomers **XIVa** and **XIVb**. Increase of the reaction time to 25 min leads to the formation of a mixture of *cis* and *trans* isomers **XIII** and **XIV** at a ratio 1:3. Further heating favors increased concentration of *cis* isomers **XIIIa** and **XIIIb**.

To conclude, we have found that thermolysis of compounds **XIa**–**XId** should be carried out in the absence of basic reagents to obtain tricyclic derivatives.

Scheme 4.



IXa, **IXb** **XIIIa**, **XIIIb** **XIVa**, **XIVb**

R = Me (**a**), $PhCH_2$ (**b**).

EXPERIMENTAL

The progress of reactions and the purity of the isolated compounds were monitored by TLC on alumina plates using chloroform as eluent; spots were visualized by treatment with iodine vapor in a moist chamber. The IR spectra were recorded from samples dispersed in mineral oil on a Specord 75IR spectrometer. The ^{1}H NMR spectra were obtained on a Varian Unity 300 instrument at 300 MHz using the residual solvent proton signals as reference ($CHCl_3$, δ 7.25 ppm; DMSO-d_5, δ 2.50 ppm).

1-Allyl-1*H*-benzimidazol-2-amine (I). A solution of 65.9 g (1 mol) of 85% KOH in 74 ml of water was added under stirring to a suspension of 66.5 g (0.5 mol) of 1*H*-benzimidazol-2-amine in 300 ml of acetone. The mixture was stirred for 10–15 min at room temperature and cooled to –2 to –3°C, and 46 ml (0.53 mol) of allyl bromide was added over a period of 15 min. The mixture warmed up to 3–5°C; it was stirred for 30–40 min at 0–5°C, allowed to spontaneously warm up to 20°C, and stirred for 2–2.5 h at that temperature. The organic phase was separated, and the aqueous phase was treated with 100 ml of acetone. The acetone extract was combined with the organic phase and evaporated, 200 ml of cold water was added to the residue, and (after 30 min) the precipitate was filtered off, washed on a filter with several portions of cold water, and dried at 100–105°C. Yield 81.4–84.0 g (94–97%). Amine **I** thus isolated was chromatographically pure, and no additional purification was necessary for subsequent transformations. The product can be recrystallized from benzene (2 g/10 ml) or from water (1 g/35–40 ml), mp 128–129°C. IR spectrum, ν, cm^{-1}: 3445, 3335 (NH_2); 1630 (C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.57d (2H, NCH_2, J = 4.8 Hz), 5.00–5.20 m (2H, CH_2), 5.80–5.97 m (1H, CH), 6.20 s (2H, NH_2), 6.75–7.18 m (4H, H_{arom}). Found, %: C 69.28; H 6.37; N 24.35. $C_{10}H_{11}N_3$. Calculated, %: C 69.34; H 6.40; N 24.26.

1-(2-Bromopropyl)-1*H*-benzimidazol-2-amine hydrobromide (II). A solution of 3.5 g (20 mmol) of amine **I** in 20 ml of 48% hydrobromic acid was heated for 10 h under reflux. The mixture was cooled, and the precipitate was filtered off, repeatedly washed with acetone to remove HBr, and dried in air. Yield 4.6 g (68%), mp 186–187°C (from *i*-PrOH). IR spectrum, ν, cm^{-1}: 3250, 3160 (NH_2); 1670 (C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.75 d (3H, CH_3, J = 7.1 Hz), 4.40–4.75 m (3H, CH_2, CH), 7.17–7.70 m (4H, H_{arom}), 8.77 s (2H, NH_2), 12.70 s (1H, N^+H). Found, %: C 35.78; H 3.88; Br 47.74; N 12.60. $C_{10}H_{12}BrN_3 \cdot HBr$. Calculated, %: C 35.85; H 3.91; Br 47.70; N 12.54.

Hydrobromide **II**, 3.4 g (10 mmol), was dissolved in 10 ml of water on heating, and 22% aqueous ammonia was added to the hot solution until pH 9–10. The mixture was cooled, and the precipitate was filtered off, washed with water, dried in air, and recrystallized from benzene. Yield 2.3 g (89%), mp 127–128°C. Found, %: C 47.32; H 4.81; Br 31.38; N 16.49. $C_{10}H_{12}BrN_3$. Calculated, %: C 47.26; N 4.76; Br 31.44; N 16.54.

1-(Prop-2-en-1-yl)-1*H*-benzimidazol-2-amine (V/VI, a mixture of *cis* and *trans* isomers**).** Amine **II**, 0.9 g (5 mmol), was dissolved in 5 ml of DMSO, 3 ml of a 0.5 M solution of potassium *tert*-butoxide in *tert*-butyl alcohol was added, and the mixture was heated for 4 h at 75–80°C, diluted with 50 ml of water, and extracted with chloroform. The extract was washed with water, dried over Na_2SO_4, and evaporated. The crystalline residue was a mixture of *cis* and *trans* isomers **V** and **VI** at a ratio 5:6. Yield 0.7 g (80%), mp 120–121°C (from benzene). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: **V**: 1.67 d.d (3H, CH_3, ^3J = 7.8, ^4J = 1.8 Hz), 5.12 (2H, NH_2), 5.95–6.12 m (1H, CH), 6.38 d.d (1H, NCH, ^3J = 7.8, ^4J = 1.8 Hz), 6.93–7.44 m (4H, H_{arom}); **VI**: 1.92 d.d (3H, CH_3, ^3J = 6.8, ^4J = 1.7 Hz), 5.12 br.s (2H, NH_2), 5.95–6.12 m (1H, CH), 6.50 d.d (1H, NCH, ^3J = 14.0, ^4J = 1.7 Hz), 6.93–7.44 m (4H, H_{arom}).

1-(2-Morpholinopropyl)-1*H*-benzimidazol-2-amine (VII). A mixture of 1.7 g (6 mmol) of hydrobromide **II** and 5 ml of morpholine was heated for 20 h under reflux. The mixture was treated with 15–20 ml of water and extracted with chloroform. The extract was washed with water to remove excess morpholine and passed through a layer of Al_2O_3 (1.5×10 cm) using chloroform as eluent. The eluate was evaporated to obtain white crystalline product which was a mixture of *cis* and *trans* isomers of 1-(prop-2-en-1-yl)benzimidazol-2-amine **V** and **VI** and compound **VII** at a ratio of 2:9:9. Yield 0.9 g. ^{1}H NMR spectrum of **VII** ($CDCl_3$), δ, ppm: 1.10 d (3H, CH_3, J = 7.1 Hz), 2.49–2.75 m (4H, NCH_2), 3.60–3.80 m (4H, OCH_2), 3.81–4.06 m (3H, CH_2, CH), 5.94 s (2H, NH_2), 6.93–7.47 m (4H, H_{arom}).

3-Substituted 1-allyl-2-amino-1*H*-benzimidazolium bromides VIIIa–VIIId (*general procedure*). *a*. Allyl bromide, 0.9 ml (10 mmol), was added to a solution of 10 mmol of 1-alkyl(benzyl)-1*H*-benzimidazol-2-amine in 10 ml of DMF, and the mixture was heated under reflux until the reaction was complete (TLC) and left overnight. The precipitate was filtered off and washed with acetone. Yield 86–98%.

3-Substituted 1-allyl-2-amino-1*H*-benzimidazolium halides were also synthesized by reaction of 1-allyl-1*H*-benzimidazol-2-amine with the corresponding alkyl halides.

b. Allyl bromide, 0.9 ml (10 mmol), was added to a solution of 10 mmol of 1-(2-dialkylaminoethyl)-1*H*-benzimidazol-2-amine in 30 ml of acetonitrile or 50 ml of acetone, and the mixture was heated for 5 h under reflux. After cooling, the precipitate was filtered off and washed with acetone. Yield 82–85%.

1-Allyl-2-amino-3-methyl-1*H*-benzimidazolium bromide (VIIIa). Yield 93%, mp 293–294°C (decomp., from water).

1-Allyl-2-amino-3-benzyl-1*H*-benzimidazolium bromide (VIIIb). Yield 86–88%, mp 298–299°C (decomp., from water).

3-Allyl-2-amino-1-(2-diethylaminoethyl)-1*H*-benzimidazolium bromide (VIIIc). Yield 83%, mp 272–273°C (decomp., from *i*-PrOH). IR spectrum, ν, cm^{-1}: 3315, 3235 (NH_2), 1650, 1605, 1580, 1505, 1465, 1455 (C=C, C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.00 t (6H, CH_3, J = 6.7 Hz), 2.64 q (4H, NCH_2), 2.92 t (2H, CH_2N, J = 7.5 Hz), 4.23 t (2H, NCH_2, J = 7.5 Hz), 4.64–4.71 m (2H, CH_2), 4.95–5.28 m (2H, CH_2), 5.86–6.02 m (1H, CH), 7.27–7.47 m (4H, H_{arom}). Found, %: C 54.45; H 7.20; Br 22.58; N 15.77. $C_{16}H_{25}BrN_4$. Calculated, %: C 54.39; H 7.13; Br 22.62; N 15.86.

3-Allyl-2-amino-1-(2-morpholinoethyl)-1*H*-benzimidazolium bromide (VIIId). Yield 85%, mp 256–257°C (from EtOH).

1-Allyl-3-methyl-2,3-dihydro-1*H*-benzimidazol-2-imine (IXa) was obtained by treatment of bromide **VIIIa** with 10 ml of a 30% solution of sodium hydroxide, followed by extraction of the free base into benzene. Yield 99%, mp 67–68°C (from hexane). IR spectrum, ν, cm^{-1}: 3350 (NH), 1635, 1600, 1490, 1445 (C=C, C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.05 (2H, NH_2), 3.35 s (3H, CH_3), 4.42 d.d (2H, NCH_2, ^2J = 5.0, ^3J = 1.6 Hz), 5.10–5.27 m (2H, CH_2), 5.77–5.97 m (1H, CH), 6.76–7.03 m (4H, H_{arom}). Found, %: C 70.49; H 6.97; N 22.54. $C_{11}H_{13}N_3$. Calculated, %: C 70.56; H 7.00; N 22.44.

Compounds **IXb–IXd** were synthesized in a similar way.

1-Allyl-3-benzyl-2,3-dihydro-1*H*-benzimidazol-2-imine (IXb). Yield 95%, mp 107–108°C (from hexane). IR spectrum, ν, cm^{-1}: 3265 (NH), 1630, 1610, 1590, 1475, 1445 (C=C, C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.50 d (2H, NCH_2, J = 4.9 Hz), 5.07 s (2H, Ph**C**$\mathbf{H}_2$), 5.10–5.24 m (2H, CH_2), 5.80–6.00 m (1H, CH), 6.72–7.30 m (9H, H_{arom}). Found, %: C 77.47; H 6.60; N 15.93. $C_{17}H_{17}N_3$. Calculated, %: C 77.54; H 6.51; N 15.95.

3-Allyl-1-(2-diethylaminoethyl)-2,3-dihydro-1*H*-benzimidazol-2-imine (IXc). Yield 90%. Unstable oily substance.

1-Allyl-3-(2-morpholinoethyl)-2,3-dihydro-1*H*-benzimidazol-2-imine (IXd). Yield 87%, mp 80–81°C (from hexane). IR spectrum, ν, cm^{-1}: 3280 (NH), 1600, 1580, 1475, 1440 (C=C, C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.54 t (4H, NCH_2, J = 4.5 Hz), 2.66 t (2H, CH_2N, J = 7.1 Hz), 3.07 br.s (2H, N^+H_2), 3.69 t (4H, OCH_2, J = 4.5 Hz), 3.95 t (2H, NCH_2, J = 7.1Hz), 4.43 d.d (2H, NCH_2, ^3J = 3.3, ^4J = 1.6 Hz), 5.10–5.24 m (2H, CH_2), 5.77–5.95 m (1H, CH), 6.77–7.01 m (4H, H_{arom}). Found, %: C 67.04; H 7.69; N 19.65. $C_{16}H_{22}N_4O$. Calculated, %: C 67.11; H 7.74; N 19.56.

3-Substituted 2-amino-1-(2-bromopropyl)-1*H*-benzimidazolium bromides Xa–Xd (*general procedure*). A mixture of 10 mmol of 3-R-1-allyl-2-aminobenzimidazolium bromide and 25 ml of 48% hydrobromic acid was heated for 10 h (30 h in the reaction with **VIIIb**) under reflux. The acid was removed from

the mixture by distillation on a rotary evaporator, the residue was diluted with acetone, and the precipitate was filtered off, washed with acetone to remove residual HBr, and dried in air.

2-Amino-1-(2-bromopropyl)-3-methyl-1*H*-benzimidazolium bromide (Xa). Yield 80%, mp 251–252°C (decomp., from *i*-PrOH). IR spectrum, ν, cm^{-1}: 3265, 3205 (NH_2), 1660, 1600, 1540, 1490, 1460 (C=C, C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.19 d (3H, CH_3, J = 5.3 Hz), 3.67 s (3H, NCH_3), 3.94–4.19 m (3H, CH_2, CH), 7.25–7.36 m (2H, 5-H, 6-H), 7.50–7.62 m (2H, 4-H, 7-H), 8.68 s (2H, N^+H_2). Found, %: C 37.92; H 4.29; Br 45.81; N 11.98. $C_{11}H_{15}Br_2N_3$. Calculated, %: C 37.85; H 4.33; Br 45.78; N 12.04.

2-Amino-3-benzyl-1-(2-bromopropyl)-1*H*-benzimidazolium bromide (Xb). Yield 77%, mp 257–258°C (from aq. EtOH).

2-Amino-1-(2-bromopropyl)-3-(2-diethylaminoethyl)-1*H*-benzimidazolium bromide hydrobromide (Xc). Yield 69%, mp 264–265°C (decomp., from EtOH). IR spectrum, ν, cm^{-1}: 3255, 3215 (NH_2), 1660, 1610, 1580, 1460 (C=C, C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.45 t (6H, CH_3, J = 6.4 Hz), 1.64 d (3H, CH_3, J = 6.7 Hz), 3.31 q (4H, $CH_3C\mathbf{H}_2$), 3.54 t (2H, CH_2N, J = 7.2 Hz), 4.04–4.21 m (2H, NCH_2), 4.32–4.55 m (3H, NCH_2, CH, J = 7.2 Hz), 7.18–7.52 m (4H, H_{arom}). Found, %: C 37.26; H 5.31; Br 46.60; N 10.83. $C_{16}H_{26}Br_2N_4 \cdot HBr$. Calculated, %: C 37.31; H 5.28; Br 46.53; N 10.88.

2-Amino-1-(2-bromopropyl)-3-(2-morpholinoethyl)-1*H*-benzimidazolium bromide hydrobromide (Xd). Yield 70%, mp 287–288°C (from aq. EtOH). IR spectrum, ν, cm^{-1}: 3270, 3205 (NH_2), 1660, 1600, 1580, 1505, 1450 (C=C, C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.64 d (3H, CH_3, J = 6.5 Hz), 3.31 s (4H, NCH_2), 3.50 t (2H, CH_2N, J = 7.4 Hz), 3.83 s (4H, OCH_2), 4.30–4.80 m (3H, CH_2N, CH_2, CH), 7.20–7.50 m (4H, H_{arom}). Found, %: C 36.40; N 4.81; Br 45.20; N 10.54. $C_{16}H_{24}Br_2N_4O \cdot HBr$. Calculated, %: C 36.32; H 4.76; Br 45.30; N 10.59.

3-Substituted 1-(2-bromopropyl)-2,3-dihydro-1*H*-benzimidazol-2-imines XIa–XId (*general procedure*). Compound **Xa**–**Xd**, 5 mmol, was dissolved on heating in 10–40 ml of water, the solution was cooled to 50–60°C, and 22% aqueous ammonia was added until pH 9–10. The precipitate was filtered off, washed with water, and dried in air.

1-(2-Bromopropyl)-3-methyl-2,3-dihydro-1*H*-benzimidazol-2-imine (XIa). Yield 86%, mp 66–67°C (intramolecular cyclization occurred on melting).

1-Benzyl-3-(2-bromopropyl)-2,3-dihydro-1*H*-benzimidazol-2-imine (XIb). Yield 80%, mp 118–119°C (from EtOAc). IR spectrum, ν, cm^{-1}: 3280 (NH), 1630, 1615, 1590, 1480, 1445 (C=C, C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.76 d (3H, CH_3, J = 6.7 Hz), 4.10–4.22 m (2H, NCH_2), 4.50–4.65 m (1H, CH), 4.99 s (2H, $C\mathbf{H}_2Ph$), 6.70–7.38 m (9H, H_{arom}). Found, %: C 59.34; H 5.32; Br 23.16; N 12.18. $C_{17}H_{18}BrN_3$. Calculated, %: C 59.31; H 5.27; Br 23.21; N 12.21.

1-(2-Bromopropyl)-3-(2-diethylaminoethyl)-2,3-dihydro-1*H*-benzimidazol-2-imine (XIc). Yield 67%, oily substance. Compound **XIc** underwent intramolecular cyclization on storage to give unstable 9-(2-diethylaminoethyl)-2-methyl-2,3-dihydroimidazo[1,2-*a*]-benzimidazole hydrobromide.

1-(2-Bromopropyl)-3-(2-morpholinoethyl)-2,3-dihydro-1*H*-benzimidazol-2-imine (XId). Yield 72%, oily substance. Compound **XId** underwent intramolecular cyclization on storage to give unstable 2-methyl-9-(2-morpholinoethyl)-2,3-dihydroimidazo[1,2-*a*]-benzimidazole hydrobromide.

9-Substituted 2-methyl-2,3-dihydroimidazo[1,2-*a*]benzimidazole hydrohalides XIIa–XIId (*general procedure*). Compound **XIa**–**XId**, 3 mmol, was heated above its melting point by 15–20°C until its complete conversion (30–90 min, TLC). The melt was cooled and ground with acetone, and the precipitate was filtered off, washed with acetone, and recrystallized from appropriate solvent. If purification of **XIIa**–**XIId** from decomposition products was necessary (a spot at the start on TLC), the melt was ground with 22% aqueous ammonia, the free base was extracted into chloroform, and the extract was passed through a layer of Al_2O_3 (3×4 cm) using chloroform as eluent. The eluate was evaporated, the residue was dissolved in 15–20 ml of acetone, and the free base was converted into hydrochloride by adding a solution of HCl in isopropyl alcohol.

2,9-Dimethyl-2,3-dihydroimidazo[1,2-*a*]benzimidazole hydrobromide (XIIa) was obtained in 98% yield by heating imine **XIa** at 80–85°C. mp 236–237°C (from EtOH). IR spectrum, ν, cm^{-1}: 1660, 1600, 1535, 1495, 1465 (C=C, C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.75 d (3H, CH_3, J = 5.8 Hz), 3.66 s (3H, NCH_3), 4.41–4.73 m (3H, CH_2, CH), 7.23–7.73 m (4H, H_{arom}), 8.94 br.s (1H, N^+H). Found, %: C 49.34; H 5.32; Br 29.75; N 15.59. $C_{11}H_{13}N_3 \cdot HBr$. Calculated, %: C 49.27; H 5.26; Br 29.80; N 15.67. Hydrobromide **XIIa** can also be obtained by heating

2 mmol of imine **XIa** in 8 ml of boiling anhydrous toluene over a period of 30 min.

9-Benzyl-2-methyl-2,3-dihydroimidazo[1,2-*a*]-benzimidazole hydrobromide (XIIb) was obtained by heating imine **XIb** for 2 h at 125–130°C. Yield 95%, mp 230–232°C (from EtOH). IR spectrum, ν, cm^{-1}: 1660, 1600, 1620, 1540, 1500, 1475 (C=C, C=N). Found, %: C 59.40; H 5.18; Br 23.15; N 12.27. $C_{17}H_{17}N_3 \cdot HBr$. Calculated, %: C 59.31; H 5.27; Br 23.21; N 12.21. ^{1}H NMR spectrum of free base **XIIb** ($CDCl_3$), δ, ppm: 1.37 d (3H, CH_3, J = 6.5 Hz), 3.35 t (1H, 3-H_{ax}, J = 6.5 Hz), 3.98 t (1H, 3-H_{eq}, J = 8.6 Hz), 4.50–4.68 m (1H, CH), 4.94 q (2H, NCH_2), 6.54–7.36 m (9H, H_{arom}).

9-(2-Diethylaminoethyl)-2-methyl-2,3-dihydro-imidazo[1,2-*a*]benzimidazole dihydrochloride (XIIc). Hydrobromide **Xc**, 5.2 g (10 mmol), was dissolved in 25 ml of water, 5 ml of 22% aqueous ammonia was added, and the free base was extracted into chloroform (2×25 ml). The extracts were combined, dried over Na_2SO_4, and evaporated, and the residue was heated in 25 ml of boiling toluene until the reaction was complete (TLC, Al_2O_3, $CHCl_3$). The mixture was then treated with water (2×15 ml), the aqueous extracts were combined and made alkaline by adding aqueous ammonia, and free base **XIIc** was extracted into chloroform (3×10 ml). The extracts were combined and passed through a layer of Al_2O_3 (3×4 cm), the sorbent was eluted with chloroform, the eluate was evaporated, and the residue was dissolved in 15–20 ml of acetone and acidified to pH 2–3 with a solution of HCl in isopropyl alcohol. Yield 41%, mp 241–242°C (decomp., from MeCN or EtOH). IR spectrum, ν, cm^{-1}: 1660, 1620, 1600, 1540, 1500, 1475 (C=C, C=N). Found, %: C 55.74; H 7.65; Cl 20.43; N 16.18. $C_{16}H_{24}N_4 \cdot 2HCl$. Calculated, %: C 55.65; H 7.59; Cl 20.53; N 16.23. ^{1}H NMR spectrum of the free base ($CDCl_3$), δ, ppm: 0.98 t (6H, CH_3, J = 7.2 Hz), 1.37 d (3H, CH_3, J = 7.1 Hz), 2.50–2.67 m (6H, CH_2N), 2.76 t (2H, NCH_2, J = 7.2 Hz), 3.32 t (1H, 3-H_{ax}, J = 7.9 Hz), 3.70–4.05 m (3H, NCH_2, 3-H_{eq}), 4.50–4.67 m (1H, CH), 6.62–6.96 m (4H, H_{arom}).

2-Methyl-9-(2-morpholinoethyl)-2,3-dihydro-imidazo[1,2-*a*]benzimidazole dihydrochloride (XIId) was synthesized as described above for dihydrochloride **XIIc**. Yield 47%, mp 237–238°C (decomp., from EtOH). IR spectrum, ν, cm^{-1}: 1660, 1610, 1500, 1475 (C=C, C=N). Found, %: C 53.58; H 6.65; Cl 19.82; N 15.51. $C_{16}H_{22}N_4O \cdot 2HCl$. Calculated, %: C 53.49; H 6.73; Cl 19.73; N 15.59. ^{1}H NMR spectrum of the free base ($CDCl_3$), δ, ppm: 1.36 d (3H, CH_3, J = 7.0 Hz), 2.43–2.60 m (4H, NCH_2), 2.63–2.76 m (2H, CH_2N), 3.33 t (1H, 3-H_{ax}, J = 7.5 Hz), 3.60–3.72 m (4H, CH_2O), 3.80–4.02 m (3H, NCH_2, 3-H_{eq}), 4.49–4.64 m (1H, CH), 6.63–6.95 m (4H, H_{arom}).

1-Methyl-3-[(*E*)-prop-2-en-1-yl]-2,3-dihydro-1*H*-benzimidazol-2-imine (XIVa). A solution of 0.9 g (5 mmol) of imine **IXa** in 10 ml of a 5% solution of potassium hydroxide in dimethyl sulfoxide was heated for 15 min at 100°C. The mixture was cooled, diluted with 100 ml of water, and extracted with chloroform. The extract was washed with water and evaporated. Yield 81%, mp 50–51°C (from petroleum ether). IR spectrum, ν, cm^{-1}: 3285 (NH); 1660, 1635, 1615, 1500, 1475 (C=C, C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.89 d.d (3H, CH_3, ^3J = 6.8, ^4J = 1.7 Hz), 3.41 s (3H, NCH_3), 5.86–6.08 m (1H, CH), 6.43 d.d (1H, NCH, ^3J = 14.1, ^4J = 1.5 Hz), 6.65–7.10 m (4H, H_{arom}). Found, %: C 70.49; H 7.05; N 22.46. $C_{11}H_{13}N_3$. Calculated, %: C 70.56; H 7.00; N 22.44.

After prolonged heating, a mixture of two isomers was formed with gradually increasing fraction of 1-methyl-3-[(*Z*)-prop-2-en-1-yl]-2,3-dihydro-1*H*-benzimidazol-2-imine (**XIIIa**). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.65 d.d (3H, CH_3, ^3J = 7.1, ^4J = 1.7 Hz), 3.34 s (3H, NCH_3), 5.86–6.08 m (1H, CH), 6.15 d.d (1H, NCH, ^3J = 7.5, ^4J = 1.5 Hz), 6.65–7.10 m (4H, H_{arom}).

3-Benzyl-1-(prop-2-en-1-yl)-2,3-dihydro-1*H*-benzimidazol-2-imine (XIIIb/XIVb, a mixture of *cis* and *trans* isomers**)**. Isomer mixture **XIIIb**/**XIVb** was synthesized according to the procedure described above for isomers of **XIVa**. ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: *cis* isomer: 1.69 d.d (3H, CH_3, ^3J = 6.8, ^4J = 1.6 Hz), 5.10 s (2H, C**H**$_2$Ph), 5.88–6.12 m (1H, CH), 6.21 d.d (1H, NCH, ^3J = 8.7, ^4J = 1.5 Hz), 6.67–7.43 m (9H, H_{arom}); *trans* isomer: 1.91 d.d (3H, CH_3, ^3J = 7.7, ^4J = 1.6 Hz), 5.04 s (2H, C**H**$_2$Ph), 5.88–6.12 m (1H, CH), 6.49 d.d (1H, NCH, ^3J = 13.7, ^4J = 1.5 Hz), 6.67–7.43 m (9H, H_{arom}).

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