ISSN 1070-4280, Russian Journal of Organic Chemistry, 2011, Vol. 47, No. 9, pp. 1354–1361. © Pleiades Publishing, Ltd., 2011.
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Imidazo[1,2-*a*]benzimidazole Derivatives: XXIX.* 1-Allyl-2-amino-3-acylmethylbenzimidazolium Halides and Syntheses on Their Base

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Received January 26, 2011

Abstract—Cyclization of 1-allyl-2-amino-3-acylmethylbenzimidazolium halides under alkaline conditions gave 9-allyl-substituted imidazo[1,2-*a*]benzimidazoles. Cyclization of the same compounds on heating in concentrated hydrobromic acid was accompanied by addition of hydrogen bromide at the exocyclic double bond. Competing cyclizations with participation of the 1-(2-bromopropyl) and 3-acylmethyl substituents in 2-imino-2,3-dihydro-1*H*-benzimidazole were studied. Functionalization of the imidazo[1,2-*a*]benzimidazole system was performed via introduction of substituents into the 3-position and replacement of bromine in the 2-bromopropyl group in the 9-position.

DOI: 10.1134/S1070428011090168

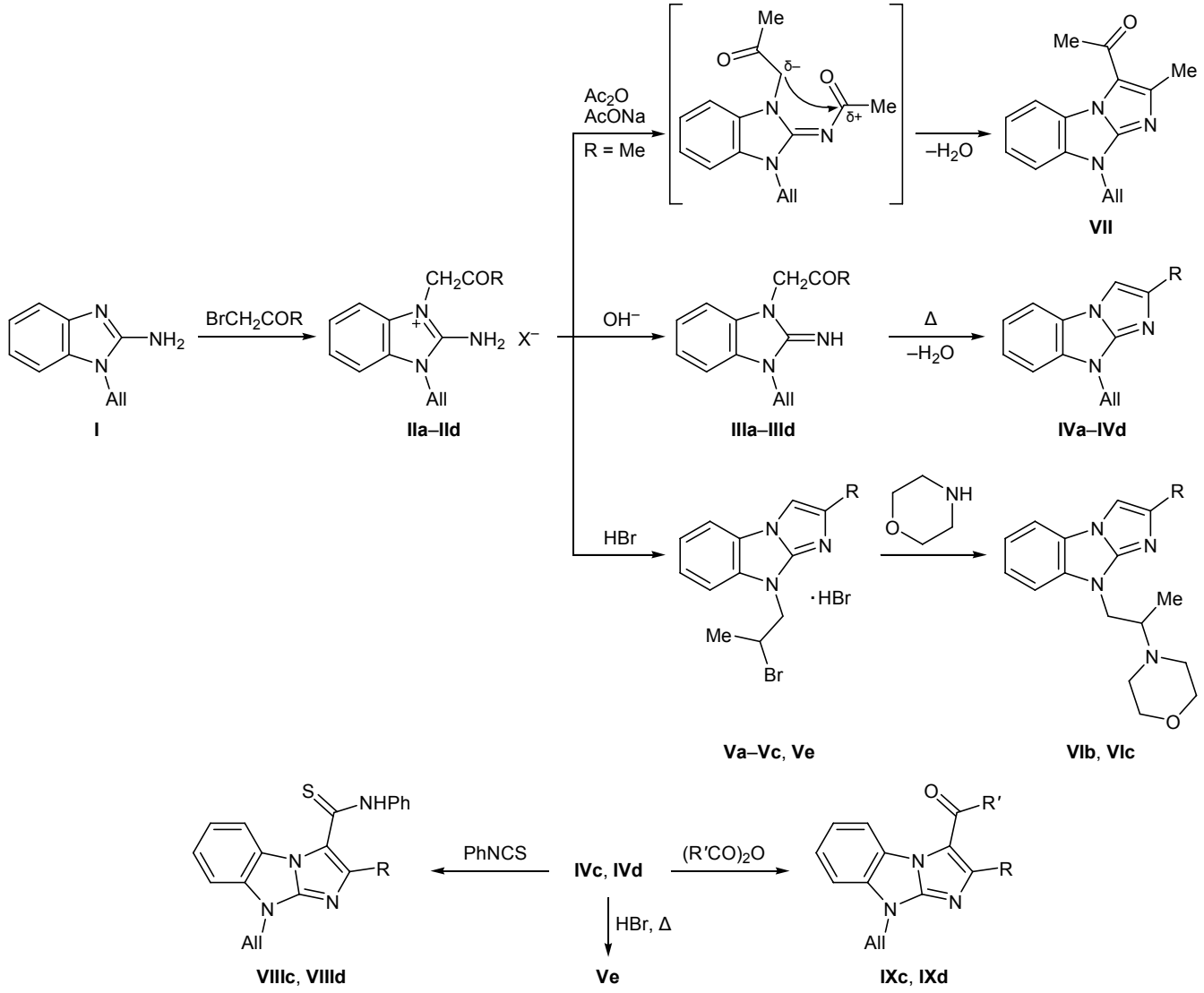
Taking into account that a large number of biologically active compounds with various properties (about 50 kinds of biological activity) were found among imidazo[1,2-*a*]benzimidazole derivatives and intermediate products in their synthesis [2–5], we continued our studies on new synthetic routes to derivatives of this tricyclic system. As shown in [1], 1-allyl-3-alkyl(arylalkyl, dialkylaminoalkyl)-2-imino-2,3-dihydro-1*H*-benzimidazoles take up hydrogen bromide at the allyl group, and next follows heterocyclization with formation of 9-substituted 2-methyl-2,3-dihydroimidazo[1,2-*a*]benzimidazoles. Some cyclization products exhibited interesting biological properties [6]. In continuation of these studies, we synthesized 1-allyl-2-aminobenzimidazoles containing an acylmethyl group in the 3-position. We anticipated that these polyfunctional compounds could give rise to various derivatives via reactions involving both allyl and carbonyl groups.

1-Allyl-1*H*-benzimidazol-2-amine (**I**) was subjected to quaternization with acylmethyl bromides in acetone [7] or acetonitrile; alternatively, compound **I** was fused with a small excess of chloroacetone. By cyclization of benzimidazolium halides **IIa**–**IId** on heating in boiling aqueous alcohol in the presence of $NaHCO_3$ or Na_2CO_3 we obtained 2-R-9-allylimidazo[1,2-*a*]benzimidazoles **IVa**–**IVd** (Scheme 1). However, the latter were formed much more readily when imines **IIIa**–**IIId** (obtained from bromides **IIa**–**IId** by treatment with an ammonia solution) were heated for a short time at the melting point. Closure of new imidazole ring resulted in disappearance of CH_2 (δ 5.45–6.05 ppm) and NH_2 (NH) proton signals from the ^{1}H NMR spectra of cyclization products **IV**, as well as of absorption band typical of stretching vibrations of carbonyl (1724–1690 cm^{-1} for salts **II** and 1690–1675 cm^{-1} for free bases **III**), amino (3340–3190 and 3175–3150 cm^{-1}), and imino groups (3280–3240 cm^{-1}) from the IR spectra.

Like 1-allyl-3-alkyl(arylalkyl)-2-aminobenzimidazolium salts [1], compounds **IIa**–**IIc** take up hydrogen bromide at the allyl group on heating in boiling concentrated hydrobromic acid; simultaneously, intramolecular cyclization with participation of the amino and carbonyl groups occurred to give tricyclic 2-R-9-(2-bromopropyl)imidazo[1,2-*a*]benzimidazoles **Va**–**Vc** [8]. The latter can also be obtained by heating 9-allyl derivatives **IVa**–**IVc** with concentrated hydrobromic acid. The ^{1}H NMR spectrum of **V** contained a doublet at 1.76–1.82 ppm (J_{HH} = 6.7 Hz) from the methyl protons instead of signals typical of vinyl group ($CH=CH_2$) in initial compounds **II** or **IV**. In the reaction with salt **IId**, the cyclization and hydrogen

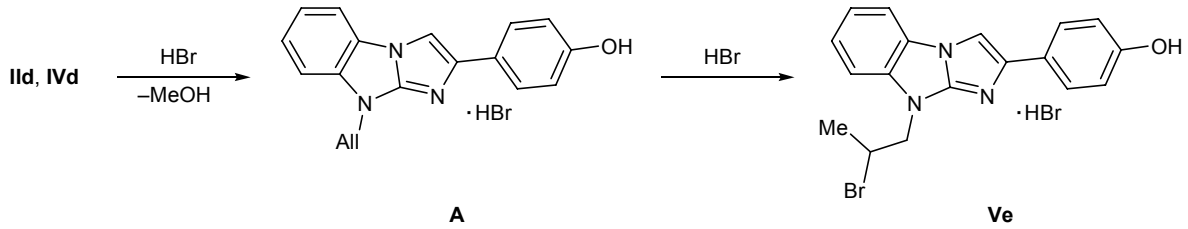
* For communication XXVIII, see [1].

Scheme 1.



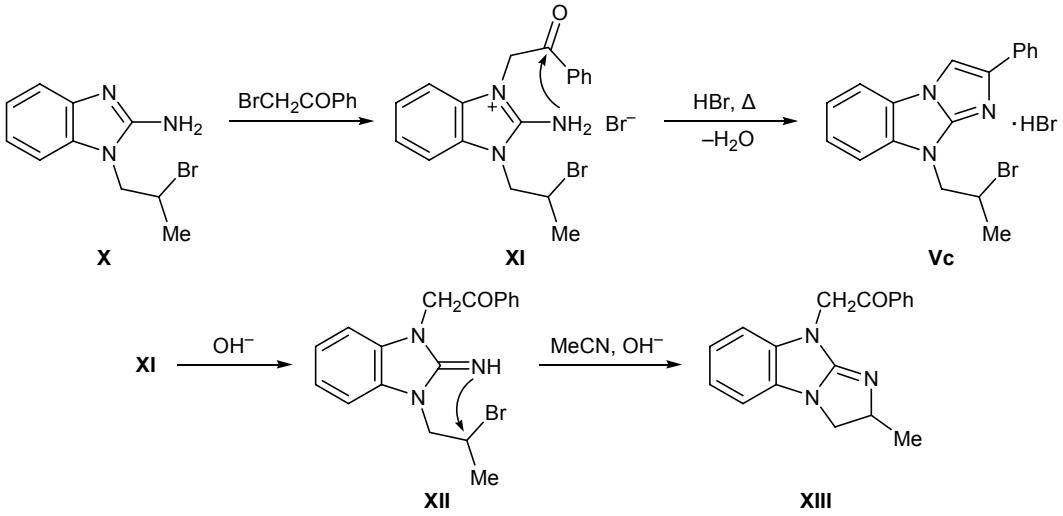
II–**IX**, R = Me (**a**), *t*-Bu (**b**), Ph (**c**), 4-$MeOC_6H_4$ (**d**), 4-HOC_6H_4 (**e**); **IX**, R′ = Me (**c**), Et (**d**); X = Cl, Br.

Scheme 2.



bromide addition were accompanied by hydrolysis of methoxy group in the aromatic ring. According to the ^{1}H NMR data, the reaction begins with hydrolysis of the ether moiety and simultaneous cyclization (the MeO signal at δ 3.88 ppm disappeared) with formation of poorly soluble phenol **A**, and then addition of HBr at the allyl double bond starts (Scheme 2). Insofar as the reaction requires fairly severe conditions, both processes occur simultaneously, thus leading to a mixture of products that are difficult to separate. Compound **Ve** becomes the major product only when the reaction time is considerably increased. Prolonged

Scheme 3.



heating of compound **IVd** in concentrated hydrobromic acid also led to the formation of 2-bromopropyl derivative **Ve**.

The halogen atom in bromopropyl derivatives **Va**–**Vc** and **Ve** is fairly labile; it is readily replaced by morpholino group on heating to give previously unknown 9-(2-morpholinopropyl) derivatives **VIb** and **VIc**. Introduction of a bulky morpholine fragment creates steric hindrances to rotation of the 9-alkyl group, so that protons in the methylene group on N^9 become magnetically nonequivalent, and they resonate as two multiplets at δ 3.96–4.13 and 4.25–4.40 ppm.

Acylmethyl derivatives **II** can be used to obtain 3-acyl-9-allyl-2-R-imidazo[1,2-*a*]benzimidazoles [9]. Heating of salt **IIa** in acetic anhydride in the presence of sodium acetate resulted in acetylation of the imino group and subsequent cyclization with participation of the carbonyl group on the nitrogen atom and acylmethyl substituent with formation of ketone **VII** (Scheme 1).

Imidazo[1,2-*a*]benzimidazoles **IV** are π-excessive heterocycles [10–12] and are capable of reacting with electrophiles at the C^3 atom. For example, the reaction of compounds **IVc** and **IVd** with such a weak electrophile as phenyl isocyanate afforded the corresponding 3-carbothioamides **VIIIc** and **VIIId** in almost quantitative yield. The structure of compounds **VIII** is confirmed by the presence in their ^{1}H NMR spectra of additional signals from aromatic protons and of a downfield singlet at δ 11.64–11.89 ppm due to NH proton. Likewise, reactions of **IVc** and **IVd** with carboxylic acid anhydrides gave 3-acetyl and 3-propanoyl derivatives **IXc** and **IXd** whose ^{1}H NMR spectra lacked 3-H signal but contained signals from the COAlk fragment. The carbonyl absorption band appeared in the IR spectra of **IXc** and **IXd** at 1640–1615 cm^{-1}.

Quaternization of 1-(2-bromopropyl)-1*H*-benzimidazol-2-amine (**X**) [1] with phenacyl bromide in acetone gave salt **XI** which was found to undergo cyclization along two pathways, depending on the conditions. By heating bromide **XI** with excess 48% hydrobromic acid we obtained hydrobromide **Vc** (Scheme 3). In this case, the reaction followed the above pattern [7] involving interaction of the carbonyl and amino groups and subsequent aromatization via elimination of water. The ^{1}H NMR spectrum of the product contained signals belonging to bromopropyl substituent, whereas those assignable to CH_2CO fragment were absent.

By treatment of salt **XI** with alkali we obtained imine **XII** which was converted into 2-methyl-9-phenacyl-2,3-dihydroimidazo[1,2-*a*]benzimidazole hydrobromide (**XIII**) on heating in acetonitrile (Scheme 3). Here, the cyclization occurred as a result of intramolecular nucleophilic attack by the imino group on the CHBr carbon atom and elimination of HBr molecule. Ketone **XIII** displayed in the ^{1}H NMR spectrum a doublet at δ 5.21 ppm (J = 6.5 Hz) from the 9-C$\mathbf{H}_2$COPh substituent, and protons in the C^3H_2 methylene group resonated as two triplets at δ 3.41 (J_{HH} = 7.9 Hz, axial) and 4.03 ppm (J_{HH} = 8.5 Hz, equatorial). The IR spectrum of **XIII** contained an absorption band at 1695 cm^{-1} due to stretching vibrations of the carbonyl group.

We can conclude that 1-allyl-2-amino-3-acylmethyl- and 2-amino-3-acylmethyl-1-(2-bromopropyl)-benzimidazolium halides are convenient initial com-

pounds for the synthesis of imidazo[1,2-*a*]benzimidazole and 2,3-dihydroimidazo[1,2-*a*]benzimidazole derivatives.

EXPERIMENTAL

The progress of reactions was monitored, and the purity of the isolated compounds was checked, by TLC on aluminum oxide using chloroform as eluent; spots were visualized by treatment with iodine vapor in a moist chamber. The IR spectra were recorded on a Specord 75IR spectrometer from samples dispersed in mineral oil. The ^{1}H NMR spectra were obtained on a Varian XL-300 spectrometer at 300 MHz.

1-Allyl-1*H*-benzimidazol-2-amine (**I**) was synthesized according to the procedure described in [1].

1-Allyl-2-amino-3-(2-oxopropyl)benzimidazolium chloride (IIa). A mixture of 1.7 g (10 mmol) of amine **I**, 1.5 ml of chloroacetone, and 5 ml of acetone (or 1.5 ml of methanol) was heated to 60–70°C and was kept at that temperature until the solvent (acetone or methanol) evaporated completely. The mixture was then heated to 85–90°C and kept for 30 min at that temperature. After cooling, the melt was ground with acetone (20–25 ml), and the precipitate was filtered off and washed with acetone. Yield 2.5 g (94%), colorless fiber-like crystals, mp 189–190°C (decomp., from EtOH). IR spectrum, ν, cm^{-1}: 3190, 3150 (NH_2), 1715 (C=O), 1665 (C=N), 1600, 1525, 1490 (C=C). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.29 s (3H, CH_3), 4.92 d (2H, CH_2, J = 5.3 Hz), 5.03–5.28 m (2H, CH_2), 5.45 s (2H, CH_2CO), 5.81–6.01 m (1H, CH), 7.21–7.61 m (4H, H_{arom}), 9.34 s (2H, NH_2). Found, %: C 58.69; H 6.12; Cl 13.40; N 15.9. $C_{13}H_{16}ClN_3O$. Calculated, %: C 58.76; H 6.07; Cl 13.34; N 15.75.

1-Allyl-2-amino-3-(3,3-dimethyl-2-oxobutyl)-benzimidazolium bromide (IIb). Amine **I**, 1.7 g (10 mmol), was dissolved in 60 ml of acetone, 2.2 ml of technical grade 1-bromo-3,3-dimethylbutan-2-one was added, and the mixture was thoroughly stirred and left to stand overnight at room temperature. The precipitate was filtered off and washed with acetone. Yield 3.3 g (98%), white fiber-like highly electrifiable crystals, mp 261–262°C (decomp., from EtOH, sweats at 234–235°C). IR spectrum, ν, cm^{-1}: 3330, 3150 (NH_2), 1724 (C=O), 1669, 1607, 1525, 1490, 1470 (C=C, C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.23 s [9H, $C(CH_3)_3$], 4.90 d (2H, CH_2, J = 4.9 Hz), 5.05–5.23 m (2H, CH_2), 5.56 s (2H, CH_2CO), 5.85–6.03 m (1H, CH), 7.22–7.33 q (2H, 5-H, 6-H), 7.41 d (1H, 7-H, J = 7.7 Hz), 7.56 d (1H, 4-H, J = 7.7 Hz), 8.91 s (2H, NH_2). Found, %: C 54.62; H 6.20; Br 22.63; N 12.00. $C_{16}H_{22}BrN_3O$. Calculated, %: C 54.55; H 6.29; Br 22.68; N 11.93.

1-Allyl-2-amino-3-(2-oxo-2-phenylethyl)benzimidazolium bromide (IIc) was synthesized in a similar way from 1.7 g (10 mmol) of amine **I** and 2.0 g (10 mmol) of phenacyl bromide in 40 ml of acetone. Yield 3.6 g (97%), mp 242–244°C (from EtOH). IR spectrum, ν, cm^{-1}: 3200, 3150 (NH_2), 1690 (C=O), 1665, 1600, 1500, 1460 (C=C, C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 4.95 d (2H, CH_2, J = 5.4 Hz), 5.19–5.33 m (2H, CH_2), 5.90–6.05 m (3H, CH, CH_2CO), 7.21–7.35 m (2H, 5-H, 6-H), 7.49–7.78 m (5H, H_{arom}), 8.10 d (1H, 4-H, J = 7.4 Hz), 8.95 s (2H, NH_2). Found, %: C 58.00; H 4.95; Br 21.54; N 11.22. $C_{18}H_{18}BrN_3O$. Calculated, %: C 58.08; H 4.87; Br 21.46; N 11.29.

1-Allyl-2-amino-3-[2-(4-methoxyphenyl)-2-oxoethyl]benzimidazolium bromide (IId) was synthesized from equivalent amounts of amine **I** and 4-methoxyphenacyl bromide in acetone. Yield 99%, mp 239–241°C (decomp., from EtOH). IR spectrum, ν, cm^{-1}: 3340, 3175 (NH_2), 1690 (C=O), 1675, 1610, 1475 (C=C, C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.88 s (3H, OCH_3), 4.47 d (2H, CH_2, J = 5.7 Hz), 5.12–5.22 m (2H, CH_2), 5.35 s (2H, CH_2CO), 5.80–5.95 m (1H, CH), 6.72–6.89 (4H, H_{arom}), 7.03 d (2H, 5-H, 6-H, J = 8.7 Hz), 8.05 d (2H, 4-H, 7-H, J = 8.7 Hz). Found, %: C 56.78; H 5.09; Br 20.77; N 10.38. $C_{19}H_{20}BrN_3O_2$. Calculated, %: C 56.73; H 5.01; Br 19.86; N 10.45.

1-(3-Allyl-2-imino-2,3-dihydro-1*H*-benzimidazol-1-yl)propan-2-one (IIIa). Chloride **IIa**, 2.7 g (10 mmol), was treated with 15 ml of 22% aqueous ammonia at room temperature. After 3 h, the precipitate was filtered off and dried in air. Yield quantitative, mp 80–85°C. Melting was accompanied by cyclization into 9-allyl-2-methylimidazo[1,2-*a*]benzimidazole (**IVa**). Imine **IIIa** underwent spontaneous cyclization upon attempted recrystallization or storage at room temperature. IR spectrum, ν, cm^{-1}: 3280 (NH), 1675 (C=O), 1615, 1475, 1435 (C=C, C=N). Found, %: C 68.15; H 6.62; N 18.43. $C_{13}H_{15}N_3O$. Calculated, %: C 68.10; H 6.59; N 18.35.

Compounds **IIIb**–**IIId** were synthesized in a similar way.

1-(3-Allyl-2-imino-2,3-dihydro-1*H*-benzimidazol-1-yl)-3,3-dimethylbutan-2-one (IIIb). Yield 98%, mp 107–108°C (from hexane). IR spectrum, ν, cm^{-1}: 3280 (NH), 1675 (C=O), 1615, 1475, 1435 (C=C,

C=N). Found, %: C 70.88; H 7.74; N 15.55. $C_{16}H_{21}N_3O$. Calculated, %: C 70.82; H 7.80; N 15.48.

2-(3-Allyl-2-imino-2,3-dihydro-1*H*-benzimidazol-1-yl)-1-phenylethanone (IIIc). Yield 95–98%, mp 157–158°C (from MeCN). IR spectrum, ν, cm^{-1}: 3240 (NH), 1690 (C=O), 1630, 1620, 1600, 1500, 1475, 1455 (C=C, C=N). Found, %: C 74.16; H 5.90; N 14.48. $C_{18}H_{17}N_3O$. Calculated, %: C 74.21; H 5.88; N 14.42.

2-(3-Allyl-2-imino-2,3-dihydro-1*H*-benzimidazol-1-yl)-1-(4-methoxyphenyl)ethanone (IIId). Yield quantitative, mp 148–149°C (from MeCN). IR spectrum, ν, cm^{-1}: 3245 (NH), 1695 (C=O), 1630, 1600, 1510, 1475 (C=C, C=N). Found, %: C 70.94; H 6.04; N 12.98. $C_{19}H_{19}N_3O_2$. Calculated, %: C 71.01; H 5.96; N 13.07.

9-Allyl-2-methylimidazo[1,2-*a*]benzimidazole (IVa). Imine **IIIa**, 2.3 g (10 mmol), was placed into an open test tube and was heated at 80–90°C until the reaction was complete (10–15 min; the reaction was accompanied by liberation of water). The resulting material was dissolved in a minimal amount of chloroform, the solution was passed through a layer of Al_2O_3 with elution with chloroform, and the first fraction was collected. Evaporation of the eluate gave colorless crystals. Yield 1.8 g (85%), mp 82–83°C (from hexane). IR spectrum, ν, cm^{-1}: 1645 (C=N), 1600, 1505, 1475, 1460 (C=C). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 2.48 s (3H, CH_3), 5.09 d (2H, CH_2, J = 5.8 Hz), 5.27–5.45 m (2H, CH_2), 6.02–6.13 m (1H, CH), 7.38–7.54 m (2H, 6-H, 7-H), 7.76 d (1H, 5-H, J = 8.4 Hz), 7.95 s (1H, 3-H), 8.05 d (1H, 8-H, J = 8.4 Hz). Found, %: C 73.85; H 6.20; N 19.95. $C_{13}H_{13}N_3$. Calculated, %: C 73.91; H 6.20; N 19.89.

9-Allyl-2-*tert*-butylimidazo[1,2-*a*]benzimidazole hydrochloride (IVb). *a*. Free base **IVb** was synthesized by heating 1.1 g (4 mmol) of imine **IIIb** at 140–145°C (20–25 min, R_f 0.9). Chromatographic purification gave an oily substance which was dissolved in acetone, and the solution was acidified with a solution of HCl in isopropyl alcohol. Yield 1.1 g (93%), mp 261–262°C (from *i*-PrOH). IR spectrum, ν, cm^{-1}: 2385–2670 (N^+H), 1660, 1605, 1520, 1480, 1460 (C=C, C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.40 s [9H, $C(CH_3)_3$], 5.19–5.42 m (4H, NCH_2, CH_2), 5.96–6.16 m (1H, CH), 7.40–7.56 m (2H, 6-H, 7-H), 7.72 d (1H, 5-H, J = 8.6 Hz), 7.95 s (1H, 3-H), 8.04 d (1H, 8-H, J = 8.6 Hz). Found, %: C 66.24; H 7.04; Cl 12.15; N 14.57. $C_{16}H_{19}N_3 \cdot HCl$. Calculated, %: C 66.31; H 6.96; Cl 12.23; N 14.50.

b. Benzimidazolium salt **IIb**, 0.8 g, was heated in 30 ml of a 5% solution of Na_2CO_3 at the boiling point. When the reaction was complete (12–15 h), the mixture was cooled, free base **IVb** was isolated by extraction, and hydrochloride **IVb** was obtained as described above in *a*. Yield 0.6 g (91%), mp 261–262°C.

9-Allyl-2-phenylimidazo[1,2-*a*]benzimidazole (IVc) was synthesized by heating imine **IIIc** at 160–165°C over a period of 15 min. Yield 95%, mp 101–102°C (from *i*-PrOH or EtOAc). Found, %: C 79.18; H 5.49; N 15.33. $C_{18}H_{15}N_3$. Calculated, %: C 79.10; H 5.53; N 15.37.

9-Allyl-2-phenylimidazo[1,2-*a*]benzimidazole hydrochloride was obtained by acidification of a solution of free base **IVc** in acetone with concentrated hydrochloric acid. Yield 95%, mp 234–236°C (decomp., from EtOH). IR spectrum, ν, cm^{-1}: 1650 (C=N), 1625, 1620, 1610, 1500, 1475, 1455 (C=C). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 5.21–5.57 m (4H, NCH_2, CH_2), 6.02–6.17 m (1H, CH), 7.31–7.58 m (5H, H_{arom}), 7.71 d (1H, H_{arom}, J = 8.0 Hz), 7.92–8.05 m (3H, H_{arom}), 8.62 s (1H, 3-H), 15.37 br.s (1H, N^+H). Found, %: C 69.88; H 5.15; Cl 11.35; N 13.62. $C_{18}H_{15}N_3 \cdot HCl$. Calculated, %: C 69.79; H 5.21; Cl 11.44; N 13.56.

9-Allyl-2-(4-methoxyphenyl)imidazo[1,2-*a*]benzimidazole (IVd). *a*. A mixture of 8 g (20 mmol) of bromide **IId**, 4 g of Na_2CO_3, and 100 ml of water was heated at the boiling point until the cyclization was complete (~12 h). The mixture was cooled and extracted with chloroform, the extract was passed through a layer of γ-Al_2O_3 (eluent $CHCl_3$), the eluate was evaporated, and the residue was recrystallized from isopropyl alcohol or acetonitrile. Yield 5.4–5.8 g (90–96%), mp 128–129°C. Found, %: C 75.28; H 5.59; N 13.93. $C_{19}H_{17}N_3O$. Calculated, %: C 75.23; H 5.65; N 13.85.

b. Imine **IIId** was heated at 150°C until water no longer evolved (10–15 min). The melt was recrystallized from acetonitrile. Yield 89%.

9-Allyl-2-(4-methoxyphenyl)imidazo[1,2-*a*]benzimidazole hydrochloride was obtained by acidification of a solution of free base **IVd** in acetone with concentrated hydrochloric acid. Yield 96%, mp 252–254°C (decomp., from EtOH). IR spectrum, ν, cm^{-1}: 1655, 1620, 1610, 1505, 1475, 1450 (C=C, C=N). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 3.84 s (3H, OCH_3), 5.33 d (2H, CH_2, J = 5.7 Hz), 5.40–5.61 m (2H, CH_2), 6.03–6.20 m (1H, CH), 6.98 d (2H, H_{arom}, J = 4.5 Hz), 7.35–7.52 m (2H, H_{arom}), 7.76 d (1H, H_{arom}, J = 6.4 Hz), 7.92–8.04 m (3H, H_{arom}), 8.36 s

(1H, 3-H). Found, %: C 67.22; H 5.29; Cl 10.35; N 12.44. $C_{19}H_{17}N_3O \cdot HCl$. Calculated, %: C 67.16; H 5.34; Cl 10.43; N 12.37.

9-(2-Bromopropyl)-2-methylimidazo[1,2-*a*]benzimidazole (Va). A mixture of 1.3 g (5 mmol) of chloride **IIa** and 15 ml of concentrated hydrobromic acid (bp 128°C) was heated for 18 h under reflux. The mixture was evaporated to a small volume under reduced pressure (water-jet pump), and the residue was left to stand in a refrigerator. The precipitate of salt **Va** was filtered off, thoroughly washed with acetone to remove traces of acid, dried in air, and treated with a 22% solution of ammonia at room temperature. Yield 0.9 g (62%), mp 81–82°C (from hexane). IR spectrum, ν, cm^{-1}: 1625, 1600, 1555, 1500, 1470 (C=C, C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.76 d (3H, CH_3, J = 6.7 Hz), 2.36 s (3H, CH_3), 4.37–4.46 m (2H, CH_2), 4.60–4.77 m (1H, CH), 7.00–7.50 m (5H, H_{arom}). Found, %: C 53.36; H 4.79; Br 27.41; N 14.44. $C_{13}H_{14}BrN_3$. Calculated, %: C 53.44; H 4.83; Br 27.35; N 14.38.

2-*tert*-Butyl-9-(2-bromopropyl)imidazo[1,2-*a*]benzimidazole hydrobromide (Vb). A mixture of 3.5 g (10 mmol) of bromide **IIb** and 40 ml of 48% hydrobromic acid was heated for 12–15 h under reflux. After cooling, the precipitate was filtered off on a glass filter, thoroughly squeezed, and washed with acetone. Yield 2.9 g, mp 233–234°C (from EtOH). IR spectrum, ν, cm^{-1}: 3100, 2550–2720 (N^+H), 1645, 1615, 1515, 1470 (C=C, C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.40 s [9H, $C(CH_3)_3$], 1.77 d (3H, CH_3, J = 6.7 Hz), 4.70–4.90 m (3H, CH_2, CH), 7.40–7.62 m (2H, H_{arom}), 7.93–8.10 m (3H, H_{arom}), 13.75 br.s (1H, N^+H). Found, %: C 46.20; H 5.24; Br 38.57; N 10.19. $C_{16}H_{20}BrN_3 \cdot HBr$. Calculated, %: C 46.29; H 5.10; Br 38.49; N 10.12.

9-(2-Bromopropyl)-2-phenylimidazo[1,2-*a*]benzimidazole hydrobromide (Vc). *a*. A mixture of 7.4 g (20 mmol) of bromide **IIc** and 80 ml of 48% hydrobromic acid was heated for 10 h under reflux (R_f values of the initial compound and final product 0.3 and 0.9, respectively). Bromide **IIc** did not dissolve during the process but was transformed into a difficultly filterable solid. Therefore, the mixture was cooled, diluted with an equal volume of acetone, and thoroughly stirred. After 2 h, the precipitate was filtered off and washed with acetone. Yield 7.6 g (87%), mp 231–232°C (from 50% EtOH). Found, %: C 49.59; H 3.89; Br 36.81; N 9.71. $C_{18}H_{16}BrN_3 \cdot HBr$. Calculated, %: C 49.68; H 3.94; Br 36.72; N 9.66.

b. Compound **XI** was heated in boiling concentrated hydrobromic acid over a period of 3 h. Yield 90%.

Free base **Vc** was isolated from the hydrobromide by treatment with alkali. Yield quantitative. mp 42–43°C (from EtOAc). IR spectrum, ν, cm^{-1}: 1635, 1600, 1550, 1500, 1475 (C=C, C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.80 d (3H, CH_3, J = 6.7 Hz), 4.45–4.54 m (2H, CH_2), 4.68–4.88 m (1H, CH), 7.14–7.44 m (6H, H_{arom}), 7.52 d (1H, H_{arom}, J = 7.4 Hz), 7.63 s (1H, 3-H), 7.84 d (2H, 5-H, 8-H, J = 7.6 Hz). Found, %: C 61.10; H 4.48; Br 22.48; N 11.94. $C_{18}H_{16}BrN_3$. Calculated, %: C 61.03; H 4.55; Br 22.56; N 11.86.

9-(2-Bromopropyl)-2-(4-hydroxyphenyl)imidazo[1,2-*a*]benzimidazole hydrobromide (Ve). A mixture of 2.0 g (5 mmol) of bromide **IId** and 30 ml of 48% hydrobromic acid was heated for 30 h at the boiling point. The mixture was cooled, and the precipitate of hydrobromide **Ve** was filtered off and washed with acetone. Yield 1.8 g (81%), mp 239–240°C (decomp., from EtOH–DMF). IR spectrum, ν, cm^{-1}: 3410, 1640, 1600, 1550, 1500, 1475 (C=C, C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 1.84 d (3H, CH_3, J = 5.7 Hz), 4.74–4.98 m (3H, CH_2, CH), 7.37–7.63 m (5H, H_{arom}), 7.80–8.08 m (3H, H_{arom}), 8.60 s (1H, 3-H). Found, %: C 47.84; H 3.74; Br 35.51; N 9.40. $C_{18}H_{16}BrN_3O \cdot HBr$. Calculated, %: C 47.92; H 3.80; Br 35.42; N 9.31.

Salt **Vd** was synthesized by prolonged heating of compound **IVd** or its hydrobromide in concentrated hydrobromic acid. Yield 85%.

2-*tert*-Butyl-9-(2-morpholinopropyl)imidazo[1,2-*a*]benzimidazole (VIb). A mixture of 2.1 g (5 mmol) of hydrobromide **Vb** and 8 ml of morpholine was heated for 6–8 h under reflux. The mixture was cooled and diluted with 30–40 ml of water, the oily material was extracted into chloroform, and the extract was washed with water to remove excess morpholine, dried over anhydrous sodium sulfate, and passed through a layer of γ-Al_2O_3 (3×5 cm) using chloroform as eluent. The eluate was evaporated to isolate compound **VIb** as a colorless oily substance. Yield 1.8 g (87%). IR spectrum, ν, cm^{-1}: 1640, 1600, 1590, 1460 (C=C, C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.02 d (3H, CH_3, J = 7.4 Hz), 1.33 s [9H, $C(CH_3)_3$], 2.28–2.40 m (2H, CH_2), 2.60–2.78 m [4H, $N(CH_2)_2$], 3.18–3.31 m (1H, CH), 3.35–3.53 m [4H, $O(CH_2)_2$], 3.96–4.10 m and 4.25–4.37 m (1H each, 9-CH_2), 7.00 s (1H, 3-H), 7.06–7.23 m (3H, 6-H, 7-H, 8-H), 7.42 d (1H, 5-H, J = 7.8 Hz). Found, %: C 70.49; H 8.35; N 16.51. $C_{20}H_{28}N_4O$. Calculated, %: C 70.56; H 8.29; N 16.46.

2-*tert*-Butyl-9-(2-morpholinopropyl)imidazo-[1,2-*a*]benzimidazole dihydrochloride was obtained by acidification of a solution of free base **VIb** in acetone with a solution of HCl in isopropyl alcohol to pH 1–2. Yield 84%, mp 232–233°C (decomp., from acetonitrile).

9-(2-Morpholinopropyl)-2-phenylimidazo[1,2-*a*]-benzimidazole (VIc) was synthesized as described above for **VIb**. Yield 94%, colorless oily substance. IR spectrum, ν, cm^{-1}: 1660, 1615, 1600, 1495, 1480 (C=N, C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.08 d (3H, CH_3, J = 7.7 Hz), 2.40–2.53 m (2H, CH_2), 2.69–2.82 m (4H, NCH_2), 3.24–3.40 m (1H, CH), 3.44–3.61 m (4H, OCH_2), 4.01–4.13 m and 4.27–4.40 m (1H each, 9-CH_2), 7.10–7.44 m (6H, H_{arom}), 7.52 d (1H, H_{arom}, J = 8.8 Hz), 7.62 s (1H, 3-H), 7.84 d (2H, 5-H, 8-H, J = 7.7 Hz). Found, %: C 73.25; H 6.65; N 15.62. $C_{22}H_{24}N_4O$. Calculated, %: C 73.31; H 6.71; N 15.54.

9-(2-Morpholinopropyl)-2-phenylimidazo[1,2-*a*]-benzimidazole dihydrochloride. Yield 88%, mp 252–253°C (from EtOH).

1-(9-Allyl-2-methylimidazo[1,2-*a*]benzimidazol-3-yl)ethanone (VIIa). A mixture of 1.3 g (5 mmol) of chloride **IIa**, 10 ml of acetic anhydride, and 1.0 g of anhydrous sodium acetate was heated for 1 h under reflux. The mixture was cooled, poured into 30 ml of cold water, and (after decomposition of excess acetic anhydride) neutralized with sodium hydrogen carbonate. The oily material was extracted into chloroform, the extract was passed through a column charged with γ-Al_2O_3 using chloroform as eluent, the eluate was evaporated, and the residue was recrystallized from a small amount of ethyl acetate. Yield 1.1 g (84%), mp 79–80°C. IR spectrum, ν, cm^{-1}: 1645 (C=N), 1600, 1505, 1475, 1460 (C=C). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.13 s (3H, CH_3), 2.62 s (3H, CH_3), 4.92 d (2H, CH_2, J = 5.7 Hz), 5.18–5.30 m (2H, CH_2), 5.92–6.06 m (1H, CH), 7.21–7.32 m (3H, 6-H, 7-H, 8-H), 8.46 d (1H, 5-H, J = 7.7 Hz). Found, %: C 71.18; H 5.90; N 16.67. $C_{15}H_{15}N_3O$. Calculated, %: C 71.13; H 5.97; N 16.59.

9-Allyl-2,*N*-diphenylimidazo[1,2-*a*]benzimidazole-3-carbothioamide (VIIIc). A mixture of 5 mmol of free base **IVc** and 1.5 ml of phenyl isothiocyanate was heated until it became homogeneous and was then heated for 15–20 min on a boiling water bath. The mixture was cooled and ground with diethyl ether, and the precipitate was filtered off and washed with diethyl ether. Yield quantitative, mp 234–235°C (from DMF). IR spectrum, ν, cm^{-1}: 1625, 1600, 1545, 1500, 1475 (C=C, C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 4.92 d (2H, CH_2, J = 5.5 Hz), 5.11–5.28 m (2H, CH_2), 5.95–6.14 m (1H, CH), 7.14–7.90 m (13H, H_{arom}), 8.06 d (1H, 5-H, J = 8.2 Hz), 11.89 s (1H, NH). Found, %: C 73.44; H 5.00; N 13.80; S 7.76. $C_{25}H_{20}N_4S$. Calculated, %: C 73.51; H 4.93; N 13.71; S 7.85.

9-Allyl-2-(4-methoxyphenyl)-*N*-phenylimidazo-[1,2-*a*]benzimidazole-3-carbothioamide (VIIId) was synthesized in a similar way. Yield 96%, mp 211–212°C (from DMF). IR spectrum, ν, cm^{-1}: 1620, 1600, 1545, 1500, 1475 (C=C, C=N). ^1H NMR spectrum (DMSO-d_6), δ, ppm: 3.76 s (3H, OCH_3), 4.91 d (2H, CH_2, J = 5.8 Hz), 5.20–5.33 m (2H, CH), 5.99–6.14 m (1H, CH), 6.76–7.93 m (12H, H_{arom}), 8.10 d (1H, 5-H, J = 7.8 Hz), 11.64 s (1H, NH). Found, %: C 71.14; H 5.12; N 12.86; S 7.22. $C_{26}H_{22}N_4OS$. Calculated, %: C 71.21; H 5.06; N 12.78; S 7.31.

1-(9-Allyl-2-phenylimidazo[1,2-*a*]benzimidazol-3-yl)ethanone (IXc). A mixture of 1.4 g (5 mmol) of compound **IVc** and 10 ml of acetic anhydride was heated for 2.5 h under reflux. The mixture was poured into 50 ml of cold water and (after decomposition of excess acetic anhydride) neutralized with sodium hydrogen carbonate. The precipitate was filtered off and purified first by column chromatography on Al_2O_3 using chloroform as eluent and then by recrystallization from acetonitrile or ethyl acetate. Yield 1.3 g (79%), mp 143–144°C. IR spectrum, ν, cm^{-1}: 1640 (C=O), 1620, 1610, 1505, 1475 (C=C, C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.13 s (3H, CH_3), 4.91 d (2H, CH_2, J = 6.0 Hz), 5.20–5.31 m (2H, CH_2), 5.91–6.07 m (1H, CH), 7.23–7.61 m (8H, H_{arom}), 8.77 d (1H, 5-H, J = 7.5 Hz). Found, %: C 76.26; H 5.35; N 13.26. $C_{20}H_{17}N_3O$. Calculated, %: C 76.17; H 5.43; N 13.32.

1-[9-Allyl-2-(4-methoxyphenyl)imidazo[1,2-*a*]-benzimidazol-3-yl]propan-1-one (IXd) was synthesized by heating 1.2 g (4 mmol) of compound **IVd** in 10 ml of propionic anhydride under reflux over a period of 3.5 h. The product was isolated as described above for **IXc**. Yield 1.1 g (78%), mp 137–138°C (from EtOAc). IR spectrum, ν, cm^{-1}: 1630 (C=O), 1615, 1475 (C=C, C=N). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 1.10 t (3H, CH_3), 2.55 q (2H, $COCH_2$), 3.88 s (3H, OCH_3), 5.33–5.60 m (4H, NCH_2, CH_2), 5.95–6.20 m (1H, CH), 7.02–7.73 m (7H, H_{arom}), 8.81 d (1H, 5-H). Found, %: C 73.45; H 5.94; N 11.78. $C_{22}H_{21}N_3O_2$. Calculated, %: C 73.52; H 5.89; N 11.69.

2-Amino-1-(2-bromopropyl)-3-(2-oxo-2-phenylethyl)benzimidazolium bromide (XIa). Phenacyl

bromide, 1.1 g (5.5 mmol), was added to a solution of 1.3 g (5 mmol) of amine **X** [1] in 20 ml of acetone, and the mixture was stirred and left overnight at room temperature. The precipitate was filtered off and washed with acetone. Yield 96%, mp 223–224°C (from aqueous EtOH). IR spectrum, ν, cm^{-1}: 3152, 3327 (NH_2), 1690 (C=O), 1663 (C=N), 1630, 1603, 1524, 1492, 1467 (C=C). Found, %: C 47.64; H 4.31; Br 35.19; N 9.35. $C_{18}H_{19}Br_2N_3O$. Calculated, %: C 47.71; H 4.23; Br 35.26; N 9.27.

2-[3-(2-Bromopropyl)-2-imino-2,3-dihydrobenzimidazol-1-yl]-1-phenylethanone (XII). Bromide **XI**, 1.8 g (4 mmol), was treated with 20 ml of 22% aqueous ammonia at 20–25°C. After 3 h, the precipitate was filtered off, washed with water, and dried in air. Yield 1.4 g (92%), mp 76–78°C (from EtOAc). IR spectrum, ν, cm^{-1}: 3285 (NH), 1670 (C=O), 1620, 1560, 1495, 1475, 1435 (C=C, C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.74 d (3H, CH_3, J = 6.7 Hz), 4.00–4.23 m (2H, CH_2), 4.37–4.52 m (1H, CH), 5.27 s (2H, CH_2CO), 6.67 m (1H, H_{arom}), 6.88–7.04 m (3H, H_{arom}), 7.45–7.68 m (3H, H_{arom}), 8.04 d (2H, 5-H, 8-H, J = 7.2 Hz). Found, %: C 58.00; H 4.94; Br 21.54; N 11.20. $C_{18}H_{18}BrN_3O$. Calculated, %: C 58.08; H 4.87; Br 21.46; N 11.29.

2-(2-Methyl-2,3-dihydroimidazo[1,2-*a*]benzimidazol-9-yl)-1-phenylethanone (XIII). A mixture of 0.74 g (2 mmol) of imine **XII** and 10 ml of acetonitrile was heated for 5–6 h under reflux. The mixture was evaporated, and the residue, compound **XIII** hydrobromide, was recrystallized from ethanol. Yield 0.7 g (94%), mp 223–224°C.

Free base **XIII** was isolated by treatment of its hydrobromide with 22% aqueous ammonia, followed by extraction with chloroform. Evaporation of the extract gave yellowish crystals. Yield 96%, mp 133–134°C (from MeCN). IR spectrum, ν, cm^{-1}: 1695 (C=O), 1640, 1585, 1475, 1445 (C=C, C=N). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.39 d (3H, CH_3, J = 6.5 Hz), 3.41 t (1H, 3-H_{ax}, J = 7.9 Hz), 4.03 t (1H, 3-H_{eq}, J = 8.5 Hz), 4.53–4.68 m (1H, CH), 5.21 d (2H, CH_2CO, J = 4.8 Hz), 6.58–7.00 m (4H, H_{arom}), 7.40–7.66 m (3H, H_{arom}), 7.98–8.08 m (2H, 5-H, 8-H). Found, %: C 74.30; H 5.82; N 14.35. $C_{18}H_{17}N_3O$. Calculated, %: C 74.21; H 5.88; N 14.42.

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