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Polyfunctional Imidazoles: VI.* Synthesis of 2-Amino-1-aryl-4-chloro-1*H*-imidazole-5-carboxylic Acids Derivatives

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Abstract—Aryl-2,4-dichloro-5-formylimidazoles by a successive treatment with hydroxylamine and thionyl chloride were converted into 1-aryl-2,4-dichloroimidazole-5-carbonitriles which by the action of sodium azide and tin(II) chloride were transformed into 2-amino-1-aryl-4-chloroimidazole-5-carbonitriles. The consecutive reactions of 2-azido-1-aryl-4-chloro-5-formylimidazoles with N-bromosuccinimide, methanol, or amides led to the formation of methyl esters and amides of 2-azido-1-aryl-4-chloroimidazole-5-carboxylic acids. The reduction of the latter with tin(II) chloride resulted in the corresponding derivatives of 2-amino-1-aryl-4-chloroimidazole-5-carboxylic acids, and the reduction of 2-azido-1-aryl-4-chloroimidazole-5-carboxylic acids was accompanied with decarboxylation and yielded 2-amino-1-aryl-4-chloroimidazoles.

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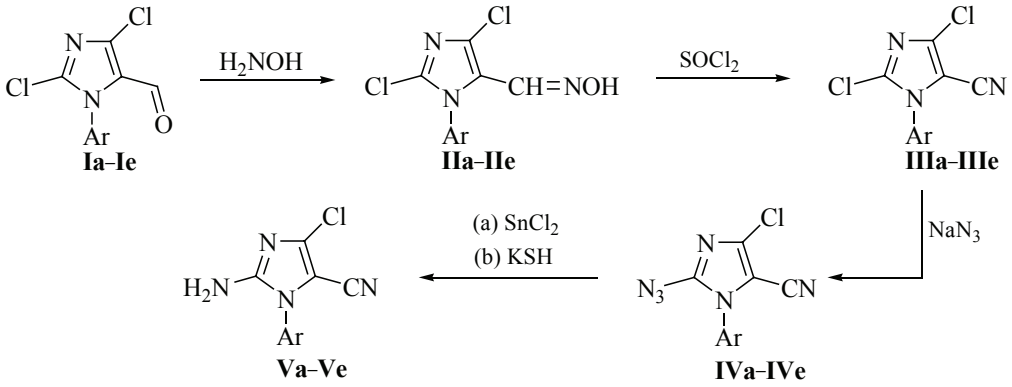
2-Aminoimidazoles are widely used in the synthesis of compounds with a pronounced biological action [2–4]. Besides the structural fragment of 2-aminoimidazole is present in the composition of some alkaloids isolated from sea animals [5–7].

Two approaches are commonly used in the synthesis of 2-aminoimidazole and its derivatives. The first one includes the formation of the imidazole ring with the simultaneous introduction of the amine function and consists in the condensation of α-aminocarbonyl compounds with cyanamide [8–10], α-diketones with guanidine [11]. or α-haloketones with *N*-acetylguanidine [12]. The second approach involves the introduction of the amine function into the position *2* of the imidazole ring by (a) coupling with aryldiazonium salts followed by reduction [13], (b) metallation with subsequent treatment with arylazides and acids [14], (c) exchange reaction of 2-chloroimidazoles with *N*,*N*-dialkylamines [15]. Yet the mentioned transformations are unsuitable for the preparation of imidazole derivatives with a free amino group in the position *2*. Therefore we regarded as useful the development of efficient procedures for the synthesis of 2-aminoimidazoles containing in the position *4* a chlorine atom, and the position *5* a nitrile, carboxy, ester , or amido group. The introduction into the imidazole ring of a chlorine atom supplies it with fungicidal properties[16, 17], and of a cyano group results in the fungicidal [18] and herbicidal [19] activity. The ester group turned out to be very useful for the chemical modification of the imidazole ring [2, 4].

For the purposeful introduction of the amino group we chose the recently synthesized [15] 1-aryl-2,4-dichloro-5-formylimidazoles **Ia–Ie** which were turned with the use of hydroxylamine into oximes **IIa–IIe** and further by treating with thionyl chloride were converted into nitriles **IIIa–IIIe**. The direct replacement of the chlorine atom in the position *2* of compounds **III** by heating with alcoholic ammonia failed, and therefore we used the introduction of an azido group in the mentioned position. 2,4-Dichloro-5-cyanoimidazoles **IIIa–IIIe** under mild conditions (DMF, 20°C) cleanly reacted with sodium azide giving 2-azido-substituted derivatives **IVa–IVe** whose reduction with tin(II) chloride (procedure *a*) or with potassium hydrogen sulfide (procedure *b*) afforded 2-amino-4-chloroimidazole-5-carbonitriles **Va–Ve**.

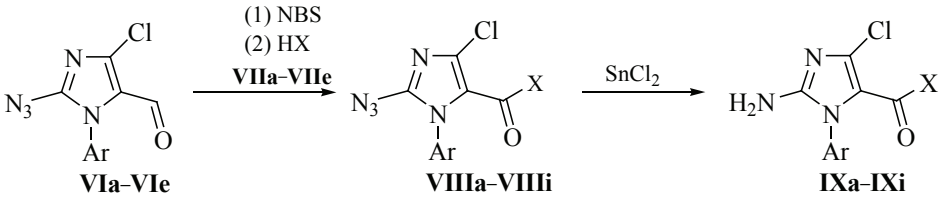
* For Communication V, see [1].



Ar = Ph (**a**), 4-FC_6H_4 (**b**), 4-BrC_6H_4 (**c**), 4-MeC_6H_4 (**d**), 4-$MeOC_6H_4$ (**e**).

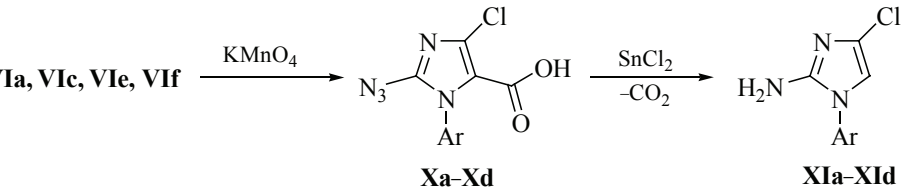
The structure of aminonitriles **Va–Ve** is in agreement with their spectral characteristics. The IR spectra contain the absorption bands of the C≡N (2215–2225 cm^{-1}) and NH_2 (3415–3430 cm^{-1}) groups. In the ^1H NMR spectra the signal of the amino group is observed in the range 6.64–6.72 ppm The characteristic signals in the ^{13}C NMR spectra are the singlets of the carbon atoms of the imidazole ring: 95–96 (C^5), 132–139 (C^2), 147–151ppm (C^4) and of C≡N group (109–111ppm).

The synthesis of esters and amides of 2-amino-4-chloro-imidazole-5-carboxylic acids was performed with the use of 2-azido-4-chloro-5-formylimidazoles **VIa–VIe** [15]. Their bromination with *N*-bromosuccinimide followed by the treatment of the obtained acyl bromides with methanol (**VIIa**) or amines (**VIIb–VIIe**) furnished esters **VIIIa–VIIIe** and amides **VIIIf–VIIIi** of 2-azido-4-chloroimidazole-5-carboxylic acids. The latter by the reaction with tin(II) chloride were mildly reduced into derivatives of 2-amino-4-chloro-imidazole-5-carboxylic acids **IXa–IXi**.



VI, Ar = Ph (**a**), 4-FC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 4-BrC_6H_4 (**d**), 4-MeC_6H_4(**e**); **VII, X** = MeO (**a**), $PhCH_2NH$ (**b**), 4-MeC_6H_4NH (**c**), 3-FC_6H_4NH (**d**), $(CH_2)_5N$ (**e**); **VIII, IX, X** = MeO, Ar = Ph (**a**), 4-FC_6H_4 (**b**), 4-ClC_6H_4 (**c**), 4-BrC_6H_4 (**d**), 4-MeC_6H_4 (**e**); X = $PhCH_2NH$, Ar =Ph (**f**); X = 4-MeC_6H_4NH, Ar = 4-ClC_6H_4 (**g**); X = 3-FC_6H_4NH, Ar = 4-MeC_6H_4 (**h**); X = $(CH_2)_5N$, Ar = 4-BrC_6H_4 (**i**).

Formerly [20] the alkaline hydrolysis of esters of 2-amino-4-cyanoimidazole-5-carboxylic acids made it possible to obtain the proper acids that are prone to decarboxylation at the temperature over 200°C. Our attempt to hydrolyze esters **IXa, IXb** with lithium hydroxide under mild conditions was unsuccessful. In the formed complex mixture of compounds no corresponding acids were detected. We tried to synthesize them from azidoaldehydes **VIa, VIc, VIe, VIf** by first oxidation of the aldehyde group and further reduction of the azido group. The oxidation of these aldehydes with potassium permanganate was an ambiguous process, and azidoacids **Xa–Xd** were isolated only in 20–25% yield. At the reduction of the latter products with tin(II) chloride under mild



VI, Ar = 4-$MeOC_6H_4$ (**f**); **X, XI**, Ar = Ph (**a**), 4-ClC_6H_4 (**b**), 4-MeC_6H_4 (**c**), 4-$MeOC_6H_4$ (**d**).

conditions alongside the reduction of the azido group decarboxylation occurred giving previously unknown 4-chloroimidazol-2-amines **XIa–XId** whose ^{1}H NMR spectra besides the singlets of the protons of NH_2 group (5.58–5.63 ppm) contained the singlets of the protons H^5 of the imidazole ring at 6.82–6.91 ppm.

EXPERIMENTAL

IR spectra were recorded on a spectrophotometer UR-20 from pellets with KBr (compound **IXf** from solution in CH_2Cl_2). ^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker Avance DRX-500 (500.13, 125.75 MHz respectively) from solutions in DMSO-d_6, internal reference TMS. GC-MS measurements were carried out on an instrument Aligent 1100/DAD/HSD/VLG119562.

Oximes IIa–IIe. To a solution of 0.05 mol of aldehyde **Ia–Ie** in 20 ml of ethanol was added a solution of 3.5 g (0.05 mol) of hydroxylamine hydrochloride and 6.8 g (0.05 mol) of sodium acetate trihydrate in 25 ml of water, the mixture was heated to boiling and diluted with 150 ml of water. The separated precipitate was filtered off, washed with water, and dried.

1-Phenyl-2,4-dichloro-1*H*-imidazole-5-carbaldehyde oxime (IIa). Yield 90%, mp 153–154°C. IR spectrum, cm^{-1}: 3410 (OH), 1625 (C=N). ^{1}H NMR spectrum, δ, ppm: 7.51–7.60 m ($5H_{arom}$), 7.63 s (1H, CH=), 11.52 s (1H, OH). Found, %: C 46.67; H 2.82; N 16.55. $C_{10}H_7Cl_2N_3O$. Calculated, %: C 46.90; H 2.76; N 16.41.

1-(4-Fluorophenyl)-2,4-dichloro-1*H*-imidazole-5-carbaldehyde oxime (IIb). Yield 82%, mp 178–180°C. IR spectrum, cm^{-1}: 3400 (OH), 1630 (C=N). ^{1}H NMR spectrum, δ, ppm: 7.41–7.63 m ($4H_{arom}$), 7.70 s (1H, CH=), 11.82 s (1H, OH). Found, %: C 43.57; H 2.32; N 15.45. $C_{10}H_6Cl_2FN_3O$. Calculated, %: C 43.82; H 2.21; N 15.33.

1-(4-Bromophenyl)-2,4-dichloro-1*H*-imidazole-5-carbaldehyde oxime (IIc). Yield 78%, mp 136–137°C. IR spectrum, cm^{-1}: 3415 (OH), 1625 (C=N). ^{1}H NMR spectrum, δ, ppm: 7.51 d ($2H_{arom}$, *J* 7.2 Hz), 7.73 s (1H, CH=), 7.78 d ($2H_{arom}$, *J* 7.2 Hz), 11.79 s (1H, OH). Found, %: C 35.67; H 1.72; N 12.75. $C_{10}H_6BrCl_2N_3O$. Calculated, %: C 35.86; H 1.81; N 12.54.

1-(4-Methylphenyl)-2,4-dichloro-1*H*-imidazole-5-carbaldehyde oxime (IId). Yield 85%, mp 145–146°C. IR spectrum, cm^{-1}: 3430 (OH), 1620 (C=N). ^{1}H NMR spectrum, δ, ppm: 2.40 s (3H, CH_3), 7.39 br.s ($4H_{arom}$), 7.64 s (1H, CH=), 11.81 s (1H, OH). Found, %: C 48.77; H 3.42; N 15.65. $C_{11}H_9Cl_2N_3O$. Calculated, %: C 48.91; H 3.36; N 15.56.

1-(4-Methoxyphenyl)-2,4-dichloro-1*H*-imidazole-5-carbaldehyde oxime (IIe). Yield 86%, mp 155–157°C. IR spectrum, cm^{-1}: 3405 (OH), 1620 (C=N). ^{1}H NMR spectrum, δ, ppm: 3.84 s (3H, CH_3O), 7.11 d ($2H_{arom}$, *J* 8.5 Hz), 7.43 d ($2H_{arom}$, *J* 8.5 Hz), 7.63 s (1H, CH=), 11.59 s (1H, OH). Found, %: C 46.07; H 3.22; N 14.55. $C_{11}H_9Cl_2N_3O_2$. Calculated, %: C 46.18; H 3.17; N 14.69.

Nitriles IIIa–IIIe. To a slurry of 0.03 mol of oxime **IIa–IIe** in 60 ml of toluene was added 3.9 g (0.033 mol) of thionyl chloride, and the mixture was boiled for 3 h. The solvent was evaporated, the residue was washed with water, filtered off, dried, and crystallized from 80% aqueous ethanol.

1-Phenyl-2,4-dichloro-1*H*-imidazole-5-carbonitrile (IIIa). Yield 80%, mp 63–64°C. IR spectrum, cm^{-1}: 2220 (C≡N). ^{1}H NMR spectrum, δ, ppm: 7.59–7.68 m ($5H_{arom}$). Found, %: C 50.12; H 2.22; N 17.53. $C_{10}H_5Cl_2N_3$. Calculated, %: C 50.45; H 2.12; N 17.65.

1-(4-Fluorophenyl)-2,4-dichloro-1*H*-imidazole-5-carbonitrile (IIIb). Yield 70%, mp 99–100°C. IR spectrum, cm^{-1}: 2220 (C≡N). ^{1}H NMR spectrum, δ, ppm: 7.54 t ($2H_{arom}$, *J* 8.2 Hz), 7.79–7.84 m ($2H_{arom}$). Found, %: C 46.77; H 1.42; N 16.55. $C_{10}H_4Cl_2FN_3$. Calculated, %: C 46.91; H 1.57; N 16.41.

1-(4-Bromophenyl)-2,4-dichloro-1*H*-imidazole-5-carbonitrile (IIIc). Yield 68%, mp 84–85°C. IR spectrum, cm^{-1}: 2225 (C≡N). ^{1}H NMR spectrum, δ, ppm: 7.71 d ($2H_{arom}$, *J* 8.4 Hz), 7.90 d ($2H_{arom}$, *J* 8.4 Hz). Found, %: C 37.98; H 1.42; N 13.45. $C_{10}H_4BrCl_2N_3$. Calculated, %: C 37.89; H 1.27; N 13.26.

1-(4-Methylphenyl)-2,4-dichloro-1*H*-imidazole-5-carbonitrile (IIId). Yield 78%, mp 75°C. IR spectrum, cm^{-1}: 2220 (C≡N). ^{1}H NMR spectrum, δ, ppm: 2.42 s (3H, CH_3), 7.40 d ($2H_{arom}$, *J* 8.0 Hz), 7.46 d ($2H_{arom}$, *J* 8.0 Hz). ^{13}C NMR spectrum, δ, ppm: 20.38 (CH_3), 105.79 (C^5), 109.06 (C≡N), 126.66, 129.77, 135.15, 137.10 (C_{arom}), 130.25 (C^2), 141.03 (C^4). Found, %: C 52.58; H 2.72; N 16.78. $C_{11}H_7Cl_2N_3$. Calculated, %: C 52.41; H 2.80; N 16.67.

1-(4-Methoxyphenyl)-2,4-dichloro-1*H*-imidazole-5-carbonitrile (IIIe). Yield 76%, mp 83°C. IR spectrum, cm^{-1}: 2220 (C≡N). ^{1}H NMR spectrum, δ, ppm: 3.86 s (3H, CH_3O), 7.18 d ($2H_{arom}$, *J* 8.8 Hz), 7.62 d ($2H_{arom}$, *J* 8.8 Hz). ^{13}C NMR spectrum, δ, ppm: 55.61 (CH_3O), 106.04 (C^5), 109.14 (C≡N), 114.95, 125.38, 128.83, 160.76

(C_{arom}), 135.43 (C^2), 136.91 (C^4). Found, %: C 49.17; H 2.52; N 15.82. $C_{11}H_7Cl_2N_3O$. Calculated, %: C 49.28; H 2.63; N 15.67.

Nitriles IVa–IVe. To a solution of 0.01 mol of nitrile **IIIa–IIIe** in 10 ml of DMF was added 0.98 g (0.015 mol) of sodium azide, and the mixture was stirred at room temperature over 12 h. The reaction mixture was poured into 50 ml of water, the precipitate was filtered off, dried, and crystallized from ethanol.

2-Azido-1-phenyl-4-chloro-1*H*-imidazole-5-carbonitrile (IVa). Yield 79%, mp 79–80°C. IR spectrum, cm^{-1}: 2245 (C≡N), 2165 (N_3). ^1H NMR spectrum, δ, ppm: 7.54–7.63 m ($5H_{arom}$). Found, %: C 49.23; H 2.22; N 34.17. $C_{10}H_5ClN_6$. Calculated, %: C 49.10; H 2.06; N 34.35.

2-Azido-1-(4-fluorophenyl)-4-chloro-1*H*-imidazole-5-carbonitrile (IVb). Yield 72%, mp 83–84°C. IR spectrum, cm^{-1}: 2160 (N_3), 2235 (C≡N). ^1H NMR spectrum, δ, ppm: 7.59–7.84 m ($4H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 102.31 (C^5), 109.61 (C≡N), 116.75 d (C_{arom}, $^2J_{C-F}$ 25.2 Hz), 128.47, 128.97, 162.60 d ($^1J_{C-F}$ 252.4 Hz) (C_{arom}), 137.39 (C^2), 143.23 (C^4). Found, %: C 45.57; H 1.42; N 32.15. $C_{10}H_4ClFN_6$. Calculated, %: C 45.73; H 1.54; N 32.00.

2-Azido-1-(4-bromophenyl)-4-chloro-1*H*-imidazole-5-carbonitrile (IVc). Yield 70%, mp 116–117°C. IR spectrum, cm^{-1}: 2240 (C≡N), 2165 (N_3). ^1H NMR spectrum, δ, ppm: 7.59 d ($2H_{arom}$, *J* 8.8 Hz), 7.85 d ($2H_{arom}$, *J* 8.8 Hz). Found, %: C 37.31; H 1.18; N 25.78. $C_{10}H_4BrClN_6$. Calculated, %: C 37.12; H 1.25; N 25.98.

2-Azido-1-(4-methylphenyl)-4-chloro-1*H*-imidazole-5-carbonitrile (IVd). Yield 77%, mp 59–60°C. IR spectrum, cm^{-1}: 2165 (N_3), 2240 (C≡N). ^1H NMR spectrum, δ, ppm: 2.40 s (3H, CH_3), 7.41 d ($2H_{arom}$, *J* 8.0 Hz), 7.48 d ($2H_{arom}$, *J* 8.0 Hz). ^{13}C NMR spectrum, δ, ppm: 20.67 (CH_3), 102.13 (C^5), 109.66 (C≡N), 126.02, 129.68, 130.09, 140.32 (C_{arom}), 137.32 (C^2), 143.18 (C^4). Found, %: C 50.98; H 2.62; N 32.68. $C_{11}H_7ClN_6$. Calculated, %: C 51.14; H 2.73; N 32.49.

2-Azido-1-(4-methoxyphenyl)-4-chloro-1*H*-imidazole-5-carbonitrile (IVe). Yield 71%, mp 101–102°C. IR spectrum, cm^{-1}: 2240 (C≡N), 2160 (N_3). ^1H NMR spectrum, δ, ppm: 3.84 c (3H, CH_3O), 7.14 d ($2H_{arom}$, *J* 8.4 Hz), 7.53 d ($2H_{arom}$, *J* 8.4 Hz). ^{13}C NMR spectrum, δ, ppm: 55.61 (CH_3O), 102.43 (C^5), 109.76 (C≡N), 114.78, 124.78, 127.82, 160.36 (C_{arom}), 135.05 (C^2), 143.18 (C^4). Found, %: C 47.87; H 2.42; N 30.79. $C_{11}H_7ClN_6O$. Calculated, %: C 48.10; H 2.57; N 30.60.

Nitriles Va–Ve. *a*. To a solution of 1.7 g (7.5 mmol) of tin(II) chloride dihydrate in 10 ml of conc. HCl was added 20 ml of ethanol, then at stirring and cooling 0.0075 mol of nitrile **IVa–IVe** was added by small portions within 0.5 h. The reaction mixture was poured into 100 ml of water, the reaction product was extracted into ethyl acetate (2 × 20 ml), the organic layer was dried with anhydrous sodium sulfate, the solvent was evaporated, and the residue was crystallized from ethanol.

b. To a solution of 7.5 mmol of nitrile **IVa–IVe** in 20 ml of ethanol at 10–20°C was added dropwise within 2 h 1.44 g (0.02 mol) of potassium hydrogen sulfide in 50 ml of 80% aqueous ethanol. The reaction mixture was poured into 100 ml of water, the precipitate was filtered off, washed with water, dried, and crystallized from ethanol.

2-Amino-1-phenyl-4-chloro-1*H*-imidazole-5-carbonitrile (Va). Yield 69% (*a*), 74% (*b*), mp 151–152°C. IR spectrum, cm^{-1}: 3415 (NH_2), 2220 (C≡N). ^1H NMR spectrum, δ, ppm: 6.78 s (2H, NH_2), 7.50–7.61 m ($5H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 96.17 (C^5), 111.52 (C≡N), 126.59, 129.47, 129.98, 138.73 (C_{arom}), 133.22 (C^2), 150.90 (C^4). Found, %: C 54.78; H 3.14; N 25.47. $[M + 1]^+$ 219. $C_{10}H_7ClN_4$. Calculated, %: C 54.93; H 3.23; N 25.62. *M* 218.65

2-Amino-1-(4-fluorophenyl)-4-chloro-1*H*-imidazole-5-carbonitrile (Vb). Yield 58% (*a*), 65% (*b*), mp 159–160°C. IR spectrum, cm^{-1}: 3430 (NH_2), 2225 (C≡N). ^1H NMR spectrum, δ, ppm: 6.70 s (2H, NH_2), 7.50–7.56 m ($2H_{arom}$), 7.81–7.88 m ($2H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 95.98 (C^5), 109.04 (C≡N), 117.00 d (C_{arom}, $^2J_{C-F}$ 25.1 Hz), 129.13 (C_{arom}), 129.73 d (C_{arom}, $^2J_{C-F}$ 8.7 Hz), 135.39 (C^2), 147.17 (C^4), 162.98 d (C_{arom}, $^1J_{C-F}$ 251.5 Hz). Found, %: C 50.57; H 2.70; N 23.45. $[M + 1]^+$ 237. $C_{10}H_6ClFN_4$. Calculated, %: C 50.76; H 2.56; N 23.68. *M* 236.64.

2-Amino-1-(4-bromophenyl)-4-chloro-1*H*-imidazole-5-carbonitrile (Vc). Yield 57% (*a*), 55% (*b*), mp 163–164°C. IR spectrum, cm^{-1}: 3420 (NH_2) 2220 (C≡N). ^1H NMR spectrum, δ, ppm: 6.75 br.s (1H, NH_2), 7.49 d ($2H_{arom}$, *J* 8.8 Hz), 7.79 d ($2H_{arom}$, *J* 8.8 Hz). ^{13}C NMR spectrum, δ, ppm: 96.12 (C^5), 111.41 (C≡N), 122.76, 129.01, 132.97, 138.87 (C_{arom}), 132.49 (C^2), 150.93 (C^4). Found, %: C 40.15; H 1.88; N 18.61. $[M + 1]^+$ 298. $C_{10}H_6BrClN_4$. Calculated, %: C 40.37; H 2.03; N 18.83. *M* 297.54.

2-Amino-1-(4-methylphenyl)-4-chloro-1*H*-

imidazole-5-carbonitrile (Vd). Yield 62% (*a*), 69% (*b*), mp 152–153°C. IR spectrum, cm^{-1}: 3415 (NH_2), 2215 (C≡N). ^{1}H NMR spectrum, δ, ppm: 2.40 c (3H, CH_3), 6.72 c (2H, NH_2), 7.32–7.42 m (4H_{arom}). ^{13}C NMR spectrum, δ, ppm: 20.70 (CH_3), 96.21 (C^5), 111.58 (C≡N), 126.46, 130.43, 130.65, 138.50 (C_{arom}), 139.26 (C^2), 150.99 (C^4), Found, %: C 57.05; H 3.72; N 24.19. [*M* + 1]$^+$ 233. $C_{11}H_9ClN_4$. Calculated, %: C 56.78; H 3.90; N 24.08. *M* 232.67.

2-Amino-1-(4-methoxyphenyl)-4-chloro-1*H*-imidazole-5-carbonitrile (Ve). Yield 60% (*a*), 63% (*b*), mp 155–157°C. IR spectrum, cm^{-1}: 3425 (NH_2), 2220 (C≡N). ^{1}H NMR spectrum, δ, ppm: 3.84 s (3H, CH_3O), 6.62 br.s (NH_2), 7.12 d (2H_{arom}, *J* 8.4 Hz), 7.42 d (2H_{arom}, *J* 8.4 Hz). ^{13}C NMR spectrum, δ, ppm: 55.53 (CH_3O), 96.54 (C^5), 111.60 (C≡N), 115.09, 125.75, 128.28, 159.84 (C_{arom}), 138.19 (C^2), 151.22 (C^4). Found, %: C 52.97; H 3.48; N 22.72. [*M* + 1]$^+$ 249. $C_{11}H_9ClN_4O$. Calculated, %: C 53.13; H 3.65; N 22.53. *M* 248.67.

Methyl 2-azido-1-aryl-4-chloro-1*H*-imidazole-5-carboxylates VIIIa–VIIIe. To a solution of 0.01 mol aldehyde **VIa–VIe** in 20 ml of tetrachloromethane was added 2.67 g (0.015 mol) of *N*-bromosuccinimide, 0.01 g of azobisisobutyronitrile, and the mixture was boiled for 2 h. The reaction mixture was cooled, the precipitate of succinimide was filtered off, 1.6 g (0.05 mol) of methanol was added to the filtrate, and the solution was boiled for 1 h. The solvent was evaporated, the precipitate was filtered off, washed with water, dried, and crystallized from aqueous methanol.

Methyl 2-azido-1-phenyl-4-chloro-1*H*-imidazole-5-carboxylate (VIIIa). Yield 78%, mp 103–104°C. IR spectrum, cm^{-1}: 2160 (N_3), 1730 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.65 s (3H, CH_3O), 7.41–7.52 m (5H_{arom}). Found, %: C 47.81; H 2.72; N 25.40. [*M* + 1]$^+$ 278. $C_{11}H_8ClN_5O_2$. Calculated, %: C 47.58; H 2.90; N 25.22. *M* 277.67.

Methyl 2-azido-1-(4-fluorophenyl)-4-chloro-1*H*-imidazole-5-carboxylate (VIIIb). Yield 70%, mp 113–114°C. IR spectrum, cm^{-1}: 1730 (C=O), 2165 (N_3). ^{1}H NMR spectrum, δ, ppm: 3.62 s (3H, CH_3O), 7.32–7.51 m (4H_{arom}). Found, %: C 44.41; H 2.42; N 23.63. [*M* + 1]$^+$ 296. $C_{11}H_7ClFN_5O_2$. Calculated, %: C 44.69; H 2.39; N 23.69. *M* 295.66.

Methyl 2-azido-4-chloro-1-(4-chlorophenyl)-1*H*-imidazole-5-carboxylate (VIIIc). Yield 67%, mp 109–110°C. IR spectrum, cm^{-1}: 2165 (N_3), 1725 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.63 s (3H, CH_3O), 7.47 d (2H_{arom}, *J* 8.8 Hz), 7.58 d (2H_{arom}, *J* 8.8 Hz). Found, %: C 42.50; H 2.39; N 22.20. [*M* + 1]$^+$ 312. $C_{11}H_7Cl_2N_5O_2$. Calculated, %: C 42.33; H 2.26; N 22.44. *M* 312.12.

Methyl 2-azido-1-(4-bromophenyl)-4-chloro-1*H*-imidazole-5-carboxylate (VIIId). Yield 50%, mp 104–105°C. IR spectrum, cm^{-1}: 2165 (N_3), 1730 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.64 s (3H, CH_3O), 7.40 d (2H_{arom}, *J* 8.4Hz), 7.71 d (2H_{arom}, *J* 8.4 Hz). Found, %: C 36.68; H 2.11; N 19.83. [*M* + 1]$^+$ 357. $C_{11}H_7BrClN_5O_2$. Calculated, %: C 37.05; H 1.98; N 19.64. *M* 356.57.

Methyl 2-azido-1-(4-methylphenyl)-4-chloro-1*H*-imidazole-5-carboxylate (VIIIe). Yield 90%, mp 145–148°C. IR spectrum, cm^{-1}: 2160 (N_3), 1730 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 3.62 s (3H, CH_3O), 7.29 br.s (4H_{arom}). Found, %: C 49.65; H 3.53; N 24.09. [*M* + 1]$^+$ 292. $C_{12}H_{10}ClN_5O_2$. Calculated, %: C 49.41; H 3.46; N 24.01. *M* 291.70.

Methyl 2-amino-1-aryl-4-chloro-1*H*-imidazole-5-carboxylates IXa–IXe. To a solution of 1.7 g (7.5 mmol) of tin(II) chloride dihydrate in 10 ml of concn. HCl and 20 ml of ethanol was added and then at stirring and cooling to 0–5°C was added within 0.5 h by small portions 7.5 mmol of ester **VIIIa–VIIIe**. The reaction mixture was poured into в 100 ml of water, the reaction product was extracted into ethyl acetate (2 × 20 ml), the organic layer was dried with anhydrous sodium sulfate, the solvent was evaporated, and the residue was crystallized from methanol.

Methyl 2-amino-1-phenyl-4-chloro-1*H*-imidazole-5-carboxylate (IXa). Yield 84%, mp 119–120°C. IR spectrum, cm^{-1}: 3390 (NH_2), 1720 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.51 s (3H, CH_3O), 6.22 s (2H, NH_2), 7.24–7.32 m (2H_{arom}), 7.44–7.50 m (3H_{arom}). ^{13}C NMR spectrum, δ, ppm: 50.61 (CH_3O), 112.57 (C^5), 127.57, 128.51, 129.12, 151.63 (C_{arom}), 135.59 (C^2), 136.35 (C^4), 158.24 (C=O). Found, %: C 52.23; H 4.06; N 16.67. [*M* + 1]$^+$ 252. $C_{11}H_{10}ClN_3O_2$. Calculated, %: C 52.50; H 4.01; N 16.70. *M* 251.67.

Methyl 2-amino-1-(4-fluorophenyl)-4-chloro-1*H*-imidazole-5-carboxylate (IXb). Yield 76%, mp 179–180°C. IR spectrum, cm^{-1}: 3400 (NH_2), 1725 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.52 s (3H, CH_3O), 6.31 s (2H, NH_2), 7.29–7.43 m (4H_{arom}). Found, %: C 48.72; H 3.43; N 15.39. [*M* + 1]$^+$ 270. $C_{11}H_9ClFN_3O_2$. Calculated, %: C 49.00; H 3.36; N 15.58. *M* 269.66.

Methyl 2-amino-4-chloro-1-(4-chlorophenyl)--

imidazole-5-carboxylate (IXc). Yield 79%, mp 188–189°C. IR spectrum, cm^{-1}: 3385 (NH_2), 1720 (C=O). ^1H NMR spectrum, δ, ppm: 3.53 s (3H, CH_3O), 6.36 s (2H, NH_2), 7.35 d (2H_{arom}, *J* 8.4 Hz), 7.54 d (2H_{arom}, *J* 8.4 Hz). Found, %: C 46.41; H 3.06; N 14.52. [*M*+1]+ 286. $C_{11}H_9Cl_2N_3O_2$. Calculated, %: C 46.18; H 3.17; N 14.69. *M* 286.12.

Methyl 2-amino-1-(4-bromophenyl)-4-chloro-1*H*-imidazole-5-carboxylate (IXd). Yield 64%, mp 181–182°C. IR spectrum, cm^{-1}: 3395 (NH_2), 1720 (C=O). ^1H NMR spectrum, δ, ppm: 3.50 s (3H, CH_3O), 6.31 s (2H, NH_2), 7.43 d (2H_{arom}, *J* 8.6 Hz), 7.75 d (2H_{arom}, *J* 8.6 Hz). Found, %: C 40.24; H 2.70; N 12.54. [*M* + 1]$^+$ 331. $C_{11}H_9BrClN_3O_2$. Calculated, %: C 39.97; H 2.74; N 12.71. *M* 330.57.

Methyl 2-amino-1-(4-methylphenyl)-4-chloro-1*H*-imidazole-5-carboxylate (IXe). Yield 80%, mp 156–157°C. IR spectrum, cm^{-1}: 3405 (NH_2), 1725 (C=O),. ^1H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3), 3.52 s (3H, CH_3O), 6.21 s (2H, NH_2), 7.16 d (2H_{arom}, *J* 7.4 Hz), 7.33d (2H_{arom}, *J* 7.4 Hz). ^{13}C NMR spectrum, δ, ppm: 20.55 (CH_3), 50.36 (CH_3O), 112.59 (C^5), 127.37, 129.71, 137.99, 151.69 (C_{arom}), 132.96 (C^2), 136.45 (C^4), 158.29 (C=O). Found, %: C 54.08; H 4.32; N 15.64. [*M* + 1]$^+$ 266. $C_{12}H_{12}ClN_3O_2$. Calculated, %: C 54.25; H 4.55; N 15.81. *M* 265.70.

2-Amino-1-aryl-4-chloro-1*H*-imidazole-5-carboxamides IXf–IXi. To a solution of 0.01 mol of aldehyde **VIa, VIc–VIe** in 20 ml of tetrachloromethane was added 2.67 g (0.015 mol) of *N*-bromosuccinimide, 0.01 g of azobisisobutyronitrile, and the mixture was boiled for 2 h. The reaction mixture was cooled to room temperature, the precipitate of succinimide was filtered off The filtrate was evaporated, to the residue was added 20 ml of acetonitrile, 0.015 mol of amine **VIIb–VIIe** and 1.5 g (0.015 mol) of triethylamine. The reaction mixture was boiled for 1 h, the solvent was evaporated, to the residue 50 ml of water was added, the reaction product was extracted into ethyl acetate (2 × 20 ml), the organic layer was dried with anhydrous sodium sulfate, the solvent was evaporated. To the obtained oily residue of azidoamide **VIIIf–VIIIi** was added at stirring and cooling within 0.5 h 1.7 g (0.02mol) of tin(II) chloride dihydrate in 10 ml of concn. HCl and 20 ml of ethanol. The reaction mixture was poured into в 100 ml of water, the reaction product was extracted into ethyl acetate (2 × 20 ml), the organic layer was dried with anhydrous sodium sulfate, the solvent was evaporated. Amides **IXf–IXi** were purified by reprecipitation in hexane from benzene or by crystallization from ethanol.

2-Amino-*N*-benzyl-1-phenyl-4-chloro-1*H*-imidazole-5-carboxamide (IXf). Yield 63%, viscous oily substance. IR spectrum, cm^{-1}: 3380–3350 (NH), 1660 (C=O). ^1H NMR spectrum, δ, ppm: 4.32 d (2H, CH_2, *J* 6.0 Hz), 5.92 s (2H, NH_2), 7.15–7.54 m (10H_{arom}), 8.94 t (1H, NH, *J* 6.0 Hz). Found, %: C 62.76; H 4.39; N 17.39. [*M* + 1]$^+$ 327. $C_{17}H_{15}ClN_4O$. Calculated, %: C 62.48; H 4.63; N 17.14. *M* 326.79.

2-Amino-*N*-(4-methylphenyl)-4-chloro-1-(4-chlorophenyl)-1*H*-imidazole-5-carboxamide (IXg). Yield 58%, mp 125–126°C. IR spectrum, cm^{-1}: 3345–3320 (NH), 1670 (C=O). ^1H NMR spectrum, δ, ppm: 2.28 s (3H, CH_3), 6.18 s (2H, NH_2), 7.38 d (2H, CH_2, *J* 8.0 Hz), 7.56 d (2H, CH_2, *J* 8.0 Hz), 9.64 c (1H, NH). Found, %: C 56.30; H 3.73; N 15.28. [*M* + 1]$^+$ 361. $C_{17}H_{14}Cl_2N_4O$. Calculated, %: C 56.53; H 3.91; N 15.51. *M* 361.23.

2-Amino-1-(4-methylphenyl)-*N*-(3-fluorophenyl)-4-chloro-1*H*-imidazole-5-carboxamide (IXh). Yield 65%, mp 199–200°C. IR spectrum, cm^{-1}: 3350–3320 (NH), 1675 (C=O). ^1H NMR spectrum, δ, ppm: 2.35 s (3H, CH_3), 6.11 s (2H, NH_2), 7.17–7.42 m (8H_{arom}), 9.99 s (1H, NH). Found, %: C 59.19; H 4.11; N 16.27. [*M* + 1]$^+$ 345. $C_{17}H_{14}ClFN_4O$. Calculated, %: C 59.22; H 4.09; N 16.25. *M* 344.78.

2-Amino-1-(4-bromophenyl)-4-chloro-1*H*-imidazol-5-yl(piperidin-1-yl)methanone (IXi). Yield 68%, mp 200–202°C. IR spectrum, cm^{-1}: 3375 (NH), 1660 (C=O). ^1H NMR spectrum, δ, ppm: 1.41–1.56 m (6H, 3CH_2), 3.38–3.42 m (4H, 2CH_2), 6.02 s (2H, NH_2), 7.21 d (2H_{arom}, *J* 8.8 Hz), 7.68 (2H_{arom}, *J* 8.8 Hz). Found, %: C 46.76; H 4.38; N 14.47. [*M* + 1]$^+$ 384. $C_{15}H_{16}BrClN_4O$. Calculated, %: C 46.96; H 4.20; N 14.60. *M* 383.68.

2-Azido-1-aryl-4-chloro-1*H*-imidazole-5-carboxylic acids Xa–Xd. To a solution of 0.01 mol of aldehyde **VIa, VIc,VIe, VIf** in 20 ml of 80% aqueous pyridine at stirring and cooling with water was added 4.74 g (0.03 mol) of potassium permanganate. The reaction mixture was stirred for 0.5 h, poured in 100 ml of water, the precipitate of manganese(IV) oxide was filtered off, the filtrate was acidified with hydrochloric acid, the separated precipitate was filtered off and dried.

2-Azido-1-phenyl-4-chloro-1*H*-imidazole-5-carboxylic acid (Xa). Yield 24%, mp 186–187°C. IR

spectrum, cm^{-1}: 2830–2550 (COOH), 2165 (N_3), 1715 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.33–7.49 m ($5H_{arom}$), 13.03 br.s (1H, COOH). Found, %: C 45.33; H 2.11; N 26.38. $[M + 1]^+$ 264. $C_{10}H_6ClN_5O_2$. Calculated, %: C 45.56; H 2.29; N 26.56. *M* 263.64.

2-Azido-4-chloro-1-(4-chlorophenyl)-1*H*-imidazole-5-carboxylic acid (Xb). Yield 25%, mp 169–170°C. IR spectrum, cm^{-1}: 2850–2520 (COOH), 2160 (N_3), 1710 (C=O). ^{1}H NMR spectrum, δ, ppm: 7.44 d ($2H_{arom}$, *J* 7.8 Hz), 7.55 d ($2H_{arom}$, *J* 7.8 Hz), 13.10 br.s (1H, COOH). Found, %: C 40.06; H 1.77; N 23.62. $[M + 1]^+$ 298. $C_{10}H_5Cl_2N_5O_2$. Calculated, %: C 40.29; H 1.69; N 23.79. *M* 298.09.

2-Azido-1-(4-methylphenyl)-4-chloro-1*H*-imidazole-5-carboxylic acid (Xc). Yield 24%, mp 173–175°C. IR spectrum, cm^{-1}: 2870–2520 (COOH), 2165 (N_3), 1715 (C=O). ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 7.22–7.28 m ($4H_{arom}$), 12.99 br.s (1H, COOH). Found, %: C 47.76; H 2.73; N 25.34. $[M + 1]^+$ 278. $C_{11}H_8ClN_5O_2$. Calculated, %: C 47.58; H 2.90; N 25.22. *M* 277.67.

2-Azido-1-(4-methoxyphenyl)-4-chloro-1*H*-imidazole-5-carboxylic acid (Xd). Yield 20%, mp 153–154°C. IR spectrum, cm^{-1}: 2860–2520 (COOH), 2165 (N_3), 1715 (C=O). ^{1}H NMR spectrum, δ, ppm: 3.82 s (3H, CH_3O), 6.99 d ($2H_{arom}$, *J* 8.4 Hz), 7.29 d ($2H_{arom}$, *J* 8.4 Hz), 13.00 br.s (1H, COOH). Found, %: C 45.24; H 2.70; N 23.68. $[M + 1]^+$ 294. $C_{11}H_8ClN_5O_3$. Calculated, %: C 44.99; H 2.75; N 23.85. *M* 293.67.

1-Aryl-4-chloro-1*H*-imidazole-2-amines XIa–XId. To a solution of 1.7 g (7.5mmol) of tin(II) chloride dihydrate in 10 ml of 20% sodium hydroxide was added by small portions at stirring while cooling to 0–5°C 5 mmol of acid **Xa–Xd**, the reaction mixture was stirred at room temperature for 0.5 h. The solution obtained was neutralized with 10% solution of hydrochloric acid, the amine was extracted into benzene (2 × 10 ml), the benzene solution was dried with anhydrous sodium sulfate. The solvent was evaporated, the residue was crystallized from 50% aqueous ethanol.

1-Phenyl-4-chloro-1*H*-imidazole-2-amine (XIa). Yield 67%, mp 125–126°C. IR spectrum, cm^{-1}: 3315 (NH_2). ^{1}H NMR spectrum, δ, ppm: 5.62 s (2H, NH_2), 6.91 s (H^5), 7.39–7.51 m ($5H_{arom}$). Found, %: C 55.59; H 4.08; N 21.57. $[M + 1]^+$ 194. $C_9H_8ClN_3$. Calculated, %: C 55.83; H 4.16; N 21.70. *M* 193.64.

4-Chloro-1-(4-chlorophenyl)-1*H*-imidazole-2-amine (XIb). Yield 69%, mp 106–107°C. IR spectrum, cm^{-1}: 3325 (NH_2). ^{1}H NMR spectrum, δ, ppm: 5.56 s (2H, NH_2), 6.84 s (H^5), 7.44 d ($2H_{arom}$, *J* 8.2 Hz), 7.60 d ($2H_{arom}$, *J* 8.2 Hz). Found, %: C 47.72; H 3.21; N 18.65. $[M + 1]^+$ 228. $C_9H_7Cl_2N_3$. Calculated, %: C 47.40; H 3.09; N 18.42. *M* 228.08.

1-(4-Methylphenyl)-4-chloro-1*H*-imidazole-2-amine (XIc). Yield 63%, mp 138–139°C. IR spectrum, cm^{-1}: 3310 (NH_2). ^{1}H NMR spectrum, δ, ppm: 5.63 s (2H, NH_2), 6.87 s (H^5), 7.33 s ($4H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 20.51 (CH_3), 110.18 (C^5), 124.13, 130.00, 136.77, 147.39 (C_{arom}), 124.79 (C^2), 133.90 (C^4). Found, %: C 57.99; H 4.66; N 20.10. $[M + 1]^+$ 208. $C_{10}H_{10}ClN_3$. Calculated, %: C 57.84; H 4.85; N 20.23. *M* 207.66.

1-(4-Methoxyphenyl)-4-chloro-1*H*-imidazole-2-amine (XId). Yield 59%, mp 123–124°C. IR spectrum, cm^{-1}: 3320 (NH_2). ^{1}H NMR spectrum, δ, ppm: 5.58 s (2H, NH_2), 6.82 s (H^5), 7.04 d ($2H_{arom}$, *J* 8.8 Hz), 7.34 d ($2H_{arom}$, *J* 8.8Hz). ^{13}C NMR spectrum, δ, ppm: 55.42 (CH_3O), 111.63 (C^5), 115.84, 126.07, 130.95, 158.76 (C_{arom}), 125.32 (C^2), 134.58 (C^4). Found, %: C 53.47; H 4.72; N 18.59. $[M + 1]^+$ 224. $C_{10}H_{10}ClN_3O$. Calculated, %: C 53.70; H 4.51; N 18.79. *M* 223.66.

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