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Polyfunctional Imidazoles: VIII.* 1-Aryl-4-chloro-5-[R-sulfanyl(R-sulfonyl)methyl]-1*H*-imidazoles

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Abstract—Alkylation of (1-aryl-4-chloro-1*H*-imidazol-5-yl)methanethiols with alkyl halides, propargyl bromide, or chloroacetic acid gave 1-aryl-5-(R-sulfanylmethyl)-4-chloro-1*H*-imidazoles. 1-Aryl-4-chloro-5-(methylsulfanylmethyl)-1*H*-imidazoles and [(1-aryl-4-chloro-1*H*-imidazol-5-yl)methylsulfanyl]acetic acids were oxidized to the corresponding sulfones with potassium permanganate.

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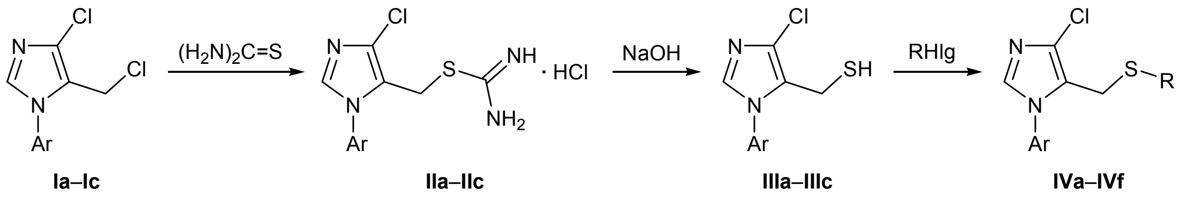
1*H*-Imidazol-5-ylmethylsulfanyl group and its S-oxidized derivatives are pharmacophores which are used in the design of biologically active compounds. In particular, it was used to modify pyrimidine structures possessing anti-inflammatory, analgesic, and antiepileptic activity [2], *N*-aryl ureas exhibiting anti-atherosclerotic properties [3], and cephalosporins with pronounced bactericidal effect [4]. 1*H*-Imidazol-5-ylmethylsulfinate and -sulfonate fragments turned out to be quite valuable for the design of anti-HIV agents in the series of benzoazepines [5] and benzoazocines [6]. Taking into account the above stated, as well as the effect of substituents in the ring (e.g., of a chlorine atom in position *4*) [7–10] on the biological properties of imidazole derivatives, we focused on an important synthetic problem, search for approaches to new sulfur-containing imidazole derivatives. It seemed reasonable to start the study with the development of a procedure for the synthesis of 5-(R-sulfanylmethyl)-1-aryl-4-chloro-1*H*-imidazoles.

In the preceding communication [1] we reported on the reaction of 4-chloro-5-chloromethyl-1*H*-imidazole with benzenethiols and hetarene-2-thiols, which afforded the corresponding aryl(or hetaryl)sulfanylmethyl-substituted imidazoles. However, the use of environmentally unsafe thiols involves some experimental difficulties and is not always justified. Therefore, we now propose a different procedure for the synthesis of 5-(alkylsulfanylmethyl)-1*H*-imidazoles, which is based on the alkylation of (1-aryl-4-chloro-1*H*-imidazol-5-yl)methanethiol with alkyl halides.

For this purpose, initial 1-aryl-4-chloro-5-chloromethyl-1*H*-imidazoles **Ia**–**Ic** [1] were brought into reaction with thiourea in boiling dioxane. We thus obtained 80–89% of thiuronium salts **IIa**–**IIc** whose

Scheme 1.



I–**III**, Ar = 4-FC_6H_4 (**a**), 4-ClC_6H_4 (**b**), 4-MeC_6H_4 (**c**); **IV**, R = Me, Ar = 4-FC_6H_4 (**a**), 4-ClC_6H_4 (**b**), 4-MeC_6H_4 (**c**); R = Bu, Ar = 4-ClC_6H_4 (**d**); R = $PhCH_2$, Ar = 4-ClC_6H_4 (**e**), 4-MeC_6H_4 (**f**).

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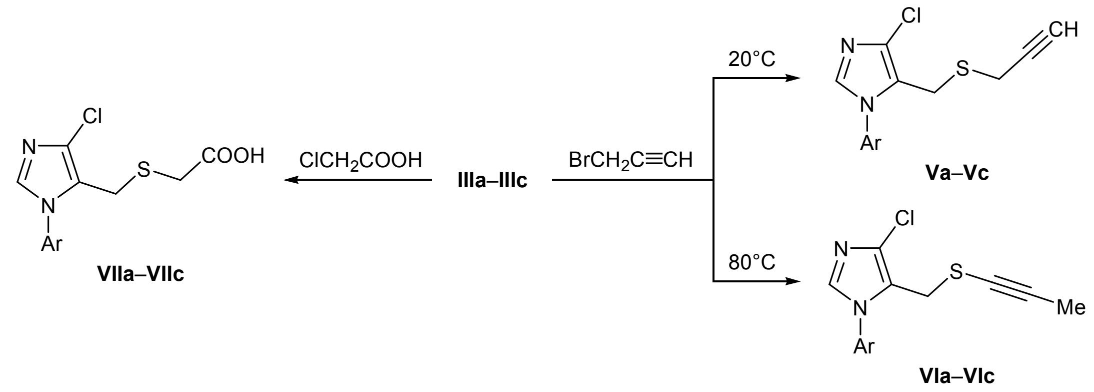
* For communication VII, see [1].

Scheme 2.



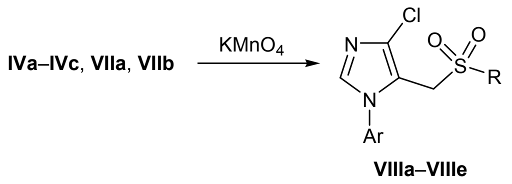
Ar = 4-FC_6H_4 (**a**), 4-ClC_6H_4 (**b**), 4-MeC_6H_4 (**c**).

hydrolysis with an alcoholic solution of sodium hydroxide at room temperature gave (1-aryl-1*H*-imidazol-5-yl)methanethiols **IIIa**–**IIIc**. The latter were isolated as solids having almost no mercaptan odor. Treatment of **IIIa**–**IIIc** in alcoholic solution with methyl iodide in the presence of sodium hydroxide afforded 80–86% of *S*-methyl derivatives **IVa**–**IVc** (method *a*). Compounds **IVa**–**IVc** can also be obtained in approximately the same yields by methylation of thiols **IIIa**–**IIIc** without their isolation from the reaction mixture (method *b*). This one-pot procedure turned out to be convenient for the preparation of R-sulfanyl derivatives **IVd**–**IVf** by alkylation of thiols **III** with butyl bromide and benzyl chloride (Scheme 1).

Taking into account synthetic importance of functionalized sulfanyl derivatives, we examined the alkylation of thiols **IIIa**–**IIIc** with propargyl bromide and chloroacetic acid. The reaction of **IIIa**–**IIIc** with propargyl bromide in alkaline medium at room temperature afforded 1-aryl-5-[(prop-2-yn-1-ylsulfanyl)-methyl]-1*H*-imidazoles **Va**–**Vc**, whereas in boiling ethanol isomeric 1-aryl-5-[(prop-1-ynylsulfanyl)-methyl]-1*H*-imidazoles **VIa**–**VIc** were obtained (method *a*) as a result of base-catalyzed isomerization of primary alkylation products **Va**–**Vc** at elevated temperature. This is consistent with published data [11, 12], as well as with our results on the transformation of **Vb** into isomer **VIb** (method *b*). The alkylation of thiols **IIIa**–**IIIc** with chloroacetic acid under mild conditions led to the formation of [(1*H*-imidazol-5-ylmethyl)sulfanyl]acetic acids **VIIa**–**VIIc** in high yield (Scheme 2).

The presence of a chlorine atom in position *4* of the imidazole ring of compounds **IV**–**VII** essentially affects the behavior of the sulfanylmethyl group toward oxidation. Unlike 4-unsubstituted analogs [3, 6], compounds **IV**–**VII** are not oxidized to sulfinyl or sulfonyl derivatives with *m*-chloroperoxybenzoic acid or hydrogen peroxide. The use of such a strong oxidant as potassium permanganate turned out to be efficient for the oxidation of sulfides **IVa**–**IVc**, **VIIa**, and **VIIb** to sulfones **VIIIa**–**VIIIe** (Scheme 3). However, analogous reaction with compounds **Va** and **VIa** gave complex oily mixtures of products, and we failed to isolate individual substances therefrom.

Scheme 3.



R = Me, Ar = 4-FC_6H_4 (**a**), 4-ClC_6H_4 (**b**), 4-MeC_6H_4 (**c**);
R = CH_2COOH, Ar = 4-FC_6H_4 (**d**), 4-ClC_6H_4 (**e**).

The structure of the synthesized compounds was confirmed by the IR, ^1H and ^{13}C NMR, and GC/MS data. Sulfanylmethylimidazoles **IV**–**VII** characteristically showed in the ^1H NMR spectra singlets at δ 3.63–4.00 ppm from methylene groups separating the imidazole ring and sulfur atom. In the spectra of **VIIIa**–**VIIId** the corresponding signals were observed in a weaker field, at δ 4.29–4.53 ppm. The prop-2-yn-1-ylsulfanyl fragment in **Va**–**Vc** gave rise to singletes at δ 3.11 (CH) and 3.22 ppm (CH_2), while isomeric compounds **VIa**–**VIc** displayed only a singlet at δ 1.81–1.83 ppm from the terminal methyl group.

EXPERIMENTAL

The IR spectra were recorded in KBr on a UR-20 spectrometer. The ^1H and ^{13}C NMR spectra were measured on a Bruker Avance DRX-500 spectrometer at

500.13 and 127.75 MHz, respectively, from solutions in DMSO-d_6 using tetramethylsilane as internal reference. The mass spectra were obtained on an Aligent 1100/DAD/HSD/ VLG119562 instrument.

Compounds IIa–IIc (*general procedure*)**.** Thiourea, 0.76 g (10 mmol), was added to a solution of 10 mmol of 1-aryl-4-chloro-5-chloromethyl-1*H*-imidazole **Ia–Ic** in 20 mL of anhydrous dioxane. The mixture was heated for 0.5 h under reflux and cooled, and the precipitate was filtered off and dried.

[4-Chloro-1-(4-fluorophenyl)-1*H*-imidazol-5-yl]-methyl carbamimidothioate hydrochloride (IIa). Yield 85%, mp 246–248°C. IR spectrum: ν 3360–3385 cm^{-1} (NH). ^{1}H NMR spectrum, δ, ppm: 4.53 s (2H, $\mathrm{CH_2}$), 7.43–7.49 m (2H, $\mathrm{H_{arom}}$), 7.58–7.63 m (2H, $\mathrm{H_{arom}}$), 7.98 s (1H, 2-H), 9.35 br.s (4H, NH). Found, %: C 41.19; H 3.50; N 17.61. *m*/*z* 322 $[M + 1]^+$. $\mathrm{C_{11}H_{10}ClFN_4S \cdot HCl}$. Calculated, %: C 41.07; H 3.42; N 17.44. *M* 321.24.

[4-Chloro-1-(4-chlorophenyl)-1*H*-imidazol-5-yl]-methyl carbamimidothioate hydrochloride (IIb). Yield 80%, mp 215–217°C. IR spectrum: ν 3360–3380 cm^{-1} (NH). ^{1}H NMR spectrum, δ, ppm: 4.57 s (2H, $\mathrm{CH_2}$), 7.59 d (2H, $\mathrm{H_{arom}}$, *J* = 8.4 Hz), 7.67 d (2H, $\mathrm{H_{arom}}$, *J* = 8.4 Hz), 7.80 s (1H, 2-H), 9.39 br.s (4H, NH). Found, %: C 39.20; H 3.15; N 16.44. *m*/*z* 338 $[M + 1]^+$. $\mathrm{C_{11}H_{10}Cl_2N_4S \cdot HCl}$. Calculated, %: C 39.12; H 3.25; N 16.59. *M* 337.70.

[4-Chloro-1-(4-methylphenyl)-1*H*-imidazol-5-yl]-methyl carbamimidothioate hydrochloride (IIc). Yield 89%, mp 205–207°C. IR spectrum: ν 3365–3380 cm^{-1} (NH). ^{1}H NMR spectrum, δ, ppm: 2.40 s (3H, $\mathrm{CH_3}$), 4.51 s (2H, $\mathrm{CH_2}$), 7.40 s (4H, $\mathrm{H_{arom}}$), 7.94 s (1H, 2-H), 9.35 br.s (4H, NH). Found, %: C 45.29; H 3.98; N 17.77. *m*/*z* 318. $[M + 1]^+$. $\mathrm{C_{12}H_{13}ClN_4S \cdot HCl}$. Calculated, %: C 45.42; H 4.09; N 17.65. *M* 317.28.

Compounds IIIa–IIIc (*general procedure*)**.** Sodium hydroxide, 0.4 g (10 mmol), was added to a solution of 5 mmol of thiuronium salt **IIa–IIc** in 20 mL of ethanol, and the mixture was stirred for 1 h at room temperature. The mixture was poured into 50 mL of water and acidified to pH 4–5 with dilute hydrochloric acid, and the precipitate was filtered off, washed with water (3×20 mL), dried, and recrystallized from 70% aqueous ethanol.

[4-Chloro-1-(4-fluorophenyl)-1*H*-imidazol-5-yl]-methanethiol (IIIa). Yield 85%, mp 65–66°C. IR spectrum: ν 2565 cm^{-1} (SH). ^{1}H NMR spectrum, δ, ppm: 2.83 t (1H, SH, *J* = 6.8 Hz), 3.68 d (2H, $\mathrm{CH_2}$, *J* = 6.8 Hz), 7.39–7.65 m (4H, $\mathrm{H_{arom}}$), 7.85 s (1H, 2-H). Found, %: C 49.69; H 3.24; N 11.44. *m*/*z* 243 $[M + 1]^+$. $\mathrm{C_{10}H_8ClFN_2S}$. Calculated, %: C 49.49; H 3.32; N 11.54. *M* 242.70.

[4-Chloro-1-(4-chlorophenyl)-1*H*-imidazol-5-yl]-methanethiol (IIIb). Yield 83%, mp 99–100°C. IR spectrum: ν 2260 cm^{-1} (SH). ^{1}H NMR spectrum, δ, ppm: 2.85 t (1H, SH, *J* = 6.6 Hz), 3.82 t (2H, $\mathrm{CH_2}$, *J* = 6.6 Hz), 7.50 d (2H, $\mathrm{H_{arom}}$, *J* = 8.4 Hz), 7.65 d (2H, $\mathrm{H_{arom}}$, *J* = 8.4 Hz), 7.87 s (1H, 2-H). Found, %: C 45.09; H 3.03; N 11.01. *m*/*z* 260 $[M + 1]^+$. $\mathrm{C_{10}H_8Cl_2N_2S}$. Calculated, %: C 46.35; H 3.11; N 10.81. *M* 259.16.

[4-Chloro-1-(4-methylphenyl)-1*H*-imidazol-5-yl]-methanethiol (IIIc). Yield 83%, mp 69–70°C. IR spectrum: ν 2265 cm^{-1} (SH). ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, $\mathrm{CH_3}$), 2.78 t (1H, SH, *J* = 6.8 Hz), 3.66 d (2H, $\mathrm{CH_2}$, *J* = 6.8 Hz), 7.33–7.39 m (4H, $\mathrm{H_{arom}}$), 7.83 s (1H, 2-H). Found, %: C 55.12; H 4.70; N 11.90. *m*/*z* 239 $[M + 1]^+$. $\mathrm{C_{11}H_{11}ClN_2S}$. Calculated, %: C 55.34; H 4.64; N 11.73. *M* 238.74.

Compounds IVa–IVc (*general procedure*)**.** *a*. Thiol **IIIa–IIIc**, 3 mmol, was dissolved in 15 mL of ethanol, 0.24 g (6 mmol) of sodium hydroxide and 0.43 g (3 mmol) of methyl iodide were added in succession, and the mixture was stirred for 2 h and poured into 20 mL of water. The precipitate was filtered off, washed with water, dried, and recrystallized from 70% aqueous ethanol.

b. Sodium hydroxide, 0.36 g (9 mmol), was added to a solution of 3 mmol of thiuronium salt **IIa–IIc** in 20 mL of ethanol, the mixture was stirred for 1 h, 0.43 g (3 mmol) of methyl iodide was added, and the mixture was stirred for 2 h and poured into 30 mL of water. The precipitate was filtered off, washed with water, dried, and recrystallized from 70% aqueous ethanol.

4-Chloro-1-(4-fluorophenyl)-5-[(methylsulfanyl)-methyl]-1*H*-imidazole (IVa). Yield 83 (*a*), 86% (*b*), mp 86–87°C. ^{1}H NMR spectrum, δ, ppm: 1.91 s (3H, $\mathrm{CH_3}$), 3.68 s (2H, $\mathrm{CH_2}$), 7.40–7.46 m (2H, $\mathrm{H_{arom}}$), 7.59–7.64 m (2H, $\mathrm{H_{arom}}$), 7.87 s (1H, 2-H). Found, %: C 51.19; H 3.84; N 11.14. *m*/*z* 257 $[M + 1]^+$. $\mathrm{C_{11}H_{10}ClFN_2S}$. Calculated, %: C 51.46; H 3.93; N 10.91. *M* 256.73.

4-Chloro-1-(4-chlorophenyl)-5-[(methylsulfanyl)-methyl]-1*H*-imidazole (IVb). Yield 85 (*a*), 86% (*b*), mp 109–110°C. ^{1}H NMR spectrum, δ, ppm: 1.91 s (3H, $\mathrm{CH_3}$), 3.71 s (2H, $\mathrm{CH_2}$), 7.40 d (2H, $\mathrm{H_{arom}}$, *J* =

8.8 Hz), 7.64 d (2H, H_{arom}, J = 8.8 Hz), 7.91 s (1H, 2-H). Found, %: C 48.49; H 3.74; N 10.34. *m*/*z* 274 $[M + 1]^+$. $C_{11}H_{10}Cl_2N_2S$. Calculated, %: C 48.36; H 3.69; N 10.25. *M* 273.19.

4-Chloro-1-(4-methylphenyl)-5-[(methylsulfanyl)methyl]-1*H*-imidazole (IVc). Yield 80 (*a*), 83% (*b*), mp 101–102°C. ^{1}H, δ, ppm: 1.93 s (3H, CH_3), 2.38 s (3H, CH_3), 3.65 s (2H, CH_2), 7.36 d (2H, H_{arom}, J = 8.0 Hz), 7.40 d (2H, H_{arom}, J = 8.0 Hz), 7.82 s (1H, 2-H). Found, %: C 57.19; H 5.09; N 10.94. *m*/*z* 253 $[M + 1]^+$. $C_{12}H_{13}ClN_2S$. Calculated, %: C 57.02; H 5.18; N 11.08. *M* 252.77.

Compounds **IVd**–**IVf**, **Va**–**Vc**, and **VIIa**–**VIIc** were synthesized in a similar way (method *b*).

5-[(Butylsulfanyl)methyl]-4-chloro-1-(4-chlorophenyl)-1*H*-imidazole (IVd). Yield 80%, mp 54–55°C. ^{1}H NMR spectrum, δ, ppm: 0.81 t (3H, CH_3, J = 8.4 Hz), 1.35–1.43 m (2H, CH_2), 2.39 t (2H, CH_2, J = 8.0 Hz), 3.72 s (2H, CH_2), 7.58 d (2H, H_{arom}, J = 8.8 Hz), 7.65 d (2H, H_{arom}, J = 8.8 Hz), 7.89 s (1H, 2-H). Found, %: C 53.49; H 5.21; N 9.02. *m*/*z* 316 $[M + 1]^+$. $C_{14}H_{16}Cl_2N_2S$. Calculated, %: C 53.34; H 5.12; N 8.89. *M* 315.27.

5-[(Benzylsulfanyl)methyl]-4-chloro-1-(4-chlorophenyl)-1*H*-imidazole (IVe). Yield 86%, mp 77–78°C. ^{1}H NMR spectrum, δ, ppm: 3.63 s (2H, CH_2), 3.66 s (2H, CH_2), 7.15–7.29 m (5H, H_{arom}), 7.49 d (2H, H_{arom}, J = 8.4 Hz), 7.56 d (2H, H_{arom}, J = 8.4 Hz), 7.87 s (1H, 2-H). Found, %: C 58.69; H 4.14; N 7.84. *m*/*z* 350 $[M + 1]^+$. $C_{17}H_{14}Cl_2N_2S$. Calculated, %: C 58.46; H 4.04; N 8.02. *M* 349.28.

5-[(Benzylsulfanyl)methyl]-4-chloro-1-(4-methylphenyl)-1*H*-imidazole (IVf). Yield 84%, mp 60–61°C. ^{1}H NMR spectrum, δ, ppm: 2.38 (3H, CH_3), 3.63 s (2H, CH_2), 3.65 s (2H, CH_2), 7.15–7.39 m (9H, H_{arom}), 7.81 s (1H, 2-H). Found, %: C 65.49; H 5.14; N 8.34. *m*/*z* 329 $[M + 1]^+$. $C_{18}H_{17}ClN_2S$. Calculated, %: C 65.74; H 5.21; N 8.52. *M* 328.87.

4-Chloro-1-(4-fluorophenyl)-5-[(prop-2-yn-1-ylsulfanyl)methyl]-1*H*-imidazole (Va). Yield 82%, mp 69–70°C. ^{1}H NMR spectrum, δ, ppm: 3.11 s (1H, HC≡), 3.22 s (2H, $CH_2C≡$), 3.86 s (2H, CH_2), 7.38–7.62 m (4H, H_{arom}), 7.87 s (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 18.75 (CH_2), 22.78 (**C**$H_2C≡$), 73.56 (≡CH), 79.96 (CH_2**C**≡), 116.48 d ($C^{3'}$, $^2J_{CF}$ = 23.8 Hz), 122.92, 128.03 (C_{arom}), 128.33 (C^5), 131.87 (C^4), 136.86 (C^2), 161.92 d ($C^{4'}$, $^1J_{CF}$ = 248.6 Hz). Found, %: C 55.89; H 3.68; N 10.14. *m*/*z* 281 $[M + 1]^+$. $C_{13}H_{10}ClFN_2S$. Calculated, %: C 55.62; H 3.59; N 9.98. *M* 280.75.

4-Chloro-1-(4-chlorophenyl)-5-[(prop-2-yn-1-ylsulfanyl)methyl]-1*H*-imidazole (Vb). Yield 84%, mp 87–88°C. ^{1}H NMR spectrum, δ, ppm: 3.11 s (1H, HC≡), 3.22 s (2H, $CH_2C≡$), 3.88 s (2H, CH_2), 7.58 d (2H, H_{arom}, J = 8.4 Hz), 7.64 d (2H, H_{arom}, J = 8.4 Hz), 7.89 s (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 18.36 (CH_2), 23.13 (**C**$H_2C≡$), 74.22 (≡CH), 80.17 (CH_2**C**≡), 123.43, 125.55, 129.66, 138.17 (C_{arom}), 128.62 (C^5), 132.40 (C^4), 136.14 (C^2). Found, %: C 52.79; H 3.34; N 9.34. *m*/*z* 298 $[M + 1]^+$. $C_{13}H_{10}Cl_2N_2S$. Calculated, %: C 52.54; H 3.39; N 9.43. *M* 297.21.

4-Chloro-1-(4-methylphenyl)-5-[(prop-2-yn-1-ylsulfanyl)methyl]-1*H*-imidazole (Vc). Yield 84%, mp 75–76°C. ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3), 3.11 s (1H, HC≡), 3.22 s (2H, $CH_2C≡$), 3.86 s (2H, CH_2), 7.35 d (2H, H_{arom}, J = 8.0 Hz), 7.44 d (2H. H_{arom}, J = 8.0 Hz), 7.83 s (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 18.82 (CH_2), 20.45 (CH_3), 22.89 (**C**$H_2C≡$), 73.37 (≡CH), 79.97 (CH_2**C**≡), 122.79, 125.27, 129.85, 138.55 (C_{arom}), 128.21 (C^5), 133.00 (C^4), 136.35 (C^2). Found, %: C 60.42; H 4.62; N 10.24. *m*/*z* 277 $[M + 1]^+$. $C_{14}H_{13}ClN_2S$. Calculated, %: C 60.75; H 4.73; N 10.12. *M* 276.79.

{[4-Chloro-1-(4-fluorophenyl)-1*H*-imidazol-5-yl]methyl}sulfanylacetic acid (VIIa). Yield 84%, mp 139–140°C. IR spectrum, ν, cm^{-1}: 1685 (C=O), 2430–2850 (OH). ^{1}H NMR spectrum, δ, ppm: 3.17 s (2H, CH_2), 3.82 s (2H, CH_2), 7.36–7.43 m (2H, H_{arom}), 7.60–7.65 m (2H, H_{arom}), 7.87 s (1H, 2-H), 12.55 br.s (1H, OH). Found, %: C 47.79; H 3.27; N 9.44. *m*/*z* 301 $[M + 1]^+$. $C_{12}H_{10}ClFN_2O_2S$. Calculated, %: C 47.93; H 3.35; N 9.31. *M* 300.74.

{[4-Chloro-1-(4-chlorophenyl)-1*H*-imidazol-5-yl]methyl}sulfanylacetic acid (VIIb). Yield 85%, mp 86–87°C. IR spectrum, ν, cm^{-1}: 1680 (C=O), 2450–2840 (OH). ^{1}H NMR spectrum, δ, ppm: 3.17 s (2H, CH_2), 3.85 s (2H, CH_2), 7.57–7.63 m (4H, H_{arom}), 7.90 s (1H, 2-H), 12.60 br.s (1H, OH). Found, %: C 45.18; H 3.27; N 8.74. *m*/*z* 318 $[M + 1]^+$. $C_{12}H_{10}Cl_2N_2O_2S$. Calculated, %: C 45.44; H 3.18; N 8.83. *M* 317.20.

{[4-Chloro-1-(4-methylphenyl)-1*H*-imidazol-5-yl]methyl}sulfanylacetic acid (VIIc). Yield 82%, mp 111–113°C. IR spectrum, ν, cm^{-1}: 1680 (C=O), 2450–2820 (OH). ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, CH_3), 3.17 s (2H, CH_2), 3.82 s (2H, CH_2), 7.36 d (2H, H_{arom}, J = 8.0 Hz), 7.41 d (2H, H_{arom}, J = 8.0 Hz), 7.83 s (1H, 2-H), 12.54 br.s (1H, OH). Found, %:

C 52.78; H 4.27; N 9.60. *m*/*z* 297 [*M* + 1]$^+$. $C_{13}H_{13}ClN_2O_2S$. Calculated, %: C 52.61; H 4.42; N 9.44. *M* 296.78.

Compound VIa–VIc (*general procedure*). *a*. Sodium hydroxide, 0.36 g (9 mmol), was added to a solution of 3 mmol of thiuronium salt **IIa–IIc** in 20 mL of ethanol, the mixture was stirred for 1 h, a solution of 0.47 g (4 mmol) of propargyl bromide in 5 ml of ethanol was added, and the mixture was heated for 0.5 h, cooled, and poured into 20 mL of water. The precipitate was filtered off, washed with water (3 × 20 mL), dried, and recrystallized from 70% aqueous ethanol.

b. Sodium hydroxide, 0.08 g (2 mmol), was added to a solution of 2 mmol of compound **Vb** in 10 mL of ethanol, the mixture was heated for 0.5 h under reflux, cooled, and poured into 10 mL of water. The precipitate was filtered off, washed with water (3 × 10 mL), dried, and recrystallized from 70% aqueous ethanol.

4-Chloro-1-(4-fluorophenyl)-5-[(prop-1-yn-1-ylsulfanyl)methyl]-1*H*-imidazole (VIa). Yield 85% (*a*), mp 80–81°C. ^{1}H NMR spectrum, δ, ppm: 1.83 s (3H, CH_3), 3.97 s (2H, CH_2), 7.40–7.63 m (4H, H_{arom}), 7.89 s (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 4.38 ($\mathbf{C}H_3C\equiv$), 27.08 (CH_2), 65.66 ($SC\equiv$), 92.91 ($\equiv SCH_3$), 116.20 d ($C^{3'}$, $C^{5'}$, $^2J_{CF}$ = 25.3 Hz), 122.34 (C_{arom}), 128.01 d ($C^{2'}$, $C^{6'}$, $^3J_{CF}$ = 6.8 Hz), 129.33 (C^5), 131.70 (C^4), 136.99 (C^2), 161.93 d ($C^{4'}$, $^1J_{CF}$ = 245.0 Hz). Found, %: C 55.84; H 3.49; N 9.84. *m*/*z* 281 [*M* + 1]$^+$. $C_{13}H_{10}ClFN_2S$. Calculated, %: C 55.62; H 3.59; N 9.98. *M* 280.75.

4-Chloro-1-(4-chlorophenyl)-5-[(prop-1-yn-1-ylsulfanyl)methyl]-1*H*-imidazole (VIb). Yield 84 (*a*), 78% (*b*), mp 85–86°C. ^{1}H NMR spectrum, δ, ppm: 1.81 s (3H, CH_3), 4.00 s (2H, CH_2), 7.55 d (2H, H_{arom}, *J* = 8.4 Hz), 7.65 d (2H, H_{arom}, *J* = 8.4 Hz), 7.93 s (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 4.41 ($\mathbf{C}H_3C\equiv$), 27.03 (CH_2), 65.57 ($SC\equiv$), 92.84 ($\equiv\mathbf{C}CH_3$), 122.15, 127.59, 129.57, 134.18 (C_{arom}), 129.54 (C^5), 133.66 (C^4), 136.65 (C^2). Found, %: C 52.79; H 3.34; N 9.34. *m*/*z* 298 [*M* + 1]$^+$. $C_{13}H_{10}Cl_2N_2S$. Calculated, %: C 52.54; H 3.39; N 9.43. *M* 297.21.

4-Chloro-1-(4-methylphenyl)-5-[(prop-1-yn-1-ylsulfanyl)methyl]-1*H*-imidazole (VIc). Yield 85% (*a*), mp 79–80°C. ^{1}H NMR spectrum, δ, ppm: 1.82 s (3H, CH_3), 2.38 s (3H, CH_3), 3.97 s (2H, CH_2), 7.38 s (4H, H_{arom}), 7.86 s (1H, 2-H). ^{13}C NMR spectrum, δ_C, ppm: 4.31 ($\mathbf{C}H_3C\equiv$), 20.69 (CH_3), 27.15 (CH_2), 65.72 ($SC\equiv$), 92.78 ($\equiv\mathbf{C}CH_3$), 122.03, 125.31, 129.84, 138.69 (C_{arom}), 129.25 (C^5), 132.78 (C^4), 136.72 (C^2). Found, %: C 60.59; H 4.64; N 10.01. *m*/*z* 277 [*M* + 1]$^+$. $C_{14}H_{13}ClN_2S$. Calculated, %: C 60.75; H 4.73; N 10.12. *M* 276.79.

Compounds VIIIa–VIIIe (*general procedure*). Potassium permanganate, 0.48 g (3 mmol), was added under stirring over a period of 0.5 h to a suspension of 2 mmol of 5-[(R-sulfanyl)methyl]imidazole **IVa–IVc**, **VIIa**, or **VIIb** in 2 mL of water, and the mixture was stirred for 2 h. The mixture was then treated with solid sodium sulfite until violet color disappeared and extracted with benzene. The organic phase was dried over sodium sulfate and evaporated, and the residue was recrystallized from 70% aqueous ethanol.

4-Chloro-1-(4-fluorophenyl)-5-[(methylsulfonyl)methyl]-1*H*-imidazole (VIIIa). Yield 50%, mp 129–130°C. ^{1}H NMR spectrum, δ, ppm: 2.93 s (3H, CH_3), 4.49 s (2H, CH_2), 7.36–7.72 m (4H, H_{arom}), 7.98 s (1H, 2-H). Found, %: C 45.89; H 3.54; N 9.84. *m*/*z* 289 [*M* + 1]$^+$. $C_{11}H_{10}ClFN_2O_2S$. Calculated, %: C 45.76; H 3.49; N 9.70. *M* 288.73.

4-Chloro-1-(4-chlorophenyl)-5-[(methylsulfonyl)methyl]-1*H*-imidazole (VIIIb). Yield 48%, mp 117–119°C. ^{1}H NMR spectrum, δ, ppm: 2.95 s (3H, CH_3), 4.53 s (2H, CH_2), 7.56 d (2H, H_{arom}, *J* = 8.4 Hz), 7.63 d (2H, H_{arom}, *J* = 8.4 Hz), 8.01 s (1H, 2-H). Found, %: C 43.49; H 3.40; N 9.04. *m*/*z* 306 [*M* + 1]$^+$. $C_{11}H_{10}Cl_2N_2O_2S$. Calculated, %: C 43.29; H 3.30; N 9.18. *M* 305.18.

4-Chloro-1-(4-methylphenyl)-5-[(methylsulfonyl)methyl]-1*H*-imidazole (VIIIc). Yield 45%, mp 115–117°C. ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, CH_3), 2.90 s (3H, CH_3), 4.48 s (2H, CH_2), 7.37 s (4H, H_{arom}), 7.95 s (1H, 2-H). Found, %: C 50.49; H 4.49; N 9.94. *m*/*z* 285 [*M* + 1]$^+$. $C_{12}H_{13}ClN_2O_2S$. Calculated, %: C 50.61; H 4.60; N 9.84. *M* 284.77.

{[4-Chloro-1-(4-fluorophenyl)-1*H*-imidazol-5-yl]methylsulfonyl}acetic acid (VIIId). Yield 54%, mp 178–180°C. ^{1}H NMR spectrum, δ, ppm: 4.29 s (2H, CH_2), 4.71 s (2H, CH_2), 7.37–7.58 m (4H, H_{arom}), 7.97 s (1H, 2-H), 13.48 br.s (1H, OH). Found, %: C 43.59; H 2.97; N 8.54. *m*/*z* 333 [*M* + 1]$^+$. $C_{12}H_{10}ClFN_2O_4S$. Calculated, %: C 43.32; H 3.03; N 8.42. *M* 332.74.

{[4-Chloro-1-(4-chlorophenyl)-1*H*-imidazol-5-yl]methylsulfonyl}acetic acid (VIIIe). Yield 55%, mp 208–210°C. IR spectrum, ν, cm^{-1}: 1680 (C=O), 2450–2840 (OH). ^{1}H NMR spectrum, δ, ppm: 4.30 s (2H, CH_2), 4.73 s (2H, CH_2), 7.54 d (2H, H_{arom}, *J* =

8.4 Hz), 7.61 d (2H, H_{arom}, J = 8.4 Hz), 8.02 s (1H, 2-H), 13.50 br.s (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 47.50 (CH_2), 57.36 (CH_2), 114.69 (C^5), 128.89, 129.29, 133.77, 134.19 (C_{arom}), 132.03 (C^4), 135.42 (C^2), 164.37 (C=O). Found, %: C 41.48; H 2.77; N 7.90. m/z 350 $[M + 1]^+$. $C_{12}H_{10}Cl_2N_2O_4S$. Calculated, %: C 41.28; H 2.89; N 8.02. M 349.20.

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