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Synthesis of 4,5-Dichloroisothiazole-3-carboxylic Acid Amides and Esters

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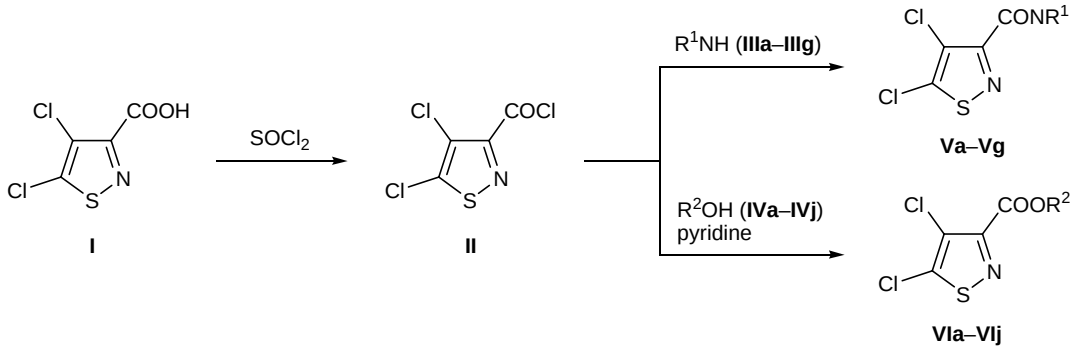
Abstract—Previously unknown 4,5-dichloroisothiazole-3-carboxylic acid amides and esters were synthesized by reactions of 4,5-dichloroisothiazole-3-carbonyl chloride with ammonia, heterocyclic and aromatic amines, and functionally substituted alcohols and phenols.

Extensive development of the chemistry of isothiazole and its derivatives in the recent years resulted from a wide range of useful properties of these compounds, primarily their high biological activity; some isothiazole derivatives were shown to be effective agrochemicals and medicines [1]. A considerable number of studies in the field of the isothiazole chemistry dealt with the synthesis of isothiazolecarboxylic acid esters which were found to exhibit a high antimicrobial activity [2] and isothiazolylamides which possess fungicide [3–5] and herbicide properties [6]. The use of isothiazole derivatives as herbicides in combination with other pesticides is characterized by synergistic effect; isothiazole derivatives were shown to enhance the activity of such known preparations as Dicamba, Glyphosate, and herbicides based on phenoxybutyric and phenoxypropionic acids [7].

We previously described a convenient procedure for synthesizing 4,5-dichloroisothiazole-3-carboxylic acid (**I**) via a new reaction involving isothiazole ring closure [8]. Preliminary experiments showed that acid **I** is weakly reactive toward aliphatic alcohols in the presence of concentrated mineral acids [9].

With the goal of obtaining a series of new amides (compounds **Va**–**Vg**) and esters (**VIa**–**VIj**), as initial compounds we selected aromatic and heterocyclic amines **IIIa**–**IIIf**, ammonia (**IIIg**), long-chain aliphatic alcohols, and functionally substituted phenols (**IVa**–**IVj**). Most compounds **IIIa**–**IIIf** and **IVa**–**IVj** *per se* exhibit various kinds of biological activity. It should be also noted that biological activity of carboxylic acid esters is usually higher than the activity of the parent acids and their salts [10]. Therefore, we anticipated that biological activity of amides and esters derived

Scheme 1.



III, **V**, R^1N = 3,5-dimethylpyrazol-1-yl (**a**), 1-benzotriazolyl (**b**), PhNH (**c**), 2-$MeOC_6H_4NH$ (**d**), 4-IC_6H_4NH (**e**), 4-MeC_6H_4NH (**f**), NH_2 (**g**); **IV**, **VI**, R^2 = Ph (**a**), 4-FC_6H_4 (**b**), furfuryl (**c**), cyclohexyl (**d**), 2-$MeOCOC_6H_4$ (**e**), 4,4'-bis(methoxycarbonylbiphenyl-3-yl (**f**), 8-quinolyl (**g**), $C_{15}H_{31}$ (**h**), $C_{16}H_{33}$ (**i**), $C_{17}H_{35}$ (**j**).

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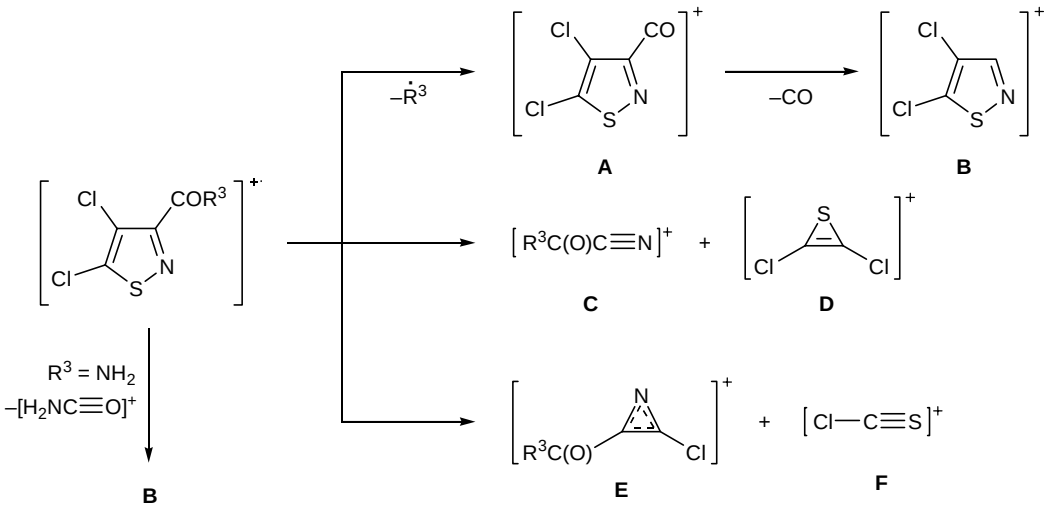
from 4,5-dichloroisothiazole-3-carboxylic acid (**I**) and amines and alcohols having pharmacophoric fragments (**IIIa**–**IIIf** and **IVa**–**IVj**) should be fairly high. We hoped to observe so-called internal synergistic effect arising from mutual influence of pharmacophoric fragments in the target compounds.

Amides **Va**–**Vg** and esters **VIa**–**VIj** were synthesized by reaction of the corresponding amines and alcohols with 4,5-dichloroisothiazole-3-carbonyl chloride (**II**) in anhydrous diethyl ether (Scheme 1). Acyl chloride **II** was obtained in 98.3% yield by heating 4,5-dichloroisothiazole-3-carboxylic acid (**I**) with thionyl chloride in boiling carbon tetrachloride [11]. The procedure for the synthesis of amides **V** and esters **VI** is advantageous due to its simplicity, mild conditions, easy isolation of the products, and good reproducibility [12]. The corresponding amides **Va**–**Vg** and esters **VIa**–**VIj** were isolated in 75–93% yield. According to the GC–MS data, the products contained 97.5–99.8% of the main substance. Their structure was confirmed by the elemental analyses and IR, UV, ^{1}H NMR, and mass spectra. In the IR spectra of amides **Va**–**Vg**, stretching vibrations of the amide carbonyl group appeared as strong bands in the region 1656–1720 cm^{-1}, and N–H bonds in compounds **Vc**–**Vg** were characterized by absorption bands at 3249–3432 cm^{-1}. The IR spectra of esters **VIa**–**VIj** contained no O–H absorption bands typical of the initial alcohols, but stretching vibrations of the carbonyl and C–O groups were observed at 1719–1757 and 1008–1285 cm^{-1}, respectively. The isothiazole ring in both amides **V** and esters **VI** characteristically gives rise to three absorption bands in the range from 1311 to 1512 cm^{-1}.

The ^{1}H NMR spectra of **Va**–**Vg** and **VIa**–**VIj** contained signals from protons in the amine and alcohol fragments. The NH signal of amides **Vc**–**Vg** appeared as a broadened singlet at δ 8.15–9.53 ppm. In the UV spectra of **Va**–**Vg** and **VIa**–**VIj** we observed three absorption bands, the most intense of which was located at λ 204–208 nm. Exceptions were pyrazole derivative **Va** and quinolyl ester **VIg**; in the spectra of these compounds, the most intense absorption band was observed at λ 254 and 243 nm, respectively. Obviously, the long-wave shift of the absorption maximum results from the presence of a strong chromophoric group (pyrazole or quinoline ring) in their molecules.

Convincing proofs for the assumed structure of amides **Va**–**Vg** and esters **VIa**–**VIj** were obtained by analysis of their mass spectra which contained molecular ion clusters with an isotope ratio indicating the presence of two chlorine atoms (100:65) [13, 14]. Fragmentation of the molecular ions includes several pathways. The main pathways may be decomposition of the amide or ester group [15] to give ions **A** and **B**, elimination of chlorine, and cleavage of the heteroring with formation of ions **C**–**F**, which is typical of isothiazoles [16, 17] (Scheme 2). Among these, the predominant pathway is fragmentation of the side chain, as follows from the presence in the mass spectra of peaks from ions **A** [*m*/*z* 180 (hereinafter, ions containing ^{35}Cl isotope are meant)] and **B** (*m*/*z* 152), as well as from those formed by elimination of chlorine

Scheme 2.



Vb–**Vf,** $R^3 = R^1$; **VIa**–**VIj**, $R^3 = OR^2$.

therefrom. Ions **C** and **E**, which might be formed by cleavage of the isothiazole ring in the molecular ion, were not detected, presumably due to concurrent fragmentation of the amide or ester group. However, peaks from ions **D** (*m*/*z* 126) and **F** (*m*/*z* 79) were present in the spectra; these ions could be formed by fragmentation of both the molecular ion and ions **A** and **B**.

EXPERIMENTAL

The IR spectra were recorded on a Protege-460 Fourier spectrometer from samples prepared as KBr pellets. The ^{1}H NMR spectra were obtained on a Tesla-587A spectrometer (80 MHz) from solutions in $CDCl_3$; the chemical shifts were measured relative to octamethyltrisiloxane. The UV spectra were measured on a Specord UV-Vis spectrophotometer from 1×10^{-4} M solutions in 1-butanol (**Va**–**Vg**, **VIa**–**VIj**) or hexane (**II**). The mass spectra (electron impact, 50 eV) were recorded on an MKh-1320 spectrometer. Gas chromatographic–mass spectrometric analysis was performed on a Hewlett-Packard HP 5972 mass-selective detector coupled with an HP 5890 gas chromatograph.

4,5-Dichloroisothiazole-3-carbonyl chloride (II). Thionyl chloride, 7.14 g (60 mmol), was added to a solution of 1.98 g (10 mmol) of 4,5-dichloroisothiazole-3-carboxylic acid (**I**) in 30 ml of carbon tetrachloride. The mixture was heated for 16 h under reflux, and the solvent and excess thionyl chloride were distilled off under reduced pressure. The dry residue was washed with hexane on a filter and recrystallized from hexane–diethyl ether (1:2). Yield 2.12 g (98%), mp 66–68°C. IR spectrum, ν, cm^{-1}: 1765 (C=O); 1477, 1440, 1353, 1320 (isothiazole); 865, 853, 735 (C–Cl). UV spectrum, λ_{max}, nm (ε): 214 (12000), 249 (6000), 284 (4000). Mass spectrum, *m*/*z* (I_{rel}, %): 215 (7) $[M]^+$, 180 (100), 152 (20), 126 (11), 117 (39), 82 (32), 79 (17), 44 (28). Found, %: C 22.24; Cl 48.89; N 6.51; S 14.72. M^+ 215. C_4Cl_3NOS. Calculated, %: C 22.19; Cl 49.13; N 6.47; S 14.81. *M* 216.46.

4,5-Dichloro-3-(3,5-dimethylpyrazol-1-ylcarbonyl)isothiazole (Va). A solution of 1.92 g (20 mmol) of 3,5-dimethylpyrazole in 20 ml of anhydrous diethyl ether was added dropwise at 10–15°C to a solution of 2.17 g (10 mmol) of 4,5-dichloroisothiazole-3-carbonyl chloride (**II**) in 30 ml of anhydrous diethyl ether. The mixture was stirred for 2 h at 20–25°C, and the precipitate was filtered off, washed with water and diethyl ether, dried under reduced pressure, and recrystallized from chloroform–hexane (2:1). Yield 2.44 g (88%), mp 92–93°C. IR spectrum, ν, cm^{-1}: 3115 (=CH); 2993, 2936 (C–H_{aliph}); 1712 (C=O); 1620 (C=C); 1596 (C=N); 1502, 1408, 1339 (isothiazole). UV spectrum, λ_{max}, nm (ε): 204 (6000), 220 (6000), 254 (12000). ^{1}H NMR spectrum, δ, ppm: 2.18 s (3H, CH_3), 2.64 s (3H, CH_3), 6.07 s (1H, =CH). Mass spectrum, *m*/*z* (I_{rel}, %): 275 (5) $[M]^+$, 240 (84), 180 (61), 152 (20), 126 (7), 117 (18), 95 (100), 79 (7). Found, %: C 39.43; H 2.48; Cl 25.39; N 14.92; S 11.94. M^+ 275. $C_9H_7Cl_2N_3OS$. Calculated, %: C 39.14; H 2.56; Cl 25.67; N 15.22; S 11.61. *M* 276.15.

Compounds **Vb**–**Vf** were synthesized in a similar way from 4,5-dichloroisothiazole-3-carbonyl chloride (**II**) and the corresponding N-nucleophiles **IIIb**–**IIIf**.

3-(1-Benzotriazolylcarbonyl)-4,5-dichloroisothiazole (Vb). Yield 87%, mp 150–151°C (from methanol). IR spectrum, ν, cm^{-1}: 3102 (=CH); 1720 (C=O); 1620, 1590 (C=C); 1500, 1390, 1357 (isothiazole). UV spectrum, λ_{max}, nm (ε): 207 (21000), 260 (9000), 274 (8000). ^{1}H NMR spectrum, δ, ppm: 7.33–7.59 m (2H, H_{arom}), 7.74–7.98 m (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 298 (4) $[M]^+$, 263 (72), 180 (58), 152 (17), 126 (6), 118 (100), 79 (10). Found, %: C 40.27; H 1.30; Cl 23.49; N 18.81; S 11.00. M^+ 298. $C_{10}H_4Cl_2N_4OS$. Calculated, %: C 40.15; H 1.35; Cl 23.70; N 18.73; S 11.00. *M* 299.14.

***N*-Phenyl-4,5-dichloroisothiazole-3-carboxamide (Vc).** Yield 80%, mp 160–162°C (from chloroform–hexane, 2:1). IR spectrum, ν, cm^{-1}: 3251 (NH); 3075 (=CH); 1665 (C=O); 1602, 1560, 1540 (C=C); 1496, 1355, 1312 (isothiazole). UV spectrum, λ_{max}, nm (ε): 205 (12000), 237 (9000), 278 (5000). ^{1}H NMR spectrum, δ, ppm: 6.98–7.86 m (5H, H_{arom}), 8.85 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 272 (49) $[M]^+$, 237 (9), 180 (100), 152 (20), 126 (7), 117 (17), 92 (14), 79 (10). Found, %: C 44.12; H 2.17; Cl 26.02; N 10.28; S 11.68. M^+ 272. $C_{10}H_6Cl_2N_2OS$. Calculated, %: C 43.97; H 2.22; Cl 25.96; N 10.26; S 11.74. *M* 273.14.

***N*-(2-Methoxyphenyl)-4,5-dichloroisothiazole-3-carboxamide (Vd).** Yield 85%, mp 132–133°C (from chloroform–hexane, 2:1). IR spectrum, ν, cm^{-1}: 3371 (NH); 3020 (=CH); 1686 (C=O); 1603, 1533 (C=C); 1486, 1377, 1347 (isothiazole). UV spectrum, λ_{max}, nm (ε): 208 (23000), 242 (14000), 312 (7000). ^{1}H NMR spectrum, δ, ppm: 3.93 s (3H, OCH_3), 6.92–7.13 m (3H, H_{arom}), 8.40–8.55 m (1H, H_{arom}), 9.53 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 302 (23) $[M]^+$, 267 (11), 180 (100), 152 (25), 126 (4), 122 (15), 92 (18), 79 (11). Found, %: C 43.81; H 2.81; Cl 23.18; N 8.91;

S 10.72. M^+ 302. $C_{11}H_8Cl_2N_2O_2S$. Calculated, %: C 43.58; H 2.67; Cl 23.39; N 9.24; S 10.57. *M* 303.17.

***N*-(4-Iodophenyl)-4,5-dichloroisothiazole-3-carboxamide (Ve).** Yield 89%, mp 153–155°C (from chloroform–hexane, 2:1). IR spectrum, ν, cm^{-1}: 3400 (NH); 1656 (C=O); 1606, 1563 (C=C); 1485, 1393, 1311 (isothiazole). UV spectrum, λ_{max}, nm (ε): 205 (23000), 250 (17000), 310 (1000). ^{1}H NMR spectrum, δ, ppm: 6.63 d (2H, H_{arom}, ^3J = 8.7 Hz), 7.42 d (2H, H_{arom}, ^3J = 8.7 Hz), 8.43 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 398 (12) $[M]^+$, 363 (12), 218 (35), 180 (100), 152 (28), 126 (6), 117 (19), 79 (6). Found, %: C 29.89; H 1.32; Cl 17.83; I 31.86; N 7.04; S 7.99. M^+ 398. $C_{10}H_5Cl_2IN_2OS$. Calculated, %: C 30.10; H 1.27; Cl 17.77; I 31.80; N 7.02; S 8.03. *M* 399.03.

***N*-(4-Methylphenyl)-4,5-dichloroisothiazole-3-carboxamide (Vf).** Yield 84%, mp 127–129°C (from chloroform–hexane, 2:1). IR spectrum, ν, cm^{-1}: 3249 (NH); 3063 (=CH); 1662 (C=O); 1603, 1556 (C=C); 1512, 1354, 1312 (isothiazole). UV spectrum, λ_{max}, nm (ε): 206 (19000), 238 (13000), 280 (7000). ^{1}H NMR spectrum, δ, ppm: 2.34 s (3H, CH_3), 7.15 d (2H, H_{arom}, ^3J = 7.7 Hz), 7.55 d (2H, H_{arom}, ^3J = 7.7 Hz), 8.82 br.s (1H, NH). Mass spectrum, *m*/*z* (I_{rel}, %): 286 (19) $[M]^+$, 251 (23), 180 (100), 152 (25), 126 (10), 117 (21), 106 (17), 79 (12). Found, %: C 45.87; H 2.96; Cl 24.41; N 10.02; S 10.93. M^+ 286. $C_{11}H_8Cl_2N_2OS$. Calculated, %: C 46.00; H 2.81; Cl 24.69; N 9.76; S 11.16. *M* 287.17.

4,5-Dichloroisothiazole-3-carboxamide (Vg). Aqueous ammonia (25%), 10 ml, was added at 20–25°C to 2.17 g (10 mmol) of 4,5-dichloroisothiazolecarbonyl chloride (**II**), and the mixture was stirred for 4 h. The precipitate was filtered off, washed with water, dried under reduced pressure, and recrystallized from methanol. Yield 1.71 g (87%), mp 173–174°C. IR spectrum, ν, cm^{-1}: 3432 (NH_2); 1712 (C=O); 1613 (δNH_2); 1440, 1347, 1311 (isothiazole). UV spectrum, λ_{max}, nm (ε): 205 (8000), 228 (5000), 270 (5000). ^{1}H NMR spectrum, δ, ppm: 8.15 br.s (2H, NH_2). Mass spectrum, *m*/*z* (I_{rel}, %): 196 (46) $[M]^+$, 180 (22), 152 (32), 126 (7), 117 (56), 79 (17), 44 (100). Found, %: C 24.63; H 1.14; Cl 36.01; N 14.19; S 16.32. M^+ 196. $C_4H_2Cl_2N_2OS$. Calculated, %: C 24.38; H 1.03; Cl 35.98; N 14.22; S 16.27. *M* 197.04.

Phenyl 4,5-dichloroisothiazole-3-carboxylate (VIa). 4,5-Dichloroisothiazolecarbonyl chloride (**II**), 2.17 g (10 mmol), was added at 20–25°C to a solution of 1.12 g (10 mmol) of phenol in 50 ml of anhydrous diethyl ether, and 0.79 g (10 mmol) of pyridine was added in one portion to the resulting solution. The mixture was vigorously stirred for 5 min and was left to stand for 24–36 h at 20–25°C. The precipitate of pyridine hydrochloride was filtered off, and the filtrate was diluted with diethyl ether, washed with water and a 5% solution of sodium hydrogen carbonate, and dried over calcium chloride. The drying agent was filtered off, the solvent was distilled off from the filtrate, and the residue was purified by low-temperature crystallization from 96% ethanol. Yield 2.04 g (75%), mp 110–112°C. IR spectrum, ν, cm^{-1}: 3070 (=CH); 1723 (C=O); 1640, 1545, 1490 (C=C); 1440, 1363, 1337 (isothiazole); 1207, 1086 (C–O). UV spectrum, λ_{max}, nm (ε): 205 (9000), 236 (3000), 270 (4000). ^{1}H NMR spectrum, δ, ppm: 7.62–7.92 m (3H, H_{arom}), 8.10–8.44 m (2H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 273 (9) $[M]^+$, 180 (100), 152 (24), 126 (11), 117 (12), 93 (10), 79 (8). Found, %: C 44.02; H 1.78; Cl 26.00; N 5.14; S 11.83. M^+ 273. $C_{10}H_5Cl_2NO_2S$. Calculated, %: C 43.81; H 1.84; Cl 25.86; N 5.11; S 11.70. *M* 274.12.

Compounds **VIb**–**VIj** were synthesized in a similar way from 4,5-dichloroisothiazolecarbonyl chloride (**II**) and the corresponding alcohol or phenol.

4-Fluorophenyl 4,5-dichloroisothiazole-3-carboxylate (VIb). Yield 82%, mp 124–125°C (from ethanol). IR spectrum, ν, cm^{-1}: 3075 (=CH); 1747 (C=O); 1598, 1505 (C=C); 1480, 1399, 1358 (isothiazole); 1201, 1081 (C–O), 1177 (C–F). UV spectrum, λ_{max}, nm (ε): 206 (16000), 240 (4000), 270 (5000). ^{1}H NMR spectrum, δ, ppm: 7.05–7.13 m (4H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 291 (5) $[M]^+$, 272 (4), 180 (100), 152 (18), 126 (3), 117 (18), 111 (8), 95 (10), 82 (29), 79 (7). Found, %: C 41.24; H 1.41; Cl 24.13; F 6.46; N 4.95; S 10.79. M^+ 291. $C_{10}H_4Cl_2FNO_2S$. Calculated, %: C 41.11; H 1.38; Cl 24.27; F 6.50; N 4.80; S 10.98. *M* 292.11.

Furfuryl 4,5-dichloroisothiazole-3-carboxylate (VIc). Yield 71%, mp 87–89°C (from ethanol). IR spectrum, ν, cm^{-1}: 3133 (=CH); 1724 (C=O); 1615, 1569 (C=C); 1501, 1414, 1353 (isothiazole); 1228, 1084 (C–O). UV spectrum, λ_{max}, nm (ε): 207 (16000), 220 (14000), 274 (6000). ^{1}H NMR spectrum, δ, ppm: 5.38 s (2H, OCH_2), 6.32–6.46 m (1H, =CH), 6.56 d (1H, =CH, ^3J = 3.2 Hz), 7.45 d (1H, =CHO, ^3J = 1.8 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 277 (3) $[M]^+$, 242 (3), 180 (7), 152 (14), 126 (3), 117 (8), 97 (100), 81 (63), 79 (8). Found, %: C 38.65; H 2.01; Cl 25.32;

N 4.99; S 11.61. M^+ 277. $C_9H_5Cl_2NO_3S$. Calculated, %: C 38.87; H 1.82; Cl 25.49; N 5.04; S 11.53. *M* 278.11.

Cyclohexyl 4,5-dichloroisothiazole-3-carboxylate (VId). Yield 78%, mp 45–46°C (from ethanol). IR spectrum, ν, cm^{-1}: 2938, 2857 (CH_{aliph}); 1731 (C=O); 1480, 1383, 1345 (isothiazole); 1236, 1008 (C–O). UV spectrum, λ_{max}, nm (ε): 205 (11000), 240 (5000), 276 (6000). ^{1}H NMR spectrum, δ, ppm: 1.10–2.15 m (10H, CH_2), 4.85–5.35 m (1H, 1-H, cyclohexyl). Mass spectrum, *m*/*z* (I_{rel}, %): 279 (3) $[M]^+$, 244 (6), 196 (71), 180 (100), 152 (17), 126 (5), 117 (23), 99 (19), 83 (29), 79 (14). Found, %: C 42.65; H 4.01; Cl 25.32; N 4.99; S 11.59. M^+ 279. $C_{10}H_{11}Cl_2NO_2S$. Calculated, %: C 42.87; H 3.97; Cl 25.31; N 5.00; S 11.44. *M* 280.18.

2-(Methoxycarbonyl)phenyl 4,5-dichloroisothiazole-3-carboxylate (VIe). Yield 89%, mp 77–78°C (from ethanol). IR spectrum, ν, cm^{-1}: 3070, 3005 (=CH); 2957 (CH_3); 1757, 1719 (C=O); 1606, 1579 (C=C); 1488, 1399, 1352 (isothiazole); 1204, 1192, 1083, 1070 (C–O). UV spectrum, λ_{max}, nm (ε): 205 (27000), 226 (15000), 274 (8000). ^{1}H NMR spectrum, δ, ppm: 3.80 s (3H, OCH_3), 7.2–7.7 m (3H, H_{arom}), 8.10 d (1H, H_{arom}, ^3J = 7.2 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 331 (5) $[M]^+$, 296 (9), 196 (17), 180 (100), 152 (32), 135 (21), 126 (9), 117 (16), 82 (19), 79 (8). Found, %: C 43.33; H 2.10; Cl 21.22; N 4.19; S 9.63. M^+ 331. $C_{12}H_7Cl_2NO_4S$. Calculated, %: C 43.39; H 2.13; Cl 21.35; N 4.22; S 9.65. *M* 332.16.

Dimethyl 3-(4,5-dichloroisothiazol-3-ylcarbonyloxy)biphenyl-4,4'-dicarboxylate (VIf). Yield 93%, mp 104–105°C (from ethanol). IR spectrum, ν, cm^{-1}: 3074, 3001 (=CH); 2952 (CH_3); 1746, 1724 (C=O); 1609, 1560, 1521 (C=C); 1492, 1391, 1355 (isothiazole); 1285, 1249, 1208, 1193, 1113 (C–O). UV spectrum, λ_{max}, nm (ε): 204 (28000), 274 (17000), 330 (3000). ^{1}H NMR spectrum, δ, ppm: 3.92 s (3H, CH_3), 3.96 s (3H, CH_3), 7.47–7.63 m (4H, H_{arom}), 7.93–8.20 m (3H, H_{arom}). Mass spectrum, *m*/*z* (I_{rel}, %): 465 (4) $[M]^+$, 196 (14), 180 (100), 152 (32), 135 (29), 126 (11), 117 (14), 79 (8). Found, %: C 51.56; H 2.71; Cl 15.12; N 3.08; S 6.83. M^+ 465. $C_{20}H_{13}Cl_2NO_6S$. Calculated, %: C 51.51; H 2.82; Cl 15.20; N 3.00; S 6.88. *M* 466.30.

8-Quinolyl 4,5-dichloroisothiazole-3-carboxylate (VIg). Yield 77%, mp 157–158°C (from ethanol). IR spectrum, ν, cm^{-1}: 3010 (=CH); 1747 (C=O); 1625, 1595, 1500 (C=C); 1470, 1388, 1350 (isothiazole); 1232, 1087 (C–O). UV spectrum, λ_{max}, nm (ε): 205 (21000), 243 (36000), 272 (5000), 318 (2000). ^{1}H NMR spectrum, δ, ppm: 7.26–7.86 m (4H, H_{arom}), 8.19 d.d (1H, H_{arom}, ^3J = 8.2 Hz), 8.89 d.d (1H, H_{arom}, ^3J = 4.7 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 324 (9) $[M]^+$, 289 (5), 261 (34), 245 (8), 180 (100), 152 (19), 126 (6), 117 (14), 79 (5). Found, %: C 47.96; H 1.81; Cl 21.91; N 8.59; S 9.92. M^+ 324. $C_{13}H_6Cl_2N_2O_2S$. Calculated, %: C 48.01; H 1.86; Cl 21.80; N 8.62; S 9.86. *M* 325.17.

Pentadecyl 4,5-dichloroisothiazole-3-carboxylate (VIh). Yield 81%, mp 34–35°C (from ethanol). IR spectrum, ν, cm^{-1}: 2955, 2919, 2853 (CH_{aliph}); 1734 (C=O); 1411, 1376, 1355 (isothiazole); 1224, 1086 (C–O). UV spectrum, λ_{max}, nm (ε): 207 (10000), 237 (4000), 270 (5000). ^{1}H NMR spectrum, δ, ppm: 0.85 t (3H, CH_3, ^3J = 5.6 Hz), 1.20–1.67 m [26H, $(CH_2)_{13}$], 4.40 t (2H, CH_2O, ^3J = 7.0 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 407 (4) $[M]^+$, 372 (14), 328 (24), 211 (5), 198 (100), 180 (82), 152 (13), 126 (7), 117 (10), 79 (7). Found, %: C 55.91; H 7.70; Cl 17.09; N 3.52; S 7.69. M^+ 407. $C_{19}H_{31}Cl_2NO_2S$. Calculated, %: C 55.86; H 7.67; Cl 17.36; N 3.43; S 7.85. *M* 408.47.

Hexadecyl 4,5-dichloroisothiazole-3-carboxylate (VIi). Yield 80%, mp 37–38°C (from ethanol). IR spectrum, ν, cm^{-1}: 2956, 2918, 2852 (CH_{aliph}); 1735 (C=O); 1410, 1376, 1356 (isothiazole); 1223, 1087 (C–O). UV spectrum, λ_{max}, nm (ε): 207 (10000), 238 (4000), 271 (5000). ^{1}H NMR spectrum, δ, ppm: 0.87 t (3H, CH_3, ^3J = 5.8 Hz), 1.20–1.65 m [28H, $(CH_2)_{14}$], 4.40 t (2H, CH_2O, ^3J = 7.3 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 421 (5) $[M]^+$, 386 (15), 342 (23), 225 (4), 198 (100), 180 (77), 152 (11), 126 (8), 117 (10), 79 (6). Found, %: C 57.10; H 8.03; Cl 16.50; N 3.18; S 7.34. M^+ 421. $C_{20}H_{33}Cl_2NO_2S$. Calculated, %: C 56.86; H 7.87; Cl 16.78; N 3.32; S 7.59. *M* 422.50.

Heptadecyl 4,5-dichloroisothiazole-3-carboxylate (VIj). Yield 81%, mp 42–43°C (from ethanol). IR spectrum, ν, cm^{-1}: 2955, 2918, 2852 (CH_{aliph}); 1733 (C=O); 1410, 1377, 1356 (isothiazole); 1222, 1087 (C–O). UV spectrum, λ_{max}, nm (ε): 206 (10000), 238 (4000), 274 (5000). ^{1}H NMR spectrum, δ, ppm: 0.85 t (3H, CH_3, ^3J = 5.4 Hz), 1.20–1.75 m [30H, $(CH_2)_{15}$], 4.38 t (2H, CH_2O, ^3J = 6.5 Hz). Mass spectrum, *m*/*z* (I_{rel}, %): 435 (4) $[M]^+$, 400 (13), 356 (22), 239 (5), 198 (100), 180 (70), 152 (10), 126 (7), 117 (9), 79 (5). Found, %: C 57.86; H 7.92; Cl 16.05; N 3.30; S 6.99. M^+ 435. $C_{21}H_{35}Cl_2NO_2S$. Calculated, %: C 57.78; H 8.10; Cl 16.24; N 3.21; S 7.34. *M* 436.53.

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