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# Synthesis of Functionally Substituted Isoxazole and Isothiazole Derivatives

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**Abstract**—Acylation of benzene and toluene with 5-phenyl- and 5-(*p*-tolyl)isoxazole-3-carbonyl chlorides gave 5-phenyl(or *p*-tolyl)isoxazol-3-yl phenyl(or *p*-tolyl)ketones which were reduced to the corresponding alcohols with sodium tetrahydridoborate in propan-2-ol. Selective reduction of the carboxy group in 4,5-dichloroisothiazole-3-carboxylic acid was achieved by the action of $BH_3$, and the aldehyde group in 4-formyl-2-methoxyphenyl 5-arylisoxazole-3-carboxylates and 4,5-dichloroisothiazole-3-carboxylates was reduced to hydroxymethyl group with sodium triacetoxyhydridoborate in benzene. Acylation of the resulting hydroxymethyl derivatives with 5-arylisoxazole- and 4,5-dichloroisothiazole-3-carbonyl chlorides afforded the corresponding esters containing two azole fragments in their molecules.

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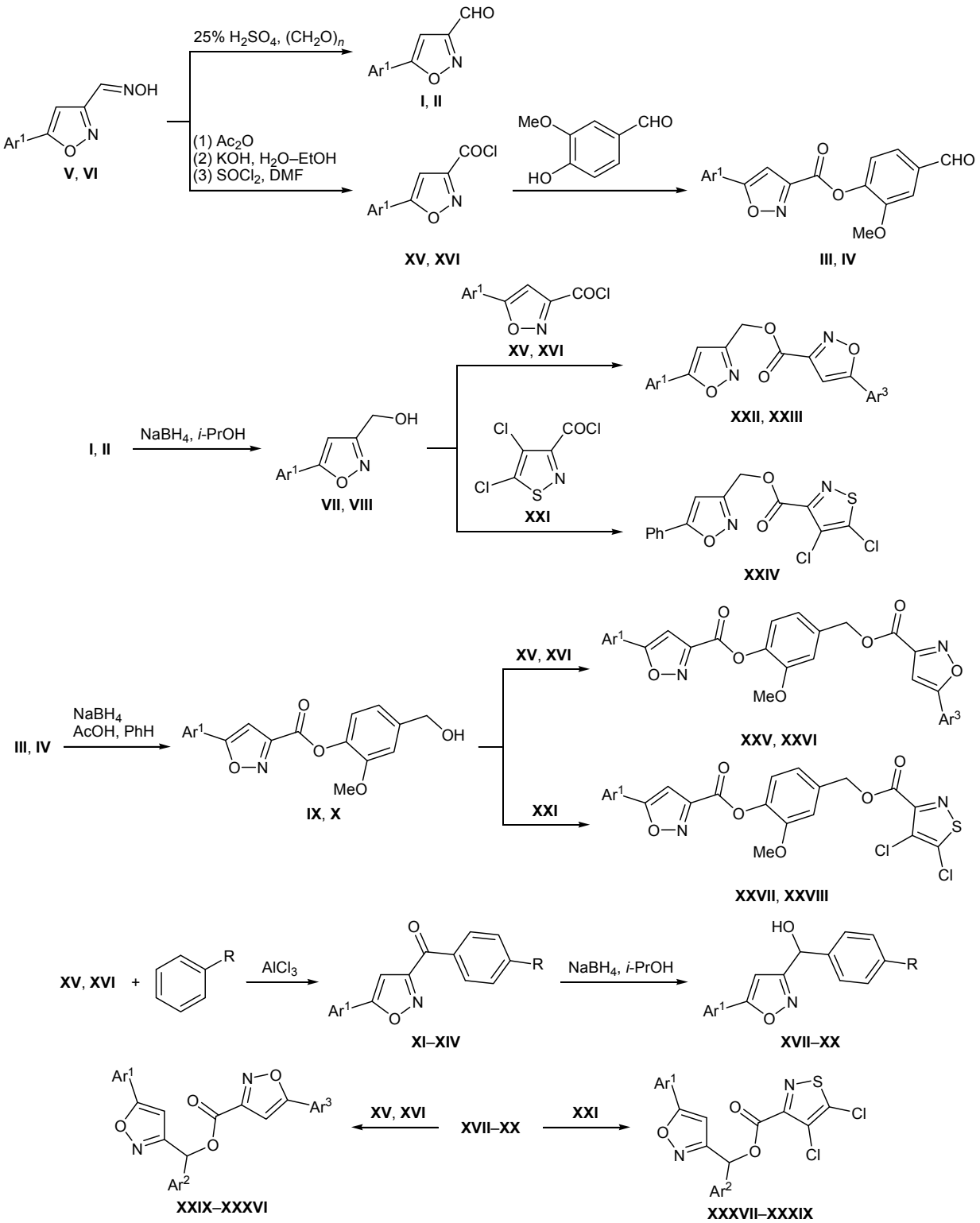
A number of isoxazole and isothiazole derivatives were found to exhibit high biological activity. Isoxazole heteroring constitutes a structural fragment of various pharmaceuticals, in particular of antibacterial drugs Sulfamethoxazole and Sulfisoxazole, Edonentan used for the treatment of hypertension and cardiovascular diseases, antidepressant Isocarboxazide, antirheumatic Leflunomide, and anti-inflammatory Valdecoxib [1]. Some isoxazole derivatives showed antitumor effect [2]. Compounds possessing high cytostatic activity were revealed among isothiazole derivatives [3]. For instance, a compound belonging to the (3-aryl-4-carboxamidoisothiazol-3-yl)urea series is an efficient tyrosine kinase inhibitor and is studied as promising antitumor agent (CP-547632) [4].

We have recently synthesized a series of functionally substituted isothiazolylureas and their isoxazolyl-substituted analogs (as CP-547632 isosteres), some of which have shown cytotoxic effect (according to bioassay at the Institute of Physiology, National Academy of Sciences of Belarus), as well as the ability to enhance the effect of known antitumor agents, in particular of Cisplatin and Carboplatin, which makes it possible to reduce therapeutic dose of these toxic drugs [5]. However, there remains a problem related to water solubility and tumor-seeking properties of isothiazole and isoxazole derivatives. This problem may be solved by selective and purposeful functionalization of their molecules.

The goal of the present study was to develop methods of synthesis of functionally substituted isoxazoles and isothiazoles possessing a hydroxy group which enhances their hydrophilicity, as well as to obtain their *O*-acyl derivatives containing several 1,2-azole fragments in a single molecule. With a view to synthesize functionally substituted 5-phenyl-(*p*-tolyl)isoxazoles with a primary hydroxy group we selected as starting compounds 5-phenyl- and 5-(*p*-tolyl)isoxazole-3-carbaldehydes **I** and **II** and 4-formyl-2-methoxyphenyl 5-phenyl- and 5-(*p*-tolyl)isoxazole-3-carboxylates **III** and **IV** which are readily prepared from accessible 5-phenyl- and 5-(*p*-tolyl)isoxazole-3-carbaldehyde oximes **V** and **VI** [6, 7]. We have improved the known method of synthesis of **I** and **II** by hydrolysis of **V** and **VI** with 70% $H_2SO_4$ [6]. Our experiments showed that the hydrolysis of **V** and **VI** with 25% $H_2SO_4$ in the presence of $(CH_2O)_n$ ensures 84–88% yield of **I** and **II** against 52–54% according to the known procedure.

**Scheme 1.**



**I**, **III**, **V**, **VII**, **IX**, **XI**, **XV**, **XVII**, **XVIII**, **XXII**, **XXV**, **XXVII**, **XXIX**–**XXXII**, **XXXVII**, **XXXVIII**, $Ar^1$ = Ph; **II**, **IV**, **VI**, **VIII**, **X**, **XIII**, **XIV**, **XVI**, **XIX**, **XX**, **XXIII**, **XXVI**, **XXVIII**, **XXXIII**–**XXXVI**, **XXXIX**, $Ar^1$ = 4-$MeC_6H_4$; **XI**, **XIII**, **XVII**, **XIX**, R = H; **XXIX**, **XXX**, **XXXIII**, **XXXIV**, **XXXVII**, **XXXIX**, $Ar^2$ = Ph; **XII**, **XIV**, **XVIII**, **XX**, R = Me; **XXII**, **XXXI**, **XXXII**, **XXXV**, **XXXVI**, **XXXVIII**, $Ar^2$ = 4-$MeC_6H_4$; **XXII**, **XXV**, **XXIX**, **XXXI**, **XXXIII**, **XXXV**, $Ar^3$ = Ph; **XXIII**, **XXVI**, **XXX**, **XXXII**, **XXXIV**, **XXXVI**, $Ar^3$ = 4-$MeC_6H_4$.

The aldehyde group in **I** and **II** was reduced with sodium tetrahydridoborate in propan-2-ol, and the corresponding hydroxymethyl derivatives, 5-phenyl- and 5-(*p*-tolyl)isoxazol-3-ylmethanols **VII** and **VIII**, were obtained in 75% yield. However, this procedure turned out to be inapplicable to the reduction of the aldehyde group in **III** and **IV** because of hydrolysis of the ester group with formation of sodium 5-arylisoxazole-3-carboxylates and 4-hydroxymethyl-2-methoxyphenol. We succeeded in selectively reducing the aldehyde group in esters **III** and **IV** with the use of $NaBH_4$ in AcOH to generate *in situ* sodium triacetoxyhydridoborate $Na[BH(OAc)_3]$ as a mild reducing agent. As a result, the corresponding 4-hydroxymethyl-2-methoxyphenyl 5-arylisoxazole-3-carboxylates **IX** and **X** were formed in 83–87% yield.

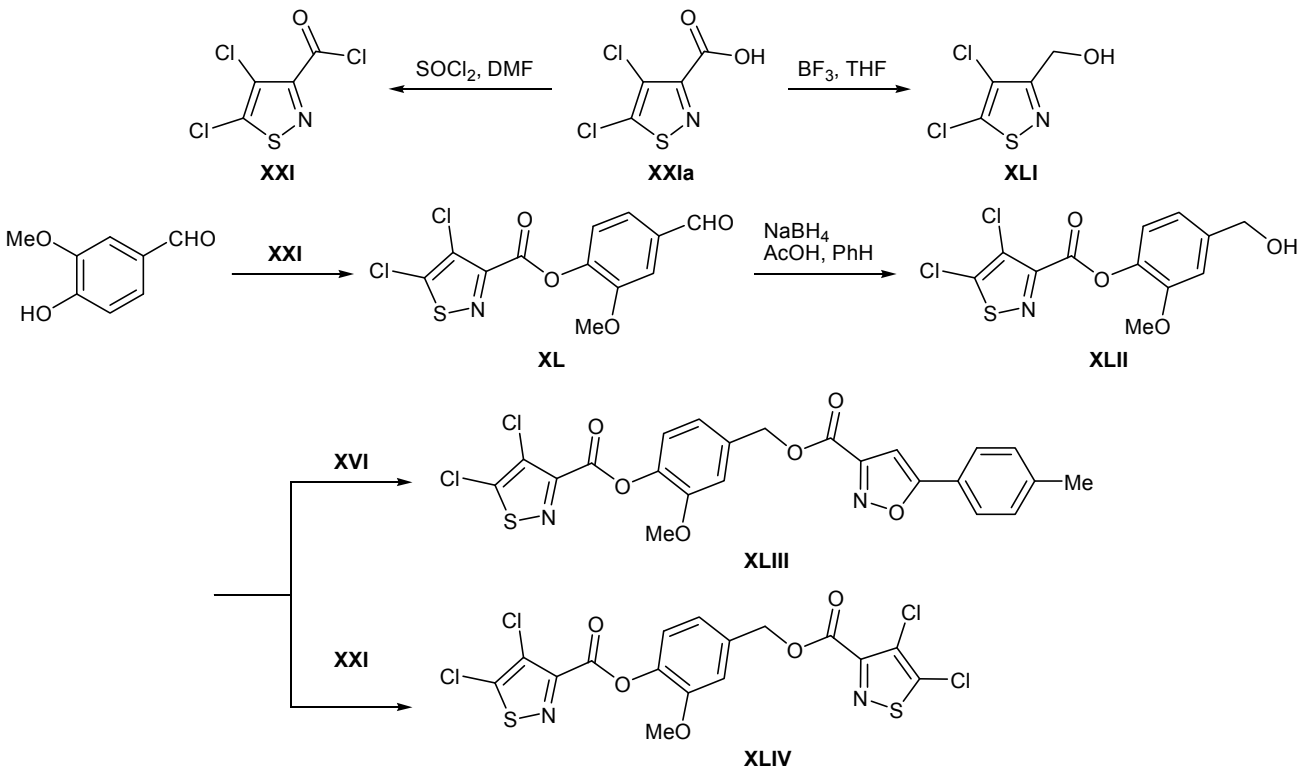
Isoxazole derivatives containing a secondary hydroxy group were synthesized by reduction of aryl 5-arylisoxazol-3-yl ketones **XI**–**XIV** which were prepared in turn by Friedel–Crafts acylation of benzene and toluene with 5-arylisoxazole-3-carbonyl chlorides **XV** and **XVI** in the presence of aluminum chloride. We previously described a preparative synthesis of acid chlorides **XV** and **XVI** from the corresponding carboxylic acids by heating with 5 equiv of thionyl chloride [7]. Addition of a catalytic amount of dimethylformamide to the reaction mixture allowed us to shorten the reaction time from 4 to 3 h and reduce the amount of $SOCl_2$ from 5 to 1.2 equiv, the high yield (98%) of **XV** and **XVI** being retained.

Like 5-arylisoxazole-3-carbaldehydes **I** and **II**, ketones **XI**–**XIV** were reduced with $NaBH_4$ in propan-2-ol; the reaction time was 4 h, and the yields of aryl (5-arylisoxazol-3-yl)methanols **XVII**–**XX** were 77–99%. In this case, the use of $Na[BH(OAc)_3]$, as in the reduction of aldehydes **I** and **II**, did not ensure complete conversion of the substrates and acceptable reaction rate, and the yields of the target alcohols were considerably lower.

The acylation of hydroxy-containing 5-arylisoxazole derivatives **VII**–**X** and **XVII**–**XX** with 5-arylisoxazole-3-carbonyl chlorides **XV** and **XVI** and 4,5-dichloroisothiazole-3-carbonyl chloride (**XXI**) afforded a number of esters **XXII**–**XXXIX** containing two 1,2-azole fragments in their molecules (Scheme 1).

The synthesis of functionalized isothiazole derivatives containing a secondary hydroxy group was described by us previously [8]. Functionally substituted isothiazoles having a primary hydroxy group were synthesized by reduction of the carboxy group in 4,5-dichloroisothiazole-3-carboxylic acid (**XXIa**) and of the aldehyde group in 4-formyl-2-methoxyphenyl 4,5-di-

**Scheme 2.**



chloroisothiazole-3-carboxylate (**XL**). Acid **XXIa** was reduced with borane in THF under argon, and (4,5-dichloroisothiazol-3-yl)methanol (**XLI**) was selectively formed in 71% yield. Ester **XL** was prepared acylation of vanillin with 4,5-dichloroisothiazole-3-carbonyl chloride (**XXI**) [9]. As in the synthesis of acid chlorides **XV** and **XVI**, we succeeded in considerably improving the procedure for the preparation of chloride **XXI** [10, 11] by adding a catalytic amount of DMF to a mixture of acid **XXIa** and thionyl chloride. As a result, the amount of $SOCl_2$ was reduced from 5 [10] or 15 equiv [11] to 1.2 equiv, and the reaction time was shortened from 16 to 3 h. By selective reduction of the aldehyde group in **XL** with $Na[BH(OAc)_3]$ in benzene we obtained 4-hydroxymethyl-2-methoxyphenyl 4,5-dichloroisothiazole-3-carboxylate (**XLII**) in 97% yield. The acylation of **XLII** with 5-(*p*-tolyl)isoxazole-3-carbonyl chloride (**XVI**) and 4,5-dichloroisothiazole-3-carbonyl chloride (**XXI**) gave esters **XLIII** and **XLIV**, respectively, which are hetero analogs of **XXV**–**XXVIII** (Scheme 2).

The structure of the newly synthesized compounds was determined on the basis of their elemental compositions and IR, $^1$H and $^{13}$C NMR, and mass spectra. Hydroxy derivatives **VII**–**X**, **XVII**–**XX**, **XLI**, and **XLII** displayed no IR absorption bands in the region 1649–1712 $cm^{-1}$, which are typical of carbonyl stretching vibrations in the spectra of the corresponding initial compounds, while broadened bands due to stretching vibrations of hydroxy group appeared at 3248–3476 $cm^{-1}$. The hydroxy proton in hydroxymethyl derivatives **IX**, **X**, and **XLII** resonated in the $^1$H NMR spectra at δ 2.07–2.53 ppm, and the OH signal of alcohols **VII**, **VIII**, and **XLI** was located at δ 3.16–3.33 ppm. Secondary alcohols **XVII**–**XX** showed OH signal in the region δ 2.87–3.84 ppm. The C**H**$_2$OH signal of **VII**–**X**, **XLI**, and **XLII** appeared at δ 4.63–4.79 ppm, and the C**H**OH proton in **XVII**–**XX** gave rise to a singlet at δ 5.97–6.02 ppm.

The mass spectra of ketones **XI**–**XIV**, their reduction products **XVII**–**XX**, and primary alcohols **VII**–**X** and **XLI** contained the molecular ion peaks and those resulting from their fragmentation. The isotope ratio of the molecular ion clusters of **XLI** and **XLII** was 100:65:11, indicating the presence of two chlorine atoms in their molecules [12].

The obtained hydroxy derivatives were found to be low-toxic on intraperitoneal and intragastric administration in white rats. Some primary alcohols showed neurotropic activity in rat brain slice preparations; the mode of signal transmission in nervous tissue changed, depending on their concentration. Biological testing of the synthesized compounds *in vitro* and *in vivo* is now in progress.

## EXPERIMENTAL

The IR spectra were recorded in KBr on a Nicolet Protégé-460 spectrometer. The $^1$H and $^{13}$C NMR spectra were measured on a Bruker Avance-500 spectrometer from solutions in $CDCl_3$ using the residual proton and carbon signals of the solvent as reference ($CHCl_3$, δ 7.26 ppm; $CDCl_3$, $\delta_C$ 77.2 ppm). The mass spectra (electron impact, 70 eV) were obtained on a Hewlett Packard 5890/5972 GC/MS system (HP-5MS capillary column, 30 m × 0.25 mm, film thickness 0.25 μm; injector temperature 250°C).

**5-Phenyl and 5-(4-methylphenyl)-1,2-oxazole-3-carbaldehydes I and II (*general procedure*).** A suspension of 23 mmol of oxime **V** or **VI** and 46 mmol of paraformaldehyde in 70 ml of 25% $H_2SO_4$ was heated for 6 h under reflux. The mixture was cooled and extracted with chloroform, the extract was dried over calcium chloride and evaporated, and the solid residue was recrystallized from hexane. The yields of aldehydes **I** and **II** were 84 and 88%, respectively; their physical constants and spectral parameters were consistent with those reported in [6].

**Aryl 5-arylisoxazol-3-yl ketones XI–XIV (*general procedure*).** A mixture of 10 mmol of acid chloride **XV** or **XVI**, 12 mmol of anhydrous $AlCl_3$, and 200 mmol of anhydrous benzene or toluene was stirred for 30 min at 20°C and for 3 h at 80°C. The mixture was then diluted with 100 ml of chloroform, treated with 10 ml of water, thoroughly stirred, and poured into water acidified to pH 3–4. The organic phase was separated, washed with water, a dilute solution of potassium carbonate, and water again, and dried over calcium chloride. The solvent was distilled off under reduced pressure, and the solid residue was recrystallized from chloroform–hexane (1:2).

**Phenyl(5-phenyl-1,2-oxazol-3-yl)methanone (XI).** Yield 97%, mp 86–87°C. IR spectrum, ν, $cm^{-1}$: 1655 (C=O), 1610, 1597, 1579, 1571, 1493, 1449, 1441, 1426 (C=C, C=N). $^1$H NMR spectrum, δ, ppm: 7.06 s (1H, 4-H), 7.49 m (3H, $H_{arom}$), 7.54 d.d (2H, $H_{arom}$, $^3J$ = 7.6 Hz), 7.66 d.d (1H, $H_{arom}$, $^3J$ = 7.6 Hz), 7.85 d (2H, $H_{arom}$, $^3J$ = 7.6 Hz), 8.35 d (2H, $H_{arom}$, $^3J$ = 7.6 Hz). $^{13}$C NMR spectrum, $\delta_C$, ppm: 100.40 ($C^4$), 126.14 (2C, $CH_{arom}$), 128.74 (2C, $CH_{arom}$), 129.30 (2C,

$CH_{arom}$), 130.85 (2C, $CH_{arom}$), 130.88 ($CH_{arom}$), 134.21 ($CH_{arom}$); 126.85, 135.88, 162.57, 170.92 ($C_{quat}$); 185.94 (C=O). Found, %: C 77.21; H 4.32; N 5.65. *m*/*z* 249 $[M]^+$. $C_{16}H_{11}NO_2$. Calculated, %: C 77.10; H 4.45; N 5.62. *M* 249.28.

**(4-Methylphenyl)(5-phenyl-1,2-oxazol-3-yl)-methanone (XII).** Yield 91%, mp 116–117°C. IR spectrum, ν, $cm^{-1}$: 1650 (C=O), 1604, 1592, 1571, 1563, 1495, 1441, 1427 (C=C, C=N). $^1H$ NMR spectrum, δ, ppm: 2.44 s (3H, $CH_3$), 7.03 s (1H, 4-H), 7.32 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz), 7.49 m (3H, $H_{arom}$), 7.83 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz), 8.26 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.90 ($CH_3$), 100.40 ($C^4$), 126.05 (2C, $CH_{arom}$), 129.22 (2C, $CH_{arom}$), 129.42 (2C, $CH_{arom}$), 130.76 ($CH_{arom}$), 130.95 (2C, $CH_{arom}$); 126.82, 133.31, 145.27, 162.64, 170.68 ($C_{quat}$); 185.38 (C=O). Found, %: C 77.62; H 4.77; N 5.35. *m*/*z* 263 $[M]^+$. $C_{17}H_{13}NO_2$. Calculated, %: C 77.55; H 4.98; N 5.32. *M* 263.31.

**[5-(4-Methylphenyl)-1,2-oxazol-3-yl]phenyl-methanone (XIII).** Yield 96%, mp 120–121°C. IR spectrum, ν, $cm^{-1}$: 1661 (C=O), 1610, 1595, 1578, 1566, 1506, 1452, 1445, 1431 (C=C, C=N). $^1H$ NMR spectrum, δ, ppm: 2.38 s (3H, $CH_3$), 6.97 s (1H, 4-H), 7.26 d (2H, $H_{arom}$, $^3J$ = 7.8 Hz), 7.52 d.d (2H, $H_{arom}$, $^3J$ = 7.6 Hz), 7.63 d.d (1H, $H_{arom}$, $^3J$ = 7.6 Hz), 7.71 d (2H, $H_{arom}$, $^3J$ = 7.8 Hz), 8.35 d (2H, $H_{arom}$, $^3J$ = 7.6 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.56 ($CH_3$), 99.69 ($C^4$), 125.94 (2C, $CH_{arom}$), 128.60 (2C, $CH_{arom}$), 129.86 (2C, $CH_{arom}$), 130.75 (2C, $CH_{arom}$), 134.04 ($CH_{arom}$); 124.02, 135.82, 141.13, 162.43, 170.95 ($C_{quat}$); 185.80 (C=O). Found, %: C 77.47; H 5.10; N 5.30. *m*/*z* 263 $[M]^+$. $C_{17}H_{13}NO_2$. Calculated, %: C 77.55; H 4.98; N 5.32. *M* 263.31.

**(4-Methylphenyl)[5-(4-methylphenyl)-1,2-oxaz-ol-3-yl]methanone (XIV).** Yield 93%, mp 139–141°C. IR spectrum, ν, $cm^{-1}$: 1649 (C=O), 1604, 1567, 1509, 1442 (C=C, C=N). $^1H$ NMR spectrum, δ, ppm: 2.41 s (3H, $CH_3$), 2.45 s (3H, $CH_3$), 6.98 s (1H, 4-H), 7.29 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.33 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz), 7.73 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 8.27 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.61 ($CH_3$), 21.89 ($CH_3$), 99.75 ($C^4$), 125.96 (2C, $CH_{arom}$), 129.38 (2C, $CH_{arom}$), 129.88 (2C, $CH_{arom}$), 130.92 (2C, $CH_{arom}$); 124.10, 133.33, 141.11, 145.18, 162.59, 170.85 ($C_{quat}$); 185.42 (C=O). Found, %: C 77.72; H 5.62; N 5.16. *m*/*z* 277 $[M]^+$. $C_{18}H_{15}NO_2$. Calculated, %: C 77.96; H 5.45; N 5.05. *M* 277.33.

**Reduction of aldehydes I and II and ketones XI–XIV (*general procedure*).** Sodium tetrahydridoborate, 10 mmol, was added to a solution of 10 mmol of carbonyl compound **I**, **II**, or **XI**–**XIV**, and the mixture was stirred for 4 h, poured into water, and extracted with chloroform. The extract was dried over sodium sulfate and evaporated on a rotary evaporator, and the residue was purified by recrystallization from diethyl ether–hexane (2:1).

**(5-Phenyl-1,2-oxazol-3-yl)methanol (VII).** Yield 75%, mp 97–99°C. IR spectrum, ν, $cm^{-1}$: 3327 (OH), 1613, 1592, 1574, 1502, 1470, 1453 (C=C, C=N), 1062 (C–O). $^1H$ NMR spectrum, δ, ppm: 3.29 br.s (1H, OH), 4.79 s (2H, $CH_2$), 6.58 s (1H, 4-H), 7.42 m (3H, $H_{arom}$), 7.73 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 57.00 ($CH_2$), 98.50 ($C^4$), 125.95 (2C, $CH_{arom}$), 129.11 (2C, $CH_{arom}$), 130.41 ($CH_{arom}$); 127.33, 164.46, 170.43 ($C_{quat}$). Found, %: C 68.69; H 5.01; N 8.09. *m*/*z* 175 $[M]^+$. $C_{10}H_9NO_2$. Calculated, %: C 68.56; H 5.18; N 8.00. *M* 175.19.

**[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methanol (VIII).** Yield 75%, mp 102–104°C. IR spectrum, ν, $cm^{-1}$: 3454 (OH), 1614, 1598, 1567, 1513, 1479, 1462 (C=C, C=N), 1071 (C–O). $^1H$ NMR spectrum, δ, ppm: 2.38 s (3H, $CH_3$), 3.33 br.s (1H, OH), 4.79 s (2H, $CH_2$), 6.52 s (1H, 4-H), 7.22 d (2H, $H_{arom}$, $^3J$ = 7.4 Hz), 7.61 d (2H, $H_{arom}$, $^3J$ = 7.4 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.60 ($CH_3$), 57.01 ($CH_2$), 97.89 ($C^4$), 125.89 (2C, $CH_{arom}$), 129.77 (2C, $CH_{arom}$); 124.66, 140.69, 164.42, 170.62 ($C_{quat}$). Found, %: C 69.79; H 6.03; N 7.33. *m*/*z* 189 $[M]^+$. $C_{11}H_{11}NO_2$. Calculated, %: C 69.83; H 5.86; N 7.40. *M* 189.22.

**Phenyl(5-phenyl-1,2-oxazol-3-yl)methanol (XVII).** Yield 99%, mp 141–142°C. IR spectrum, ν, $cm^{-1}$: 3449 (OH), 1612, 1591, 1572, 1494, 1466, 1451, 1422 (C=C, C=N). $^1H$ NMR spectrum, δ, ppm: 3.84 br.s (1H, OH), 6.02 s (1H, CH), 6.43 s (1H, 4-H), 7.31 d.d (1H, $H_{arom}$, $^3J$ = 7.2 Hz), 7.39 m (5H, $H_{arom}$), 7.49 d (2H, $H_{arom}$, $^3J$ = 7.5 Hz), 7.68 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 69.20 (CH), 97.86 ($C^4$), 125.92 (2C, $CH_{arom}$), 126.40 (2C, $CH_{arom}$), 128.33 ($CH_{arom}$), 128.81 (2C, $CH_{arom}$), 129.01 (2C, $CH_{arom}$), 130.35 ($CH_{arom}$); 127.30, 140.89, 167.22, 170.32 ($C_{quat}$). Found, %: C 76.80; H 5.00; N 5.46. *m*/*z* 251 $[M]^+$. $C_{16}H_{13}NO_2$. Calculated, %: C 76.48; H 5.21; N 5.57. *M* 251.29.

**(4-Methylphenyl)(5-phenyl-1,2-oxazol-3-yl)-methanol (XVIII).** Yield 77%, mp 107–109°C. IR spectrum, ν, $cm^{-1}$: 3338, 3248 (OH), 1613, 1592, 1574, 1513, 1463, 1452, 1412 (C=C, C=N). $^1H$ NMR spectrum, δ, ppm: 2.34 s (3H, $CH_3$), 3.36 d (1H, OH, $^3J$ = 3.3 Hz), 5.98 d (1H, CH, $^3J$ = 3.3 Hz), 6.43 s (1H,

4-H), 7.18 d (2H, $H_{arom}$, $^3J$ = 7.9 Hz), 7.37 d (2H, $H_{arom}$, $^3J$ = 7.9 Hz), 7.41 m (3H, $H_{arom}$), 7.71 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.31 ($CH_3$), 69.29 (CH), 97.85 ($C^4$), 125.95 (2C, $CH_{arom}$), 126.39 (2C, $CH_{arom}$), 129.04 (2C, $CH_{arom}$), 129.54 (2C, $CH_{arom}$), 130.35 ($CH_{arom}$); 127.41, 138.00, 138.21, 167.28, 170.31 ($C_{quat}$). Found, %: C 77.05; H 5.54; N 5.33. *m*/*z* 265 $[M]^+$. $C_{17}H_{15}NO_2$. Calculated, %: C 76.96; H 5.70; N 5.28. *M* 265.32.

**[5-(4-Methylphenyl)-1,2-oxazol-3-yl]phenylmethanol (XIX).** Yield 87%, mp 167–168°C. IR spectrum, ν, $cm^{-1}$: 3444 (OH), 1614, 1596, 1585, 1567, 1514, 1470, 1452, 1432 (C=C, C=N). $^1H$ NMR spectrum, δ, ppm: 2.36 s (3H, $CH_3$), 5.35 d (1H, OH, $^3J$ = 4.2 Hz), 5.98 d (1H, CH, $^3J$ = 4.2 Hz), 6.74 s (1H, 4-H), 7.29 m (3H, $H_{arom}$), 7.36 d.d (2H, $H_{arom}$, $^3J$ = 7.5 Hz), 7.53 d (2H, $H_{arom}$, $^3J$ = 7.7 Hz), 7.72 d (2H, $H_{arom}$, $^3J$ = 7.7 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.72 ($CH_3$), 69.49 (CH), 98.55 ($C^4$), 126.77 (2C, $CH_{arom}$), 127.36 (2C, $CH_{arom}$), 128.73 ($CH_{arom}$), 129.51 (2C, $CH_{arom}$), 130.91 (2C, $CH_{arom}$); 126.15, 141.60, 143.68, 169.23, 170.79 ($C_{quat}$). Found, %: C 76.78; H 5.89; N 5.30. *m*/*z* 265 $[M]^+$. $C_{17}H_{15}NO_2$. Calculated, %: C 76.96; H 5.70; N 5.28. *M* 265.32.

**(4-Methylphenyl)[5-(4-methylphenyl)-1,2-oxazol-3-yl]methanol (XX).** Yield 96%, mp 113–114°C. IR spectrum, ν, $cm^{-1}$: 3342, 3266 (OH), 1617, 1595, 1567, 1511, 1463, 1443, 1424 (C=C, C=N). $^1H$ NMR spectrum, δ, ppm: 2.34 s (3H, $CH_3$), 2.38 s (3H, $CH_3$), 3.34 d (1H, OH, $^3J$ = 3.8 Hz), 5.97 d (1H, CH, $^3J$ = 3.8 Hz), 6.37 s (1H, 4-H), 7.18 d (2H, $H_{arom}$, $^3J$ = 7.9 Hz), 7.21 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.37 d (2H, $H_{arom}$, $^3J$ = 7.9 Hz), 7.59 d (2H, $H_{arom}$, $^3J$ = 8 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.31 ($CH_3$), 21.62 ($CH_3$), 69.29 (CH), 97.20 ($C^4$), 125.88 (2C, $CH_{arom}$), 126.39 (2C, $CH_{arom}$), 129.52 (2C, $CH_{arom}$), 129.71 (2C, $CH_{arom}$); 124.70, 138.04, 138.16, 140.62, 167.21, 170.51 ($C_{quat}$). Found, %: C 77.55; H 6.01; N 5.09. *m*/*z* 279 $[M]^+$. $C_{18}H_{17}NO_2$. Calculated, %: C 77.40; H 6.13; N 5.01. *M* 279.35.

**5-Phenyl and 5-(4-methylphenyl)-1,2-oxazol-3-carbonyl chlorides XV and XVI and 4,5-dichloro-1,2-thiazole-3-carbonyl chloride (XXI) (***general procedure***).** Thionyl chloride, 1.43 g (12 mmol), was added to 10 mmol of the corresponding acid, 3 drops of DMF were then added, and the mixture was heated under reflux until it became homogeneous (~3 h). Excess thionyl chloride was distilled off under reduced pressure, the residue was dissolved in hexane, the solution was passed through a layer of silica gel (5–40 μm), and the solvent was distilled off under reduced pressure to isolate acid chloride **XV**, **XVI**, or **XXI** in 98% yield. The physical constants and spectral parameters of the products were consistent with published data [7, 10].

**Reduction of the aldehyde group in compounds III, IV, and XL (***general procedure***).** Glacial acetic acid, 36 mmol, was added in portions under stirring to a suspension of 12 mmol of sodium tetrahydridoborate in 50 ml of anhydrous benzene, 10 mmol of aldehyde **III**, **IV**, or **XL** was then added, and the mixture was stirred for 4 h. The mixture was treated with 100 ml of water and 100 ml of chloroform, the organic phase was separated and dried over sodium sulfate, the solvent was distilled off under reduced pressure, and the residue was recrystallized from hexane–chloroform (4:1).

**4-(Hydroxymethyl)-2-methoxyphenyl 5-phenyl-1,2-oxazole-3-carboxylate (IX).** Yield 87%, mp 151–152°C. IR spectrum, ν, $cm^{-1}$: 3476 (OH), 1748 (C=O), 1609, 1590, 1575, 1514, 1470, 1450, 1439, 1423 (C=C, C=N), 1229, 1149, 1129, 1119 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 2.18 br.s (1H, OH), 3.84 s (3H, $CH_3$), 4.70 s (2H, $CH_2$), 6.96 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.06 s (1H, 4-H), 7.07 s (1H, $H_{arom}$), 7.16 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.50 m (3H, $H_{arom}$), 7.84 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 56.08 ($CH_3$), 65.03 ($CH_2$), 100.55 ($C^4$), 111.25 ($CH_{arom}$), 119.06 ($CH_{arom}$), 122.62 ($CH_{arom}$), 126.13 (2C, $CH_{arom}$), 129.35 (2C, $CH_{arom}$), 131.09 ($CH_{arom}$); 126.29, 138.39, 140.90, 151.16, 156.40, 158.11 ($C_{quat}$); 172.22 (C=O). Found, %: C 66.76; H 4.73; N 4.45. *m*/*z* 325 $[M]^+$. $C_{18}H_{15}NO_5$. Calculated, %: C 66.46; H 4.65; N 4.31. *M* 325.32.

**4-Hydroxymethyl-2-methoxyphenyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (X).** Yield 83%, mp 171–172°C. IR spectrum, ν, $cm^{-1}$: 3472 (OH), 1752 (C=O), 1610, 1594, 1575, 1509, 1466, 1442, 1422 (C=C, C=N), 1232, 1150, 1128, 1118 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 2.07 br.s (1H, OH), 2.42 s (3H, $CH_3$), 3.83 s (3H, $OCH_3$), 4.70 s (2H, $CH_2$), 6.96 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.01 s (1H, 4-H), 7.07 s (1H, $H_{arom}$), 7.16 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.30 m (2H, $H_{arom}$, $^3J$ = 7.5 Hz), 7.73 m (2H, $H_{arom}$, $^3J$ = 7.5 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.71 ($CH_3$), 56.08 ($CH_3$), 65.05 ($CH_2$), 99.96 ($C^4$), 111.24 ($CH_{arom}$), 119.06 ($CH_{arom}$), 122.64 ($CH_{arom}$), 126.07 (2C, $CH_{arom}$), 130.02 (2C, $CH_{arom}$); 124.01, 138.42, 140.84, 141.54, 151.18, 156.34, 158.19 ($C_{quat}$); 172.42 (C=O). Found, %: C 67.27; H 5.34; N 4.21. *m*/*z* 339 $[M]^+$. $C_{19}H_{17}NO_5$. Calculated, %: C 67.25; H 5.05; N 4.13. *M* 339.34.

**4-Hydroxymethyl-2-methoxyphenyl 4,5-dichloro-1,2-thiazole-3-carboxylate (XLII).** Yield 97%, mp 111–113°C. IR spectrum, ν, $cm^{-1}$: 3327 (OH), 3186, 3005, (=C–H), 2976, 2935, 2917, 2853 (C–H), 1743 (C=O), 1609, 1515, 1483, 1465, 1451, 1418 (C=C, C=N), 1205, 1150 (C–O–C), 871, 821 (C–Cl). $^1$H NMR spectrum, δ, ppm: 2.53 br.s (1H, OH), 3.79 s (3H, $CH_3$), 4.63 s (2H, $CH_2$), 6.91 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.02 s (1H, $H_{arom}$), 7.12 d (1H, $H_{arom}$, $^3J$ = 8 Hz). $^{13}$C NMR spectrum, $\delta_C$, ppm: 56.03 ($CH_3$), 64.78 ($CH_2$), 111.11 ($CH_{arom}$), 118.93 ($CH_{arom}$), 122.49 ($CH_{arom}$); 126.42, 138.24, 140.89, 150.99, 151.05, 153.46 ($C_{quat}$); 157.01 (C=O). Found, %: C 42.87; H 3.04; Cl 20.99; N 3.95; S 9.25. *m*/*z* 333 $[M]^+$. $C_{12}H_9Cl_2NO_4S$. Calculated, %: C 43.13; H 2.71; Cl 21.22; N 4.19; S 9.60. *M* 334.18.

**(4,5-Dichloro-1,2-thiazol-3-yl)methanol (XLI).** A 1 M solution of 15 mmol of $BH_3$ in THF was added dropwise at –20°C under stirring in an argon atmosphere to 3.0 g (15 mmol) of 4,5-dichloro-1,2-thiazole-3-carboxylic acid (**XXIa**), and the mixture was stirred for 12 h, allowing it to gradually warm up to room temperature. Methanol, 50 ml, was then added, the mixture was stirred for 1 h, the solvent was removed on a rotary evaporator, the residue was treated with 100 ml of 1 N aqueous HCl, and the mixture was heated for 12 h under reflux and evaporated to dryness. The residue was purified by column chromatography on silica gel (100–160 μm) using hexane–acetone (5:2) as eluent. Yield 71%, mp 49–50°C. IR spectrum, ν, $cm^{-1}$: 3341 (OH), 2940, 2866 (CH), 1517, 1442, 1422, 1393, 1312 (C=C, C=N), 1098, 1067, 971, 845, 815 (C–Cl), 622, 560, 506. $^1$H NMR spectrum, δ, ppm: 3.16 br.s (1H, OH), 4.67 s (2H, $CH_2O$). $^{13}$C NMR spectrum, $\delta_C$, ppm: 61.28 ($CH_2O$); 123.20, 148.31, 168.04 ($C_{quat}$). Found, %: C 26.22; H 2.01; Cl 38.77; N 7.59; S 17.50. *m*/*z* 183 $[M]^+$. $C_4H_3Cl_2NOS$. Calculated, %: C 26.10; H 1.64; Cl 38.53; N 7.61; S 17.42. *M* 184.04.

**Esters XXII–XXXIX, XLIII, and XLIV (*general procedure*).** Acid chloride **XV**, **XVI**, or **XXI**, 10 mmol, was added in portions under stirring to a solution of 10 mmol of compound **VII**–**X** or **XVII**–**XX** and 10 mmol of anhydrous triethylamine in 50 ml of anhydrous diethyl ether. The mixture was heated for 5 h under reflux, and the precipitate was filtered off, washed with diethyl ether and water (3×100 ml), and dried under reduced pressure over $P_2O_5$.

**(5-Phenyl-1,2-oxazol-3-yl)methyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (XXII).** Yield 83%, mp 142–143°C. IR spectrum, ν, $cm^{-1}$: 1753 (C=O), 1615, 1594, 1576, 1506, 1461, 1456, 1432 (C=C, C=N), 1249, 1148 (C–O–C). $^1$H NMR spectrum, δ, ppm: 2.40 s (3H, $CH_3$), 5.54 s (2H, $CH_2$), 6.69 s and 6.90 s (1H each, 4-H, 4′-H), 7.28 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.45 m (3H, $H_{arom}$), 7.68 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.77 m (2H, $H_{arom}$). $^{13}$C NMR spectrum, $\delta_C$, ppm: 21.64 ($CH_3$), 58.97 ($CH_2$), 99.33 and 99.54 ($C^4$, $C^{4'}$), 126.01 (4C, $CH_{arom}$), 129.15 (2C, $CH_{arom}$), 129.97 (2C, $CH_{arom}$), 130.59 ($CH_{arom}$); 123.87, 127.15, 141.54, 156.25, 159.55, 159.78, 171.07 ($C_{quat}$); 172.40 (C=O). Found, %: C 69.72; H 4.75; N 7.81. $C_{21}H_{16}N_2O_4$. Calculated, %: C 69.99; H 4.48; N 7.77.

**[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (XXIII).** Yield 73%, mp 133–134°C. IR spectrum, ν, $cm^{-1}$: 1736 (C=O), 1616, 1596, 1569, 1513, 1451, 1437, 1412 (C=C, C=N), 1237, 1147 (C–O–C). $^1$H NMR spectrum, δ, ppm: 2.39 s (3H, $CH_3$), 2.40 s (3H, $CH_3$), 5.53 s (2H, $CH_2$), 6.63 s and 6.90 s (1H each, 4-H, 4′-H), 7.26 m (4H, $H_{arom}$), 7.67 m (4H, $H_{arom}$). $^{13}$C NMR spectrum, $\delta_C$, ppm: 21.61 ($CH_3$), 21.64 ($CH_3$), 59.02 ($CH_2$), 98.73 and 99.55 ($C^4$, $C^{4'}$), 125.95 (2C, $CH_{arom}$), 126.02 (2C, $CH_{arom}$), 129.84 (2C, $CH_{arom}$), 129.98 (2C, $CH_{arom}$); 123.90, 124.48, 140.94, 141.54, 156.27, 159.49, 159.79, 171.28 ($C_{quat}$); 172.39 (C=O). Found, %: C 70.49; H 4.97; N 7.53. $C_{22}H_{18}N_2O_4$. Calculated, %: C 70.58; H 4.85; N 7.48 .

**(5-Phenyl-1,2-oxazol-3-yl)methyl 4,5-dichloro-1,2-thiazole-3-carboxylate (XXIV).** Yield 70%, mp 123–125°C. IR spectrum, ν, $cm^{-1}$: 1729 (C=O), 1615, 1593, 1577, 1473, 1455, 1436, 1405 (C=C, C=N), 1219, 1179 (C–O–C), 844, 807 (C–Cl). $^1$H NMR spectrum, δ, ppm: 5.53 s (2H, $CH_2$), 6.67 s (1H, 4-H), 7.45 m (3H, $H_{arom}$), 7.77 m (2H, $H_{arom}$). $^{13}$C NMR spectrum, $\delta_C$, ppm: 56.20 ($CH_2$), 99.31 ($C^4$), 126.01 (2C, $CH_{arom}$), 129.16 (2C, $CH_{arom}$), 130.61 ($CH_{arom}$); 126.13, 127.13, 151.10, 153.49, 158.71, 159.42 ($C_{quat}$); 171.08 (C=O). Found, %: C 47.28; H 2.39; Cl 19.78; N 7.93; S 9.13. $C_{14}H_8Cl_2N_2O_3S$. Calculated, %: C 47.34; H 2.27; Cl 19.96; N 7.89; S 9.03.

**3-Methoxy-4-[(5-phenyl-1,2-oxazol-3-yl)carbonyloxy]benzyl 5-phenyl-1,2-oxazole-3-carboxylate (XXV).** Yield 84%, mp 146–147°C. IR spectrum, ν, $cm^{-1}$: 1739 (C=O), 1610, 1592, 1573, 1510, 1462, 1445, 1422 (C=C, C=N), 1247, 1238, 1222, 1152, 1132 (C–O–C). $^1$H NMR spectrum, δ, ppm: 3.86 s (3H, $CH_3$), 5.43 s (2H, $CH_2$), 6.95 s and 7.06 s (1H each, 4-H, 4′-H), 7.12 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.15 s (1H, $H_{arom}$), 7.22 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.48 m (6H,

$H_{arom}$), 7.80 m (2H, $H_{arom}$), 7.83 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 56.15 ($CH_3$), 67.36 ($CH_2$), 100.13 and 100.51 ($C^4$, $C^{4'}$), 113.11 ($CH_{arom}$), 121.29 ($CH_{arom}$), 122.92 ($CH_{arom}$), 126.05 (2C, $CH_{arom}$), 126.08 (2C, $CH_{arom}$), 129.27 (2C, $CH_{arom}$), 129.30 (2C, $CH_{arom}$), 130.99 ($CH_{arom}$), 131.05 ($CH_{arom}$), 126.62 (2C, $C_{quat}$); 134.61, 139.36, 151.23, 156.28, 156.75, 157.86, 159.92 ($C_{quat}$); 172.00 and 172.19 (C=O). Found, %: C 67.79; H 4.15; N 5.73. $C_{28}H_{20}N_2O_7$. Calculated, %: C 67.74; H 4.06; N 5.64.

**3-Methoxy-4-{[5-(4-methylphenyl)-1,2-oxazol-3-yl]carbonyloxy}benzyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (XXVI).** Yield 79%, mp 173–174°C. IR spectrum, ν, $cm^{-1}$: 1750, 1729 (C=O), 1611, 1594, 1570, 1510, 1471, 1446, 1424 (C=C, C=N), 1244, 1233, 1212, 1160, 1133 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 2.40 s (3H, $CH_3$), 2.41 s (3H, $CH_3$), 3.86 s (3H, $OCH_3$), 5.42 s (2H, $CH_2$), 6.88 s and 7.00 s (1H each, 4-H, 4′-H), 7.12 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.14 s (1H, $H_{arom}$), 7.22 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.26 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz), 7.29 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz), 7.68 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz), 7.72 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.64 (2C, $CH_3$), 56.14 ($CH_3$), 67.31 ($CH_2$), 99.52 and 99.91 ($C^4$, $C^{4'}$), 113.09 ($CH_{arom}$), 121.27 ($CH_{arom}$), 122.91 ($CH_{arom}$), 125.98 (2C, $CH_{arom}$), 126.01 (2C, $CH_{arom}$), 129.93 (2C, $CH_{arom}$), 129.97 (2C, $CH_{arom}$), 123.94 (2C, $C_{quat}$); 134.61, 139.36, 141.42, 141.49, 151.23, 156.22, 156.69, 157.94, 159.99 ($C_{quat}$); 172.19 and 172.39 (C=O). Found, %: C 68.88; H 4.84; N 5.41. $C_{30}H_{24}N_2O_7$. Calculated, %: C 68.70; H 4.61; N 5.34.

**4-[(4,5-Dichloro-1,2-thiazol-3-yl)carbonyloxymethyl]-2-methoxyphenyl 5-phenyl-1,2-oxazole-3-carboxylate (XXVII).** Yield 83%, mp 135–136°C. IR spectrum, ν, $cm^{-1}$: 3144, 3128, 3053 (=C–H), 2983, 2948, 2924, 2853 (C–H), 1756, 1726 (C=O), 1608, 1590, 1572, 1518, 1474, 1438, 1403 (C=C, C=N), 1237, 1228, 1213, 1160, 1135 (C–O–C), 859, 809 (C–Cl). $^1H$ NMR spectrum, δ, ppm: 3.86 s (3H, $CH_3$), 5.43 s (2H, $CH_2$), 7.06 s (4-H), 7.12 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.16 s (1H, $H_{arom}$), 7.22 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.50 m (3H, $H_{arom}$), 7.84 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 56.19 ($CH_3$), 67.61 ($CH_2$), 100.55 ($C^4$), 113.11 ($CH_{arom}$), 121.32 ($CH_{arom}$), 122.98 ($CH_{arom}$), 126.13 (2C, $CH_{arom}$), 129.35 (2C, $CH_{arom}$), 131.09 ($CH_{arom}$); 125.95, 126.68, 134.55, 139.39, 150.94, 151.26, 154.08, 156.31, 157.88 ($C_{quat}$); 159.00 and 172.23 (C=O). Found, %: C 52.38; H 2.91; Cl 14.36; N 5.68; S 6.27. $C_{22}H_{14}Cl_2N_2O_6S$. Calculated, %: C 52.29; H 2.79; Cl 14.03; N 5.54; S 6.35.

**4-[(4,5-Dichloro-1,2-thiazol-3-yl)carbonyloxymethyl]-2-methoxyphenyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (XXVIII).** Yield 87%, mp 144–145°C. IR spectrum, ν, $cm^{-1}$: 3135, 3085, 3055, 3024 (=C–H), 2973, 2923, 2853 (C–H), 1743, 1724 (C=O), 1608, 1567, 1515, 1477, 1448, 1418 (C=C, C=N), 1243, 1233, 1213, 1159, 1138 (C–O–C), 865, 811 (C–Cl). $^1H$ NMR spectrum, δ, ppm: 2.42 s (3H, $CH_3$), 3.85 s (3H, $OCH_3$), 5.43 s (2H, $CH_2$), 7.00 s (1H, 4-H), 7.12 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.15 s (1H, $H_{arom}$), 7.21 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.30 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.73 d (2H, $H_{arom}$, $^3J$ = 8 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.72 ($CH_3$), 56.20 ($OCH_3$), 67.62 ($CH_2$), 99.95 ($C^4$), 113.12 ($CH_{arom}$), 121.32 ($CH_{arom}$), 123.00 ($CH_{arom}$), 126.08 (2C, $CH_{arom}$), 130.02 (2C, $CH_{arom}$); 124.00, 125.96, 134.51, 139.43, 141.54, 150.93, 151.28, 154.10, 156.26, 157.97 ($C_{quat}$); 159.00 and 172.44 (C=O). Found, %: C 53.39; H 3.47; Cl 13.77; N 5.27; S 5.91. $C_{23}H_{16}Cl_2N_2O_6S$. Calculated, %: C 53.19; H 3.11; Cl 13.65; N 5.39; S 6.17.

**Phenyl(5-phenyl-1,2-oxazol-3-yl)methyl 5-phenyl-1,2-oxazole-3-carboxylate (XXIX).** Yield 79%, mp 170–172°C. IR spectrum, ν, $cm^{-1}$: 1736 (C=O), 1613, 1591, 1574, 1494, 1465, 1450, 1423 (C=C, C=N), 1239, 1136 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 6.63 s (1H, CH), 6.99 s and 7.32 s (1H each, 4-H, 4′-H), 7.39 d.d (1H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.43 m (5H, $H_{arom}$), 7.48 m (3H, $H_{arom}$), 7.61 d (2H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.76 m (2H, $H_{arom}$), 7.81 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 71.78 (CH), 98.29 and 100.31 ($C^4$, $C^{4'}$), 126.03 (2C, $CH_{arom}$), 126.11 (2C, $CH_{arom}$), 127.21 (2C, $CH_{arom}$), 129.13 (4C, $CH_{arom}$), 129.28 ($CH_{arom}$), 129.33 (2C, $CH_{arom}$), 130.61 ($CH_{arom}$), 131.09 ($CH_{arom}$); 126.61, 127.16, 136.57, 156.50, 158.94, 163.30, 170.95 ($C_{quat}$); 172.16 (C=O). Found, %: C 79.88; H 4.39; N 6.57. $C_{26}H_{18}N_2O_4$. Calculated, %: C 79.92; H 4.29; N 6.63.

**Phenyl(5-phenyl-1,2-oxazol-3-yl)methyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (XXX).** Yield 58%, mp 129–131°C. IR spectrum, ν, $cm^{-1}$: 1742 (C=O), 1611, 1591, 1573, 1500, 1495, 1449, 1423 (C=C, C=N), 1238, 1136 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 2.41 s (3H, $CH_3$), 6.63 s (1H, CH), 6.93 s and 7.31 s (1H each, 4-H, 4′-H), 7.29 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.43 m (5H, $H_{arom}$), 7.51 d (1H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.60 d (2H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.69 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.75 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.69 ($CH_3$), 71.73 (CH), 98.30 and 99.71 ($C^4$, $C^{4'}$), 126.04 (4C, $CH_{arom}$), 127.20 (2C, $CH_{arom}$), 129.12 (4C, $CH_{arom}$),

129.25 ($CH_{arom}$), 129.99 (2C, $CH_{arom}$), 130.59 ($CH_{arom}$); 123.93, 127.41, 136.62, 141.54, 156.44, 159.02, 163.33, 170.93 ($C_{quat}$); 172.37 (C=O). Found, %: C 74.23; H 4.89; N 6.55. $C_{27}H_{20}N_2O_4$. Calculated, %: C 74.30; H 4.62; N 6.42.

**(4-Methylphenyl)(5-phenyl-1,2-oxazol-3-yl)-methyl 5-phenyl-1,2-oxazole-3-carboxylate (XXXI).** Yield 88%, mp 140–141°C. IR spectrum, ν, $cm^{-1}$: 1737 (C=O), 1614, 1590, 1572, 1516, 1498, 1463, 1449, 1439 (C=C, C=N), 1229, 1136 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 2.36 s (3H, $CH_3$), 6.62 s (1H, CH), 6.98 s and 7.27 s (1H each, 4-H, 4′-H), 7.24 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.44 m (3H, $H_{arom}$), 7.49 m (5H, $H_{arom}$), 7.76 m (2H, $H_{arom}$), 7.81 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.42 ($CH_3$), 71.81 (CH), 98.32 and 100.32 ($C^4$, $C^{4'}$), 126.05 (2C, $CH_{arom}$), 126.12 (2C, $CH_{arom}$), 127.27 (2C, $CH_{arom}$), 129.14 (2C, $CH_{arom}$), 129.34 (2C, $CH_{arom}$), 129.80 (2C, $CH_{arom}$), 130.58 ($CH_{arom}$), 131.08 ($CH_{arom}$); 124.11, 126.67, 133.67, 139.29, 156.59, 159.00, 163.45, 170.89 ($C_{quat}$); 172.13 (C=O). Found, %: C 74.51; H 4.93; N 6.47. $C_{27}H_{20}N_2O_4$. Calculated, %: C 74.30; H 4.62; N 6.42.

**(4-Methylphenyl)(5-phenyl-1,2-oxazol-3-yl)-methyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (XXXII).** Yield 74%, mp 141–143°C. IR spectrum, ν, $cm^{-1}$: 1742 (C=O), 1615, 1592, 1574, 1513, 1465, 1445, 1427 (C=C, C=N), 1230, 1138 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 2.36 s (3H, $CH_3$), 2.41 s (3H, $CH_3$), 6.62 s (1H, CH), 6.92 s and 7.27 s (1H each, 4-H, 4′-H), 7.23 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.29 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.44 m (3H, $H_{arom}$), 7.48 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.70 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.76 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.41 ($CH_3$), 21.71 ($CH_3$), 71.75 (CH), 98.33 and 99.71 ($C^4$, $C^{4'}$), 126.05 (4C, $CH_{arom}$), 127.25 (2C, $CH_{arom}$), 129.13 (2C, $CH_{arom}$), 129.79 (2C, $CH_{arom}$), 130.00 (2C, $CH_{arom}$), 130.57 ($CH_{arom}$); 123.97, 126.25, 133.69, 139.26, 141.53, 156.52, 159.06, 163.47, 170.86 ($C_{quat}$); 172.32 (C=O). Found, %: C 74.58; H 5.21; N 6.33. $C_{28}H_{22}N_2O_4$. Calculated, %: C 74.65; H 4.92; N 6.22.

**[5-(4-Methylphenyl)-1,2-oxazol-3-yl](phenyl)-methyl 5-phenyl-1,2-oxazole-3-carboxylate (XXXIII).** Yield 82%, mp 171–173°C. IR spectrum, ν, $cm^{-1}$: 1735 (C=O), 1615, 1597, 1573, 1513, 1493, 1467, 1450, 1445 (C=C, C=N), 1240, 1136 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 2.38 s (3H, $CH_3$), 6.57 s (1H, CH), 6.99 s and 7.31 s (1H each, 4-H, 4′-H), 7.24 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.38 d.d (1H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.43 d.d (2H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.48 m (3H, $H_{arom}$), 7.61 d (2H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.65 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.81 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.65 ($CH_3$), 71.81 (CH), 97.66 and 100.31 ($C^4$, $C^{4'}$), 125.96 (2C, $CH_{arom}$), 126.10 (2C, $CH_{arom}$), 127.21 (2C, $CH_{arom}$), 129.10 (2C, $CH_{arom}$), 129.24 ($CH_{arom}$), 129.33 (2C, $CH_{arom}$), 129.81 (2C, $CH_{arom}$), 131.07 ($CH_{arom}$); 124.48, 126.63, 136.65, 140.93, 156.53, 158.95, 163.23, 171.14 ($C_{quat}$); 172.14 (C=O). Found, %: C 74.39; H 4.79; N 6.37. $C_{27}H_{20}N_2O_4$. Calculated, %: C 74.30; H 4.62; N 6.42.

**[5-(4-Methylphenyl)-1,2-oxazol-3-yl](phenyl)-methyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (XXXIV).** Yield 82%, mp 180–181°C. IR spectrum, ν, $cm^{-1}$: 1738 (C=O), 1616, 1594, 1568, 1517, 1510, 1469, 1446, 1412 (C=C, C=N), 1236, 1134 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 2.38 s (3H, $CH_3$), 2.41 s (3H, $CH_3$), 6.57 s (1H, CH), 6.93 s and 7.30 s (1H each, 4-H, 4′-H), 7.24 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.29 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.38 d.d (1H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.43 d.d (2H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.60 d (2H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.65 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.70 d (2H, $H_{arom}$, $^3J$ = 8 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.64 ($CH_3$), 21.68 ($CH_3$), 71.75 (CH), 97.67 and 99.71 ($C^4$, $C^{4'}$), 125.97 (2C, $CH_{arom}$), 126.04 (2C, $CH_{arom}$), 127.20 (2C, $CH_{arom}$), 129.09 (2C, $CH_{arom}$), 129.21 ($CH_{arom}$), 129.80 (2C, $CH_{arom}$), 129.99 (2C, $CH_{arom}$); 123.98, 124.51, 136.70, 140.91, 141.52, 156.47, 159.02, 163.27, 171.12 ($C_{quat}$); 172.34 (C=O). Found, %: C 74.51; H 5.09; N 6.15. $C_{28}H_{22}N_2O_4$. Calculated, %: C 74.65; H 4.92; N 6.22.

**(4-Methylphenyl)[5-(4-methylphenyl)1,2-oxazol-3-yl]methyl 5-phenyl-1,2-oxazole-3-carboxylate (XXXV).** Yield 87%, mp 151–153°C. IR spectrum, ν, $cm^{-1}$: 1737 (C=O), 1616, 1597, 1571, 1514, 1466, 1440, 1410 (C=C, C=N), 1231, 1136 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 2.36 s (3H, $CH_3$), 2.38 s (3H, $CH_3$), 6.57 s (1H, CH), 6.98 s and 7.27 s (1H each, 4-H, 4′-H), 7.23 m (4H, $H_{arom}$), 7.48 m (5H, $H_{arom}$), 7.64 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.80 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.40 ($CH_3$), 21.65 ($CH_3$), 71.85 (CH), 97.70 and 100.31 ($C^4$, $C^{4'}$), 125.98 (2C, $CH_{arom}$), 126.11 (2C, $CH_{arom}$), 127.26 (2C, $CH_{arom}$), 129.32 (2C, $CH_{arom}$), 129.77 (2C, $CH_{arom}$), 129.80 (2C, $CH_{arom}$), 131.05 ($CH_{arom}$); 124.54, 126.67, 133.73, 139.23, 140.89, 156.59, 158.98, 163.37, 171.07 ($C_{quat}$); 172.10 (C=O). Found, %: C 74.75; H 5.20; N 6.36. $C_{28}H_{22}N_2O_4$. Calculated, %: C 74.65; H 4.92; N 6.22.

**(4-Methylphenyl)[5-(4-methylphenyl)-1,2-oxazol-3-yl]methyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (XXXVI).** Yield 71%, mp 83–84°C. IR

spectrum, ν, $cm^{-1}$: 1740 (C=O), 1616, 1596, 1574, 1512, 1466, 1441, 1412 (C=C, C=N), 1231, 1135 (C–O–C). $^1H$ NMR spectrum, δ, ppm: 2.36 s (3H, $CH_3$), 2.38 s (3H, $CH_3$), 2.41 s (3H, $CH_3$), 6.58 s (1H, CH), 6.92 s and 7.27 s (1H each, 4-H, 4′-H), 7.23 m (4H, $H_{arom}$), 7.28 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.49 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.64 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.69 d (2H, $H_{arom}$, $^3J$ = 8 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.37 ($CH_3$), 21.61 ($CH_3$), 21.67 ($CH_3$), 71.77 (CH), 97.69 and 99.69 ($C^4$, $C^{4'}$), 125.95 (2C, $CH_{arom}$), 126.01 (2C, $CH_{arom}$), 127.24 (2C, $CH_{arom}$), 129.74 (2C, $CH_{arom}$), 129.77 (2C, $CH_{arom}$), 129.96 (2C, $CH_{arom}$); 123.95, 133.75, 138.14, 139.18, 140.85, 141.47, 156.50, 159.03, 163.39, 171.03 ($C_{quat}$); 172.27 (C=O). Found, %: C 75.11; H 5.41; N 6.15. $C_{29}H_{24}N_2O_4$. Calculated, %: C 74.98; H 5.21; N 6.03.

**Phenyl(5-phenyl-1,2-oxazol-3-yl)methyl 4,5-dichloro-1,2-thiazole-3-carboxylate (XXXVII).** Yield 82%, mp 111–113°C. IR spectrum, ν, $cm^{-1}$: 1731 (C=O), 1613, 1591, 1573, 1494, 1465, 1449, 1426, 1406 (C=C, C=N), 1208, 1080 (C–O–C), 978, 833 (C–Cl). $^1H$ NMR spectrum, δ, ppm: 6.60 s (1H, CH), 7.28 s (1H, 4-H), 7.42 m (6H, $H_{arom}$), 7.60 m (2H, $H_{arom}$), 7.73 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 72.05 (CH), 98.29 ($C^4$), 125.99 (2C, $CH_{arom}$), 127.30 (2C, $CH_{arom}$), 129.10 (4C, $CH_{arom}$), 129.27 ($CH_{arom}$), 130.57 ($CH_{arom}$); 126.11, 127.12, 136.50, 150.99, 153.62, 157.87, 163.21 ($C_{quat}$); 170.88 (C=O). Found, %: C 55.94; H 2.98; Cl 16.35; N 6.44; S 7.51. $C_{20}H_{12}Cl_2N_2O_3S$. Calculated, %: C 55.70; H 2.80; Cl 16.44; N 6.50; S 7.43.

**(4-Methylphenyl)(5-phenyl-1,2-oxazol-3-yl)-methyl 4,5-dichloro-1,2-thiazole-3-carboxylate (XXXVIII).** Yield 80%, mp 102–103°C. IR spectrum, ν, $cm^{-1}$: 1739 (C=O), 1613, 1593, 1574, 1516, 1464, 1452, 1417, 1404 (C=C, C=N), 1208, 1080 (C–O–C), 979, 833 (C–Cl). $^1H$ NMR spectrum, δ, ppm: 2.36 s (3H, $CH_3$), 6.60 s (1H, CH), 7.23 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.25 s (1H, 4-H), 7.43 m (3H, $H_{arom}$), 7.49 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.74 m (2H, $H_{arom}$). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.38 ($CH_3$), 72.07 (CH), 98.31 ($C^4$), 125.99 (2C, $CH_{arom}$), 127.36 (2C, $CH_{arom}$), 129.09 (2C, $CH_{arom}$), 129.76 (2C, $CH_{arom}$), 130.54 ($CH_{arom}$); 126.07, 127.18, 133.58, 139.26, 150.92, 153.73, 157.93, 163.34 ($C_{quat}$); 170.80 (C=O). Found, %: C 56.82; H 3.37; Cl 16.15; N 6.19; S 7.31. $C_{21}H_{14}Cl_2N_2O_3S$. Calculated, %: C 56.64; H 3.17; Cl 15.92; N 6.29; S 7.20.

**[5-(4-Methylphenyl)-1,2-oxazol-3-yl](phenyl)-methyl 4,5-dichloro-1,2-thiazole-3-carboxylate (XXXIX).** Yield 87%, mp 125–127°C. IR spectrum, ν, $cm^{-1}$: 1743 (C=O), 1618, 1597, 1567, 1514, 1470, 1435, 1402 (C=C, C=N), 1210, 1081 (C–O–C), 979, 833 (C–Cl). $^1H$ NMR spectrum, δ, ppm: 2.38 s (3H, $CH_3$), 6.55 s (1H, CH), 7.23 d (2H, $H_{arom}$, $^3J$ = 8 Hz), 7.27 s (1H, 4-H), 7.38 d.d (1H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.42 d.d (2H, $H_{arom}$, $^3J$ = 7.3 Hz), 7.60 m (2H, $H_{arom}$), 7.63 d (2H, $H_{arom}$, $^3J$ = 8 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.64 ($CH_3$), 72.10 (CH), 97.69 ($C^4$), 125.95 (2C, $CH_{arom}$), 127.32 (2C, $CH_{arom}$), 129.09 (2C, $CH_{arom}$), 129.25 ($CH_{arom}$), 129.79 (2C, $CH_{arom}$); 124.45, 126.14, 136.57, 140.94, 151.00, 153.66, 157.89, 163.15 ($C_{quat}$); 171.10 (C=O). Found, %: C 56.79; H 3.29; Cl 16.12; N 6.35; S 7.29. $C_{21}H_{14}Cl_2N_2O_3S$. Calculated, %: C 56.64; H 3.17; Cl 15.92; N 6.29; S 7.20.

**4-[(4,5-Dichloro-1,2-thiazol-3-yl)carbonyloxy]-3-methoxybenzyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (XLIII).** Yield 88%, mp 162–163°C. IR spectrum, ν, $cm^{-1}$: 3141, 3063, 3024 (=C–H), 2947, 2921, 2854 (C–H), 1750, 1731 (C=O), 1610, 1594, 1509, 1470, 1446, 1423 (C=C, C=N), 1247, 1165, 1142 (C–O–C), 870, 821 (C–Cl). $^1H$ NMR spectrum, δ, ppm: 2.41 s (3H, $CH_3$), 3.86 s (3H, $CH_3$), 5.43 s (2H, $CH_2$), 6.89 s (1H, 4-H), 7.12 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.14 s (1H, $H_{arom}$), 7.21 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.29 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz), 7.70 d (2H, $H_{arom}$, $^3J$ = 8.1 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 21.71 ($CH_3$), 56.25 ($OCH_3$), 67.37 ($CH_2$), 99.58 ($C^4$), 113.11 ($CH_{arom}$), 121.35 ($CH_{arom}$), 122.96 ($CH_{arom}$), 126.06 (2C, $CH_{arom}$), 130.00 (2C, $CH_{arom}$); 124.03, 126.59, 134.69, 139.43, 141.49, 151.13, 151.25, 153.50, 156.75, 156.87 ($C_{quat}$); 160.07 and 172.27 (C=O). Mass spectrum: *m*/*z* 518 $[M]^+$. Found, %: C 53.65; H 3.19; Cl 13.22; N 5.21; S 5.87. $C_{23}H_{16}Cl_2N_2O_6S$. Calculated, %: C 53.19; H 3.11; Cl 13.65; N 5.39; S 6.17. *M* 519.35.

**4-[(4,5-Dichloro-1,2-thiazol-3-yl)carbonyloxy]-3-methoxybenzyl 4,5-dichloro-1,2-thiazole-3-carboxylate (XLIV).** Yield 54%, mp 137–138°C. IR spectrum, ν, $cm^{-1}$: 3016 (=C–H), 2941 (C–H), 1749, 1731 (C=O), 1608, 1513, 1461, 1407 (C=C, C=N), 1236, 1214, 1156 (C–O–C), 876, 839, 815 (C–Cl). $^1H$ NMR spectrum, δ, ppm: 3.85 s (3H, $CH_3$), 5.42 s (2H, $CH_2$), 7.11 d (1H, $H_{arom}$, $^3J$ = 8 Hz), 7.15 s (1H, $H_{arom}$), 7.20 d (1H, $H_{arom}$, $^3J$ = 8 Hz). $^{13}C$ NMR spectrum, $\delta_C$, ppm: 56.20 ($CH_3$), 67.59 ($CH_2$), 113.06 ($CH_{arom}$), 121.31 ($CH_{arom}$), 122.95 ($CH_{arom}$); 125.93, 126.55, 134.53, 139.39, 150.91, 151.10, 151.20, 153.43, 154.08 ($C_{quat}$); 156.80 and 158.97 (C=O). Mass spectrum: *m*/*z* 512 $[M]^+$. Found, %: C 37.79; H 1.73; Cl 27.13; N 5.01; S 11.94. $C_{16}H_8Cl_4N_2O_5S_2$. Calculated, %: C 37.37; H 1.57; Cl 27.58; N 5.45; S 12.47. *M* 514.19.

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