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Synthesis of Functional Isoxazole Derivatives Proceeding from (5-Arylisoxazol-3-yl)chloromethanes

V. I. Potkin[a], N. A. Bumagin[b], S. K. Petkevich[a], E. A. Dikusar[a], E. V. Semenova[a], P. V. Kurman[c], R. M. Zolotar'[c], S. G. Pashkevich[d], T. A. Gurinovich[d], and V. A. Kul'chitskii[d]

[a] *Institute of Physical Organic Chemistry, National Academy of Sciences of Belarus, ul. Surganova 13, Minsk, 220072 Belarus*
e-mail: potkin@ifoch.bas-net.by

[b] *Lomonosov Moscow State University, Moscow, Russia*

[c] *Institute of Bioorganic Chemistry, National Academy of Sciences of Belarus, Minsk, Belarus*

[d] *Physiology Institute, National Academy of Sciences of Belarus, Minsk, Belarus*

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Abstract—Reaction of 3-chloromethyl-5-phenyl(*p*-tolyl)isoxazoles with substituted phenols under the conditions of Williamson reaction afforded the corresponding 3-aryloxymethyl-5-phenyl(*p*-tolyl)isoxazoles. Treating the latter with sodium methylate, sodium phenyl(benzyl, furfuryl)thiolates and morpholine in methanol resulted in the replacement of the chlorine atom in 3-chloromethyl-5-phenyl(*p*-tolyl)isoxazoles by methoxy-, phenyl-(benzyl, furfuryl)sulfanyl groups and morpholine residue.

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Functionally substituted isoxazoles attract a constantly growing attention due to the high biological activity exhibited by specimens of this compounds class [1]. The isoxazole heterocycle is a fragment of molecules of quite a number of pharmaceuticals, e.g., of leflunomide (drug for treating rheumatoid arthritis), isocarboxazid (antidepressant), valdecoxib (antiphlogistic drug), edonentan (antihypertensive drug), sulfamethoxazole, sulfisoxazole (antibacterial drugs) [2–5]. Among isoxazole derivatives kinase inhibitors, antagonists of glutamate receptors, and antitumor agents were found [6–9]. We recently performed the synthesis of substituted isoxazolylureas, and they were found to increase the cytotoxicity of antitumor pharmaceuticals cisplatin and carboplatin thus permitting the reduction of the therapeutic dose of these very toxic substances [10].

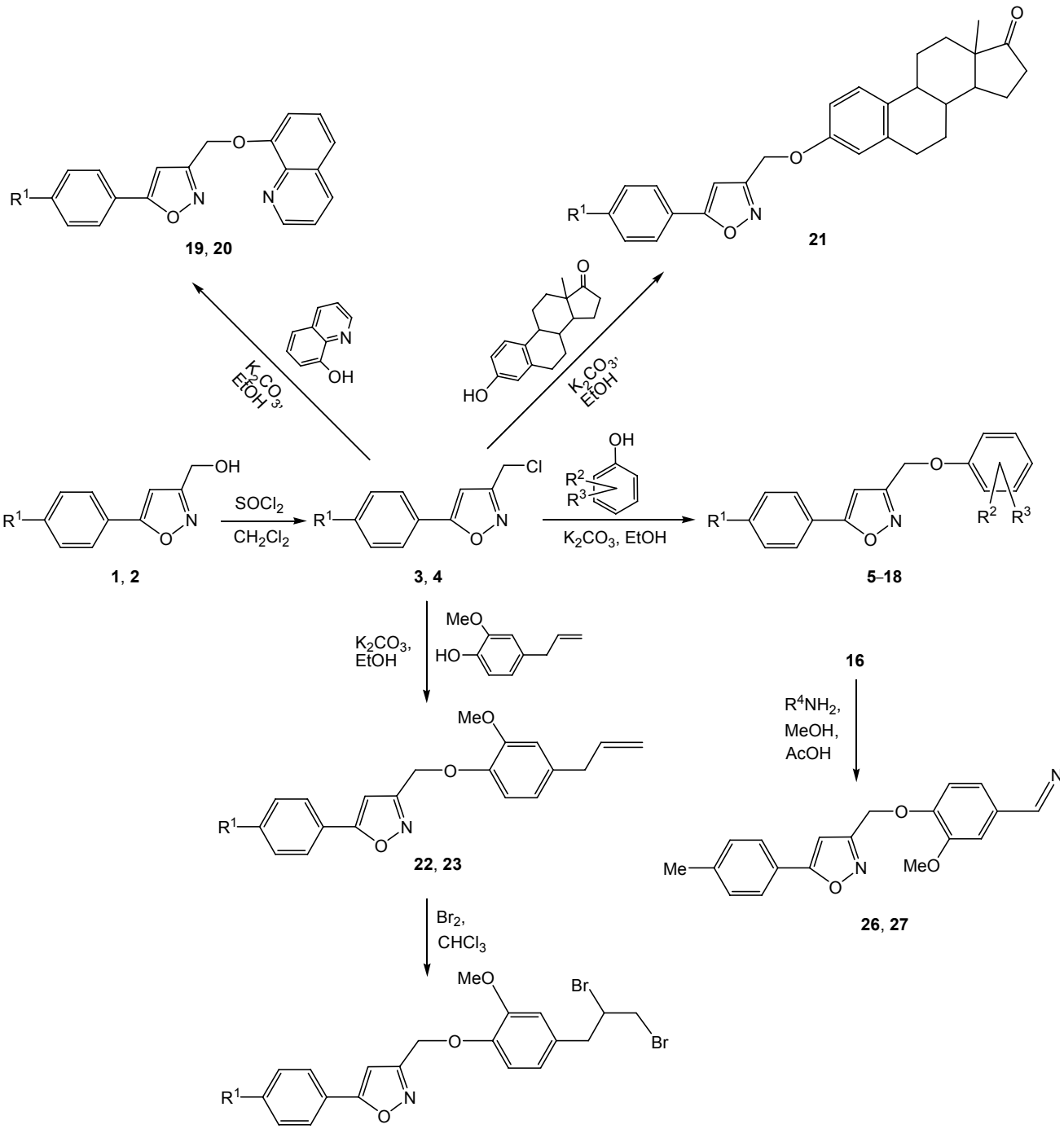
Beside the biologic action isoxazoles are able to form complexes with palladium(II) that exhibit a high catalytic activity in the cross-coupling reactions in water and water-alcoholic media and can be successfully applied to the preparation of various practically valuable substances [11]. The immobilization of the complexes on various carriers opens a way to reusable catalytic systems [12].

The complexing properties of substituted isoxazoles and their biological activity are considerably determined by the functional surrounding of the heterocycle [13, 14]. Therefore the development of approaches to the formation of desired exocyclic functionality of isoxazoles, synthesis of their new derivatives promising for biotesting and application as ligands in metal complex catalysts are extremely important tasks.

The aim of our work consisted in the preparation of 5-arylisoxazoles derivatives containing in the position *3* of the heterocycle substituents of diverse nature, in particular, pharmacophoric fragments. As initial compounds available 5-(arylisoxazol-3-yl)methanols **1** and **2** were chosen whose synthesis had been formerly developed based on successive transformations of trichloroethylene dimer [15].

The exocyclic hydroxymethyl group of compounds **1** and **2** was first converted into a chloromethyl fragment by treating with thionyl chloride to obtain the corresponding 5-aryl-3-chloromethylisoxazoles **3** and

Scheme 1.



R^1 = H (**1**, **3**, **5**, **6**, **9**–**13**, **19**, **22**, **24**), Me (**2**, **4**, **7**, **8**, **14**–**18**, **20**, **21**, **23**, **25**); $R^2 = R^3$ = H (**5**, **6**); R^2 = H, R^3 = 4-$Me_3CCH_2CMe_2$ (**7**, **8**); R^2 = H, R^3 = 2-CHO (**9**, **14**), 4-CHO (**10**, **15**); R^2 = 2-OMe, R^3 = 4-CHO (**11**, **16**); R^2 = 2-OEt, R^3 = 4-CHO (**12**, **17**); R^2 = 2-OMe, R^3 = 5-CHO (**13**, **18**); R^4 = Ph (**26**), 4-PhC_6H_4 (**27**).

4 in 74–87% yield. Further transformations were carried out using the synthetic potential of the reactive chloromethyl group.

By treating 5-aryl-3-chloromethylisoxazoles **3** and **4** with substituted synthetic and natural phenols (among them salicylaldehyde, vanillin, their analogs, 8-hydroxy-

quinoline, eugenol, and also estrone, etc.) in ethanol in the presence of potassium carbonate under the conditions of Williamson reaction we synthesized 3-aryloxymethyl-5-arylisoxazoles **5–23**. The process was performed in an argon atmosphere under reflux of reaction mixture for 5 days, the yields of ethers **5–23** were 76–92% (Scheme 1). A number or the compounds contain reactive substituents, for instance, an aldehyde fragment (derivatives of aldehydephenols), keto group (estrone), allyl residue (derivatives of eugenol). Therefore it is possible to bring the synthesized ethers into further directed transformations.

We carried out the bromination of eugenol derivatives **22** and **23** with elemental bromine in tetrachloromethane under mild conditions at room temperature. The reaction proceeded selectively by bromine addition to the exocyclic double bond, it completed within 10 h, and the yields of dibromo adducts **24** and **25** were 81–84%. The presence of two reactive bromine atoms in obtained compounds **24** and **25** increases their synthetic potential. Besides the introduction of halogen atoms increases as a rule the biologic activity of the substance and makes it more attractive for bio testing, in particular, for investigating the pesticide activity [16, 17].

By the condensation of vanillin derivative **16** with aniline or *p*-biphenylamine in boiling anhydrous methanol with added glacial acetic acid we obtained the corresponding azomethines **26** and **27** in 77 and 79% yields respectively.

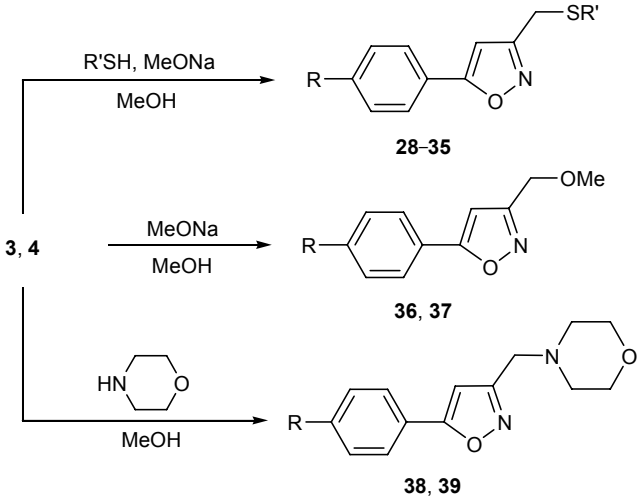
We brought the initial 3-(chloromethyl)isoxazoles **3** and **4** into the nucleophilic substitution reactions with other nucleophiles as well. By the treatment with sodium methylate, sodium phenyl(benzyl, furfuryl) thiolates, and morpholine in methanol the chlorine atom was substituted for methoxy fragment, phenyl (benzyl, furfuryl)sulfanyl groups, and morpholine residue respectively. The reactions with sodium methylate and morpholine were carried out in boiling methanol, the reaction with sodium thiolates readily occurred at 20°C. The yield of the products of chlorine substitution for the nucleophile residues was 82–97%, only in the case of mercaptoethanol derivative the yield of sulfide **31** did not exceed 66% (Scheme 2).

The synthesized compounds **3–39** were identified based on the data of elemental analysis, IR, ^{1}H and ^{13}C NMR, and mass spectra.

IR spectra of 3-(chloromethyl)isoxazoles **3** and **4** lack the absorption band of stretching vibrations of the OH group that is present in the spectra of initial 5-(arylisoxazol-3-yl)methanols **1** and **2**. The presence of the chloromethyl fragment is confirmed by the singlet signals in the ^{1}H NMR spectra of isoxazoles **3** and **4** in the region 4.61–4.62 ppm and the signals δ 35.82 ppm in the ^{13}C NMR spectra. In the IR spectra of ethers **5–27** the absorption bands are observed of the C=C bonds in the phenol residues, and also of the C=C and C=O bonds in the corresponding substituents in the aromatic fragments of the molecules. In the ^{1}H NMR spectra of compounds **5–27** the CH_2O groups give rise to singlets at 5.16–5.47 ppm, the single proton H^4 of the isoxazole heterocycle appears as a singlet in the region 6.52–7.23 ppm. Besides the multiplets of aromatic protons are observed, and in the spectra of aldehydophenols derivatives **9–18**, singlets of aldehyde fragments in the range 9.84–10.53 ppm. The presence of the azomethine fragment in compounds **26** and **27** is indicated by the singlets at 8.35–8.42 ppm in the ^{1}H NMR spectra, and also the signals at δ 159.58–159.78 ppm in the ^{13}C NMR spectra. Azomethines **26** and **27** apparently form as *E*-isomers as show the close values δ of the azomethine group signals and similar signals in the spectra of analogous compounds [18].

^{1}H and ^{13}C NMR spectra of compounds **28–39** contain the signals of molecular fragments of the nucleophile residues of the corresponding multiplicity [singlet of the methoxy group (**36** and **37**), multiplets of thiol residues (**28–35**) and of morpholine rest (**38** and **39**)], and in the IR spectra the absorption bands are present characteristic of the bonds forming these fragments.

Scheme 2.



R = H (**28–31**, **36**, **38**), Me (**32–35**, **37**, **39**); R' = Ph (**28**, **32**), Bn (**29**, **33**), 2-FuCH_2 (**30**, **34**), CH_2CH_2OH (**31**, **35**).

Synthesized derivatives of aldehydophenols **9–18** and azomethines **26** and **27** are isosteres of sinergists of insecticides [19, 20] and are now under bio testing in binary mixtures with neonicotinoid insecticide Kerber against Colorado potato beetle. Derivatives of morpholine **38** and **39** are structural analogs of compounds possessing antitumor activity and increasing the cytotoxic action of cisplatin and carboplatin drugs [10, 14], and they have been transferred to Physiology Institute, National Academy of Sciences of Belarus', for medico-biologic investigations. A series of obtained isoxazole derivatives are promising as ligands for palladium complexes and modifier of polymer matrices for development of cross-coupling catalysts.

EXPERIMENTAL

IR spectra were recorded on a Fourier spectrophotometer Nicolet Protégé-460 from pellets with KBr (compounds **36** and **37**, from thin films). ^{1}H and ^{13}C NMR spectra were registered on a spectrometer Bruker Avance-500 in $CDCl_3$ (**3–9**, **14**, and **21–37)** and $(CD_3)_2SO$ (**10–13** and **15–20)**. The chemical shifts were measured from the residual signals of the deuterated solvents [$CDCl_3$: δ_H 7.26, δ_C 77.2 ppm; $(CD_3)_2SO$: δ_H 2.50, δ_C 40.1 ppm]. Mass spectra were measured on an instrument Agilent 5975 inert MSD/6890N Network GC System in the electron impact mode, ionizing electrons energy 70 eV; capillary column HP-5MS (30 m × 0.25 mm × 0.25 μm); stationary phase 5% PhMe Silicone; vaporizer temperature 250°C.

Chloromethylisoxazoles (3 and 4). General procedure. To 20 mmol of an appropriate alcohol **1** and **2** in 40 mL of anhydrous dichloromethane at 10°C was added 2.86 g (24 mmol) of thionyl chloride. The reaction mixture was stirred at 20°C till the end of HCl liberation (2 h), then it was boiled for 4 h more. On cooling the solution was poured in 150 mL of water, the organic layer was separated, washed with water solution of sodium hydrogen carbonate, and dried with calcium chloride. The solvent was distilled off at a reduced pressure, the residue was recrystallized from hexane.

5-Phenyl-3-(chloromethyl)isoxazole (3). Yield 87%, mp 70–71°C. IR spectrum, ν, cm^{-1}: 3119, 3058, 3043, 3022, 2925, 2853, 1646, 1612, 1591, 1574, 1502, 1464, 1452, 1423, 1265, 1152, 1048, 1012, 949, 921, 821, 766, 735, 693, 685, 667, 619, 507. ^{1}H NMR spectrum, δ, ppm: 4.62 s (1H, CH_2), 6.61 s (1H$_{isox}$), 7.44 m (3H$_{arom}$), 7.75 m (2H$_{arom}$). ^{13}C NMR spectrum, δ, ppm: 35.82 (CH_2), 99.11 (CH$_{isox}$), 125.88 (2CH$_{arom}$), 129.09 (2CH$_{arom}$), 130.54 (1CH$_{arom}$), 127.04, 161.47, 170.90 (3C$_{quat}$). Found, %: C 61.95; H 4.02; Cl 18.50; N 7.21. $[M]^+$ 193. $C_{10}H_8ClNO$. Calculated, %: C 62.03; H 4.16; Cl 18.31; N 7.23. *M* 193.63.

5-(4-Methylphenyl)-3-(chloromethyl)isoxazole (4). Yield 74%, mp 47.5–48°C. IR spectrum, ν, cm^{-1}: 3136, 3058, 3024, 2920, 2854, 1619, 1599, 1587, 1566, 1513, 1458, 1450, 1429, 1409, 1266, 1114, 1047, 1019, 948, 927, 827, 803, 739, 726, 715, 673, 634, 505. ^{1}H NMR spectrum, δ, ppm: 2.37 s (3H, Me), 4.61 s (1H, CH_2), 6.54 s (1H$_{isox}$), 7.23 d (2H$_{arom}$, *J* 8 Hz), 7.63 d (2H$_{arom}$, *J* 8 Hz). ^{13}C NMR spectrum, δ, ppm: 21.48 (Me), 35.82 (CH_2), 98.45 (CH$_{isox}$), 125.76 (2CH$_{arom}$), 129.71 (2CH$_{arom}$), 124.31, 140.82, 161.36, 171.05 (4C$_{quat}$). Found, %: C 63.54; H 4.90; Cl 17.12; N 6.68. $[M]^+$ 207. $C_{11}H_{10}ClNO$. Calculated, %: C 63.62; H 4.85; Cl 17.07; N 6.75. *M* 207.66.

Ethers (5–23). General procedure. A mixture of 20 mmol of chloromethylisoxazole **3** and **4**, 60 mmol of substituted phenol, and 8.29 g (60 mmol) of anhydrous K_2CO_3 in 40 mL of 96% ethanol was boiled at reflux for 5 days in an argon atmosphere. On cooling the reaction mixture was poured in 100 mL of 10% water NaCl solution. The separated precipitate was filtered off, washed with 500 mL of water, and dried at 30–35°C. The final purification was performed by column chromatography on silica gel (100–160 μm), eluent benzene (for compounds **5–18** and **21–23**), or by low temperature crystallization from a mixture benzene–hexane, 1 : 1 (for compounds **19** and **20**).

5-Phenyl-3-(phenoxymethyl)isoxazole (5). Yield 90%, mp 61–62°C. IR spectrum, ν, cm^{-1}: 3127, 3065, 3040, 2922, 2853, 1600, 1588, 1574, 1496, 1470, 1453, 1434, 1368, 1292, 1246, 1227, 1171, 1154, 1110, 1081, 1051, 1023, 923, 847, 807, 752, 689. ^{1}H NMR spectrum, δ, ppm: 5.21 s (2H, CH_2), 6.66 s (1H$_{isox}$), 6.98–7.08 m (3H$_{arom}$), 7.33 t (2H$_{arom}$, *J* 7.4 Hz), 7.40–7.51 m (3H$_{arom}$), 7.73–7.83 m (2H$_{arom}$). ^{13}C NMR spectrum, δ, ppm: 61.84 (CH_2), 98.96 (CH$_{isox}$), 114.87 (2CH$_{arom}$), 121.71 (1CH$_{arom}$), 125.97 (2CH$_{arom}$), 129.10 (2CH$_{arom}$), 129.76 (2CH$_{arom}$), 130.43 (1CH$_{arom}$), 127.33, 158.16, 161.62, 170.59 (4C$_{quat}$). Found, %: C 76.91; H 5.28; N 5.23. $[M]^+$ 251. $C_{16}H_{13}NO_2$. Calculated, %: C 76.48; H 5.21; N 5.57. *M* 251.28.

3-{[4-(2,4,4-Trimethylpentan-2-yl)phenoxy]methyl}-5-phenylisoxazole (6). Yield 92%, mp 118–119°C. IR spectrum, ν, cm^{-1}: 3133, 3064, 3043, 2954, 2884,

2872, 1610, 1593, 1573, 1509, 1467, 1453, 1395, 1385, 1373, 1364, 1284, 1246, 1232, 1183, 1131, 1112, 1098, 1052, 1019, 947, 929, 856, 826, 814, 763, 682, 585. ^{1}H NMR spectrum, δ, ppm: 0.74 s (9H, 3Me), 1.36 s (6H, 2Me), 1.73 s (2H, CH_2), 5.19 s (2H, OCH_2), 6.67 s (1H$_{isox}$), 6.94 d (2H$_{arom}$, *J* 8.5 Hz), 7.32 d (2H$_{arom}$, *J* 8.5 Hz), 7.40–7.52 m (3H$_{arom}$), 7.73–7.83 m (2H$_{arom}$). ^{13}C NMR spectrum, δ, ppm: 31.79 (2MeC), 31.93 (3MeC), 57.15 (CH_2), 61.96 (OCH_2), 99.08 (CH$_{isox}$), 114.12 (2CH$_{arom}$), 126.02 (2CH$_{arom}$), 127.40 (2CH$_{arom}$), 129.14 (2CH$_{arom}$), 130.47 (1CH$_{arom}$), 32.48, 38.16, 127.37, 143.42, 155.87, 161.87, 170.57 (7C$_{quat}$). Found, %: C 79.66; H 8.27; N 3.35. $[M]^+$ 363. $C_{24}H_{29}NO_2$. Calculated, %: C 79.30; H 8.04; N 3.85. *M* 363.50.

5-(4-Methylphenyl)-3-(phenoxymethyl)isoxazole (7). Yield 92%, mp 103–104°C. IR spectrum, ν, cm^{-1}: 3121, 3066, 3033, 3023, 3013, 2963, 2922, 2855, 1618, 1600, 1587, 1519, 1496, 1474, 1454, 1437, 1369, 1242, 1172, 1080, 1056, 1018, 920, 841, 821, 755, 692, 515. ^{1}H NMR spectrum, δ, ppm: 2.41 sc (3H, Me), 5.20 s (2H, CH_2), 6.61 s (1H$_{isox}$), 6.97–7.09 m (3H$_{arom}$), 7.27 d (2H$_{arom}$, *J* 8 Hz), 7.33 t (2H$_{arom}$, *J* 7.6 Hz), 7.68 d (2H$_{arom}$, *J* 8 Hz). ^{13}C NMR spectrum, δ, ppm: 21.61 (Me), 61.89 (CH_2), 98.36 (CH$_{isox}$), 114.88 (2CH$_{arom}$), 121.68 (1CH$_{arom}$), 125.92 (2CH$_{arom}$), 129.76 (2CH$_{arom}$), 129.79 (2CH$_{arom}$), 124.67, 140.75, 158.21, 161.56, 170.81 (5C$_{quat}$). Found, %: C 77.20; H 5.85; N 7494. $[M]^+$ 265. $C_{17}H_{15}NO_2$. Calculated, %: C 76.96; H 5.70; N 5.28. *M* 265.31.

5-(4-Methylphenyl)-3-{[4-(2,4,4-trimethylpentan-2-yl)-phenoxy]methyl}isoxazole (8). Yield 91%, mp 109–110°C. IR spectrum, ν, cm^{-1}: 3136, 3100, 3065, 3038, 2956, 2922, 2886, 2866, 1616, 1598, 1581, 1568, 1511, 1473, 1459, 1442, 1365, 1285, 1252, 1188, 1180, 1113, 1055, 1020, 920, 825, 813, 798, 581, 509. ^{1}H NMR spectrum, δ, ppm: 0.74 s (9H, 3Me), 1.37 s (6H, 2Me), 1.73 s (2H, CH_2), 2.41 s (3H, Me), 5.18 s (2H, OCH_2), 6.61 s (1H$_{isox}$), 6.95 d (2H$_{arom}$, *J* 8.8 Hz), 7.27 d (2H$_{arom}$, *J* 8.1 Hz), 7.32 d (2H$_{arom}$, *J* 8.8 Hz), 7.68 d (2H$_{arom}$, *J* 8.1 Hz). ^{13}C NMR spectrum, δ, ppm: 21.62 (Me), 31.78 (2MeC), 31.91 (3MeC), 57.13 (CH_2), 61.99 (OCH_2), 98.43 (CH$_{isox}$), 114.09 (2CH$_{arom}$), 125.93 (2CH$_{arom}$), 127.36 (2CH$_{arom}$), 129.79 (2CH$_{arom}$), 32.47, 38.14, 124.75, 140.68, 143.31, 155.93, 161.74, 170.70 (8C$_{quat}$). Found, %: C 79.90; H 8.27; N 3.45. $[M]^+$ 377. $C_{25}H_{31}NO_2$. Calculated, %: C 79.54; H 8.28; N 3.71. *M* 377.53.

2-[(5-Phenylisoxazol-3-yl)methoxy]benzaldehyde (9). Yield 78%, mp 125–126°C. IR spectrum, ν, cm^{-1}: 1685 (C=O), 3134, 3070, 3047, 3040, 3008, 2958, 2922, 2883, 2855, 2783, 1599, 1574, 1490, 1473, 1459, 1450, 1443, 1428, 1406, 1375, 1303, 1292, 1257, 1241, 1191, 1166, 1105, 1049, 947, 850, 762, 754, 686, 679, 636, 529. ^{1}H NMR spectrum, δ, ppm: 5.30 s (2H, CH_2), 6.66 s (1H$_{isox}$), 7.07 t (1H$_{arom}$, *J* 7.5 Hz), 7.11 d (1H$_{arom}$, *J* 8.4 Hz), 7.42–7.47 m (3H$_{arom}$), 7.54 d.d (1H$_{arom}$, *J* 7.9, 1.8 Hz), 7.74–7.79 m (2H$_{arom}$), 7.85 d.d (1H$_{arom}$, *J* 7.7, 1.8 Hz), 10.53 s (1H, =CHO). ^{13}C NMR spectrum, δ, ppm: 62.34 (CH_2), 98.69 (CH$_{isox}$), 112.85 (1CH$_{arom}$), 121.76 (1CH$_{arom}$), 125.95 (2CH$_{arom}$), 128.88 (1CH$_{arom}$), 129.13 (2CH$_{arom}$), 130.60 (1CH$_{arom}$), 136.11 (1CH$_{arom}$), 125.25, 127.05, 160.24, 160.73, 170.98 (5C$_{quat}$), 189.39 (C=O). Found, %: C 73.56; H 4.88; N 4.86. $[M]^+$ 279. $C_{17}H_{13}NO_3$. Calculated, %: C 73.11; H 4.69; N 5.02. *M* 279.30.

4-[(5-Phenylisoxazol-3-yl)methoxy]benzaldehyde (10). Yield 81%, mp 105–106°C. IR spectrum, ν, cm^{-1}: 1696 (C=O), 3151, 3069, 3008, 2960, 2923, 2852, 2821, 2796, 1597, 1576, 1507, 1454, 1423, 1385, 1307, 1257, 1233, 1217, 1164, 1110, 1051, 1038, 1007, 928, 866, 832, 814, 797, 764, 688, 607. ^{1}H NMR spectrum, δ, ppm: 5.38 s (2H, CH_2), 7.17 s (1H$_{isox}$), 7.25 d (2H$_{arom}$, *J* 8.8 Hz), 7.47–7.53 m (3H$_{arom}$), 7.86–7.89 m (2H$_{arom}$), 7.89 d (2H$_{arom}$, *J* 8.8 Hz), 9.89 s (1H, =CHO). ^{13}C NMR spectrum, δ, ppm: 62.20 (CH_2), 100.57 (CH$_{isox}$),115.83 (2CH$_{arom}$), 126.22 (2CH$_{arom}$), 129.81 (2CH$_{arom}$), 131.14 (1CH$_{arom}$), 132.40 (2CH$_{arom}$), 127.17, 130.81, 161.37, 163.19, 170.28 (5C$_{quat}$), 191.88 (C=O). Found, %: C 73.52; H 4.85; N 5.20. $[M]^+$ 279. $C_{17}H_{13}NO_3$. Calculated, %: C 73.11; H 4.69; N 5.02. *M* 279.30.

3-Methoxy-4-[(5-phenylisoxazol-3-yl)-methoxy]-benzaldehyde (11). Yield 79%, mp 132–133°C. IR spectrum, ν, cm^{-1}: 1679 (C=O), 3139, 3078, 3049, 3014, 2963, 2925, 2855, 2840, 2767, 1600, 1588, 1576, 1512, 1467, 1456, 1426, 1405, 1375, 1347, 1279, 1268, 1231, 1158, 1138, 1048, 1032, 1012, 863, 838, 811, 798, 762, 730, 690, 642. ^{1}H NMR spectrum, δ, ppm: 3.85 s (3H, OMe), 5.37 s (2H, CH_2), 7.17 s (1H$_{isox}$), 7.34 d (1H$_{arom}$, *J* 8.3 Hz), 7.44 d (1H$_{arom}$, *J* 1.8 Hz), 7.50–7.55 m (3H$_{arom}$), 7.57 d.d (1H$_{arom}$, *J* 8.3, 1.8 Hz), 7.88–7.91 m (2H$_{arom}$), 9.86 s (1H, =CHO). ^{13}C NMR spectrum, δ, ppm: 56.25 (OMe), 62.52 (CH_2), 100.81 (CH$_{isox}$), 110.61 (1CH$_{arom}$), 113.54 (1CH$_{arom}$), 126.30 (2CH$_{arom}$), 126.32 (1CH$_{arom}$), 129.93 (2CH$_{arom}$), 131.26 (1CH$_{arom}$), 127.18, 131.01, 150.02, 153.07, 161.36, 170.31 (6C$_{quat}$), 192.15 (C=O). Found, %: C 70.12; H 4.98; N 4.25. $[M]^+$ 309. $C_{18}H_{15}NO_4$. Calculated, %: C 69.89; H 4.89; N 4.53. *M* 309.32.

4-[(5-Phenylisoxazol-3-yl)methoxy]-3-ethoxybenzaldehyde (12). Yield 76%, mp 86–87°C. IR spectrum, ν, cm^{-1}: 1692 (C=O), 3141, 3078, 3065, 3016, 2976, 2925, 2883, 2852, 2823, 2784, 1588, 1511, 1455, 1436, 1397, 1333, 1266, 1228, 1169, 1134, 1121, 1036, 1005, 863, 807, 765, 688. ^{1}H NMR spectrum, δ, ppm: 1.34 t (3H, MeCH$_2$, *J* 7 Hz), 4.09 q (MeCH$_2$, *J* 7 Hz), 5.38 s (2H, OCH$_2$), 7.14 s (1H$_{isox}$), 7.33 d (1H$_{arom}$, *J* 8.3 Hz), 7.42 d (1H$_{arom}$, *J* 1.8 Hz), 7.48–7.53 m (3H$_{arom}$), 7.54 d.d (1H$_{arom}$, *J* 8.3, 1.8 Hz), 7.85–7.89 m (2H$_{arom}$), 9.85 s (1H, =CHO). ^{13}C NMR spectrum, δ, ppm: 15.12 (MeCH$_2$), 62.56 (MeCH$_2$), 64.56 (OCH$_2$), 100.66 (CH$_{isox}$), 111.79 (1CH$_{arom}$), 113.88 (1CH$_{arom}$), 126.00 (1CH$_{arom}$), 126.22 (2CH$_{arom}$), 129.83 (2CH$_{arom}$), 131.16 (1CH$_{arom}$), 127.15, 131.02, 149.24, 153.18, 161.42, 170.24 (6C$_{quat}$), 192.02 (C=O). Found, %: C 70.87; H 5.47; N 4.01. $[M]^+$ 323. $C_{19}H_{17}NO_4$. Calculated, %: C 70.58; H 5.30; N 4.33. *M* 323.35.

4-Methoxy-3-[(5-phenylisoxazol-3-yl)methoxy]-benzaldehyde (13). Yield 87%, mp 103–104°C. IR spectrum, ν, cm^{-1}: 1680 (C=O), 3142, 3080, 3062, 3007, 2956, 2924, 2852, 2766, 1598, 1584, 1512, 1469, 1455, 1433, 1406, 1372, 1263, 1238, 1158, 1133, 1018, 808, 764, 690, 639. ^{1}H NMR spectrum, δ, ppm: 3.88 s (3H, OMe), 5.32 s (2H, CH$_2$), 7.14 s (1H$_{isox}$), 7.19 d (1H$_{arom}$, *J* 8.3 Hz), 7.48–7.54 m (3H$_{arom}$), 7.59 s (1H$_{arom}$), 7.60 d.d (1H$_{arom}$, *J* 8.3, 1.8 Hz), 7.88–7.91 m (2H$_{arom}$), 9.84 s (1H, =CHO). ^{13}C NMR spectrum, δ, ppm: 56.55 (OMe), 62.49 (CH$_2$), 100.71 (CH$_{isox}$), 112.31 (1CH$_{arom}$), 112.36 (1CH$_{arom}$), 126.22 (2CH$_{arom}$), 127.47 (1CH$_{arom}$), 129.81 (2CH$_{arom}$), 131.12 (1CH$_{arom}$), 127.20, 130.16, 148.16, 155.09, 161.55, 170.19 (6C$_{quat}$), 191.77 (C=O). Found, %: C 70.10; H 5.04; N 4.20. $[M]^+$ 309. $C_{18}H_{15}NO_4$. Calculated, %: C 69.89; H 4.89; N 4.53. *M* 309.32.

2-{[5-(4-Methylphenyl)isoxazol-3-yl]methoxy}-benzaldehyde (14). Yield 91%, mp 140–141°C. IR spectrum, ν, cm^{-1}: 1686 (C=O), 3139, 3067, 3031, 3011, 2952, 2920, 2887, 2858, 2783, 1619, 1600, 1568, 1517, 1490, 1470, 1458, 1438, 1408, 1373, 1305, 1269, 1253, 1242, 1194, 1185, 1164, 1105, 1055, 1050, 948, 921, 851, 837, 819, 756, 715, 643, 499. ^{1}H NMR spectrum, δ, ppm: 2.30 s (3H, Me), 5.21 s (2H, CH$_2$), 6.52 s (1H$_{isox}$), 6.98 t (1H$_{arom}$, *J* 7.5 Hz), 7.03 d (1H$_{arom}$, *J* 8.4 Hz), 7.17 d (2H$_{arom}$, *J* 8 Hz), 7.46 d.d (1H$_{arom}$, *J* 7.9, 1.8 Hz), 7.58 d (2H$_{arom}$, *J* 8 Hz), 7.77 d.d (1H$_{arom}$, *J* 7.7, 1.8 Hz), 10.45 s (1H, =CHO). ^{13}C NMR spectrum, δ, ppm: 21.59 (Me), 62.41 (CH$_2$), 98.08 (CH$_{isox}$), 112.88 (1CH$_{arom}$), 121.74 (1CH$_{arom}$), 125.91 (2CH$_{arom}$), 128.86 (1CH$_{arom}$), 129.82 (2CH$_{arom}$), 136.11 (1CH$_{arom}$), 124.39, 125.28, 140.97, 160.31, 160.69, 171.20 (6C$_{quat}$), 189.41 (C=O). Found, %: C 74.06; H 5.22; N 4.41. $[M]^+$ 293. $C_{18}H_{15}NO_3$. Calculated, %: C 73.71; H 5.15; N 4.78. *M* 293.32.

4-{[5-(4-Methylphenyl)isoxazol-3-yl]methoxy}-benzaldehyde (15). Yield 88%, mp 93–94°C. IR spectrum, ν, cm^{-1}: 1686 (C=O), 3127, 3076, 3041, 3010, 2974, 2924, 2853, 2757, 1618, 1602, 1579, 1517, 1509, 1470, 1439, 1396, 1368, 1315, 1254, 1215, 1162, 1109, 948, 916, 864, 839, 813, 803, 745, 716, 509. ^{1}H NMR spectrum, δ, ppm: 2.35 s (3H, Me), 5.37 s (2H, CH$_2$), 7.10 s (1H$_{isox}$), 7.26 d (2H$_{arom}$, *J* 8.8 Hz), 7.33 d (2H$_{arom}$, *J* 8.1 Hz), 7.77 d (2H$_{arom}$, *J* 8.1 Hz), 7.90 d (2H$_{arom}$, *J* 8.8 Hz), 9.89 s (1H, =CHO). ^{13}C NMR spectrum, δ, ppm: 21.56 (Me), 62.19 (CH$_2$), 99.91 (CH$_{isox}$), 115.84 (2CH$_{arom}$), 126.18 (2CH$_{arom}$), 130.38 (2CH$_{arom}$), 132.39 (2CH$_{arom}$), 124.52, 130.81, 141.10, 161.31, 163.21, 170.43 (6C$_{quat}$), 191.91 (C=O). Found, %: C 74.23; H 5.19; N 4.35. $[M]^+$ 293. $C_{18}H_{15}NO_3$. Calculated, %: C 73.71; H 5.15; N 4.78. *M* 293.32.

4-{[5-(4-Methylphenyl)isoxazol-3-yl]methoxy}-3-methoxybenzaldehyde (16). Yield 86%, mp 103–104°C. IR spectrum, ν, cm^{-1}: 1686 (C=O), 3142, 3076, 3060, 3032, 2958, 2920, 2852, 2763, 1619, 1600, 1587, 1513, 1476, 1463, 1445, 1422, 1400, 1374, 1344, 1281, 1264, 1231, 1159, 1135, 1045, 1033, 1013, 915, 860, 819, 798, 754, 727, 510. ^{1}H NMR spectrum, δ, ppm: 2.35 s (3H, Me), 3.85 s (3H, OMe), 5.35 s (2H, CH$_2$), 7.09 s (1H$_{isox}$), 7.34 m (3H$_{arom}$), 7.44 d (1H$_{arom}$, *J* 1.8 Hz), 7.57 d.d (1H$_{arom}$, *J* 8.2, 1.8 Hz), 7.78 d (2H$_{arom}$, *J* 8.1 Hz), 9.86 s (1H, =CHO). ^{13}C NMR spectrum, δ, ppm: 21.58 (Me), 56.19 (OMe), 62.49 (CH$_2$), 100.08(CH$_{isox}$), 110.54 (1CH$_{arom}$), 113.46 (1CH$_{arom}$), 126.20 (2CH$_{arom}$), 126.27 (1CH$_{arom}$), 130.40 (2CH$_{arom}$), 124.51, 130.96, 141.12, 149.98, 153.05, 161.23, 170.43 (7C$_{quat}$), 192.03 (C=O). Found, %: C 70.92; H 5.37; N 4.11. $[M]^+$ 323. $C_{19}H_{17}NO_4$. Calculated, %: C 70.58; H 5.30; N 4.33. *M* 323.35.

4-{[5-(4-Methylphenyl)isoxazol-3-yl]methoxy}-3-ethoxybenzaldehyde (17). Yield 85%, mp 61–62°C. IR spectrum, ν, cm^{-1}: 1693 (C=O), 3140, 3083, 3055, 3028, 2975, 2921, 2868, 2823, 2785, 1620, 1586, 1514, 1462, 1449, 1397, 1336, 1273, 1231, 1177, 1133, 1120, 1037, 1008, 948, 848, 810, 791, 737, 505. ^{1}H NMR spectrum, δ, ppm: 1.34 t (3H, MeCH$_2$, *J* 7 Hz), 2.34 s (3H, Me), 4.10 q (MeCH$_2$, *J* 7 Hz), 5.37 s (2H, OCH$_2$), 7.07 s (1H$_{isox}$), 7.33 m (3H$_{arom}$), 7.42 d (1H$_{arom}$, *J* 1.8 Hz), 7.54 d.d (1H$_{arom}$, *J* 8.3, 1.8 Hz), 7.76 d

($2H_{arom}$, *J* 8.1 Hz), 9.85 s (1H, =CHO). ^{13}C NMR spectrum, δ, ppm: 15.12 ($\underline{Me}CH_2$), 21.56 (Me), 62.56 ($Me\underline{C}H_2$), 64.56 (OCH_2), 100.10 (CH_{isox}), 111.80 ($1CH_{arom}$), 113.88 ($1CH_{arom}$), 125.99 ($1CH_{arom}$), 126.16 ($2CH_{arom}$), 130.37 ($2CH_{arom}$), 124.50, 131.01, 141.09, 149.24, 153.20, 161.33, 170.40 ($7C_{quat}$), 192.00 (C=O). Found, %: C 71.65; H 5.84; N 4.21. $[M]^+$ 337. $C_{20}H_{19}NO_4$. Calculated, %: C 71.20; H 5.68; N 4.15. *M* 337.37.

3-{[5-(4-Methylphenyl)isoxazol-3-yl]-methoxy}-4-methoxybenzaldehyde (18). Yield 89%, mp 134–135°C. IR spectrum, ν, cm^{-1}: 1680 (C=O), 3138, 3079, 3034, 3017, 2974, 2923, 2871, 2849, 2766, 1617, 1599, 1586, 1518, 1507, 1475, 1436, 1403, 1367, 1263, 1236, 1225, 1160, 1137, 1049, 1021, 948, 901, 864, 822, 806, 793, 764, 640, 503. ^1H NMR spectrum, δ, ppm: 2.36 s (3H, Me), 3.89 s (3H, OCH_3), 5.30 s (2H, CH_2), 7.08 s ($1H_{isox}$), 7.22 d ($1H_{arom}$, *J* 8.3 Hz), 7.34 d ($2H_{arom}$, *J* 8.1 Hz), 7.58 d ($1H_{arom}$, *J* 1.8 Hz), 7.61 d.d ($1H_{arom}$, *J* 8.3, 1.8 Hz), 7.78 d ($2H_{arom}$, *J* 8.1 Hz), 9.84 s (1H, =CHO). ^{13}C NMR spectrum, δ, ppm: 21.59 (Me), 56.59 (OMe), 62.48 (CH_2), 100.08 (CH_{isox}), 112.37 ($1CH_{arom}$), 112.38 ($1CH_{arom}$), 126.19 ($2CH_{arom}$), 127.47 ($1CH_{arom}$), 130.40 ($2CH_{arom}$), 124.54, 130.15, 141.08, 148.16, 155.09, 161.47, 170.32 ($7C_{quat}$), 191.84 (C=O). Found, %: C 70.87; H 5.44; N 4.09. $[M]^+$ 323. $C_{19}H_{17}NO_4$. Calculated, %: C 70.58; H 5.30; N 4.33. *M* 323.35.

5-Phenyl-3-[(quinolin-8-yloxy)methyl]isoxazole (19). Yield 80%, mp 72–73°C. IR spectrum, ν, cm^{-1}: 3044, 2953, 2850, 1599, 1575, 1497, 1465, 1424, 1387, 1371, 1324, 1312, 1281, 1268, 1231, 1109, 1034, 873, 823, 803, 789, 745, 732, 506. ^1H NMR spectrum, δ, ppm: 5.47 s (2H, CH_2), 7.23 s ($1H_{isox}$), 7.39 d ($1H_{arom}$, *J* 7.2 Hz), 7.48–7.59 m ($6H_{arom}$), 7.90 d ($2H_{arom}$, *J* 6.7 Hz), 8.33 d.d ($1H_{arom}$, *J* 8.1, 1.1 Hz), 8.88 d.d ($1H_{arom}$, *J* 3.7, 1.1 Hz). ^{13}C NMR spectrum, δ, ppm: 62.70 (CH_2), 100.90 (CH_{isox}), 111.27 ($1CH_{arom}$), 121.29 ($1CH_{arom}$), 122.55 ($1CH_{arom}$), 126.23 ($2CH_{arom}$), 127.27 ($1CH_{arom}$), 129.84 ($2CH_{arom}$), 131.12 ($1CH_{arom}$), 136.46 ($1CH_{arom}$), 149.82 ($1CH_{arom}$), 127.24, 129.72, 140.36, 154.16, 161.88, 170.13 ($6C_{quat}$). Found, %: C 75.79; H 4.86; N 8.97. $C_{19}H_{14}N_2O_2$. Calculated, %: C 75.48; H 4.67; N 9.27.

5-(4-Methylphenyl)-3-[(quinolin-8-yloxy)methyl]-isoxazole (20). Yield 82%, mp 66–67°C. IR spectrum, ν, cm^{-1}: 3042, 2958, 2921, 2854, 1600, 1578, 1502, 1469, 1425, 1384, 1371, 1327, 1262, 1109, 1035, 822, 803, 790, 744, 513. ^1H NMR spectrum, δ, ppm: 2.37 s (3H, Me), 5.45 s (2H, CH_2), 7.16 s ($1H_{isox}$), 7.35 d ($2H_{arom}$, *J* 8.1 Hz), 7.38 d ($1H_{arom}$, *J* 7.2 Hz), 7.53 t ($1H_{arom}$, *J* 7.9 Hz), 7.55–7.61 m ($2H_{arom}$), 7.80 d ($2H_{arom}$, *J* 8.1 Hz), 8.34 d.d ($1H_{arom}$, *J* 8.3, 1.5 Hz), 8.88 d.d ($1H_{arom}$, *J* 4, 1.5 Hz). ^{13}C NMR spectrum, δ, ppm: 21.60 (Me), 62.68 (CH_2), 100.27 (CH_{isox}), 111.23 ($1CH_{arom}$), 121.27 ($1CH_{arom}$), 122.58 ($1CH_{arom}$), 126.21 ($2CH_{arom}$), 127.30 ($1CH_{arom}$), 130.43 ($2CH_{arom}$), 136.49 ($1CH_{arom}$), 149.84 ($1CH_{arom}$), 124.61, 130.06, 144.22, 150.06, 154.17, 162.62, 170.31 ($7C_{quat}$). Found, %: C 76.27; H 5.28; N 8.49. $C_{20}H_{16}N_2O_2$. Calculated, %: C 75.93; H 5.10; N 8.86.

(8*R*,9*S*,13*S*,14*S*)-13-Methyl-3-{[5-(4-methylphenyl)isoxazol-3-yl]methoxy}-6,7,8,9,11,12,13,14,15,16-decahydro-17*H*-cyclopenta[*a*]phenanthren-17-one (21). Yield 74%, mp 156–157°C. IR spectrum, ν, cm^{-1}: 3130, 3066, 3035, 2955, 2936, 2918, 2884, 2864, 2853, 2818, 1746, 1618, 1607, 1599, 1501, 1468, 1455, 1372, 1253, 1234, 1166, 1043, 1024, 1019, 921, 812, 795, 504. ^1H NMR spectrum, δ, ppm: 0.91 s (3H, Me_{aliph}), 1.40–1.66 m ($6H_{aliph}$), 1.93–2.09 m ($3H_{aliph}$), 2.10–2.19 m ($1H_{aliph}$), 2.21–2.29 m ($1H_{aliph}$), 2.35–2.39 m ($1H_{aliph}$), 2.40 s (3H, 4-Me), 2.46–2.54 m ($1H_{aliph}$), 2.85–2.93 m ($2H_{aliph}$), 5.16 s (2H, OCH_2), 6.59 s ($1H_{isox}$), 6.75 d ($1H_{arom}$, *J* 2.7 Hz), 6.82 d.d ($1H_{arom}$, *J* 8.6, 2.7 Hz), 7.22 d ($1H_{arom}$, *J* 8.6 Hz), 7.26 d ($1H_{arom}$, *J* 8.1 Hz), 7.67 d ($1H_{arom}$, *J* 8.1 Hz). ^{13}C NMR spectrum, δ, ppm: 14.01 (Me_{aliph}), 21.65 (CH), 21.74 (CH_2), 26.04 (CH_2), 26.65 (CH_2), 29.81 (CH_2), 31.73 (CH_2), 36.02 (CH_2), 38.44 (CH), 44.14 (CH), 50.57 (CH), 61.97 (CH_2), 98.39 (CH_{isox}), 112.51 ($1CH_{arom}$), 114.94 ($1CH_{arom}$), 125.95 ($2CH_{arom}$), 126.66 ($1CH_{arom}$), 129.82 ($2CH_{arom}$), 48.15, 124.74, 133.14, 138.17, 140.77, 156.28, 161.75, 170.79 ($8C_{quat}$), 221.03 (C=O). Found, %: C 79.02; H 7.15; N 3.09. $[M]^+$ 441. $C_{29}H_{31}NO_3$. Calculated, %: C 78.88; H 7.08; N 3.17. *M* 441.57.

3-[(4-Allyl-2-methoxyphenoxy)methyl]-5-phenyl-isoxazole (22). Yield 91%, mp 61–62°C. IR spectrum, ν, cm^{-1}: 3151, 3074, 3063, 3038, 2990, 2950, 2934, 2923, 2857, 2829, 1636, 1612, 1591, 1574, 1517, 1469, 1450, 1433, 1419, 1373, 1336, 1305, 1261, 1230, 1192, 1158, 1142, 1042, 1017, 993, 949, 921, 912, 831, 810, 771, 694. ^1H NMR spectrum, δ, ppm: 3.34 d (2H, $\underline{CH_2}CH=CH_2$, *J* 6.7 Hz), 3.89 s (3H, OMe), 5.04–5.12 m (2H, $CH_2CH=\underline{CH_2}$), 5.25 s (2H, OCH_2), 5.90–6.00 m (1H, $CH_2\underline{CH}=CH_2$), 6.69 s ($1H_{isox}$), 6.71 d.d ($1H_{arom}$, *J* 8.2, 2 Hz), 6.75 d ($1H_{arom}$, *J* 2 Hz), 6.94 d ($1H_{arom}$, *J* 8.2 Hz), 7.40–7.47 m ($3H_{arom}$), 7.73–7.80 m ($2H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 39.95 ($\underline{C}H_2CH=CH_2$), 55.99 (OMe), 63.29 (CH_2), 99.10

(CH_{isox}), 112.57 ($1CH_{arom}$), 114.74 ($1CH_{arom}$), 115.93 ($CH_2CH=\underline{C}H_2$), 120.67 ($1CH_{arom}$), 125.97 ($2CH_{arom}$), 129.08 ($2CH_{arom}$), 130.36 ($1CH_{arom}$), 137.57 ($CH_2-\underline{C}H=CH_2$), 127.43, 134.41, 145.87, 149.75, 161.87, 170.50 ($6C_{quat}$). Found, %: C 61.95; H 4.02; N 7.21. $[M]^+$ 321. $C_{20}H_{19}NO_3$. Calculated, %: C 74.75; H 5.96; N 4.36. *M* 321.38.

3-[(4-Allyl-2-methoxyphenoxy)methyl]-5-(4-methylphenyl)isoxazole (23). Yield 92%, mp 84–85°C. IR spectrum, ν, cm^{-1}: 3130, 3076, 3063, 3043, 3031, 2999, 2976, 2958, 2941, 2919, 2865, 2833, 1638, 1611, 1593, 1514, 1464, 1437, 1414, 1368, 1261, 1229, 1185, 1143, 1094, 1054, 1036, 999, 921, 841, 816, 756, 510. ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, Me), 3.34 d (2H, $\underline{CH_2}CH=CH_2$, *J* 6.7 Hz), 3.89 s (3H, OMe), 5.03–5.13 m (2H, $CH_2CH=C\underline{H_2}$), 5.24 s (2H, OCH_2), 5.90–6.01 m (1H, $CH_2C\underline{H}=CH_2$), 6.64 s ($1H_{isox}$), 6.71 d.d ($1H_{arom}$, *J* 8.2, 1.8 Hz), 6.75 d ($1H_{arom}$, *J* 1.8 Hz), 6.95 d ($1H_{arom}$, *J* 8.2 Hz), 7.24 d ($2H_{arom}$, *J* 8.1 Hz), 7.66 d ($2H_{arom}$, *J* 8.1 Hz). ^{13}C NMR spectrum, δ, ppm: 21.52 (Me), 39.89 ($\underline{C}H_2CH=CH_2$), 55.92 (OMe), 63.24 (CH_2), 98.44 (CH_{isox}), 112.51 ($1CH_{arom}$), 114.66 ($1CH_{arom}$), 115.85 ($CH_2CH=\underline{C}H_2$), 120.61 ($1CH_{arom}$), 125.84 ($2CH_{arom}$), 129.69 ($2CH_{arom}$), 137.52 ($CH_2\underline{C}H=CH_2$), 124.68, 134.29, 140.56, 145.87, 149.69, 161.73, 170.62 ($7C_{quat}$). Found, %: C 75.53; H 4.28; N 3.90. $[M]^+$ 335. $C_{21}H_{21}NO_3$. Calculated, %: C 75.20; H 6.31; N 4.18. *M* 335.40.

Bromination of ethers (22 and 23). General procedure. To 20 mmol of allyl isoxazole derivative **22** or **23** in 40 mL of anhydrous CCl_4 at 10°C was added 3.4 g (21 mmol) of Br_2. The solution was stirred at 20°C till complete discoloration (10 h). The solvent was distilled off at a reduced pressure, the residue was purified by column chromatography on silica gel (100–160 μm), eluent benzene, and by low temperature crystallization from a mixture of benzene with hexane.

3-{[4-(2,3-Dibromopropyl)-2-methoxyphenoxy]methyl}-5-phenylisoxazole (24). Yield 81%, mp 74–75°C. IR spectrum, ν, cm^{-1}: 3130, 3061, 3043, 3025, 3000, 2963, 2921, 2852, 1614, 1592, 1575, 1515, 1463, 1452, 1428, 1418, 1379, 1334, 1289, 1262, 1248, 1226, 1210, 1167, 1143, 1086, 1071, 1034, 1015, 912, 845, 807, 764, 685, 573, 555, 499. ^{1}H NMR spectrum, δ, ppm: 3.07–3.12, 3.37–3.42 m (2H, CH_2Br), 3.58–3.62, 3.78–3.81 m (2H, $ArC\underline{H_2}CHBr$), 3.90 s (3H, OMe), 4.30–4.36 m (1H, CHBr), 5.26 s (2H, OCH_2), 6.69 s ($1H_{isox}$), 6.80 d.d ($1H_{arom}$, *J* 8.2, 1.9 Hz), 6.85 d ($1H_{arom}$, *J* 1.9 Hz), 6.97 d ($1H_{arom}$, *J* 8.2 Hz), 7.41–7.48 m ($3H_{arom}$), 7.75–7.80 m ($2H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 36.14 (CH_2Br), 41.61 ($Ar\underline{C}H_2CHBr$), 52.56 (CHBr), 56.10 (OMe), 63.14 (OCH_2), 99.08 (CH_{isox}), 113.49 ($1CH_{arom}$), 114.36 ($1CH_{arom}$), 121.89 ($1CH_{arom}$), 125.98 ($2CH_{arom}$), 129.10 ($2CH_{arom}$), 130.41 ($1CH_{arom}$), 127.38, 130.83, 146.73, 149.60, 161.67, 170.59 ($6C_{quat}$). Found, %: C 49.89; H 4.12; Br 32.91; N 7.21. $[M - HBr]^+$ 399. $C_{20}H_{19}Br_2NO_3$. Calculated, %: C 49.42; H 3.98; Br 33.21; N 2.91. *M* 481.18.

3-{[4-(2,3-Dibromopropyl)-2-methoxyphenoxy]methyl}-5-(4-methylphenyl)isoxazole (25). Yield 84%, mp 93–94°C. IR spectrum, ν, cm^{-1}: 3134, 3083, 3058, 3033, 3016, 2954, 2920, 2853, 2830, 1618, 1600, 1590, 1518, 1463, 1450, 1428, 1382, 1354, 1335, 1263, 1227, 1208, 1174, 1145, 1120, 1088, 1035, 1016, 948, 924, 842, 803, 646, 571, 545, 504. ^{1}H NMR spectrum, δ, ppm: 2.38 s (3H, Me), 3.06–3.12, 3.36–3.42 m (2H, CH_2Br), 3.57–3.63, 3.77–3.82 m (2H, $ArC\underline{H_2}CHBr$), 3.90 s (3H, OMe), 4.28–4.37 m (1H, CHBr), 5.24 s (2H, OCH_2), 6.63 s ($1H_{isox}$), 6.80 d.d ($1H_{arom}$, *J* 8.2, 1.9 Hz), 6.85 d ($1H_{arom}$, *J* 1.9 Hz), 6.97 d ($1H_{arom}$, *J* 8.2 Hz), 7.24 d ($2H_{arom}$, *J* 8.1 Hz), 7.65 d ($2H_{arom}$, *J* 8.1 Hz). ^{13}C NMR spectrum, δ, ppm: 21.58 (Me), 36.14 (CH_2Br), 41.57 ($Ar\underline{C}H_2CHBr$), 52.55 (CHBr), 56.05 (OMe), 63.10 (OCH_2), 98.44 (CH_{isox}), 113.44 ($1CH_{arom}$), 114.30 ($1CH_{arom}$), 121.84 ($1CH_{arom}$), 125.87 ($2CH_{arom}$), 129.73 ($2CH_{arom}$), 124.64, 130.73, 140.65, 146.73, 149.54, 161.54, 170.72 ($7C_{quat}$). Found, %: C 51.22; H 4.36; Br 31.89; N 2.45. $[M - HBr]^+$ 413. $C_{21}H_{21}Br_2NO_3$. Calculated, %: C 50.93; H 4.27; Br 32.27; N 2.83. *M* 495.20.

Isoxazole-containing azomethines (26 and 27). General procedure. To a solution of 3 mmol of substituted benzaldehyde **16** in 30 mL of anhydrous methanol was added 3.1 mmol of aniline or *p*-biphenylamine and 0.05 mL of glacial acetic acid. The mixture was boiled for 6 and cooled to 5°C. The separated precipitate was filtered off, washed with 5 mL of cold methanol, dried in a vacuum, and recrystallized from a mixture benzene–hexane, 1 : 1.

(*E*)-1-(3-Methoxy-4-{[5-(4-methylphenyl)isoxazol-3-yl]methoxy}phenyl)-*N*-phenylmethanimine (26). Yield 77%, mp 109–110°C. IR spectrum, ν, cm^{-1}: 3145, 3078, 3059, 3040, 3017, 2955, 2922, 2875, 2852, 1625, 1600, 1583, 1511, 1467, 1458, 1439, 1420, 1376, 1266, 1234, 1213, 1160, 1143, 1052, 1030, 921, 814, 791, 771, 694, 506. ^{1}H NMR spectrum, δ, ppm: 2.39 s (3H, Me), 4.00 s (3H, OMe),

5.33 s (2H, CH_2), 6.64 s (1H, CH_{isox}), 7.08 d (1H_{arom}, *J* 8.2 Hz), 7.20 t (2H_{arom}, *J* 7.5 Hz), 7.22–7.30 m (4H_{arom}), 7.38 t (2H_{arom}, *J* 7.8 Hz), 7.64–7.68 m (3H_{arom}), 8.35 s (1H, CH=N). ^{13}C NMR spectrum, δ, ppm: 21.60 (Me), 56.21 (OMe), 62.96 (CH_2), 98.39 (CH_{isox}), 109.68 (1CH_{arom}), 113.25 (1CH_{arom}), 120.99 (2CH_{arom}), 124.35 (1CH_{arom}), 125.85 (1CH_{arom}), 125.95 (2CH_{arom}), 129.26 (2CH_{arom}), 129.80 (2CH_{arom}), 159.78 (CH=N), 124.63, 130.78, 140.80, 150.14, 150.49, 152.28, 161.17, 171.01 (8C_{quat}). Found, %: C 75.46; H 5.44; N 7.09. $C_{25}H_{22}N_2O_3$. Calculated, %: C 75.36; H 5.57; N 7.03.

(*E*)-*N*-[(1,1'-Biphenyl)-4-yl]-1-(3-methoxy-4-{[5-(4-methylphenyl)isoxazol-3-yl]methoxy}phenyl)-methanimine (27). Yield 79%, mp 173–174°C. IR spectrum, ν, cm^{-1}: 3130, 3082, 3055, 3027, 2961, 2920, 2852, 1633, 1621, 1595, 1585, 1510, 1461, 1431, 1418, 1376, 1362, 1334, 1276, 1238, 1219, 1191, 1153, 1140, 1049, 1032, 1005, 968, 948, 911, 863, 825, 811, 769, 753, 717, 692, 619, 505. ^{1}H NMR spectrum, δ, ppm: 2.40 s (3H, Me), 4.02 s (3H, OMe), 5.34 s (2H, CH_2), 6.65 s (1H, CH_{isox}), 7.10 d (1H_{arom}, *J* 8.2 Hz), 7.26 d (2H_{arom}, *J* 8 Hz), 7.27–7.32 m (3H_{arom}), 7.35 t (1H_{arom}, *J* 7.4 Hz), 7.45 t (2H_{arom}, *J* 7.7 Hz), 7.60–7.65 m (4H_{arom}), 7.67 d (2H_{arom}, *J* 8.2 Hz), 7.69 d (1H_{arom}, *J* 1.8 Hz), 8.42 s (1H, CH=N). ^{13}C NMR spectrum, δ, ppm: 21.63 (Me), 56.24 (OMe), 62.96 (CH_2), 98.40 (CH_{isox}), 109.67 (1CH_{arom}), 113.24 (1CH_{arom}), 121.51 (2CH_{arom}), 124.44 (1CH_{arom}), 125.97 (2CH_{arom}), 127.04 (2CH_{arom}), 127.31 (1CH_{arom}), 127.97 (2CH_{arom}), 128.93 (2CH_{arom}), 129.82 (2CH_{arom}), 159.58 (CH=N), 124.64, 130.81, 138.81, 140.78, 140.83, 150.15, 150.54, 151.39, 161.17, 171.04 (10C_{quat}). Found, %: C 78.60; H 5.45; N 5.93. $C_{31}H_{26}N_2O_3$. Calculated, %: C 78.46; H 5.52; N 5.90.

Reaction of chloromethylisoxazoles (3 and 4) with thiols. General procedure. To a solution of sodium methylate obtained by dissolving 0.21 g (9.1 mmol) of Na in 30 mL of anhydrous methanol was added 8 mmol of thiol, the mixture was stirred for 30 min, and then 8.3 mmol of chloromethylisoxazole **3** or **4** was added. The slurry was stirred for 2 h at 20°C, 150 mL of water was added, the precipitate was filtered off, washed with water, and dried in a vacuum.

5-Phenyl-3-[(phenylsulfanyl)methyl]isoxazole (28). Yield 82%, mp 61–62°C. IR spectrum, ν, cm^{-1}: 3112, 3065, 3049, 3026, 3014, 3000, 2965, 2921, 2853, 1614, 1592, 1574, 1498, 1470, 1450, 1438, 1418, 1408, 1259, 1187, 1141, 1067, 1051, 1025, 946, 914, 825, 766, 749, 691, 679, 490. ^{1}H NMR spectrum, δ, ppm: 4.12 s (2H, CH_2), 6.46 s (1H_{isox}), 7.17 t (1H_{arom}, *J* 7.4 Hz), 7.25 t (2H_{arom}, *J* 7.4 Hz), 7.33–7.43 m (5H_{arom}), 7.64–7.72 m (2H_{arom}). ^{13}C NMR spectrum, δ, ppm: 29.08 (CH_2), 99.26 (CH_{isox}), 125.78 (2CH_{arom}), 126.90 (1CH_{arom}), 128.96 (2CH_{arom}), 129.12 (2CH_{arom}), 129.83 (2CH_{arom}), 130.23 (1CH_{arom}), 127.28, 134.78, 161.98, 170.18 (4C_{quat}). Found, %: C 71.98; H 4.75; N 5.20; S 12.12. $[M]^+$ 267. $C_{16}H_{13}NOS$. Calculated, %: C 71.88; H 4.90; N 5.24; S 11.99. *M* 267.35.

3-[(Benzylsulfanyl)methyl]-5-phenylisoxazole (29). Yield 90%, mp 97–98°C. IR spectrum, ν, cm^{-1}: 3125, 3083, 3066, 3054, 3024, 3003, 2962, 2925, 2853, 2816, 1613, 1593, 1573, 1493, 1464, 1451, 1425, 1410, 1327, 1259, 1228, 1136, 1070, 1049, 1028, 946, 913, 810, 764, 734, 699, 684, 666, 562, 487, 474. ^{1}H NMR spectrum, δ, ppm: 3.48 s (2H, CH_2), 3.55 s (2H, CH_2), 6.34 s(1H_{isox}), 7.10 t (1H_{arom}, *J* 7.1 Hz), 7.14–7.25 m (4H_{arom}), 7.25–7.35 m (3H_{arom}), 7.56–7.66 m (2H_{arom}). ^{13}C NMR spectrum, δ, ppm: 25.60 (SCH_2), 35.65 ($S\underline{C}H_2Ph$), 99.31 (CH_{isox}), 125.78 (2CH_{arom}), 127.18 (1CH_{arom}), 128.56 (2CH_{arom}), 128.98 (2CH_{arom}), 129.23 (2CH_{arom}), 130.20 (1CH_{arom}), 127.36, 137.58, 162.29, 170.13 (4C_{quat}). Found, %: C 72.63; H 5.32; N 5.00; S 11.46. $[M]^+$ 281. $C_{17}H_{15}NOS$. Calculated, %: C 72.57; H 5.37; N 4.98; S 11.39. *M* 281.37.

5-Phenyl-3-{[(furan-2-ylmethyl)sulfanyl]methyl}-isoxazole (30). Yield 90%, mp 85–85.5°C. IR spectrum, ν, cm^{-1}: 3124, 3057, 3042, 2973, 2928, 2852, 1612, 1593, 1574, 1502, 1461, 1451, 1426, 1413, 1398, 1329, 1246, 1148, 1125, 1065, 1050, 1011, 946, 937, 913, 810, 767, 742, 710, 684, 667, 597, 488. ^{1}H NMR spectrum, δ, ppm: 3.70 s (4H, $2CH_2$), 6.24–6.28 m (1H_{furan}), 6.28–6.31 m (1H_{furan}), 6.50 s (1H_{isox}), 7.33–7.37 m (1H_{furan}), 7.38–7.46 m (3H_{arom}), 7.71–7.77 m (2H_{arom}). ^{13}C NMR spectrum, δ, ppm: 25.81 (SCH_2), 27.74 ($S\underline{C}H_2Fu$), 99.19 (CH_{isox}), 108.44 (1CH_{furan}), 110.46 (1CH_{furan}), 125.73 (2CH_{arom}), 128.94 (2CH_{arom}), 130.19 (1CH_{arom}), 142.32 (1CH_{furan}), 127.28, 150.40, 162.04, 170.16 (4C_{quat}). Found, %: C 66.56; H 4.80; N 5.10; S 11.93. $[M]^+$ 271. $C_{15}H_{13}NO_2S$. Calculated, %: C 66.40; H 4.83; N 5.16; S 11.82. *M* 271.33.

2-{[(5-Phenylisoxazole-3-yl)methyl]sulfanyl}-ethanol (31). Yield 66%, mp 29–30°C. IR spectrum, ν, cm^{-1}: 3295 (OH), 3118, 3058, 3043, 2956, 2922, 2874, 1614, 1593, 1574, 1500, 1451, 1423, 1293, 1261, 1187, 1154, 1071, 1048, 1018, 946, 918, 812, 764,

735, 691, 666, 494. ^{1}H NMR spectrum, δ, ppm: 2.69 t (2H, SC$\underline{H}_2$CH$_2$OH, *J* 7.4 Hz), 2.90 br.s (1H, OH), 3.70–3.79 m (4H, SCH$_2$, SCH$_2$C$\underline{H}_2$OH), 6.55 s (1H$_{isox}$), 7.35–7.45 m (3H$_{arom}$), 7.67–7.75 m (2H$_{arom}$). ^{13}C NMR spectrum, δ, ppm: 26.03 (SCH$_2$), 34.38 (SC$\underline{H}_2$CH$_2$OH), 60.63 (SCH$_2$C$\underline{H}_2$OH), 99.19 (CH$_{isox}$), 125.83 (2CH$_{arom}$), 129.03 (2CH$_{arom}$), 130.37 (1CH$_{arom}$), 127.20, 162.36, 170.42 (3C$_{quat}$). Found, %: C 61.40; H 5.50; N 5.94; S 13.77. $[M]^+$ 235. $C_{12}H_{13}NO_2S$. Calculated, %: C 61.25; H 5.57; N 5.95; S 13.63. *M* 235.30.

5-(*p*-Tolyl)-3-[(phenylsulfanyl)methyl]isoxazole (32). Yield 82%, mp 78–79°C. IR spectrum, ν, cm^{-1}: 3122, 3078, 3055, 3024, 2916, 2853, 1613, 1597, 1583, 1567, 1513, 1481, 1459, 1439, 1427, 1407, 1375, 1259, 1240, 1184, 1115, 1093, 1073, 1051, 1024, 1019, 997, 947, 918, 823, 793, 768, 734, 688, 502, 472. ^{1}H NMR spectrum, δ, ppm: 2.39 s (3H, Me), 4.16 s (2H, CH$_2$), 6.45 s (1H$_{isox}$), 7.18–7.26 m (3H$_{arom}$), 7.30 t (2H$_{arom}$, *J* 7.6 Hz), 7.36–7.43 m (2H$_{arom}$), 7.62 d (2H$_{arom}$, *J* 8.2 Hz). ^{13}C NMR spectrum, δ, ppm: 21.52 (Me), 29.16 (CH$_2$), 98.69 (CH$_{isox}$), 125.78 (2CH$_{arom}$), 126.90 (1CH$_{arom}$), 129.14 (2CH$_{arom}$), 129.67 (2CH$_{arom}$), 129.86 (2CH$_{arom}$), 124.67, 134.92, 140.54, 161.94, 170.44 (5C$_{quat}$). Found, %: C 72.66; H 5.23; N 4.91; S 11.49. $[M]^+$ 281. $C_{17}H_{15}NOS$. Calculated, %: C 72.57; H 5.37; N 4.98; S 11.39. *M* 281.37.

3-[(Benzylsulfanyl)methyl]-5-(4-methylphenyl)-isoxazole (33). Yield 86%, mp 132–133°C. IR spectrum, ν, cm^{-1}: 3126, 3083, 3062, 3026, 3006, 2962, 2924, 2854, 1619, 16000, 1567, 1514, 1493, 1466, 1453, 1431, 1413, 1319, 1228, 1136, 1070, 1047, 946, 914, 797, 769, 743, 699, 678, 564, 498. ^{1}H NMR spectrum, δ, ppm: 2.41 s (3H, Me), 3.63 s (2H, SC$\underline{H}_2$C$_6$H$_5$), 3.70 s (2H, SCH$_2$), 6.46 s (1H$_{isox}$), 7.23–7.29 m (3H$_{arom}$), 7.30–7.38 m (4H$_{arom}$), 7.67 d (2H$_{arom}$, *J* 8.2 Hz). ^{13}C NMR spectrum, δ, ppm: 21.64 (Me), 25.78 (SCH$_2$), 35.79 (S$\underline{C}$H$_2$C$_6$H$_5$), 98.79 (CH$_{isox}$), 125.88 (2CH$_{arom}$), 127.30 (1CH$_{arom}$), 128.70 (2CH$_{arom}$), 129.36 (2CH$_{arom}$), 129.79 (2CH$_{arom}$), 124.84, 137.72, 140.63, 162.37, 170.53 (5C$_{quat}$). Found, %: C 73.30; H 5.69; N 4.68; S 10.95. $[M]^+$ 295. $C_{18}H_{17}NOS$. Calculated, %: C 73.19; H 5.80; N 4.74; S 10.85. *M* 295.40.

5-(4-Methylphenyl)-3-{[(furan-2-ylmethyl)sulfanyl]methyl}isoxazole (34). Yield 82%, mp 115–116°C. IR spectrum, ν, cm^{-1}: 3126, 3063, 3030, 2965, 2925, 2856, 1618, 1600, 1567, 1513, 1504, 1466, 1454, 1431, 1416, 1400, 1383, 1317, 1256, 1247, 1213, 1144, 1122, 1113, 1068, 1048, 1068, 1048, 1009, 939, 912, 883, 828, 810, 798, 736, 710, 673, 596, 500. ^{1}H NMR spectrum, δ, ppm: 2.34 s (3H, Me), 3.65 s (2H, CH$_2$), 3.66 s (2H, SC$\underline{H}_2$Fu), 6.19–6.24 m (1H$_{furan}$), 6.24–6.29 m (1H$_{furan}$), 6.41 s (1H$_{isox}$), 7.21 d (2H$_{arom}$, *J* 7.9 Hz), 7.32 s (1H$_{furan}$), 7.61 d (2H$_{arom}$, *J* 7.9 Hz). ^{13}C NMR spectrum, δ, ppm: 21.57 (Me), 25.95 (SCH$_2$), 27.86 (SCH$_2$ furan), 98.66 (CH$_{isox}$), 108.56 (1CH$_{furan}$), 110.56 (1CH$_{furan}$), 125.81 (2CH$_{arom}$), 129.74 (2CH$_{arom}$), 142.44 (1CH$_{furan}$), 124.74, 140.59, 150.52, 162.09, 170.53 (5C$_{quat}$). Found, %: C 67.54; H 5.22; N 4.78; S 11.44. $[M]^+$ 285. $C_{16}H_{15}NO_2S$. Calculated, %: C 67.34; H 5.30; N 4.91; S 11.23. *M* 285.36.

2-({[5-(4-Methylphenyl)isoxazol-3-yl]methyl}-sulfanyl)ethanol (35). Yield 83%, mp 53–54°C. IR spectrum, ν, cm^{-1}: 3336 (OH), 3125, 3065, 3036, 3017, 2921, 2866, 1620, 1600, 1567, 1513, 1464, 1431, 1406, 1365, 1295, 1244, 1182, 1148, 1112, 1064, 1047, 1020, 1002, 946, 913, 802, 728, 715, 671, 631, 497. ^{1}H NMR spectrum, δ, ppm: 2.39 s (3H, Me), 2.56 t (1H, OH, *J* 7.4 Hz), 2.71 t (2H, SC$\underline{H}_2$CH$_2$OH, *J* 7.4 Hz), 3.70–3.79 m (4H, SCH$_2$, SCH$_2$C$\underline{H}_2$OH), 6.50 s (1H$_{isox}$), 7.25 d (2H$_{arom}$, *J* 8.1 Hz), 7.64 d (2H$_{arom}$, *J* 8.1 Hz). ^{13}C NMR spectrum, δ, ppm: 21.61 (Me), 26.07 (SCH$_2$), 34.58 (S$\underline{C}$H$_2$CH$_2$OH), 60.62 (SCH$_2$$\underline{C}H_2$OH), 98.58 (CH$_{isox}$), 125.88 (2CH$_{arom}$), 129.79 (2CH$_{arom}$), 124.63, 140.78, 162.33, 170.77 (4C$_{quat}$). Found, %: C 62.79; H 5.94; N 5.60; S 13.04. $[M]^+$ 249. $C_{13}H_{15}NO_2S$. Calculated, %: C 62.63; H 6.06; N 5.62; S 12.86. *M* 249.33.

Reaction of chloromethylisoxazoles (3 and 4) with sodium methylate. General procedure. To a solution of sodium methylate obtained by dissolving 0.11 g of Na (4.78 mmol) in 30 mL of anhydrous methanol was added 3.3 mmol of chloromethylisoxazole **3** and **4**, the mixture was boiled for 8 h, afterwards 150 mL of water was added, the reaction product was extracted with dichloromethane, the extract was dried with calcium chloride, and the solvent was removed in a vacuum. Obtained compounds **36** and **37** did not require further purification.

3-(Methoxymethyl)-5-phenylisoxazole (36). Yield 92%, oily substance. IR spectrum, ν, cm^{-1}: 3129, 3063, 3042, 2989, 2930, 2895, 2823, 1614, 1593, 1574, 1502, 1464, 1452, 1427, 1365, 1260, 1193, 1182, 1158, 1109, 1074, 1049, 1024, 962, 949, 908, 807, 766, 691, 499. ^{1}H NMR spectrum, δ, ppm: 3.36 s (3H, Me), 4.50 s (2H, CH$_2$), 6.51 s (1H$_{isox}$), 7.33–7.39 m

($3H_{arom}$), 7.68–7.73 m ($2H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 58.33 (Me), 65.66 (CH_2), 98.60 (CH_{isox}), 125.61 ($2CH_{arom}$), 128.82 ($2CH_{arom}$), 130.04 ($1CH_{arom}$), 127.19, 161.87, 170.01 ($3C_{quat}$). Found, %: C 69.80; H 5.97; N 7.33. $[M]^+$ 189. $C_{11}H_{11}NO_2$. Calculated, %: C 69.83; H 5.86; N 7.40. *M* 189.21.

3-(Methoxymethyl)-5-(4-methylphenyl)isoxazole (37). Yield 95%, oily substance. IR spectrum, ν, cm^{-1}: 3131, 3058, 3032, 2988, 2925, 2894, 2862, 2823, 1619, 1599, 1568, 1515, 1466, 1451, 14391365, 1316, 1260, 1188, 1109, 1046, 1021, 949, 907, 822, 799, 758, 716, 681, 507. ^1H NMR spectrum, δ, ppm: 2.34 s (3H, Me), 3.39 s (3H, OMe), 4.52 s (2H, CH_2), 6.49 s ($1H_{isox}$), 7.20 d ($2H_{arom}$, *J* 8 Hz), 7.62 d ($2H_{arom}$, *J* 8 Hz). ^{13}C NMR spectrum, δ, ppm: 21.38 (Me), 58.47 (OMe), 65.83 (CH_2), 98.06 (CH_{isox}), 125.69 ($2CH_{arom}$), 129.62 ($2CH_{arom}$), 124.65, 140.43, 161.91, 170.38 ($4C_{quat}$). Found, %: C 70.88; H 6.41; N 6.96. $[M]^+$ 203. $C_{12}H_{13}NO_2$. Calculated, %: C 70.92; H 6.45; N 6.89. *M* 203.24.

Reaction of chloromethylisoxazoles (3 and 4) with morpholine. General procedure. To a solution of 3 mmol of chloromethylisoxazole **3** and **4** in 15 mL of anhydrous methanol was added 1.05 g (12 mmol) of morpholine, and the mixture was boiled for 12 h. Then it was diluted with 150 mL of brine, the precipitate was filtered off, washed with water, dried in a vacuum, and recrystallized from hexane.

4-[(5-Phenylisoxazol-3-yl)methyl]morpholine (38). Yield 87%, mp 90.5–91°C. IR spectrum, ν, cm^{-1}: 3132, 3070, 3053, 2961, 2934, 2858, 2803, 2751, 1612, 1593, 1574, 1502, 1467, 1451, 1350, 1331, 1290, 1267, 1210, 1133, 1114, 1074, 1047, 1005, 947, 911, 865, 820, 801, 764, 688, 615, 496. ^1H NMR spectrum, δ, ppm: 2.52 t (4H, $2CH_2N$, *J* 4.5 Hz), 3.61 s (2H, CH_2), 3.71 t (4H, $2CH_2O$, *J* 4.5 Hz), 6.55 s ($1H_{isox}$), 7.37–7.50 m ($3H_{arom}$), 7.71–7.82 m ($2H_{arom}$). ^{13}C NMR spectrum, δ, ppm: 53.64 (2C, $2CH_2N$), 53.86 (CH_2), 66.94 (2C, $2CH_2O$), 99.63 (CH_{isox}), 125.86 ($2CH_{arom}$), 129.06 ($2CH_{arom}$), 130.25 ($1CH_{arom}$), 127.52, 161.70, 170.12 ($3C_{quat}$). Found, %: C 68.98; H 6.45; N 11.40. $[M]^+$ 244. $C_{14}H_{16}N_2O_2$. Calculated, %: C 68.83; H 6.60; N 11.47. *M* 244.29.

4-{[5-(4-Methylphenyl)isoxazol-3-yl]methyl}-morpholine (39). Yield 97%, mp 97–98°C. IR spectrum, ν, cm^{-1}: 3132, 3059, 3043, 2975, 2960, 2935, 2919, 2858, 2810, 1618, 1600, 1587, 1569, 1516, 1471, 1447, 1354, 1335, 1294, 1271, 1261, 1135, 1112, 1078, 1045, 1005, 947, 910, 866, 818, 802, 505. ^1H NMR spectrum, δ, ppm: 2.37 s (3H, Me), 2.52 t (4H, $2CH_2N$, *J* 4.5 Hz), 3.60 s (2H, CH_2), 3.71 t (4H, $2CH_2O$, *J* 4.5 Hz), 6.49 s ($1H_{isox}$), 7.23 d ($2H_{arom}$, *J* 8 Hz), 7.64 d ($2H_{arom}$, *J* 8 Hz). ^{13}C NMR spectrum, δ, ppm: 21.55 (Me), 53.64 (2C, $2CH_2N$), 53.90 (CH_2), 66.96 (2C, $2CH_2O$), 99.02 (CH_{isox}), 125.79 ($2CH_{arom}$), 129.73 ($2CH_{arom}$), 124.83, 140.50, 161.67, 170.29 ($4C_{quat}$). Found, %: C 69.87; H 7.00; N 10.69. $[M]^+$ 258. $C_{15}H_{18}N_2O_2$. Calculated, %: C 69.74; H 7.02; N 10.84. *M* 258.32.

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