Synthesis of Functional Isoxazole and Isothiazole Derivatives from [(5-Arylisoxazol-3-yl)methoxy]arylmethanols

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Abstract—A procedure has been developed for the synthesis of functional isoxazole and isothiazole derivatives by reduction of (5-aryl-1,2-oxazol-3-yl)methoxybenzaldehydes to (5-aryl-1,2-oxazol-3-yl)methoxyarylmethanols and subsequent acylation of the latter with isoxazole- and isothiazolecarbonyl chlorides.

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Biological activity of substituted isoxazoles and isothiazoles is largely determined by functional environment of the corresponding heterocycles and their variable combinations [1–3]. Purposeful development of synthetic approaches to required exocyclic functionalities of isoxazoles and isothiazoles and preparation of their derivatives containing fragments of natural compounds, which may be promising for biological screening and use as ligands for metal complex catalysts, seem to be reasonable and important [4–6].

Herein, we describe a procedure for the synthesis of variable functional isoxazole and isothiazole deriva-

tives **4–9** by reduction of [(5-aryl-1,2-oxazol-3-yl)methoxy]benzaldehydes **1a–1f** [7] with sodium tetrahydridoborate in anhydrous isopropyl alcohol at 20– 23°C to the corresponding [(5-aryl-1,2-oxazol-3-yl)methoxy]arylmethanols **2a–2f**, followed by acylation with 1,2-oxazole- and 1,2-thiazole-3-carboxylic acid chlorides **3a–3d** in anhydrous diethyl ether in the presence of triethylamine at 20–23°C (Scheme 1). Compounds **2a–2f**, **4a–4d**, **5a–5d**, **6a–6d**, **7a–7d**, **8a– 8d**, **9c**, and **9d** were identified on the basis of their elemental compositions and IR, ¹H and ¹³C NMR, and mass spectra.



1a, 2a, 4a–4d, R¹ = H, R² = 2-[(5-phenyl-1,2-oxazol-3-yl)methoxy]; 1b, 2b, 5a–5d, R¹ = H, R² = 2-{[5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy}; 1c, 2c, 6a–6d, R¹ = H, R² = 4-{[5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy}; 1d, 2d, 7a–7d, R¹ = 4-MeO, R² = 2-{[5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy}; 1e, 2e, 8a–8d, R¹ = 3-MeO, R² = 4-{[5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy}; 1f, 2f, 9c, 9d, R¹ = 3-EtO, R² = 4-{[5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy}; 3–9, R³ = 5-phenyl-1,2-oxazol-3-yl]methoxy}; 1a, 5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy}; 1b, 2b, 5-(2,5-dimethylphenyl)-1,2-oxazol-3-yl]methoxy}; 3-9, R³ = 5-phenyl-1,2-oxazol-3-yl]methoxy}; 1a, 5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy}; 1b, 5-(2,5-dimethylphenyl)-1,2-oxazol-3-yl]methoxy}; 3-9, R³ = 5-phenyl-1,2-oxazol-3-yl]methoxy}; 1a, 5-(4-methylphenyl)-1,2-oxazol-3-yl]methox}; 3-9, R³ = 5-phenyl-1,2-oxazol-3-yl]methox}; 3

Alcohols 2a-2f and esters 4-9 are structural analogs of compounds exhibiting antitumor activity and enhancing the cytotoxic effect of such antitumor agents as cisplatin and carboplatin [2, 8]. They are now under medical and biological testing at the Institute of Physiology, National Academy of Sciences of Belarus. Some of the synthesized isoxazole derivatives attract interest as ligands for the preparation of palladium complexes and polymer modifiers with the aim of developing cross-coupling catalysts [1].

EXPERIMENTAL

The IR spectra were recorded in KBr on a Nicolet Protégé-460 spectrometer. The ¹H and ¹³C NMR spectra were measured on a Bruker Avance-500 spectrometer using CDCl₃ as solvent and reference (CHCl₃, δ 7.26 ppm; CDCl₃, δ_C 77.2 ppm). The mass spectra were obtained on an Agilent 5975 inert MSD/6890N Network GC System (electron impact, 70 eV; HP-5MS capillary column, 30 m×0.25 mm, film thickness 0.25 µm; injector temperature 250°C).

Initial [(5-aryl-1,2-oxazol-3-yl)methoxy]benzaldehydes **1a–1f** were synthesized by the Williamson reaction [7], and isoxazole- and isothiazolecarbonyl chlorides **3a–3d** were prepared as described in [9–11].

[(5-Aryl-1,2-oxazol-3-yl)methoxy]arylmethanols 2a–2f (general procedure). Aldehyde 1a–1f, 10 mmol, was dissolved in 50 mL of anhydrous isopropyl alcohol, 10 mmol of NaBH₄ was added, and the mixture was stirred for 24 h at 20–23°C. The mixture was then poured into 150 mL of 5% aqueous sodium carbonate and stirred for 3 h, and the precipitate was filtered off, washed with 500 mL of cold water, and dried under reduced pressure. Alcohols 2a–2f were purified by low-temperature crystallization from methylene chloride–hexane.

2-[(5-Phenyl-1,2-oxazol-3-yl)methoxy]phenylmethanol (2a). Yield 83%, mp 79–80°C. IR spectrum, v, cm⁻¹: 3311, 3150, 3138, 3064, 3042, 2919, 2860, 1602, 1592, 1574, 1493, 1468, 1449, 1426, 1368, 1288, 1240, 1181, 1161, 1119, 1060, 1050, 996, 947, 918, 873, 844, 801, 764, 754, 687. ¹H NMR spectrum, δ , ppm: 2.59 br.s (1H, OH), 4.75 s (2H, CH₂OH), 5.24 s (2H, CH₂), 6.61 s (1H, 4'-H), 6.80–7.20 m (2H, H_{arom}), 7.28 d.d (1H, H_{arom}, *J* = 7.9, 1.7 Hz), 7.34 d.d (1H, H_{arom}, *J* = 7.9, 1.7 Hz), 7.43–7.63 m (3H, H_{arom}), 7.76–7.79 m (2H, H_{arom}). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 61.70 (CH₂), 62.14 (CH₂), 98.63 (C^{4'}), 111.72 (CH_{arom}), 121.82 (CH_{arom}), 126.02 (2C, CH_{arom}), 129.15 (3C, CH_{arom}), 129.17 (CH_{arom}), 130.57 (CH_{arom}), 127.20, 129.82, 155.97, 161.37, 170.85. Found, %: C 72.74; H 5.48; N 4.66. *m*/*z* 281 [*M*]⁺. C₁₇H₁₅NO₃. Calculated, %: C 72.58; H 5.37; N 4.98. *M* 281.31.

2-{[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methoxy}phenylmethanol (2b). Yield 87%, mp 86-87°C. IR spectrum, v, cm⁻¹: 3450, 3128, 3079, 3059, 3034, 3010, 2921, 2856, 1616, 1594, 1568, 1517, 1495, 1469, 1452, 1434, 1369, 1290, 1238, 1188, 1160, 1117, 1056, 1021, 976, 948, 919, 821, 750, 503. ¹H NMR spectrum, δ , ppm: 2.40 s (3H, Me), 2.58 t (1H, OH, J = 6.5 Hz), 4.75 d (2H, CH₂OH, J =6.5 Hz), 5.23 s (2H, CH₂), 6.56 s (1H, 4'-H), 6.94-7.04 m (2H, H_{arom}), 7.25 d (2H, H_{arom} , J = 8 Hz), 7.28 d.d (1H, H_{arom} , J = 7.9, 1.8 Hz), 7.35 d.d (1H, H_{arom} , J = 7.9, 1.8 Hz), 7.66 d (2H, H_{arom} , J = 8 Hz). 13 C NMR spectrum, δ_{C} , ppm: 21.63 (Me), 61.74 (CH₂), 62.18 (CH₂), 98.01 (C^{4'}), 111.72 (CH_{arom}), 121.79 (CH_{arom}), 125.96 (2C, CH_{arom}), 129.14 (CH_{arom}), 129.16 (CHarom), 129.83 (2C, CHarom and Cquat), 124.52, 140.91, 156.01, 161.30, 171.04. Found, %: C 73.48; H 5.96; N 4.31. m/z 276 $[M - H_2O - H]^+$. C₁₈H₁₇NO₃. Calculated, %: C 73.20; H 5.80; N 4.74. M 295.34.

4-{[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methoxy}phenylmethanol (2c). Yield 89%, mp 137-138°C. IR spectrum, v, cm⁻¹: 3252, 3133, 3067, 3037, 2950, 2921, 2870, 2856, 1612, 1586, 1572, 1510, 1466, 1452, 1367, 1300, 1244, 1226, 1211, 1175, 1113, 1050, 1009, 860, 829, 803, 783, 505. ¹H NMR spectrum, δ , ppm: 1.79 t (1H, OH, J = 5.2 Hz), 2.40 s (3H, Me), 4.62 d (2H, CH₂OH, J = 5.2 Hz), 5.17 s (2H, CH₂), 6.59 s (1H, 4'-H), 6.99 d (2H, H_{arom}, J = 8.5 Hz), 7.26 d (2H, H_{arom}, J = 8 Hz), 7.31 d (2H, H_{arom}, J =8.5 Hz), 7.66 d (2H, H_{arom}, J = 8 Hz). ¹³C NMR spectrum, δ_{C} , ppm: 21.66 (Me), 62.04 (CH₂), 65.06 (CH₂), 98.35 (C^{4'}), 115.00 (2C, CH_{arom}), 125.97 (2C, CH_{arom}), 128.88 (2C, CH_{arom}), 129.84 (2C, CH_{arom}), 124.66, 134.25, 140.84, 157.80, 161.51, 170.91. Found, %: C 73.45; H 5.93; N 4.44. m/z 276 $[M - H_2O - H]^+$. C₁₈H₁₇NO₃. Calculated, %: C 73.20; H 5.80; N 4.74. M 295.34.

(4-Methoxy-3-{[5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy}phenyl)methanol (2d). Yield 81%, mp 85–86°C. IR spectrum, v, cm⁻¹: 3398, 3138, 3058, 3033, 2921, 2853, 1618, 1594, 1570, 1519, 1465, 1445, 1425, 1377, 1322, 1261, 1243, 1183, 1162, 1136, 1030, 1020, 947, 815, 800, 504. ¹H NMR spectrum, δ , ppm: 2.10 br.s (1H, OH), 2.39 s (3H, Me), 3.87 s (3H, OMe), 4.59 s (2H, CH₂), 5.23 s (2H, CH₂), 6.63 s (1H, 4'-H), 6.87 d (1H, H_{arom}, J = 8.2 Hz), 6.95 d.d (1H, H_{arom}, J = 8.2, 1.6 Hz), 7.04 d (1H, H_{arom}, J = 1.6 Hz), 7.24 d (2H, H_{arom}, J = 8 Hz), 7.64 d (2H, H_{arom}, J = 8 Hz). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 21.63 (Me), 56.17 (OMe), 63.08 (CH₂), 65.07 (CH₂), 98.53 (C^{4'}), 111.99 (CH_{arom}), 113.57 (CH_{arom}), 120.98 (CH_{arom}), 125.94 (2C, CH_{arom}), 129.79 (2C, CH_{arom}), 124.70, 133.96, 140.74, 147.63, 149.30, 161.54, 170.80. Found, %: C 70.42; H 5.97; N 4.15. *m*/*z* 325 [*M*]⁺. C₁₉H₁₉NO₄. Calculated, %: C 70.14; H 5.89; N 4.31. *M* 325.36.

(3-Methoxy-4-{[5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy}phenyl)methanol (2e). Yield 82%, mp 103–104°C. IR spectrum, v, cm⁻¹: 3396, 3137, 3077, 3034, 2959, 2921, 2888, 2837, 1612, 1595, 1570, 1522, 1468, 1438, 1419, 1372, 1333, 1298, 1264, 1236, 1167, 1141, 1114, 1038, 1010, 948, 916, 850, 820, 790, 639, 502. ¹H NMR spectrum, δ, ppm: 2.03 br.s (1H, OH), 2.38 s (3H, Me), 3.88 s (3H, OMe), 4.60 s (2H, CH₂), 5.23 s (2H, CH₂), 6.62 s (1H, 4'-H), 6.83 d.d (1H, H_{arom} , J = 8.2, 1.9 Hz), 6.95 d (1H, H_{arom} , J = 1.9 Hz), 6.96 d (1H, H_{arom} , J = 8.2 Hz), 7.24 d (2H, H_{arom}, J = 8 Hz), 7.64 d (2H, H_{arom}, J = 8 Hz). ¹³C NMR spectrum, δ_{C} , ppm: 21.60 (Me), 56.05 (OMe), 63.23 (CH₂), 65.22 (CH₂), 98.48 (C^{4'}), 111.17 (CH_{arom}), 114.52 (CH_{arom}), 119.47 (CH_{arom}), 125.94 (2C, CH_{arom}), 129.79 (2C, CH_{arom}), 124.70, 135.32, 140.74, 147.04, 149.97, 161.64, 170.82. Found, %: C 70.37; H 5.99; N 4.10. m/z 306 $[M - H_2O - H]^+$. C₁₉H₁₉NO₄. Calculated, %: C 70.14; H 5.89; N 4.31. M 325.36.

(3-Ethoxy-4-{[5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy{phenyl)methanol (2f). Yield 80%, mp 62–63°C. IR spectrum, v, cm⁻¹: 3355, 3148, 3054, 3021, 2975, 2923, 2870, 1619, 1600, 1568, 1517, 1457, 1430, 1400, 1372, 1263, 1236, 1223, 1168, 1138, 1112, 1038, 1018, 949, 907, 873, 841, 821, 804, 502. ¹H NMR spectrum, δ , ppm: 1.46 t (3H, OCH₂Me, J = 7 Hz), 1.97 br.s (1H, OH), 2.39 s (3H, Me), 4.11 g $(2H, OCH_2Me, J = 7 Hz), 4.59 s (2H, CH_2), 5.22 s$ $(2H, CH_2), 6.63 \text{ s} (1H, 4'-H), 6.82 \text{ d.d} (1H, H_{arom}, J =$ 8.3, 1.9 Hz), 6.95 d (1H, H_{arom} , J = 1.9 Hz), 6.96 d (1H, H_{arom} , J = 8.3 Hz), 7.25 d (2H, H_{arom} , J = 8 Hz), 7.65 d (2H, H_{arom}, J = 8 Hz). ¹³C NMR spectrum, δ_{C} , ppm: 15.04 (OCH₂Me), 21.62 (Me), 63.59 (CH₂), 64.57 (CH₂), 65.24 (CH₂), 98.51 (C^{4'}), 112.66 (CH_{arom}), 115.52 (CH_{arom}), 119.51 (CH_{arom}), 125.92 (2C, CH_{arom}), 129.79 (2C, CH_{arom}), 124.74, 135.54, 140.71, 147.32, 149.51, 161.87, 170.67. Found, %: C 71.15; H 6.39; N 3.88. m/z 339 $[M]^+$. C₂₀H₂₁NO₄. Calculated, %: C 70.78; H 6.24; N 4.13. M 339.39.

Esters 4–9 (general procedure). Alcohol 2a–2f, 10 mmol, was dissolved in 50 mL of anhydrous diethyl ether, 11 mmol of acid chloride 3a–3d and 11 mmol of anhydrous triethylamine were added, and the mixture

was stirred for 8 h at 23°C. The precipitate was filtered off, washed with 5–10 mL of cold (5–10°C) diethyl ether, 200–300 mL of cold water (15–20°C), 150–200 mL of 5% aqueous NaHCO₃, and 200–300 mL of warm water (45–50°C), dried under reduced pressure, and purified by low-temperature crystallization from methylene chloride–hexane.

2-[(5-Phenyl-1,2-oxazol-3-yl)methoxy]benzyl 5-phenyl-1,2-oxazole-3-carboxylate (4a). Yield 83%, mp 153–154°C. IR spectrum, v, cm⁻¹: 3423, 3146, 3133, 3063, 3033, 2924, 2858, 1728 (C=O), 1607, 1591, 1574, 1497, 1471, 1445, 1364, 1291, 1253, 1147, 1123, 1048, 1020, 1001, 947, 924, 817, 764, 689, 677. ¹H NMR spectrum, δ , ppm: 5.29 s (2H, CH₂), 5.55 s (2H, CH₂), 6.80 s and 6.92 s (4'-H, 4"-H), 7.00–7.07 m (2H, H_{arom}), 7.35 d.d (1H, H_{arom} , J = 7.9, 1.7 Hz), 7.37–7.42 m (3H, H_{arom}), 7.45–7.51 m (4H, H_{arom}), 7.74–7.80 m (4H, H_{arom}). ¹³C NMR spectrum, δ_{C} , ppm; 62.05 (CH₂), 63.74 (CH₂), 99.17 and 100.21 (C^{4'}, C^{4''}), 111.95 (CH_{arom}), 121.58 (CH_{arom}), 126.07 (4C, CH_{arom}), 129.07 (2C, CH_{arom}), 129.33 (2C, CH_{arom}), 130.40 (CH_{arom}), 130.60 (CH_{arom}), 131.01 (CH_{arom}), 131.09 (CH_{arom}), 123.74, 126.75, 127.38, 156.49, 157.09, 160.12, 161.57, 170.77, 171.91. Found, %: C 71.89; H 4.57; N 5.86. m/z 452 $[M]^+$. C₂₇H₂₀N₂O₅. Calculated, %: C 71.67; H 4.46; N 6.19. *M* 452.47.

2-[(5-Phenyl-1,2-oxazol-3-yl)methoxy]benzyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (4b). Yield 86%, mp 130–131°C. IR spectrum, v, cm^{-1} : 3435, 3133, 3067, 3042, 2920, 2854, 1726 (C=O), 1605, 1593, 1573, 1505, 1469, 1447, 378, 1367, 1292, 1254, 1241, 1139, 1124, 1050, 1001, 947, 920, 820, 804, 764, 754, 694, 500. ¹H NMR spectrum, δ, ppm: 2.41 s (3H, Me), 5.28 s (2H, CH₂), 5.54 s (2H, CH₂), 6.80 s and 6.86 s (1H each, 4'-H, 4"-H), 6.98-7.06 m $(2H, H_{arom})$, 7.28 d $(2H, H_{arom})$, J = 8 Hz), 7.35 d.d (1H, J) H_{arom} , J = 7.9, 1.4 Hz), 7.36–7.43 m (3H, H_{arom}), 7.47 d.d (1H, H_{arom} , J = 7.4, 1.2 Hz), 7.66 d (2H, H_{arom} , J = 8 Hz), 7.74–7.81 m (2H, H_{arom}). ¹³C NMR spectrum, δ_C, ppm: 21.67 (Me), 62.01 (CH₂), 63.65 (CH₂), 99.16 and 99.59 (C^{4'}, C^{4''}), 111.91 (CH_{arom}), 121.53 (CH_{arom}), 125.98 (2C, CH_{arom}), 126.04 (2C, CH_{arom}), 129.04 (2C, CH_{arom}), 129.96 (2C, CH_{arom}), 130.35 (CH_{arom}), 130.54 (CH_{arom}), 131.04 (CH_{arom}), 123.74, 124.03, 127.35, 141.41, 156.45, 157.00, 160.16, 161.55, 170.72, 172.08. Found, %: C 72.30; H 4.91; N 5.74. m/z 466 $[M]^+$. C₂₈H₂₂N₂O₅. Calculated, %: C 72.09; H 4.75; N 6.01. M 466.49.

2-[(5-Phenyl-1,2-oxazol-3-yl)methoxy]benzyl 5-(2,5-dimethylphenyl)-1,2-oxazole-3-carboxylate (4c). Yield 88%, mp 127–129°C. IR spectrum, v, cm⁻¹: 3165, 3067, 3046, 2955, 2922, 2855, 1733 (C=O), 1607, 1592, 1571, 1502, 1469, 1450, 1390, 1366, 1293, 1241, 1180, 1151, 1124, 1049, 1018, 1002, 951, 930, 910, 812, 769, 751, 692. ¹H NMR spectrum, δ, ppm: 2.37 s (3H, Me), 2.43 s (3H, Me), 5.30 s (2H, CH₂), 5.56 s (2H, CH₂), 6.82 s and 6.83 s (1H each, 4'-H, 4"-H), 7.00-7.07 m (2H, H_{arom}), 7.19 s (2H, H_{arom}), 7.35 d.d (1H, H_{arom} , J = 7.9, 1.5 Hz), 7.37– 7.42 m (3H, H_{arom}), 7.48 d.d (1H, H_{arom} , J = 8.4, 1.2 Hz), 7.53 s (1H, H_{arom}), 7.78-8.01 m (2H, H_{arom}). ¹³C NMR spectrum, δ_{C} , ppm: 20.98 (Me), 21.06 (Me), 61.96 (CH₂), 63.70 (CH₂), 99.20 and 103.08 (C^{4'}, C^{4''}), 111.91 (CH_{arom}), 121.54 (CH_{arom}), 126.04 (2C, CH_{arom}), 129.03 (3C, CH_{arom}), 130.38 (CH_{arom}), 130.56 (CH_{arom}), 131.07 (CH_{arom}), 131.58 (2C, CH_{arom}), 123.70, 125.95, 133.39, 136.11, 156.44, 156.67, 160.28, 161.59, 162.40, 170.73, 172.11. Found, %: C 72.84; H 5.13; N 5.56. m/z 480 $[M]^+$. C₂₉H₂₄N₂O₅. Calculated, %: C 72.49; H 5.03; N 5.83. M 480.52.

2-[(5-Phenyl-1,2-oxazol-3-yl)methoxy]benzyl 4,5-dichloro-1,2-thiazole-3-carboxylate (4d). Yield 88%, mp 114–115°C. IR spectrum, v, cm⁻¹: 3131, 3054, 3033, 3013, 2924, 2854, 1725 (C=O), 1606, 1592, 1573, 1494, 1453, 1408, 1363, 1354, 1256, 1241, 1211, 1162, 1123, 1080, 1041, 1018, 966, 914, 847, 763, 750, 684. ¹H NMR spectrum, δ, ppm: 5.26 s (2H, CH₂), 5.54 s (2H, CH₂), 6.73 s (4'-H), 6.99-7.04 m (2H, H_{arom}), 7.33 d.d (1H, H_{arom} , J = 7.9, 1.4 Hz), 7.42-7.49 m (4H, H_{arom}), 7.73-7.79 m (2H, H_{arom}). ¹³C NMR spectrum, δ_C , ppm: 62.09 (CH₂), 63.60 (CH₂), 99.02 (C^{4'}), 111.94 (CH_{arom}), 121.60 (CHarom), 125.96 (2C, CHarom), 129.05 (2C, CHarom), 130.40 (CH_{arom}), 130.44 (CH_{arom}), 130.88 (CH_{arom}), 123.65, 126.00, 127.29, 150.62, 154.40, 156.28, 159.10, 161.48, 170.59. Found, %: C 54.89; H 3.38; Cl 15.07; N 5.66; S 6.60. m/z 460 $[M]^+$. C₂₁H₁₄Cl₂N₂O₄S. Calculated, %: C 54.68; H 3.06; Cl 15.37; N 6.07; S 6.95. M 461.31.

2-{[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methoxy}benzyl 5-phenyl-1,2-oxazole-3-carboxylate (**5a**). Yield 84%, mp 133–135°C. IR spectrum, v, cm⁻¹: 3134, 3067, 3038, 2960, 2920, 2875, 2852, 1729, 1605, 1590, 1573, 1497, 1475, 1444, 1362, 1291, 1252, 1145, 1122, 1047, 1019, 1000, 948, 926, 845, 810, 771, 762, 690. ¹H NMR spectrum, δ , ppm: 2.35 s (3H, Me), 5.27 s (2H, CH₂), 5.55 s (2H, CH₂), 6.71 s and 6.91 s (1H each, 4'-H, 4"-H), 7.02 t (1H, H_{arom}, *J* = 7.5 Hz), 7.04 d (1H, H_{arom}, *J* = 8.4 Hz), 7.18 d (2H, H_{arom}, *J* = 8 Hz), 7.35 d.d (1H, H_{arom}, *J* = 7.8, 1.3 Hz), 7.42–7.52 m (4H, H_{arom}), 7.64 d (2H, H_{arom}, *J* = 8 Hz), 7.72–7.82 m (2H, H_{arom}). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 21.61 (Me), 62.11 (CH₂), 63.70 (CH₂), 98.52 and 100.20 (C^{4'}, C^{4''}), 111.99 (CH_{arom}), 121.55 (CH_{arom}), 125.98 (2C, CH_{arom}), 126.08 (2C, CH_{arom}), 129.29 (2C, CH_{arom}), 129.75 (2C, CH_{arom}), 130.55 (CH_{arom}), 130.96 (CH_{arom}), 131.02 (CH_{arom}), 123.78, 124.70, 126.79, 140.65, 156.52, 157.08, 160.09, 161.46, 170.95, 171.88. Found, %: C 72.38; H 4.87; N 5.81. *m/z* 466 [*M*]⁺. C₂₈H₂₂N₂O₅. Calculated, %: C 72.09; H 4.75; N 6.01. *M* 466.49.

2-{[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methoxy{benzyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (5b). Yield 88%, mp 136-138°C. IR spectrum, v, cm⁻¹: 3146, 3133, 3038, 2948, 2920, 2854, 1723, 1617, 1607, 1594, 1498, 1467, 1448, 1412, 1368, 1289, 1257, 1230, 1200, 1186, 1135, 1040, 1005, 973, 948, 911, 808, 772, 755, 737, 497. ¹H NMR spectrum, δ, ppm: 2.34 s (3H, Me), 2.40 s (3H, Me), 5.26 s (2H, CH₂), 5.54 s (2H, CH₂), 6.72 s and 6.85 s (1H each, 4'-H, 4"-H), 7.02 t (1H, H_{arom} , J = 7.5 Hz), 7.04 d (1H, H_{arom}, J = 8.2 Hz), 7.17 d (2H, H_{arom}, J =8 Hz), 7.27 d (2H, H_{arom}, J = 8 Hz), 7.34 d.d (1H, H_{arom} , J = 7.9, 1.6 Hz), 7.47 d.d (1H, H_{arom} , J = 7.4, 1.4 Hz), 7.58 d (2H, H_{arom} , J = 8 Hz), 7.58 d (2H, H_{arom} , J = 8 Hz). ¹³C NMR spectrum, δ_{C} , ppm: 21.54 (Me), 21.60 (Me), 62.01 (CH₂), 63.57 (CH₂), 98.48 and 99.54 (C^{4'}, C^{4''}), 111.89 (CH_{arom}), 121.47 (CH_{arom}), 125.91 (2C, CH_{arom}), 125.94 (2C, CH_{arom}), 129.68 (2C, CH_{arom}), 129.89 (2C, CH_{arom}), 130.45 (CH_{arom}), 130.92 (CH_{arom}), 123.74, 124.02, 124.62, 140.55, 141.32, 156.43, 156.95, 160.09, 161.40, 170.86, 172.00. Found, %: C 72.80; H 5.24; N 5.41. m/z 480 $[M]^+$. C₂₉H₂₄N₂O₅. Calculated, %: C 72.49; H 5.03; N 5.83. M 480.52.

2-{[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methoxy}benzyl 5-(2,5-dimethylphenyl)-1,2-oxazole-3carboxylate (5c). Yield 89%, mp 121-122°C. IR spectrum, v, cm⁻¹: 3128, 3067, 3048, 3012, 2955, 2922, 2854, 1730, 1606, 1595, 1561, 1518, 1504, 1473, 1445, 1376, 1365, 1294, 1255, 1187, 1147, 1127, 1060, 1005, 923, 827, 810, 791, 758, 501. ¹H NMR spectrum, δ, ppm: 2.33 s (3H, Me), 2.35 s (3H, Me), 2.41 s (3H, Me), 5.25 s (2H, CH₂), 5.55 s (2H, CH₂), 6.74 s and 6.80 s (1H each, 4'-H, 4"-H), 7.01 t (1H, H_{arom} , J =7.5 Hz), 7.03 d (1H, H_{arom}, J = 8.3 Hz), 7.12–7.22 m $(4H, H_{arom})$, 7.34 d.d (1H, H_{arom}, J = 7.9, 1.7 Hz), 7.47 d.d (1H, H_{arom} , J = 7.4, 1.5 Hz), 7.64 d (2H, H_{arom} , J = 8.2 Hz). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 20.85 (Me), 20.93 (Me), 21.45 (Me), 61.90 (CH₂), 63.54 (CH₂), 98.44 and 102.94 (C^{4'}, C^{4"}), 111.80 (CH_{arom}), 121.37 (CH_{arom}), 125.80 (2C, CH_{arom}), 128.87 (CH_{arom}), 129.59

N 5.83. M 480.52.

(2C, CH_{arom}), 130.40 (CH_{arom}), 130.90 (CH_{arom}), 131.40 (CH_{arom}), 131.47 (CH_{arom}), 123.63, 124.54, 125.85, 133.26, 135.96, 140.46, 156.37, 156.59, 160.11, 161.33, 170.74, 171.90. Found, %: C 73.05; H 5.51; N 5.50. m/z 494 $[M]^+$. C₃₀H₂₆N₂O₅. Calculated, %: C 72.86; H 5.30; N 5.66. M 494.55.

2-{[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methoxy{benzyl 4,5-dichloro-1,2-thiazole-3-carboxylate (5d). Yield 85%, mp 121–123°C. IR spectrum, v, cm⁻¹: 3130, 3067, 3032, 3009, 2924, 2869, 1728, 1618, 1594, 1567, 1513, 1497, 1459, 1450, 1407, 1355, 1322, 1255, 1205, 1164, 1122, 1082, 1043, 1019, 966, 949, 915, 846, 815, 751, 728, 636, 503. ¹H NMR spectrum, δ, ppm: 2.39 s (3H, Me), 5.25 s (2H, CH₂), 5.55 s $(2H, CH_2), 6.67 \text{ s} (1H, 4'-H), 7.01 \text{ t} (1H, H_{arom}, J =$ 7.5 Hz), 7.02 d (1H, H_{arom}, J = 8.4 Hz), 7.25 d (2H, H_{arom}, J = 8 Hz), 7.33 d.d (1H, H_{arom}, J = 7.9, 1.6 Hz), 7.48 d.d (1H, H_{arom} , J = 7.4, 1.4 Hz), 7.65 d (2H, H_{arom} , J = 8 Hz). ¹³C NMR spectrum, δ_{C} , ppm: 21.62 (Me), 62.20 (CH₂), 63.64 (CH₂), 98.42 (C^{4'}), 112.01 (CH_{arom}), 121.60 (CH_{arom}), 125.95 (2C, CH_{arom}), 129.76 (2C, CH_{arom}), 130.45 (CH_{arom}), 130.87 (CH_{arom}), 123.72, 124.67, 125.85, 140.72, 150.62, 154.48, 156.36, 159.14, 161.45, 170.83. Found, %: C 55.84; H 3.45; Cl 14.66; N 5.60; S 6.61. m/z 474 $[M]^+$. C₂₂H₁₆Cl₂N₂O₄S. Calculated, %: C 55.59; H 3.39; Cl 14.92; N 5.89; S 6.75. M 475.34.

4-{[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methoxy{benzyl 5-phenyl-1,2-oxazole-3-carboxylate (6a). Yield 88%, mp 134–135°C. IR spectrum, v, cm^{-1} : 3149, 3128, 3053, 3038, 2971, 2920, 2857, 1729, 1614, 1588, 1572, 1515, 1471, 1444, 1381, 1298, 1241, 1184, 1137, 1063, 1051, 1007, 982, 948, 828, 802, 766, 687, 507. ¹H NMR spectrum, δ, ppm: 2.38 s (3H, Me), 5.19 s (2H, CH₂), 5.37 s (2H, CH₂), 6.58 s and 6.89 s (1H each, 4'-H, 4"-H), 7.03 d (2H, H_{arom}, J = 8.7 Hz), 7.24 d (2H, H_{arom}, J = 8.1 Hz), 7.43 d (2H, H_{arom} , J = 8.7 Hz), 7.44–7.53 m (3H, H_{arom}), 7.65 d $(2H, H_{arom}, J = 8.1 Hz), 7.72-7.82 m (2H, H_{arom}).$ ¹³C NMR spectrum $\delta_{\rm C}$, ppm: 21.57 (Me), 61.99 (CH₂), 67.49 (CH₂), 98.28 and 100.07 (C^{4'}, C^{4"}), 115.04 (2C, CHarom), 125.91 (2C, CHarom), 126.01 (2C, CHarom), 129.22 (2C, CH_{arom}), 129.77 (2C, CH_{arom}), 130.74 (2C, CH_{arom}), 130.90 (CH_{arom}), 124.60, 126.69, 128.12, 140.76, 156.90, 158.53, 159.98, 161.27, 170.89, 171.83. Found, %: C 72.31; H 4.82; N 5.94. m/z 466 $[M]^+$. C₂₈H₂₂N₂O₅. Calculated, %: C 72.09; H 4.75; N 6.01. M 466.49.

4-{[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methoxy}benzyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (6b). Yield 87%, mp 143-144°C. IR spectrum, v, cm⁻¹: 3141, 3121, 3047, 2966, 2920, 2858, 1728, 1613, 1599, 1589, 1511, 1461, 1448, 1431, 1412, 1369, 1302, 1266, 1244, 1175, 1135, 1113, 1063, 1008, 981, 949, 840, 820, 775, 501. ¹H NMR spectrum, δ, ppm: 2.39 s (3H, Me), 2.40 s (3H, Me), 5.20 s (2H, CH₂), 5.37 s (2H, CH₂), 6.58 s and 6.84 s (1H each, 4'-H, 4"-H), 7.02 d (2H, H_{arom} , J = 8.7 Hz), 7.25 d (2H, H_{arom}, J = 8.2 Hz), 7.27 d (2H, H_{arom}, J =8.7 Hz), 7.43 d (2H, H_{arom}, J = 8.2 Hz), 7.66 d (2H, H_{arom} , J = 8.2 Hz), 7.67 d (2H, H_{arom} , J = 8.2 Hz). ¹³C NMR spectrum, δ_{C} , ppm: 21.63 (Me), 21.66 (Me), 62.07 (CH₂), 67.50 (CH₂), 98.32 and 99.53 ($C^{4'}$, $C^{4''}$), 115.10 (2C, CHarom), 125.98 (2C, CHarom), 126.02 (2C, CH_{arom}), 129.83 (2C, CH_{arom}), 129.96 (2C, CH_{arom}), 130.78 (2C, CH_{arom}), 124.10, 124.68, 128.23, 140.82, 141.39, 156.90, 158.58, 160.13, 161.35, 170.97, 172.12. Found, %: C 72.66; H 5.19; N 5.48. m/z 480 [M]⁺. C₂₉H₂₄N₂O₅. Calculated, %: C 72.49; H 5.03;

4-{[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methoxy}benzyl 5-(2,5-dimethylphenyl)-1,2-oxazole-3carboxylate (6c). Yield 90%, mp 121-122°C. IR spectrum, v, cm⁻¹: 3127, 3115, 3085, 3038, 2963, 2922, 2867, 1731, 1613, 1587, 1570, 1518, 1468, 1453, 1374, 1360, 1304, 1263, 1249, 1184, 1144, 1116, 1060, 1010, 981, 949, 832, 820, 808, 790, 777, 505. ¹H NMR spectrum, δ, ppm: 2.37 s (3H, Me), 2.39 s (3H, Me), 2.45 s (3H, Me), 5.21 s (2H, CH₂), 5.38 s (2H, CH₂), 6.59 s and 6.81 s (1H each, 4'-H, 4"-H), 7.03 d (2H, H_{arom} , J = 8.6 Hz), 7.18 s (2H, H_{arom}), 7.26 d (2H, H_{arom} , J = 8 Hz), 7.44 d (2H, H_{arom} , J = 8.6 Hz), 7.53 s (1H, H_{arom}), 7.67 d (2H, H_{arom}, J = 8 Hz). ¹³C NMR spectrum, δ_C, ppm: 21.00 (Me), 21.06 (Me), 21.65 (Me), 62.02 (CH₂), 67.58 (CH₂), 98.36 and 103.05 (C^{4'}, C^{4"}), 115.10 (2C, CH_{arom}), 126.01 (2C, CH_{arom}), 129.12 (CH_{arom}), 129.85 (2C, CH_{arom}), 130.87 (2C, CH_{arom}), 131.58 (2C, CH_{arom}), 124.59, 125.89, 128.22, 133.44, 136.16, 140.93, 156.82, 158.56, 160.24, 161.39, 171.02, 172.19. Found, %: C 72.99; H 5.43; N 5.41. m/z 494 $[M]^+$. C₃₀H₂₆N₂O₅. Calculated, %: C 72.86; H 5.30; N 5.66. *M* 494.55.

4-{[5-(4-Methylphenyl)-1,2-oxazol-3-yl]methoxy}benzyl 4,5-dichloro-1,2-thiazole-3-carboxylate (6d). Yield 84%, mp 149–150°C. IR spectrum, v, cm⁻¹: 3125, 3066, 3038, 2951, 2921, 2876, 1724, 1615, 1599, 1589, 1570, 1513, 1476, 1461, 1445, 1404, 1364, 1348, 1299, 1226, 1177, 1088, 1053, 1024, 994, 964, 857, 813, 801, 725, 509. ¹H NMR spectrum, δ, ppm: 2.39 s (3H, Me), 5.19 s (2H, CH₂), 5.36 s (2H, CH₂), 6.57 s (1H, 4'-H), 7.01 d (2H, H_{arom}, *J* = 8.6 Hz), 7.25 d (2H, H_{arom}, J = 8.1 Hz), 7.43 d (2H, H_{arom}, J = 8.6 Hz), 7.66 d (2H, H_{arom}, J = 8.1 Hz). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 21.64 (Me), 62.06 (CH₂), 67.80 (CH₂), 98.31 (C⁴), 115.12 (2C, CH_{arom}), 125.98 (2C, CH_{arom}), 129.83 (2C, CH_{arom}), 130.84 (2C, CH_{arom}), 124.67, 125.79, 128.08, 140.83, 150.72, 154.39, 158.60, 159.13, 161.33, 170.96. Found, %: C 55.86; H 3.31; Cl 14.60; N 5.62; S 6.48. *m/z* 474 [*M*]⁺. C₂₂H₁₆Cl₂N₂O₄S. Calculated, %: C 55.59; H 3.39; Cl 14.92; N 5.89; S 6.74. *M* 475.34.

4-Methoxy-3-{[5-(4-methylphenyl)-1,2-oxazol-3yl]methoxy}benzyl 5-phenyl-1,2-oxazole-3-carboxvlate (7a). Yield 83%, mp 163–164°C. IR spectrum, v. cm⁻¹: 3133, 3063, 2958, 2922, 2854, 1737 (C=O), 1611, 1592, 1571, 1523, 1467, 1446, 1370, 1268, 1235, 1164, 1137, 1017, 949, 850, 819, 764, 687, 503. ¹H NMR spectrum, δ , ppm: 2.36 s (3H, Me), 3.90 s (3H, OMe), 5.29 s (2H, CH₂), 5.35 s (2H, CH₂), 6.63 s (1H, 4'-H or 4"-H), 6.91 d (2H, H_{arom} , J = 8.2 Hz), 6.92 s (1H, 4"-H or 4'-H), 7.09 d.d (1H, H_{arom} , J = 8.2, 1.8 Hz), 7.18 d (1H, H_{arom}, J = 1.8 Hz), 7.21 d (2H, H_{arom}, J = 8 Hz), 7.42–7.52 m (3H, H_{arom}), 7.62 d (2H, H_{arom} , J = 8 Hz), 7.75–7.84 m (2H, H_{arom}). ¹³C NMR spectrum, δ_C, ppm: 21.62 (Me), 56.18 (OMe), 62.17 (CH_2) , 67.69 (CH_2) , 98.52 and 100.16 $(C^{4'}, C^{4''})$, 111.92 (CH_{arom}), 115.24 (CH_{arom}), 123.21 (CH_{arom}), 125.95 (2C, CH_{arom}), 126.11 (2C, CH_{arom}), 129.28 (2C, CH_{arom}), 129.78 (2C, CH_{arom}), 130.93 (CH_{arom}), 124.70, 126.80, 127.65, 140.70, 147.60, 150.24, 156.91, 159.99, 161.39, 170.88, 171.89. Found, %: C 70.38; H 4.97; N 5.34. m/z 496 $[M]^+$. C₂₉H₂₄N₂O₆. Calculated, %: C 70.15; H 4.87; N 5.64. *M* 496.52.

4-Methoxy-3-{[5-(4-methylphenyl)-1,2-oxazol-3vl]methoxy}benzyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (7b). Yield 84%, mp 160-161°C. IR spectrum, v, cm⁻¹: 3129, 3058, 3013, 2920, 2854, 1721 (C=O), 1612, 1593, 1570, 1523, 1466, 1446, 1432, 1377, 1367, 1295, 1271, 1243, 1165, 1144, 1054, 1039, 1018, 949, 914, 847, 819, 772, 504. ¹H NMR spectrum, δ, ppm: 2.36 s (3H, Me), 2.41 s (3H, Me), 3.90 s (3H, OMe), 5.28 s (2H, CH₂), 5.34 s (2H, CH₂), 6.63 s and 6.86 s (1H each, 4'-H, 4"-H), 6.91 d (2H, H_{arom} , J = 8.2 Hz), 7.09 d.d (1H, H_{arom} , J = 8.2, 1.8 Hz), 7.17 d (1H, H_{arom}, J = 1.8 Hz), 7.21 d (2H, H_{arom} , J = 8 Hz), 7.27 d (2H, H_{arom} , J = 8 Hz), 7.63 d $(2H, H_{arom}, J = 8 Hz), 7.68 d (2H, H_{arom}, J = 8 Hz).$ ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 21.62 (Me), 21.68 (Me), 56.17 (OMe), 63.17 (CH₂), 67.64 (CH₂), 98.52 and 99.56 (C^{4'}, C^{4''}), 111.91 (CH_{arom}), 115.25 (CH_{arom}), 123.22 (CH_{arom}), 125.95 (2C, CH_{arom}), 126.04 (2C, CH_{arom}), 129.77 (2C, CH_{arom}), 129.94 (2C, CH_{arom}), 124.11, 124.71, 127.68, 140.69, 141.35, 147.59, 150.23, 156.85, 160.07, 161.38, 170.86, 172.09. Found, %: C 70.74; H 5.26; N 5.32. m/z 510 $[M]^+$. C₃₀H₂₆N₂O₆. Calculated, %: C 70.58; H 5.13; N 5.49. M 510.55.

4-Methoxy-3-{[5-(4-methylphenyl)-1,2-oxazol-3yl|methoxy}benzyl 5-(2,5-dimethylphenyl)-1,2-oxazole-3-carboxylate (7c). Yield 88%, mp 133-135°C. IR spectrum, v, cm⁻¹: 3126, 3062, 3025, 2960, 2922, 2850, 1732 (C=O), 1614, 1597, 1560, 1524, 1469, 1445, 1429, 1367, 1271, 1253, 1241, 1184, 1148, 1052, 1023, 1013, 1003, 949, 871, 814, 799, 781, 521, 502. ¹H NMR spectrum, δ , ppm: 2.35 s (3H, Me), 2.36 s (3H, Me), 2.44 s (3H, Me), 3.89 s (3H, OMe), 5.28 s (2H, CH₂), 5.35 s (2H, CH₂), 6.31 s and 6.80 s (1H each, 4'-H, 4"-H), 6.91 d (2H, H_{arom} , J = 8.2 Hz), 7.11 d.d (1H, H_{arom} , J = 8.2, 1.6 Hz), 7.18 s (3H, H_{arom}), 7.20 d (2H, H_{arom} , J = 8 Hz), 7.53 s (1H, H_{arom}), 7.62 d (2H, H_{arom}, J = 8 Hz). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 20.97 (Me), 21.05 (Me), 21.57 (Me), 56.13 (OMe), 63.16 (CH₂), 67.64 (CH₂), 98.48 and 103.01 (C^{4'}, C^{4''}), 111.89 (CH_{arom}), 115.31 (CH_{arom}), 123.28 (CHarom), 125.89 (2C, CHarom), 129.07 (CHarom), 129.73 (2C, CH_{arom}), 131.48 (CH_{arom}), 131.53 (CH_{arom}), 124.66, 126.03, 127.66, 133.39, 136.08, 140.64, 147.58, 150.23, 156.53, 160.14, 161.33, 170.81, 172.06. Found, %: C 71.18; H 5.44; N 5.10. m/z 524 $[M]^+$. C₃₁H₂₈N₂O₆. Calculated, %: C 70.98; H 5.38; N 5.34. M 524.57.

4-Methoxy-3-{[5-(4-methylphenyl)-1,2-oxazol-3yl|methoxy}benzyl 4,5-dichloro-1,2-thiazole-3-carboxylate (7d). Yield 85%, mp 137-138°C. IR spectrum, v, cm⁻¹: 3142, 3128, 3067, 3005, 2967, 2934, 2890, 2858, 1732 (C=O), 1615, 1598, 1567, 1519, 1471, 1460, 1434, 1407, 1371, 1353, 1272, 1257, 1241, 1203, 11163, 1141, 1081, 1052, 1023, 966, 856, 812, 520, 503. ¹H NMR spectrum, δ, ppm: 2.38 s (3H, Me), 3.89 s (3H, OMe), 5.26 s (2H, CH₂), 5.33 s (2H, CH₂), 6.61 s (1H, 4'-H), 6.90 d (2H, H_{arom}, J = 8.2 Hz), 7.09 d.d (1H, H_{arom} , J = 8.2, 1.8 Hz), 7.15 d (1H, H_{arom} , J = 1.8 Hz), 7.24 d (2H, H_{arom}, J = 8 Hz), 7.64 d (2H, H_{arom}, J = 8 Hz). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 21.63 (Me), 56.15 (OMe), 63.23 (CH₂), 67.94 (CH₂), 98.46 (C^4) , 111.92 (CH_{arom}), 115.28 (CH_{arom}), 123.30 (CH_{arom}), 125.94 (2C, CH_{arom}), 129.78 (2C, CH_{arom}), 124.71, 125.84, 127.53, 140.71, 147.63, 150.26, 150.68, 154.28, 159.06, 161.37, 170.80. Found, %: C 54.93; H 3.67; Cl 13.84; N 5.18; S 6.11. m/z 504 $[M]^+$. C₂₃H₁₈Cl₂N₂O₅S. Calculated, %: C 54.66; H 3.59; Cl 14.03; N 5.54; S 6.34. M 505.37.

3-Methoxy-4-{[5-(4-methylphenyl)-1,2-oxazol-3vl]methoxy}benzyl 5-phenyl-1,2-oxazole-3-carboxvlate (8a). Yield 82%, mp 135–136°C. IR spectrum, v, cm⁻¹: 3148, 3133, 3068, 3033, 2962, 2923, 2852, 1731, 1611, 1596, 1572, 1519, 1468, 1449, 1441, 1422, 1367, 1329, 1273, 1252, 1234, 1166, 1142, 1035, 1016, 993, 949, 819, 806, 763, 686, 676, 499. ¹H NMR spectrum, δ, ppm: 2.34 s (3H, Me), 3.90 s (3H, OMe), 5.24 s (2H, CH₂), 5.34 s (2H, CH₂), 6.60 s and 6.88 s (1H each, 4'-H, 4"-H), 7.00 s (2H, H_{arom}), 7.04 s (1H, H_{arom}), 7.20 d (2H, H_{arom} , J = 8 Hz), 7.37–7.47 m (3H, H_{arom}), 7.62 d (2H, H_{arom} , J = 8 Hz), 7.68–7.78 m (2H, H_{arom}). ¹³C NMR spectrum, δ_{C} , ppm: 21.47 (Me), 56.00 (OMe), 62.92 (CH₂), 67.68 (CH₂), 98.33 and 99.99 (C^{4'}, C^{4''}), 112.74 (CH_{arom}), 114.03 (CH_{arom}), 121.78 (CH_{arom}), 125.78 (2C, CH_{arom}), 125.89 (2C, CH_{arom}), 129.13 (2C, CH_{arom}), 129.65 (2C, CH_{arom}), 130.83 (CH_{arom}), 124.51, 126.53, 128.80, 140.59, 147.84, 149.70, 156.77, 159.87, 161.30, 170.71, 171.74. Found, %: C 70.36; H 4.96; N 5.30. m/z 496 $[M]^+$. C₂₉H₂₄N₂O₆. Calculated, %: C 70.15; H 4.87; N 5.64. M 496.52.

3-Methoxy-4-{[5-(4-methylphenyl)-1,2-oxazol-3vl]methoxy}benzyl 5-(4-methylphenyl)-1,2-oxazole-3-carboxylate (8b). Yield 84%, mp 164–165°C. IR spectrum, v, cm⁻¹: 3130, 3062, 3029, 2962, 2923, 2852, 1729, 1614, 1595, 1567, 1522, 1474, 1445, 1424, 1381, 1357, 1330, 1273, 1253, 1236, 1172, 1148, 1138, 1118, 1060, 1034, 1016, 984, 948, 851, 818, 780, 499. ¹H NMR spectrum, δ, ppm: 2.37 s (3H, Me), 2.38 s (3H, Me), 3.91 s (3H, OMe), 5.26 s (2H, CH₂), 5.35 s (2H, CH₂), 6.61 s and 6.84 s (1H each, 4'-H, 4"-H), 7.01 s (2H, H_{arom}), 7.04 s (1H, H_{arom}), 7.23 d (2H, H_{arom} , J = 8 Hz), 7.25 d (2H, H_{arom} , J =8 Hz), 7.64 d (2H, H_{arom}, J = 8 Hz), 7.65 d (2H, H_{arom}, J = 8 Hz). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 21.56 (Me), 21.60 (Me), 56.10 (OMe), 63.03 (CH₂), 67.72 (CH₂), 98.39 and 99.47 (C4', C4"), 112.80 (CHarom), 114.12 (CH_{arom}), 121.86 (CH_{arom}), 125.88 (2C, CH_{arom}), 125.93 (2C, CH_{arom}), 129.73 (2C, CH_{arom}), 129.89 (2C, CH_{arom}), 123.95, 124.61, 128.91, 140.68, 141.34, 147.89, 149.78, 156.79, 160.05, 161.41, 170.82, 172.05. Found, %: C 70.72; H 5.21; N 5.36. m/z 510 $[M]^+$. C₃₀H₂₆N₂O₆. Calculated, %: C 70.58; H 5.13; N 5.49. M 510.55.

3-Methoxy-4-{[5-(4-methylphenyl)-1,2-oxazol-3-yl]methoxy}benzyl 5-(2,5-dimethylphenyl)-1,2-oxazole-3-carboxylate (8c). Yield 86%, mp 140–141°C. IR spectrum, v, cm⁻¹: 3143, 3125, 3059, 3023, 2963, 2925, 2851, 1733, 1608, 1596, 1559, 1523, 1473, 1453, 1437, 1379, 1331, 1273, 1255, 1237, 1186,

1145, 1033, 1016, 986, 822, 811, 778, 501. ¹H NMR spectrum, δ, ppm: 2.37 s (3H, Me), 2.39 s (3H, Me), 2.45 s (3H, Me), 3.92 s (3H, OMe), 5.27 s (2H, CH₂), 5.37 s (2H, CH₂), 6.62 s and 6.80 s (1H each, 4'-H, 4"-H), 7.02 s (2H, H_{arom}), 7.05 s (1H, H_{arom}), 7.18 s $(2H, H_{arom})$, 7.25 d $(2H, H_{arom}, J = 8 Hz)$, 7.53 s (1H, J) H_{arom}), 7.65 d (2H, H_{arom} , J = 8 Hz). ¹³C NMR spectrum, δ_{C} , ppm: 21.01 (Me), 21.08 (Me), 21.65 (Me), 56.19 (OMe), 63.13 (CH₂), 67.82 (CH₂), 98.45 and 103.06 ((C^{4'}, C^{4"}), 112.92 (CH_{arom}), 114.20 (CH_{arom}), 121.99 (CH_{arom}), 125.98 (2C, CH_{arom}), 129.11 (CH_{arom}), 129.81 (2C, CH_{arom}), 131.57 (CH_{arom}), 131.59 (CH_{arom}), 124.70, 126.02, 128.98, 133.42, 136.16, 140.77, 147.98, 149.85, 156.59, 160.25, 161.49, 170.93, 172.17. Found, %: C 71.10; H 5.43; N 5.18. m/z 524 [M]⁺. C₃₁H₂₈N₂O₆. Calculated, %: C 70.98; H 5.38; N 5.34. M 524.57.

3-Methoxy-4-{[5-(4-methylphenyl)-1,2-oxazol-3yl]methoxy}benzyl 4,5-dichloro-1,2-thiazole-3-carboxylate (8d). Yield 86%, mp 119-120°C. IR spectrum, v, cm⁻¹: 3144, 3056, 2957, 2920, 2852, 1731, 1615, 1595, 1572, 1521, 1473, 1450, 1402, 1352, 1331, 1271, 1233, 1201, 1195, 1169, 1145, 1079, 1054, 1036, 1020, 975, 934, 908, 851, 821, 806, 792, 639, 507. ¹H NMR spectrum, δ , ppm: 2.35 s (3H, Me), 3.88 s (3H, OMe), 5.23 s (2H, CH₂), 5.33 s (2H, CH₂), 6.59 s (1H, 4'-H), 6.99 s (2H, H_{arom}), 7.02 s (1H, H_{arom}), 7.20 d (2H, H_{arom} , J = 8 Hz), 7.61 d (2H, H_{arom} , J = 8 Hz). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 21.50 (Me), 56.01 (OMe), 62.93 (CH₂), 67.90 (CH₂), 98.32 ($C^{4'}$), 112.68 (CHarom), 114.06 (CHarom), 121.76 (CHarom), 125.79 (2C, CH_{arom}), 129.65 (2C, CH_{arom}), 124.52, 125.70, 128.70, 140.59, 147.82, 149.69, 150.61, 154.13, 158.92, 161.30, 170.71. Found, %: C 54.85; H 3.64; Cl 13.80; N 5.27; S 6.03. m/z 504 $[M]^+$. C₂₃H₁₈Cl₂N₂O₅S. Calculated, %: C 54.66; H 3.59; Cl 14.03; N 5.54; S 6.34. M 505.37.

3-Ethoxy-4-{[5-(4-methylphenyl)-1,2-oxazol-3yl]methoxy}benzyl 5-(2,4-dimethylphenyl)-1,2-oxazole-3-carboxylate (9c). Yield 81%, mp 131–132°C. IR spectrum, v, cm⁻¹: 3152, 3138, 3063, 3033, 2974, 2928, 2877, 1729 (C=O), 1617, 1592, 1560, 1520, 1465, 1449, 1429, 1398, 1379, 1363, 1333, 1290, 1255, 1243, 1229, 1183, 1152, 1136, 1113, 1057, 1039, 1014, 963, 943, 843, 815, 803, 780, 504. ¹H NMR spectrum, δ , ppm: 1.48 t (3H, OCH₂Me, *J* = 7 Hz), 2.36 s (3H, Me), 2.38 s (3H, Me), 2.44 s (3H, Me), 4.14 q (2H, OCH₂Me, *J* = 7 Hz), 5.26 s (2H, CH₂), 5.36 s (2H, CH₂), 6.63 s and 6.80 s (1H each, 4'-H, 4"-H), 7.01 s (2H, H_{arom}), 7.06 s (1H, H_{arom}), 7.18 s (2H, H_{arom}), 7.24 d (2H, H_{arom}, *J* = 8 Hz), 7.53 s (1H, H_{arom}), 7.65 d (2H, H_{arom}, J = 8 Hz). ¹³C NMR spectrum, δ_C, ppm: 14.99 (OCH₂**Me**), 20.97 (Me), 21.04 (Me), 21.60 (Me), 63.44 (CH₂), 64.70 (CH₂), 67.78 (CH₂), 98.45 and 103.01 (C⁴', C⁴''), 114.44 (CH_{arom}), 115.22 (CH_{arom}), 121.91 (CH_{arom}), 125.91 (2C, CH_{arom}), 129.05 (CH_{arom}), 129.77 (2C, CH_{arom}), 131.52 (CH_{arom}), 131.54 (CH_{arom}), 124.71, 125.98, 129.17, 133.36, 136.11, 140.69, 148.26, 149.39, 156.56, 160.19, 161.69, 170.72, 172.10. Found, %: C 71.69; H 5.80; N 5.01. *m*/*z* 538 [*M*]⁺. C₃₂H₃₀N₂O₆. Calculated, %: C 71.36; H 5.61; N 5.20. *M* 538.60.

3-Ethoxy-4-{[5-(4-methylphenyl)-1,2-oxazol-3vl]methoxy{benzyl 4,5-dichloro-1,2-thiazole-3-carboxylate (9d). Yield 80%, mp 126-127°C. IR spectrum, v, cm⁻¹: 3146, 3080, 3077, 2962, 2924, 2872, 2855, 1731 (C=O), 1617, 1604, 1593, 1523, 1476, 1448, 1434, 1407, 1371, 1352, 1298, 1271, 1253, 1241, 1207, 1171, 1140, 1112, 1079, 1041, 964, 877, 814, 801, 650, 503. ¹H NMR spectrum, δ, ppm: 1.46 t $(3H, OCH_2Me, J = 7 Hz), 2.38 s (3H, Me), 4.12 q (2H, Me))$ OCH_2Me , J = 7 Hz), 5.25 s (2H, CH₂), 5.34 s (2H, CH₂), 6.61 s (1H, 4'-H), 6.99 s (2H, H_{arom}), 7.04 s (1H, H_{arom}), 7.24 d (2H, H_{arom} , J = 8 Hz), 7.64 d (2H, H_{arom} , J = 8 Hz). ¹³C NMR spectrum, $\delta_{\rm C}$, ppm: 14.98 (OCH₂Me), 21.61 (Me), 63.43 (CH₂), 64.66 (CH₂), 68.04 (CH₂), 98.44 (C^{4'}), 114.35 (CH_{arom}), 115.23 (CHarom), 121.87 (CHarom), 125.91 (2C, CHarom), 129.77 (2C, CH_{arom}), 124.70, 125.81, 129.00, 140.69, 148.25, 149.37, 150.73, 154.30, 159.07, 161.68, 170.71. Found, %: C 55.79; H 3.96; Cl 13.28; N 5.17; S 5.86. m/z 518 $[M]^+$. C₂₄H₂₀Cl₂N₂O₅S. Calculated, %: C 55.50; H 3.88; Cl 13.65; N 5.39; S 6.17. M 519.39.

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