

Synthesis of 1,2,4- and 1,3,4-Oxadiazoles from 1-Aryl-5-methyl-1*H*-1,2,3-triazole-4-carbonyl Chlorides

N. D. Obushak, N. T. Pokhodylo, N. I. Pidlypnyi, and V. S. Matiichuk

Ivan Franko Lviv National University, ul. Kirilla i Mefodiya 6, Lviv, 79005 Ukraine
e-mail: obushak@in.lviv.ua

Received January 14, 2008

Abstract—5-Substituted 2-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)-1,3,4-oxadiazoles were synthesized by reaction of 1-aryl-5-methyl-1*H*-1,2,3-triazole-4-carbonyl chlorides with the corresponding 5-substituted 1*H*-tetrazoles. 5-Methyl-1-phenyl-1*H*-1,2,3-triazole-4-carbonyl chloride reacted with *N'*-hydroxybenzimidamides to give 3-aryl-5-(5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-1,2,4-oxadiazoles. Reactions of 4-(5-methyl-1*H*-1,2,3-triazol-1-yl)benzoic acid with *N'*-hydroxybenzimidamides resulted in the formation of 3-aryl-5-[4-(5-methyl-1*H*-1,2,3-triazol-1-yl)phenyl]-1,2,4-oxadiazoles.

DOI: 10.1134/S1070428008100217

1,3,4-Oxadiazoles constitute an important class of heterocyclic compounds [1]. Numerous 1,3,4-oxadiazole derivatives exhibit biological activity, in particular antiphlogistic and hypotensive [2], bactericidal [3], hypoglycemic [4], myorelaxant [5], fungicidal [6], insecticidal [7], and pesticidal [8]. Central nervous system stimulators were found among 1,3,4-oxadiazole derivatives [9], and such medical agents as Vadrin, Eudormil, and SC27166 are based on compounds of this class [10–12]. 1,2,4-Oxadiazoles have also found application, e.g., as hydrolytically stable bioisosters of amide and ester groups [13], antidepressants [14], 5-HT_{1D} receptor agonists [15], and antiviral agents [16]. Compounds containing a 1,2,3-triazole ring also possess biological activity [17].

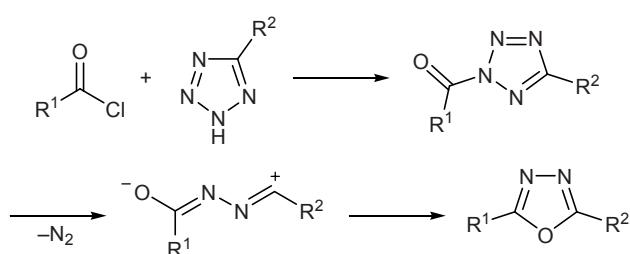
In the present work we tried to find synthetic approaches to compounds including both 1,2,3-triazole and oxadiazole fragments. It is known that 2,5-disubstituted 1,3,4-oxadiazoles can be obtained by reaction of carboxylic acid chlorides with tetrazoles [18], which

is accompanied by thermal rearrangement with liberation of nitrogen (Scheme 1). However, it is more likely that elimination of nitrogen molecule and formation of oxadiazole ring follow a synchronous mechanism [19]. Analogous reactions of triazolecarboxylic acid chlorides were not reported. Such reactions might be expected to involve competing processes due to opening of the triazole ring with formation of highly reactive intermediates.

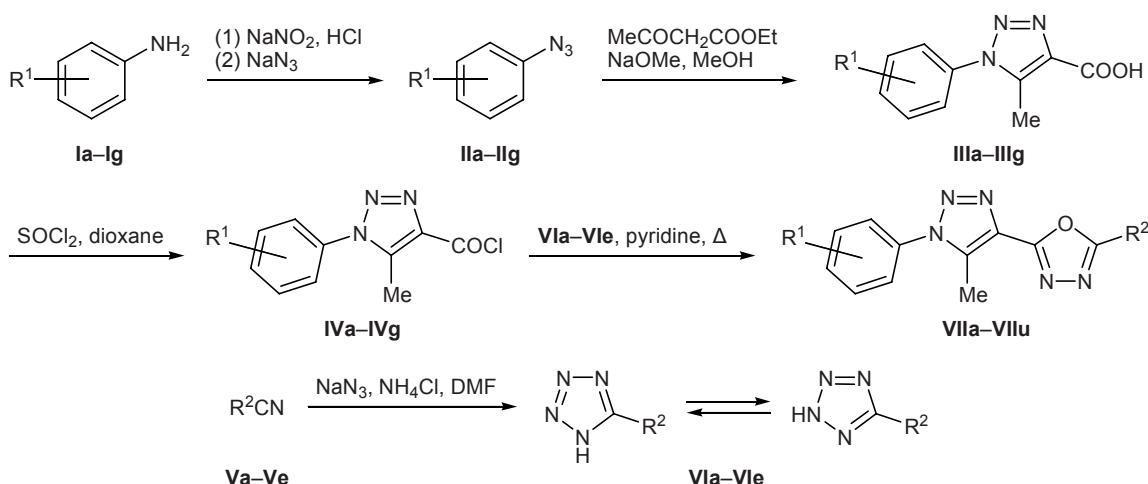
We have found that 5-substituted tetrazoles VIa–VIe react with 1-aryl-5-methyl-1*H*-1,2,3-triazole-4-carbonyl chlorides IVa–IVg to give in all cases the corresponding 1,3,4-oxadiazoles VIIa–VIIu having a triazolyl substituent in the 5-position. The reactions start at a temperature of about 60°C and are complete in 30 min, and the yields of compounds VIIa–VIIu range from 54 to 83% (Scheme 2). Initial tetrazoles VIa–VIe were obtained by 1,3-dipolar cycloaddition of sodium azide to nitriles Va–Ve [20], and triazolecarboxylic acids IIIa–IIIg were prepared by cycloaddition of aryl azides IIa–IIg to ethyl acetoacetate. Compounds IIa–IIg were synthesized in turn from substituted anilines Ia–Ig via diazotization followed by treatment with sodium azide.

We also examined reactions of acid chloride IVa with *N'*-hydroxybenzimidamides IXa–IXc. The reactions were carried out in pyridine at room temperature, and the mixture was then heated in DMF for 3 h at 80°C. These conditions allowed us to avoid decom-

Scheme 1.



Scheme 2.



I–IV, R¹ = H (**a**), 2-Me (**b**), 3-Me (**c**), 4-Me (**d**), 4-F (**e**), 2-MeO (**f**), 3-MeO (**g**); V, VI, R² = Ph (**a**), 2-MeC₆H₄ (**b**), 4-MeC₆H₄ (**c**), 2-ClC₆H₄ (**d**), 2-furyl (**e**); VII, R¹ = H, R² = Ph (**a**), 2-MeC₆H₄ (**b**), 4-MeC₆H₄ (**c**), 2-ClC₆H₄ (**d**), 2-furyl (**e**); R¹ = 2-Me, R² = Ph (**f**), 4-MeC₆H₄ (**g**), 2-furyl (**h**); R¹ = 3-Me, R² = Ph (**i**), 2-MeC₆H₄ (**j**); R¹ = 4-Me, R² = Ph (**k**), 2-MeC₆H₄ (**l**), 4-MeC₆H₄ (**m**), 2-furyl (**n**); R¹ = 4-F, R² = Ph (**o**), 2-MeC₆H₄ (**p**), 2-furyl (**q**); R¹ = 2-MeO, R² = Ph (**r**), 4-MeC₆H₄ (**s**); R¹ = 3-MeO, R² = Ph (**t**), 2-MeC₆H₄ (**u**).

position of the triazole ring and tarring; as a result, almost no by-products were formed, and compounds **Xa** and **Xb** were isolated in high yields (Scheme 3). Thus the proposed procedure may be regarded as a preparative method of synthesis of compounds simultaneously containing both 1,2,3-triazole and 1,2,4-oxadiazole fragments. N'-Hydroxybenzimidamides **IXa**–**IXc** were synthesized by addition of hydroxylamine to nitriles **VIIIa**–**VIIIc**.

Compounds containing 1,2,4-oxadiazole and triazole rings were also obtained starting from triazolyl-substituted benzoic acid **XII** which was synthesized from 4-azidobenzoic acid (**IIh**) and phosphorane **XI**. The corresponding acid chloride **XIII** smoothly reacted with amide oximes **IXb** and **IXc**, yielding compounds **XIVa** and **XIVb**, respectively (Scheme 4).

Thus the results of our study demonstrate the possibility for synthesizing molecular ensembles including oxadiazole and triazole rings in different combinations by reactions of triazolecarboxylic acid chlorides with tetrazoles or N'-hydroxybenzimidamides.

EXPERIMENTAL

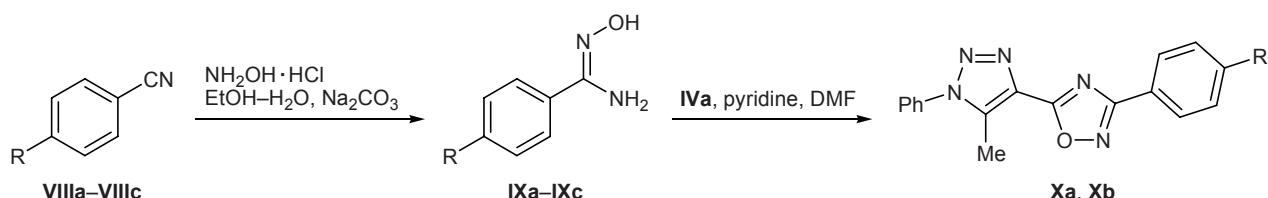
The ¹H NMR spectra were measured on a Varian Mercury spectrometer (400 MHz) using DMSO-*d*₆ as solvent and tetramethylsilane as internal reference.

Aryl azides IIa–IIh were synthesized according to the procedure reported in [21]: **IIa**, yield 63%, bp 52–53°C (10 mm); **IIb**, yield 46%, bp 62°C (10 mm); **IIc**, yield 67%, bp 78°C (10 mm); **IId**, yield 70%, bp 70°C (10 mm); **IIe**, yield 78%; **IIf**, yield 57%, bp 87–89°C (1 mm); **IIg**, yield 78%; **IIh**, yield 87%, mp 179–180°C (from aqueous ethanol); azides **IIe** and **IIg** were used without additional purification.

Acids IIIa–IIIg were prepared as described in [22] and were purified by recrystallization from aqueous alcohol: **IIIa**, yield 84%, mp 137–138°C; **IIIb**, yield 65%, mp 134–135°C; **IIIc**, yield 54%, mp 158–159°C; **IId**, yield 76%, mp 183–184°C; **IIIe**, yield 88%, mp 187–188°C; **IIIf**, yield 63%, mp 175–176°C; **IIIg**, yield 68%, mp 133–134°C.

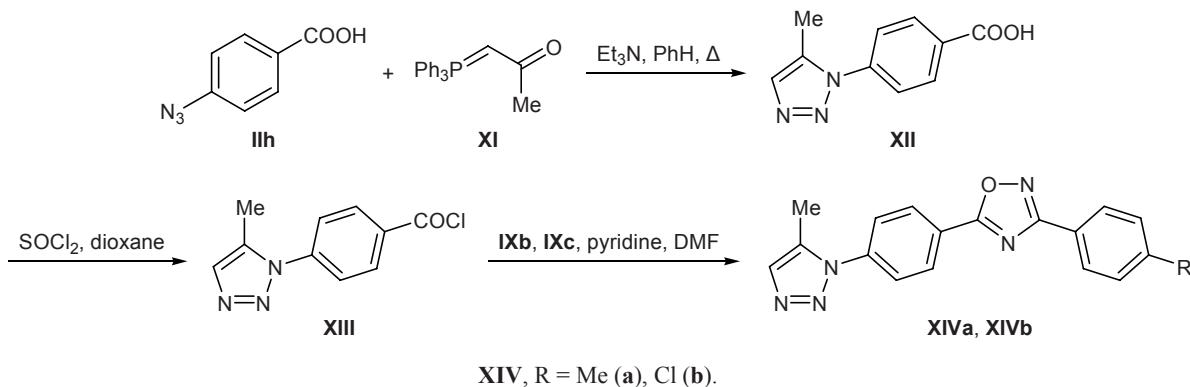
Acid chlorides IVa–IVg and XIII (general procedure). A mixture of 50 mmol of the corresponding

Scheme 3.



VIII, IX, R = H (**a**), Me (**b**), Cl (**c**); X, R = H (**a**), Me (**b**).

Scheme 4.



carboxylic acid and 4.4 ml (60 mmol) of thionyl chloride in 30 ml of dioxane was heated under reflux until hydrogen chloride no longer evolved. The mixture was cooled to room temperature, 30 ml of hexane was added, and the precipitate was filtered off, washed with hexane on a filter, and dried in air: **IVa**, yield 95%, mp 126–127°C; **IVb**, yield 89%, mp 143–144°C; **IVc**, yield 91%, mp 75–76°C; **IVd**, yield 97%, mp 142–143°C; **IVe**, yield 96%, mp 85–86°C; **IVf**, yield 84%, mp 122–123°C; **IVg**, yield 88%, mp 125–126°C; **XIII**, yield 63%, mp 175–176°C.

Tetrazoles VIa–VIe were synthesized according to the procedure described in [20]: **VIa**, yield 82%, mp 218–219°C; **VIb**, yield 61%, mp 150–151°C; **VIc**, yield 87%, mp 257–258°C; **VID**, yield 74%, mp 176–177°C; **VIe**, yield 75%, mp 201–202°C.

N'-Hydroxybenzimidamides IXa–IXc were prepared as described in [23]: **IXa**, yield 70%, mp 71°C; **IXb**, yield 83%, mp 155°C; **IXc**, yield 72%, mp 129°C.

4-Azidobenzoic acid (XII) was obtained as described in [24]. Yield 82%, mp 243–244°C.

1,3,4-Oxadiazoles VIIa–VIIu (general procedure). Acid chloride **IVa–IVg**, 5 mmol, was added to a solution of 5 mmol of tetrazole **VIa–VIe** in 5 ml of pyridine. The mixture was heated until nitrogen no longer evolved, heated for 30 min under reflux, cooled, and diluted with 50 ml of water. The precipitate was filtered off, washed on a filter with water (up to 50 ml), dried in air, and purified by recrystallization.

2-(5-Methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-5-phenyl-1,3,4-oxadiazole (VIIa). Yield 79%, mp 137°C. ^1H NMR spectrum, δ , ppm: 2.73 s (3H, Me), 7.60–7.70 m (8H, H_{arom}), 8.14 m (2H, H_{arom}). Found, %: C 67.14; H 4.41; N 22.98. $\text{C}_{17}\text{H}_{13}\text{N}_5\text{O}$. Calculated, %: C 67.32; H 4.32; N 23.09.

2-(2-Methylphenyl)-5-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-1,3,4-oxadiazole (VIIb). Yield

63%, mp 149°C. ^1H NMR spectrum, δ , ppm: 2.72 s (3H, Me), 2.75 s (3H, Me), 7.38–7.52 m (3H, H_{arom}), 7.62–7.68 m (5H, H_{arom}), 8.04 d (1H, 6-H, J = 7.6 Hz). Found, %: C 68.22; H 4.82; N 21.95. $\text{C}_{18}\text{H}_{15}\text{N}_5\text{O}$. Calculated, %: C 68.13; H 4.76; N 22.07.

2-(4-Methylphenyl)-5-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-1,3,4-oxadiazole (VIIc). Yield 78%, mp 155°C. ^1H NMR spectrum, δ , ppm: 2.47 s (3H, Me), 2.72 s (3H, Me), 7.41 d (2H, 3-H, 5-H in 4-MeC₆H₄, J = 8.0 Hz), 7.62–7.69 m (5H, C₆H₅), 8.02 d (2H, 2-H, 6-H in 4-MeC₆H₄, J = 8.0 Hz). Found, %: C 67.84; H 4.66; N 22.15. $\text{C}_{18}\text{H}_{15}\text{N}_5\text{O}$. Calculated, %: C 68.13; H 4.76; N 22.07.

2-(2-Chlorophenyl)-5-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-1,3,4-oxadiazole (VIId). Yield 59%, mp 145°C. ^1H NMR spectrum, δ , ppm: 2.73 s (3H, Me), 7.57 pseudotriplet (1H, 4-H in C₆H₄), 7.61–7.69 m (7H, H_{arom}), 8.10 d (1H, 6-H in C₆H₄, J = 8.0 Hz). Found, %: C 60.49; H 3.50; N 20.87. $\text{C}_{17}\text{H}_{12}\text{ClN}_5\text{O}$. Calculated, %: C 60.45; H 3.58; N 20.73.

2-(2-Furyl)-5-(5-methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-1,3,4-oxadiazole (VIIe). Yield 70%, mp 137°C. ^1H NMR spectrum, δ , ppm: 2.72 s (3H, Me), 6.76 d.d (1H, 4'-H, J = 1.6, 3.2 Hz), 7.38 d (1H, 3'-H, J = 3.2 Hz), 7.62–7.69 m (5H, H_{arom}), 7.99 d (1H, 5'-H, J = 1.6 Hz). Found, %: C 61.09; H 3.65; N 23.91. $\text{C}_{15}\text{H}_{11}\text{N}_5\text{O}_2$. Calculated, %: C 61.43; H 3.78; N 23.88.

2-[5-Methyl-1-(2-methylphenyl)-1H-1,2,3-triazol-4-yl]-5-phenyl-1,3,4-oxadiazole (VIIf). Yield 72%, mp 144°C. ^1H NMR spectrum, δ , ppm: 2.09 s (3H, Me), 2.53 s (3H, Me), 7.42–7.64 m (7H, H_{arom}), 8.13–8.16 m (2H, H_{arom}). Found, %: C 68.01; H 4.82; N 21.94. $\text{C}_{18}\text{H}_{15}\text{N}_5\text{O}$. Calculated, %: C 68.13; H 4.76; N 22.07.

2-[5-Methyl-1-(2-methylphenyl)-1H-1,2,3-triazol-4-yl]-5-(4-methylphenyl)-1,3,4-oxadiazole

(VIIg). Yield 74%, mp 127°C. ^1H NMR spectrum, δ , ppm: 2.09 s (3H, Me), 2.46 s (3H, Me), 2.52 s (3H, Me), 7.41 d (2H, 3-H, 5-H in 4-MeC₆H₄, J = 8.0 Hz), 7.46 d (1H, 3-H in 2-MeC₆H₄, J = 8.0 Hz), 7.48–7.59 m (3H, 2-MeC₆H₄), 8.02 d (2H, 2-H, 6-H in 4-MeC₆H₄, J = 8.0 Hz). Found, %: C 68.98; H 5.14; N 21.01. C₁₉H₁₇N₅O. Calculated, %: C 68.87; H 5.17; N 21.13.

2-(2-Furyl)-5-[5-methyl-1-(2-methylphenyl)-1*H*-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (VIIh). Yield 54%, mp 117°C. ^1H NMR spectrum, δ , ppm: 2.08 s (3H, Me), 2.50 s (3H, Me), 6.77 d.d (1H, 4'-H, J = 1.2, 3.6 Hz), 7.38 d (1H, 3'-H, J = 3.6 Hz), 7.42–7.58 m (4H, C₆H₄), 7.99 d (1H, 5'-H, J = 1.2 Hz). Found, %: C 62.45; H 4.19; N 22.85. C₁₆H₁₃N₅O₂. Calculated, %: C 62.53; H 4.26; N 22.79.

2-[5-Methyl-1-(3-methylphenyl)-1*H*-1,2,3-triazol-4-yl]-5-phenyl-1,3,4-oxadiazole (VIIi). Yield 76%, mp 119°C. ^1H NMR spectrum, δ , ppm: 2.49 s (3H, Me), 2.72 s (3H, Me), 7.41–7.48 m (3H, C₆H₄), 7.52 pseudotriplet (1H, 5-H in C₆H₄), 7.58–7.63 m (3H, C₆H₅), 8.12–8.16 m (2H, C₆H₅). Found, %: C 68.22; H 4.85; N 22.13. C₁₈H₁₅N₅O. Calculated, %: C 68.13; H 4.76; N 22.07.

2-[5-Methyl-1-(3-methylphenyl)-1*H*-1,2,3-triazol-4-yl]-5-(2-methylphenyl)-1,3,4-oxadiazole (VIIj). Yield 65%, mp 129°C. ^1H NMR spectrum, δ , ppm: 2.49 s (3H, Me), 2.71 s (3H, Me), 2.75 s (3H, Me), 7.39–7.56 m (7H, H_{arom}), 8.05 d (1H, 6-H in 2-MeC₆H₄, J = 7.6 Hz). Found, %: C 68.53; H 5.07; N 20.89. C₁₉H₁₇N₅O. Calculated, %: C 68.87; H 5.17; N 21.13.

2-[5-Methyl-1-(4-methylphenyl)-1*H*-1,2,3-triazol-4-yl]-5-phenyl-1,3,4-oxadiazole (VIIk). Yield 80%, mp 182°C. ^1H NMR spectrum, δ , ppm: 2.48 s (3H, Me), 2.70 s (3H, Me), 7.45 d (2H, 3-H, 5-H in C₆H₄, J = 8.4 Hz), 7.53 d (2H, 2-H, 6-H in C₆H₄, J = 8.4 Hz), 7.60–7.63 m (3H, C₆H₅), 8.12–8.16 m (2H, 2-H, 6-H in C₆H₅). Found, %: C 67.80; H 4.71; N 21.97. C₁₈H₁₅N₅O. Calculated, %: C 68.13; H 4.76; N 22.07.

2-[5-Methyl-1-(4-methylphenyl)-1*H*-1,2,3-triazol-4-yl]-5-(2-methylphenyl)-1,3,4-oxadiazole (VIII). Yield 74%, mp 148°C. ^1H NMR spectrum, δ , ppm: 2.48 s (3H, Me), 2.70 s (3H, Me), 2.75 s (3H, Me), 7.39–7.56 m (7H, H_{arom}), 8.05 d (1H, 6-H in 2-MeC₆H₄, J = 7.6 Hz). Found, %: C 68.98; H 5.12; N 21.22. C₁₉H₁₇N₅O. Calculated, %: C 68.87; H 5.17; N 21.13.

2-[5-Methyl-1-(4-methylphenyl)-1*H*-1,2,3-triazol-4-yl]-5-(4-methylphenyl)-1,3,4-oxadiazole (VIIIm). Yield 82%, mp 186°C. ^1H NMR spectrum, δ , ppm: 2.46 s (3H, Me), 2.48 s (3H, Me), 2.69 s (3H, Me), 7.41 (2H, 3-H, 5-H in C₆H₄N, J = 8.2 Hz), 7.45 (2H, 3-H, 5-H in C₆H₄, J = 8.0 Hz), 7.53 (2H, 2-H, 6-H in C₆H₄N, J = 8.2 Hz), 8.01 (2H, 2-H, 6-H in C₆H₄, J = 8.0 Hz). Found, %: C 68.48; H 5.06; N 21.09. C₁₉H₁₇N₅O. Calculated, %: C 68.87; H 5.17; N 21.13.

2-(2-Furyl)-5-[5-methyl-1-(4-methylphenyl)-1*H*-1,2,3-triazol-4-yl]-1,3,4-oxadiazole (VIIIn). Yield 79%, mp 174°C. ^1H NMR spectrum, δ , ppm: 2.48 s (3H, Me), 2.69 s (3H, Me), 6.76 d.d (1H, 4'-H, J = 1.6, 3.2 Hz), 7.38 d (1H, 3'-H, J = 3.2 Hz), 7.44 d (2H, 3-H, 5-H in C₆H₄, J = 8.0 Hz), 7.53 d (2H, 2-H, 6-H in C₆H₄, J = 8.0 Hz), 7.99 br.s (1H, 5'-H). Found, %: C 62.41; H 4.21; N 22.70. C₁₆H₁₃N₅O₂. Calculated, %: C 62.53; H 4.26; N 22.79.

2-[1-(4-Fluorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-5-phenyl-1,3,4-oxadiazole (VIIo). Yield 79%, mp 169°C. ^1H NMR spectrum, δ , ppm: 2.70 s (3H, Me), 7.43 pseudotriplet (2H, 3-H, 5-H in 4-FC₆H₄), 7.58–7.62 m (3H, C₆H₅), 7.74 d.d (2H, 2-H, 6-H in 4-FC₆H₄, J_{HF} = 4.8, J_{HH} = 8.8 Hz), 8.11–8.14 m (2H, C₆H₅). Found, %: C 63.61; H 3.63; N 21.78. C₁₇H₁₂FN₅O. Calculated, %: C 63.55; H 3.76; N 21.80.

2-[1-(4-Fluorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-5-(2-methylphenyl)-1,3,4-oxadiazole (VIIp). Yield 83%, mp 127°C. ^1H NMR spectrum, δ , ppm: 2.70 s (3H, Me), 2.74 s (3H, Me), 7.38–7.52 m (5H, H_{arom}), 7.75 d.d (2H, 2-H, 6-H in 4-FC₆H₄, J_{HF} = 4.8, J_{HH} = 8.8 Hz), 8.04 d (1H, 6-H in 2-MeC₆H₄, J = 7.6 Hz). Found, %: C 64.28; H 4.24; N 20.97. C₁₈H₁₄FN₅O. Calculated, %: C 64.47; H 4.21; N 20.88.

2-[1-(4-Fluorophenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-5-(2-furyl)-1,3,4-oxadiazole (VIIq). Yield 75%, mp 184°C. ^1H NMR spectrum, δ , ppm: 2.70 s (3H, Me), 6.77 d.d (1H, 4'-H, J = 1.2, 3.6 Hz), 7.39 d (1H, 3'-H, J = 3.6 Hz), 7.44 pseudotriplet (2H, 3-H, 5-H in 4-FC₆H₄), 7.74 d.d (2H, 2-H, 6-H in 4-FC₆H₄, J_{HF} = 4.8, J_{HH} = 8.8 Hz), 7.99 d (1H, 5'-H, J = 1.2 Hz). Found, %: C 57.61; H 3.28; N 22.41. C₁₅H₁₀FN₅O₂. Calculated, %: C 57.88; H 3.24; N 22.50.

2-[1-(2-Methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-5-phenyl-1,3,4-oxadiazole (VIIr). Yield 61%, mp 164°C. ^1H NMR spectrum, δ , ppm: 2.49 s (3H, Me), 3.89 s (3H, MeO), 7.19 pseudotriplet (1H, 5-H in C₆H₄), 7.32 d (1H, 3-H in C₆H₄, J = 8.4 Hz), 7.48 d (1H, 6-H in C₆H₄, J = 8.0 Hz), 7.58–7.66 m

(4H, H_{arom}), 8.12–8.15 m (2H, 2-H, 6-H in C₆H₅). Found, %: C 64.69; H 4.46; N 20.93. C₁₈H₁₅N₅O₂. Calculated, %: C 64.86; H 4.54; N 21.01.

2-[1-(2-Methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-5-(4-methylphenyl)-1,3,4-oxadiazole (VII^s). Yield 72%, mp 135°C. ¹H NMR spectrum, δ, ppm: 2.46 s (3H, Me), 2.52 s (3H, Me), 3.87 s (3H, MeO), 7.19 pseudotriplet (1H, 5-H in 2-MeOC₆H₄), 7.33 d (1H, 3-H in 2-MeOC₆H₄, *J* = 8.4 Hz), 7.41 d (2H, 3-H, 5-H in 4-MeC₆H₄, *J* = 7.8 Hz), 7.48 d (1H, 6-H in 2-MeOC₆H₄, *J* = 7.6 Hz), 7.64 pseudotriplet (1H, 4-H in 2-MeOC₆H₄), 8.02 d (2H, 2-H, 6-H in 4-MeC₆H₄, *J* = 7.8 Hz). Found, %: C 65.72; H 4.80; N 20.04. C₁₉H₁₇N₅O₂. Calculated, %: C 65.69; H 4.93; N 20.16.

2-[1-(3-Methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-5-phenyl-1,3,4-oxadiazole (VII^t). Yield 78%, mp 129°C. ¹H NMR spectrum, δ, ppm: 2.73 s (3H, Me), 3.89 s (3H, MeO), 7.14–7.24 m (3H, H_{arom}), 7.55 pseudotriplet (1H, H_{arom}), 7.60–7.63 m (3H, H_{arom}), 8.13–8.16 m (2H, 2-H, 6-H in C₆H₅). Found, %: C 64.94; H 4.62; N 20.86. C₁₈H₁₅N₅O₂. Calculated, %: C 64.86; H 4.54; N 21.01.

2-[1-(3-Methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-5-(2-methylphenyl)-1,3,4-oxadiazole (VII^u). Yield 62%, mp 152°C. ¹H NMR spectrum, δ, ppm: 2.72 s (3H, Me), 2.74 s (3H, Me), 3.88 s (3H, MeO), 7.15–7.23 m (3H, H_{arom}), 7.39–7.57 m (4H, H_{arom}), 8.07 d (1H, 6-H in 2-MeC₆H₄, ³J = 8.0 Hz). Found, %: C 65.54; H 4.77; N 20.07. C₁₉H₁₇N₅O₂. Calculated, %: C 65.69; H 4.93; N 20.16.

1,2,4-Oxadiazoles X^a, X^b, XIV^a, and XIV^b (general procedure). Compound IV^a or XIII, 5 mmol, was added to a solution of 5 mmol of amide oxime IX^a–IX^c in 2 ml of pyridine. The mixture was kept for 0.5 h, 5 ml of DMF was added, and the mixture was heated for 3 h at 80°C, cooled to room temperature, and mixed with 30 ml of water. The precipitate was filtered off, washed with water on a filter, recrystallized from alcohol, and dried in air.

5-(5-Methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl)-3-phenyl-1,2,4-oxadiazole (X^a). Yield 77%, mp 137°C. ¹H NMR spectrum, δ, ppm: 2.78 s (3H, Me), 7.55–7.59 m (3H, H_{arom}), 7.65–7.69 m (5H, H_{arom}), 8.12–8.15 m (2H, H_{arom}). Found, %: C 67.45; H 4.43; N 22.89. C₁₇H₁₃N₅O. Calculated, %: C 67.32; H 4.32; N 23.09.

3-(4-Methylphenyl)-5-[5-methyl-1-phenyl-1*H*-1,2,3-triazol-4-yl]-1,2,4-oxadiazole (X^b). Yield 82%,

mp 142°C. ¹H NMR spectrum, δ, ppm: 2.48 s (3H, Me), 2.77 s (3H, Me), 7.35 d (2H, H_{arom}, *J* = 8.0 Hz), 7.64–7.69 m (5H, H_{arom}), 8.01 d (2H, 2-H, 6-H in C₆H₄, *J* = 8.0 Hz). Found, %: C 68.03; H 4.67; N 21.95. C₁₈H₁₅N₅O. Calculated, %: C 68.13; H 4.76; N 22.07.

5-[4-(5-Methyl-1*H*-1,2,3-triazol-1-yl)phenyl]-3-(4-methylphenyl)-1,2,4-oxadiazole (XIV^a). Yield 75%, mp 176°C. ¹H NMR spectrum, δ, ppm: 2.44 s (3H, Me), 2.46 s (3H, Me), 7.35 d (2H, 3-H, 5-H in 4-MeC₆H₄, *J* = 7.8 Hz), 7.63 s (1H, 4'-H), 7.89 d (2H, 3-H, 5-H in C₆H₄, *J* = 8.4 Hz), 7.99 d (2H, 2-H, 6-H in 4-MeC₆H₄, *J* = 7.8 Hz), 8.39 d (2H, 2-H, 6-H in C₆H₄, *J* = 8.4 Hz). Found, %: C 68.01; H 4.62; N 21.95. C₁₈H₁₅N₅O. Calculated, %: C 68.13; H 4.76; N 22.07.

3-(4-Chlorophenyl)-5-[4-(5-methyl-1*H*-1,2,3-triazol-1-yl)phenyl]-1,2,4-oxadiazole (XIV^b). Yield 84%, mp 222°C. ¹H NMR spectrum, δ, ppm: 2.43 s (3H, Me), 7.69 d (2H, 3-H, 5-H in 4-ClC₆H₄, *J* = 8.4 Hz), 7.76 s (1H, 4'-H), 7.94 d (2H, 3-H, 5-H in C₆H₄, *J* = 8.4 Hz), 8.12 d (2H, 2-H, 6-H in 4-ClC₆H₄, *J* = 8.4 Hz), 8.40 d (2H, 2-H, 6-H in C₆H₄, *J* = 8.4 Hz). Found, %: C 60.32; H 3.50; N 20.54. C₁₇H₁₂ClN₅O. Calculated, %: C 60.45; H 3.58; N 20.73.

REFERENCES

- Hill, J., *Comprehensive Heterocyclic Chemistry*, Katritzky, A.R. and Rees, C.W., Eds., Oxford: Pergamon, 1984, vol. 6, p. 427.
- Deshmukh, A.A., Sattur, P.B., and Sheth, U.K., *Indian J. Exp. Biol.*, 1976, vol. 4, p. 166.
- Brown, P., Best, D.J., Broom, N.J.P., Cassels, R., O'Hanlon, P.J., Mitchell, T.J., Osborne, N.F., and Wilson, J.M., *J. Med. Chem.*, 1997, vol. 40, p. 2563; Girges, M.M., *Arzneim.-Forsch. Drug Res.*, 1994, vol. 44, p. 490.
- O'Neal, J.B., Rosen, H., Russel, P.B., Adams, A.C., and Blumenthal, A., *J. Med. Pharm. Chem.*, 1962, vol. 5, p. 617; Kurzer, F., *Org. Compd. Sulphur, Selenium, Tellurium*, 1974, vol. 4, p. 417.
- Yale, H.L. and Losee, K., *J. Med. Chem.*, 1966, vol. 9, p. 478.
- Singh, H. and Yadav, L.D.S., *Agric. Biol. Chem.*, 1976, vol. 40, p. 759; Singh, H., Yadav, L.D.S., and Chaudhary, J.P., *Acta Chim. Hung.*, 1985, vol. 118, p. 11.
- Sen Gupta, A.K., Garg, M., and Chandra, U., *J. Indian Chem. Soc.*, 1979, vol. 56, p. 1230.
- Ram, V.J. and Vlietinck, A.J., *J. Heterocycl. Chem.*, 1988, vol. 25, p. 253.
- Derappe, C., Rips, R., Albert, O., and Aurousseau, M., *Chim. Ther.*, 1968, vol. 3, p. 181.

10. Wilder Smith, A.E., *Arzneim.-Forsch.*, 1962, vol. 12, p. 275.
11. Vincent, M., Maillard, J., and Bernard, M., *Bull. Soc. Chim.*, 1962, p. 1580.
12. Kleemann, A., Engel, J., Kutscher, B., and Reichert, D., *Pharmaceutical Substances: Syntheses, Patents, Applications*, Stuttgart: Thieme, 2001.
13. Andersen, K.E., Jørgensen, A.S., and Bræstrup, C., *Eur. J. Med. Chem.*, 1994, vol. 29, p. 393; Diana, G.D., Volkots, D.L., Nitz, T.J., Bailey, T.R., Long, M.A., Vescio, N., Aldous, S., Pevear, D.C., and Dutko, F.J., *J. Med. Chem.*, 1994, vol. 37, p. 2421; Saunders, J., Cassidy, M., Freedman, S.B., Harley, E.A., Iversen, L.L., Kneen, C., Mac-Leod, A.M., Merchant, K.J., Snow, R.J., and Baker, R., *J. Med. Chem.*, 1990, vol. 33, p. 1128.
14. Harfenist, M., Heuser, D.J., Joyner, C.T., Batchelor, J.F., and White, H.L., *J. Med. Chem.*, 1996, vol. 39, p. 1857.
15. Street, L.J., Baker, R., Davey, W.B., Guiblin, A.R., Jolley, R.A., Reeve, A.J., Routledge, H., Sternfeld, F., Watt, A.P., Beer, M.S., Middlemiss, D.N., Noble, A.J., Stanton, J.A., Scholey, K., Hargreaves, R.J., Sohal, B., Graham, M.I., and Matassa, V.G., *J. Med. Chem.*, 1995, vol. 38, p. 1799.
16. Diana, G.D., Rudewicz, P., Pevear, D.C., Nitz, T.J., Aldous, S.C., Aldous, D.J., Robinson, D.T., Draper, T., Dutko, F.J., Aldi, C., Gendron, G., Oglesby, R.C., Volkots, D.L., Reuman, M., Bailey, T.R., Czerniak, R., Block, T., Roland, R., and Opperman, J., *J. Med. Chem.*, 1995, vol. 38, p. 1355.
17. Sanghvi, Y.S., Bhattacharya, B.K., Kini, G.D., Matsu-moto, S.S., Larson, S.B., Jolley, W.B., Robins, R.K., and Revankar, G.R., *J. Med. Chem.*, 1990, vol. 33, p. 336;
18. Buckle, D.R., Rockell, C.J.M., Smith, H., and Spicer, B.A., *J. Med. Chem.*, 1986, vol. 29, p. 2262; Hupe, D.J., Boltz, R., Cohen, C.J., Felix, J., Ham, E., Miller, D., Soderman, D., and van Skiver, D., *J. Biol. Chem.*, 1991, vol. 266, p. 10136; Bascal, Z., Holden-Dye, L., Willis, R.J., Smith, S.W.G., and Walker, R.J., *Parasitology*, 1996, vol. 112, p. 253; Biagi, G., Giorgi, I., Livi, O., Lucacchini, A., Martini, C., and Scartoni, V., *J. Pharm. Sci.*, 1993, vol. 82, p. 893; Moltzen, E.K., Pedersen, H., Bøgesø, K.P., Meier, E., Frederiksen, K., Sanchez, C., and Lembøl, H.L., *J. Med. Chem.*, 1994, vol. 37, p. 4085; Chakrabarti, J.K., Hotten, T.M., Pullar, I.A., and Steggles, D.J., *J. Med. Chem.*, 1989, vol. 32, p. 2375.
19. Huisgen, R., Sauer, J., Sturm, H.J., and Markgraf, J.H., *Chem. Ber.*, 1960, vol. 93, p. 2106; Faber, K. and Kappe, T., *J. Heterocycl. Chem.*, 1984, vol. 21, p. 1881; Jilale, A., Nechitailo, P., Decroix, B., and Végh, D., *J. Heterocycl. Chem.*, 1993, vol. 30, p. 881.
20. Kadaba, P.K., *Synthesis*, 1973, p. 71.
21. *Organic Syntheses*, Schreiber, R.S., Ed., New York: Wiley, 1951, vol. 31, p. 14.
22. Sun, X.-W., Xu, P.-F., and Zhang, Z.-Y., *Magn. Reson. Chem.*, 1998, vol. 36, p. 459.
23. Tietze, L.-F. and Eicher, T., *Reactions and Syntheses in the Organic Chemistry Laboratory*, Mill Valley, California: University Science Books, 1989. Translated under the title *Preparativnaya organicheskaya khimiya*, Moscow: Mir, 1999, p. 365.
24. Pokhodylo, N., Obushak, M., and Matichuk, V., *Vestn. L'viv. Univ., Ser. Khim.*, 2007, vol. 48, no. 2, p. 20.