

## 2-Aryl-5-arylsulfanyl-1,3-oxazole-4-carboxylic Acids and Their Derivatives

S. G. Pil'ko, V. M. Prokopenko, V. S. Brovarets, and B. S. Drach<sup>†</sup>

*Institute of Bioorganic and Petroleum Chemistry, National Academy of Sciences of Ukraine,  
ul. Murmanskaya 1, Kiev, 02660 Ukraine  
e-mail: brovarets@bpki.kiev.ua*

Received June 18, 2009

**Abstract**—A convenient preparative procedure has been developed for the synthesis of previously unknown 2-aryl-5-arylsulfanyl-1,3-oxazole-4-carboxylic acids and their functional derivatives from accessible multicenter substrates of the general formula  $\text{Cl}_2\text{C}=\text{C}(\text{NHCOR})\text{C}(\text{O})\text{OMe}$ . The products turned out to be suitable for various subsequent transformations. Some oxazole-4-carboxylic acid hydrazide derivatives containing a substituted oxazol-5-yl fragment at the  $\text{N}^2$  atom in the hydrazine moiety underwent recyclization on heating in acetic acid; as a result, one oxazole ring was converted into 1,3,4-oxadiazole.

**DOI:** 10.1134/S1070363210070212

Extensive development of the chemistry of functional 1,3-oxazole derivatives over the past two decades was undoubtedly related to search for effective bioregulators. The role of 1,3-oxazole derivatives in vital processes turned out to be more significant than it was believed previously; this followed from the recent isolation of numerous bio-active oxazole compounds from natural sources [1–3]. Among these, virginiamycin, madumycin **II**, griseoviridin, dendroamide **A**, and other antibiotics are derivatives of oxazole-4-carboxylic acid, which exhibit not only strong bactericidal but also antitumor effect [4–7].

It is quite obvious that studies performed in 1950–60 [1, 8–10] on the development of methods for the preparation of oxazole-4-carboxylic acid derivatives should be continued with account taken of considerable improvement of synthetic tools in the chemistry of oxazole, which was attained in the recent years.

In the present work we used accessible methyl 2-acylamino-3,3-dichloroacrylates **I** and their cyclization products **II** to develop convenient synthetic approaches to numerous new 5-sulfanyl-1,3-oxazole-4-carboxylic acid derivatives **III–XIII** (Scheme 1). The first reaction in Scheme 1 was reported previously [11–13], while all other reactions were performed for the first time.

The key transformation sequence **II** → **III** → **V** afforded reactive compounds, 2-aryl-5-arylsulfanyl-1,3-oxazole-4-carbonyl chlorides which were brought into further transformations to obtain the corresponding hydrazides **IV** and *N*-arylamides **IX** (Table 1). It is more convenient to synthesize compounds **IV** from substrates **II**, while acid chlorides **V** are indispensable for the synthesis of **IX** and **X**.

More profound modification of the substituent on  $\text{C}^4$  in the oxazole ring can be achieved following the transformation sequences **IV** → **VII** and **V** → **X** → **XIII**. The first process is a particular case of cyclization of carboxylic acid hydrazides with triethyl orthoformate [14]. On the other hand, the second process is much more complex, for it is likely to involve regioselective reaction of compounds **V** and **VIII**, probable prototropic transformation **X** ↔ **XI**, and subsequent recyclization **XI** → **XII** → **XIII**. Analogous recyclization was recently examined in detail for simpler acylation products of methyl 2-aryl-5-hydrazino-1,3-oxazole-4-carboxylates [13].

The structure of all new oxazole derivatives shown in Scheme 1 directly followed from their synthesis and was confirmed by IR and  $^1\text{H}$  NMR spectroscopy (Table 2). The products obtained by alkaline hydrolysis of ester **II** lacked signal at  $\delta$  3.87 ppm (MeO) in the  $^1\text{H}$  NMR spectra, but displayed a downfield signal at  $\delta$  13.21 ppm due to proton in the carboxyl group of acid

<sup>†</sup> Deceased.



**Table 1.** Yields, melting points, and elemental analyses of compounds **II–VII** and **IX–XIII**

Comp. no.	Yield, %	mp, °C (solvent)	Found, %		Formula	Calculated, %	
			N (Cl)	S		N (Cl)	S
<b>IIa</b>	64	93–95 (EtOH)	4.22	9.79	C <sub>18</sub> H <sub>15</sub> NO <sub>3</sub> S	4.30	9.85
<b>IIb</b>	65	98–100 (EtOH)	3.95	9.35	C <sub>19</sub> H <sub>17</sub> NO <sub>3</sub> S	4.13	9.45
<b>IIc</b>	69	126–129 <sup>a</sup> (EtOH)	3.78 (9.80)	8.85	C <sub>18</sub> H <sub>14</sub> ClNO <sub>3</sub> S	3.89 (9.85)	8.91
<b>IIIa</b>	70	188–190 (EtOH)	4.52	10.27	C <sub>17</sub> H <sub>13</sub> NO <sub>3</sub> S	4.50	10.30
<b>IIIb</b>	75	191–194 (EtOH)	4.21	9.80	C <sub>18</sub> H <sub>15</sub> NO <sub>3</sub> S	4.30	9.85
<b>IIIc</b>	75	205–208 (EtOH)	3.95 (10.31)	9.29	C <sub>17</sub> H <sub>12</sub> ClNO <sub>3</sub> S	4.05 (10.25)	9.27
<b>IVa</b>	84 <sup>b</sup>	162–163 (EtOH)	12.85	9.80	C <sub>17</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub> S	12.91	9.85
<b>IVb</b>	82	125–127 (EtOH)	12.34	9.44	C <sub>18</sub> H <sub>17</sub> N <sub>3</sub> O <sub>2</sub> S	12.38	9.45
<b>IVc</b>	85	176–178 (EtOH)	11.61 (9.92)	8.83	C <sub>17</sub> H <sub>14</sub> ClN <sub>3</sub> O <sub>2</sub> S	11.68 (9.85)	8.91
<b>Va</b>	80	118–120 <sup>c</sup>	4.12 (10.83)	9.58	C <sub>17</sub> H <sub>12</sub> ClNO <sub>2</sub> S	4.25 (10.75)	9.72
<b>Vb</b>	80	153–155 <sup>c</sup>	3.85 (10.43)	9.12	C <sub>18</sub> H <sub>14</sub> ClNO <sub>2</sub> S	4.07 (10.31)	9.33
<b>Vc</b>	85	140–142 <sup>c</sup>	3.70 (19.56)	8.68	C <sub>17</sub> H <sub>11</sub> Cl <sub>2</sub> NO <sub>2</sub> S	3.85 (19.47)	8.80
<b>VIa</b>	76	190–192 (EtOH)	3.89	9.21	C <sub>17</sub> H <sub>13</sub> NO <sub>5</sub> S	4.08	9.34
<b>VIb</b>	80	178–180 (EtOH)	3.90	8.99	C <sub>18</sub> H <sub>15</sub> NO <sub>5</sub> S	3.92	8.97
<b>VIc</b>	80	192–196 (EtOH)	3.65 (9.40)	8.55	C <sub>17</sub> H <sub>12</sub> ClNO <sub>5</sub> S	3.71 (9.38)	8.49
<b>VIIa</b>	60	112–115 (EtOH)	12.39	9.50	C <sub>18</sub> H <sub>13</sub> N <sub>3</sub> O <sub>2</sub> S	12.53	9.56
<b>VIIb</b>	62	128–132 (EtOH)	11.85	9.03	C <sub>19</sub> H <sub>15</sub> N <sub>3</sub> O <sub>2</sub> S	12.03	9.18
<b>VIIc</b>	65	135–138 (EtOH)	9.40	8.52	C <sub>18</sub> H <sub>12</sub> ClN <sub>3</sub> O <sub>2</sub> S	9.59	8.67
<b>IXa</b>	80	146–148 (MeCN)	6.71	7.68	C <sub>25</sub> H <sub>22</sub> N <sub>2</sub> O <sub>2</sub> S	6.76	7.74
<b>IXb</b>	80	170–173 (MeCN)	6.28 (8.19)	7.22	C <sub>24</sub> H <sub>19</sub> ClN <sub>2</sub> O <sub>2</sub> S	6.44 (8.15)	7.37
<b>IXc</b>	78	168–172 (MeCN)	6.30 (8.20)	7.25	C <sub>24</sub> H <sub>19</sub> ClN <sub>2</sub> O <sub>2</sub> S	6.44 (8.15)	7.37
<b>IXd</b>	80	180–184 (MeCN)	6.03 (15.63)	6.88	C <sub>23</sub> H <sub>16</sub> Cl <sub>2</sub> N <sub>2</sub> O <sub>2</sub> S	6.15 (15.57)	7.04
<b>Xa</b>	82	212–216 (MeCN–DMF, 3:1)	10.69	6.01	C <sub>28</sub> H <sub>22</sub> N <sub>4</sub> O <sub>5</sub> S	10.64	6.09
<b>Xb</b>	82	222–224 (MeCN–DMF, 3:1)	10.25	5.89	C <sub>29</sub> H <sub>24</sub> N <sub>4</sub> O <sub>5</sub> S	10.36	5.93
<b>Xc</b>	85	222–224 (MeCN–DMF, 3:1)	10.45	5.90	C <sub>29</sub> H <sub>24</sub> N <sub>4</sub> O <sub>5</sub> S	10.36	5.93
<b>Xd</b>	85	220–224 (MeCN–DMF, 3:1)	9.85 (6.40)	5.75	C <sub>28</sub> H <sub>21</sub> ClN <sub>4</sub> O <sub>5</sub> S	9.99 (6.32)	5.72
<b>XIIIa</b>	76	179–182 (EtOH)	10.55	6.12	C <sub>28</sub> H <sub>22</sub> N <sub>4</sub> O <sub>5</sub> S	10.64	6.09
<b>XIIIb</b>	78	172–175 (EtOH)	10.30	5.98	C <sub>29</sub> H <sub>24</sub> N <sub>4</sub> O <sub>5</sub> S	10.36	5.93
<b>XIIIc</b>	75	190–192 (AcOH)	10.40	5.91	C <sub>29</sub> H <sub>24</sub> N <sub>4</sub> O <sub>5</sub> S	10.36	5.93
<b>XIIId</b>	75	215–217 (AcOH)	9.88 (6.30)	5.75	C <sub>28</sub> H <sub>21</sub> ClN <sub>4</sub> O <sub>5</sub> S	9.99 (6.32)	5.72

<sup>a</sup> The melting point corresponds to published data [16]. <sup>b</sup> Yield according to method *a*. <sup>c</sup> After washing with hexane.

**III.** The transformation **IV** → **VII** leading to closure of oxadiazole ring is accompanied by disappearance from the IR spectra of absorption bands typical of carbonyl and hydrazine groups in the regions 1645–1800 and 3050–3600 cm<sup>−1</sup>, respectively. Recyclization **X** → **XIII** characteristically gives rise to CH–NH proton

signals (<sup>3</sup>*J*<sub>HH</sub> = 7.5 Hz) in the <sup>1</sup>H NMR spectrum of **XIII**, which is consistent with published data [13].

To conclude, it should be noted that acids **III** smoothly undergo oxidation with hydrogen peroxide in acetic acid to produce previously unknown 2-aryl-5-

**Table 2.** IR and  $^1\text{H}$  NMR spectra of compounds **II–VII** and **IX–XIII**

Comp. no.	IR spectrum (KBr), $\nu$ , $\text{cm}^{-1}$	$^1\text{H}$ NMR spectrum, $\delta$ , ppm ( $\text{DMSO}-d_6$ )
<b>IIa</b>	1730 (C=O)	2.37 s (3H, $\text{CH}_3$ ), 3.87 s (3H, $\text{OCH}_3$ ), 7.30–7.79 m (9H, $\text{H}_{\text{arom}}$ )
<b>IIb</b>	1728 (C=O)	2.37 s (6H, $2\text{CH}_3$ ), 3.87 s (3H, $\text{OCH}_3$ ), 7.28–7.68 m (8H, $\text{H}_{\text{arom}}$ )
<b>IIIa</b>	1687 (C=O), 3667 (OH, assoc.)	2.37 s (3H, $\text{CH}_3$ ), 7.30–7.72 m (9H, $\text{H}_{\text{arom}}$ ), 13.21 br.s (1H, COOH)
<b>IIIb</b>	1693 (C=O), 3640 (OH, assoc.)	2.31 s (3H, $\text{CH}_3$ ), 2.35 s (3H, $\text{CH}_3$ ), 7.24–7.72 m (8H, $\text{H}_{\text{arom}}$ ), 13.21 br.s (1H, COOH)
<b>IIIc</b>	1690 (C=O), 3590 (OH, assoc.)	2.38 s (3H, $\text{CH}_3$ ), 7.30–7.74 m (8H, $\text{H}_{\text{arom}}$ ), 13.21 br.s (1H, COOH)
<b>IVa</b>	1654 (C=O) <sup>a</sup> , 3208 (NH, $\text{NH}_2$ , assoc.)	2.33 s (3H, $\text{CH}_3$ ), 4.48 br.s (2H, $\text{NH}_2$ ), 7.24–7.86 m (9H, $\text{H}_{\text{arom}}$ ), 9.47 s (1H, NH)
<b>IVb</b>	1657 (C=O) <sup>a</sup> , 3252 (NH, $\text{NH}_2$ , assoc.)	2.33 s (3H, $\text{CH}_3$ ), 2.38 s (3H, $\text{CH}_3$ ), 4.46 br.s (2H, $\text{NH}_2$ ), 7.30–7.80 m (8H, $\text{H}_{\text{arom}}$ ), 9.40 s (1H, NH)
<b>IVc</b>	1660 (C=O) <sup>a</sup> , 3210 (NH, $\text{NH}_2$ , assoc.)	2.38 s (3H, $\text{CH}_3$ ), 4.55 br.s (2H, $\text{NH}_2$ ), 7.30–7.80 m (8H, $\text{H}_{\text{arom}}$ ), 9.50 s (1H, NH)
<b>VIa</b>	1149, 1303 ( $\text{SO}_2$ ), 1723 (C=O) <sup>a</sup> , 3250 (NH, assoc.)	2.44 s (3H, $\text{CH}_3$ ), 7.44–8.01 m (9H, $\text{H}_{\text{arom}}$ )
<b>VIb</b>	1122, 1305 ( $\text{SO}_2$ ), 1735 (C=O) <sup>a</sup> , 3232 (NH, assoc.)	2.42 s (6H, $2\text{CH}_3$ ), 7.43–8.03 m (8H, $\text{H}_{\text{arom}}$ )
<b>VIc</b>	1118, 1301 ( $\text{SO}_2$ ), 1729 (C=O) <sup>a</sup> , 3228 (NH, assoc.)	2.41 s (3H, $\text{CH}_3$ ), 7.41–8.15 m (8H, $\text{H}_{\text{arom}}$ )
<b>VIIa</b>	1645–1800, 3050–3600 (no absorption)	2.32 s (3H, $\text{CH}_3$ ), 7.24–7.96 m (9H, $\text{H}_{\text{arom}}$ ), 9.40 s (1H, 5'-H)
<b>VIIb</b>	1645–1800, 3050–3600 (no absorption)	2.29 s (3H, $\text{CH}_3$ ), 2.39 s (3H, $\text{CH}_3$ ), 7.24–7.87 m (8H, $\text{H}_{\text{arom}}$ ), 9.47 s (1H, 5'-H)
<b>VIIc</b>	1645–1800, 3050–3600 (no absorption)	2.39 s (3H, $\text{CH}_3$ ), 7.40–7.94 m (8H, $\text{H}_{\text{arom}}$ ), 9.44 s (1H, 5'-H)
<b>IXa</b>	1672 (C=O), 3390 (NH, assoc.)	2.28 s (3H, $\text{CH}_3$ ), 2.32 s (3H, $\text{CH}_3$ ), 2.37 s (3H, $\text{CH}_3$ ), 7.24–7.88 m (12H, $\text{H}_{\text{arom}}$ ), 10.07 s (1H, NH)
<b>IXb</b>	1679 (C=O), 3392 (NH, assoc.)	2.33 s (3H, $\text{CH}_3$ ), 2.37 s (3H, $\text{CH}_3$ ), 7.30–7.86 m (12H, $\text{H}_{\text{arom}}$ ), 10.30 s (1H, NH)
<b>IXc</b>	1670 (C=O), 3380 (NH, assoc.)	2.28 s (3H, $\text{CH}_3$ ), 2.38 s (3H, $\text{CH}_3$ ), 7.20–7.84 m (12H, $\text{H}_{\text{arom}}$ ), 10.13 s (1H, NH)
<b>IXd</b>	1675 (C=O), 3375 (NH, assoc.)	2.38 s (3H, $\text{CH}_3$ ), 7.40–7.94 m (12H, $\text{H}_{\text{arom}}$ ), 10.37 s (1H, NH)
<b>Xa</b>	1634 (C=O), 1677 (C=O), 3284 (NH, assoc.)	2.34 s (3H, $\text{CH}_3$ ), 3.82 s (3H, $\text{OCH}_3$ ), 7.32–7.94 m (14H, $\text{H}_{\text{arom}}$ ), 9.32 s (1H, NH), 10.75 s (1H, NH)
<b>Xb</b>	1641 (C=O), 1681 (C=O), 3265 (NH, assoc.)	2.34 s (6H, $2\text{CH}_3$ ), 3.81 s (3H, $\text{OCH}_3$ ), 7.26–7.92 m (13H, $\text{H}_{\text{arom}}$ ), 9.27 s (1H, NH), 10.72 s (1H, NH)
<b>Xc</b>	1638 (C=O), 1685 (C=O), 3310 (NH, assoc.)	2.34 s (3H, $\text{CH}_3$ ), 2.40 s (3H, $\text{CH}_3$ ), 3.82 s (3H, $\text{OCH}_3$ ), 7.30–7.87 m (13H, $\text{H}_{\text{arom}}$ ), 9.28 s (1H, NH), 10.69 s (1H, NH)
<b>Xg</b>	1643 (C=O), 1679 (C=O), 3292 (NH, assoc.)	2.40 s (3H, $\text{CH}_3$ ), 3.81 s (3H, $\text{OCH}_3$ ), 7.40–7.84 m (13H, $\text{H}_{\text{arom}}$ ), 9.35 s (1H, NH), 10.80 s (1H, NH)
<b>XIIIa</b>	1642 (C=O), 1762 (C=O), 3264 (NH, assoc.)	2.31 s (3H, $\text{CH}_3$ ), 3.82 s (3H, $\text{OCH}_3$ ), 6.24 d (1H, CH, $^3J_{\text{HH}} = 7.5$ Hz), 7.26–7.97 m (14H, $\text{H}_{\text{arom}}$ ), 9.73 d (1H, NH, $^3J_{\text{HH}} = 7.5$ Hz)
<b>XIIIb</b>	1646 (C=O), 1755 (C=O), 3198 (NH, assoc.)	2.31 s (3H, $\text{CH}_3$ ), 2.39 s (3H, $\text{CH}_3$ ), 3.82 s (3H, $\text{OCH}_3$ ), 6.25 d (1H, CH, $^3J_{\text{HH}} = 7.5$ Hz), 7.30–8.03 m (13H, $\text{H}_{\text{arom}}$ ), 9.63 d (1H, NH, $^3J_{\text{HH}} = 7.5$ Hz)
<b>XIIIc</b>	1645 (C=O), 1758 (C=O), 3205 (NH, assoc.)	2.31 s (3H, $\text{CH}_3$ ), 2.40 s (3H, $\text{CH}_3$ ), 3.83 s (3H, $\text{OCH}_3$ ), 6.24 d (1H, CH, $^3J_{\text{HH}} = 7.5$ Hz), 7.22–7.96 m (13H, $\text{H}_{\text{arom}}$ ), 9.70 d (1H, NH, $^3J_{\text{HH}} = 7.5$ Hz)
<b>XIIId</b>	1642 (C=O), 1763 (C=O), 3244 (NH, assoc.)	2.41 s (3H, $\text{CH}_3$ ), 3.82 s (3H, $\text{OCH}_3$ ), 6.27 d (1H, CH, $^3J_{\text{HH}} = 7.5$ Hz), 7.36–7.98 m (13H, $\text{H}_{\text{arom}}$ ), 9.71 d (1H, NH, $^3J_{\text{HH}} = 7.5$ Hz)

<sup>a</sup> Band with a shoulder.

arylsulfonyl-1,3-oxazole-4-carboxylic acids **VI**. The properties of acids **VI** and their analogs **III** having a bivalent sulfur atom will be compared elsewhere.

## EXPERIMENTAL

The IR spectra were recorded in KBr on a Vertex 70 spectrometer. The  $^1\text{H}$  NMR spectra were measured on a Varian VXR-300 spectrometer from solutions in  $\text{DMSO}-d_6$  using tetramethylsilane as internal reference.

Methyl 2-acylamino-3,3-dichloroacrylates **Ia** and **Ib** were synthesized according to the procedure reported in [11]. Methyl 2-aryl-5-arylsulfanyl-1,3-oxazole-4-carboxylates (**IIa–IIc**) were prepared as described in [15].

**2-Aryl-5-arylsulfanyl-1,3-oxazole-4-carboxylic acid IIIa–IIc (general procedure).** A solution of 0.015 mol of sodium hydroxide in 5 ml of water was added to a solution of 0.01 mol of compound **IIa–IIc** in 30 ml of ethanol, and the mixture was stirred for 1 h on heating. After cooling, the mixture was neutralized to pH  $\sim 7\text{--}6$  with hydrochloric acid, the solvent was removed under reduced pressure, the residue was treated with water, and the precipitate was filtered off and purified by recrystallization.

**2-Aryl-5-arylsulfanyl-1,3-oxazole-4-carboxylic acid hydrazides IVa–IVc.** *a.* Hydrazine hydrate, 0.015 mol, was added to a solution of 0.005 mol of compound **IIa–IIc** in 20 ml of ethanol. The mixture was heated for 3 h under reflux and was then left to stand for 12 h at room temperature. The precipitate was filtered off, washed with water, and purified by recrystallization.

*b.* A solution of 0.03 mol of hydrazine hydrate in 50 ml of water was cooled with ice water, a solution of 0.01 mol of compound **Va** in 15 ml of anhydrous acetonitrile was added dropwise under stirring, and the mixture was stirred for 1 h. The precipitate was filtered off and purified by recrystallization. Yield of compound **IVa** 88%. Samples of **IVa** obtained by the two methods (*a* and *b*) showed no depression of the melting point on mixing, and their IR and  $^1\text{H}$  NMR spectra were identical.

**2-Aryl-5-arylsulfanyl-1,3-oxazole-4-carbonyl chlorides Va–Vc (general procedure).** Thionyl chloride, 0.006 mol, was added to a solution of 0.005 mol of compound **IIIa–IIc** in 20 ml of anhydrous benzene. The solution was heated under reflux until gaseous products no longer evolved, the solvent was

removed under reduced pressure, the residue was treated with anhydrous hexane, and the precipitate was filtered off, dried under reduced pressure, and used in further syntheses without additional purification.

**2-Aryl-5-arylsulfanyl-1,3-oxazole-4-carboxylic acids VIa–VIc (general procedure).** A solution of 0.005 mol of compound **IIIa–IIc** in 10 ml of glacial acetic acid was heated to the boiling point, a 30% solution of hydrogen peroxide was added to the hot mixture in three 1-ml portions over a period of 1 h, the mixture was kept for 8 h at room temperature, the solvent was removed under reduced pressure, the residue was treated with water, and the precipitate was filtered off and purified by recrystallization.

**2-(2-Aryl-5-arylsulfanyl-1,3-oxazol-4-yl)-1,3,4-oxadiazoles VIIa–VIIc (general procedure).** A mixture of 0.001 mol of compound **IVa–IVc** and 0.005 mol of triethyl orthoformate was heated for 12 h under reflux and was then left to stand for 12 h at room temperature. The resulting oily material was treated with water, and the precipitate was filtered off and purified by recrystallization.

**2-Aryl-5-arylsulfantl-1,3-oxazole-4-carbox-amides IXa–IXd (general procedure).** The corresponding amine, 0.001 mol, was dissolved in 20 ml of anhydrous acetonitrile, 0.001 mol of triethylamine and 0.001 mol of compound **Va–Vc** were added, and the mixture was heated to the boiling point and left to stand for 12 h at room temperature. The precipitate was treated with water, filtered off, and purified by recrystallization.

**Methyl 2-aryl-5-[2-(2-aryl-5-arylsulfanyl-1,3-oxazole-4-carbonyl)hydrazino]-1,3-oxazole-4-carboxylates Xa–Xd (general procedure).** Compound **VIIIa** or **VIIIb**, 0.005 mol, was dissolved in 30 ml of anhydrous acetonitrile, 0.005 mol of dimethylaniline and 0.005 mol of compound **Va–Vc** was added, and the mixture was heated to the boiling point and left to stand for 12 h at room temperature. The precipitate was treated with water, filtered off, and purified by recrystallization.

**Methyl acylamino[5-(2-aryl-5-arylsulfanyl-1,3-oxazol-4-yl)-1,3,4-oxadiazol-2-yl]acetates XIIIa–XIIIc (general procedure).** A solution of 0.005 mol of compound **Xa–Xd** in 20 ml of glacial acetic acid was heated for 8 h under reflux and was then left to stand for 12 h at room temperature. The solvent was removed under reduced pressure, the residue was

treated with water, and the precipitate was filtered off and purified by recrystallization.

#### REFERENCES

1. Clarke, H.T., Johnson, J.R., and Robinson, R., *The Chemistry of Penicillin*, Princeton: Princeton Univ., 1949, p. 688.
2. *The Chemistry of Heterocyclic Compounds: Oxazoles*, Turchi, I.J., Ed., New York: Wiley, 1986, vol. 45, p. 109.
3. *Oxazoles: Synthesis, Reactions, and Spectroscopy*, Palmer, D.C., Ed., Hoboken: Wiley, 2003, part A, vol. 60, p. 255.
4. Chamberlin, J.W. and Chen, S., *J. Antibiot.*, 1977, vol. 30, no. 3, p. 197.
5. Jansen, R., Kunze, B., Reichenbach, H., Jurkiewicz, E., Hunsmann, G., and Höfle, G., *Justus Liebigs Ann. Chem.*, 1992, no. 4, p. 357.
6. Moody, C.J. and Bagley, M.C., *J. Chem. Soc., Perkin Trans. 1*, 1998, no. 3, p. 601.
7. Bertram, A. and Pattenden, G., *Synlett*, 2001, no. 12, p. 1873.
8. Cornforth, J.W. and Cornforth, R.H., *J. Chem. Soc.*, 1947, p. 96.
9. Cornforth, J.W. and Huang, H.T., *J. Chem. Soc.*, 1948, p. 1964.
10. Cornforth, J.W. and Cooxon, E., *J. Chem. Soc.*, 1952, p. 1085.
11. Drach, B.S. and Mis'kevich, G.N., *Zh. Org. Khim.*, 1974, vol. 10, no. 11, p. 2315.
12. Drach, B.S., Mis'kevich, G.N., and Martynyuk, A.P., *Zh. Org. Khim.*, 1978, vol. 14, no. 3, p. 508.
13. Golovchenko, A.V., Pil'o, S.G., Brovarets, V.S., Chernega, A.N., and Drach, B.S., *Russ. J. Gen. Chem.*, 2005, vol. 75, no. 3, p. 425.
14. Ainsworth, C., *J. Am. Chem. Soc.*, 1955, vol. 77, no. 5, p. 1148.
15. Matsumura, K., Miyashita, O., Shimadzu, H., and Hashimoto, N., *Chem. Pharm. Bull.*, 1976, vol. 24, no. 5, p. 948.
16. Pil'o, S.G., Brovarets, V.S., Vinogradova, T.K., Golovchenko, A.V., and Drach, B.S., *Russ. J. Gen. Chem.*, 2002, vol. 72, no. 11, p. 1714.