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Amidophenacylating Reagents in Synthesis of New Derivatives of 1,3-Oxazole- and 1,3-Thiazole-4-sulfonyl Chlorides and Corresponding Sulfonamides

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Abstract—Derivatives of 4-benzylsulfanyl-1,3-oxazole and 4-benzylsulfanyl-1,3-thiazole were synthesized using available amidophenacylating reagents. By the oxidative chlorination compounds obtained were converted to 1,3-oxazole-4-sulfonyl and 1,3-thiazol-4-sulfonyl chlorides. The latter were used to prepare the corresponding sulfonamides.

Keywords: 1,3-thiazole, 1,3-oxazole, sulfonyl chlorides, sulfonamides

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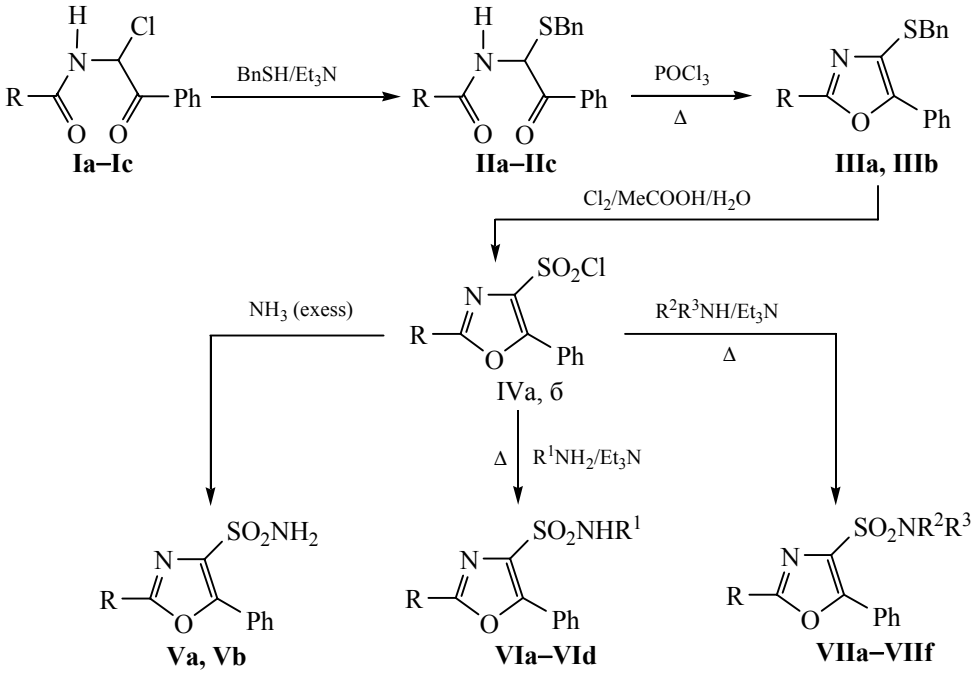
In the past decade, a significant number of natural and synthetic biologically active compounds containing 1,3-oxazole or 1,3-thiazole fragments were prepared [1–5]. It stimulates the studies of reactivity and search for the ways of heterocycles functionnalization. In the present work we developed new methods of the synthesis of 1,3-oxazole- and 1,3-thiazole-4-sulfonyl chlorides as well as the corresponding sulfonamides.

Available amidophenacylating reagents **I**, which are convenient syntons for the preparation of a number of functionally substituted oxazoles and thiazoles [6, 7], were used as starting substrates. 2-Aryl-5-phenyl-4-benzylsulfanyl-1,3-oxazoles **III** were obtained through simple sequence of the reactions **I** → **II** → **III** (Scheme 1). The oxidative chlorination of these compounds (Cl_2, $MeCOOH/H_2O$, 0°C) afforded 2-aryl-5-phenyl-1,3-oxazole-4-sulfonyl chlorides **IV**. The latter were purified by recrystallization from aprotic solvents and stored for a long time without any changes. Treating with excess aqueous ammonia, primary or secondary amines in the presence of triethylamine in dioxane resulted in high yields of the corresponding sulfonamides **V**–**VII**. 1,3-Oxazole-4-sulfonyl chlorides **IV** and 1,3-oxazole-4-sulfonamides **V**–**VII** were synthesized for the first time.

Heating substrates **II** with the Lawesson's reagent in dioxane afforded the thiazole derivatives **VIII** (Scheme 2). The latter were converted into 2-aryl-(methyl)-5-phenyl-1,3-thiazole-4-sulfonyl chlorides **IX** by the action of chlorine in acetic acid. Chlorides **IX** were used to obtain a series of appropriate sulfonamides **X**–**XII**. It should be noted that similar 1,3-thiazole-4-sulfonyl chlorides and 1,3-thiazole-4-sulfonamides have been known [8–17], however 2,5-disubstituted 1,3-thiazole-4-sulfonyl chlorides **IX** and sulfonamides **X**–**XII** we prepared for the first time.

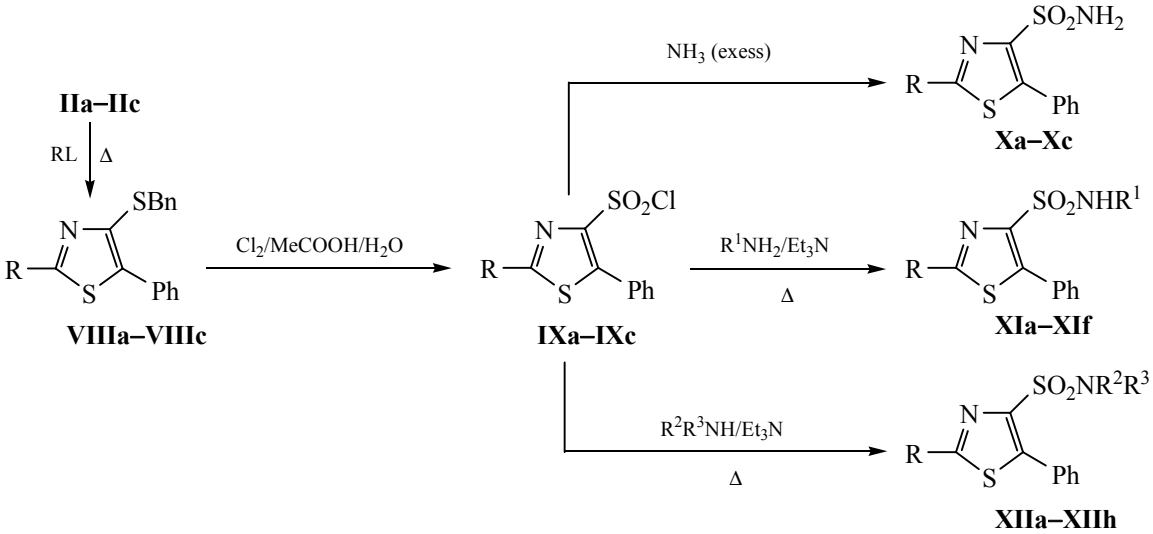
The composition and structure of new compounds were confirmed by elemental analysis (Table 1), IR, ^{1}H and ^{13}C NMR spectra and by LC-MS spectrometry (Table 2). The formation of azole rings as a result of transformations **II** → **III** and **II** → **VIII** was proved by the disappearance of the signals of >CHNH group in ^{1}H NMR spectra and intensive absorption bands in the ranges of 1635–1649 (C=O), 1677–1686 (C=O), and 3256–3396 cm^{-1} (N–H) in the IR spectra and by appearance of the absorption bands at 1143–1384 cm^{-1} belonging to SO_2 group. ^{1}H and ^{13}C NMR spectra of the synthesized compounds contain all the necessary signals. In GC-MS spectra there are peaks corresponding to protonated molecular ions $[M + 1]^+$.

Scheme 1.



R = Ph (**Ia–VIIa, VIc, VIIc, VIIe**), 4-MeC_6H_4 (**Ib–VIIb, VId, VIId, VIIf**), Me (**Ic, IIc**); R^1NH = $PhCH_2NH$ (**VIa, VIb**), PhNH (**VIc, VId**); R^2R^3N = Me_2N (**VIIa, VIIb**), $(CH_2)_5N$ (**VIIc, VIId**), $O(CH_2)_4N$ (**VIIe, VIIf**).

Scheme 2.



R = Ph (**IIa, VIIIa–XIIa, XId, XIIc, XIIf**), 4-MeC_6H_4 (**IIb, VIIIb–XIIb, XIe, XIId, XIIg**), Me (**IIc, VIIIc–XIc, XIf, XIIe, XIIh**); R^1NH = $PhCH_2NH$ (**XIa–XIc**), PhNH (**XId–XIf**); R^2R^3N = Me_2N (**XIIa, XIIb**), $(CH_2)_5N$ (**XIIc–XIIe**), $O(CH_2)_4N$ (**XIIf–XIIh**); RL =

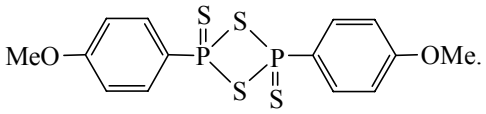


Table 1. Yields, melting points, and elemental analyses of compounds **II–XII**

Comp. no.	Yield, %	mp, °C (solvent for recrystallization)	Found, %		Formula	Calculated, %	
			N	S		N	S
IIa	85	122–123 (MeCN)	3.95	8.81	$C_{22}H_{19}NO_2S$	3.87	8.87
IIb	83	102–104 (EtOH)	3.68	8.51	$C_{23}H_{21}NO_2S$	3.73	8.54
IIc	80	134–135 (EtOH)	4.55	10.73	$C_{17}H_{17}NO_2S$	4.68	10.71
IIIa	70	89–91 (EtOH)	4.00	9.36	$C_{22}H_{17}NOS$	4.08	9.34
IIIb	70	95–96 (EtOH)	3.89	8.95	$C_{23}H_{19}NOS$	3.92	8.97
IVa	75	147–148 (toluene)	4.21	9.94	$C_{15}H_{10}ClNO_3S$[a]	4.38	10.03
IVb	72	102–103 (cyclohexane)	4.12	9.52	$C_{16}H_{12}ClNO_3S$[b]	4.20	9.61
Va	80	248–249 (MeCN)	9.39	10.65	$C_{15}H_{12}N_2O_3S$	9.33	10.68
Vb	81	254–256 (MeCN)	8.93	10.20	$C_{16}H_{14}N_2O_3S$	8.91	10.20
VIa	86	153–154 (MeCN)	7.21	8.21	$C_{22}H_{18}N_2O_3S$	7.17	8.21
VIb	85	175–176 (MeCN)	6.99	7.91	$C_{23}H_{20}N_2O_3S$	6.93	7.93
VIc	85	204–205 (MeCN)	7.41	8.56	$C_{21}H_{16}N_2O_3S$	7.44	8.52
VId	84	213–214 (MeCN)	7.19	8.24	$C_{22}H_{18}N_2O_3S$	7.17	8.21
VIIa	79	129–130 (EtOH)	8.42	9.79	$C_{17}H_{16}N_2O_3S$	8.53	9.76
VIIb	80	126–127 (EtOH)	8.11	9.33	$C_{18}H_{18}N_2O_3S$	8.18	9.36
VIIc	84	100–101 (EtOH)	7.56	8.79	$C_{20}H_{20}N_2O_3S$	7.60	8.70
VIId	84	142–143 (EtOH)	7.27	8.33	$C_{21}H_{22}N_2O_3S$	7.32	8.38
VIIe	87	119–121 (EtOH)	7.58	8.64	$C_{19}H_{18}N_2O_4S$	7.56	8.66
VIIf	87	122–123 (EtOH)	7.31	8.31	$C_{20}H_{20}N_2O_4S$	7.29	8.34
VIIIa	70	88–89 (MeCN)	3.81	17.86	$C_{22}H_{17}NS_2$	3.90	17.84
VIIIb	70	105–106 (MeCN)	3.55	17.25	$C_{23}H_{19}NS_2$	3.75	17.17
VIIIc	65	Oil	4.75	21.52	$C_{17}H_{15}NS_2$	4.71	21.56
IXa	74	131–132 (cyclohexane)	4.02	19.00	$C_{15}H_{10}ClNO_2S_2$[c]	4.17	19.10
IXb	74	121–122 (cyclohexane)	3.35	18.25	$C_{16}H_{12}ClNO_2S_2$[d]	4.00	18.33
IXc	67	98–99 (hexane)	5.02	23.38	$C_{10}H_8ClNO_2S_2$[e]	5.12	23.42
Xa	80	236–237 (MeCN)	8.91	20.21	$C_{15}H_{12}N_2O_2S_2$	8.85	20.27
Xb	80	264–265 (MeCN)	8.52	19.33	$C_{16}H_{14}N_2O_2S_2$	8.48	19.41
Xc	72	148 (EtOH)	11.04	25.21	$C_{10}H_{10}N_2O_2S_2$	11.01	25.21
XIa	85	135–136 (MeCN)	6.92	15.81	$C_{22}H_{18}N_2O_2S_2$	6.89	15.77
XIb	85	158–159 (MeCN)	6.70	15.20	$C_{23}H_{20}N_2O_2S_2$	6.66	15.25
XIc	80	174–175 (MeCN)	8.21	18.57	$C_{17}H_{16}N_2O_2S_2$	8.13	18.62
XId	83	162–163 (MeCN)	7.16	16.31	$C_{21}H_{16}N_2O_2S_2$	7.14	16.34
XIe	83	171–172 (MeCN)	6.84	15.76	$C_{22}H_{18}N_2O_2S_2$	6.89	15.77
XIf	80	199–200 (MeCN)	8.37	19.44	$C_{16}H_{14}N_2O_2S_2$	8.48	19.41
XIIa	80	174–175 (MeCN)	8.10	18.66	$C_{17}H_{16}N_2O_2S_2$	8.13	18.62
XIIb	82	209–210 (MeCN)	7.75	17.87	$C_{18}H_{18}N_2O_2S_2$	7.81	17.89
XIIc	85	135–136 (EtOH)	7.11	16.72	$C_{20}H_{20}N_2O_2S_2$	7.29	16.68
XIId	85	146–147 (MeCN)	7.07	16.04	$C_{21}H_{22}N_2O_2S_2$	7.03	16.09
XIIe	80	131–132 (cyclohexane)	8.57	19.93	$C_{15}H_{18}N_2O_2S_2$	8.69	19.89
XIIf	86	173–174 (MeCN)	7.19	16.59	$C_{19}H_{18}N_2O_3S_2$	7.25	16.59
XIIg	87	132–133 (MeCN)	7.09	16.00	$C_{20}H_{20}N_2O_3S_2$	6.99	16.01
XIIh	80	171–173 (toluene)	8.60	19.71	$C_{14}H_{16}N_2O_3S_2$	8.63	19.77

[a] Found Cl, %: 11.14. Calculated Cl, %: 11.09. [b] Found Cl, %: 10.81. Calculated Cl, %: 10.62. [c] Found Cl, %: 10.72. Calculated Cl, %: 10.56. [d] Found Cl, %: 10.27. Calculated Cl, %: 10.13. [e] Found Cl, %: 13.16. Calculated Cl, %: 12.95.

Table 2. Spectral data for compounds **II–XII**

Comp. no.	IR spectrum (KBr), ν, cm^{-1}	^1H NMR spectrum (DMSO-d_6)[a], δ, ppm	Mass spectrum, *m*/*z*
IIa	1347, 1524; 1635 (C=O), 1686 (C=O); 3297 (NH)	3.86 d, 4.02 d (2H, CH_2S, $^2J_{HH}$ 13.0 Hz), 6.65 d (1H, CH, $^3J_{HH}$ 7.8 Hz), 7.32–7.90 m (15H, $3C_6H_5$), 9.25 d (1H, NH, $^3J_{HH}$ 7.8 Hz)	362 $[M+1]^+$
IIb	1344,1485; 1649 (C=O), 1677 (C=O); 3396 (NH)	2.38 s (3H, CH_3), 3.86 d, 4.02 d (2H, CH_2S, $^2J_{HH}$ 13.0 Hz), 6.63 d (1H, CH, $^3J_{HH}$ 7.8 Hz), 7.27–7.87 m (14H, $2C_6H_5$, C_6H_4), 9.14 d (1H, NH, $^3J_{HH}$ 7.8 Hz)	376 $[M+1]^+$
IIc	1331, 1522; 1647 (C=O), 1684 (C=O); 3256 (NH)	1.97 s (3H, CH_3), 3.79 d, 3.94 d (2H, CH_2S, $^2J_{HH}$ 13.0 Hz), 6.44 d (1H, CH, $^3J_{HH}$ 8.0 Hz), 7.28–7.82 m (10H, $2C_6H_5$), 8.94 d (1H, NH, $^3J_{HH}$ 8.0 Hz)	300 $[M+1]^+$
IIIa[b]	1482, 1552, 1600	4.38 s (2H, CH_2), 7.26–8.13 m (15H, $3C_6H_5$)	344 $[M+1]^+$
IIIb	1495, 1556, 1601	2.40 s (3H, CH_3), 4.36 s (2H, CH_2), 7.19–8.01 m (14H, $2C_6H_5$, C_6H_4)	358 $[M+1]^+$
IVa	1170, 1384 (SO_2); 1487, 1559, 1606	7.28–8.19 m (10H, $2C_6H_5$)	–
IVb	1170, 1393 (SO_2); 1498, 1564, 1611	–	–
Va	1157, 1353 (SO_2); 1487, 1567; 3206, 3336 (NH_2)	7.55–8.11 m (12H, NH_2, $2C_6H_5$)	301 $[M+1]^+$
Vb	1158, 1352 (SO_2); 1496, 1568, 1612; 3198, 3325 (NH_2)	2.41 s (3H, CH_3), 7.42–8.00 m (11H, NH_2, C_6H_5, C_6H_4)	315 $[M+1]^+$
VIa	1155, 1336 (SO_2); 1448, 1485, 1547; 3243 (NH)	4.27 s (2H, CH_2), 7.23–8.08 m (15H, $3C_6H_5$), 8.77 s (1H, NH)	391 $[M+1]^+$
VIb	1151, 1328 (SO_2); 1448, 1493, 1555, 1612; 3148 (NH)	2.42 s (3H, CH_3), 4.27 s (2H, CH_2), 7.25–7.97 m (14H, $2C_6H_5$, C_6H_4), 8.72 s (1H, NH)	405 $[M+1]^+$
VIc	1152, 1343 (SO_2); 1408, 1485, 1554; 3269 (NH)	7.05–8.04 m (15H, $3C_6H_5$), 10.80 s (1H, NH)	377 $[M+1]^+$
VId	1158, 1339 (SO_2); 1413, 1497, 1556, 1612; 3251 (NH)	2.39 s (3H, CH_3), 7.05–7.93 m (14H, $2C_6H_5$, C_6H_4), 10.78 s (1H, NH)	391 $[M+1]^+$
VIIa[c]	1150, 1338 (SO_2); 1449, 1488, 1556	2.94 s (6H, $2CH_3$), 7.57–8.12 m (10H, $2C_6H_5$)	329 $[M+1]^+$
VIIb	1155, 1347 (SO_2); 1449, 1499, 1557, 1612	2.41 s (3H, CH_3), 2.93 s (6H, $2CH_3$), 7.40–7.99 m (9H, C_6H_5, C_6H_4)	343 $[M+1]^+$
VIIc	1165, 1336 (SO_2); 1447, 1488, 1554	1.48–1.59 m (6H, $3CH_2$, piperidine), 3.28–3.33 m (4H, $2CH_2$, piperidine), 7.57–8.12 m (10H, $2C_6H_5$)	369 $[M+1]^+$
VIId	1162, 1351 (SO_2); 1442, 1498, 1561, 1614	1.47–1.55 m (6H, $3CH_2$, piperidine), 2.38 s (3H, CH_3), 3.27–3.37 m (4H, $2CH_2$, piperidine), 7.41–8.00 m (9H, C_6H_5, C_6H_4)	383 $[M+1]^+$
VIIe	1157, 1344 (SO_2); 1448, 1487, 1555	3.30–3.33 m (4H, $2CH_2$, morpholine), 3.67–3.70 m (4H, $2CH_2$, morpholine), 7.57–8.13 m (10H, $2C_6H_5$)	371 $[M+1]^+$
VIIf	1160, 1345 (SO_2); 1455, 1497, 1556, 1615	2.42 s (3H, CH_3), 3.31–3.34 m (4H, $2CH_2$, morpholine), 3.66–3.69 m (4H, $2CH_2$, morpholine), 7.41–8.00 m (9H, C_6H_5, C_6H_4)	385 $[M+1]^+$
VIIIa	1436, 1451, 1465, 1497, 1595	4.49 s (2H, CH_2), 7.21–8.02 m (15H, $3C_6H_5$)	360 $[M+1]^+$
VIIIb[d]	1413, 1450, 1468, 1493, 1596	2.39 s (3H, CH_3), 4.49 s (2H, CH_2), 7.29–7.90 m (14H, $2C_6H_5$, C_6H_4)	374 $[M+1]^+$
IXa	1161, 1383 (SO_2); 1441, 1464	7.51–8.03 m (10H, $2C_6H_5$)	–

Table 2. (Contd.)

Comp. no.	IR spectrum (KBr), ν, cm^{-1}	^1H NMR spectrum (DMSO-d_6)[a], δ, ppm	Mass spectrum, *m*/*z*
IXb	1157, 1372 (SO_2); 1463	–	–
IXc	1168, 1384 (SO_2); 1466, 1498	2.81 s (3H, CH_3), 7.48–7.53 m (5H, C_6H_5)	–
Xa	1146, 1334 (SO_2); 1439, 1457, 1470; 3222, 3333 (NH_2)	7.49–8.03 m (12H, NH_2, $2C_6H_5$)	317 $[M+1]^+$
Xb	1151, 1347 (SO_2); 1455, 1472, 1566; 3192, 3350 (NH_2)	2.37 s (3H, CH_3), 7.38–7.92 m (11H, NH_2, C_6H_5, C_6H_4)	331 $[M+1]^+$
Xc	1149, 1346 (SO_2); 1442, 1469, 1492, 1555; 3282, 3346 (NH_2)	2.71 s (3H, CH_3), 7.43–7.55 m (7H, NH_2, C_6H_5)	255 $[M+1]^+$
XIa	1145, 1325 (SO_2); 1427, 1455, 1469; 3294 (NH)	4.29 s (2H, CH_2), 7.25–7.98 m (15H, $3C_6H_5$), 8.62 s (1H, NH)	407 $[M+1]^+$
XIb	1143, 1340 (SO_2); 1408, 1454, 1470; 3308 (NH)	2.41 s (3H, CH_3), 4.29 s (2H, CH_2), 7.21–7.87 m (14H, $2C_6H_5$, C_6H_4), 8.58 s (1H, NH)	421 $[M+1]^+$
XIc	1145, 1338 (SO_2); 1420, 1443, 1499; 3290 (NH)	2.67 s (3H, CH_3), 4.16 s (2H, CH_2), 7.22–7.52 m (10H, $2C_6H_5$), 8.47 s (1H, NH)	345 $[M+1]^+$
XId	1148, 1349 (SO_2); 1408, 1474, 1502, 1598; 3241 (NH)	7.15–7.92 m (15H, $3C_6H_5$), 10.65 s (1H, NH)	393 $[M+1]^+$
XIe	1149, 1348 (SO_2); 1412, 1457, 1473, 1494, 1597; 3241 (NH)	2.38 s (3H, CH_3), 7.16–7.80 m (14H, $2C_6H_5$, C_6H_4), 10.62 s (1H, NH)	407 $[M+1]^+$
XIf	1155, 1356 (SO_2); 1426, 1487, 1595; 3127 (NH)	2.67 s (3H, CH_3), 7.03–7.46 m (10H, $2C_6H_5$), 10.49 s (1H, NH)	331 $[M+1]^+$
XIIa	1145, 1352 (SO_2); 1440, 1459	2.95 s (6H, $2CH_3$), 7.51–8.07 m (10H, $2C_6H_5$)	345 $[M+1]^+$
XIIb[e]	1145, 1352 (SO_2); 1460	2.41 s (3H, CH_3), 2.92 s (6H, $2CH_3$), 7.38–7.89 m (9H, C_6H_5, C_6H_4)	359 $[M+1]^+$
XIIc	1166, 1334 (SO_2); 1440, 1455, 1470	1.50–1.58 m (6H, $3CH_2$, piperidine), 3.30–3.34 m (4H, $2CH_2$, piperidine), 7.51–8.00 m (10H, $2C_6H_5$)	385 $[M+1]^+$
XIId	1158, 1343 (SO_2); 1473	1.52–1.57 m (6H, $3CH_2$, piperidine), 2.40 s (3H, CH_3), 3.29–3.33 m (4H, $2CH_2$, piperidine), 7.40–7.89 m (9H, C_6H_5, C_6H_4)	399 $[M+1]^+$
XIIe	1146, 1344 (SO_2); 1442, 1470, 1500	1.47–1.53 m (6H, $3CH_2$, piperidine), 2.72 s (3H, CH_3), 3.17–3.33 m (4H, $2CH_2$, piperidine), 7.46–7.50 m (5H, C_6H_5)	323 $[M+1]^+$
XIIf	1157, 1356 (SO_2); 1442, 1458	3.27–3.31 m (4H, $2CH_2$, morpholine), 3.65–3.68 m (4H, $2CH_2$, morpholine), 7.52–8.01 m (10H, $2C_6H_5$)	387 $[M+1]^+$
XIIg	1158, 1356 (SO_2); 1452	2.40 s (3H, CH_3), 3.30–3.34 m (4H, $2CH_2$, morpholine), 3.67–3.70 m (4H, $2CH_2$, morpholine), 7.38–7.89 m (9H, C_6H_5, C_6H_4)	401 $[M+1]^+$
XIIh	1157, 1350 (SO_2); 1451, 1499	2.74 s (3H, CH_3), 3.18–3.22 m (4H, $2CH_2$, morpholine), 3.60–3.64 m (4H, $2CH_2$, morpholine), 7.46–7.51 m (5H, C_6H_5)	325 $[M+1]^+$

[a] ^1H NMR spectra of **IVa, IXa, IXc** were recorded in $CDCl_3$. [b] ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 37.59 (SCH_2), 125.61, 126.65, 126.68, 127.63, 127.69, 128.85, 128.92, 129.33, 129.70, 130.41, 131.54, 138.21, 147.89 (C^4, oxazoline), 159.76 (C^2, oxazoline). [c] ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 38.46 [$N(CH_3)_2$], 126.00, 126.15, 127.06, 128.97, 129.12, 129.78, 131.06, 132.19, 134.34 (C^4, oxazoline), 151.95, 159.71 (C^2, oxazoline). [d] ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 21.51 (CH_3), 37.86 (SCH_2), 126.39, 127.55, 128.72, 128.83, 128.99, 129.33, 130.36, 130.42, 130.95, 131.67, 138.65, 141.13, 144.14 (C^4, oxazoline), 165.26 (C^2, oxazoline). [e] ^{13}C NMR spectrum (DMSO-d_6), δ_C, ppm: 21.54 (CH_3), 38.65 [$N(CH_3)_2$], 126.66, 128.89, 129.57, 130.10, 130.53, 141.94, 142.06, 146.62, 155.41 (C^4, oxazoline), 166.35 (C^2, oxazoline).

Some 1,3-thiazole-4-sulfonamides were screened for anticancer activity within the International Scientific Program of the National Cancer Institute (USA) [18–21]. The screening was performed *in vitro* at 60 cancer cell lines under the action of the substance in a concentration of 1×10^{-5} M, whereby the cancer cells growth index (GI) was determined in comparison with reference (100%). Among the investigated compounds, sulfonamide **XIb** showed moderate activity as inhibitor of the growth of leukemia cell lines (K-562, GI = 43.77%; MOLT-4, GI = 44.21%), prostate cancer (PS-3, GI = 40.44%), breast cancer (T-47D, GI = 42.51%); sulfonamide **XId** showed moderate activity as inhibitor of the growth of leukemia cell lines (RPMI, GI = 48.16%), lung cancer (A549/ATCC, GI = 48.18%), intestines cancer (HCT-116, GI = 31.46%), breast cancer (T-47D, GI = 46.42%) and a significant activity against renal cancer lines (UO-31 , GI = –56.83%).

In summary, starting from available amidophenacylating reagents we have developed new methods for the synthesis of 1,3-oxazole- and 1,3-thiazole-4-sulfonyl chlorides and sulfonamides, which are potential bioactive compounds.

EXPERIMENTAL

IR spectra were recorded on a Vertex 70 instrument from KBr pellets. ^{1}H and ^{13}C NMR spectra were obtained on a Bruker AVANCE DRX-500 spectrometer operating at 500 and 125 MHz, respectively, internal reference TMS. LC-MS spectra were registered on an Agilent 1100 Series HPLC chromatograph equipped with a diode array with a mass selective detector Agilent LC\MSD SL. GC-MS analysis parametersare as follows: column Zorbax SB-C18, 1.18 μm, 4.6 × 15 mm (PN 821975-932); acetonitrile–water (95 : 5), 0.1% aqueous trifluoroacetic acid, flow rate of the eluent 3 mL min^{-1}, injection volume 1 μL; UV detecting at 215, 254, 285 nm; chemical ionization at atmospheric pressure (APCI), scan range *m*/*z* 80–1000. Melting points were measured on a Fisher-Johns instrument.

Carboxylic acids *N*-(1-benzylsulfanyl-2-oxo-2-phenylethyl)amides (IIa–IIc). To a solution of 0.05 mol of compound **Ia–Ic** [6, 22] in 200 mL of anhydrous acetonitrile were added benzylthiol (0.05 mol) and Et_3N (0.05 mol). The mixture was refluxed and then maintained at 20–25°C for 12 h. To the solution was added 400 mL of water. The precipitate was filtered off, dried, and purified by recrystallization.

2-Aryl-4-benzylsulfanyl-5-phenyl-1,3-oxazoles (IIIa, IIIb). A solution of 0.025 mol of compound **IIa** or **IIb** in 30 mL of $POCl_3$ was refluxed for 5 h, then maintained at 20–25°C for 12 h and poured into ice. The formed precipitate was filtered off, dried, and purified by recrystallization.

2-Aryl-5-phenyl-1,3-oxazole-4-sulfonyl chlorides (IVa, IVb). To a solution of 0.01 mol of compound **IIIa** or **IIIb** in 30 mL of 95% acetic acid was bubbled at stirring Cl_2 for 0.5 h maintaining the reaction temperature in the range of 0–5°C. Then the mixture was maintained at this temperature for 12 h and poured into ice. The formed precipitate was filtered off, dried in a vacuum desiccator over phosphorus pentoxide and purified by recrystallization.

2-Aryl-5-phenyl-1,3-oxazole-4-sulfonamides (Va, Vb). To a solution (50 mL) of 25% aqueous ammonia while stirring and cooling with ice water was added dropwise a solution of 0.005 mol of compound **IVa** or **VIb** in 15 mL of anhydrous dioxane. The slurry was stirred at 20–25°C for 0.5 h. The formed precipitate was filtered off, dried, and purified by recrystallization.

2-Aryl-*N*-benzyl(phenyl)-5-phenyl-1,3-oxazole-4-sulfonamides (VIa–VId). To a solution of 0.005 mol of sulfonyl chloride **IVa** or **IVb** in 15 mL of anhydrous dioxane was added 0.005 mol of the appropriate amine (benzylamine or aniline) and 0.005 mol of Et_3N. The mixture was refluxed for 2 h, and then maintained at 20–25°C for 12 h. The solvent was removed in a vacuum, and the residue was treated with water. The formed precipitate was filtered off, dried, and purified by recrystallization.

2-Aryl-*N*,*N*-dimethyl-5-phenyl-1,3-oxazole-4-sulfonamides (VIIa, VIIb). To 50 mL of 40% aqueous dimethylamine with stirring and cooling with ice water was added a solution of 0.005 mol of compound **IVa** or **IVb** in 15 mL of anhydrous dioxane. The slurry was stirred at 20–25°C for 0.5 h, and the formed precipitate was filtered off, dried and purified by recrystallization.

2-Aryl-*N*,*N*-R^1R^2-5-phenyl-1,3-oxazole-4-sulfonamides (VIIc–VIIf) were prepared similarly to compounds **VIa–VId** from **IVa** or **IVb** and morpholine or piperidine.

2-Aryl(methyl)-4-benzylsulfanyl-5-phenyl-1,3-thiazoles (VIIIa–VIIIc). A mixture of 0.025 mol of compound **IIa–IIc** and 0.025 mol of the Lawesson's

reagent in 120 mL of anhydrous dioxane was refluxed for 8 h, and then maintained at 20–25°C for 12 h. The solvent was removed in a vacuum. The residue was treated with 5% aqueous sodium hydroxide solution. The precipitate was filtered off and dried. Compounds **VIIIa, VIIIb** were purified by recrystallization. Compound **VIIIc** was extracted with chloroform, the extract was dried over anhydrous magnesium sulfate and concentrated in a vacuum to afford **VIIIc** which was used in the next steps without further purification.

2-Aryl(methyl)-5-phenyl-1,3-thiazole-4-sulfonyl chlorides (IXa–IXc) were prepared similarly to compounds **IVa, IVb** from corresponding thiazoles **VIIIa–VIIIc**.

2-Aryl(methyl)-5-phenyl-1,3-thiazole-4-sulfonamides (Xa–Xc) were prepared similarly to compounds **Va, Vb** from corresponding sulfonyl chlorides **IXa–IXc** and aqueous ammonia solution.

2-Aryl(methyl)-*N*-benzyl(phenyl)-5-phenyl-1,3-thiazole-4-sulfonamides (XIa–XIf) were prepared similarly to compounds **VIa–VId** from corresponding sulfonyl chlorides **IXa–IXc** and benzylamine or aniline.

2-Aryl-*N*,*N*-dimethyl-5-phenyl-1,3-thiazole-4-sulfonamides (XIIa, XIIb) were prepared similarly to compounds **VIIa, VIIb** from corresponding sulfonyl chlorides **IXa, IXb** and dimethylamine aqueous solution.

2-Aryl(methyl)-*N*,*N*-R^1R^2-5-phenyl-1,3-thiazole-4-sulfonamides (XIIc–XIIh) were prepared similarly to compounds **VIa–VId** from corresponding sulfonyl chlorides **IXa–IXc** and piperidine or morpholine.

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