ISSN 1070-3632, Russian Journal of General Chemistry, 2017, Vol. 87, No. 3, pp. 407–413. © Pleiades Publishing, Ltd., 2017.
Original Russian Text © R.N. Solomyannii, S.G. Pil'o, S.R. Slivchuk, V.M. Prokopenko, E.B. Rusanov, V.S. Brovarets, 2017, published in Zhurnal Obshchei Khimii, 2017, Vol. 87, No. 3, pp. 398–404.

Synthesis of 5-Methylsulfonylpyrimidines and Their Fused Derivatives

R. N. Solomyannii[a], S. G. Pil'o[a], S. R. Slivchuk[a], V. M. Prokopenko[a], E. B. Rusanov[b], and V. S. Brovarets[a]*

[a] *Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences of Ukraine, ul. Murmanskaya 1, Kiev, 02660 Ukraine*
**e-mail: brovarets@bpci.kiev.ua*

[b] *Institute of Organic Chemistry, National Academy of Sciences of Ukraine, Kiev, Ukraine*

Received September 29, 2016

Abstract—The interaction of available 2-methylsulfonyl-3-ethoxyacrylonitrile with amidine, their analogs, and aminoazoles containing amidine fragment, yielding earlier unknown 4-amino-5-methylsulfonylpyrimidines and their fused derivatives has been studied.

Keywords: 2-methylsulfonyl-3-ethoxyacrylonitrile, aminoazole, 4-amino-5-methylsulfonylpyrimidine, imidazo-[1,2-*a*]pyrimidine, pyrazolo[1,5-*a*]pyrimidine, heterocyclization

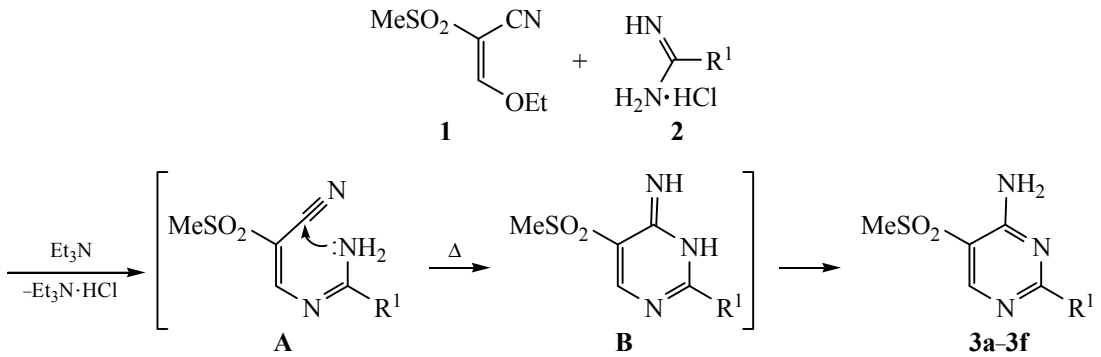
DOI: 10.1134/S1070363217030082

Pyrimidine derivatives play important part in biochemical processes in living organisms [1–4] and exhibit a wide range of biological activity [5–9]. Methylsulfonyl group is found in certain natural compounds [10–15]; therefore, its introduction in pyrimidine molecule leads to various biological activity of the resulting derivatives [16–20].

This work aimed to study the interaction of available 2-methylsulfonyl-3-ethoxyacrylonitrile **1** [21] with amidines, their analogs, and aminoazoles in order to prepare novel 5-methylsulfonylpyrimidines and their fused derivatives. We observed that substrate **1** reacts with amidines **2** on reflux in ethanol in the presence of triethylamine to form 4-amino-2-aryl(arylthio)-5-methylsulfonylpyrimidines **3a–3f** (Scheme 1). Most probably, the transformation scheme includes initial substitution of ethoxy group yielding intermediate **A** (cf. [22, 23]), followed by intramolecular heterocyclization **A→B** and isomerization into the target products **3**.

Composition and structure of pyrimidines **3a–3f** were confirmed by elemental analysis (Table 1), IR, ^{1}H NMR, and ^{13}C NMR spectroscopy, and chromato–mass spectrometry (Table 2) data. IR spectra of the

Scheme 1.



A **B** **3a**–**3f**

R^1 = Ph (**a**), 4-FC_6H_4 (**b**), 4-$MeOC_6H_4$ (**c**), PhS (**d**), 4-MeC_6H_4S (**e**), 4-$MeOC_6H_4S$ (**f**).

Table 1. Yields, melting points, and elemental analysis data of compounds **3**, **5**, **7**, **9**

Comp. no.	Yield, %	mp, °C	Found, %				Formula	Calculated, %			
			C	H	N	S		C	H	N	S
3a[a]	65	185–187 (EtOH)	53.08	4.40	16.69	12.96	$C_{11}H_{11}N_3O_2S$	53.01	4.42	16.86	12.86
3b	53	185–186 (EtOH)	49.60	3.71	15.91	12.14	$C_{11}H_{10}FN_3O_2S$	49.62	3.76	15.72	12.00
3c	55	187–188 (EtOH)	51.55	4.66	15.18	11.35	$C_{12}H_{13}N_3O_3S$	51.61	4.66	15.04	11.48
3d	57	209–210 (EtOH)	46.94	3.90	15.05	22.63	$C_{11}H_{11}N_3O_2S_2$	46.98	3.91	14.93	22.79
3e	69	213 (decomp.) (EtOH)	48.80	4.45	14.39	21.51	$C_{12}H_{13}N_3O_2S_2$	48.81	4.41	14.23	21.71
3f	79	215 (decomp.) (EtOH)	48.40	4.37	13.57	20.43	$C_{12}H_{13}N_2O_3S_2$	48.48	4.38	13.49	20.59
5a	73	202–203 (dioxane)	39.60	3.70	26.55	15.02	$C_7H_8N_4O_2S$	39.62	3.77	26.40	15.11
5b	60	205–206 (dioxane)	42.53	4.35	24.85	14.05	$C_8H_{10}N_4O_2S$	42.48	4.42	24.76	14.17
7	70	>250 (dioxane)	39.52	3.70	26.29	15.23	$C_7H_8N_4O_2S$	39.62	3.77	26.40	15.11
9	90	>250 (dioxane)	50.33	3.90	21.50	12.11	$C_{11}H_{10}N_4O_2S$	50.38	3.82	21.36	12.22

[a] mp 188–189°C [16].

Table 2. Spectral parameters of compounds **3**, **5**, **7**, **9**

Comp. no.	ν, cm^{-1}	δ, ppm	*m*/*z*, $[M + 1]^+$
3a[a,b]	1142, 1277 (SO_2); 1418, 1440, 1470, 1569, 1625, 3123, 3269, 3456	3.25 s (3H, CH_3), 7.10 br.s (1H, NH), 7.47–7.64 m (3H, C_6H_5), 8.22 br.s (1H, NH), 8.32–8.40 m (2H, C_6H_5), 8.68 s (1H, CH)	250
3b	1140, 1282 (SO_2); 1226, 1418, 1571, 1601, 1631, 3080, 3418, 3446	3.30 s (3H, CH_3), 7.14 br.s (1H, NH), 7.30–7.39 m (2H, C_6H_4), 8.24 br.s (1H, NH), 8.45–8.46 m (2H, C_6H_4), 8.67 s (1H, CH)	268
3c	1145, 1247 (SO_2); 1403, 1535, 1562, 1634, 3358, 3460	3.27 s (3H, CH_3), 3.86 s (3H, CH_3O), 7.00 br.s (1H, NH), 7.08 d (2H, C_6H_4, *J* = 8.5 Hz), 8.10 br.s (1H, NH), 8.34 d (2H, C_6H_4, *J* = 8.5 Hz), 8.63 m (1H, CH)	280
3d	1126, 1282 (SO_2); 1357, 1458, 1529, 1562, 1629, 3344, 3453	3.23 s (3H, CH_3), 7.06 br.s (1H, NH), 7.48–7.62 m (5H, C_6H_5), 8.19 br.s (1H, NH), 8.31 s (1H, CH)	282
3e[c]	1128, 1283 (SO_2); 1528, 1562, 1634, 3344, 3442	2.37 s (3H, CH_3), 3.23 s (3H, CH_3), 7.03 br.s (1H, NH), 7.27 d (2H, C_6H_4, *J* 8.5 Hz), 7.46 d (2H, C_6H_4, *J* = 8.5 Hz), 8.17 br.s (1H, NH), 8.29 s (1H, CH)	296
3f	1127, 1285 (SO_2); 1249, 1528, 1564, 1632, 3340, 3445	3.23 s (3H, CH_3), 3.82 s (3H, CH_3O), 7.02 d (2H, C_6H_4, *J* = 8.5 Hz), 7.19 br.s (1H, NH), 7.50 d (2H, C_6H_4, *J* = 8.5 Hz), 8.15 br.s (1H, NH), 8.29 s (1H, CH)	312
5a[d]	1130, 1290 (SO_2); 1199, 1311, 1458, 1495, 1586, 1637, 1680, 3129, 3333, 3456	3.32 s (3H, CH_3), 6.61 s (1H, CH), 8.28 s (1H, CH), 8.40 br.s (2H, NH_2), 8.41 s (1H, CH)	213
5b[e]	1118, 1293 (SO_2); 1223, 1563, 1603, 1641, 3006, 3413	2.45 s (3H, CH_3), 3.37 s (3H, CH_3), 6.43 s (1H, CH), 8.35 s (1H, CH), 8.40 br.s (2H, NH_2)	227
7[f]	1127, 1292 (SO_2); 1560, 1578, 1662, 3128, 3393	3.28 s (3H, CH_3), 7.63 s (1H, CH), 8.17 s (1H, CH), 8.40 br.s (2H, NH_2), 8.41 s (1H, CH)	213
9	1124, 1288 (SO_2); 1212, 1420, 1452, 1569, 1606, 1637, 3173, 3420	3.33 s (3H, CH_3), 7.39–7.58 m (7H, CH, C_6H_4, NH_2)	263

[a] IR spectrum, ν, cm^{-1}: 1410, 1530, 1560, 1620, 3100, 3440 [16]. ^{1}H NMR spectrum, δ, ppm: 3.23 s (3H, CH_3), 7.52–8.18 m (7H, C_6H_5, NH_2), 8.68 s (1H) [16]. [b] ^{13}C NMR spectrum, δ_C, ppm: 43.4 (SO_2CH_3), 113.9 (C^5), 128.8 (CH_{Ar}), 129.1 (CH_{Ar}), 132.1 (CH_{Ar}), 136.9 (C_{Ar}), 158.4 (C^6H), 159.7 (C^4), 166.7 (C^2). [c] ^{13}C NMR spectrum, δ_C, ppm: 21.2 (CH_3), 43.5 (SO_2CH_3), 112.7 (C^5), 125.5 (C_{Ar}), 130.4 (CH_{Ar}), 135.6 (CH_{Ar}), 139.7 (C_{Ar}), 157.9 (C^6H), 158.9 (C^4), 175.9 (C^2). [d] ^{13}C NMR spectrum, δ_C, ppm: 44.9 (SO_2CH_3), 97.7 (C^3H), 100.3 (C^6), 146.7 (C^5H), 147.0 (C^{3a}), 149.1 (C^2H), 149.5 (C^7). [e] ^{13}C NMR spectrum, δ_C, ppm: 14.9 (CH_3), 44.9 (SO_2CH_3), 97.7 (C^3H), 100.0 (C^6), 146.4 (C^{3a}), 149.0 (C^5H), 150.1 (C^7), 156.4 (C^2). [f] ^{13}C NMR spectrum, δ_C, ppm: 44.6 (SO_2CH_3), 100.5 (C^6), 109.3 (C^3H), 134.6 (C^2H), 147.7 (C^5), 149.8 (C^{8a}), 150.1 (C^7H).

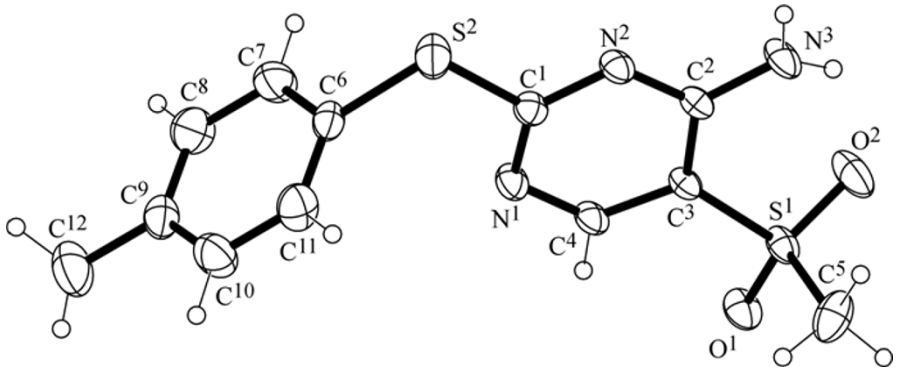


Fig. 1. General view of molecule of compound **3e** (thermal ellipsoids with 30% probability, hydrogen atoms omitted).

products contained the absorption bands at 1126–1145 and 1247–1285 cm^{-1} assigned to symmetric and asymmetric stretching of SO_2 group and the bands at 3269–3460 cm^{-1} corresponding to NH_2 stretching. The absence of the nitrile band evidenced the participation of that group in cyclization.

^{1}H NMR spectra of compounds **3a–3f** did not contain the signal of the EtO fragment but contained two broadened singlets at δ 7.02–7.14 and 8.15–8.27 ppm assigned to amino group. ^{13}C NMR spectra contained the expected signals of carbon atoms. On top of that, product **3a** has been earlier prepared via a different route [24], and its constants were identical to those of the **1**→**3a** transformation product.

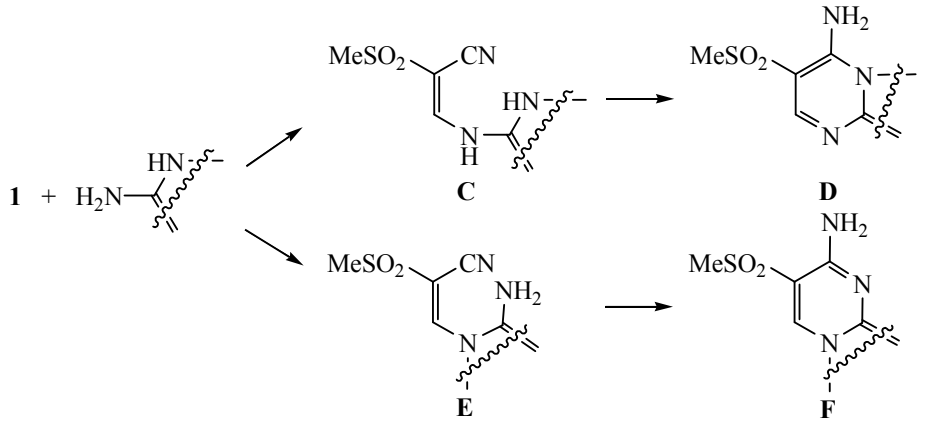
To unambiguously elucidate the structure of compounds **3**, we performed X-ray diffraction analysis of one of them (**3e**). General view of its molecule is shown in Fig. 1, and the basic geometry parameters are collected in Table 3. The bond lengths and angles in the central pyrimidine cycle fell within the expected ranges and coincided with the suggested structure of the compound. In detain, the transannular bonds were delocalized, and their lengths were typical of the delocalized structures. The pyrimidine cycle was planar, the mean square deviation of the atoms off the plane being as low as 0.0113 Å, the S^1, S^2, and N^3 atoms deviated from the plane by 0.1594(30), 0.0680(29), and –0.0652(34) Å, respectively, and the phenyl cycle C^6–C^{11} was rotated with respect to the plane by 84.76(7)°. The C^2–N^3 bond, 1.334(3) Å, was strongly shortened as compared to the length typical of the ordinary C–N bonds (1.45 Å), whereas the sum of bond angles at the amino group nitrogen atom equaled 359(3)°, evidencing the efficient conjugation of the lone-electron pair of the N^3 atom with the heterocycle π-system. Intramolecular (N^3–$H^1\cdots O^2$) as well as intermolecular (N^3–$H^2\cdots O^{1\#1}$ and N^3–$H^1\cdots O^{2\#2}$) hydrogen bonds with the following parameters were formed in the crystal: N^3–H^1 0.85(3), $N^3\cdots O^2$ 2.978(3) Å, $N^3H^1O^2$ 128(3)°; N^3–H^2 0.82(2), $N^3\cdots O^{1\#1}$ 3.038(3) Å, $N^3H^2O^{1\#1}$ 167(2)° and N^3–H^1 0.85(3)°, $N^3\cdots O^{2\#2}$ 2.958(3) Å, $N^3H^1O^{2\#2}$ 147(3)° (the #1 and #2 symbols denote the atoms related to the basic ones via the symmetry operations *x*, –*y* – 0.5, *z* – 0.5 and –*x* + 1, –*y* – 1, –*z*, respectively).

Aiming to prepare fused derivatives of 5-methylsulfonylpyrimidines annulated via the bond *a*, we studied the interaction of 2-methylsulfonyl-3-ethoxyacrylonitrile **1** with aminoazoles: 5-amino-3-R-1*H*-pyrazoles **4**, 2-amino-1*H*-imidazole **6**, and 2-amino-1*H*-benzimidazole **8**, containing three labile hydrogen atoms (Scheme 2). The reactions occurred on refluxing the equimolar amounts of the reagents and triethylamine in dioxane. In contrast to the expected cyclocon-

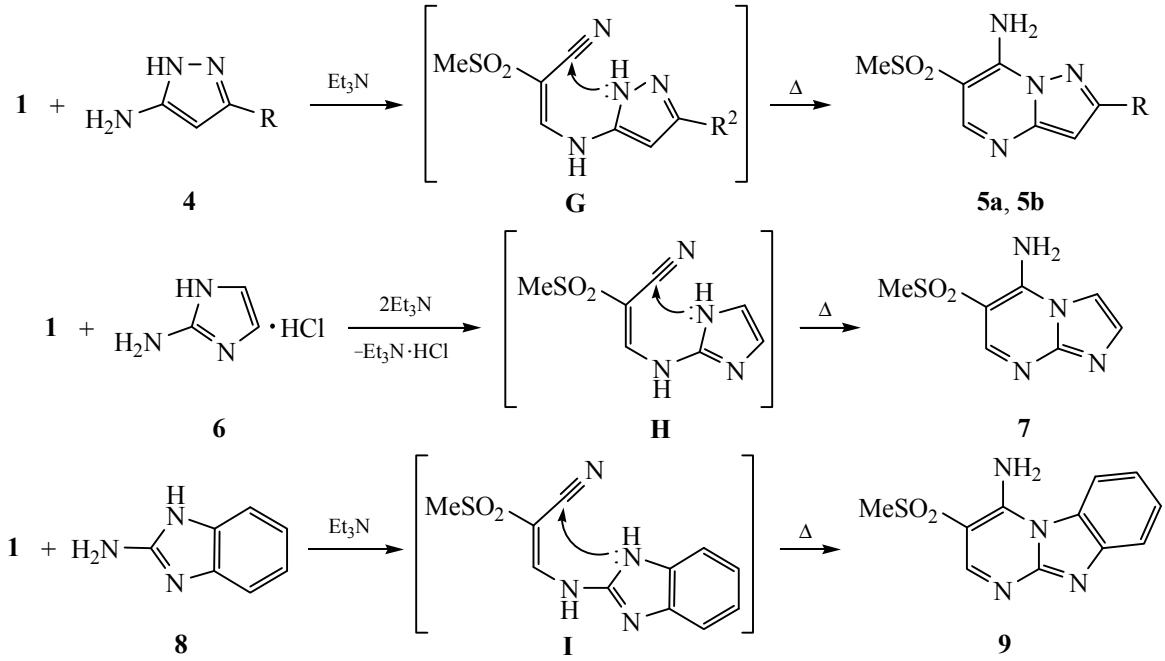
Table 3. Major bond lengths and bond angles in molecule of compound **3e**

Bond length	*d*, Å	Bond angle	ω, deg
C^1–N^1	1.334(3)	$N^2C^1N^1$	128.0(2)
C^1–N^2	1.332(3)	$C^1N^2C^2$	117.31(19)
C^2–N^2	1.345(3)	$N^2C^2C^3$	119.23(19)
C^2–C^3	1.419(3)	$C^4C^3C^2$	116.9(2)
C^3–C^4	1.373(3)	$N^1C^4C^3$	124.6(2)
C^4–N^1	1.328(3)	$C^4N^1C^1$	113.92(19)
C^2–N^3	1.334(3)	$C^3S^1C^5$	104.17(12)
C^1–S^2	1.754(2)	$C^1S^2C^6$	103.25(11)
C^6–S^2	1.771(2)		
C^3–S^1	1.742(2)		
C^5–S^1	1.743(3)		

Scheme 2.



Scheme 3.



R = H (**a**), Me (**b**).

densation **1**→**3**, the initial pathway of the interaction between compound **1** and the aminoazoles could involve the primary amino group as well as the cyclic nitrogen atom, resulting in the formation of intermediates **C** and **E** that would afford linear (**D**) or angular (**F**) products.

According to the data in [25–27], the **1**→**C**→**D** path involving the formation of intermediates **G**, **H**, and **I** (Scheme 3) should be preferred. The latter intermediates, rapidly cyclizing in the fused systems **5**, **7**, and **9**, were not isolated.

Composition and structure of compounds **5**, **7**, and **9** were confirmed by the data of elemental analysis, spectroscopy, and X-ray diffraction. The IR spectroscopy data confirmed the disappearance of the CN group during the heterocyclization and the presence of SO_2 and NH_2 groups in the reaction products. The ^1H NMR spectra contained the signal of the NH_2 group at 8.40–8.75 ppm, coinciding the reference data for similar systems [26, 27].

Structure of compound **5a** was unambiguously elucidated by means of X-ray diffraction. General view

of the molecule is shown in Fig. 2, and the basic geometry parameters are collected in Table 4. The central bicyclic fragment $N^1N^2N^4C^{1-6}$ was planar within 0.006 Å. The distribution of bond lengths and angles evidenced delocalization of electronic density in the heterocyclic scaffold. The C^6–N^3 bond (1.315 Å) was strongly shortened as compared to the length typical of the C–N ordinary bond (1.45 Å), and the sum of bond angles at the nitrogen atom was 360(3)°, pointing at conjugation of the lone-electron pair of the N^3 atom of the amino group with π-system of the heterocycle. It is interesting that the S–C bond lengths were identical within the experimental accuracy (1.740 Å). Intermolecular (N^3–$H^{32}\cdots O^{1A}$) as well as strong intramolecular (N^3–$H^{31}\cdots O^2$) bonds with the following parameters were observed in the crystal: N^3–H^{32} 0.90(3), $N^3\cdots O^{1A}$ 2.925(3) Å, $N^3H^{32}O^{1A}$ 147(3)°; N^3–H^{31} 0.82(3), $N^3\cdots O^2$ 2.794(3) Å, $N^3H^{31}O^2$ 132(3)°. The "A" sign denotes the atom related with the basic ones via the following symmetry operation: $x + 1$, y, z.

In summary, the interaction of 2-methylsulfonyl-3-ethoxyacrylonitrile with amidines and their analogs yielded 4-amino-5-methylsulfonylpyrimidines. The reactions of the same substrate with aminoazoles (5-amino-3-R-1*H*-pyrazoles, 2-amino-1*H*-imidazole, and 2-amino-1*H*-benzimidazole) occurred regioselectively to afford 7-amino-6-(methylsulfonyl)pyrazolo[1,5-*a*]-pyrimidines, 5-amino-6-(methylsulfonyl)imidazo[1,2-*a*]pyrimidine, and 4-amino-3-(methylsulfonyl)pyrimido[1,2-*a*]benzimidazole. These products are interesting in view of further modification and screening for biologically active compounds.

EXPERIMENTAL

^{1}H and ^{13}C NMR spectra were recorded using a Varian Mercury instrument (400 and 100 MHz) in DMSO-d_6 with TMS as internal reference. IR spectra were recorded using a Vertex-70 spectrometer (KBr pellets). Chromato–mass spectra were recorded using an Agilent 1100 Series chromatograph equipped with a diode matrix and an Agilent LC\MSD SL mass-selective detector. Parameters of the analysis: column Zorbax SB-C18, 1.8 μm, 4.6×15 mm; solvents: MeCN–H_2O, 95 : 5, 0.1% CF_3COOH (A); 0.1% aqueous CF_3COOH (B); eluent flow rate 3 mL/min, injected volume 1 μL, UV detectors 215, 254, and 285 nm, chemical ionization at atmospheric pressure. Elemental analysis was performed at Laboratory of Analytical Chemistry, Institute of Bioorganic Chemistry and Petrochemistry, National Academy of Sciences of Ukraine. Contents of carbon and hydrogen were determined using gravimetric Pregl method, content of nitrogen was determined using gasometric Dumas micromethod, and sulfur content was determined using titrimetric Schoeniger method [28]. Melting points were determined using a Fisher–Johns instrument.

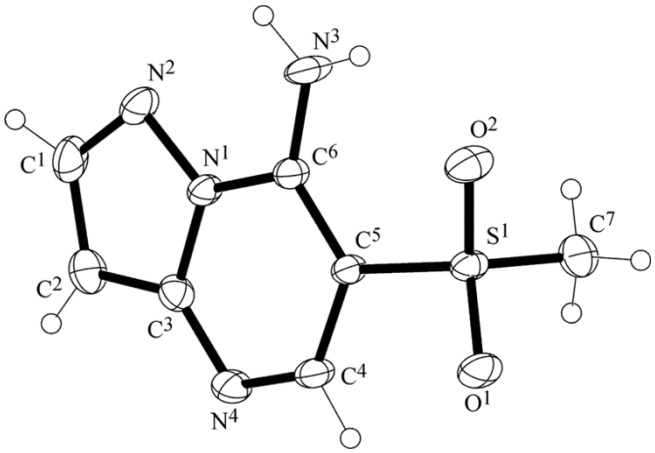


Fig. 2. General view of molecule of compound **5a** (thermal ellipsoids with 30% probability, hydrogen atoms omitted).

Table 4. Major bond lengths and bond angles in molecule of compound **5a**

Bond length	*d*, Å	Bond angle	ω, deg
N^2–N^1	1.364(3)	$C^1C^2C^3$	105.3(3)
N^2–C^1	1.329(4)	$C^1N^2N^1$	101.9(2)
C^2–C^1	1.376(5)	$C^2C^3N^1$	104.6(2)
C^3–C^2	1.379(4)	$N^2C^1C^2$	114.8(3)
C^3–N^1	1.387(3)	$N^4C^3N^1$	121.6(2)
C^3–N^4	1.350(3)	$N^2N^1C^3$	113.4(2)
C^4–N^4	1.314(3)	$N^2N^1C^6$	122.5(2)
C^4–C^5	1.414(3)	$C^6N^1C^3$	124.0(2)
C^6–N^3	1.314(3)	$N^4C^3C^2$	133.7(3)
C^6–N^1	1.369(3)	$C^4N^4C^3$	115.5(2)
C^6–C^5	1.387(3)	$C^6C^5C^4$	119.7(2)
		$N^3C^6N^1$	116.9(2)
		$N^3C^6C^5$	129.1(2)
		$N^1C^6C^5$	113.9(2)
		$N^4C^4C^5$	125.1(3)

X-ray diffraction study of a monocrystal of compound **3e** (0.10×0.15×0.26 mm) was performed at room temperature using a Bruker Smart Apex II diffractometer (MoK_α-radiation, graphitic monochromator, θ_{max} 28.89°, $-14 \le h \le 16$, $-11 \le k \le 11$, $-19 \le l \le 19$). Total reflections collected: 15100, 3582 of them being independent (*R*-factor of averaging 0.0512). Crystals of compound **3e** were monoclinic, $C_{12}H_{13}N_3O_2S_2$, *M* 295.37, space group *C*2/*c*, *a*.8777(4), *b* 8.3561(3), *c* 14.4812(5) Å, β106.937(2)°, *V* 1374.94 (8) Å^3, *Z* 4, d_{calc} 1.427, μ 0.388 mm^{-1}, *F*(000) 616. The absorption was corrected for by means of multiscanning using SADABS software (T_{min}/T_{max} = 0.804262/0.9697). The structure was solved via direct method and refined using least squares method implemented in Bruker SHELXTL software package [29]. The non-hydrogen atoms were refined under anisotropic approximation. Positions and thermal parameters of the CH hydrogen atoms were refined using a *rider* model along with the respective parameters of the adjacent carbon atoms; the hydrogen atoms adjacent to nitrogen were localized via differential Fourier synthesis, and their positions were refined under isotropic approximation. 2306 reflections with $I > 2\sigma(I)$ were used in the refinement (180 fitted parameters, 12.8 reflections per a parameter); the weighing scheme $\omega = 1/[\sigma^2(Fo^2) + (0.0537P)^2 + 0.5368P]$ with $P = (Fo^2 + 2Fc^2)/3$ was applied. Final values of the divergence factors: $R_1(F)$ 0.0503, $wR_2(F^2)$ 0.1105 over reflections with $I > 2\sigma(I)$ and $R_1(F)$ 0.0922, $wR_2(F^2)$ 0.1303, GOF 1.018 over all reflections. Residual electronic density from the differential Fourier series after the last cycle of refinement 0.34 and –0.41 *e*/Å^3. Complete crystallographic data were deposited at the Cambridge Crystallographic Data Centre (CCDC 1502961).

X-ray diffraction study of a monocrystal of compound **5a** (0.39×0.35×0.15 mm) was performed at room temperature using a Bruker Smart Apex II diffractometer (MoK_α-radiation, graphitic monochromator, θ_{max} 29.57°, $-9 \le h \le 9$, $-11 \le k \le 11$, $-11 \le l \le 11$). Total reflections collected: 5370, 2290 of them being independent (*R*-factor of averaging 0.0429). Crystals of compound **5a** were triclinic, $C_7H_8N_4O_2S$, *M* 212.23, space group *P*-1, *a* 7.2727(12), *b* 8.2714(13), *c* 8.3057(14) Å, α 96.932(11), β 114.398(9), γ 100.789(9)°, *V* 435.88(12) Å^3, *Z* 2, d_{calc} 1.617, μ 0.349 mm^{-1}, *F*(000) 220. The absorption was corrected for by means of multiscanning using SADABS software (T_{min}/T_{max} = 0.652028) and isotropic extinction factor [0.0041(9)]. The structure was solved via direct method and refined using least squares method implemented in Bruker SHELXTL software package [29]. Hydrogen atoms were localized and refined under isotropic approximation. 1516 reflections with $I > 2\sigma(I)$ were used in the refinement (159 fitted parameters, 9.5 reflections per a parameter); the weighing scheme $\omega = 1/[\sigma^2(Fo^2) + (0.0446P)^2 + 0.870P]$ with $P = (Fo^2 + 2Fc^2)/3$ was applied. The ratio of the highest (average) shift to the inaccuracy at the last cycle 0.014(0.001). Final values of the divergence factors: $R_1(F)$ 0.0566, $wR_2(F^2)$ 0.1227 over reflections with $I > 2\sigma(I)$ and $R_1(F)$ 0.0973, $wR_2(F^2)$ 0.1458, GOF 1.082 over all reflections. Residual electronic density from the differential Fourier series after the last cycle of refinement 0.66 and –0.35 *e*/Å^3. Complete crystallographic data were deposited at the Cambridge Crystallographic Data Centre (CCDC 1502977).

Commercial chemicals and solvents were used.

4-Amino-2-aryl(arylthio)-5-methylsulfonylpyrimidines (3a–3f). A mixture of 0.52 g (3 mmol) of 2-methylsulfonyl-3-ethoxyacrylonitrile **1**, 3 mmol of the corresponding amidine hydrochloride, and 0.84 mL (6 mmol) of triethylamine were refluxed during 6 h in 10 mL of ethanol and then kept at room temperature during 12 h. The solvent was removed in vacuum, the residue was treated with water, the precipitate was filtered off, dried, and recrystallized.

7-Amino-6-(methylsulfonyl)pyrazolo[1,5-*a*]pyrimidine (5a). A mixture of 0.52 g (3 mmol) of 2-methylsulfonyl-3-ethoxyacrylonitrile **1**, 0.25 g (3 mmol) of 5-amino-1*H*-pyrazole, and 0.42 mL (3 mmol) of triethylamine was refluxed during 3 h in 5 mL of dioxane. The solvent was removed in vacuum, the residue was treated with water, the precipitate was filtered off, dried, and recrystallized.

7-Amino-2-methyl-6-(methylsulfonyl)pyrazolo-[1,5-*a*]pyrimidine (5b) was prepared similarly from 2-methylsulfonyl-3-ethoxyacrylonitrile **1** and 5-amino-3-methyl-1*H*-pyrazole.

5-Amino-6-(methylsulfonyl)imidazo[1,2-*a*]pyrimidine (7). A mixture of 0.52 g (3 mmol) of 2-methylsulfonyl-3-ethoxyacrylonitrile **1**, 0.36 g (3 mmol) of 2-amino-1*H*-imidazole hydrochloride, and 0.84 mL (6 mmol) of triethylamine was refluxed during 3 h in 10 mL of dioxane. The solvent was removed in vacuum, the residue was treated with water, the precipitate was filtered off, dried, and recrystallized.

4-Amino-3-(methylsulfonyl)pyrimido[1,2-*a*]benzimidazole (9). A mixture of 0.52 g (3 mmol) of 2-methylsulfonyl-3-ethoxyacrylonitrile **1**, 0.40 g (3 mmol) of 2-amino-1*H*-benzimidazole, and 0.42 mL (3 mmol) of triethylamine was refluxed during 3 h in 5 mL of dioxane. The formed precipitate was filtered off, washed with ethanol, and recrystallized.

ACKNOWLEDGMENTS

This work was financially supported by National Research Foundation of Ukraine (project no. 16DF037-02).

REFERENCES

1. Joule, J.A. and Smith, G.F., *Heterocyclic Chemistry*, New York: Van Nostrand and Reinhold, 1972.
2. Gilchrist, T.L., *Heterocyclic Chemistry*, Pitman: Marshfield, MA, 1985.
3. Walker, S.R., Carter, E.J., Huff, B.C., and Morris, J.C., *Chem. Rev*., 2009, vol. 109, no. 7, p. 3080. doi 10.1021/cr900032s
4. Koroleva, E.V., Gusak, K.N., and Ignatovich, Zh.V., *Russ. Chem. Rev*., 2010, vol. 79, no. 8, p. 655. doi 10.1070/RC2010v079n08ABEH004116.
5. Bruno, O., Brullo, C., Schenone, S., Bondavalli, F., Ranise, A., Tognolini, M., Ballabeni, V., and Barocelli, E., *Bioorg. Med. Chem*., 2004, vol. 12, no. 3, p. 553. doi 10.1016/j.bmc.2003.11.018
6. Ingarsal, N., Saravanan, G., Amutha, P., and Nagarajan, S., *Eur. J. Med. Chem*., 2007, vol. 42, no. 4, p. 517. doi 10.1016/j.ejmech.2006.09.012
7. Amin, K.M., Hanna, M.M., Abo-Youssef, H.E., and George, R.F., *Eur. J. Med. Chem*., 2009, vol. 44, no. 11, p. 4572. doi 10.1016/j.ejmech.2009.06.028
8. Amin, K.M., Awadalla, F.M., Eissa, A.A.M., Abou-Seri, S.M., and Hassan, G.S., *Bioorg. Med. Chem*., 2011, vol. 19, no. 20, p. 6087. doi 10.1016/j.bmc.2011.08.037
9. Ramesh, L.S., Varsha, I.S., Ganesh, D.J., and Jyoti, B.W., *Med. Chem. Res*., 2012, vol. 21, no. 8, p. 1825. doi 10.1007/s00044-011-9700-7
10. Lin, Y.-L., Tsai, W.-Y., and Kuo, Y.-H., *Phytochem*., 1995, vol. 39, no. 4, p. 919. doi 10.1016/0031-9422(95)00005-R
11. Kouokam, J.C., Zapp, J., and Becker, H., *Phytochem*., 2002, vol. 60, no. 4, p. 403. doi 10.1016/S0031-9422(02)00125-5
12. Park, H.-S., Yoda, N., Fukaya, H., Aoyagi, Y., and Takeya, K., *Tetrahedron*, 2004, vol. 60, no. 1, p. 171. doi 10.1016/j.tet.2003.10.083
13. Semenov, A.A. and Kartsev, V.G., *Osnovy khimii prirodnyhk soedinenii* (Fundamentals of Chemistry of Natural Compounds), vol. 2, Moscow: ICSPF, 2009.
14. Putra, M.Y., Ianaro, A., Panza, E., Bavestrello, G., Cerrano, C., Fattorusso, E., and Taglialatela-Scafati, O., *Tetrahedron Lett*., 2012, vol. 53, no. 30, p. 3937. doi 10.1016/j.tetlet.2012.05.095
15. Chen, M., Shao, C.-L., Fu, X.-M., Kong, C.-J., She, Z.-G., and Wang, C.-Y., *J. Nat. Prod*., 2014, vol. 77, no. 7, p. 1601. doi 10.1021/np5001686.
16. Hoegerle, K. and Tobler, H., US Patent 4560402, 1985.
17. Straub, A., Stasch, J.P., Alonso-Alija, C., Benet-Buchholz, J., Ducke, B., Feurer, A., and Fürstner, C., *Bioorg. Med. Chem. Lett*., 2001, vol. 11, no. 6, p. 781. doi 10.1016/S0960-894X(01)00073-7
18. Siddiqui, M.A., Nan, Y., Patel, M.F., Reddy, P.A.P., Mansoor, U.F., Meng, Z., Vitharana, L.D., Zhao, L., Mandal, A.K., Liu, D., Tang, S., Mcriner, A., Belanger, D.B., Curran, P.J., Dai, C., Angeles, A.R., and Yang, L., Daniels, M.H., WO Patent 2011090935, 2011.
19. Kim, C., Nakai, T., Wai-Ho, L.T., Moore, J., Perl, N.R., Rohde, J., Iyengar, R.R., and Mermerian, A., WO Patent 2012003405, 2012.
20. Hitchcock, M., Mengel, A., Richter, A., Briem, H., Eis, K., Putter, V., Siemeister, G., Prechtl, S., Fernandez-Montalvan, A.E., Stegmann, C., Holton, S., Gnoth, M.J., and Preusse, C., WO Patent 2013092512, 2013.
21. Lunt, E., Newton, C.G., Smith, C., Stevens, G.P., Stevens, M.F.G., Straw, C.G., Walsh, R.J.A., Warren, P.J., Fizames, C., Lavelle, F., Langdon, S.P., and Vickers, L.M., *J. Med. Chem*., 1987, vol. 30, no. 2, p. 357. doi 10.1021/jm00385a018
22. Pigošováa, J., Gatiala, A., Milatab, V., Černuchováb, P., Prónayovác, N., Liptajc, T., and Matějkad, P., *J. Mol. Struct*., 2005, vols. 744–747, p. 315. doi 10.1016/j.molstruc.2004.10.053
23. Slivchuk, S.R., Brovarets, V.S., and Drach, B.S., *Dop. NAN Ukraïni*, 2006, no. 3, p. 146.
24. Takahashi, M., Mamiya, T., and Wakao, M., *J. Het. Chem*., 1986, vol. 23, p. 77. doi 10.1002/jhet.5570230116
25. Slivchuk, S.R., Rusanov, E.B., and Brovarets, V.S., *Zh. Org. Fiz. Khim*., 2006, vol. 4, no. 3, p. 62.
26. Shaaban, M.R., *Heterocycles*, 2008, vol. 75, no. 12, p. 3005. doi 10.3987/COM-08-11471
27. Tominaga, Y., Sakai, S., Kohra, S., Tsuka, J., Matsuda, Y., and Kobayashi, G., *Chem. Pharm. Bull*., 1985, vol. 33, no. 3, p. 962. doi 10.1248/cpb.33.962
28. Klimova, V.A., *Osnovnye mikrometody analiza organicheskikh soedinenii* (Basic Micromethods of Analysis of Organic Compounds), Moscow: Khimiya, 1975.
29. Sheldrick, G.M., *Acta Crystallogr. (A)*, 2008, vol. 64, p. 112. doi 10.1107/S0108767307043930