Reactions of ethyl methylsulfonylpyruvate and its sodium salt with a mixture of aromatic aldehyde and arylamine

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The reactions of ethyl methylsulfonylpyruvate and its sodium salt with a mixture of aromatic aldehyde and arylamine afforded 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones. The spatial structure of 1,5-diphenyl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-one was established by X-ray diffraction analysis.

Key words: ethyl methylsulfonylpyruvate, ethyl methylsulfonylpyruvate sodium salt, aromatic aldehydes, arylamines, 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones, ^{1}H NMR spectroscopy, X-ray diffraction analysis.

It has previously[1] been shown that the reactions of ethyl arylsulfonylpyruvates with Schiff´s bases in the presence of potassium carbonate afford 5-arylsulfonylmethylene-2,3-diphenyloxazolidin-4-ones, which are isomerized by an acid to form 4-arylsulfonyl-1,5-diphenylpyrrolidine-2,3-diones. The latter can also be prepared by the three-component reaction of equimolar amounts of arylsulfonylpyruvate, benzaldehyde, and aromatic amine.

Continuing the study of the syntheses of sulfonyl-substituted 3-hydroxy-3-pyrrolin-2-ones and their structural peculiarities, in this work we studied the reaction of ethyl methylsulfonylpyruvate or its sodium salt with a mixture of aromatic aldehyde and arylamine.

It has been established that the reaction of sodium salt of ethyl methylsulfonylpyruvate (method *A*) or ethyl methylsulfonylpyruvate (method *B*) with a mixture of aromatic aldehyde and arylamine (Scheme 1) affords pyrroline salts **1g—l,q** and **2a—h,m—p**, respectively. Pyrroline sodium salts **1g—l,q** isolated from the reaction mixture were treated with HCl without preliminary purification, except for salt **1g**. The ^{1}H NMR spectrum of the purified salt **1g** virtually coincides with the spectrum of compound **3g**.

Salts **2a—h,m—p** (method *B*), six of which (**2a—f**) were isolated and purified, are formed as intermediates due to the relatively high acidity of the enolic hydroxyl group, which is explained by the electron-withdrawing properties of the methylsulfonyl substituents in position 4 of the heterocycle.

The hydrolysis of both pyrroline sodium salts **1g—l,q** (method *A*) and pyrroline salts with arylamines **2a—h,m—p** (method *B*) produces 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones **3a—q** (see Scheme 1).

Compounds **2a—f** and **3a—q** are colorless or light yellow crystalline substances, which are highly soluble in acetone, DMSO, and DMF.

The IR spectra of pyrrolinones **3a—q** exhibit the absorption bands of the lactamic carbonyl group at 1692—1732 cm^{-1}, C=C double bond at 1638—1680 cm^{-1}, enolic hydroxyl at 3078—3164 cm^{-1}, and sulfonyl group at 1134—1150 and 1310—1366 cm^{-1}.

The reaction of compounds **2a—f** and **3a—q** with an alcohol solution of iron(III) chloride shows the presence of the enolic hydroxyl group. The ^{1}H NMR spectroscopic data are presented in Table 1. The results of elemental analysis and the yields of compounds **2a—f** and **3a—q** are presented in Table 2.

In order to reveal the spatial structure of the compounds synthesized, crystals of pyrrolinone **3g** obtained by slow crystallization from an alcohol solution were studied by X-ray diffraction analysis.

The unit cell contains two crystallographically independent molecules **A** and **B**, which are close structurally in general outline. The structures of the molecules projected to the heterocycle plane are shown in Fig. 1. Compound **3g** is based on the five-membered planar heterocycle with the localized C(9)=C(10) double bond (1.345 Å (**A**), 1.331 Å (**B**)). The main bond lengths and bond angles (Table 3) in molecules **A** and **B** are the same

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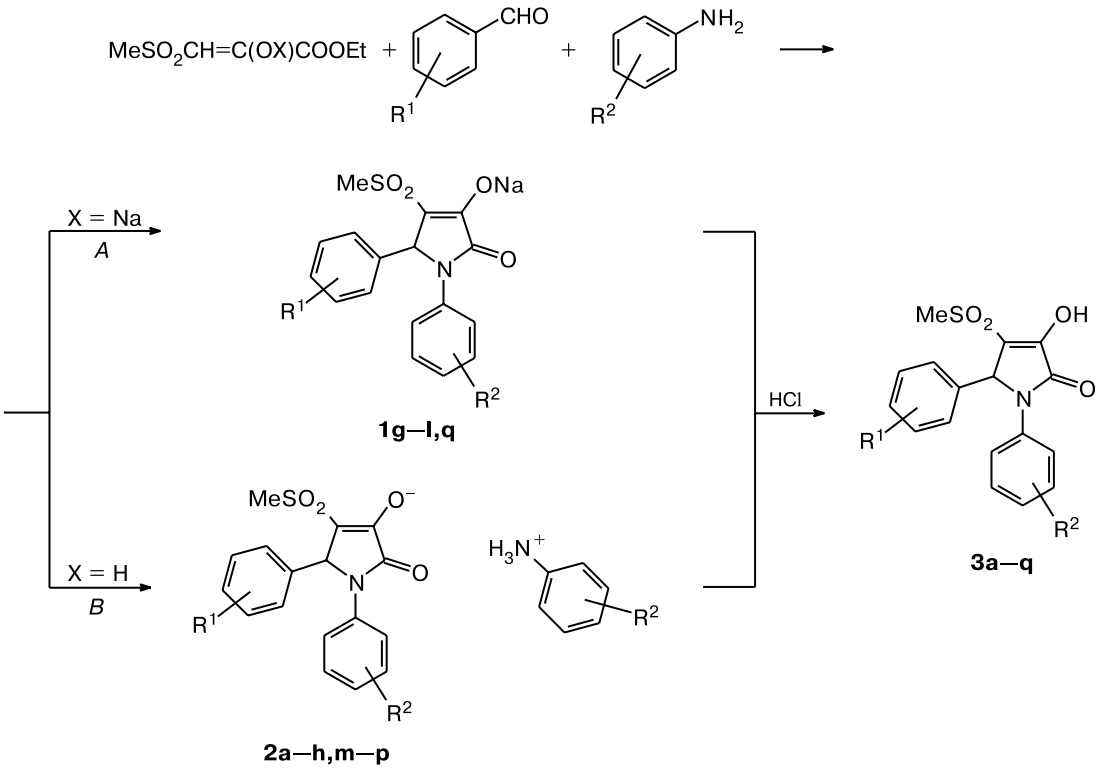
Scheme 1



2a, **3a:** R^1 = 4-F, R^2 = H; **2b**, **3b:** R^1 = 4-Me, R^2 = H; **2c**, **3c:** R^1 = 3,4-$(MeO)_2$, R^2 = H; **2d**, **3d:** R^1 = 4-Cl, R^2 = H; **2e**, **3e:** R^1 = 4-NO_2, R^2 = H; **2f**, **3f:** R^1 = 4-MeO, R^2 = H; **1g**, **2g**, **3g:** $R^1 = R^2$ = H; **1h**, **2h**, **3h:** R^1 = H, R^2 = 4-MeO; **1i**, **3i:** R^1 = H, R^2 = 4-Me ; **1j**, **3j:** R^1 = H, R^2 = 4-MeNHCO; **1k**, **3k:** R^1 = H, R^2 = 4-EtOOC; **1l**, **3l:** R^1 = H, R^2 = 3-CF_3; **2m**, **3m:** R^1 = H, R^2 = 4-Br; **2n**, **3n:** R^1 = H; R^2 = 4-I; **2o**, **3o:** R^1 = H, R^2 = 4-NO_2; **2p**, **3p:** R^1 = H, R^2 = 4-NH_2SO_2; **2q**, **3q:** R^1 = 4-Br, R^2 = H

within the accuracy and are close to the values of the corresponding bonds. Some difference is observed in the orientation of the substituents (see Fig. 1). In molecule **B**, the Ph substituent at the C(11) atom is localized in the plane perpendicular to the plane of the pyrrolidine cycle (the N(6)—C(11)—C(12)—C(13) torsion angle is 61.5°), and the plane of the Ph substituent at N(6) forms with the latter an angle of 36° (the C(8)—N(6)—C(18)—C(19)

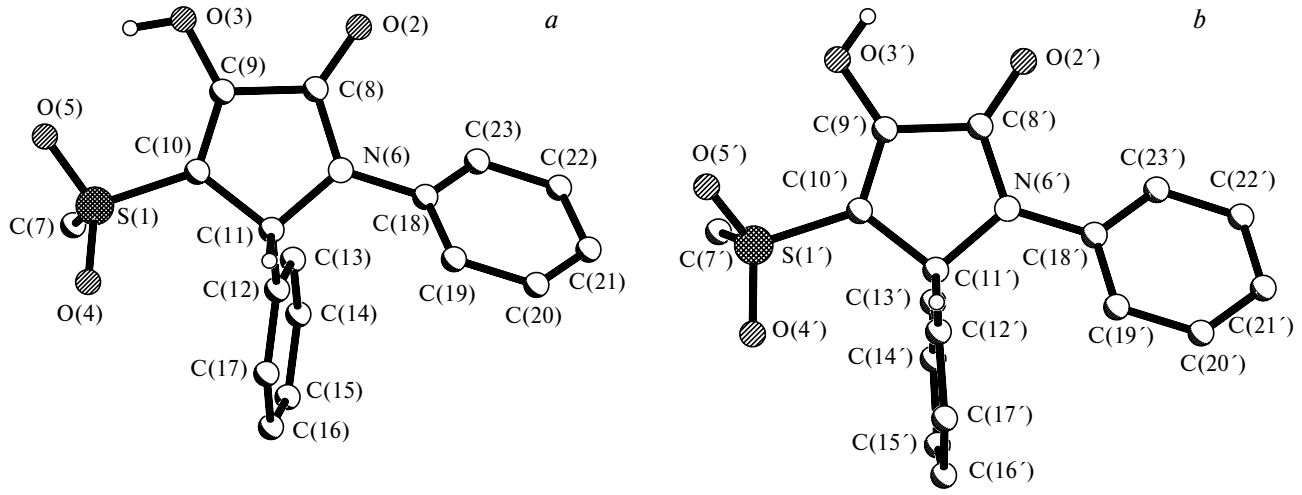


Fig. 1. Structures of molecules **A** (*a*) and **B** (*b*) of compound **3g** in the projection to the heterocycle plane.

Table 1. ^{1}H NMR spectroscopic data for compounds **2a—f** and **3a—q**

Compound	^{1}H NMR, δ			
	CH_3SO_2 (s, 3 H)	C(5)H (s, 1 H)	Ar	Other protons
2a	2.94	6.27	7.24 (m, 14 H)	6.59 (br.s, 3 H)
2b	2.76	6.19	6.22, 7.24 (both m, 14 H)	2.12 (s, 3 H); 6.02 (br.s, 3 H)
2c	2.79	6.18	6.81 (m, 13 H)	3.68 (s, 6 H); 5.18 (br.s, 3 H)
2d	2.88	6.27	7.36 (m, 14 H)	6.64 (br.s, 3 H)
2e	2.96	6.51	7.71 (m, 14 H)	6.71 (br.s, 3 H)
2f	2.73	6.14	7.14 (m, 14 H)	3.65 (s, 3 H); 5.30 (br.s, 3 H)
3a	2.45	6.84	7.15 (m, 9 H)	—
3b	2.76	6.20	7.21 (m, 9 H)	2.17 (s, 3 H)
3c	2.78	6.19	6.91, 7.34 (both m, 8 H)	3.66 (s, 6 H)
3d	2.86	6.29	7.34 (m, 9 H)	—
3e	2.99	6.51	8.16 (m, 9 H)	—
3f	2.73	6.19	6.84, 7.43 (both m, 9 H)	3.63 (s, 3 H)
3g	2.70	6.12	7.28, 7.55 (both m, 10 H)	—
3h	2.94	6.28	7.04, 7.69 (both m, 9 H)	3.56 (s, 3 H)
3i	2.80	6.30	7.51 (m, 9 H)	2.19 (s, 3 H)
3j	2.73	6.13	7.29, 7.49 (both m, 9 H)	1.96 (s, 3 H); 10.02 (s, 1 H)
3k	2.76	6.29	7.37, 7.83 (both m, 9 H)	1.25 (s, 3 H); 4.64 (s, 2 H)
3l	2.71	6.25	7.23, 7.93 (both m, 9 H)	—
3m	2.78	6.29	7.37 (m, 9 H)	—
3n	2.73	6.24	7.47 (m, 9 H)	—
3o	2.73	6.41	7.37, 8.11 (both m, 9 H)	—
3p	3.19	6.34	7.31 (m, 9 H)	7.05 (s, 2 H)
3q	2.82	6.14	7.25, 7.34 (both m, 9 H)	—

Table 2. Main physicochemical characteristics of compounds **2a—f** and **3a—q**

Compound	Yield (%) (method of synthesis)	M.p. /°C	Found / Calculated (%)			Molecular formula
			C	H	N	
2a	27 (*B*)	180—181	62.95 / 62.71	4.76 / 4.81	6.49 / 6.36	$C_{23}H_{21}FN_2O_4S$
2b	40 (*B*)	166—168	66.24 / 66.05	5.41 / 5.55	9.59 / 6.43	$C_{24}H_{24}N_2O_4S$
2c	14 (*B*)	131—133	62.36 / 62.23	5.29 / 5.43	5.70 / 5.81	$C_{25}H_{26}N_2O_6S$
2d	59 (*B*)	173—175	60.57 / 60.46	4.48 / 4.63	6.27 / 6.13	$C_{23}H_{21}Cl\,N_2O_4S$
2e	21 (*B*)	173—175	53.19 / 53.10	4.49 / 4.53	8.87 / 8.98	$C_{23}H_{21}N_3O_6S$
2f	43 (*B*)	168—170	63.44 / 63.69	5.25 / 5.35	6.31 / 6.19	$C_{24}H_{24}N_2O_5S$
3a	30 (*B*)	189—190	58.61 / 58.78	4.17 / 4.06	4.18 / 4.03	$C_{17}H_{14}FNO_4S$
3b	35 (*B*)	208—209	62.83 / 62.95	5.15 / 4.98	4.13 / 4.08	$C_{18}H_{17}NO_4S$
3c	12 (*B*)	184—186	58.78 / 58.61	5.13 / 4.92	3.68 / 3.59	$C_{19}H_{19}NO_6S$
3d	21 (*B*)	195—197	56.27 / 56.12	3.78 / 3.88	3.71 / 3.85	$C_{17}H_{14}ClNO_4S$
3e	25 (*B*)	207—209	54.67 / 54.54	3.81 / 3.77	7.55 / 7.48	$C_{17}H_{14}N_2O_6S$

(*to be continued*)

Table 2 (*continued*)

Compound	Yield (%) (method of synthesis)	M.p. /°C	Found / Calculated (%)			Molecular formula
			C	H	N	
3f	24 (*B*)	181—183	60.24	4.87	3.98	$C_{18}H_{17}NO_5S$
			60.15	4.76	3.90	
3g	25 (*A*), 33 (*B*)	215—217	62.07	4.50	4.31	$C_{17}H_{15}NO_4S$
			61.99	4.54	4.25	
3h	17 (*A*), 40 (*B*)	177—178	60.25	4.93	3.97	$C_{18}H_{17}NO_5S$
			60.15	4.76	3.90	
3i	25 (*A*)	116—118	62.79	5.17	4.00	$C_{18}H_{17}NO_4S$
			62.95	4.98	4.08	
3j	28 (*A*)	230—232	59.21	4.85	7.28	$C_{19}H_{18}N_2O_5S$
			59.05	4.69	7.25	
3k	28 (*A*)	154—156	59.96	4.70	3.55	$C_{20}H_{19}NO_6S$
			59.84	4.77	3.49	
3l	28 (*A*)	143—145	54.32	3.61	3.50	$C_{18}H_{14}F_3NO_4S$
			54.40	3.55	3.52	
3m	20 (*B*)	148—150	50.16	3.37	3.59	$C_{17}H_{14}BrNO_4S$
			50.01	3.46	3.43	
3n	27 (*B*)	170—172	44.68	3.01	2.98	$C_{17}H_{14}INO_4S$
			44.85	3.10	3.08	
3o	22 (*B*)	173—174	54.57	3.88	7.28	$C_{17}H_{14}N_2O_6S$
			54.55	3.77	7.48	
3p	21 (*B*)	248—249	49.74	4.11	6.93	$C_{17}H_{16}N_2O_6S_2$
			49.99	3.95	6.86	
3q	37 (*A*)	190—192	50.24	3.57	3.29	$C_{17}H_{14}BrNO_4S$
			50.01	3.46	3.43	

Table 3. Main bond lengths (*d*) and bond angles (ω) in two independent molecules of compound **3g**

Parameter	**A**	**B**	Parameter	**A**	**B**
Bond	*d*/Å		Angle	ω/deg	
S(1)—O(4)	1.428(2)	1.422(2)	C(10)—S(1)—C(7)	105.7(1)	104.3(2)
S(1)—C(10)	1.728(2)	1.742(2)	C(8)—N(6)—C(18)	124.7(2)	125.4(2)
O(2)—C(8)	1.214(3)	1.227(3)	C(8)—N(6)—C(11)	113.4(2)	112.2(2)
N(6)—C(8)	1.361(3)	1.353(3)	C(18)—N(6)—C(11)	121.6(2)	122.3(2)
N(6)—C(11)	1.466(3)	1.479(3)	O(2)—C(8)—N(6)	127.9(2)	127.8(2)
C(9)—C(10)	1.345(3)	1.331(3)	O(2)—C(8)—C(9)	126.4(2)	125.5(2)
S(1)—O(5)	1.434(2)	1.434(2)	N(6)—C(8)—C(9)	105.7(2)	106.7(2)
S(1)—C(7)	1.748(3)	1.764(4)	O(3)—C(9)—C(10)	134.3(2)	128.5(2)
O(3)—C(9)	1.317(3)	1.323(3)	O(3)—C(9)—C(8)	116.7(2)	122.3(2)
N(6)—C(18)	1.422(3)	1.422(3)	C(10)—C(9)—C(8)	109.0(2)	109.2(2)
C(8)—C(9)	1.495(3)	1.490(3)	C(9)—C(10)—C(11)	110.5(2)	110.6(2)
Angle	ω/deg		C(9)—C(10)—S(1)	126.0(2)	125.4(2)
O(4)—S(1)—O(5)	118.0(1)	119.6(1)	C(11)—C(10)—S(1)	123.5(2)	124.0(2)
O(4)—S(1)—C(10)	109.2(1)	108.5(1)	N(6)—C(11)—C(12)	111.6(2)	112.8(2)
O(5)—S(1)—C(10)	106.0(1)	107.4(1)	N(6)—C(11)—C(10)	101.2(2)	101.4(2)
O(4)—S(1)—C(7)	109.0(2)	108.3(2)	C(12)—C(11)—C(10)	114.8(2)	114.4(2)
O(5)—S(1)—C(7)	108.1(2)	107.7(2)			

torsion angle is 142.2°). In molecule **A**, similar angles between the planes are 99.4 and 48°, respectively, whereas the torsion angles are 46.9 and 136.8°. The orientation of the sulfonyl groups is characterized by the O(5)—S(1)—C(10)—C(9) torsion angles equal to 17.4° (**A**) and 36.2° (**B**). The difference in orientation of the hydroxyl groups in two independent molecules is most substantial. In molecule **A**, the H(3) atom of the enolic hydroxyl group is oriented toward the sulfonyl group, while in molecule **B** it is oriented toward the carbonyl fragment.

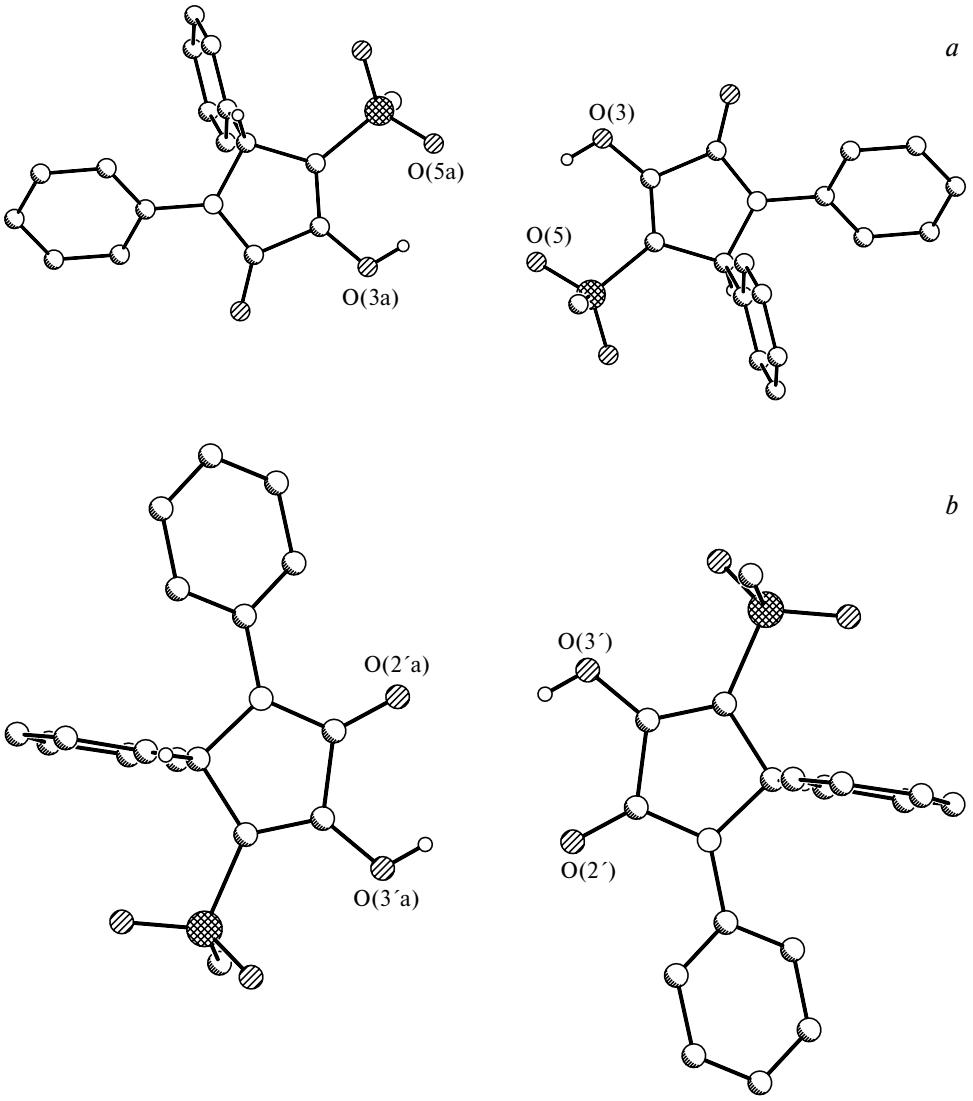


Fig. 2. Crystal structures of compound **3g**: **A** (*a*) and **B** (*b*).

The objective localization of the hydroxylic H atoms of two molecules is confirmed by the crystal structure (Fig. 2). Both molecules in crystal exist as dimeric center-symmetric associates, which are bound by rather strong hydrogen bonds. In the dimeric associate of molecules **A** with the symmetry center in the point of coordinate origin of the cell, the hydrogen bond with the 2.73 Å length is formed by the hydroxyl group and the O(5) atom of the sulfonyl group (O(5)...H) 2.01 Å, the angle at the H(3) atom is 140°). The dimeric associates of molecules **B** with the coordinates of the symmetry center 0, 0.5, 0 are formed by the O(3´)—H(3´)...O(2´) intermolecular hydrogen bonds involving the carbonyl group. This hydrogen bond has the following parameters: O(3´)...O(2´) 2.60 Å, H(3´)...O(2´) 1.84 Å, and the angle at the H(3´) atom is 151°. Thus, molecules **B** are bound by stronger hydrogen bonds to form dimeric associates.

Experimental

Purity of substances was monitored by TLC using Silufol UV-254 plates in a benzene—ethyl acetate (5 : 1) mixture. ^{1}H NMR spectra were recorded with a Bruker WM-250 spectrometer in DMSO-d_6 using HMDS as an internal standard. IR spectra were recorded with a UR-20 instrument as a paste in Nujol.

3-Hydroxy-4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-one (3g). Method *A*. A solution of ethyl methylsulfonylpyruvate sodium salt (0.01 mol) in AcOH (5 mL) was added to a mixture of benzaldehyde (0.01 mol) and aniline (0.01 mol) in AcOH (5 mL). The reaction mixture was heated to boiling and stored for 1 day at ~20 °C, and a precipitate that formed was filtered off. The resulting sodium salt was boiled for 1 h and cooled, and crystals precipitated were filtered off. The yield of pyrrolinone **3g** (from EtOH) was 1.10 g (33%). IR (Nujol), ν/cm^{-1}: 3116 (OH); 1720 (CON); 1676 (C=C); 1320, 1155 (SO_2).

Compounds **3h—l,q** were synthesized similarly. Their yields and ^{1}H NMR spectroscopic data are presented in Tables 1 and 2.

Salt of aniline and 3-hydroxy-5-(4-methylphenyl)-4-methylsulfonyl-1-phenyl-3-pyrrolin-2-one (2b). Method *B*. A solution of ethyl methylsulfonylpyruvate (0.01 mol) in AcOH (5 mL) was added to a mixture of 4-methylbenzaldehyde (1.18 mL, 0.01 mol) and aniline (1.82 mL, 0.02 mol) in AcOH (5 mL). The reaction mixture was heated to boiling and stored for 24 h at ~20 °C, and a precipitate that formed was filtered off. The yield of pyrrolinone **2b** (from EtOH) was 1.73 g (40%).

Compounds **2a,c—f** were synthesized similarly. Their yields and ^{1}H NMR spectroscopic data are presented in Tables 1 and 2.

3-Hydroxy-5-(4-methylphenyl)-4-methylsulfonyl-1-phenyl-3-pyrrolin-2-one (3b). Method *B*. Concentrated HCl (10 mL) was added to a mixture of the aniline salt and 3-hydroxy-5-(4-methylphenyl)-4-methylsulfonyl-1-phenyl-3-pyrrolin-2-one **2b** (1.40 g, 0.004 mol), and the resulting mixture was boiled for 1 h. A precipitate was filtered off. The yield of pyrrolinone **3b** (from EtOH) was 0.72 g (40%).

Compounds **3a,c—h,m—p** were synthesized similarly. Their yields and ^{1}H NMR spectroscopic data are presented in Tables 1 and 2.

X-ray diffraction study of compound 3g. Crystals **3g** are monoclinic, a = 27.839(6), b = 8.981(2), c = 26.616(5) Å, β = 110.37(3)°, V = 6238(2) Å^3, M = 658.72, d_{calc} = 1.403 g cm^{-3}, Z = 16, space group $C2/c$. Unit cell parameters and a set of experimental reflections were measured with an KM-4 automated four-circle diffractometer (KUMA DIFFRACTION) with χ geometry using the θ—2θ scan mode on the monochromatized Cu-Kα radiation in the interval of angles $4° < \theta < 80°$, measuring 6261 independent reflections. Correction to absorption were not introduced (μ = 2.03 mm^{-1}). The structure was solved by the direct statistical method followed by the series of calculations of the electron density maps. Hydrogen atoms of the phenyl substituents were specified geometrically. The methinic and hydroxylic H atoms were objectively localized from the difference electron density syntheses. The full-matrix anisotropic (isotropic for H atoms) refinement by the least-squares method was completed at R = 0.048 against 4772 reflections with $I \geq 2\sigma(I)$. The atomic coordinates were deposited at the Cambridge Bank of Structural Data. All calculations were performed on a PC/AT using the SHELX-97 program package.[2]

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