Chemistry of Heterocyclic Compounds, Vol. 43, No. 11, 2007

REACTION OF 1,5-DIARYL-3-HYDROXY-4-METHYLSULFONYL-3-PYRROLIN-2-ONES WITH UREA, HYDRAZINE, ETHYLENEDIAMINE, AND *o*-PHENYLENEDIAMINE

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With urea 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones form the 3-amino derivatives of pyrrolones. In reactions with hydrazine hydrate and ethylenediamine the corresponding salts are formed. With ethylenediamine at 180-185°C the double salt of 3-hydroxy-4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-one forms N,N'-di(4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-on-3-yl)-ethylenediamine. The reaction with o-phenylenediamine gives 2,3-diaryl-4-methylsulfonylpyrrolo-[2,3-b]quinoxalines.

Keywords: 3-amino-1,5-diaryl-4-methylsulfonyl-3-pyrrolin-2-ones, 2,3-diaryl-4-methylsulfonylpyrrolo-[2,3-*b*]quinoxalines, binucleophilic reagents.

Earlier it was established that the reaction of ethyl ester of methylsulfonylpyruvic acid or its sodium salt with a mixture of aromatic aldehyde and arylamine leads to the formation of 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones [1], fusion of which with *o*-phenylenediamine gives 2,3-diaryl-4-methylsulfonylpyrrolo-[2,3-*b*]quinoxalines [2].

While continuing research into the properties of 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones in relation to binucleophilic reagents we studied their reaction with urea, hydrazine hydrate, ethylenediamine, and *o*-phenylenediamine.

It was established that the reaction of 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones with urea at 170-180°C leads to the formation of 3-amino-1,5-diaryl-4-methylsulfonyl-3-pyrrolin-2-ones **1a**-**f**.

The obtained compounds **1a**-**f** (Table 1) are pinkish crystalline substances insoluble in water and soluble in DMSO and DMF.

The formation of compounds **1a**-**f** is probably explained by the fact that the urea decomposes to ammonia under the reaction conditions and acts as an aminating reagent [3].

In addition to the absorption bands of the sulfonyl and lactam groups, the IR spectra of compounds **1a**-**f** (Table 2) contain absorption bands for the stretching vibrations of the amino group at 3252-3490 cm^{-1}.

In the ^{1}H NMR spectra of compounds **1a**-**f** (Table 3) there is a signal for the two protons of the amino group at 6.51-6.60 ppm and a characteristic signal for the methine proton at position 5 of the heterocycle at 5.85-6.09 ppm.

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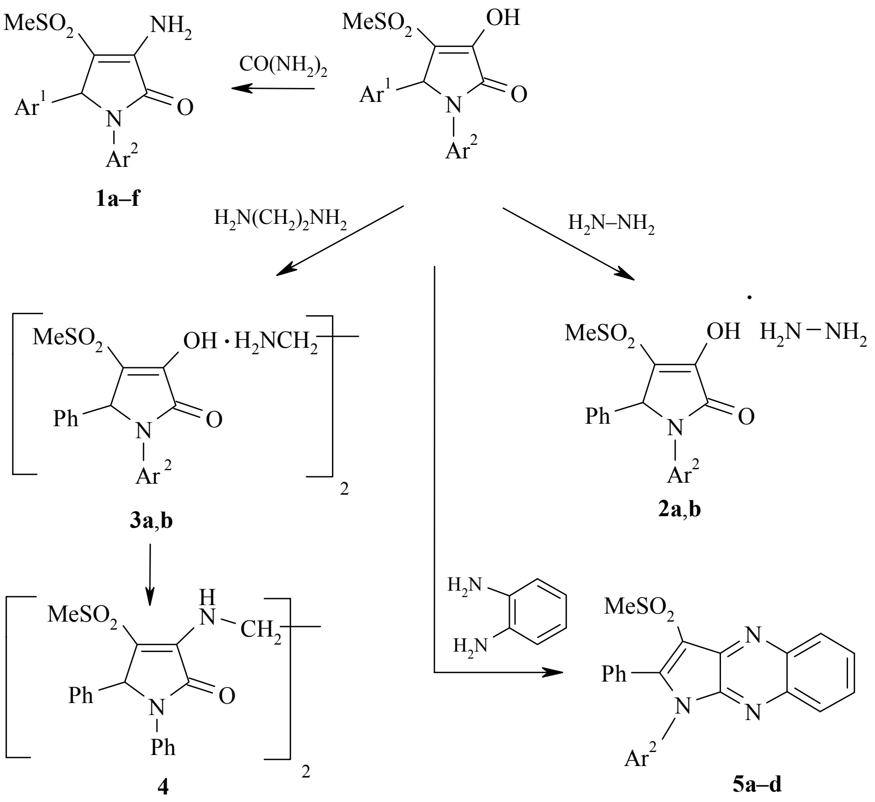

1a,b,d,f Ar^1 = Ph, **c** Ar^1 = 4-$MeOC_6H_4$, **e** Ar^1 = 4-BrC_6H_4; **1a,c, 2a,3a** Ar^2 = Ph; **1b**, **5b** Ar^2 = 4-ClC_6H_4;
1d Ar^2 = 4-FC_6H_4; **1e** Ar^2 = 4-BrC_6H_4; **1f, 2b,3b, 5a** Ar^2 = 4-HOC_6H_4; **5c** Ar^2 = 4-$H_2NSO_2C_6H_4$; **5d** Ar^2 = CH_2Ph

Thus, the spectral data indicate that compounds **1a-f** exist in the enamine form.

The basicity of the amino group in compounds **1a-f** is quite strongly reduced as a result, probably, of conjugation of the electron pair of the nitrogen atom with the double bond and the strong electron-withdrawing effect of the sulfonyl substituent at position 4 of the heterocycle. This is demonstrated by the fact that it was not possible to obtain the corresponding Schiff base during investigation of the reaction of 3-amino-4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-one **1a** with benzaldehyde.

Good yields of the salts of 1-aryl-3-hydroxy-4-methylsulfonyl-5-phenyl-3-pyrrolin-2-ones with hydrazine **2a**,**b** are formed in the reaction of 3-hydroxy-4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-one and 3-hydroxy-1-(4-hydroxyphenyl)-4-methylsulfonyl-5-phenyl-3-pyrrolin-2-one with 50% hydrazine hydrate in dioxane. The formation of the salts is evidently explained by the acidic characteristics of the enolic hydroxyl at position 3 of the heterocycle.

The obtained compounds **2a**,**b** (Table 1) are colorless crystalline substances soluble in DMSO and DMF.

In the IR spectra of compounds **2a**,**b** (Table 2) there are bands for the stretching vibrations of the OH group at 3019-3160 cm^{-1} and the NH_2 groups at 3305-3547 cm^{-1}.

The signals of the amino group are not seen in the ^1H NMR spectra of compounds **2a**,**b** (Table 3), but unlike the initial compounds [1] an upfield shift of all the signals is observed. The absence of signals for the amino groups is probably explained by their broadening on account of exchange processes.

Compounds **2a**,**b** give a cherry-red color with an alcohol solution of $FeCl_3$, which together with the spectral data indicates that they exist in the enolic form.

TABLE 1. The Characteristics of the Synthesized Compounds

Com-pound	Empirical formula	Found, % / Calculated, %			mp, °C*	Yield,%
		C	H	N		
1a	$C_{17}H_{16}N_2O_3S$	62.17 62.29	4.91 4.85	8.53 8.65	157-158	48
1b	$C_{17}H_{15}ClN_2O_3S$	56.27 56.11	4.17 4.29	7.72 7.70	157-159	54
1c	$C_{18}H_{18}N_2O_4S$	60.32 60.39	5.06 5.19	7.82 7.69	179-180	50
1d	$C_{17}H_{15}FN_2O_3S$	58.94 58.80	4.37 4.19	8.09 8.01	174-175	40
1e	$C_{17}H_{14}Br_2N_2O_3S$	41.99 41.80	2.90 2.75	5.76 5.67	240-241	31
1f	$C_{17}H_{16}N_2O_4S$	59.29 59.09	4.68 4.79	8.14 8.25	260-261	33
2a	$C_{17}H_{19}N_3O_4S$	56.30 56.50	5.48 5.30	11.85 11.63	115-117	85
2b	$C_{17}H_{19}N_3O_5S$	54.30 54.10	5.21 5.07	11.01 11.13	163-164	81
3a	$C_{36}H_{38}N_4O_8S_2$	60.34 60.15	5.21 5.33	7.58 7.79	198-200	65
3b	$C_{36}H_{38}N_4O_{10}S_2$	57.70 57.95	5.01 5.10	7.68 7.46	134-141	74
5a	$C_{23}H_{17}N_3O_3S$	66.59 66.49	4.01 4.13	10.29 10.11	294-295	52
5b	$C_{23}H_{16}ClN_3O_2S$	63.91 63.66	3.62 3.72	9.50 9.68	232-233	53
5c	$C_{23}H_{18}N_4O_4S_2$	57.60 57.73	3.60 3.79	11.93 11.71	>300	42
5d	$C_{24}H_{19}N_3O_3S$	69.79 69.71	4.81 4.63	10.03 10.16	196-198	50

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*Solvent: ethanol (compounds **1a**-**f**, **2a**,**b**, and **3a**,**b**), toluene (compounds **5a**-**d**).

TABLE 2. The IR Spectra of Compounds **1a**-**f**, **2a**,**b**, and **5a**-**d**

Com-pound	ν, cm^{-1}				
	SO_2	C=C	CON	NH_2	Others bonds
1a	1132, 1370	1666	1720	3328, 3362, 3424, 3490	
1b	1140, 1370	1664	1696	3342, 3442	
1c	1130, 1378	1664	1704	3338, 3298, 3252, 3190	
1d	1132, 1376	1664	1716	3348, 3452	
1e	1136, 1376	1664	1716	3454, 3336	
1f	1128, 1378	1664	1694	3328, 3434, 3116 (OH)	
2a	1152, 1347	1616			1680 (C=O), 3019 (OH), 3334, 3547 (NH_2NH_2)
2b	1149, 1347	1629			1686 (C=O), 3160 (OH), 3305 (NH_2NH_2)
5a	1130, 1340	1640			3324 (OH), 1595 (C=N)
5b	1146, 1317	1548			1539 (C=N)
5c	1139, 1316	1640			1589 (C=N), 3061; 3262, 3361; 3409 (SO_2)
5d	1139, 1307	1607			1529 (C=N)

We tried to prepare the 3-hydrazones of 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones under more rigid conditions. The reaction was conducted with 98% hydrazine hydrate by boiling in glacial acetic acid and gave a mixture of compounds that could not be separated into the individual compounds. This is probably explained by the presence of the acylated form of the 3-hydrazone in the reaction mixture in addition to 3-aminoimino-3-pyrrolin-2-one, as demonstrated by the peaks of the fragment ions in the mass spectrum of the mixture.

While studying the reaction of 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones with ethylenediamine we established that the reaction takes place at room temperature with the reagents in ratios of 1:1 or 2:1 and leads to the formation of a double salt of ethylenediamine and 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones **3a**,**b**. When the reaction was carried out under more rigid conditions, i.e., by boiling the reagents in dioxane for 1 h, the yields of the compounds were reduced.

The formation of an adduct of two molecules of the pyrrolone and one molecule of ethylenediamine is obviously due to the high basicity of the amino groups in ethylenediamine. Compounds **3a**,**b** (Table 1) are colorless crystalline substances with limited solubility in organic solvents.

The ^{1}H NMR spectra of compounds **3a**,**b** (Table 3) contain a signal for the protons of the $(CH_2)_2$ groups at 2.87-3.38 ppm.

Compounds **3a**,**b** give a cherry-red color with an alcohol solution of $FeCl_3$, indicating together with the spectral data that they exist in the enolic form.

When compound **3a** is kept at 180-185°C until the release of gases has stopped N,N′-di(4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-on-3-yl)ethylenediamine (**4**) is formed. It is a white crystalline substance soluble in DMSO and DMF and does not give a cherry-red color with an alcohol solution of $FeCl_3$. The constants and spectral data of this compound are given in the experimental section.

During further study of the reaction of 1,5-diaryl-3-hydroxy-4-methylsulfonyl-3-pyrrolin-2-ones with *o*-phenylenediamine we obtained the previously undescribed [2] 2,3-diaryl-4-methylsulfonylpyrrolo-[2,3-*b*]quinoxalines **5a-d** (Table 1), which are greenish-yellow crystalline compounds readily soluble in DMSO and DMF.

The IR spectra of compounds **5a-d** (Table 2) contain bands for the stretching vibrations of the C=N (1529-1595 cm^{-1}) and C=C (1584-1640 cm^{-1}) bonds.

In the ^{1}H NMR spectra of compounds **5a-d** (Table 3) there are a group of signals for the aromatic protons in the region of 6.72-8.34 ppm and a singlet for the three protons of the methylsulfonyl group at 3.39-3.52 ppm.

TABLE 3. The ^{1}H NMR Spectra of Compounds **1a-f**, **2a**,**b**, **3a**,**b**, and **5a-d**

Compound	Chemical shifts, δ, ppm.				
	Ar–H, m	H-5, s	$MeSO_2$, s	NH_2, s	Other protons
1a	7.05-7.60 (10H)	6.04	2.32	6.60	
1b	7.20-7.67 (9H)	6.05	2.34	6.57	
1c	6.80-7.57 (9H)	5.95	2.35	6.51	3.71 (3H, s, H_3CO)
1d	7.04-7.58 (9H)	6.02	2.34	6.57	
1e	7.20-7.53 (8H)	6.09	2.48	6.53	
1f	6.62-7.34 (9H)	5.85	2.30	5.52	9.21 (1H, s, HO)
2a	6.58-7.17 (10H)	5.79, 5.68	2.47		
2b	6.98-7.57 (9H)	5.79	2.49		9.20 (1H, s, HO)
3a	5.79 (10H)	5.61	2.41		3.28 (4H, m, $CH_2)_2$)
3b	5.61 (9H)		2.47		2.87 (4H, m, $CH_2)_2$)
5a	7.15 (13H)		3.51		9.58 (1H, s, OH)
5b	7.61 (13H)		3.52		
5c	8.34 (13H)		3.46		
5d	6.72 (14H)		3.39		5.40 (2H, s, CH_2)

The mass spectrum of compound **5b** contains a molecular ion peak with *m/z* 433 $[M]^+$ and 99.9% intensity and also peaks for fragment ions with *m/z* 354 $[M-CH_3SO_2]^+$ (30.6%) and 319 $[M-Cl]^+$ (39.39%), confirming the structure.

EXPERIMENTAL

The ^1H NMR spectra were obtained in DMSO-d_6 on a Bruker AM-300 spectrometer (300 MHz) with TMS as internal standard. The IR spectra were recorded in vaseline oil on a Specord-85 spectrometer. The mass spectra were obtained on a MAT-311A spectrometer (40 eV).

3-Amino-4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-one (1a). A mixture of 3-hydroxy-4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-one (1.64 g, 5 mmol) and urea (0.60 g, 10 mmol) was kept at 170-180°C for 1 h until the release of gases had stopped. The reaction mixture was treated with ethanol, and the precipitate was filtered off. Yield 48%; mp 157-158°C (ethanol).

Compounds 1b-f were obtained similarly.

The Salt of 3-Hydroxy-4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-one and Hydrazine (2a). A mixture of 3-hydroxy-4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-one (1.64 g, 5 mmol) and 50% hydrazine hydrate (0.16 g, 5 mmol) was boiled in dioxane (20 ml) for 1 h. The solvent was evaporated. Yield 85%; mp 115-117°C (ethanol).

Compound 2b was obtained similarly.

The Double Salt of 3-Hydroxy-4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-one and Ethylenediamine (3a). A solution of 3-hydroxy-4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-one (1.64 g, 5 mmol) and 50% ethylenediamine (0.30 g, 5 mmol) in dioxane (10 ml) was kept at room temperature for 1 h. The solvent was evaporated under vacuum, and the residue was treated with ethanol. Yield 65%; mp 198-200°C (ethanol).

Compound 3b was obtained similarly.

N,N′-Di(4-methylsulfonyl-1,5-diphenyl-3-pyrrolin-2-on-3-yl)ethylenediamine (4). Compound **3a** (2.16 g, 3 mmol) was kept at 180-185°C for 30 min, ethanol (20 ml) was added, and the crystals that separated were filtered off. Yield 50%; mp 151-153°C (ethanol). ^1H NMR spectrum, δ, ppm (*J*, Hz): 2.85 (6H, s, $(CH_3SO_2)_2$); 5.93 (1H, s, H-5); 6.00 (1H, s, H-5); 7.00-7.50 (20H, m, $4C_6H_5$); 3.90-4.20 (4H, m, $(CH_2)_2$). Found, %: N 7.96. $C_{36}H_{34}N_4O_6S_2$. Calculated, %: N 7.84.

2-(4-Hydroxyphenyl)-4-methylsulfonyl-3-phenylpyrrolo[2,3-*b*]quinoxaline (5a). A mixture of 1-(3-hydroxy-4-hydroxyphenyl-4-methylsulfonyl-5-phenyl-3-pyrrolin-2-one (1.64 g, 5 mmol) and *o*-phenylenediamine (0.54 g, 5 mmol) was kept at 190-200°C for 30 min, ethanol (20 ml) was added, and the crystals that separated were filtered off. Yield 52%; mp 294-295°C (toluene).

Compounds 5b-d were obtained similarly.

The work was carried out with financial support from the Russian Fundamental Research Fund (project No. 04-03-96042).

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