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THE REACTION OF 5-ARYL-(HETARYL)-2-AROYLMETHYLTHIO-1,3,4-OXADIAZOLES WITH ARYLDIAZONIUM TETRAFLUOROBORATES

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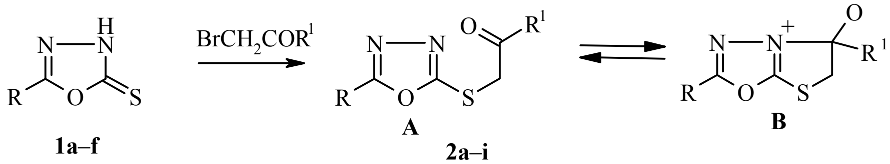
5-Aryl(hetaryl)-2-aroylmethylthio-1,3,4-oxadiazoles behave as CH acids and readily react with aryldiazonium tetrafluoroborates at the active methylene group to give azo coupling products. The spectroscopic properties of the compounds synthesized have been studied.

Keywords: 5-aryl(hetaryl)-2-aroylmethylthio-1,3,4-oxadiazoles, 5-aryl(hetaryl)-2-(1-aroyl-1-hydrazinomethylthio)-1,3,4-oxadiazole, azo coupling reaction with diazonium tetrafluoroborates.

In a continuation of a study on the synthesis and properties of compounds containing active methylene groups [1-6], 5-aryl(hetaryl)-2-aroylmethylthio-1,3,4-oxadiazoles (**2a-i**), which can exist as two tautomeric forms A and B [8], have been obtained by the reaction of 5-aryl(hetaryl)-1,3,4-oxadiazole-2(3H)-thiones (**1a-f**) with substituted phenacyl bromides [7]. Analysis of the ^{1}H NMR and IR spectroscopic data (Tables 1 and 2) shows unambiguously that compounds **2a-i** exist in the form of the open chain tautomer A, analogously to N-substituted 2-acylmethylthiobenzimidazoles [9]. In fact the protons of the methylene groups of the phenacyl substituents in compounds **2a-i** appear as a singlet in the ^{1}H NMR spectra in the 5.03-5.26 ppm region, whereas for the form B the signals characteristic of an AB system would be expected as a result of the presence of an asymmetric center. In addition the IR spectra contain bands characteristic of the C=O stretching vibrations in the region of 1670-1690 cm^{-1}, which confirms structure A.



1a–f   **2a–i**

1a R = C_6H_5; **b** R = 3-BrC_6H_4; **c** R = 4-FC_6H_4; **d** R = $C_6H_5CH_2$; **e** R = 3-C_5H_4N; **f** R = 4-C_5H_4N. **2a*** R = R^1 = C_6H_5;
b R = 3-BrC_6H_4, R^1 = C_6H_5; **c** R = 3-BrC_6H_4, R^1 = 4-ClC_6H_4; **d** R = 3-BrC_6H_4, R^1 = 4-$O_2NC_6H_4$;
e R = 4-FC_6H_4, R^1 = 4-$CH_3OC_6H_4$; **f** R = $C_6H_5CH_2$, R^1 = 4-ClC_6H_4;
g* R = 3-C_5H_4N, R^1 = C_6H_5; **h*** R = 4-C_5H_4N, R^1 = C_6H_5; **i** R = 4-C_5H_4N, R = 4-ClC_6H_4
(* compounds whose synthesis and properties have been described in [7]).

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Compounds **2a-i** are CH acids which react readily with aryldiazonium tetrafluoroborates at the active methylene group to give azo coupling products (**3a-m**). The mobility of the methylene group hydrogen atom is indicated in the ^{1}H NMR spectra of compounds **2** by the disappearance of the CH_2 proton singlet and the appearance of CH singlet at 5.0-5.1 ppm as a result of substitution of the proton on deuterium when D_2O is added.

It is theoretically possible for compounds **3a-m** to exist in three tautomeric forms: the keto hydrazone (A), azo ketone (B) or azo enol forms (C). Formation of intramolecular hydrogen bonds between atoms $O_{(1)}$ and $N_{(3)}$ of the molecules is not excluded.

The ^{1}H NMR spectra of compounds **3a-m** contain signals of the NH group protons as singlets in the 10.78-11.89 ppm region, while the IR spectra include absorption bands characteristic of the CO and NH groups at 1650-1670 and 3128-3210 cm^{-1} regions respectively (Table 2), so that they are assigned the structure of the corresponding keto hydrazones (A).

TABLE 1. Characteristics of Compounds **2a-i*** and **3a-m**

Compound	Empirical formula	Found, % Calculated, %		mp, °C	Yield, %
		N	S		
2b	$C_{16}H_{11}BrN_2O_2S$	7.39 7.47	8.45 8.54	118.5-119	81
2c	$C_{16}H_{10}BrClN_2O_2S$	6.58 6.84	7.80 7.83	162-163	85
2d	$C_{16}H_{10}BrN_3O_4S$	9.89 10.0	7.58 7.63	147-148.5	92
2e	$C_{17}H_{13}FN_2O_3S$	8.05 8.11	9.20 9.24	154-155	83
2f	$C_{17}H_{13}ClN_2O_2S$	7.98 8.12	9.21 9.30	106-107	75
2i	$C_{15}H_{10}ClN_3O_2S$	12.2 12.7	9.60 9.65	150-151	91
3a	$C_{24}H_{20}N_4O_2S$	13.5 13.1	8.02 7.48	168-171	54
3b	$C_{22}H_{14}BrN_5O_4S$	12.8 13.4	6.21 6.11	267-268	72
3c	$C_{22}H_{13}BrClN_5O_4S$	12.9 12.5	5.70 5.73	252-253	75
3d	$C_{22}H_{13}BrCl_2N_4O_2S$	11.0 10.2	6.01 5.84	184.5-185	64
3e	$C_{23}H_{16}BrN_5O_5S$	12.1 12.6	5.82 5.76	210-210.5	67
3f	$C_{23}H_{16}FN_5O_5S$	13.8 14.2	6.52 6.49	253-254.5	72
3g	$C_{24}H_{19}ClN_4O_3S$	11.3 11.7	6.73 6.69	204-205	65
3h	$C_{23}H_{16}ClN_5O_4S$	14.0 14.2	6.51 6.48	241-242	68
3i	$C_{22}H_{17}N_5O_2S$	16.4 16.9	7.93 7.70	194-194.5	75
3j	$C_{21}H_{14}N_6O_4S$	19.0 18.8	7.23 7.17	247-248.5	74
3k	$C_{21}H_{14}N_6O_4S$	18.5 18.8	7.20 7.17	196-197	70
3l	$C_{22}H_{16}ClN_5O_3S$	14.5 15.0	6.91 6.87	227-227.5	67
3m	$C_{21}H_{13}ClN_6O_4S$	17.1 17.5	6.71 6.67	262-262.5	76

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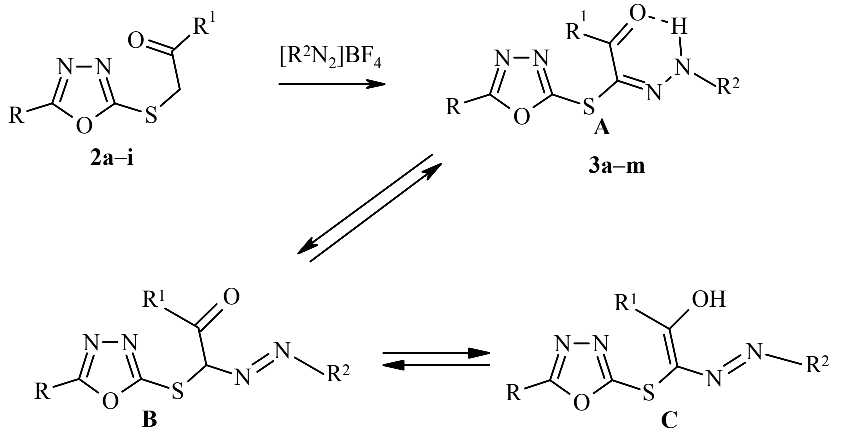
* Compounds **2a,g,h** are described in [7].



3a R = R^1 = C_6H_5, R^2 = 4-$C_2H_5C_6H_4$; **b** R = 3-BrC_6H_4, R^1 = C_6H_5, R^2 = 4-$O_2NC_6H_4$;
c R = 3-BrC_6H_4, R^1 = 4-ClC_6H_4, R^2 = 4-$O_2NC_6H_4$; **d** R = 3-BrC_6H_4, R^1 = C_6H_5,
R^2 = 2,4-$Cl_2C_6H_3$; **e** R = 3-BrC_6H_4, R^1 = 4-$O_2NC_6H_4$, R^2 = 4-$CH_3OC_6H_4$; **f** R = 4-FC_6H_4,
R^1 = 4-$CH_3OC_6H_4$, R^2 = 4-$O_2NC_6H_4$; **g** R = $C_6H_5CH_2$, R^1 = 4-ClC_6H_4, R^2 = 4-$CH_3OC_6H_4$;
h R = $C_6H_5CH_2$, R^1 = 4-ClC_6H_4, R^2 = 4-$O_2NC_6H_4$; **i** R = 3-C_5H_4N, R^1 = C_6H_5, R^2 = 4-$CH_3C_6H_4$;
j R = 3-C_5H_4N, R^1 = C_6H_5, R^2 = 4-$O_2NC_6H_4$; **k** R = 4-C_5H_4N, R^1 = C_6H_5, R^2 = 4-$O_2NC_6H_4$;
l R = 4-C_5H_4N, R^1 = 4-ClC_6H_4, R^2 = 4-$CH_3OC_6H_4$; **m** R = 4-C_5H_4N, R^1 = 4-ClC_6H_4,
R^2 = 4-$O_2NC_6H_4$

TABLE 2. ^{1}H NMR and IR Spectroscopic Data for Compounds **2a-i*** and **3a-m**

Compound	IR spectra, ν, cm^{-1}	^{1}H NMR spectra, δ, ppm			
		S–CH_2–CO (2H, s)	N–NH– (1H, s)	H–Ar (м)	other signals
2b	1672	5.22		7.56-8.12 (9H)	
2c	1670	5.18		7.52-8.12 (8H)	
2d	1672	5.26		7.52-8.43 (8H)	
2e	1690	5.12		7.08-8.05 (8H)	3.88 (3H, s, OCH_3)
2f	1670	5.03		7.29-8.01 (9H)	4.24 (2H, s, CH_2)
2i	1680	5.20		7.62-8.81 (8H)	
3a	1650, 3120		11.30	7.40-8.21 (14H)	1.23 (3H, t, CH_3); 2.70 (2H, q, CH_2)
3b	1650, 3126		11.55	7.50-8.41 (13H)	
3c	1650, 3120		11.58	7.50-8.41 (12H)	
3d	1650, 3100		11.34	7.48-8.15 (12H)	
3e	1650, 3130		11.44	7.10-8.39 (12H)	3.83 (3H, s, OCH_3)
3f	1660, 3160		11.44	7.17-8.50 (12H)	3.90 (3H, s, OCH_3)
3g	1660, 3184		10.78	7.09-8.18 (13H)	3.81 (3H, s, OCH_3); 3.53 (2H, s, CH_2)
3h	1660, 3170		10.85	7.21-8.24 (13H)	3.57 (2H, s, CH_2)
3i	1650, 3160		11.49	7.36-9.03 (13H)	2.38 (3H, s, OCH_3)
3j	1650, 3130		11.69	7.61-9.06 (13H)	
3k	1670, 3128		11.89	7.62-8.88 (13H)	
3l	1660, 3168		11.56	7.11-8.75 (12H)	3.83 (3H, s, OCH_3)
3m	1660, 3126		11.76	7.71-8.79 (12H)	

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* Compounds **2a,g,h** are described in [7].

EXPERIMENTAL

IR spectra of KBr disks were recorded with a UR-20 spectrometer. ^1H NMR spectra of DMSO-d_6 solutions with TMS as internal standard were obtained with a Bruker-300 (300 MHz) instrument.

5-R-2-Aroylmethylthio-1,3,4-oxadiazoles (2a-i). 1,3,4-Oxadiazole-2(3H)-thione (**1a-f**) (0.01 mol) was dissolved in aqueous ethanol (40 ml) containing KOH (0.56 g, 0.01 mol) and α-halo ketone (0.01 mol) dissolved in ethanol (20 ml) was added. The reaction mixture was kept for 10-15 h at 18-20°C, after which water (50 ml) was added, the precipitate was filtered off and washed with water.

5-R-2-[1-(R^2-Hydrazono)-2-R^1-2-oxoethylthio]-1,3,4-oxadiazoles (3a-m). Suspension of aryldiazonium tetrafluoroborate (0.01 mol) in mixture of AcOH (20 ml) and Ac_2O (5 ml) was added to solution of 5-R-2-aroylmethylthio-1,3,4-oxadiazole (**2a-i**) (0.01 mol) and anhydrous AcONa (1 g) in mixture of AcOH (30 ml) and Ac_2O (5 ml). The reaction mixture was kept in the dark at 18-20°C for 20-24 h and the precipitate was filtered off.

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