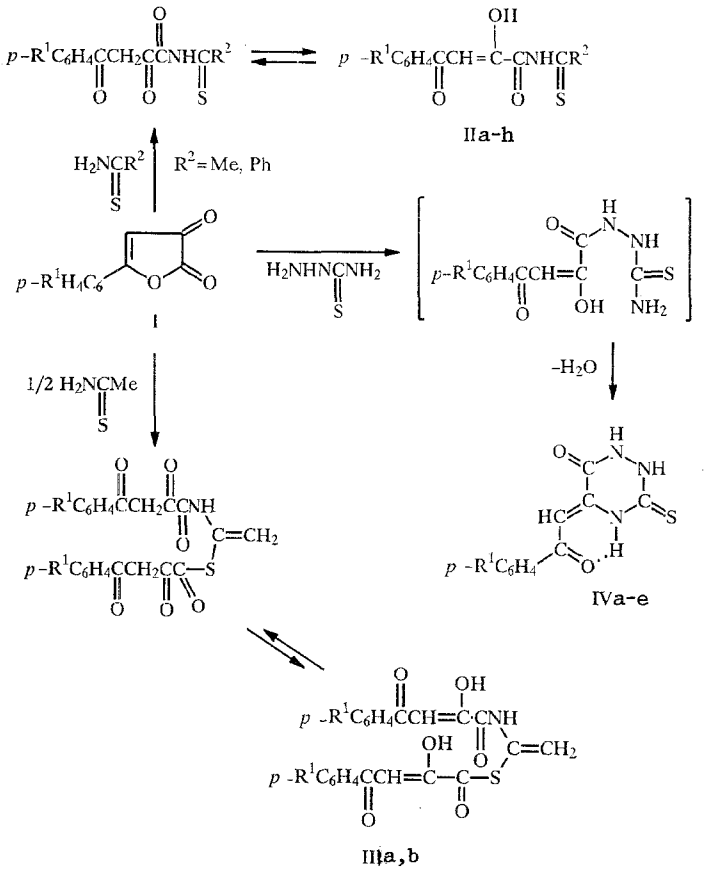
FIVE-MEMBERED 2,3-DIOXOHETEROCYCLES. 28.* REACTION OF 5-ARYL-2,3-DIHYDROFURAN-2,3-DIONES WITH THIOAMIDES AND THIOSEMICARBAZIDES

Yu. S. Andreichikov, D. D. Nekrasov, I. V. Krylova, and V. I. Bachurina

The reaction of 5-aryl-2,3-dihydrofuran-2,3-diones (I) with thiocarbonyl compounds has been described only for thiourea. The products of this reaction are 3-aryl-5-phenacylidene-4-oxoimidazolidine-2-thiones [2]. It seemed of interest to study the conversion of the furandiones (I) with a wider range of thiocarbonyl compounds such as thioamides and thiosemicarbazides.

We have established that thioacetamides and thiobenzamides open the ring of furandiones in 24 h at room temperature in absolute dioxan solution in the presence of a catalytic quantity of triethylamine with the formation of N-(aroylpyruvoyl)thioacetamides (IIa-e) and N-(aroylpyruvoyl)thiobenzamides (IIf-h), respectively.



*For Communication 27 see [1].

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The reaction does not proceed in the absence of triethylamine and attempts to activate the process by heating the reaction mixture lead to resinification. Probably triethylamine on the one hand aids polarization of the furandione causing the appearance of a positive charge on the carbon atom of the lactone carbonyl and facilitating attack on it by the amino group of the thioamide, and on the other hand it increases the nucleophilicity of the nitrogen atom of the thioamide amino group, which also facilitates opening of the furan ring.

No peak was detected in the mass spectrum of compound (IIe) for the molecular ion, which is probably due to its instability. Peaks were present with the following m/z values:* 270 (10) $[M - C_2HS]^+$, 225 (75) $[M - CH_3C(S)NHCO]^+$, 183 (100) $[BrC_6H_4CO]^+$, 155 (35) $[BrC_6H_4]^+$. The IR and PMR spectra of compounds (IIa-h) are given in Table 1. Compounds (IIa-h) were completely enolized in solution like the amides of aroylpyruvic acids [3].

Both nucleophilic centers participate in the reaction of compounds (I) with thioacetamide in anhydrous acetic acid at room temperature and 1-(aroylpyruvoylamido)-1-(aroylpyruvoylthio)ethylenes (IIIa, b) are formed.

The acetic acid acts as the solvent in this case.

The PMR spectra of compounds (IIIa, b), unlike those of compounds (IIa-e), contain a quadruplet for the methylene group at 3.85-3.88 ppm, two signals for methine protons at 6.90-6.75 and 6.93 ppm, and a multiplet for the protons of two aromatic rings which enable the structure of these compounds to be interpreted unequivocally. The absorption in the IR spectrum at 1710-1730 cm^{-1} corresponds to the absorption of the thioester and at 1670-1675 cm^{-1} to the amide carbonyl.

The reaction of compounds (I) with thiosemicarbazide proceeds in dioxan at room temperature. This is probably linked with the high nucleophilicity of the thiosemicarbazide amino group.

On opening the furan ring the intermediate 1-(aroylpyruvoyl)thiosemicarbazides split out a molecule of water and are cyclized into 5-phenacyliden-6-oxo-1,2,4-perhydrotriazine-3-thiones (IVa-e). An electron impact mass spectrum was taken for compound (IVe) with precise measurement of the mass of the molecular and fragment ions.

The found value for m/z of M^+ at 282.9961 is in good agreement with the calculated value of 282.9969 for a composition of $C_{11}H_8ClN_3O_2S$ (^{37}Cl). Decomposition of M^+ to the ions 222 (28) $[M - CHN_2O]^+$, 194 (22) $[M - CHN_3S]^+$, 139 (100) $[ClC_6H_4CO]^+$, 111 (50) $[ClC_6H_4]^+$, 89 (7) $[NHNHC(S)NH]^+$, 74 (30) $[NHC(S)NH]^+$ confirms the structure. Compounds (IVa-e) are in the form of Z-isomers due to the formation of an intramolecular hydrogen bond between the carbonyl of the phenacylidene substituent and the NH group of the triazine ring. The presence of the intramolecular hydrogen bond was confirmed by the reduction of the frequency of the vibrations of the phenacylidene carbonyl from 1630-1635 to 1600-1605 cm^{-1} (see Table 1). In the PMR spectrum the signal for the proton on the nitrogen atom at position 4 is found at 10.53-10.61 ppm, which also indicates the involvement of this proton in an intramolecular hydrogen bond.

1-Phenylthiosemicarbazide does not react with compounds (I) which is probably linked with the reduction in nucleophilicity and a diminution in the steric availability of the NH group.

It has been established that N-(aroylpyruvoyl)thioacetamides and N-(aroylpyruvoyl)thiobenzamides display weak antimicrobial and anti-inflammatory activity.

EXPERIMENTAL

The IR spectra were recorded on a UR 20 instrument in Nujol. The PMR spectra were recorded on a RYa 2310 (60 MHz) instrument in DMSO-D_6 (internal standard was HMDS). The mass spectra of compounds were obtained on a MX 1310 mass spectrometric system with SVP-5 direct insertion, at a resolution of $1.5 \cdot 10^4$ with precision determination of ion masses to at least $5 \cdot 10^{-6}$. Ionization energy was 50 eV.

The characteristics of the compounds synthesized are given in Table 1.

N-(Aroylpyruvoyl)thioamides (IIa-h). Thioacetamide or thiobenzamide (0.01 mole) and triethylamine (2-3 drops) were added to a solution of compound (I) (0.01 mole) in dioxan (20 ml). The reaction mixture was stirred well, left for 24 h, the solvent evaporated. Compounds (IIa-e) were recrystallized from chloroform or dichloroethane, compounds (IIf-h) from toluene.

*Peaks are shown for ions containing the lighter isotope of bromine.

TABLE 1. Characteristics of the Compounds Synthesized

Compound	Empirical formula	R^1	R^2	Mp, °C	IR spectrum, cm^{-1}	PMR spectrum, δ, ppm	Yield, %
IIa	$C_{12}H_{11}NO_3S$	H	Me	117...118	1160, 1470, 1605, 1650, 3190, 3225	2,38 (3H, s, CH_3); 7,07 (1H, s, CH); 7,78 (5H, m, C_6H_5); 8,38 (1H, s, NH)	65
IIb	$C_{13}H_{13}NO_3S$	Me	Me	116...117	1150, 1470, 1602, 1660, 3240, 3380	2,38 (6H, s, $2CH_3$); 7,02 (1H, s, CH), 7,78 (4H, q, C_6H_4); 9,15 (1H, s, NH)	90
IIc	$C_{14}H_{15}NO_4S$	EtO	Me	136...137	1180, 1470, 1603, 1665, 3220, 3370	1,33 (3H, t, CH_3); 2,31 (3H, s, CH_3), 4,05 (2H, q, CH_2); 6,98 (1H, s, CH); 7,45 (4H, q, C_6H_4); 9,15 (1H, NH)	80
IId	$C_{12}H_{10}ClNO_3S$	Cl	Me	165...166	1150, 1470, 1592, 1630, 3320, 3430	2,35 (3H, t, CH_3); 7,06 (1H, s, CH); 7,75 (4H, q, C_6H_4); 8,25 (1H, s, NH)	70
IIe	$C_{12}H_{10}BrNO_3S$	Br	Me	143...144	1155, 1470, 1600, 1670, 3250, 3395	2,41 (3H, s, CH_3); 7,08 (1H, s, CH); 7,80 (4H, q, C_6H_4); 8,45 (1H, s, NH)	76
IIf	$C_{17}H_{13}NO_3S$	H	Ph	113...114	1150, 1460, 1605, 1715, 3225, 3380	7,12 (1H, s, CH); 7,65 (10H, m, 2 C_6H_5); 9,62(1H, s, NH)	72
IIg	$C_{18}H_{15}NO_3S$	Me	Ph	116...117	1150, 1460, 1608, 1705, 3165, 3360	2,38 (3H, s, CH_3); 7,05 (1H, s, CH); 7,62 (9H, m, C_6H_5, C_6H_4); 9,55 (1H, s NH)	78
IIh	$C_{17}H_{12}BrNO_3S$	Br	Ph	147...149	1155, 1460, 1590, 1722, 3325, 3350	7,05 (1H, s, CH); 7,65 (9H, m, C_6H_5, C_6H_4); 9,61 (1H, s, NH)	82
IIIa	$C_{22}H_{17}NO_6S$	H		186..187	1670, 1710, 3180	3,85 (2H, q, CH_2); 6,70 (1H, s, CH); 6,93 (1H, s, CH); 7,55 (10H, m, $2C_6H_5$); 11,95 (1H, s, NH)	88
IIIb	$C_{24}H_{21}NO_6S$	Me		174...175	1675, 1738, 3170	2,35 (6H, c, $2CH_3$); 3,88 (2H, q, CH_2); 6,75 (1H, s CH); 6,93 (1H, s CH); 7,55 (8H, , $2C_6H_4$); 11,97 (1H, s NH)	79
IVa	$C_{11}H_9N_3O_2S$	H		196...198	1600, 1672, 3110, 3280, 3440	6,76 (1H, s CH); 7,06...8,12 (6H, m, C_6H_5, H); 9,06 (1H, s, NH); 10,13 (1H, s, NH)	94
IVb	$C_{12}H_{11}N_3O_2S$	Me		198...199	1595, 1670, 3120, 3300, 3435	2,38 (3H, s, CH_3); 7,11 (1H, s, CH); 7,18...8,11 (5H, m, C_6H_4, NH); 9,45 (1H, s, NH); 10,61 (1H, s, NH)	96
IVc	$C_{12}H_{11}N_3O_3S$	MeO		196...197	1605, 1690, 3140, 3270, 3340	3,80 (3H, s, CH_3O); 6,83...8,16 (6H, m, C_6H_4, CH, NH); 9,30 (1H, s, NH); 10,53 (1H, NH)	94
IVd	$C_{13}H_{13}N_3O_3S$	EtO		195...197	1600, 1680, 3120, 3315, 3460	1,30 (3H, t, CH_3); 4,00 (2H, q, CH_2); 6,73...8,10 (6H, m, C_6H_4, CH, NH); 9,36 (1H, s, NH); 10,56 (1H, s, NH)	95
IVe	$C_{11}H_8ClN_3O_2S$	Cl		220...221	1615, 1680, 3130, 3290, 3420	7,06 (1H, s, CH); 7,33...8,20 (5H, q, C_6H_4, NH); 9,43 (1H, s, NH); 10,56 (1H, s, NH)	97

1-Aroylpyruvoylamido-1-(aroylpyruvoylthio)ethylenes (IIIa, b). Compound (I) (0.01 mole) and thioacetamide (0.005 mole) were dissolved in anhydrous acetic acid (15 ml) at room temperature. The mixture was left for 24 h, the solid filtered off, washed with ether, and crystallized from benzene.

Z-5-Phenacyliden-6-oxo-1,2,4-perhydrotriazine-3-thiones (IVa-e). Thiosemicarbazide (0.01 mole) was added to a solution of compound (I) (0.01 mole) in anhydrous dioxan (10 ml) and mixed on a magnetic stirrer for 15-20 min. The precipitated solid was filtered off and recrystallized from acetonitrile.

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