# UNUSUAL TRANSFORMATIONS OF ARYLHYDRAZONOYL CHLORIDES OF ETHYL OXALATE

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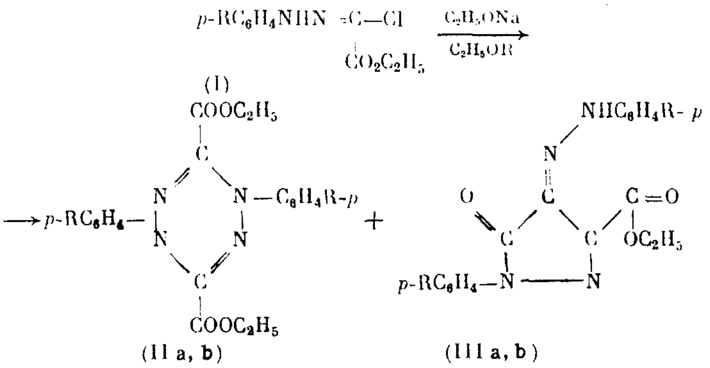
X-ray diffraction structural analysis, IR, $^{13}C$ NMR, and PMR spectroscopy was used to establish that the products of the reactions of arylhydrazonoyl chlorides of ethyl oxalate and sodium ethylate are 1,4-diaryl-3,6-dicarboethoxy-1,4-dihydro-1,2,4,5-tetrazines and 1-aryl-3-carboethoxy-4-arylhydrazono-5-pyrazolones.

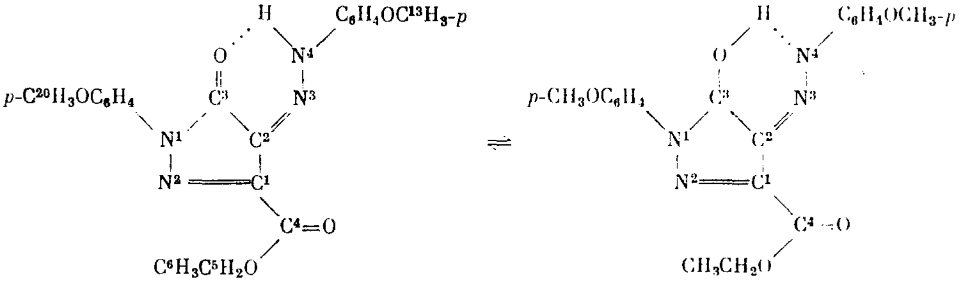
Arylhydrazonoyl chlorides of ethyl oxalate (I), containing electron-withdrawing substituents in the aryl ring, react with triethylamine to give 1,4-diaryl-3,6-dicarboethoxy-1,4-dihydro-1,2,4,5-tetrazines (II) [1, 2].

We have discovered that the reaction of (I) with sodium ethylate gives a mixture of a tetrazine (II) and 1-aryl-3-carboethoxy-4-arylhydrazono-5-pyrazolone (IIIa) or (IIIb). The yield of (III) is much greater than the yield of (II).



R = $CH_3$ (a), $OCH_3$ (b).

The structures of (IIa), (IIb), and (IIIa) were established by IR, $^{13}C$ NMR, and PMR spectroscopy. The spectra for product (IIIb) did not yield unequivocal conclusions. While the $^{13}C$ NMR and PMR data corresponded to structure (IIIb), the presence of IR bands characteristic for C=C, N=N, and OH bonds (see Experimental) was not in accord with the proposed structure. An x-ray diffraction structural analysis of monocrystals of (IIIb) showed that this compound in the crystal is a mixture of ketohydrazone (IIIb) and azoenol (IIIb') tautomers.



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Molecules of (IIIb) and (IIIb′) in the crystal differ in the bond lengths in the ketohydrazone and azoenol fragments. In (IIIb), $C^3{=}O$, 1.169(7); $C^3{-}C^2$, 1.495(2); $C^2{=}N^3$, 1.245(7); and $N^3{-}N^4$, 1.370(3) Å. In (IIIb′), $C^3{-}O$, 1.295(6); $C^3{=}C^2$, 1.345(5); $C^2{-}N^3$, 1.410(4), and $N^3{=}N^4$, 1.281(6) Å. The hydrogen atoms participating in the intramolecular $>N{-}H\cdots O{=}$ and $O{-}H\ldots N$ hydrogen bonds could not be located. The parameters of the hydrogen bonds···in (IIIb): $O\cdots N^4$, 2.667(8) Å, $\angle C^3ON^4$, 81.3(4)°, $\angle N^3N^4O$, 91.1(3)°. The parameters of the hydrogen bonds in (IIIb′): $O\cdots N^4$, 2.736(7) Å, $\angle C^3ON^4$, 77.9(3)°, and $\angle N^3N^4O$, 89.6(4)°.

The detailed results of the x-ray diffraction structural analysis of (IIIb) will be examined in a separate communication.

## EXPERIMENTAL

The IR spectra were taken on a UR-20 spectrophotometer. The PMR spectra were taken on a Bruker WP-200 spectrometer at 200 MHz in DMSO-$d_6$ and $CD_3CN$ with HMDS as the internal standard. The $^{13}C$ NMR spectra were taken on a Varian Gemini spectrometer at 50.3 MHz in DMSO-$d_6$ with HMDS as the internal standard.

1-p-Tolyl-3-carboethoxy-4-(p-tolylhydrazono)-5-pyrazolone (IIIa). A sample of 2.4 g (0.01 mole) tolylhydrazonoyl chloride of ethyl oxalate (Ia) in 50 ml abs. ethanol was added with stirring to a solution of sodium ethylate prepared from 0.23 g metallic sodium and 30 ml absolute ethanol. Slight warming of the reaction mixture was noted and a crystalline precipitate formed after 5 min. The crystalline precipitate was filtered off, washed with ethanol and water, dried, and crystallized from ethanol to give 1.2 g (33%) (IIIa), mp 135°C. IR spectrum in KBr pellet ($\nu$, $cm^{-1}$): 1730 (C=O), 1650 (C=N), 2980, 2930 ($CH_3$, $CH_2$), 3230, 3100 (N-H), 3440 (OH), 1520 ($C_6H_4$). PMR spectrum in DMSO-$d_6$ ($\delta$, ppm): 1.32 t (3H, $CH_3CH_2$), 2.28 s ($CH_3{-}C_6H_4NH$), 2.45 ($CH_3C_6H_4NC{=}O$), 4.33 m (2H, $CH_2CH_3$), 7.22 m (4H, $C_6H_4NH$), 7.74 m (4H, $C_6H_4NC{=}O$), 13.90 s (1H, HN-N=). Found: C, 65.98; H, 5.60; N, 15.29%. M 364 (mass spectrometry). Calculated for $C_{20}H_{20}N_4O_3$: C, 66.00; H, 5.50; N, 15.37%. M 364.

1-(p-Methoxyphenyl)-3-carboethoxy-4-p-methoxyphenylhydrazono-5-pyrazolone (IIIb′) was obtained by analogy. The yield was 1.7 g (43%), mp 169°C. IR spectrum in KBr pellet ($\nu$, $cm^{-1}$): 1740 (C=O), 1660 (C=N), 1620 (C=C), 1510 (N-N), 1520 ($C_6H_4$), 2990, 2940 ($CH_3$, $CH_2$), 3310 (NH-N=), 3450 (OH). PMR spectrum in DMSO-$d_6$ ($\delta$, ppm): 1.40 t (3H, $CH_3CH_2$), 3.75 s (3H, $OCH_3$), 3.76 s (3H, $OCH_3$), 4.41 m (2H, $CH_2CH_3$), 7.02 m (4H, $C_6H_4NH$), 7.66 m (4H, $C_6H_4NC{=}O$), 14.22 s (1H, NH-N=). $^{13}C$ NMR spectrum ($\delta$, ppm): 53.62, 53.68 ($C^{13}$, $C^{20}$), 10 signals from 112.46 to 132.72 ($C_{arom}$), 158.64, 157.50, 156.47, 155.74 ($C^1$, $C^2$, $C^3$, $C^4$). Found: C, 60.66; H, 4.98; N, 14.11%, M 396 (mass spectrometry). Calculated for $C_{20}H_{20}N_4O_5$: C, 60.59; H, 5.08; N, 14.13%, M 396.

1,4-Di(p-tolyl)-3,6-dicarboethoxy-1,4-dihydro-1,2,4,5-tetrazine (IIa) was obtained from the mother liquor in the preparation of (IIIa). The filtrate was evaporated in vacuum. The residue was washed with water, dried, and crystallized from ethanol to give 0.38 g (5%) (IIa), mp 157°C. IR spectrum in KBr pellet ($\nu$, $cm^{-1}$): 1730, 1750 (C=O), 1610-1590, 1590-1500, 1465-1380 (tetrazine and phenyl rings). PMR spectrum in DMSO-$d_6$ ($\delta$, ppm): 1.29 t (6H, $CH_3CH_2$), 2.13 s (6H, $CH_{3arom}$), 4.38 m (4H, $CH_2CH_3$), 7.38-7.66 (8H, $H_{arom}$). Found: C, 64.69; H, 5.89; N, 13.70%, M 408 (mass spectrometry). Calculated for $C_{22}H_{24}N_4O_4$: C, 64.69; H, 5.92; N, 13.71%, M 408.

1,4-Di(p-methoxyphenyl)-3,6-dicarboethoxy-1,4-dihydro-1,2,4,5-tetrazine (IIb) was isolated by analogy. The yield of (IIb) was 0.18 g (~1%), mp 53°C. IR spectrum in KBr pellet ($\nu$, $cm^{-1}$): 1730, 1700 (C=O), 1610-1590, 1550-1500, 1465-1380 (tetrazine and phenyl rings). PMR spectrum in $CD_3CN$ ($\delta$, ppm): 1.27 t (6H, $CH_3CH_2$), 3.85 s (6H, $OCH_3$), 4.38 m (4H, $CH_2CH_3$), 7.01-7.80 m (8H, $H_{arom}$). Found: C, 59.86; H, 5.48; N, 12.77%, M 440 (mass spectrometry). Calculated for $C_{22}H_{24}N_4O_6$: C, 59.99, H. 5.49; N, 12.72%, M 440.

X-ray Diffraction Structural Investigation. Triclinic monocrystals of (IIIb) have a characteristic ruby color. The unit cell parameters are as follows: $(C_{20}H_{20}N_4O_5)_2$, molecular mass 792.8, a = 11.859(3), b = 10.439(2), c = 7.997(1) Å, $\alpha$ = 96.40(1), $\beta$ = 79.79(2), $\gamma$ = 87.74(2)°, V = 966.5(3) Å$^3$, space group P1, Z = 1 (molecules of (IIIb) and (IIIb′) are found in an independent region). The intensities of 1712 reflections with $I \geq 2\sigma(I)$ were measured using $CuK_\alpha$ radiation and an RÉD-4 automatic four-circle diffractometer. Absorption was not taken into account, $\mu(CuK_\alpha)$ = 8.40 $cm^{-1}$. The structure was solved by the direct method and refined anisotropically to R = 0.043. All the calculations were carried out using the Roentgen-75 program set [3].

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# REACTION OF ACYLACETYLENES AND METHYL PROPIOLATE WITH N,N′-BIS(DITHIOCARBOXY)PIPERAZINE

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The reaction of N,N′-bis(dithiocarboxy)piperazine with acetylenic ketones and methyl propiolate gave N,N′-bis(acylvinyldithiocarbo)- and N,N′-bis(methoxycarbonylvinyldithiocarbo)piperazines. Heating the compounds obtained with perchloric acid leads to intramolecular cyclization with the formation of N,N′-bis[2-acyl(methoxycarbonyl)methyl-1,3-dithietanium]piperazine perchlorates.

The reaction of N-methyldithiocarbamic acid with propiolic acid in the presence of $PCl_3$ leads to 5-methyl-4-oxo-1,3-thiazine-6-thione [1], while the reaction of the triethylammonium salt of N,N-diethyldithiocarbamic acid with the dimethyl ester of acetylenedicarboxylic acid (DMEADC) in acetonitrile gives 2-(N,N-diethylamino)-4,5-dicarbomethoxy-1,3-dithiol [2] in 88% yield. The trimethylammonium salt of dithiobenzoic acid reacts analogously with DMEADC to give 2-phenyl-4,5-dicarbomethoxy-1,3-dithiol [3].

We have previously studied the reaction of α-acetylenic ketones with N,N-dialkyldithiocarbamic acids in acetonitrile at 20°C leading to the formation of S-acylvinyl-N,N- dialkyldithiocarbamates and carried out their heterocyclization to give 1,3-dithietanium perchlorates by the action of perchloric acid [4, 5].

In the present work, we studied the reaction of terminal and substituted α-acetylenic ketones (Ia)-(Ie) and methyl propiolate (If) with N,N′-bis(dithiocarboxy)piperazine (II) in order to synthesize new functionally substituted piperazines, which hold promise as pharmacological agents.

Samples of (II) were synthesized by the reaction of anhydrous piperazine with carbon disulfide in 1:2 ratio in an aprotic solvent such as chloroform or acetonitrile and were used in the reaction without separation from the reaction mixture. The reaction of dithiocarbamic acid (II) with terminal acylacetylenes (Ia) and (Ib) in 1:2 mole ratio in chloroform at 20°C gives N,N′-bis[benzoylvinyldithiocarbo]piperazine (IIIa) and N,N′-bis[(thenoyl-2)- vinyldithiocarbo]piperazine (IIIb) in 88-94% yields.

The reaction of substituted acylacetylenes (Ic)-(Ie) with (II) was carried out in chloroform in the presence of triethylamine at 60°C. The yields of (IIIc)-(IIIe) were 52-85%.

The reaction of methyl propiolate (If) with (II) was carried out in acetonitrile with a 2:1 reagent ratio at 20°C. The yield of (IIIf) was 18%.

The IR spectra of (IIIa)-(IIIf) have bands for a conjugated carbonyl group at 1615-1630 $cm^{-1}$ (1690 $cm^{-1}$ for (IIIf)), C=C bonds at 1570-1600 $cm^{-1}$, C-N bonds at 1250-1270 $cm^{-1}$, and C-S bonds at 702-705 $cm^{-1}$. The PMR spectral data for (IIIa)-(IIIf) are given in Table 1.

Careful heating of (IIId)-(IIIf) in excess 57% perchloric acid leads to the formation of N,N′-bis(2-acyl(methoxycarbonyl)methyldithietanium]piperazine perchlorates (IVd)-(IVf). Salts (IVd)-(IVf) are white, high-melting, crystalline compounds, which are soluble in hot water, aqueous ethanol, acetone, and DMSO. The IR spectra of perchlorates (IVd)-(IVf) have bands at 1670-1705 $cm^{-1}$ (C=O), 1610-1620 $cm^{-1}$ (C=N), 1460 $cm^{-1}$ ($CH_2$), 700-705 $cm^{-1}$ (C-S), and 1080-1120 $cm^{-1}$ ($ClO_4^-$). The PMR spectral data for these compounds are given in Table 1.

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