

STRUCTURE AND RING-CHAIN TAUTOMERISM OF OXOALKYL DITHIOCARBAMATES AND 4-HYDROXY-1,3-THIAZIN-2-THIONES

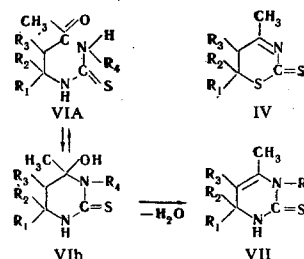
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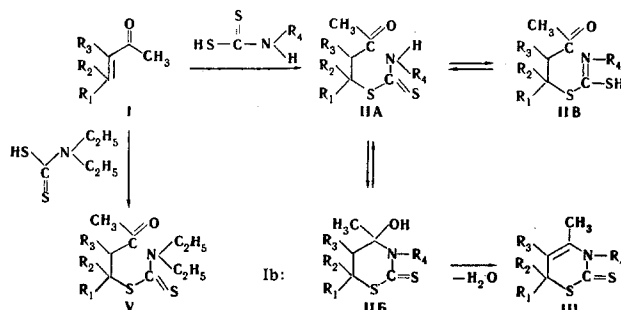
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The structures of the reaction products of some α, β -unsaturated ketones with dithiocarbamic acids have been investigated by IR spectroscopic methods. It has been shown that the adducts, in the crystalline state, may be either the acyclic oxoalkyl dithiocarbamates or the cyclic 4-hydroxytetrahydro-1,3-thiazin-2-thiones, depending on the number and positions of the substituents in the parent ketones. The existence of prototropic ring-chain tautomerism in solutions of 4-hydroxytetrahydro-1,3-thiazin-2-thiones has been established.

It has been shown previously [1, 2] that the reaction of aliphatic β -isothiocyanatoketones with primary amines gives, depending on the reaction conditions and on the nature of the starting materials, either the substituted oxoalkylthiureas (VIA) which are isomeric with the 4-hydroxyhexahydropyrimidine-2-thiones (VIB), or the tetrahydropyrimidine-2-thiones (VII). All the compounds of types VI and VII which we have prepared are effective accelerators of the vulcanization of rubber [3, 4].



As starting materials for the preparation of II, we used isopropenyl methyl ketone (Ia), and salts of unsubstituted and N-alkyl-substituted dithiocarbamic acids, prepared from equimolecular amounts of the corresponding amine, carbon disulfide, and sodium hydroxide or ammonium hydroxide [7]. The addition of dithiocarbamic acids to the double bond of the ketone Ia occurs when they are liberated from their sodium or ammonium salts at 10-40° C [6, 8]. The prod-

Ia: $R_1=R_2=H$; $R_3=CH_3$; Ib: $R_1=R_2=CH_3$; $R_3=H$.IIa: $R_1=R_2=R_4=H$; $R_3=CH_3$; IIb: $R_1=R_2=H$; $R_3=R_4=CH_3$; IIc: $R_1=R_2=H$; $R_3=CH_3$;IIc: $R_1=R_2=H$; $R_3=CH_3$; $R_4=C_2H_5$; IId: $R_1=R_2=H$; $R_3=CH_3$; $R_4=H-C_3H_7$; IIE: $R_1=R_2=H$; $R_3=CH_3$; $R_4=$ IIe: $R_1=R_2=H$; $R_3=CH_3$; $R_4=H-C_4H_9$; IIf: $R_1=R_2=R_4=CH_3$; $R_3=H$; IIg: $R_1=R_2=CH_3$; $R_3=R_4=H$.V: $R_1=R_2=H$; $R_3=CH_3$.

Examination of the structural analogs of compounds VIA, VIB, and VII, containing sulfur in place of one of the nitrogen atoms, was considered to be of interest in determining the relationship of structure to activity as vulcanization accelerators. The oxoalkyl dithiocarbamates IIA, their cyclic isomers, the 4-hydroxytetrahydro-1,3-thiazin-2-thiones IIB, and the dihydro-1,3-thiazin-2-thiones III or IV are of this type, the last compounds also being reported in the literature [5, 6] to be vulcanization accelerators.

The reaction of some α, β -unsaturated ketones with dithiocarbamic acids was examined. The products were the previously unknown oxoalkyl dithiocarbamates IIA or the corresponding cyclic compounds IIB.

ucts are viscous oils which are stable on keeping, but purification by chromatography on grade II alumina gives low melting crystalline solids which are readily soluble in organic solvents.

The chemistry of the reactions involved suggests that the first products should possess the acyclic oxoalkyl dithiocarbamate structure IIA. The other possible structure for the adducts is the isomeric cyclic 4-hydroxytetrahydro-1,3-thiazin-2-thione structure (IIB), formed by the migration of a proton from the nitrogen atom in the molecular conformation IIA and consequent bond formation between the carbonyl and amino groups.

The reaction products of α, β -unsaturated ketones with dithiocarbamic acids have previously been as-

signed the cyclic structures IIB [5,8,9]. By analogy with compounds VIA and VIB described in [1,2], however, it seems probable that structure IIB is found only in the crystalline state, with a prototropic tautomeric equilibrium existing in solution between the acyclic IIA and cyclic (IIB) forms.

The structures of our compounds II were investigated by IR spectroscopy both in the solid state, and in solution in chloroform and in carbon tetrachloride. The spectra were recorded on a UR-10 spectrometer, using a LiF prism for the 2800–3700 cm^{-1} region and NaCl for the region from 800 to 2800 cm^{-1} . Examination of the IR spectra of II in vaseline oil suspension, exemplified in Fig. 1 by compounds IIc and IId (curves 3 and 4, respectively), shows that all these compounds possess the acyclic oxoalkyl dithiocarbamate structure IIA when in the crystalline state. This is shown by the strong absorption bands at 1710–1720 cm^{-1} (C=O group), and broad bands at 3200 cm^{-1} which we attributed to the absorption of the NH group participating in intramolecular hydrogen bonding with sulfur and nitrogen atoms and carbonyl and thiocarbonyl groups of neighboring molecules.

A similar picture was observed with CCl_4 solutions of these compounds at a concentration of 0.05 M, the bands due to the carbonyl group (1710–1720 cm^{-1}) and the free NH group (3410 cm^{-1}) of the monomeric IIA being accompanied by the band at 3200 cm^{-1} due to residual intermolecular hydrogen bonding, this band disappearing completely on dilution to 0.01 M (curves 3 and 4, Fig. 2).

Since these results are in conflict with the literature [5,8,9] concerning the cyclic structure IIB for the products of the reaction between dithiocarbamic acids and aliphatic α,β -unsaturated ketones, we prepared the previously described compounds IIIf and IIg starting from mesityl oxide (Ib). These compounds had been assigned [5,8,9] the structure IIB.

The IR spectra of suspensions of IIIf and IIg in vaseline oil (curves 1 and 2, Fig. 1) confirm that these compounds, in contrast to our compounds IIA–IIe, exist in the crystalline form as the cyclic 4-hydroxy-tetrahydro-1,3-thiazine-2-thione IIB, as shown by the absence of the band at 1710–1720 cm^{-1} characteristic of the carbonyl group of the acyclic form IIA. We have attributed the absorption in the 3200–3300 cm^{-1} region to intermolecular association (or dimerization) of the cyclic forms IIB with the hydroxyl, amino and thione groups and sulfur atoms of neighboring molecules. A similar picture is seen with the spectra [2] of the crystalline forms of compounds VIB (vaseline oil suspension).

The spectra of solutions of IIIf at 0.01 M in CHCl_3 and CCl_4 (curve 1, Fig. 2), immediately after solution of the samples, show a band at 3600 cm^{-1} , attributed to the free hydroxyl group of the monomeric cyclic form IIB. Carbonyl absorption during the first few minutes after solution is absent, but spectra recorded after successive time intervals show a progressive diminution in the intensity of the band at 3600 cm^{-1} ,

accompanied by the appearance and gradual increase in intensity of the carbonyl absorption band at 1720 cm^{-1} of the acyclic form IIA. The intensity of this band increases for 1 hr, after which it attains a maximum which remains unchanged. At the same time, their appears in the spectra of solutions of IIIf a band at 3400 cm^{-1} due to the free NH group. This behavior in chloroform and CCl_4 indicates the opening of the ring IIB as a result of prototropic ring-chain tautomerism, with the establishment of the tautomeric equilibrium $\text{IIB} \rightleftharpoons \text{IIA}$ with the acyclic form IIA predominating. This may be deduced by comparing the intensity of the carbonyl absorption in the spectrum of IIIf with that of compound V in CCl_4 at the same concentration (0.01 M). The intensity of the carbonyl absorption in the model compound V was taken as 100%. Compound IIg behaved similarly in dichlorethane solution (curve 2, Fig. 2).

We have thus shown, in contrast to the findings of Iansen et al. [5,8,9], that while the compounds IIIf–IIg possess the cyclic structure IIB in the crystalline state, when in solution they are almost wholly converted into the acyclic form IIA as a result of prototropic ring-chain tautomerism in a similar way to that described in the literature [2], for example, compound VI.

Comparing compounds II with their structural analogs VI which contain a single substituent on the nitrogen atom shows that the mutual relationship between the cyclic and acyclic forms in both series is dependent on the substituents in the oxoalkyl moiety of the molecule. On the other hand, the cyclic forms of VIB are, in all cases, more stable than the corresponding cyclic forms IIB.

In those cases where compounds II and VI have a hydrogen atom in the α -position to the carbonyl group and geminal methyl groups in the β -position, in both series there is a strong tendency toward conversion of the acyclic forms IIA and VIA into the cyclic forms IIB and VIB. In this connection, compounds VIIf and VIg preserve the stable cyclic structure VIB, both in the crystalline form and in solution in CHCl_3 and CCl_4 , whereas their structural analogs IIIf and IIg exist in the cyclic form IIB only in the crystalline state, and in solution are converted to IIA. The introduction of a methyl substituent in the α -position to the carbonyl group and the replacement of the geminal methyl groups in the β -position by hydrogen atoms leads, in both series, to a reduction in the stability of the cyclic forms IIB and VIB, with the result that VIB–VID are gradually transformed in solution from VIB into VIA, while the corresponding compounds IIB–e do not exist at all in the cyclic form IIB, and irrespective of their state of aggregation possess the acyclic form IIA.

The greater stability of the cyclic forms VIB, in comparison with their analogs IIB, is apparently connected with the different electronic contributions of the nitrogen and sulfur to the total electronic systems of the molecules, i. e., to the different p- π -electron delocalization energies in the systems:

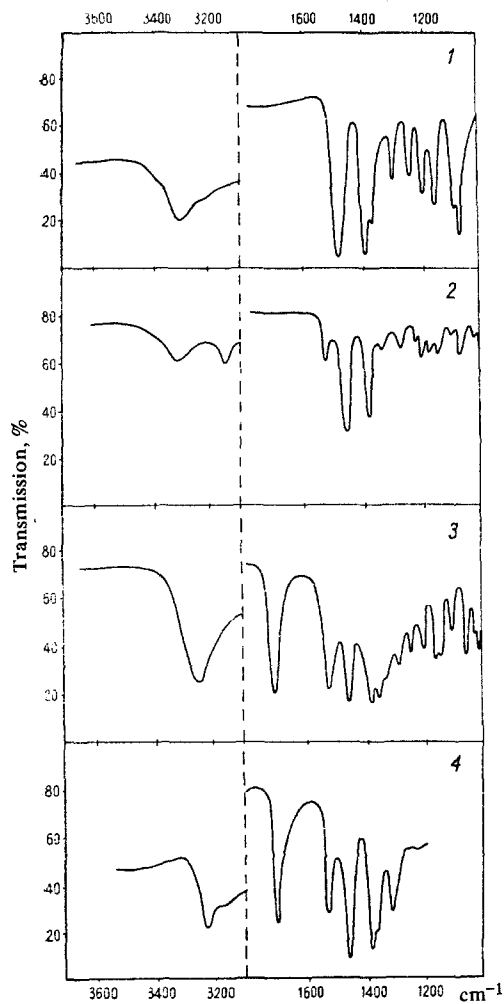


Fig. 1. IR spectra of the crystalline forms of compounds: 1) II f; 2) II g; 3) II c; 4) II d. Spectra recorded in vaseline oil.

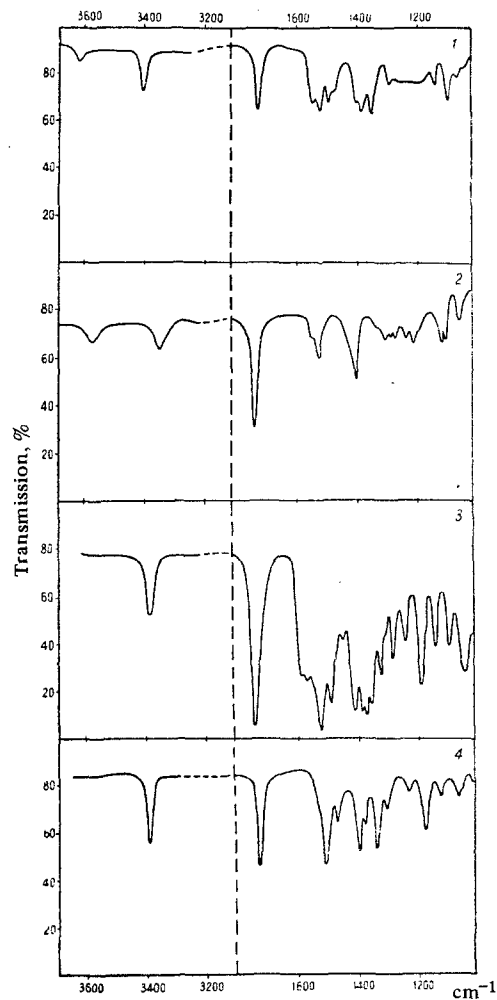
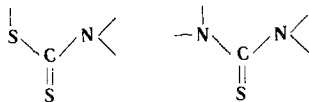


Fig. 2. IR spectra of solutions: 1) II f; 2) II g; 3) II c; 4) II d. Solvents: CCl_4 , c 0.01 M, d = 0.998 mm (compound II g was recorded in dichloroethane, c 0.005 M, d = 0.998 mm).



Compounds II can theoretically exist in both the thione (IIA) and thiol (IIB) forms. Absorption due to the SH group ($2400\text{--}2500\text{ cm}^{-1}$) is absent from the spectra of IIa–IIe and IIg, both in the crystalline form and in solution, while a strong absorption at $1520\text{--}1530\text{ cm}^{-1}$ related to the thioamide grouping [10] appears together with the NH absorption band at 3320 cm^{-1} , showing that IIa–IIe exist in the thione form IIA.

The absorption at 1530 cm^{-1} due to the thioamide group is absent from the spectrum of compound IIf in the crystalline state in which it possesses the cyclic structure IIB, but this band appears in solution as a result of its conversion to the acyclic form IIA.

Attempts to dehydrate compound IIb with 25% H_2SO_4 at 70°C were unsuccessful, unchanged IIb being recovered. The dehydration was effected in the case of compound IIa by heating in acetic anhydride at 80°C . The reaction product, a stable crystalline substance, apparently possesses the structure IIIa rather than the other possibility IVa, which has a system of conjugated double bonds.

EXPERIMENTAL

Thin-layer chromatography was carried out on alumina of grade II activity.

2-Methyl-3-oxobutyl dithiocarbamate (IIa). A 40% solution of 21.7 g (0.20 mole) of ammonium dithiocarbamate was added, with stirring during 50 min, to a mixture of 15 g (0.18 mole) of isopropyl methyl ketone (Ia), 18 ml of conc HCl and 30 ml of water, the temperature being kept at 15°C . The reaction mixture was then stirred at $55\text{--}60^\circ\text{C}$ for 1 hr, cooled, the dark-colored oil separated from the aqueous layer and kept for 24 hr at 0°C . There was obtained 18.2 g (56.9%) of IIa as a yellow crystalline solid, mp $102\text{--}103.5^\circ\text{C}$ (from hexane-alcohol), readily soluble in alcohol and acetone, but insoluble in CCl_4 , benzene, and hexane. Found, %: C 40.60; H 6.23. Calculated for $\text{C}_6\text{H}_{11}\text{NOS}_2$, %: C 40.64; H 6.26.

4,5-Dimethyl-1,3-dihydrothiazine-2-thione (IVa). A mixture of 14.7 g (0.083 mole) of IIa and 17 g (0.17 mole) of acetic anhydride with 1 drop of conc H_2SO_4 was heated at 60°C for 2 hr. To the warm dark red solution was added 20 ml of ice water, and the copious yellow precipitate filtered off, washed with water, and dried. There was obtained 11.1 g (84%) of IVa, mp $111\text{--}112^\circ\text{C}$ (from light petroleum-alcohol). Found, %: C 45.31; H 5.50; N 8.81. Calculated for $\text{C}_8\text{H}_9\text{NS}_2$, %: C 45.23; H 5.71; N 8.79.

2-Methyl-3-oxobutyl N-methyldithiocarbamate (IIb). To a mixture of 13 g (0.15 mole) of Ia was added sodium N-methylcarbamate (20 g; 0.15 mole), 25 ml of alcohol and 14 ml of conc HCl, with vigorous stirring at 0°C . The reaction mixture was stirred for 3 hr at 20°C , the organic layer separated, the aqueous layer washed with $3 \times 20\text{ ml}$ of ether, the washings combined with the organic layer and dried over calcined MgSO_4 . Removal of the ether gave 16.7 g (56%) of bright yellow oil, R_f 0.72 (3:1, benzene-acetone). Trituration of the oil with a mixture of ether and light petroleum afforded crystals, mp $34\text{--}35^\circ\text{C}$ (after washing with cold ether). Found, %: C 43.65; H 6.81. Calculated for $\text{C}_7\text{H}_{13}\text{NOS}_2$, %: C 43.99; H 6.86.

2-Methyl-3-oxobutyl N-ethylthiocarbamate (IIc). From 10 g (0.07 mole) of sodium N-ethylthiocarbamate, 5.9 g (0.07 mole) of ketone Ia and 6 ml of conc HCl at 80°C with stirring for 3 hr, there was obtained 6.77 g (47%) of IIc, mp $50\text{--}51.5^\circ\text{C}$ (from hexane), R_f 0.6 (3:1, benzene-ether). Found, %: C 46.83; H 7.38. Calculated for $\text{C}_8\text{H}_{13}\text{NOS}_2$, %: C 47.01; H 7.17.

2-Methyl-3-oxobutyl N-propyldithiocarbamate (IIId). Similarly, from 20 g (0.13 mole) of sodium N-propyldithiocarbamate, 10.7 g (0.13 mole) of Ia, and 12 ml of conc. HCl in 20 ml of water, there was obtained 13.2 g (46.5%) of IIId, which after purification by chromatography on a column of grade II alumina and recrystallization from hexane had mp $29\text{--}30.5^\circ\text{C}$, and R_f 0.6 (4:1, benzene-ether). Found, %: C 49.50; H 8.01; S 29.57. Calculated for $\text{C}_9\text{H}_{17}\text{NOS}_2$, %: C 49.51; H 7.81; S 29.40.

2-Methyl-3-oxobutyl N-isobutyldithiocarbamate (IIe). Similarly, from 20 g (0.11 mole) of potassium N-isobutyldithiocarbamate and 8.4 g (0.1 mole) of Ia there was obtained 11.7 g (50%) of a yellow oil which was purified by chromatography on a column of grade II alumina. n_D^{20} 1.5498; d_4^{20} 1.0846. Found, %: N 6.22; S 27.61; MR_D 68.53. Calculated for $\text{C}_{10}\text{H}_{19}\text{NOS}_2$, %: N 6.09; S 27.47; MR_D 68.40.

2-Methyl-3-oxobutyl N-diethylthiocarbamate (V). To a mixture of 10 g (0.12 mole) of ketone Ia, 10 ml of conc HCl, and 15 ml of water, was added 20.5 g of a 40% aqueous solution of sodium N-diethylthiocarbamate at 150°C . The mixture was stirred for 2 hr at 50°C , the organic layer separated, the aqueous layer extracted with ether, the ether extract combined with the organic layer, dried over calcined MgSO_4 , the ether was removed and the residual oil purified by chromatography on a grade II alumina column. Yield 7.46 g (32.2%) of bright yellow oil, R_f 0.75 (2:1 benzene-acetone), n_D^{20} 1.5440; d_4^{20} 1.105. Found, %: S 27.56; MR_D 68.70. Calculated for $\text{C}_{10}\text{H}_{19}\text{NOS}_2$, %: S 27.46; MR_D 68.59.

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