

THIOUREA DERIVATIVE OF β -DICARBONYL COMPOUNDS

VII. Synthesis and Study of 2-Thioxoindeno[1,2-d]imidazolin-4-one*

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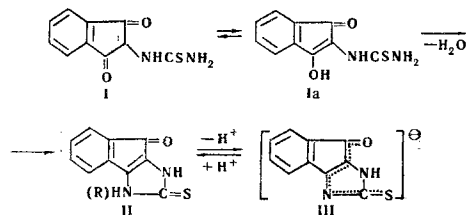
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The action of ammonium thiocyanate on the hexachlorostannate of 2-aminoindan-1,3-dione forms not 2-thioureidoindan-1,3-dione but a cyclization product, 2-thioxoindeno[1,2-d]imidazolin-4-one. The reactivity of this compound has been studied. It dissolves in alkalis with the formation of a conjugated anion. Under the action of 60% sulfuric acid it is converted into 4(5)-(o-carboxyphenyl)imidazole-2-thione. Methylation with dimethyl sulfate leads to the formation of 3-methyl-2-methylthioindeno-[1,2-d]imidazole.

α -Aminoketones are widely used as the starting materials for the synthesis of heterocyclic systems. Imidazole-2-thione derivatives have been synthesized by the action of ammonium thiocyanate on α -amino-ketone hydrochlorides [1-9].

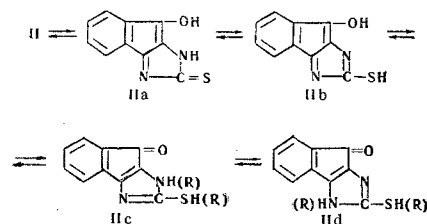
In preceding investigations, we have studied the conditions for the synthesis of 2-thioreido derivatives of 2-substituted indan-1,3-diones from the corresponding 2-aminoindan-1,3-diones and ammonium thiocyanate [10,11], and also their transformation under the action of sulfuric acid [11,12]. The synthesis of the 2-thioreido derivative of indan-1,3-dione from 2-aminoindan-1,3-dione and the investigation of its reactions encounters difficulties because of the extremely low stability of the initial 2-aminoindan-1,3-dione [3]. We have directed attention to the fact that the hexachlorostannate of 2-aminoindan-1,3-dione, which is obtained in the reduction of 2-nitrosoindan-1,3-dione with stannous chloride, is formed in good yield and is extremely stable [14]. An investigation of the reactivity of this salt in the reaction with ammonium thiocyanate in ethanolic solution in the presence of hydrochloric acid showed that, under these conditions, a product containing sulfur and nitrogen is, in fact, formed. It was possible to expect, equally, the formation of 2-thioureidoindan-1,3-dione (I), capable of existing in its enolic form (Ia), or the product of its cyclization—2-thioxoindeno[1,2-d]imidazolin-4-one (II):



The results of elementary analysis and the IR spectrum permit structure II to be ascribed to the product obtained. In the double-bond region there is only one frequency of carbonyl absorption at 1717 cm^{-1} , the

frequency of a $\text{C}=\text{C}$ at 1622 cm^{-1} , and the stretching vibrations of an aromatic ring at 1603 cm^{-1} ; the frequency at 1175 cm^{-1} can be ascribed to the vibrations of the $\text{C}=\text{S}$ bond [5]. In the $2800\text{--}3200\text{ cm}^{-1}$ region, a broad absorption band also includes the vibrations of the N-H bonds [16]. When II was subjected to oximation with hydroxylamine in 5% aqueous alkali, an oxime was formed. The IR spectrum of the oxime lacked the frequency of $\text{C}=\text{O}$ groups and had the frequency of $\text{C}=\text{N}$ and $\text{C}=\text{C}$ bonds at 1643 cm^{-1} , together with frequencies of an aromatic ring in the $1616\text{--}1590\text{ cm}^{-1}$ region. Thus, the imidazolethione structure II does not cause doubt for the solid state of the reaction product. This conclusion agrees with the literature information since imidazolethiones [15], oxazolethiones [16], and triazolethiones [17] capable of tautomerism exist in the form of the thioxoamines in the solid state.

If we turn our attention to the structure of product II, it can be seen that the system is capable of tautomeric forms:

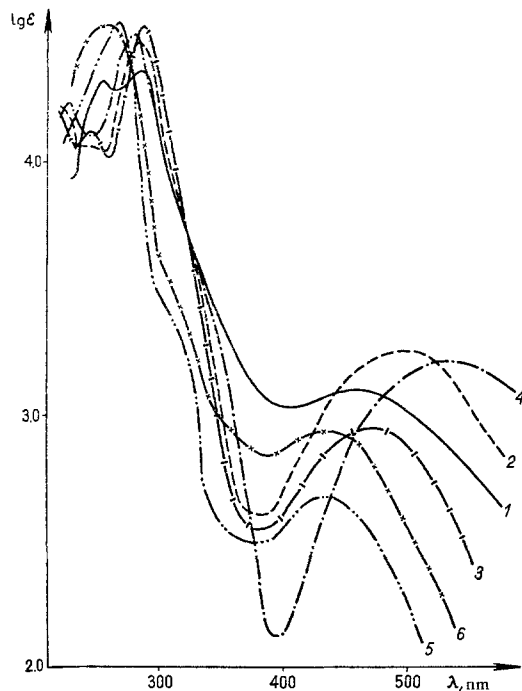


Compound II dissolves in aqueous and ethanolic solutions of alkalis with an intense coloration, which shows the formation of the conjugated anion III. The latter is responsible for the capacity of compound II for undergoing alkylation with dimethyl sulfate in an alkaline medium with the formation of a dimethylation product which, on the basis of its IR spectrum, may be regarded as a derivative of the tautomeric form IId or IIc ($\text{R} = \text{CH}_3$). No O-methylation takes place, since the IR spectrum of the methylated product retains the frequency of the carbonyl absorption of 1697 cm^{-1} but has lost the frequencies of the stretching vibrations of the $\text{C}=\text{S}$ and N-H groups. As can be seen, the IR spectrum does not enable us to choose between the forms IIc and IId ($\text{R} = \text{CH}_3$).

An investigation of the UV spectra in methanolic solution in the presence of alkali and acid showed that the anionic form has absorption at $\lambda_{\text{max}} 290\text{ nm}$ ($\log \epsilon 4.5$) and by a maximum at $515\text{--}540\text{ nm}$ ($\log \epsilon 3.20$), characterizing the conjugated system of the anion III (see figure). The absorption maximum characterizing the system of the anion at 290 nm is also retained for the methanolic and acidified methanolic solutions but

*For part VI, see [11].

in the latter case there is, in addition, a somewhat less intense band in the 250–260 nm region, apparently characterizing the undissociated form II, which is in all probability also specific to the solid state of the

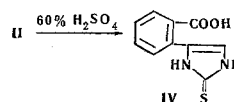


The UV spectra, concentration 10^{-4} mole/l: 1) II in methanol; 2) II in 0.1 M methanolic KOH; 3) II in 0.1 M methanolic HCl; 4) II in 1 M aqueous NaOH; 5) II_d, R = CH₃, in methanol; 6) II, R = CH₂COC₆H₅, in methanol.

substance. The long-wave maximum of II is displaced hypsochromically and is found at 470 nm. The methylation product is characterized by the maximum of the undissociated form at λ_{\max} 265 nm, and the long-wave maximum is displaced hypsochromically still more, being found at 430 nm, while the maximum of the anionic form is completely absent from the spectrum. The presence in the spectrum of the methylated product of the maximum characteristic for the undissociated form II, and also the considerable hypsochromic displacement of the long-wave maximum forces us to assume structure II_d and not II_c for the methylated product. For II_c we could expect a deepening of the color as compared with that of the starting material, since, in this case, the length of the conjugated system is increased. The process of formation of II_d apparently begins with alkylation at the nitrogen of the ketoenamine system and is completed by alkylation at the sulfur of the thione-thiol grouping. The alkylation of II with phenacyl bromide leads to the formation of the product of the monoalkylation of II (R = CH₂COC₆H₅). Alkylation takes place at the nitrogen in position 3, since the IR spectrum retains the $\nu_{\text{C=S}}$ frequency at 1201 cm⁻¹. As can be seen, the tautomeric forms II_a–II_c play no appreciable part in the reactivity of II.

Under the action of 60% sulfuric acid, II is converted into 4(5)-(o-carboxyphenyl)imidazole-2-thione

(IV), which is the parent of derivatives of this system synthesized previously [11,12].



The structure of product IV was confirmed by its UV and IR spectra. The UV spectrum has λ_{\max} at 265 (log ϵ 4.13) and 295 (log ϵ 4.10) nm and is identical in nature with that of a model substance, 4(5)-phenylimidazole-2-thione. In the IR spectrum, ν_{COOH} is found at 1682 cm⁻¹, $\nu_{\text{C=C}}$ at 1655 cm⁻¹, and the frequencies of the aromatic ring in the 1614–1599 cm⁻¹ region. Compound IV forms a salt with triethylamine which has the single broad absorption band in the 1551–1626 cm⁻¹ range that is characteristic for the COO⁻ and an aromatic system.

EXPERIMENTAL

2-Thioxoindeno[1,2-d]imidazolin-4-one (II). A solution of 2.1 g of 2-aminoindan-1,3-dione hexachlorostannate [14] and 0.6 g of ammonium thiocyanate in 15 ml of ethanol was treated with 1.5 ml of conc HCl and was immediately heated in a previously-heated water bath for 15 min. A red precipitate deposited. The solution was poured into 200 ml of water, whereupon the precipitate dissolved; a 5% solution of alkali was added, the mixture was filtered, and the filtrate was acidified with HCl. The precipitate that deposited was filtered off and washed with water, giving 0.8 g (61%) of a substance with mp 272–274° C (from dioxane). Found, %: C 59.41; H 3.15; N 13.91; S 16.10. Calculated for C₁₀H₆N₂OS, %: C 59.39; H 2.99; N 13.86; S 15.85.

Oxime of 2-thioxoindeno[1,2-d]imidazolin-4-one. Over 1 hr, 0.5 g of hydroxylamine hydrochloride was slowly added to a solution of 0.5 g of II in 15 ml of 5% alkali. The color of the solution changed from violet to yellow-brown. Then, it was acidified and the precipitate was filtered off. This gave 0.5 g (93%) of an orange-colored oxime. After two recrystallizations from dioxane, mp 256° C. Found, %: N 19.21; S 14.71. Calculated for C₁₀H₇N₃OS, %: N 19.34; S 14.76.

3-Methyl-2-methylthioindeno[1,2-d]imidazolin-4-one (II_d, R = CH₃). A solution of 0.70 g of II in 20 ml of 10% NaOH was treated with 1 ml of dimethyl sulfate and the mixture was left at room temperature for 2 hr with occasional stirring. A red-brown precipitate deposited. In this way, 0.60 g (75%) of II with mp 166° C (from ethanol) was obtained. Found, %: C 63.05; H 4.10; N 12.09; S 13.91. Calculated for C₁₂H₁₀N₂OS, %: C 63.58; H 4.37; N 12.16; S 13.92.

3-Phenacyl-2-thioxoindeno[1,2-d]imidazolin-4-one (II_d, R = CH₂COC₆H₅). A solution of 0.60 g of II and 0.54 g of phenacyl bromide in 15 ml of ethanol was heated in the water bath for 20–30 min. The reaction mixture was poured into water and extracted with benzene. The benzene solution was dried over anhydrous sodium sulfate. Evaporation of the benzene yielded 0.50 g (52%) of a substance with mp 185–187° C (from ethanol). Found, %: C 67.57; H 3.79; N 8.43; S 10.22. Calculated for C₁₈H₁₂N₂O₂S, %: C 67.51; H 3.77; N 8.74; S 10.01.

4(5)-(o-Carboxyphenyl)imidazole-2-thione (VI). With heating 0.47 g of comminuted II was dissolved in 10 ml of 60% H₂SO₄, and the solution was boiled for a further few minutes, cooled, and neutralized with a 10% solution of alkali. The precipitate that deposited was dissolved in an excess of alkali and the solution was acidified and extracted with ethyl acetate. The extract was dried over anhydrous sodium sulfate and the ethyl acetate was distilled off to give 0.30 g (58%) of faintly yellow IV with mp 238–240° C (from ethanol). Found, %: C 54.69; H 3.80; N 12.94; S 14.60. Calculated for C₁₀H₆N₂O₂S, %: C 54.53; H 3.66; N 12.73; S 14.55.

Triethylamine salt of 4(5)-(o-carboxyphenyl)imidazole-2-thione. A suspension of IV in absolute ethanol was treated with 0.2 ml of triethylamine and the mixture was heated, whereupon the solid matter dissolved. After the addition of ether, 0.15 g (51%) of the salt crystallized out. Mp 163–165° C (from ethanol with the addition of ether).

Found, %: C 59.39; H 7.02; N 13.03; S 9.88. Calculated for $C_{10}H_8N_2O_2S \cdot N(C_2H_5)_3$, %: C 59.43; H 7.16; N 12.99; S 9.91.

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