SYNTHESIS OF 3-NITRO-4-AMINO- AND 3,4-
DIAMINOTHIOCOUMARINS*

V. L. Savel'ev, T. G. Afanas'eva, and V. A. Zagorevskii

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Nitration of 4-hydroxythiocoumarin gave 3-nitro-4-hydroxythiocoumarin, which was converted to 3-nitro-4-chlorothiocoumarin by the action of phosphorus oxychloride in dimethylformamide. The corresponding 3-nitro-4-aminothiocoumarins were synthesized by reaction of 3-nitro-4-chlorothiocoumarin with ammonia or amines. The 3-nitro-4-aminothiocoumarins were hydrogenated in alcohol over Raney nickel to give 3,4-diaminothiocoumarins. The \( \beta \)-aminovinylcarbonyl form of the 4-substituted 3-aminothiocoumarins was established on the basis of the UV, IR, and PMR spectra.

In contrast to the oxygen and nitrogen heteroanalogs - coumarin and carbostyril - little study has been devoted to the chemical properties of the heterocyclic ring of 1-thiocoumarin and substituted 1-thiocoumarins [2-4], whereas polyfunctional thiocoumarin derivatives, particularly 3-substituted 4-aminothiocoumarins, may be of particular interest as subjects for chemical and physicochemical studies.

We have synthesized a number of 3-nitro-4-amino- (Ia-i) and 3,4-diaminothiocoumarins (IIa-i):

\[
\text{OH} \quad \text{HNO}_3 \quad \text{OH} \quad \text{NO}_2 \quad \text{POCl}_3 \quad \text{Cl} \quad \text{NO}_2 \quad \text{HNR'}R''
\]

\[
\begin{align*}
\text{III} & \rightarrow \text{IV} \rightarrow \text{V} \rightarrow \text{Ia-i} & \text{IIa-i} \\
& \text{HI} & \text{IIi} \text{i} \text{i}
\end{align*}
\]

1. \( R = R' = H; b \ R = H, R' \neq H; c \ R = H, R' = C_6H_5; d \ R = H, R' = C_6H_5 \text{-tert}; e \ R = H, \\
R' = CH_2C_6H_5; f \ R = H, R' = C_6H_5; g \ R = R' = C_6H_5; h \ R + R' = (C_6H_5) \)

Nitration of 4-hydroxycoumarin (III) with fuming nitric acid in a mixture of concentrated sulfuric and glacial acetic acids gave 3-nitro-4-hydroxythiocoumarin (IV), which by the action of phosphorus oxychloride in dimethylformamide (DMF) was converted to 3-nitro-4-chlorothiocoumarin (V) - the key compound for the synthesis of amino derivatives I and II. Compounds V were aminated to Ia-i by the action of excess ammonia or 2 moles of amine in absolute benzene solution. Diamines IIa-i were obtained by hydrogenation of nitro compounds Ia-i in alcohol over Raney nickel.

According to the PMR spectra, aminonitrothiocoumarins Ia-i exist in the thiocoumarin form. Thus the signal of the protons of the CH_2N group in the spectrum of Ie in solution in \((\text{CD}_3)_2\text{SO}-\text{CDCl}_3\) (1:2) appears at 4.4 ppm in the form of a doublet due to spin-spin coupling (SSC) \((J = 6 \text{ Hz})\) with the proton of the NH group, the broad signal of which is found at 8.5 ppm; when \text{CD}_3\text{OD} is added, the doublet is converted to a singlet (deuteration and exchange processes), and the signal at 8.5 ppm practically vanishes.

Dependent vibrations of the C = O group are observed at 1615 cm\(^{-1}\), i.e., in a longer-wavelength region than in the spectrum of thiocoumarin itself (1640 cm\(^{-1}\)), in the IR spectra (in chloroform) of Ig-4 (Table 1), which are model compounds with a fixed amino group; in addition, there are characteristic absorption bands of double bonds of the cyclic system (1585 and 1570 cm\(^{-1}\)) and stretching vibrations of an NO_2 group (~1525 and ~1350 cm\(^{-1}\)).

*See [1] for our preliminary communication.


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TABLE 1. Frequencies of the Characteristic Absorption Bands of 3-Nitro-4-amino- (Ia–Ii) and 3,4-Diaminothiocoumarins (IIa–IIe)

<table>
<thead>
<tr>
<th>Compound</th>
<th>ν, cm⁻¹</th>
<th>Compound</th>
<th>ν, cm⁻¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ia²</td>
<td>3465, 3400, 3360, 3245</td>
<td>Ha</td>
<td>3385, 3350, 3310, 3290</td>
</tr>
<tr>
<td>Ib²</td>
<td>3340, 3350</td>
<td>Hb²</td>
<td>3450, 3350</td>
</tr>
<tr>
<td>Ic²</td>
<td>3450, 3340</td>
<td>Hc²</td>
<td>3405, 3340, 3330</td>
</tr>
<tr>
<td>Id²</td>
<td>3340, 3350</td>
<td>He²</td>
<td>3400, 3350</td>
</tr>
<tr>
<td>Ie²</td>
<td>3450, 3340</td>
<td>Hf²</td>
<td>3400, 3340, 3330</td>
</tr>
<tr>
<td>If²</td>
<td>3340, 3350</td>
<td>Hg²</td>
<td>3400, 3350</td>
</tr>
<tr>
<td>Ig²</td>
<td>3450, 3340</td>
<td>Ih²</td>
<td>3400, 3340, 3330</td>
</tr>
<tr>
<td>Ih²</td>
<td>3340, 3350</td>
<td>IIa²</td>
<td>3385, 3350, 3310, 3290</td>
</tr>
<tr>
<td>IIb²</td>
<td>3340, 3350</td>
<td>IIc²</td>
<td>3450, 3350</td>
</tr>
<tr>
<td>IIe²</td>
<td>3340, 3350</td>
<td>IId²</td>
<td>3400, 3350</td>
</tr>
<tr>
<td>IIe²</td>
<td>3450, 3340</td>
<td>IIe²</td>
<td>3400, 3340, 3330</td>
</tr>
</tbody>
</table>

aThe IR spectra of oil suspensions were recorded. bThis band vanishes when the compound is deuterated. cSolution in chloroform (c 0.01 M, d 1.01 mm). dShoulder. eSolution in chloroform (c 0.1 M, d 0.16 mm). fSolution in chloroform (c 0.01 M, d 0.6 mm).

TABLE 2. Data from the UV Spectra of 3-Nitro-4-amino- (I) and 3,4-Diaminothiocoumarins (II)

<table>
<thead>
<tr>
<th>Compound</th>
<th>λ_max, nm</th>
<th>log ε</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ic</td>
<td>235; 261; 317</td>
<td>4.47; 4.09; 4.07</td>
</tr>
<tr>
<td>Ig</td>
<td>235; 267; 299; 353</td>
<td>4.40; 3.88; 3.87; 3.87</td>
</tr>
<tr>
<td>Ih</td>
<td>235; 267; 299; 352</td>
<td>4.32; 3.87; 3.84; 3.87</td>
</tr>
<tr>
<td>IIa</td>
<td>235; 279; 363</td>
<td>4.64; 4.06; 4.02</td>
</tr>
<tr>
<td>IIb</td>
<td>235; 277; 361</td>
<td>4.40; 4.01; 4.00; 4.02</td>
</tr>
<tr>
<td>IIc</td>
<td>235; 277; 373</td>
<td>4.54; 4.15; 4.06</td>
</tr>
<tr>
<td>IIe</td>
<td>237; 279; 372</td>
<td>4.51; 4.07; 4.06</td>
</tr>
<tr>
<td>IIh</td>
<td>227; 273; 364</td>
<td>4.47; 3.99; 3.99</td>
</tr>
<tr>
<td>Ih</td>
<td>225; 274; 366</td>
<td>4.55; 4.03; 3.99</td>
</tr>
</tbody>
</table>

The IR spectra of mineral oil suspensions of Ib–If, which have a secondary amino group, are characterized by the following absorption frequencies: 3350 (ν NH), ~1590 (broad intense band, dependent vibrations of the carbonyl group and ring double bonds), ~1530 and ~1350 cm⁻¹ (NO₂ group). The transition to solutions in chloroform in the case of Ic, e is accompanied by an increase in the frequency of the vibrations of the secondary amino group (3450 cm⁻¹) and partial resolution of the broad band in the region of the vibrations of the double bonds of the system (1597 and shoulder at 1610 cm⁻¹). In analogy with the spectra of 4-amino-3-nitrocoumarins [5], the band at 3450 cm⁻¹ should be assigned to vibrations of a free amino group. In the case of Id, f passing to solutions in chloroform does not have a special effect on the absorption and form of the bands corresponding to the vibrations of the NH group (an additional band at 3430 cm⁻¹ from the vibrations of a free amino group appears in the spectrum of thiocoumarin II) but does gives rise to substantial changes in the region of absorption of the double bonds of the system: Bands are observed at 1630 (dependent vibrations of the C=O group) and ~1595 cm⁻¹ (ring double bonds). The absence of vibrations of a free NH group in the spectrum of a solution of Id is probably determined by the great advantageousness of intramolecular hydrogen bonds between the NH and NO₂ groups due to repulsion of the bulky substituent attached to the amino group in the 4 position away from the nitro group [5].

Instead of the one long-wave absorption maximum at 317 nm observed in the spectra of I that contain a secondary amino group, the UV spectra of I (Table 2) with a tertiary amino group contain two maxima at 295 and 353 nm; this is evidently associated with the change in the electronic interaction of the amino and nitro groups with one another and with the π-electron system of the thiocoumarin ring.