Chemistry of Coumarins. Thermal Reactions of 4-Chloro-3-coumarinyl *N,N*-Dialkyldithiocarbamates and 3-Nitro-4-coumarinyl *N*-Phenyldithiocarbamate

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The thermal reactions of 4-chloro-3-coumarinyl *N,N*-dialkyldithiocarbamates **2-4** and 3-nitro-4-coumarinyl *N*-phenyldithiocarbamate, **9**, afforded the novel heterocyclic systems, *e.g.* bis-6*H*-1-benzopyrano[4,3-*b*][1,4]dithiin, **7**, and bis-6*H*-1-benzopyrano[4,3-*b*][1,4]thiazine, **14**. A possible mechanism of the formation of the reaction products is discussed.

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Introduction.

It is well documented in the literature that coumarin derivatives posses a wide range of biological activity and show interesting chemical reactivity [1-4]. In the course of our studies on the chemistry of coumarins we have investigated the reactions for the preparation of a number of polycyclic heteroaromatic compounds having the coumarin ring [5-14]. In our previous paper [8] we reported that according to Pearson's HSAB principle [15] hard nucleophiles substituted for chlorine in position 4 and soft nucleophiles substituted for a nitro group in position 3 of 4-chloro-3-nitrocoumarin (**1**). The reaction of **1** with *N,N*-dialkyldithiocarbamate, as a soft nucleophile, gave the products substituted in position 3 which were shown to be thermally unstable compounds. It is the intention of the present paper to investigate the thermal decomposition of the products.

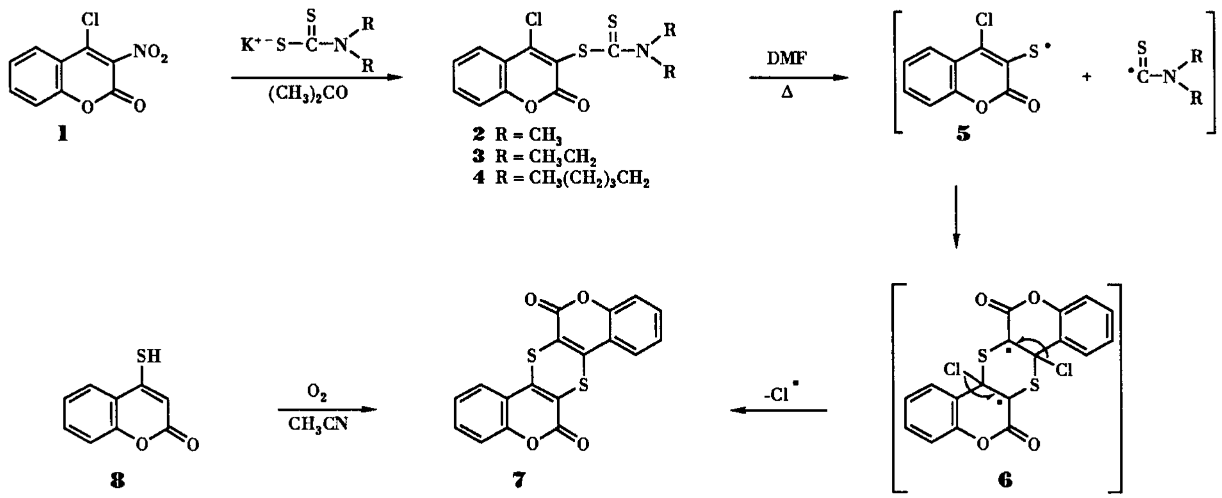
Results and Discussion.

When 4-chloro-3-coumarinyl *N,N*-dialkyldithiocarbamates **3-5** were refluxed in different solvents (DMF, acetonitrile, DMSO) the very insoluble bis-6*H*-1-benzopyrano[4,3-*b*][1,4]dithiin (**7**) was precipitated. It appeared that compound **7**, as a novel heterocyclic system, can be prepared through independent synthesis from 4-mercaptocoumarin (**8**) by air oxidation [16].

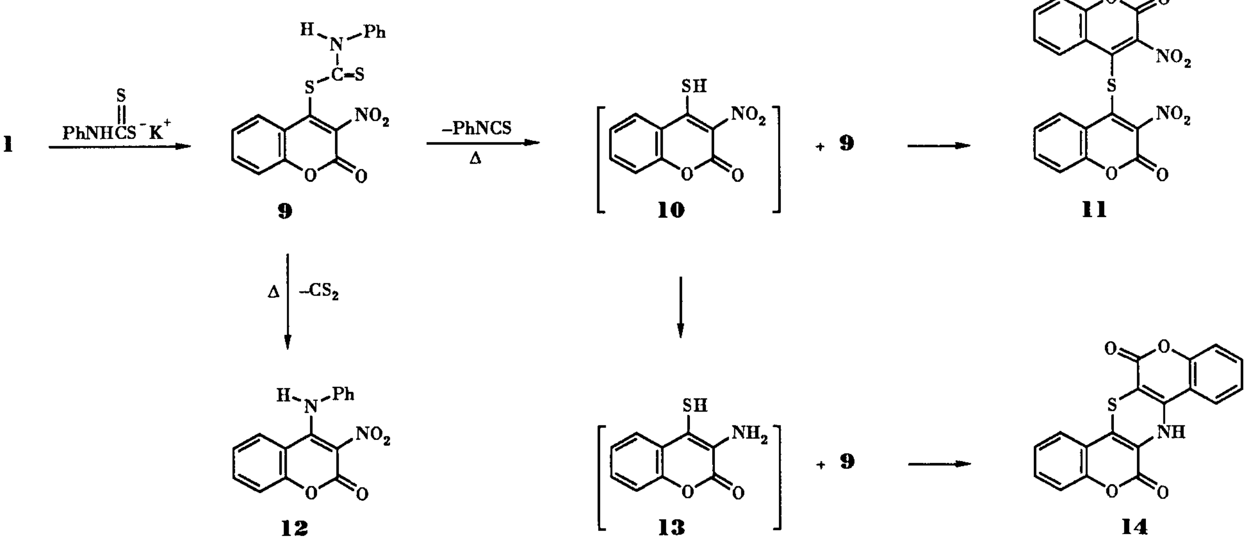
The ir spectrum of **7** shows absorption due to the carbonyl group of the pyrone ring at 1730 cm^{-1}. Additional confirmation of the structural assignment was obtained by elemental analysis and by the identification of a mass spectral peak corresponding to m/z 352 ($M^{\cdot +}$).

The proposed mechanism for the thermal decomposition of **2**, **3** and **4** is depicted in Scheme 1. 4-Chloro-3-coumarinyl *N,N*-dialkyldithiocarbamates **2-4** are homolytically cleaved to radicals **5**. Radical pair **5** resulting from thermolysis of **2**, showed CIDNP effect using ^{1}H-nmr in DMSO-d$_6$ as the solvent. The reaction is carried out in an nmr tube at 140°. Under these conditions the methyl protons showed a CIDNAP effect of the type A/E + A. Aromatic protons did not show a CIDNP effect under the same reaction conditions. The dimeric product **7** was presumably formed through attack of the nucleophilic thiyl radical at position **4** of the coumarin ring. The intermediate diradical, **6**, undergoes aromatization through the eli-

Scheme 1



Scheme 2



mination of two chlorine radicals, which could be the driving force for the reaction.

Reaction of 4-chloro-3-nitrocoumarin, **1**, and the potassium salt of *N*-phenyldithiocarbamate in acetone at 10-20° gave 3-nitro-4-coumarinyl *N*-phenyldithiocarbamate, **9**, Although *N*-phenyldithiocarbamate is a soft nucleophile it seems that the electronic factors are less important than the steric factors so that the substitution in the position 4 of the coumarin ring occurred similar to iodide [8] and benzylmercaptan [17] as a soft nucleophile. Product **9** is thermally rather unstable and cannot be purified by recrystallization. The ir spectrum of product **9** showed characteristic bands at 3300 (NH), 1730 (C=O), 1600 (C=C ar), 1540 (NO_2) and 1055 (C=S) cm^{-1} respectively.

It has been shown that the thermal decomposition of **9** is dependent upon the reaction conditions. On heating **9** in acetic acid for a few minutes bis-(3-nitro-4-coumarinyl) sulfide, **11**, was obtained. The formation of product **11** can be explained according to Scheme 2.

The decomposition of **9** takes place by elimination of phenylisocyanate leading to the intermediate 3-nitro-4-mercaptocoumarin, **10**, which reacts with **9** through nucleophilic displacement of *N*-phenyldithiocarbamate yielding **11** as the main product. The concomitant formation of isocyanate in a weakly acidic medium was considered to precede intramolecularly [18]. The reaction of **9** in refluxing DMF during 30 minutes gave rise to 3-nitro-4-anilinocoumarin, **12**, as the main product (70%) yield) and a novel heterocyclic system, bis-6*H*-1-benzopyrano[4,3-*b*][1,4]thiazine (**14**), as a minor product (12% yield). The ir spectra of **14** shows two absorption bands due to a carbonyl group at 1735 cm^{-1} and at 1685 cm^{-1} shifted due to intramolecular hydrogen bonds. The band at 3325 cm^{-1} is diagnostic for the NH group. The correct elemental analysis and the identification of a mass spectral peak at m/z 335 ($M^{+\cdot}$) are in accordance with the proposed structure.

The formation of the **11** can be explained through intramolecular elimination of carbon disulfide and compound **14** is formed presumably through the intermediate **10** which is being reduced to 3-amino-4-mercaptocoumarin, **13**, by hydrogen sulfide as a reducing species. A similar mode of decomposition of *N*-monosubstituted dithiocarbamate has been already proposed [19,20]. The intermediate compound **13**, having both hard (amino) and soft (mercapto) nucleophiles, reacts with **9** in a similar fashion as that previously described [11] leading to the final product **14**.

EXPERIMENTAL

All melting points are uncorrected. The ir spectra (potassium bromide pellets) were recorded on a Perkin-Elmer M-377 spectrophotometer, the nmr spectra were recorded on a Perkin-Elmer R 12 A spectrometer using tetramethylsilane as an internal standard and the mass spectra were recorded on a Hitachi Perkin-Elmer RMV-GL mass spectrometer.

3-Nitro-4-coumarinyl *N*-Phenyldithiocarbamate, **9**.

To a stirred and cooled solution (5°) of 4-chloro-3-nitrocoumarin, **1** (1 g, 4.4 mmoles) in acetone (50 ml) a solution of the potassium salt of *N*-phenyldithiocarbamate (0.91 g, 4.4 mmoles) in acetone (50 ml) was added dropwise at the rate so as to maintain the temperature of the reaction mixture below 10°. After stirring (4 hours) at room temperature ice-water (100 ml) was added to the reaction mixture. The resulting brown crystalline solid was filtered off to yield 1.05 g (70%) of **9** as a crude product with mp 228-234°; ir (potassium bromide): 3300, 1730, 1635, 1600, 1540, 1055, 760 cm^{-1}.

Reaction of 4-Chloro-3-coumarinyl *N*,*N*-Dimethyldithiocarbamate, (**2**) in DMF.

A solution of 4-chloro-3-coumarinyl *N*,*N*-dimethyldithiocarbamate, **2**, (0.98 g, 3.3 mmoles) in DMF (20 ml) was refluxed for 3.5

hours. During this period orange needles of **7** precipitated. After allowing the reaction mixture to stand for 1 hour at room temperature the product was collected by filtration and recrystallized from DMF to yield 0.33 g (59%) of analytically pure **7** mp >320°; ir (potassium bromide): 3060, 1730, 1600, 1590, 1530, 1450, 1305, 1130, 1045, 1015, 760, 745 cm^{-1}; ms: m/z (relative intensity) 352 (M$^{\cdot+}$, 88), 324 (10), 308 (100), 296 (20), 280 (44), 251 (30), 240 (28), 236 (30), 208 (20), 176 (44), 120 (58).

Anal. Calcd. for $C_{18}H_8O_4S_2$: C, 61.30; H, 2.27. Found: C, 61.30; H, 2.60.

Reaction of 3-Nitro-4-coumarinyl *N*-Phenyldithiocarbamate, 9, in Acetic Acid.

A solution of **9** (1 g, 2.7 mmoles) in acetic acid (50 ml) was refluxed during 3 minutes. The solution was cooled and allowed to stand overnight at room temperature. The dark brown crystalline solid was filtered off and recrystallized from acetic acid to yield 0.26 g (45%) of analytically pure **11** with mp 272-273°; ir (potassium bromide): 1745, 1605, 1595, 1545, 1450, 1310, 1270, 1060, 840, 760 cm^{-1}; ^{1}H nmr (DMSO-d$_6$): 7.15-8.21 (m, 8H, arom) ppm.

Anal. Calcd. for $C_{18}H_8N_2O_8S$: C, 52.42; H, 1.94; N, 6.79. Found: C, 52.08; H, 1.74; N, 6.60.

Reaction of 3-Nitro-4-coumarinyl *N*-Phenyldithiocarbamate, 9 in DMF.

A solution of **9** (1 g, 2.9 mmoles) was refluxed in DMF (25 ml) during 30 minutes. The product **14** precipitated on cooling and was recrystallized from DMF to give 0.11 g (12%) of analytically pure sample, mp 325-327°; ir (potassium bromide): 3325, 1735, 1685, 1600, 1595, 1500, 1465, 1370, 1145, 1130, 1050, 905, 745 cm^{-1}; ms: m/z (relative intensity) 335 (100), 319 (7), 318 (17), 317 (81), 307 (5), 303 (5), 295 (5), 288 (7), 279 (7), 278 (7), 262 (5), 261 (5), 260 (28), 178 (5), 150 (7), 149 (10), 121 (5), 120 (10), 103 (7), 102 (12), 89 (7), 88 (12), 77 (10), 76 (10).

Anal. Calcd. for $C_{18}H_9NO_4S$: C, 64.47; H, 2.68; N, 4.17. Found: C, 64.41; H, 3.03; N, 4.41.

The mother liquor after the separation of **14** was poured into ice-water (200 ml). The resulting yellow crystalline solid was filtered off and recrystallized from ethanol to yield 0.87 g (70%) of 3-anilino-4-nitrocoumarin, **12**. The ir, nmr and mp (267-268°) were the same as those obtained with an authentic sample [13].

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