A Reexamination of the Reactions of 2,3-Dichloro-1,4-naphthoquinone with Thioamides

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2,3-Dichloro-1,4-naphthoquinone reacts with thioamides and thiourea to give mixtures of condensed thiazoles and thianthrenes.

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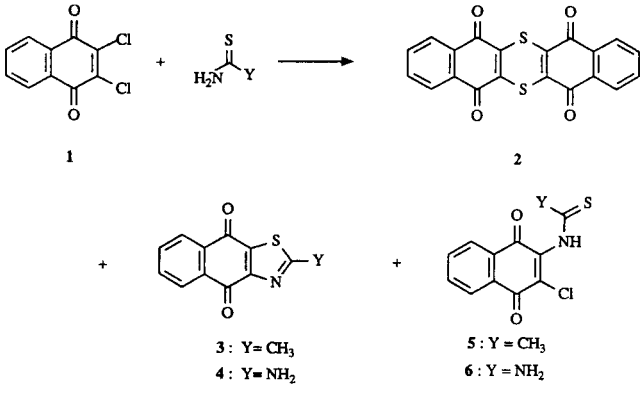
The preparations of 2-methyl- and 2-aminonaphtho[2,3-*d*]thiazole-4,9-diones **3** and **4** from the reactions of 2,3-dichloro-1,4-naphthoquinone (**1**) with thioacetamide or with thiourea, and of the bisthiazole **7** from **1** and dithiooxamide were first reported by Hammam and Bayoumy in 1985 [1]. They also claimed that the intermediates, 2-thioamido-3-chloro-1,4-naphthoquinones **5** and **6** were also isolated from the reaction medium and that **5** and **6** could separately be transformed to thiazoles by boiling in aqueous ethanol containing sodium bicarbonate.

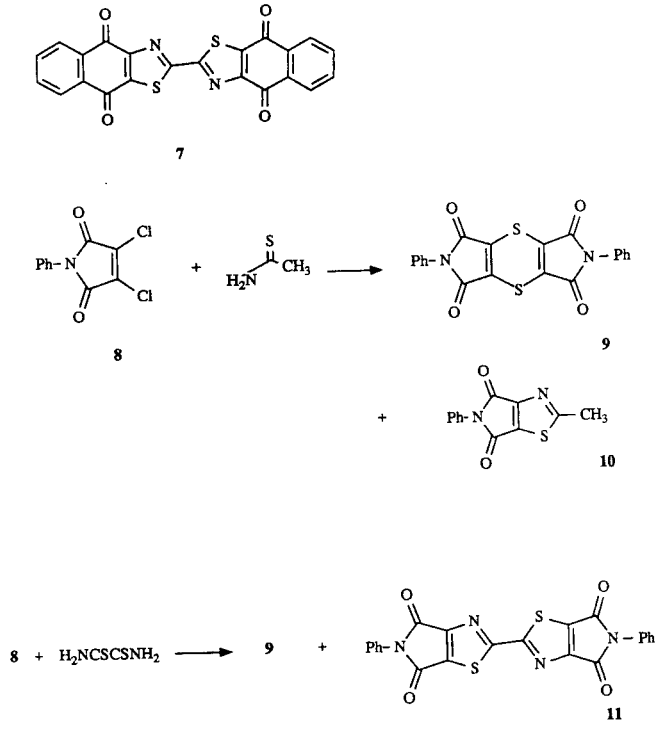
Block 1



Some years later, this work was repeated in our laboratory [2,3] and, in agreement with the earlier work, we found that 2,3-dichloro-1,4-naphthoquinone (**1**) reacted with a variety of thioamides in dimethylformamide or in dimethyl sulfoxide in the presence of triethylamine yielding the corresponding thiazoles (**3** and **4**) and with dithiooxamide to form the bisthiazole **7**, although the yields were lower than those reported by Hammam. We also found that 2,3-dichloro-*N*-phenylmaleimide (**8**) with thioamides or dithiooximide gave the analogous products **10** and **11**.

Recently, Matsuoka and co-workers [4,5] have also reported the reactions of 2,3-dichloro-1,4-naphthoquinone (**1**) with thioamides. They claimed our work was wrong, and that reactions of 2,3-dichloro-1,4-naphthoquinone (**1**) with thioacetamide, with thiourea, and with dithiooxamide all gave the same product, dibenzo[*b,i*]thianthrene-5,7,12,14-tetraone (**2**), but not the thiazoles **3, 4** and **7**. They mentioned the earlier work of Hammam and Bayoumy only in their first paper which criticized our structure **7** [4]. Similarly 2,3-dichloro-*N*-phenylmaleimide (**8**) and thioacetamide, thiourea or dithiooxamide afforded in their hands the 1,4-dithiine derivative **9** and the corresponding thiazoles **10** and **11** were not formed.

Block 2



In view of these discrepancies, we have now reexamined some of these reactions. Although the products reported to have been isolated by Matsuoka *et al.* are indeed formed, in all cases the 1,4-dithiine is accompanied by the corresponding 1,3-thiazole; however in some cases the separation is difficult.

In the present work, 2,3-dichloro-1,4-naphthoquinone (**1**) on treatment with thioacetamide in ethanol [1] or in dimethyl sulfoxide [2] in the presence of sodium bicarbonate or triethylamine gave dibenzo[*b,i*]thianthrene-5,7,12,14-tetraone (**2**) (50-60%) with the melting point and spectrum in agreement with Matsuoka's reports [4,5], together with the corresponding 2-methylnaphtho[2,3-*d*]thiazole-4,9-dione (**3**) (13-20%, Block 1). We separated and characterized **3** by its hrms, ^{1}H- and ^{13}C-nmr spectra and by its elemental analysis. Another product, probably the intermediate 2-thioacetamido-3-chloro-1,4-naphthoquinone (**5**), was also observed in less than 10% yield, mp 146-148°, Hammam reported [1] mp 145° for compound **5**.

The material we previously obtained and published [2] as structure **3** was probably a mixture of **2** and **3**; structure **3** was assigned based on the mp (>300°) compared with that given by Hammam and Bayoumy (318-320°) who followed a similar route and presumably got the same mixture. Both these reports included infrared spectra, but these would be of no use in attempting to distinguish compounds **2** and **3**. Our melting point for the carefully purified sample of **3** is 256-258° while that of pure compound **2** is 316-319° (Matsuoka gave mp 308-310° [4]).

Under the same conditions 2,3-dichloro-1,4-naphthoquinone (**1**) with thiourea gave a mixture of dibenzo[*b,i*]thianthrenetetraone (**2**, 47%), 2-aminonaphtho[2,3-*d*]thiazole-4,9-dione (**4**, 12%) and other unidentified compounds. The structure of compound **4** was indicated by the ms (M^+ = 230) and ^{1}H nmr spectrum, its analysis is good for C and H but not for N (−1.56) because as shown by the ^{1}H nmr spectrum a small amount of an impurity, assumed to be **2** was still present. Its melting point (303-307°) is below that reported by Hammam (333°). Matsuoka also described in his paper [5] the formation of 2-aminonaphtho[2,3-*d*]thiazole-4,9-dione (**4**); he detected **4** in the complex reaction mixture from the mass spectrum [5]. Our previous report [2] was based on a mixture of **2** and **4** which we thought was pure **4**. Our identification depended on the use of the literature procedure and on the mp (>300°) compared to Hammam and Bayoumy's (333° [1]). Unfortunately, an incorrect elemental analysis appeared to agree with the naphthothiazoledione structure **4**.

The reaction of 2,3-dichloro-*N*-phenylmaleimide (**8**) with thioacetamide in ethanol or in dimethyl sulfoxide in the presence of base afforded the 1,4-dithiine compound **9** as reported by Matsuoka; compound **9** was characterized by its elemental analysis. However, 2-methyl-5-phenyl-4,5-dihydro-6*H*-pyrrolo[3,4-*d*]thiazole-4,6-dione (**10**) was simultaneously formed; it was separated and characterized by its ^{1}H nmr spectrum and by its analysis. Our previous product mp >250° [2] was probably a mixture of **9** (mp >330°) and **10** (mp 208-211°). The interpretation of this as the single product **10** was based on our (wrong) interpretation of the previous reactions and on an error in the nitrogen analysis since the carbon and hydrogen analyses are closely similar for compounds **9** and **10** (see Experimental). When 2,3-dichloro-*N*-phenylmaleimide (**8**) was treated with dithiooxamide, the same 1,4-dithiine derivative **9** was obtained in 75% yield but the bisthiazole compound **11** was also present in the reaction mixture. The purification of this bisthiazole **11** was not possible but it was identified by its high resolution mass spectrum (m/z Calcd. for $C_{22}H_{10}S_2N_4O_4$: 458.0135. Found: 458.0234).

In summary, the reactions of 2,3-dichloro-1,4-naphthoquinone and 2,3-dichloro-*N*-phenylmaleimide with thioamides give mixtures of 1,4-dithiines and 1,3-thiazoles, but the separations, isolation and characterizations are difficult because of the sparingly soluble nature of the products. Unfortunately, some of the isolated products did not give full elemental analyses up to the usually accepted standard (see Experimental), but we believe we have now presented better evidence of the course of these reactions.

EXPERIMENTAL

Melting points were measured on a Kofler hot-stage microscope and are uncorrected. The ^{1}H nmr (300 MHz) and ^{13}C (75 MHz) nmr spectra were recorded on a Varian XL-300 (FT mode) spectrometer.

Reaction of **1** with Thioacetamide.

A mixture of 2,3-dichloro-1,4-naphthoquinone (2.27 g, 10 mmoles) and thioacetamide (0.75 g, 10 mmoles) was refluxed in ethanol in the presence of sodium bicarbonate [1] or heated at 80-100° in dimethylformamide in the presence of triethylamine (10 mmoles) [2]. After cooling to room temperature the precipitate was collected by filtration to give dibenzo[*b,i*]thianthrene-5,7,12,14-tetraone (**2**). The filtrate was poured into water and the resulting solid was collected and separated by column chromatography (ethyl acetate/benzene) or by recrystallization from ethanol/dioxane to give 2-methylnaphtho[2,3-*d*]thiazole-4,9-dione (**3**).

Dibenzo[*b,i*]thianthrene-5,7,12,14-tetraone (**2**).

This compound was obtained in a yield of 50-60%, mp 316-319° (lit [4] mp 308-310°).

Anal. Calcd. for $C_{20}H_8O_4S_2$: C, 63.82; H, 2.14. Found: C, 63.50; H, 2.07; hrms Calcd. 375.9864. Found: 375.9852.

2-Methylnaphtho[2,3-*d*]thiazole-4,9-dione (**3**).

This compound was obtained in a yield of 13-20%, mp 256-258°; ^{1}H nmr (chloroform-d): δ 8.32 (dd, 1H), 8.19 (dd, 1H), 7.79 (m, 2H), 2.91 (s, 3H, CH_3); ^{13}C nmr: 178.2, 177.5, 174.2, 154.2, 144.3, 134.3, 133.9, 132.8, 132.4, 127.6, 126.8, 20.2 (CH_3).

Anal. Calcd. for $C_{12}H_7NO_2S$: C, 62.87; H, 3.08; N, 6.11. Found: C, 62.30; H, 3.16; N, 5.91; hrms: Calcd. 229.0197. Found: 229.0192.

2-Aminonaphtho[2,3-*d*]thiazole-4,9-dione (**4**).

This compound was obtained from the reaction of **1** and thiourea and separated as a minor product (15-18%) from the mixture of **2** and **4** as described above, mp 303-307°; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 8.08 (d, 1H), 8.03 (d, 1H), 7.75 (t, 1H), 7.66 (t,

1H), 6.70 (br, NH_2); ms: (m/z) 230 (M^+).

Anal. Calcd. for $C_{11}H_6N_2O_2S$: C, 57.38; H, 2.63; N, 12.17. Found: C, 57.23; H, 2.98; N, 10.61.

Reaction of 2,3-Dichloro-*N*-phenylmaleimide with Thioacetamide.

The reaction was carried out under the same conditions as above, and the initial precipitation gave the 1,4-dithiine **9**. A mixture of **9** and **10** was obtained from the filtrate and separated by column chromatography (silica gel, ethyl acetate/hexane) to give **10**.

2,6-Diphenyl-1,2,5,6-tetrahydro-3*H*,7*H*-[1,4]dithiino[2,3-*c*:5,6-*c'*]-dipyrrole-1,3,5,7-tetrone (**9**).

This compound was obtained as a green solid in 60-67% yield, mp 338-340° (lit [4] mp >330°); insoluble in nmr solvents.

Anal. Calcd. for $C_{20}H_{10}N_2O_4S_2$: C, 59.11; H, 2.48; N, 6.89. Found: C, 58.46; H, 2.45; N, 6.95.

2-Methyl-5-phenyl-4,5-dihydro-6*H*-pyrrolo[3,4-*d*]thiazole-4,6-dione (**10**).

This compound was obtained as a brown solid, in 10% yield, mp 208-211°; ^1H nmr (chloroform-d): δ 8.15 (d, 2H), 7.64 (t, 1H), 7.50 (m, 2H), 2.78 (s, 3H, CH_3).

Anal. Calcd. for $C_{12}H_8N_2O_2S$: C, 59.01; H, 3.30; N, 11.47. Found: C, 58.94; H, 3.25; N, 11.45.

REFERENCES AND NOTES

[1] A. S. Hammam and B. E. Bayoumy, *Collect. Czech. Chem. Commun.*, **50**, 71 (1985).

[2] A. R. Katritzky and W. Q. Fan, *J. Heterocyclic Chem.*, **25**, 901 (1988).

[3] A. R. Katritzky, W. Q. Fan, Q. L. Li and S. Bayyuk, *J. Heterocyclic Chem.*, **26**, 885 (1989).

[4] M. Matsuoka, A. Iwamoto and T. Kitao, *J. Heterocyclic Chem.*, **28**, 1445 (1991).

[5] M. Matsuoka, A. Iwamoto, N. Furukawa and T. Kitao, *J. Heterocyclic Chem.*, **29**, 439 (1992).