

# REACTION OF 2-MERCAPTOBENZIMIDA(THIA)ZOLE WITH 1,4-NAPHTHOQUINONE AND ITS OXIDE

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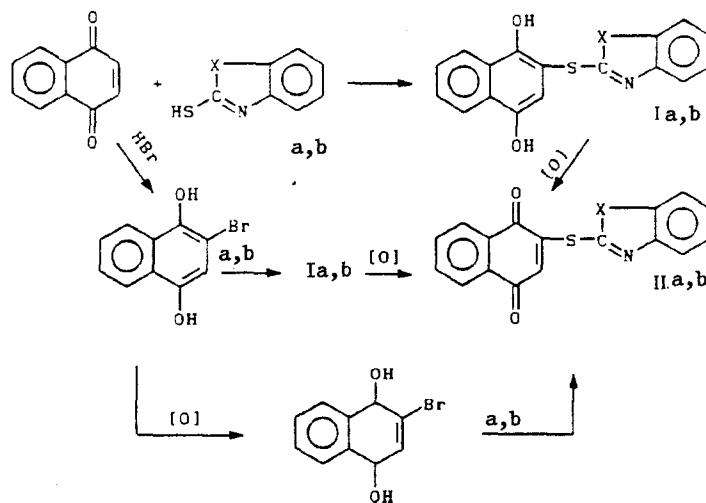
*The reaction of 2-mercaptobenzimidaza(thia)zole with 1,4-naphthoquinone proceeds as nucleophilic 1,4-addition to give the corresponding thioethers. The reaction of 1,4-naphthoquinone oxide with 2-mercaptobenzimidazole leads to benzimidazonaphthothiazole, while the reaction of the oxide with 2-mercaptobenzothiazole leads to a thioether as a consequence of the addition of the mercapto-substituted heterocycle at the oxide ring.*

The reaction of mercapto-substituted heterocycles with quinones and particularly their oxides has not been studied adequately, and only individual publications have been devoted to it [1-3].

In the present paper the reaction of 1,4-naphthoquinone and its oxide with 2-mercaptobenzimidazole (a) and 2-mercaptobenzothiazole (b) is described for the first time.

The selection of the indicated mercapto-substituted heterocycles was due to the fact that they, being close structural analogs, differ with respect to the possibility, for 2-mercaptobenzimidazole, of cyclization through the NH and OH groups (formed during addition) to a condensed heterocyclic system, which is impossible for 2-mercaptobenzothiazole.

We found that addition of the mercapto-substituted heterocycles to give thioethers Ia, b occurs in the reaction with naphthoquinone (see Table 1). The structures of the thioethers obtained were confirmed by alternative synthesis on the basis of 2-bromo-1,4-naphthohydroquinone. In addition, we accomplished the oxidation of these compounds with lead tetraacetate to 2-(2-benzimidazolylthio)-1,4-naphthoquinone (IIa) and 2-(2-benzothiazolylthio)-1,4-naphthoquinone (IIb). Compounds IIa, b were identical to samples obtained by the reaction of 2-bromo-1,4-naphthoquinone with the indicated heterocycles.



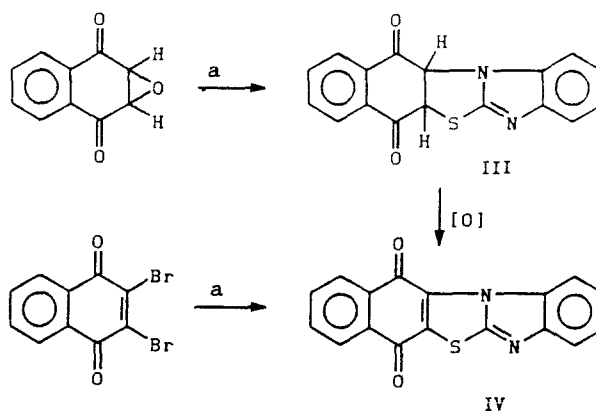
I, II a, X=NH; b, X=S.

TABLE 1. Characteristics of I-VI

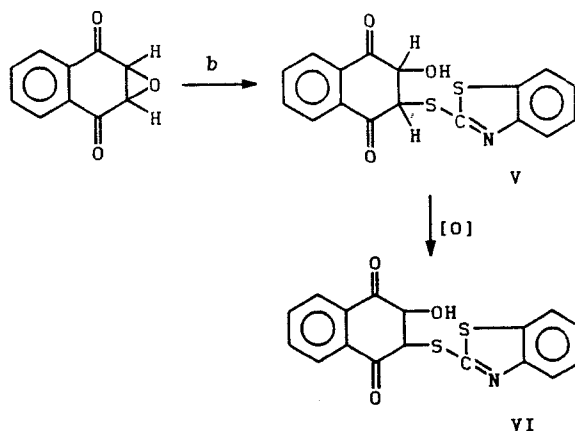
| Com-<br>pound | Empirical<br>formula                                     | Temp, °C   |     | IR spec-<br>trum, $\nu$ ,<br>$\text{cm}^{-1}$ | PMR spectrum,<br>$\delta$ , ppm                  | Yield,<br>% |    |
|---------------|--|--|-----|---|--|-------------|----|
|               |  | A  | B   |   |  | A           | B  |
| Ia            | $\text{C}_{17}\text{H}_{12}\text{N}_2\text{O}_2\text{S}$ | 154...155  | 156 | 745 (C-S-C),<br>3165 (NH),<br>3170 (OH)       | 7.7...7.9 (m, Ar);<br>3.5 (H, NH);<br>6.8 (2-OH) | 80          | 70 |
| Ib            | $\text{C}_{17}\text{H}_{11}\text{NO}_2\text{S}_2$        | [ethanol-water<br>(2:1)]<br>97...98   96...97<br>(ethanol) |     | 755 (C-S-C),<br>3420 (OH)                     | 7.8...7.9 (m, Ar);<br>6.7 (2-OH)                 | 78          | 86 |
| IIa           | $\text{C}_{17}\text{H}_{10}\text{N}_2\text{O}_2\text{S}$ | 223  | 221 | 740 (C-S-C),<br>1665 (C=O),<br>3150 (NH)      | 7.9...8.0 (m, Ar);<br>3.4 (H, NH);<br>5.1 (3-H)  | 70          | 80 |
| IIb           | $\text{C}_{17}\text{H}_9\text{NO}_2\text{S}_2$           | [ethanol-water<br>(5:1)]<br>143   142<br>(toluene)         |     | 760 (C-S-C),<br>1655 (C=O)                    | 7.7...7.9 (m, Ar);<br>5.0 (3-H)                  | 70          | 84 |
| III           | $\text{C}_{17}\text{H}_{10}\text{N}_2\text{O}_2\text{S}$ | 241<br>(ethanol)   |     | 1675 (C=O)                                    | 7.8...8.0 (m, Ar);<br>3.2 (5a, 12a-H)            | 85          |    |
| IV            | $\text{C}_{17}\text{H}_8\text{N}_2\text{O}_2\text{S}$    | 267*   | 265 | 1685 (C=O)                                    | 7.5...8.1 (m, Ar)                                | 70          | 85 |
| V             | $\text{C}_{17}\text{H}_9\text{NO}_3\text{S}_2$           | 150<br>(ethanol)   |     | 745 (C-S-C),<br>1730 (C=O),<br>3280 (OH)      | 7.6...8.0 (m, Ar);<br>3.4 (OH);<br>3.1 (2,3-H)   | 70          |    |
| VI            | $\text{C}_{17}\text{H}_9\text{NO}_3\text{S}_2$           | 160<br>(ethanol)   |     | 755 (C-S-C),<br>1675 (C=O),<br>3410 (OH)      | 7.6...8.1 (m, Ar);<br>3.5 (OH)                   | 80          |    |

\*According to [4], mp 251°C; according to [5], mp 267°C.

Naphthoquinone oxide reacts with 2-mercaptobenzimidazole to give condensed dihydrothiazole III, which, upon oxidation, is converted to benzimidazo[2,1-b]naphtho[2,3-d]thiazole-7,12-dione (IV), which was also obtained from 2,3-dibromo-1,4-naphthoquinone and 2-mercaptobenzimidazole in accordance with [4, 5].



The reaction of naphthoquinone oxide with 2-mercaptobenzothiazole terminates with the formation of addition product V, which is oxidized by lead tetraacetate to 2-hydroxy-3-benzothiazolylthio-1,4-naphthoquinone (VI). (See scheme at the top of the next page.)



## EXPERIMENTAL

The PMR spectra of solutions of the compounds in  $d_6$ -DMSO were recorded with a Tesla BS-497 C spectrometer (100 MHz) with hexamethyldisiloxane (HMDS) as the internal standard. The IR spectra of KBr pellets were obtained with an IKS-29 spectrometer. Thin-layer chromatography was carried out on Silufol UV-254 plates. Elementary microanalysis was carried out with a Janaco MT-3 C,H,N-analyzer.

The results of elementary analysis of I-VI were in agreement with the calculated values.

**2-(2-Benzimidazolylthio)-1,4-naphthohydroquinone (Ia).** A. A solution of 1.58 g (10 mmole) of 1,4-naphthoquinone and 1.50 g (10 mmole) of 2-mercaptobenzimidazole in 100 ml of ethanol was refluxed on a water bath for 3 h, after which 3/4 of the solvent was removed, and the resulting precipitate was removed by filtration and washed with ethanol.

B. A solution of 2.39 g (10 mmole) of 2-bromo-1,4-naphthohydroquinone and 1.50 g (10 mmole) of 2-mercaptobenzimidazole in 200 ml of ethanol was refluxed on a water bath for 2 h, after which the bulk (3/4) of the solvent was removed, and the resulting precipitate was removed by filtration and washed with ethanol.

**2-(2-Benzothiazolylthio)-1,4-naphthohydroquinone (Ib).** A. A solution of 1.67 g (10 mmole) of 2-mercaptobenzothiazole and 1.58 g (10 mmole) of 1,4-naphthoquinone in 150 ml of ethanol was refluxed for 3 h on a water bath, after which the solvent was removed, and the residue was recrystallized from alcohol.

B. A solution of 2.39 g (10 mmole) of 2-bromo-1,4-naphthohydroquinone and 1.67 g (10 mmole) of 2-mercaptobenzothiazole in 220 ml of ethanol was refluxed for 2 h on a water bath, after which the solvent was removed, and the residue was recrystallized from toluene.

**2-(2-Benzimidazolylthio)-1,4-naphthoquinone (IIa).** A. Lead tetraacetate (5 g) was added in portions at room temperature to a solution of 3.08 g (10 mmole) of Ia in 100 ml of glacial acetic acid, after which the mixture was allowed to stand for 2 h. Three fourths of the solvent was removed, the concentrate was diluted with two volumes of water, and the resulting precipitate was removed by filtration and washed with ethanol.

B. A solution of 2.37 g (10 mmole) of 2-bromo-1,4-naphthoquinone and 1.50 g (10 mmole) of 2-mercaptobenzimidazole in 240 ml of ethanol was refluxed on a water bath for 2 h, after which 2/3 of the solvent was removed, and the resulting precipitate was removed by filtration and washed with alcohol.

**2-(2-Benzothiazolylthio)-1,4-naphthoquinone (IIb).** A. Lead tetraacetate (5 g) was added in portions at room temperature to a solution of 3.25 g (10 mmole) of Ib in 100 ml of glacial acetic acid, after which the mixture was allowed to stand for 2 h. Three fourths of the solvent was evaporated, the concentrate was diluted with two volumes of water, and the resulting precipitate was removed by filtration and washed with ethanol.

B. A solution of 2.37 g (10 mmole) of 2-bromo-1,4-naphthoquinone and 1.67 g (10 mmole) of 2-mercaptobenzothiazole in 250 ml of ethanol was refluxed on a water bath for 2 h, after which the solvent was removed, and the residue was recrystallized from toluene.

**Benzimidazo[2,1-b]naphtho[2,3-d]thiazole-5a,12a-dihydro-7,12-dione (III).** A solution of 1.74 g (10 mmole) of 1,4-naphthoquinone oxide and 1.5 g (10 mmole) of 2-mercaptobenzimidazole in 150 ml of ethanol was refluxed on a water bath for 2 h, after which the bulk of the solvent was removed, and the resulting precipitate was removed by filtration and washed with a small amount of cold alcohol.

**Benzimidazo[2,1-b]naphtho[2,3-d]thiazole-7,12-dione (IV).** A. A 1.0-ml sample of 5%  $H_2SO_4$  and 0.06 g of potassium bromate were added to a solution of 0.31 g (1 mmole) of III in 45 ml of ethanol, after which the mixture was heated

to 70°C and then maintained at room temperature for 1 h. The bulk of the solvent was then removed, the concentrate was filtered, and the resulting precipitate was washed with water and alcohol.

**B.** A mixture of 1.58 g (5 mmole) of 2,3-dibromo-1,4-naphthoquinone, 0.75 g (5 mmole) of 2-mercaptobenzimidazole, 1.25 g of anhydrous sodium acetate, 60 ml of ethanol, and 30 ml of DMF was heated for 5 min on a boiling-water bath, during which a voluminous precipitate formed. The mixture was cooled, and the precipitate was removed by filtration and washed with water and alcohol.

**2,3-Dihydro-2-hydroxy-3-(2-benzothiazolylthio)-1,4-naphthoquinone (V).** A solution of 1.74 g (10 mmole) of 1,4-naphthoquinone oxide and 1.67 g (10 mmole) of 2-mercaptobenzothiazole in 450 ml of ethanol was refluxed for 2 h on a water bath, after which the bulk of the solvent was removed, and the resulting precipitate was removed by filtration and washed with alcohol.

**2-Hydroxy-3-(2-benzothiazolylthio)-1,4-naphthoquinone (VI).** Lead tetraacetate (1.1 g) was added at room temperature to a solution of 0.34 g (10 mmole) of dihydro compound V in 70 ml of glacial acetic acid, after which the mixture was diluted with three volumes of water after having evaporated half of the solvent. The resulting precipitate was removed by filtration and washed with water.

#### LITERATURE CITED

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