

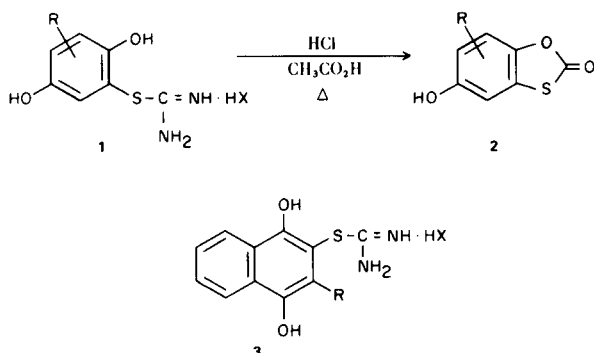
Synthesis of Some 5-Hydroxynaphth[2,1-*d*]-1,3-oxathiol-2-ones

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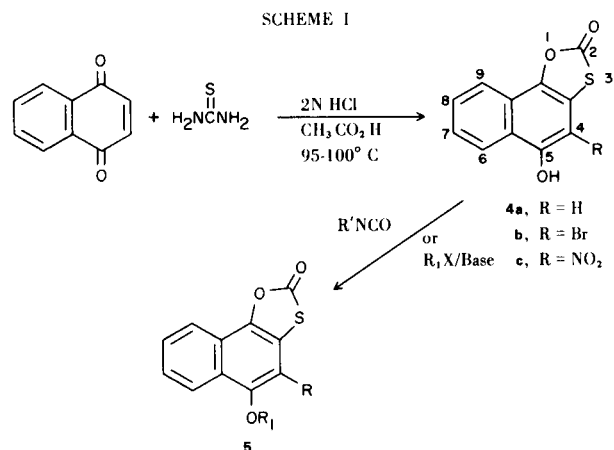
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The naphth[2,1-*d*]-1,3-oxathiol-2-one ring system has received little synthetic attention (1). Recent work by Lau and co-workers (2,3) has shown that 1,4-benzoquinones react readily with excess thiourea in the presence of aqueous mineral acids to afford a wide variety of *S*-(2,5-dihydroxyaryl)thiuronium salts (1) which upon heating in acid are easily cyclized to 5-hydroxy-1,3-benzoxathiol-2-ones (2). Although 1,4-naphthoquinones are less reactive than 1,4-benzoquinones (4), they also react with thiourea in the presence of mineral acids to give *S*-(1,4-dihydroxy-2-naphthyl)thiuronium salts (3) (3,5,6), but unlike the *S*-(aryl)thiuronium salts 1, the salts 3 have been reported (2,3) to decompose rather than undergo cyclization to give 5-hydroxynaphth[2,1-*d*]-1,3-oxathiol-2-ones (4).



We have found, however, that the 5-hydroxynaphth[2,1-*d*]-1,3-oxathiol-2-one **4a** can be prepared in 61-65% yield by a one-step procedure from 1,4-naphthoquinone and excess thiourea. In this paper we describe the preparation of **4a** and some of its reactions and derivatives. The synthetic route used for the preparation of 5-hydroxynaphth[2,1-*d*]-1,3-oxathiol-2-one (**4a**) was essentially that described by Lau and Kestner (2) for the one-step synthesis of the 5-hydroxybenzoxathiol-2-ones **2** (7), and is illustrated by Scheme I. This procedure involved heating thiourea and naphthoquinone ( $\geq 1.5:1$  molar ratios) in 2*N* hydrochloric acid-glacial acetic acid. The product **4a** was obtained as a grey photochromic (8) solid, and was characterized by elemental, nmr, and ir analyses. Several carbamoyl and phosphoryl derivatives (**5**) of the 5-hydroxyl group were prepared (Table I).



Bromination of **4a** with excess bromine afforded only the monobromo derivative **4b**. The structure of **4b** was easily established by nmr analysis, *i.e.*, the singlet absorption for the proton at position 4 in **4a** was absent in the spectrum of **4b**. Nitration of **4a** with 70% nitric acid afforded the 4-nitro derivative **4c**.

The compounds prepared in this work were screened for potential fungicidal, herbicidal, and insecticidal activity. None demonstrated any noteworthy activity.

## EXPERIMENTAL

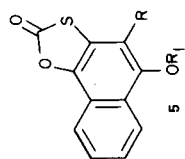
All melting points were determined with a Mel-Temp apparatus and are uncorrected. The elemental analyses were performed by the Analytical Laboratories, Chemicals and Plastics, Union Carbide Corporation. The infrared spectra were obtained in potassium bromide pellets on a Perkin-Elmer Model 221 spectrometer. The nuclear magnetic resonance spectra were determined with a Varian Associates Model A-60 instrument using tetramethylsilane as an internal standard. Chemical shifts are reported in parts per million ( $\delta$  values).

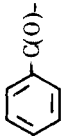
5-Hydroxynaphth[2,1-*d*]-1,3-oxathiol-2-one (**4a**).

To a solution of 68.5 g. (0.9 mole) of thiourea in 600 ml. of 2*N* hydrochloric acid was added, with stirring, a solution of 95 g. (0.6 mole) of 1,4-naphthoquinone (recrystallized from 2-propanol) in 2 liters of glacial acetic acid. The mixture was stirred for 30 minutes at room temperature, and then was heated at 95-100° for 1 hour. Water (1500 ml.) was added to the reaction mixture, and the solution was cooled and filtered. The purple precipitate was thoroughly washed with water, dried, and then was dissolved in 800 ml. of boiling ethanol. The ethanol solution was treated with decolorizing charcoal and filtered. The ethanol filtrate was

TABLE I

Physical and Analytical Data for Derivatives of 5-Hydroxynaphth[2,1-d]-1,3-oxathiol-2-one



Compound	R	R <sub>1</sub>	M.p. °C	Yield, %	Recrystallization Solvent	Empirical Formula	Analysis, %		Infrared, $\mu$		Notes	
							Calcd.	Found	Oxathiol C=O	Other C=O		
5a	H	CH <sub>3</sub> NHC(O)-	192-195	73	2-propanol	C <sub>13</sub> H <sub>9</sub> NO <sub>4</sub> S	C	56.72	C	56.80	5.72	5.85
							H	3.29	H	3.18		
							N	5.09	N	5.21		
5b	Br	CH <sub>3</sub> NHC(O)-	229	67	acetone	C <sub>13</sub> H <sub>8</sub> BrNO <sub>4</sub> S	C	44.08	C	43.95	5.65, 5.77	5.77 (broad)
							H	2.27	H	2.30		
							N	3.96	N	3.97		
5c	H	CCl <sub>3</sub> C(O)NHC(O)-	151-155	31	dimethoxyethane	C <sub>14</sub> H <sub>6</sub> Cl <sub>3</sub> NO <sub>5</sub> S	C	41.35	C	41.19	5.70	5.53 5.78 (shoulder)
							H	1.49	H	1.61		
							N	3.44	N	3.40		
5d	H	CH <sub>3</sub> NHC(O)NCH <sub>3</sub> C(O)-	207-209	50	acetonitrile	C <sub>15</sub> H <sub>12</sub> N <sub>2</sub> O <sub>5</sub> S	C	54.21	C	54.35	5.75	5.61 5.90 (shoulder)
							H	3.64	H	3.58		
							N	8.43	H	8.50		
5e	H	(CH <sub>3</sub> O-) <sub>2</sub> P(O)-	132-134	61	diisopropyl ether	C <sub>13</sub> H <sub>11</sub> O <sub>6</sub> PS	C	47.85	C	48.04	5.70	-----
							H	3.40	H	3.27		
5f	H	CF <sub>3</sub> -  -C(O)-	173-175	43	acetonitrile	C <sub>19</sub> H <sub>9</sub> F <sub>3</sub> O <sub>4</sub> S	C	58.46	C	58.21	5.75	5.72 (shoulder)
							H	2.32	H	2.36		

diluted 1:1 with water, cooled to 5°, and was filtered to give a red-brown solid which was recrystallized three times from 2-propanol to give 85 g. (65% yield) of a grey solid, m.p. 180-181°. The nmr spectrum (acetone-d<sub>6</sub>) showed a singlet at δ 6.95 ppm (1H) for the proton at the 4 position, and multiplets at δ 7.61 ppm (3H) and δ 8.25 ppm (1H) for the protons at positions 6-9. The 5-OH proton was not detected, probably due to a rapid deuterium exchange with solvent. The ir spectrum showed absorptions at 2.97 μ, -OH; 3.26 μ, aryl CH; 5.86 μ, C=O; 6.13, 6.35, and 6.6 μ, aryl C=C; 9.28 μ, aryl-S; 11.75 μ, isolated aromatic hydrogen; and 13.25 μ, four adjacent hydrogens.

*Anal.* Calcd. for C<sub>11</sub>H<sub>6</sub>O<sub>3</sub>S: C, 60.54; H, 2.77; S, 14.70. Found: C, 60.40; H, 2.98; S, 15.00.

In a second preparation of **4a**, a 1.7:1 molar ratio of thiourea: naphthoquinone was used. After 1 hour at 95-100° the mixture was cooled to 15°, but was not diluted with water, and was filtered. The red-brown solid obtained was thoroughly washed with water, and was air-dried. This solid was dissolved in boiling acetone, and the acetone solution was treated with decolorizing charcoal. After removal of the charcoal, the acetone was removed *in vacuo*, and the resulting solid was recrystallized from 2-propanol to give **4a** in 61% yield, m.p. 181-182°.

5-(*N*-Methylcarbamoyloxy)naphth[2,1-*d*]-1,3-oxathiol-2-one (**5a**).

A solution of 8.7 g. (0.04 mole) of 5-hydroxynaphth[2,1-*d*]-1,3-oxathiol-2-one (**4a**), 2.9 g. (0.05 mole) of methyl isocyanate, and 3 drops of dibutyltin diacetate in 75 ml. of diethyl ether was allowed to stand for 8 hours in a 16 oz. sealed glass pressure bottle. Then the ether solution was filtered, and the precipitate was washed with cold ether and air-dried. The solid was recrystallized from 2-propanol to give 8 g. (73% yield) of a white product, m.p. 191-195°. The nmr spectrum (DMSO-d<sub>6</sub>) showed a doublet at δ 2.79 ppm (3H, *J* = 4.5 cps) for the NH-CH<sub>3</sub> methyl protons, and singlet at δ 7.68 aromatic proton at position 4.

Similarly prepared were 4-bromo-5-(*N*-methylcarbamoyloxy)-naphth[2,1-*d*]-1,3-oxathiol-2-one (**5b**) and 5-(*N*-trichloroacetylcarbamoyloxy)naphth[2,1-*d*]-1,3-oxathiol-2-one (**5c**).

Naphth[2,1-*d*]-1,3-oxathiol-2-one-5-yl 2,4-dimethylallophanate (**5d**).

To a solution of 6.5 g. (0.03 mole) of **4a** and 3.1 g. of triethylamine in 75 ml. of acetonitrile was added, with stirring, a solution of 4.5 g. (0.03 mole) of 2,4-dimethylallophanoyl chloride in 75 ml. of acetonitrile at 25°. The mixture was stirred at 30° for 2 hours, was poured into water, and the aqueous mixture was filtered. The precipitate was washed with water, dried, and was recrystallized from acetonitrile to give 5 g. (51% yield) of a white solid, m.p. 207-209°.

Similarly prepared from **4a** and *O,O*-dimethyl phosphorochloridate and 4-trifluoromethylbenzoyl chloride were compounds **5e** and **5f**.

4-Bromo-5-hydroxynaphth[2,1-*d*]-1,3-oxathiol-2-one (**4b**).

A solution of bromine (10 g., 0.062 mole) in 50 ml. of chloroform was added dropwise with stirring to a solution of 13.0 g. (0.06 mole) of **4a** in 650 ml. of chloroform at 25°. Then the mixture was stirred for 18 hours at room temperature and filtered. The precipitate was washed with cold ether, and

recrystallized from xylene to give 12 g. (91% yield) of product, m.p. 152-155°. The nmr spectrum (DMSO-d<sub>6</sub>) showed multiplets at δ 7.59 ppm and 8.17 ppm (4H) for the ring protons, and a broad absorption at δ 10.05 ppm (1H) for the -OH proton. The ir spectrum had carbonyl absorptions at 5.65 μ and 5.77 μ (for -OC(O)- and -OC(O)S-).

*Anal.* Calcd. for C<sub>11</sub>H<sub>5</sub>BrO<sub>3</sub>S: C, 44.46; H, 1.79; Br, 26.9. Found: C, 44.52; H, 2.09; Br, 26.8.

4-Nitro-5-Hydroxynaphth[2,1-*d*]-1,3-oxathiol-2-one (**4c**).

To 150 ml. of 70% nitric acid, cooled to -15°, was added, portionwise with vigorous stirring over a 10 minute period, 10.0 g. (0.0457 mole) of **4a**. The acid mixture was stirred at -15° for 30 minutes, and then was poured into 1 liter of ice water. The solid product was collected by suction filtration, washed with water, and dried. Recrystallization from 1,4-dioxane gave 4 g. (33% yield) of a yellow product, m.p. 195-197°. The nmr spectrum (DMSO-d<sub>6</sub>) showed multiplets at δ 8.31 and 8.02 ppm for the aryl protons. The ir spectrum had carbonyl absorptions at 5.63 μ and 5.75 μ (for -OC(O)- and -OC(O)S-).

*Anal.* Calcd. for C<sub>11</sub>H<sub>5</sub>NO<sub>5</sub>S: C, 50.19; H, 1.91; N, 5.32. Found: C, 50.30; H, 1.95; N, 5.09.

Attempts to prepare polynitro derivatives of **4a** by heating the nitric acid solution led to decomposition. The use of 70% nitric acid-concentrated sulfuric acid also decomposed **4a**.

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- (7) We have reproduced the results of Lau and Kestner (2) for **2**, where R = H, 7-CH<sub>3</sub>, 4,7-(CH<sub>3</sub>)<sub>2</sub>, 6,7-(CH<sub>3</sub>)<sub>2</sub>, and 4,7-(C<sub>6</sub>H<sub>5</sub>)<sub>2</sub>, by procedures which employed heating thiourea and the appropriate benzoquinone (1.5:1 molar ratios) in 2*N* hydrochloric acid-glacial acetic acid. The actual conditions used by Lau *et al.* (2,3) in their unsuccessful attempts to prepare **4** is not specified; these authors did note, however, that when thiourea and naphthoquinones (1:2 molar ratios) are allowed to react in mineral acid 2-amino-5-hydroxynaphth[1,2-*d*]thiazoles are obtained in high yields.
- (8) Compound **4a** appeared to be weakly photochromic in that upon prolonged exposure to light it turned a cherry red color, but after being returned to the dark it reverted to its original grey color.