this method 2-oxazolidinones with a one, two, or three carbon chain at position 5 of the ring.

Experimental Section

Infrared data were obtained on a Beckman IR-5A spectrophotometer. Microanalyses were conducted by the Aldrich Analytical Division on an F & M Model 185 CHN analyzer.

Materials.—3- and 4-piperidinol and their *N*-methyl and *N*-ethyl derivatives were obtained from Aldrich Chemical Co., and used without further purification. The *N*-benzyl derivatives were prepared by alkylating the unsubstituted piperidinols with benzyl chloride. *N*-Benzyl-3-pyrrolidinol was prepared from 1,4-dibromo-2-butanol and benzylamine.[10] 1-Chloro-3-cyclohexylamino-2-propanol was prepared after McKelvey, *et al.*,[11] and cyclized to 1-cyclohexyl-3-azetidinol, using Gaertner's procedure[12] with minor modifications.

Chloroformate Hydrochlorides.—All reactions were conducted under anhydrous conditions. All chloroformates enhibited a sharp and strong carbonyl absorption at 5.61–5.65 μ.

A solution of a free amine–alcohol or its hydrochloride in dichloromethane was added with stirring into a solution of phosgene (1–1.5 molar equiv) in the same solvent. After stirring overnight, the reaction solution (filtered through Celite if turbid) was concentrated on a rotary vacuum evaporator at temperatures below 25° to afford the product as a white solid. An alternate method was to saturate a solution of the free amine–alcohol in benzene with phosgene gas. The precipitated product was collected and washed with anhydrous benzene. The materials thus obtained by either method were suitable for subsequent rearrangement reactions.

Rearrangement Reaction. Procedure A.—A suspension of a chloroformate hydrochloride in anhydrous toluene or benzene was stirred and heated to reflux. A solution of triethylamine (1–1.1 molar equiv) in a small amount of the same solvent was added. After refluxing for 1 hr, the triethylamine hydrochloride was removed by filtration and the solvent was removed *in vacuo*. The residue was fractionated on a kugelrohr distillation apparatus[13] to afford the product. In cases where carbonates **17** and chlorides **18** were produced as by-products, these substances were collected as lower boiling fractions.

Procedure B.—A solution of triethylamine (1–1.1 molar equiv) in dichloromethane was rapidly added to a solution of a chloroformate hydrochloride in the same solvent with efficient mixing. After stirring at room temperature for several hours, the reaction solution was washed with water, dried, and evaporated *in vacuo*. The product thus obtained was purified by kugelrohr distillation as in procedure A (Table II).

TABLE II
PHYSICAL PROPERTIES OF REARRANGEMENT PRODUCTS[b]

Compd	C=O absorption, μ	Kugelrohr distillations,[a] °C (mm)	$n^{20}D$	Mp, °C
9a	5.72	130–135 (0.003)		
13a	5.9	108–112 (0.001)	1.4944	
13b	5.92	180–183 (0.001)	1.5498	53–54
16a	5.72	108–115 (0.001)		95.5–97.0

[a] Temperatures given are not boiling points but are those of the air bath during the collection of the compounds. [b] Satisfactory analytical values (±0.3% for C, H, and N) were reported for all compounds in the table: Ed.

Registry No.—**9a**, 26384-64-5; **13a**, 26409-02-9; **13b**, 26384-65-6; **16a**, 26384-66-7.

Acknowledgment.—We thank Mrs. Margaret M. Weber and Mrs. Ramona H. Jules for preparing some of the starting materials.

(10) C. D. Lunsford, J. W. Ward, A. J. Pallotta, T. W. Tusing, E. K. Rose, and R. S. Murphey, *J. Med. Pharm. Chem.*, **1**, 73 (1959).
(11) J. B. McKelvey, B. G. Webre, and E. Klein, *J. Org. Chem.*, **24**, 614 (1959).
(12) V. R. Gaertner, *ibid.*, **32**, 2972 (1967).
(13) R. Graeve and G. H. Wahl, Jr., *J. Chem. Educ.*, **41**, 279 (1964).

Reaction of Quinones with Thiourea. A Novel Route to 2-Amino-6-hydroxybenzothiazoles and 2-Amino-5-hydroxynaphtho[1,2-*d*]thiazoles

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Received May 4, 1970

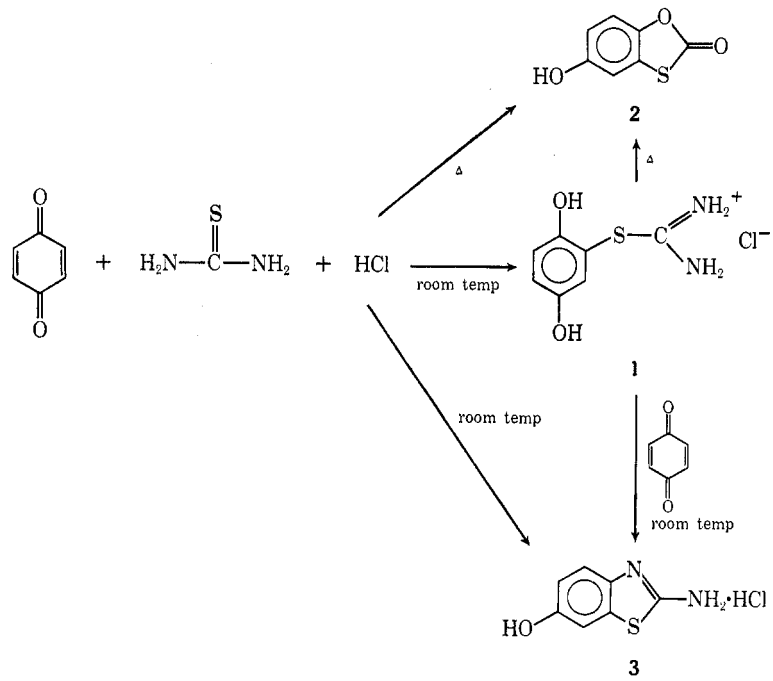
The reaction of thiourea with excess 1,4-benzoquinones and 1,4-naphthoquinones in the presence of concentrated hydrochloric acid offers a convenient route for the synthesis of a variety of 2-amino-6-hydroxybenzothiazoles (**3**) and 2-amino-5-hydroxynaphtho[1,2-*d*]thiazoles (**15**). These compounds could also be prepared by treating the corresponding *S*-(2,5-dihydroxyphenyl)thiouronium chlorides (**1**) and *S*-(1,4-dihydroxynaphthyl)thiouronium chlorides (**13**) with benzoquinones and naphthoquinones, respectively. Extension of this reaction to N-substituted thioureas gave the related N-substituted 2-aminobenzothiazolyl (**16**) and naphthothiazolyl (**17**) compounds.

The reaction of quinones with various thiol compounds has been the subject of several publications.[1-4] However, the reaction with thiourea and its derivatives has remained relatively unexplored.[5,6]

Recent work[7] in these laboratories has shown that the reaction of benzoquinones with excess thiourea in the presence of aqueous mineral acid affords, depending upon the reaction conditions, a wide variety of *S*-(2,5-dihydroxyaryl)thiouronium chlorides (**1**) and 5-hydroxy-1,3-benzoxathiol-2-ones (**2**). Further investigation has shown that, when thiourea is treated with a 1 molar excess of benzoquinone in the presence of mineral acid, none of the compounds **1** or **2** was formed. Instead, a new heterocyclic compound, 2-amino-6-hydroxybenzothiazole (**3**), was isolated in yield greater

* To whom correspondence should be addressed.
(1) H. Fiedler, *Chem. Ber.*, **95**, 1771 (1962).
(2) R. F. Porter, W. W. Rees, E. Frauenglass, H. S. Wilgus, H. G. Nawn, P. P. Chiesa, and J. W. Gates, Jr., *J. Org. Chem.*, **29**, 588 (1964).
(3) See H. S. Wilgus, E. Frauenglass, E. T. Jones, R. F. Porter, and J. W. Gates, Jr., *ibid.*, **29**, 594 (1964), and references cited therein.
(4) See K. Klemm and B. Geiger, *Justus Liebigs Ann. Chem.*, **726**, 103 (1969), and references cited therein.
(5) M. Schubert, *J. Amer. Chem. Soc.*, **69**, 712 (1947).
(6) H. Burton and S. B. David, *J. Chem. Soc.*, 2193 (1952).
(7) P. T. S. Lau and M. Kestner, *J. Org. Chem.*, **33**, 4426 (1968).

SCHEME I

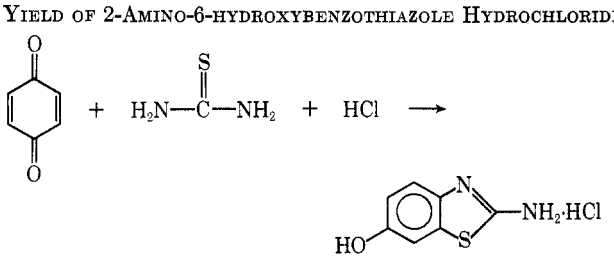


than 70%. The product was identified by nuclear magnetic resonance spectroscopy, infrared spectroscopy, and comparison with an authentic sample obtained from the hydrolysis of 2-amino-6-methoxybenzothiazole. Compound **3** can also be obtained in the same yield by treating an ethanolic solution of the thiouronium salt (**1**) with an equimolar solution of benzoquinone, which suggests that the thiouronium salt is an intermediate in this reaction. The same intermediate is involved in the synthesis of compound **2** (Scheme I).

Acid catalysis is essential; in the absence of acid only a black, amorphous, insoluble material with a melting point greater than 300° was isolated. Table I shows

TABLE I

EFFECTS OF BENZOQUINONE AND HYDROCHLORIC ACID ON THE YIELD OF 2-AMINO-6-HYDROXYBENZOTHIAZOLE HYDROCHLORIDE



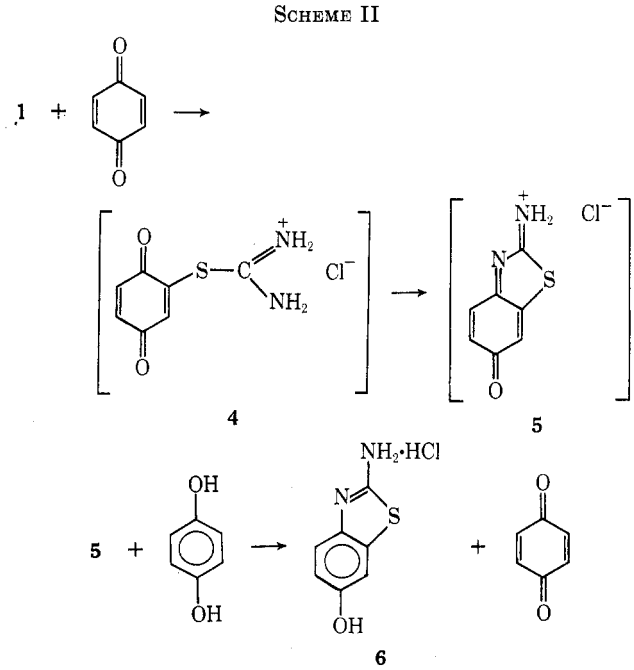
Quinone, mol	Thiourea, mol	HCl, mol	Yield, %
2.5	1.0	1.0	73
2.0	1.0	1.0	76
1.5	1.0	1.0	75
1.0	1.0	1.0	0[a]
1.5	1.0	0	0[b]
1.5	1.0	0.5	31
1.5	1.0	2.0	75

[a] *S*-(2,5-dihydroxyphenyl)thiouronium chloride was isolated exclusively. [b] A black insoluble amorphous material was obtained.

that the reaction is best run using 1 or more molar equiv of hydrochloric acid. Lower yields were obtained when less than 1 equiv of acid was used. It is important that an excess amount, preferably 1.5–2 molar equiv of benzoquinone, be present in the reaction mixture. With 1 or less than 1 molar equiv of benzoquinone, only *S*-(2,5-dihydroxyphenyl)thiouronium chloride (**1**) was formed.

A mechanism that is consistent with these observations is outlined in Scheme II. This reaction is depicted as proceeding through an oxidation–reduction pathway *via* the intermediates **1**, **4**, and **5** to give compound **6**. A detailed study of this mechanism is underway and the results will be reported in a future communication.

SCHEME II

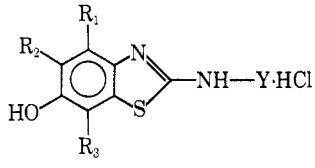


This reaction of thiourea with excess benzoquinone in hydrochloric acid appears to be a general one for the

preparation of thiazoles and can be extended to a variety of readily available benzoquinones and naphthoquinones. Thus, by taking advantage of this new synthetic method one can now obtain in one step various types of 2-amino-6-hydroxybenzothiazolyl and 2-amino-5-hydroxynaphtho[1,2-*d*]thiazolyl compounds. The results of this investigation are summarized in Tables II and III. The structure of these new compounds was established by elemental analysis, nuclear magnetic resonance, and infrared spectroscopy.

TABLE II[a,b]

2-AMINO-6-HYDROXYBENZOTHIAZOLE HYDROCHLORIDE SALTS

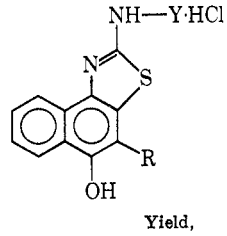


Compd	R_1	R_2	R_3	Y	Yield, %	Mp, °C
3a	H	H	H	H	75	265–266 (249–251)
3b	CH_3	CH_3	H	H	61	304–305 dec (265–266)
3c	CH_3	H	CH_3	H	92	296–297 (235–236)
9	$(CH_3)_2CH$	H	CH_3	H	80	225–227 (203–204)
7a	CH_3	H	H	H	56	284–285 dec (241–242)
7b	PhS	H	H	H	59	255–256 (203–204)
16a	H	H	H	CH_3	64	270–271 (255–256)
16b	H	H	H	$CH_2CH{=}CH_2$	78	204–205 (117–118)
16c	H	H	H	Ph	(41)	(176–177)
19	H	H	Cl	Ph	(37)	(197–198)

[a] Satisfactory analytical values (±0.3%) for C, H, and N were submitted for all compounds in the table: Ed. [b] Numbers in parentheses refer to the free base 2-amino-6-hydroxybenzothiazoles.

TABLE III[a,b]

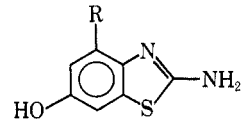
2-AMINO-5-HYDROXYNAPHTHO[1,2-*b*]THIAZOLE HYDROCHLORIDE SALTS



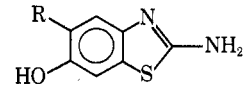
Compd	R	Y	Yield, %	Mp, °C
15a	H	H	80	294-296 dec (>320)
15b	CH_3	H	91	>320 (251-252 dec)
17a	CH_3	CH_3	75	>321 dec (285-287 dec)
17b	CH_3	C_6H_5	23	263-264 dec (174-176)

[a] Satisfactory analytical values (±0.3%) for C, H, and N were submitted for all compounds in the table: Ed. [b] Numbers in parentheses refer to the free base 2-amino-5-hydroxynaphtho[1,2-*d*]thiazoles.

The addition of thiourea to the unsubstituted and disubstituted benzoquinones gave a single product, as we had expected from the results of our previous study[7] and the fact that a common intermediate (see Scheme I) is involved in both the benzoxathione and benzothiazole reactions. Similarly, the addition to monosubstituted benzoquinones such as toluquinone and phenylmercaptobenzoquinone gave two isomeric products, shown by nmr spectroscopy to consist of 93–95% of **7** and 5–7% of **8**. Of these, only the 4-substituted isomers (**7**) could be isolated. Attempts to isolate the



7a, R = CH_3
b, R = C_6H_5S



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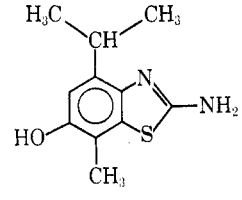
pure isomers (**8**) by fractional crystallization and by preparative thin layer chromatography were unsuccessful.

Although the reaction of thymoquinone with thiourea would theoretically give two isomeric products, **9** and **10**, only one product, identified as the 2-amino-6-hydroxy-4-isopropyl-7-methylbenzothiazole (**9**), was isolated. This structural assignment is based on steric



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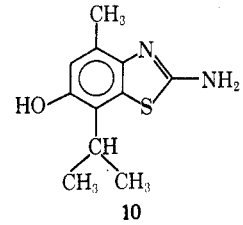

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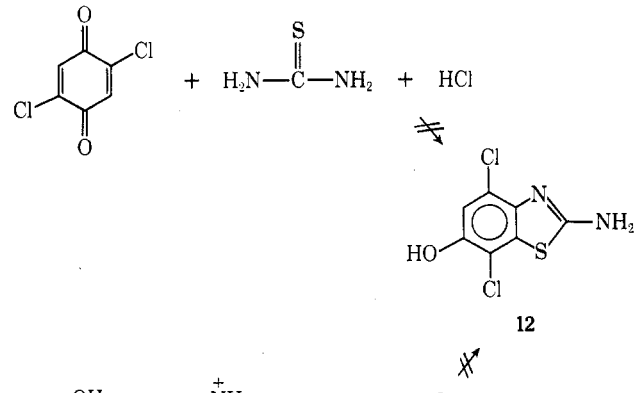
considerations and on the fact that no reaction took place when the position ortho to the methyl group was blocked, as in 3-bromothymoquinone.

Attempts to prepare 2-amino-4,7-dichloro-6-hydroxybenzothiazole (**12**) from 2,5-dichlorobenzoquinone or from its corresponding thiouronium chloride salt (**11**) were unsuccessful. In each case an impure colored product with saltlike properties was isolated.



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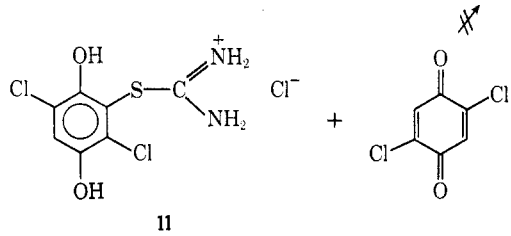

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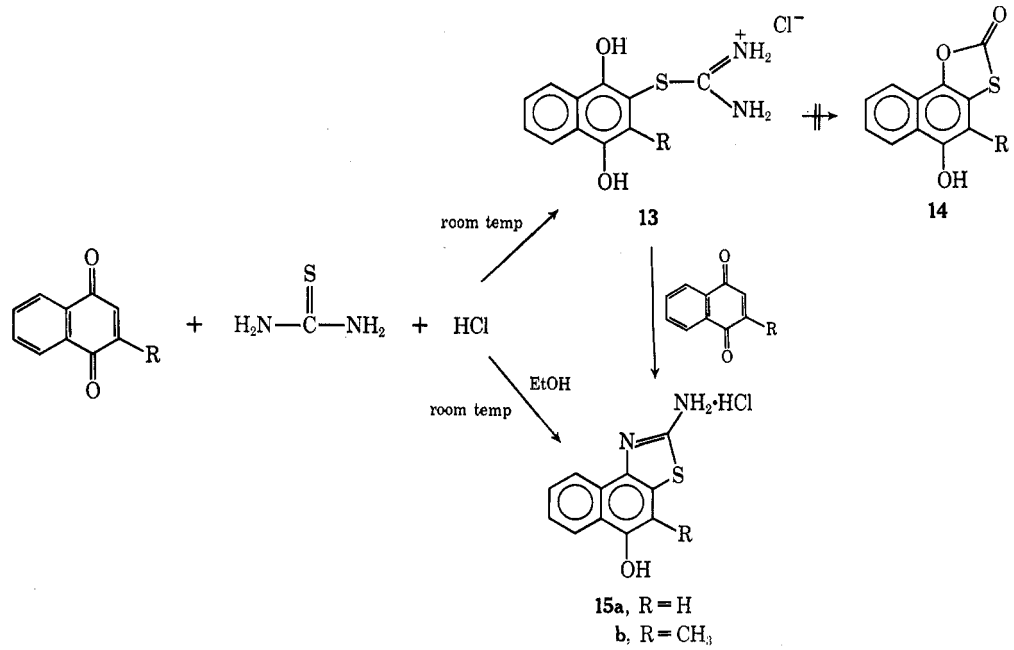
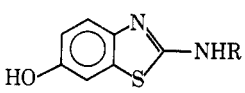
Although 1,4-naphthoquinones are less reactive[8] than 1,4-benzoquinones, they react readily with thiourea to give good yields of thiouronium salts (**13**). However, unlike benzoquinones, these salts did not undergo cyclization to give the expected 5-hydroxynaphth[2,1-*d*]-1,3-oxathiol-2-ones (**14**) when heated in aqueous acetic

(8) L. F. Fieser and M. Fieser, "Advanced Organic Chemistry," Reinhold, New York, N. Y., 1961, pp 845–878.

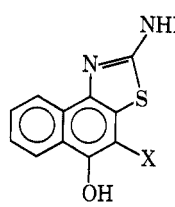


acid. Instead, they decomposed to a black gummy mixture. On the other hand, treatment of these salts with an equimolar quantity of a naphthoquinone gave excellent yields of 2-amino-5-hydroxynaphtho[1,2-*d*]-thiazoles (**15**). These compounds **15** can also be prepared in one step by treating an ethanolic solution of thiourea with a slight excess of naphthoquinone in the presence of concentrated hydrochloric acid. The products which precipitate out from the reaction mixture are especially pure (tlc) after one or two washings with boiling ethanol.

Extension of the reaction of benzoquinones and napthoquinones to *N*-methyl- and *N*-allylthioureas gave the corresponding N-substituted 2-aminothiazolyl compounds (**16** and **17**). As noted in Tables II and III, the

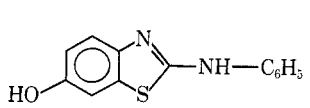


16a, R = CH_3
b, R = $CH_2CH=CH_2$
c, R = C_6H_5



17a, R = X = CH_3
b, R = C_6H_5; X = CH_3

best yields are obtained with *N*-methyl- and *N*-allylthioureas. The reaction with *N*-acetyl- and *N*-phenylthioureas required a longer time and the yield was considerably lower. In the case of *N*-acetylthiourea, the acetyl group was hydrolyzed off during the reaction to give a product that was identical in all respects with **15b**, obtained from the reaction of thiourea and 2-methyl-1,4-naphthoquinone. Depending upon the methods of isolation, treatment of *N*-phenylthiourea with benzoquinone gave two products, identified by nmr as 6-hydroxy-2-phenylaminobenzothiazole (**18**) and 7-chloro-6-hydroxy-2-phenylaminobenzothiazole (**19**).



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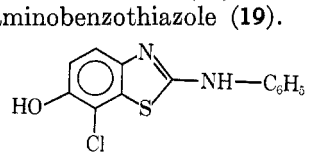

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Experimental Section

All melting points were taken on a Thomas–Hoover Unimelt apparatus and are uncorrected. Infrared spectra were recorded on a Perkin–Elmer Infracord spectrometer. Nuclear magnetic resonance spectra were determined with a Varian Associates Model A-60 instrument in deuterated dimethyl sulfoxide (DMSO-d_6). Chemical shifts are reported in parts per million (δ values) relative to an internal tetramethylsilane standard. Thin layer chromatography (tlc) on silica gel plates containing a uv indicator was employed routinely to follow the course of the reactions and to check the purity of products. Plates were developed with ethyl acetate–ethanol (4:1 v/v) and were visualized with an ultraviolet lamp equipped with a short wave filter. All reagents were Eastman Kodak Co. Chemicals.

Reaction of Benzoquinones with Thiourea and N-Substituted Thiourea. General Procedure.—The following preparation of **2-amino-6-hydroxybenzothiazole hydrochloride** (**3a**) illustrates the general procedure. To a stirred solution of 7.6 g (0.1 mol) of thiourea in 200 ml of ethanol and 9 ml (0.1 mol) of concentrated hydrochloric acid was added dropwise 21.6 g (0.2 mol) of 1,4-benzoquinone dissolved in 400 ml of hot ethanol. After the mixture had been stirred at room temperature for 24 hr, the solvent was removed in a rotary evaporator. The residue was triturated with hot acetonitrile and washed with cold ethanol until tlc analysis showed only one component. The salt was dissolved in a minimum amount of water, filtered, and reprecipitated with concentrated hydrochloric acid to give 15.2 g (75%) of white crystalline solid, mp 263–265°. This process of purification was repeated to yield an analytically pure sample, mp 265–266° (lit.[9] mp 303° dec).

Anal. Calcd for $C_7H_7ClN_2OS$: C, 41.5; H, 3.5; N, 13.8. Found: C, 41.5; H, 3.7; N, 13.8.

The free base was obtained by dissolving the salt in water and carefully neutralizing it with sodium acetate. Recrystallization from ethanol–water yielded straw-colored needles, mp 249–251 (lit.[9] mp 247°). The melting point and infrared spectra were identical with those of an authentic sample obtained from the acid hydrolysis of 2-amino-6-methoxybenzothiazole: nmr (DMSO-d_6) δ 6.83 (q, 1, J_{BX} = 2.5 Hz, J_{BA} = 9.0 Hz, ArH_B), 7.16 (d, 1, J_{XB} = 2.5 Hz, ArH_X), 7.28 (d, 1, J_{AB} = 9.0 Hz, ArH_A).

Anal. Calcd for $C_7H_6N_2OS$: C, 50.6; H, 3.6; N, 16.9. Found: C, 50.5; H, 3.6; N, 17.1.

2-Amino-4,5-dimethyl-6-hydroxybenzothiazole hydrochloride (**3b**) was prepared from 2,3-dimethylbenzoquinone, in 61% yield. For analysis the salt was recrystallized from ethanol, mp 304–305° dec.

(9) R. P. Vel'tman, *Ukr. Khim. Zh.*, **21**, 347 (1955); *Chem. Abstr.*, **49**, 14738*g* (1955).

Anal. Calcd for $C_9H_{11}ClN_2OS$: C, 46.8; H, 4.8; N, 12.1. Found: C, 47.0; H, 4.9; N, 12.4.

Recrystallization of the free base from methanol–water yielded white microcrystalline needles: mp 265–266°; nmr (DMSO-d_6) δ 2.11 (s, 3, CH_3), 2.38 (s, 3, CH_3), 6.95 (s, 1, ArH), and 7.02 (broad s, 2, NH_2).

Anal. Calcd for $C_9H_{10}N_2OS$: C, 55.6; H, 5.2; N, 14.4. Found: C, 55.4; H, 5.1; N, 14.5.

2-Amino-4,7-dimethyl-6-hydroxybenzothiazole hydrochloride (**3c**), obtained from 2,5-dimethylbenzoquinone in 92% yield, was recrystallized from ethanol to give white needles, mp 296–297°.

Anal. Calcd for $C_9H_{11}ClN_2OS$: C, 46.8; H, 4.8; N, 12.1. Found: C, 46.6; H, 4.7; N, 12.1.

The free base was recrystallized from ethanol–water to give white needles: mp 235–236°; nmr (DMSO-d_6) δ 2.20 (s, 3, $ArCH_3$), 2.36 (s, 3, $ArCH_3$), 6.63 (s, 1, ArH), and 7.15 (broad s, 2, NH_2).

Anal. Calcd for $C_9H_{10}N_2OS$: C, 55.6; H, 5.2; N, 14.4. Found: C, 55.4; H, 5.0; N, 14.3.

2-Amino-6-hydroxy-4-isopropyl-7-methylbenzothiazole hydrochloride (**9**) was prepared from thymoquinone in 80% yield. The salt was recrystallized from isopropyl alcohol to give white needles, mp 225–227°.

Anal. Calcd for $C_{11}H_{15}ClN_2OS$: C, 51.1; H, 5.8; N, 10.8. Found: C, 51.0; H, 6.0; N, 10.8.

The analytical sample of the free base was obtained from ethanol–water as yellow platelets: mp 203–204°; nmr (DMSO-d_6) δ 1.29 [d, 6, $CH(CH_3)_2$], 2.28 (s, 3, $ArCH_3$), 3.49 [q, 1, $CH(CH_3)_2$], 6.77 (s, 1, ArH), and 7.16 (broad s, 2, NH_2).

Anal. Calcd for $C_{11}H_{14}N_2OS$: C, 59.4; H, 6.4; N, 12.3. Found: C, 59.3; H, 6.3; N, 12.0.

6-Hydroxy-2-methylaminobenzothiazole hydrochloride (**16a**) was prepared in 64% yield from 1,4-benzoquinone and 1-methyl-2-thiourea. An analytical sample was obtained by recrystallization from methanol, mp 270–271°.

Anal. Calcd for $C_8H_9ClN_2OS$: C, 44.4; H, 4.2; N, 12.9. Found: C, 44.5; H, 4.1; N, 12.8.

The free base was obtained from ethanol as white needles: mp 255–256°; nmr (DMSO-d_6) δ 3.00 (s, 3, NCH_3), 6.74 and 6.86 (d, 1, J_{BX} = 2.5 Hz, J_{BA} = 9.0 Hz, ArH_B), 7.20 (d, 1, J_{XB} = 2.5 Hz, ArH_X), 7.34 (d, 1, J_{AB} = 9.0 Hz, ArH_A), 7.63 (broad s, 2, NH_2), and 9.17 (broad s, 1, OH).

2-Allylamino-6-hydroxybenzothiazole hydrochloride (**16b**), formed in 78% yield from 1,4-benzoquinone and 1-allyl-2-thiourea, was obtained from ethanol as white crystals, mp 204–205°.

Anal. Calcd for $C_{10}H_{11}ClN_2OS$: C, 49.5; H, 4.6; N, 11.5. Found: C, 49.4; H, 4.7; N, 11.5.

The free base was obtained by neutralizing **16b** with sodium acetate. When sodium carbonate or ammonium hydroxide was used, a resinous gum was formed. Recrystallization from acetonitrile–water gave white needles: mp 117–118°; nmr (DMSO-d_6) δ 2.97 (d, 2, $NCH_2CH{=}CH_2$), 5.01–6.32 (m, 3, $-CH_2CH{=}CH_2$), 6.73 (q, 1, J_{BX} = 2.5 Hz, J_{BA} = 9.0 Hz, ArH_B), 7.10 (d, 1, J_{XB} = 2.5 Hz, ArH_X), and 7.23 (d, 1, J_{AB} = 9.0 Hz, ArH_A).

Anal. Calcd for $C_{10}H_{10}N_2OS$: C, 58.2; H, 4.9; N, 13.5. Found: C, 58.1; H, 5.1; N, 13.5.

Reaction of *S*-(2,5-Dihydroxyphenyl)thiouronium Chloride with *p*-Benzoquinone.—To a well-stirred suspension of 22.1 g (0.1 mol) of *S*-(2,5-dihydroxyphenyl)thiouronium chloride[7] in 400 ml of ethanol was added portionwise 10.8 g (0.1 mol) of *p*-benzoquinone. As the reaction proceeded the suspended starting materials dissolved to give a dark brown solution. The mixture was stirred at room temperature for 24 hr. The solvent was evaporated *in vacuo* and the resulting black residue was triturated with boiling acetonitrile and washed with cold ethanol giving 15 g (75%) of a straw-colored salt, which was identical in all respects with the hydrochloride salt of **3a** prepared from *p*-benzoquinone and thiourea in concentrated hydrochloric acid.

Effects of 1,4-Benzoquinone and Hydrochloric Acid on the Yield of 2-Amino-6-hydroxybenzothiazole Hydrochloride (**3a**).—The reaction was run in the same manner as in the preparation of **3a** by using varying amounts of 1,4-benzoquinone and hydrochloric acid. The results are summarized in Table I.

2-Amino-6-hydroxy-4-methylbenzothiazole Hydrochloride (**7a**).—A solution of 12.2 g (0.1 mol) of toluquinone in 500 ml of ethanol was added dropwise to a stirred solution of 3.8 g (0.05 mol) of thiourea in 150 ml of ethanol and 4.5 ml (0.05 mol) of concentrated hydrochloric acid. After the mixture had been stirred at room temperature for 24 hr, the solvent was removed under reduced pressure, and the residue triturated repeatedly with hot acetonitrile until all the starting quinone was removed (tlc). A yield of 6.6 g (61%) of a cream-white solid was obtained, mp 257–261° dec. Tlc analysis of the crude solid showed only one spot, but analysis by nmr spectroscopy showed the presence of two isomers, consisting of approximately 93% of the 4-methyl isomer **7a** and 7% of the 5-methyl isomer **8a**. The crude mixture was crystallized from water to give 6.0 g (56%) of white crystals, mp 284–285° dec, which was identified by nmr as **7a**.

Anal. Calcd for $C_8H_9ClN_2OS$: C, 44.4; H, 4.2; N, 12.9. Found: C, 44.2; H, 4.2; N, 12.9.

Attempts to isolate the 5-methyl isomer from the filtrate by fractional crystallization and preparative thin layer chromatography were unsuccessful.

The free base of **7a** was obtained by neutralizing a water solution of it with ammonium hydroxide. Recrystallization from ethanol–water furnished a light tan solid: mp 241–242°; nmr (DMSO-d_6) δ 2.41 (s, 3, $ArCH_3$), 6.64 (d, 1, J = 2.4 Hz, ArH), 6.95 (d, 1, J = 2.4 Hz, ArH), and 7.20 (broad s, 2, NH_2).

Anal. Calcd for $C_8H_8N_2OS$: C, 53.4; H, 4.5; N, 15.5. Found: C, 53.6; H, 4.6; N, 15.7.

2-Amino-6-hydroxy-4-phenylthiobenzothiazole hydrochloride (**7b**) was prepared from 2-phenylthiobenzoquinone[10] in the same manner as in the preparation of **7a**. The crude mixture was shown by nmr spectroscopy to consist of two isomers, present approximately in the ratio of 95% of the 4-phenylthio isomer **7b** and 5% of the 5-phenylthio isomer **8b**. Of these only **7b** was isolated pure in 59% yield as white needles after crystallization from ethanol.

Anal. Calcd for $C_{13}H_{11}ClN_2OS_2$: C, 50.2; H, 3.6; N, 9.0. Found: C, 50.1; H, 3.8; N, 8.9.

The free base of **7b** was obtained from ethanol–water as white needles: mp 203–204°; nmr (DMSO-d_6) δ 6.47, 7.09 (AB q, 2, J = 2.5 Hz, ArH), 7.34 (s, 5, PhS), and 7.50 (broad s, 2, NH_2).

Anal. Calcd for $C_{13}H_{10}N_2OS_2$: C, 56.9; H, 3.7; N, 10.2. Found: C, 56.8; H, 3.8; N, 10.4.

Reaction of 1,4-Benzoquinone with 1-Phenyl-2-thiourea. A. Isolation of 6-Hydroxy-2-phenylaminobenzothiazole (**16c**).—A solution of 10.8 g (0.1 mol) of 1,4-benzoquinone dissolved in 250 ml of hot ethanol was added dropwise to a stirred mixture of 7.6 g (0.5 mol) of 1-phenyl-2-thiourea and 4.5 ml (0.05 mol) of concentrated hydrochloric acid in 250 ml of ethanol. The mixture was stirred at room temperature for 24 hr and filtered, and the solvent removed under reduced pressure to give a dark brown resinous gum. The gum was dissolved in 100 ml of ethanol and diluted with 2 *N* hydrochloric acid. Scratching and cooling caused the oil to solidify. The dark brown solid was collected and washed repeatedly with hot water. The washings were combined and neutralized with sodium carbonate giving 5 g (41%) of yellow solid. Recrystallization from glacial acetic acid–water and then from ethanol–water gave light tan needles: mp 176–177°; nmr (DMSO-d_6) δ 6.83–7.93 (m, 8, ArH) and 10.41 (broad s, 2, NH, OH).

Anal. Calcd for $C_{13}H_{10}N_2OS$: C, 64.4; H, 4.2; N, 11.5. Found: C, 64.6; H, 4.4; N, 11.3.

B. Isolation of 7-Chloro-6-hydroxy-2-phenylaminobenzothiazole (**19**).—The reaction was run in the same manner as A using 0.1 mol of 1,4-benzoquinone, 0.05 mol of *N*-phenylthiourea, and 0.1 mol of concentrated hydrochloric acid. The gummy residue, after removal of the solvent, was treated with a solution of sodium hydrosulfite and triturated with water until it solidified. Recrystallization from ethanol–water gave 4 g (31%) of white needles: mp 197–198°; nmr (pyridine-d_5) δ 7.35, 7.77 (AB q, 2, J_{AB} = 9.0 Hz, ArH), and 6.96–8.25 (m, 5, NHPh).

Anal. Calcd for $C_{13}H_9ClN_2OS$: C, 56.4; H, 3.3; N, 10.1; Cl, 12.8. Found: C, 56.4; H, 3.3; N, 9.8; Cl, 12.7.

Reaction of Naphthoquinones with Thiourea and N-Substituted Thioureas. General Procedure.—This procedure may be illustrated by the preparation of **2-amino-5-hydroxynaphtho[1,2-*d*]thiazole hydrochloride** (**15a**). To a solution of 3.8 g (0.05 mol) of thiourea and 4.5 ml (0.05 mol) of concentrated hydrochloric acid in 200 ml of ethanol was added dropwise, with stirring, 15.8 g (0.1 mol) of 1,4-naphthoquinone dissolved in 500 ml of hot ethanol. The mixture was stirred for 24 hr at room temperature, during which time a solid precipitated out. It

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was collected and washed thoroughly with boiling ethanol to give 10.0 g (80%) of a creamy white solid, mp 294–296° dec. Tlc analysis indicated one component. For elemental analysis, a sample of the solid was recrystallized from dimethyl sulfoxide–ethyl acetate with no change in melting point: nmr (DMSO-d_6) δ 7.55 (s, 1, ArH), and 7.64–8.57 (m, 2, peri-ArH).

Anal. Calcd for $C_{11}H_9ClN_2OS$: C, 52.3; H, 3.6; N, 11.1. Found: C, 52.1; H, 3.5; N, 11.0.

The free base was obtained by neutralizing a water solution of **15a** with ammonium hydroxide. Recrystallization from ethanol–water gave a light gray solid: mp >320°; nmr (DMSO-d_6) δ 7.25–8.41 (broad nondefinitive m, 5, ArH).

Anal. Calcd for $C_{11}H_8N_2OS$: C, 61.1; H, 3.7; N, 12.9. Found: C, 60.9; H, 3.6; N, 12.9.

2-Amino-5-hydroxy-4-methylnaphtho[1,2-*d*]thiazole hydrochloride (**15b**) was prepared in 91% yield from 2-methylnaphthoquinone and thiourea. The product was essentially pure after washing with boiling ethanol (tlc). An analytical sample was obtained by recrystallization from a dimethyl sulfoxide–ethyl acetate mixture, mp >320°.

Anal. Calcd for $C_{12}H_{11}ClN_2OS$: C, 54.0; H, 4.2; N, 10.4. Found: C, 53.9; H, 4.3; N, 10.2.

The free base was obtained from ethanol–water as white needles with a slight pink coloration: mp 251–252° dec; nmr (DMSO-d_6) δ 2.45 (s, 3, $ArCH_3$), 7.50–7.66 (m, 2, ArH), and 8.25–8.55 (m, 2, peri-ArH).

Anal. Calcd for $C_{12}H_{10}N_2OS$: C, 62.6; H, 4.4; N, 12.2. Found: C, 62.5; H, 4.5; N, 12.2.

5-Hydroxy-2-methylamino-4-methylnaphtho[1,2-*d*]thiazole hydrochloride (**17a**) was prepared in 75% yield from 2-methylnaphthoquinone and *N*-methylthiourea. The salt was crystallized from water–ethanol, mp 323° dec.

Anal. Calcd for $C_{13}H_{13}ClN_2OS$: C, 55.6; H, 4.7; N, 9.9. Found: C, 55.7; H, 4.7; N, 9.7.

The free base was obtained from ethanol–water as an unstable, gray solid: mp 285–287° dec; nmr (DMSO-d_6) spectrum was broad and nondefinitive.

Anal. Calcd for $C_{13}H_{12}N_2OS$: C, 63.9; H, 5.4; N, 11.5. Found: C, 63.7; H, 5.4; N, 11.2.

5-Hydroxy-4-methyl-2-phenylaminonaphtho[1,2-*d*]thiazole hydrochloride (**17b**) was obtained in 23% yield from 2-methylnaphthoquinone and 1-phenyl-2-thiourea after 3 days of stirring at room temperature. An analytical sample was prepared by recrystallization from dimethyl sulfoxide–ethyl acetate to give white needles: mp 262–265° dec; nmr (DMSO-d_6) δ 2.50 (s, 3, $ArCH_3$) and 6.92–8.59 (m, 9, ArH).

Anal. Calcd for $C_{18}H_{15}ClN_2OS$: C, 63.1; H, 4.4; N, 8.2. Found: C, 62.9; H, 4.4; N, 8.0.

The free base was recrystallized from ethanol–water to give crystalline needles: mp 174–176°; nmr (DMSO-d_6) δ 2.52 (s, 3, $ArCH_3$), 6.89–7.99 (m, 7, ArH), and 8.20–8.59 (m, 2, peri-ArH).

Anal. Calcd for $C_{18}H_{14}N_2OS$: C, 70.6; H, 4.6; N, 9.2. Found: C, 70.3; H, 4.6; N, 9.1.

Reaction of 2-Methylnaphthoquinone with *N*-Acetylthiourea.—To a solution of 5.9 g (0.05 mol) of 1-acetyl-2-thiourea in 200 ml of ethanol and 4.5 ml (0.05 mol) of concentrated hydrochloric acid was added dropwise, with stirring, a solution of 17.2 g (0.1 mol) of 2-methylnaphthoquinone in 500 ml of ethanol. After 3 days of stirring, the solid was collected and washed thoroughly with boiling ethanol to give 4.5 g (34%) of a creamy white solid, mp >320°. The product was identical in all respects with compound **15b** obtained from the reaction of 2-methylnaphthoquinone and thiourea, thus indicating that the acetyl group was hydrolyzed during the reaction.

Reaction of *S*-(1,4-Dihydroxy-2-naphthyl)thiouronium Chloride with 1,4-Naphthoquinone.—To a stirred suspension of 13.5 g (0.05 mol) of *S*-(1,4-dihydroxy-2-naphthyl)thiouronium chloride[6] in 400 ml of ethanol was added dropwise a solution of 7.9 g (0.05 mol) of 1,4-naphthoquinone in 500 ml of ethanol. After 24 hr of stirring at room temperature, the solid was collected and washed well with boiling ethanol to give 10.2 g (81%) of crystalline solid, mp 296–297° dec, which was identical in all respects with **15a** obtained from the reaction of 1,4-naphthoquinone and thiourea in the presence of hydrochloric acid.

Compound **15b** was similarly prepared in 90% yield from *S*-(1,4-dihydroxy-3-methyl-2-naphthyl)thiouronium[6] chloride and 2-methylnaphthoquinone.

Registry No.—**3a** (HCl), 26278-78-4; **3a** (base), 26278-79-5; **3b** (HCl), 26278-80-8; **3b** (base), 26278-81-9; **3c** (HCl), 26278-82-0; **3c** (base), 26278-83-1; **7a** (HCl), 26278-84-2; **7a** (base), 26278-85-3; **7b** (HCl), 26268-99-5; **7b** (base), 26269-00-1; **9** (HCl), 26269-01-2; **9** (base), 26269-02-3; **15a** (HCl), 26269-03-4; **15a** (base), 26269-04-5; **15b** (HCl), 26322-40-7; **15b** (base), 26269-05-6; **16a** (HCl), 26269-06-7; **16a** (base), 26269-07-8; **16b** (HCl), 26269-08-9; **16b** (base), 26269-09-0; **16c** (base), 26269-10-3; **17a** (HCl), 26269-11-4; **17a** (base), 26269-12-5; **17b** (HCl), 26269-13-6; **17b** (base), 26269-14-7; **19** (base), 26269-15-8.