5-*n*-butyl-2-(4-dimethylaminophenyl)-4-methylthiazole hydrobromide, 17790-40-8.

Acknowledgments.—The authors wish to thank Mrs. Ruth Stanaszek for assistance in determining the nmr spectra, Mr. Victor Rauschel and coworkers for elemental analyses, and Mr. William Washburn for some ir spectra. Helpful discussions with Dr. Milton Levenberg of these laboratories and Professor Peter Beak of the University of Illinois are appreciated.

A One-Step Synthesis of 5-Hydroxy-1,3-benzoxathiol-2-ones from Quinones and Thiourea

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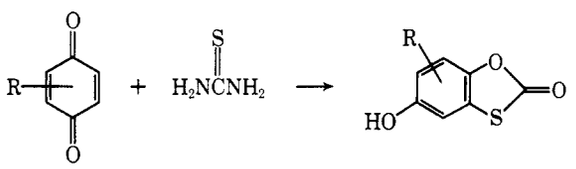
A wide variety of 5-hydroxy-1,3-benzoxathiol-2-ones were prepared in excellent yields by a one-step synthesis from readily available quinones and thiourea. Depending on the nature of the substituents and the reaction conditions, the intermediate S-(2,5-dihydroxyaryl)thiouronium salts and 5-hydroxy-2-imino-1,3-benzoxathioles could also be readily isolated. Reactions of thiourea with unsubstituted, disubstituted, or trisubstituted quinone gave only one end product. However, monosubstituted quinones gave one or more of the three possible isomeric end products, the 4-, 6-, and 7-substituted 5-hydroxy-1,3-benzoxathiol-2-ones. The directive influence of the substituent groups on the addition of thiourea and their effect on the ease of cyclization of the resulting thiouronium salts are described.

Although several methods have been reported in the literature[1,2] for the synthesis of 5-hydroxy-1,3-benzoxathiol-2-ones, these methods are, in general, characterized by low yields or by cumbersome preparative procedures.

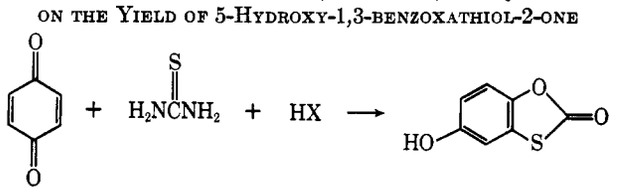
In this paper we describe a method whereby a wide variety of 5-hydroxy-1,3-benzoxathiol-2-ones can be prepared rapidly and in excellent yields by a one-step synthesis from readily available quinones and thiourea.



In general, the procedure consists in mixing a solution of thiourea in aqueous hydrochloric acid with a solution of a quinone in glacial acetic acid and heating for 1 hr on a steam bath. The product, which crystallizes from solution on cooling, is essentially pure. As can be seen from Table I, the reaction is best run with a large excess of thiourea and aqueous hydrochloric acid. Good results are also obtained with sulfuric or trifluoroacetic acid. When a weak acid such as acetic acid is used, the yield is considerably lower, and the product is generally contaminated with colored impurities which are difficult to separate. No product is formed in the absence of acid.

These observations strongly suggest that the reaction involves a 1,4 addition of thiourea to the protonated quinone, giving first an intermediate S-(2,5-dihydroxyaryl)thiouronium salt (**1**), which cyclizes to a second intermediate, 5-hydroxy-2-imino-1,3-benzoxathiole (**2**). This, in turn, is hydrolyzed to the final 5-hydroxy-1,3-benzoxathiol-2-one (**3**) (Scheme I). The formation of each intermediate, and the final product, during the course of the reaction can be readily detected and followed by thin layer chromatography (tlc). Several of the thiouronium salts (Table II) and imino salt were isolated and characterized. Upon being heated in strong aqueous acid, they were rapidly and quantitatively converted into the corresponding products.

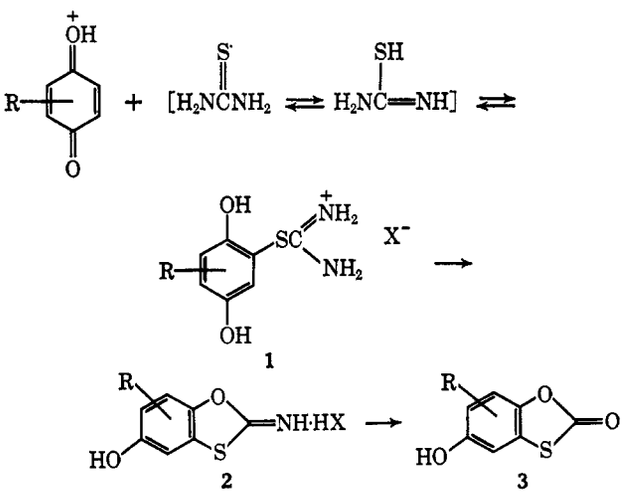
TABLE I
EFFECTS OF AMOUNT OF ACIDS, THIOUREA, AND QUINONES ON THE YIELD OF 5-HYDROXY-1,3-BENZOXATHIOL-2-ONE



Acid	Molar ratio	Benzoquinone[a] molar ratio	Thiourea[b] molar ratio	Yield, %
...	...	1.0	1.5	0
HCl	3.0	1.0	1.5	92
HCl	1.0	1.0	1.5	60
HCl	0.5	1.0	1.5	21
HCl	3.0	2.0	1.0	10
H_2SO_4	3.0	1.0	1.5	94
CF_3CO_2H	10.0	1.0	1.5	85
HOAc	10.0	1.0	1.5	45

[a] Solution in HOAc. [b] Solution in aqueous 2 *N* HCl or H_2SO_4

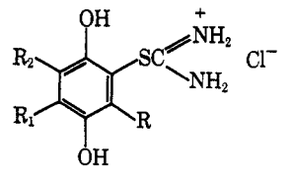
SCHEME I

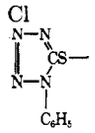


(1) H. Burton and S. B. David, *J. Chem. Soc.*, 2193 (1952).
(2) H. Fiedler, *Chem. Ber.*, **95**, 1771 (1962).

TABLE II

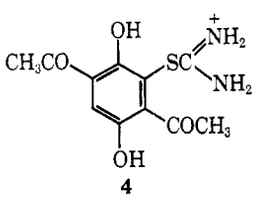
S-(2,5-DIHYDROXYARYL)THIOURONIUM CHLORIDES



R	R_1	R_2	Registry no.	Mp, dec, °C[a]	Calcd, % C	Calcd, % H	Calcd, % S	Found, % C	Found, % H	Found, % S
H	H	H	6274-93-7	156	38.2	4.1	14.5	38.3	4.0	14.2
H	H	Ph	17630-82-9	112	52.6	4.4	10.8	52.4	4.6	11.0
H	H	CH_3 [b]	17630-83-0	121	40.9	4.7	13.6	40.5	4.5	13.8
H	CH_3	H [b]	17630-84-1							
H	H	PhS	17630-85-2	160	47.5	4.0	19.5	47.5	3.9	19.3
H	H	CH_3CO	17630-86-3	195	41.2	4.2	12.2	41.1	4.3	12.2
H	H	OCH_3 [b]	17630-87-4	170	38.3	4.4	12.8	37.9	4.3	13.2[c]
H	OCH_3	H [b]	17630-88-5							
H	H	Cl	17630-89-6	140	33.0	3.1	11.0	32.7	3.2	11.0
H	Cl	H [b]	17630-90-9	145	33.0	3.1	11.0	33.3	3.2	11.3
Cl	H	H [b]	17630-91-0							
H	CH_3	CH_3	17630-92-1	110	43.5	5.3	12.8	43.5	5.4	12.5
CH_3	CH_3	H	17658-48-9	198	43.5	5.3	12.8	43.8	5.6	12.9
Cl	H	Cl	17630-93-2	160	29.3	2.4	11.1	29.0	2.8	10.8
	H	H	17630-94-3	149	42.4	3.3	16.2	42.3	3.4	16.0

[a] The temperature at which the salt turned color was taken as the decomposition point. [b] Isomeric mixtures as analyzed by nmr spectroscopy. [c] Analytically pure samples were not obtained.

Contrary to previous reports,[1,3] the thiouronium salts do not decompose to colored products when heated in strong acid. Only when the salts were heated in weak acids or failed to undergo cyclization (*e.g.*, **4** and **5**) did we observe extensive decomposition.



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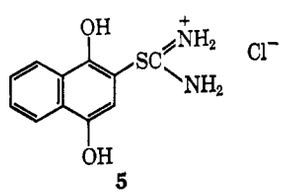

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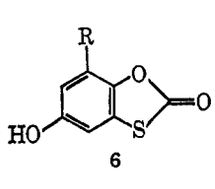
Reactions of thiourea with an unsubstituted, a disubstituted, or a trisubstituted quinone gave only a single product (Table III). No difficulty was encountered in controlling the reaction in order to obtain the monoaddition product with thiourea. However, when a monosubstituted quinone was used, the reaction was more complex. Depending on the nature of the substituent, one or more of the three possible isomers (**6**–**8**) is obtained. The results of this study, listed in Table IV, show that, when R is $-C_{18}H_{37}$ and $-C_8H_{17}$, the thiourea adds *meta* to the substituents to give exclusively the 7-substituted 5-hydroxy-1,3-benzoxathiol-2-one (**6**). With groups such as CH_3, C_6H_5S, and C_6H_5, a small amount (3–10%) of the 6-substituted isomer (**7**) is also obtained. If the position *meta* to these substituents is blocked, as in 2,6-dimethylbenzoquinone, the yield is considerably lower (Table III).



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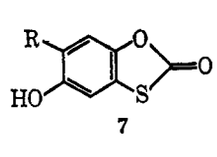

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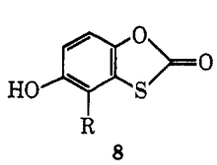

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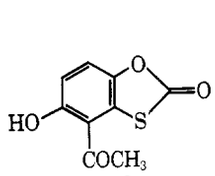
The reaction of thiourea with 2-acetylquinone, which contains an electron-withdrawing group, also gave a mixture of two isomeric products, shown by nmr and vpc to consist of 83% **9** and 17% **10**. The formation of these isomers was conveniently followed by tlc. The thiouronium chloride (**11**) was converted completely into its cyclized product (**9**), when the reaction mixture was heated on a steam bath for 40 min, while the thiouronium chloride (**12**) remained practically unchanged. Only upon prolonged heating was **12** converted into product **10**. This striking difference



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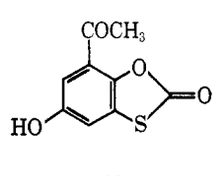

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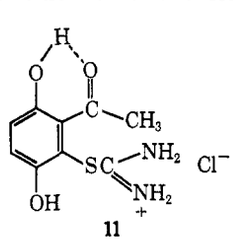

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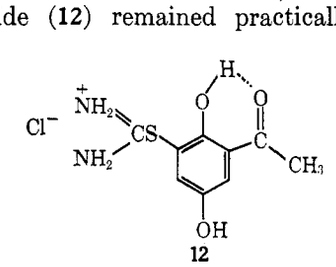
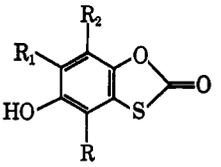


12

(3) M. Schubert, *J. Amer. Chem. Soc.*, **69**, 712 (1947).

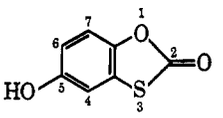
TABLE III
UNSUBSTITUTED, DISUBSTITUTED, AND TRISUBSTITUTED 5-HYDROXY-1,3-BENZOXATHIOL-2-ONES



R	R_1	R_2	Registry no.	Mp (lit.[a]), °C	Yield, %	Calcd, % C	Calcd, % H	Calcd, % S	Found, % C	Found, % H	Found, % S
H	H	H		174–175 (175–176)	92	50.0	2.4	19.0	49.9	2.7	19.0
H	CH_3	CH_3	17631-06-0	164–165	73	55.1	4.1	16.4	55.1	4.2	16.1
CH_3	CH_3	H	7735-65-1	145–146 (147–147.5)	38[b]	55.1	4.1	16.4	55.3	4.2	16.2
CH_3	H	CH_3		205–206 (205–206)	95	55.1	4.1	16.4	55.1	4.4	16.6
Cl	H	Cl		174–175 (177–178)	90	35.5	0.9	13.5	35.3	1.0	13.5
Cl	Cl	H		161–162 (162–162.5)	87	35.5	0.9	13.5	35.5	1.1	13.8
Ph	H	Ph	17630-96-5	181–182	98	71.2	3.7	10.0	71.3	4.0	10.3
CH_3	CH_3	CH_3	17630-97-6	159–160	72	57.1	4.8	15.2	56.9	4.7	15.2
CH_3	H	$CH(CH_3)_2$		156.5–157.5 (158.5–159)	96	58.9	5.4	14.3	58.8	5.3	14.5
CH_3CO	H	CH_3		217–218	82	53.6	3.6	14.3	53.6	3.9	14.0

[a] Reference 2. [b] A large amount of 2,5-dimethyl-4-chlorophenol was also isolated.

TABLE IV
MONOSUBSTITUTED 5-HYDROXY-1,3-BENZOXATHIOL-2-ONES

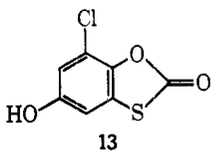


R	Registry no.	Mp, °C	Yield, %[a]	Coupling constant,[b] cps	Product ratio, %[c]	Calcd, % C	Calcd, % H	Calcd, % S	Found, % C	Found, % H	Found, % S
7-Ph		176–177	90	2.5	93	63.9	3.3	13.1	63.8	3.4	13.1
6-Ph	7735-69-5	144–145	3	<1.0	7				63.8	3.3	13.0
7-CH_3	17631-00-4	164–165	82	2.5	90	52.7	3.3	17.6	52.4	3.4	17.4
6-CH_3	17631-01-5	143–144	7	<1.0	10				52.4	3.0	17.3
4-CH_3CO		187–188	79	9.0	83	51.4	2.9	15.3	51.6	2.9	15.6
7-CH_3CO		209–210	11	2.6	17				51.5	2.7	15.3
7-Cl		180–181	53	2.5	62				41.5	1.6	15.6
6-Cl, 4-Cl		128–130	25	<1.0 9.0	20 18	41.5	1.5	15.8	41.6	1.7	16.1
7-PhS	17630-67-0	167–168	96	2.3	97	56.5	2.9	23.2	56.4	3.0	23.4
6-PhS	17630-68-1	118–119	2	<1.0	3						
7-*n*-$C_{18}H_{37}$	17630-69-2	122–123	96	2.5	100	71.4	9.6	7.6	71.5	9.7	7.7
7-*n*-C_8H_{17}	17630-70-5	108–109	99	2.5	100	64.2	7.2	11.4	64.3	7.2	11.4

[a] Isolated yield. [b] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p 85. [c] Product ratio of isomeric mixture as analyzed by nmr spectroscopy and vpc.

in reactivity, which made the separation of the cyclized products easy, may be attributed to hydrogen bonding between the carbonyl oxygen and the hydroxyl group of the thiouronium salts.

With a quinone containing a substituent such as chloro, which can withdraw as well as donate electrons, all three isomeric products were obtained. Of these, only the 7-chloro isomer (**13**) was obtained in a pure



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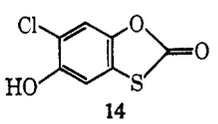

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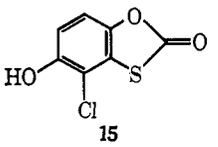

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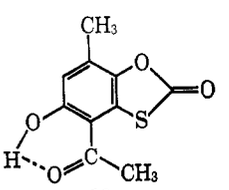
condition. The position of the chloro substituent in the ring was established by nmr spectroscopy, and the amount of each isomer present in the mixture was determined by nmr spectroscopy and vpc to be in the ratio of 62% **13**, 20% **14**, and 18% **15**.

Although reaction of thiourea with 2-acetyl-5-methylbenzoquinone would theoretically yield two isomeric products, only one product, identified as the 4-acetyl-5-hydroxy-1,3-benzoxathiol-2-one (**16**), was iso-



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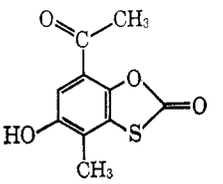

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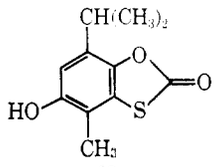
lated in excellent yield. This result again demonstrates the directive influence of the methyl and acetyl groups. Structure assignment of the product was made in favor of the intramolecularly hydrogen-bonded **16** over **17** on the basis of its nmr spectrum, which shows that the chemical shift of the hydroxyl proton is far downfield

at 12.4 ppm, indicative of hydrogen bonding. The very slight upfield shift on changing temperature from 35 to 60° and the absence of any shift on dilution suggest an intramolecular hydrogen bond, a phenomenon which is possible only for compound **16**.

The addition of thymoquinone to thiourea afforded only the 5-hydroxy-7-isopropyl-4-methyl-1,3-benzoxathiol-2-one (**18**). That the other isomer (**19**) was not formed probably results from the steric effect of the isopropyl group. This is further supported by the



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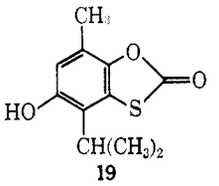

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observation that, when 3-bromothymoquinone or 2,5-di-*t*-butylbenzoquinone was used, no reaction occurred. Instead, the quinones were reduced quantitatively to their respective hydroquinones. This procedure was also useful for reducing duroquinone to durohydroquinone.

The observations made in this study indicate that, in general, strong electron-donating groups direct the addition of thiourea primarily *meta* and secondarily *para* to the substituents. Electron-withdrawing groups, on the other hand, direct *ortho* to the substituents. Addition is sterically excluded at the *ortho* position by bulky substituents such as the isopropyl or *t*-butyl groups. It is interesting to note that these reactions somewhat resemble the Thiele acetylation of quinones,[4] in that they are both acid-catalyzed reactions, and that they both give only monoaddition products. However, they differ from each other in the orientation effects of strong electron-donating groups and in the distribution of isomers.[5]

Experimental Section

All melting points were taken on a Thomas–Hoover Unimelt apparatus and are uncorrected. Infrared spectra were measured on a Perkin-Elmer Infracord spectrometer. Nuclear magnetic resonance spectra were determined with a Varian A-60 spectrometer in deuterated chloroform ($CDCl_3$) or dimethyl sulfoxide (DMSO-d_6). Chemical shifts are reported in parts per million relative to an internal tetramethysilane standard. Thin layer chromatography (tlc) was run on silica gel plates containing a uv indicator and developed in a solvent mixture of equal volumes of ethyl acetate and chloroform. Vapor phase chromatography (vpc) was done on a 0.25 in. × 10 ft column of 20% OV-17 on 80–100 mesh Anakdrom ABS, with a helium flow of 70–75 cc/min. Samples were run as trimethylsilyl derivatives, and product ratios were determined by a comparison of peak areas. Unless specified otherwise, all reagents were Eastman Kodak Co. chemicals.

Preparation of *S*-(2,5-Dihydroxyaryl)thiouronium Chlorides. General Procedure.—To a solution of 0.15 mol of thiourea in 100 ml of 2 *N* hydrochloric acid was added, with stirring, a solution of 0.1 mol of quinone in 50–100 ml of glacial acetic acid. The mixture was stirred for 30 min at room temperature. If the thiouronium chloride did not precipitate at this point, concentrated hydrochloric acid was added to the mixture. The precipitated salt was removed by suction filtration and washed with a little cold 2 *N* hydrochloric acid. The salt was purified by dissolving it in cold water, filtering the solution, and reprecipitating it with concentrated hydrochloric acid. Pertinent data concerning these compounds are reported in Table I. Most of these salts have no definite melting point; they decompose without melting over a wide range of temperatures. Their structures are confirmed by elemental and spectral analyses.

4,7-Dichloro-5-hydroxy-2-imino-1,3-benzoxathioles and 4,7-Dimethyl-5-hydroxy-2-imino-1,3-benzoxathioles.—To a solution of 5.7 g (0.075 mol) of thiourea in 30 ml of 2 *N* hydrochloric acid was added 8.9 g (0.05 mol) of 2,5-dichlorobenzoquinone in 100 ml of glacial acetic acid. The mixture was stirred for 30 min at room temperature, then heated slowly in a water bath to 50–55°. The precipitated thiouronium salt redissolved to give a clear, faintly yellow solution. After about a 10-min stirring at this temperature, a mass of white solid crystallized out of solution. Stirring was continued for 20 min more, until tlc indicated that the thiouronium salt had been completely converted into the imino product. The solid was collected by suction and washed with alcohol to remove the small amount of 4,7-dichloro-5-hydroxy-1,3-benzoxathiol-2-one present in the reaction product: yield, 7.5 g (64%); mp 213–214° dec. Its ir and nmr spectra were consistent with the structure.

Anal. Calcd for $C_7H_3Cl_2NO_2S$: C, 35.6; H, 1.3; S, 13.6. Found: C, 35.3; H, 1.5; S, 13.9.

Similarly, 4,7-dimethyl-5-hydroxy-2-imino-1,3-benzoxathiole hydrochloride salt was prepared in a yield of 81%, mp 116° dec.

Anal. Calcd for $C_9H_{10}ClNO_2S$: C, 46.7; H, 4.7; S, 13.8. Found: C, 46.9; H, 4.6; S, 13.7.

Preparation of Unsubstituted, Disubstituted, and Trisubstituted 5-Hydroxy-1,3-benzoxathiol-2-ones. General Procedure.—To a solution of 0.15 mol of thiourea in 100 ml of 2 *N* hydrochloric acid was added, with stirring, a solution of 0.1 mol of quinone in 50–70 ml of glacial acetic acid. The mixture was stirred at room temperature for 30 min, during which time a mass of crystalline thiouronium salt precipitated (with most of the quinones). Upon heating on a steam bath, the salt redissolved to give a clear solution. The mixture was heated for 1 hr, then chilled in an ice bath until crystallization was complete. The solid was collected, washed with water, and dried. For elemental analysis, the product was recrystallized from ethanol–water.

Compounds prepared by this procedure are reported in Table III. The structures were confirmed by elemental and nmr spectral analyses or by comparison of the melting point and infrared spectra with those of known authentic samples.

S-(2,5-Dihydroxy-4,6-dimethylphenyl)thiouronium Chloride and 4,6-Dimethyl-5-hydroxy-1,3-benzoxathiol-2-one.—To a stirred solution of 5.7 g (0.075 mol) of thiourea in 50 ml of 2 *N* hydrochloric acid was added, at room temperature, 6.8 g (0.05 mol) of 2,6-dimethylbenzoquinone[6] dissolved in 50 ml of glacial acetic acid. The mixture was stirred for 30 min, during which time a mass of crystalline white needles precipitated. The solid was collected by filtration and dried to give 4.7 g (38%) of a product which was identified by elemental analysis and infrared and nmr spectroscopy as the S-(2,5-dihydroxy-4,6-dimethylphenyl)thiouronium chloride. The purified colorless salt became orange at 198° and, after progressive darkening, decomposed to a black solid at 245°.

Anal. Calcd for $C_9H_{13}ClH_2O_2S$: C, 43.5; H, 5.3; S, 12.8. Found: C, 43.8; H, 5.6; S, 12.9.

The filtrate from the isolation of the thiouronium salt was mixed with an equal volume of concentrated hydrochloric acid. The resulting precipitate was collected and recrystallized from ethanol–water to give 2.6 g (33%) of white needles, mp 80–81°. Its infrared and nmr spectra were identical with those of an authentic sample of 4-chloro-2,6-dimethylphenol, and a mixture melting point was not depressed.

A 2.0-g (0.008 mol) sample of S-(2,5-dihydroxy-4,6-dimethylphenyl)thiouronium chloride prepared as just described was suspended in a mixture of 20 ml of 2 *N* hydrochloric acid and 20 ml of glacial acetic acid. The slurry was heated for 2 hr. The hot solution was diluted with 25 ml of water and allowed to stand at room temperature. The crystals which separated were collected and dried to yield 1.6 g (100%) of 4,6-dimethyl-5-hydroxy-1,3-benzoxathiol-2-one, mp 145–146° (lit.[2] mp 147–147.5°). The nmr spectrum ($CDCl_3$) showed three singlets at 2.24 (CH_3, 3 H), 2.28 (CH_3, 3 H), and 6.92 ppm (aromatic, 1 H).

Anal. Calcd for $C_9H_8O_3S$: C, 55.1; H, 4.1; S, 16.4. Found: C, 55.3; H, 4.2; S, 16.2.

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4-Acetyl-5-hydroxy-7-methyl-1,3-benzoxathiol-2-one.—A solution of 6.6 g (0.04 mol) of 2-acetyl-5-methylbenzoquinone[7] in 30 ml of glacial acetic acid was added to a stirred solution of 4.6 g (0.06 mol) of thiourea in 50 ml of 2 *N* hydrochloric acid. The mixture was stirred at room temperature for 30 min, then heated on a steam bath for 60 min. After cooling, the mixture was poured into 100 ml of ice–water. The yellow precipitate was collected, washed with water, and dried; it weighed 7.4 g (82%) and had a melting point of 215–217°. Recrystallization from aqueous ethanol yielded crystalline white needles, mp 217–218°. The nmr spectrum ($CDCl_3$) showed four singlets at 2.43 (CH_3, 3 H), 2.63 (CH_3CO, 3 H), 6.83 (aromatic, 1 H), and 12.4 ppm (OH, 1 H). In addition, the hydroxylic proton peak at 12.4 ppm showed no shift upon dilution and a very slight upfield shift to 12.27 on raising the temperature from 35 to 60°. These data are consistent with the structure of 4-acetyl-5-hydroxy-7-methyl-1,3-benzoxathiol-2-one in which the hydroxyl group is intramolecularly hydrogen bonded to the *o*-acetyl group.

Anal. Calcd for $C_{10}H_8O_4S$: C, 53.6; H, 3.6; S, 14.3. Found: C, 53.6; H, 3.9; S, 14.0.

5-Hydroxy-7-octyl-1,3-benzoxathiol-2-one.—To a stirred solution of 5.7 g (0.075 mol) of thiourea in 100 ml of 2 *N* hydrochloric acid was added 11.0 g (0.05 mol) of 2-octylbenzoquinone suspended in 50 ml of glacial acetic acid. The mixture was stirred until solution was complete, then heated for 40 min. During this time the mixture became cloudy, and an oil separated. The mixture was poured into 500 ml of water, and the solid which separated was collected by filtration to give 13.9 g (99%) of dried product, mp 97–100°. Thin layer chromatographic analysis indicated only one product, which was identified by nmr spectroscopy to be the 5-hydroxy-7-octyl-1,3-benzoxathiol-2-one. Recrystallization from ethanol–water containing Norit gave 12 g of light brown prisms, mp 108–109°. Its nmr spectrum (DMSO-d_6) showed a multiplet at 0.65–0.9 (CH_3, 3 H), a broad singlet at 1.25 ($-CH_2-$, 12 H), a multiplet at 2.49–2.78 ($Ph-CH_2-$, 2 H), and two doublets of an AB quartet centered at 6.64 and 6.97 ppm (aromatic, 2 H, J_{AB} = 2.5 cps).

Anal. Calcd for $C_{15}H_{20}O_3S$: C, 64.2; H, 7.2; S, 11.4. Found: C, 64.3; H, 7.2; S, 11.4.

Preparation and Isolation of Isomeric Monosubstituted 5-Hydroxy-1,3-benzoxathiol-2-ones. General Procedure.—This procedure may be illustrated by the preparation and isolation of 5-hydroxy-7-methyl- and 5-hydroxy-6-methyl-1,3-benzoxathiol-2-ones.

A solution of 12.2 g (0.1 mol) of 2-methylbenzoquinone in 70 ml of glacial acetic acid was added, with stirring, to a solution of 11.4 g (0.15 mol) of thiourea in 100 ml of 2 *N* hydrochloric acid. After a 30-min stirring, the mixture was heated on a steam bath for 1 hr, then diluted with 100 ml of hot water. The product was allowed to crystallize at room temperature, collected, washed with water, and recrystallized from ethanol–water, giving 14.9 g (82%) of 5-hydroxy-7-methyl-1,3-benzoxathiol-2-one, mp 163–164°. The nmr spectrum (DMSO-d_6) showed a singlet at 2.28 (CH_3, 3 H), two doublets of an AB quartet centered at 6.64 and 6.91 (aromatic, 2 H, J_{AB} = 2.5 cps), and a singlet at 13.2 ppm (OH, 1 H).

Anal. Calcd for $C_8H_6O_3S$: C, 52.7; H, 3.3; S, 17.6. Found: C, 52.4; H, 3.4; S, 17.4.

The filtrate from this procedure was diluted with 1 l. of water and allowed to stand overnight in the refrigerator. The solid which separated was collected and recrystallized from ethanol–water (1:10) to give 1.4 g (7%) of small needles, mp 143–144°, identified as the 6-methyl isomer. The nmr spectrum ($CDCl_3$) showed three sharp singlets at 2.27 (CH_3, 3 H), 6.89 (aromatic 1 H), and 7.03 ppm (aromatic 1 H).

Anal. Calcd for $C_8H_6O_3S$: C, 52.7; H, 3.3; S, 17.6. Found: C, 52.4; H, 3.0; S, 17.3.

To obtain the product ratio of the two isomers in the crude mixture, the reaction was repeated as just described. At the end of the reaction, the mixture was diluted with 1 l. of water and refrigerated overnight. The solid was collected, washed with water, and dried. Analysis of the crude mixture by nmr spectroscopy and vpc gave a product ratio of 90% 7-methyl isomer and 10% 6-methyl isomer.

Similarly prepared were 5-hydroxy-7-phenyl- and 5-hydroxy-6-phenyl-1,3-benzoxathiol-2-ones from 2-phenylbenzoquinone; and 7-phenylmercapto- and 6-phenylmercapto-1,3-benzoxathiol-2-ones from 2-phenylmercaptobenzoquinone.[8] For pertinent physical and analytical data, see Table IV.

7-Chloro-, 6-Chloro-, and 4-Chloro-5-hydroxy-1,3-benzoxathiol-2-ones.—To a stirred solution of 5.7 g (0.075 mol) of thiourea in 100 ml of 2 *N* hydrochloric acid was added 7.1 g (0.05 mol) of 2-chlorobenzoquinone[9] in 25 ml of glacial acetic acid. The mixture was stirred for 30 min, then heated for 1 hr. Water was added to the cloud point; after crystallization was complete, the solid was collected, washed with water, and recrystallized from ethanol–water to give 5 g (53%) of white needles, mp 180–181°. This material was identified as the 7-chloro isomer by its nmr spectrum (DMSO-d_6) which displayed two doublets of an AB quartet centered at 6.83 and 7.11 (aromatic, 2 H, J_{AB} = 2.5 cps) and a singlet at 13.4 ppm (OH, 1 H).

Anal. Calcd for $C_7H_3ClO_3S$: C, 41.5; H, 1.5; S, 15.8. Found: C, 41.5; H, 1.6; S, 15.6.

The filtrate from the crude mixture was diluted with 500 ml more water and set aside. The solid which separated was recrystallized from benzene to give a product which has a melting point and infrared spectrum identical with those of the 7-chloro isomer. The benzene filtrate was concentrated to one-half its volume. The solid which precipitated was recrystallized from ethanol–water to give 2.5 g of white needles, mp 128–130°. Nuclear magnetic resonance analysis indicated a mixture of both the 4- and 6-chloro isomers. All attempts to separate these two isomers by fractional crystallization were unsuccessful. The nmr spectrum (DMSO-d_6) showed two sharp singlets at 7.37 (aromatic, 1 H) and 7.56 (aromatic, 1 H), and two doublets of an AB quartet centered at 6.97 and 7.30 ppm (aromatic, 2 H, J_{AB} = 9.0 cps).

Anal. Calcd for $C_7H_3ClO_3S$: C, 41.5; H, 1.5; S, 15.8. Found: C, 41.6; H, 1.7; S, 16.1.

To obtain the product ratio of the isomers, the crude mixture was analyzed by vpc and found to consist of 62% 7-chloro isomer, 20% 6-chloro isomer, and 18% 5-chloro isomer.

7-Isopropyl-5-hydroxy-4-methyl-1,3-benzoxathiol-2-one.—A solution of 8.2 g (0.05 mol) of thymoquinone in 50 ml of glacial acetic acid was mixed with a solution of 5.3 g (0.07 mol) of thiourea in 50 ml of 2 *N* hydrochloric acid. After a 30-min stirring, at room temperature, it was heated on a steam bath for 30 min. Upon cooling, a mass of large white platelets crystallized and were collected. There was obtained 10.8 g (96%) of a solid, mp 156.5–157.5° (lit.[2] mp 158.5–159°). The nmr spectrum ($CDCl_3$) showed a doublet centered at 1.25 (CH_3, 6 H), a singlet at 2.10 ($Ph-CH_3$, 3 H), a quartet centered at 3.07 (CH, 1 H), and a singlet at 6.79 ppm (aromatic, 1 H).

2,5-Di-*t*-butylhydroquinone, Durohydroquinone, and 3-Bromothymohydroquinone.—A suspension of 11.0 g (0.05 mol) of 2,5-di-*t*-butylbenzoquinone in 100 ml of glacial acetic acid was stirred for 30 min with a solution of 5.3 g (0.07 mol) of thiourea in 100 ml of 2 *N* hydrochloric acid, then heated on a steam bath until the reddish brown suspension became colorless (2 hr). The solid was collected, washed with water, and dried, giving 11 g (99%) of pure white prisms, mp 212–214°. The melting point, R_f value, and infrared spectrum were identical with those of an authentic sample of 2,5-di-*t*-butylhydroquinone.

Similarly, reaction of duroquinone or 3-bromothymoquinone[10] with thiourea resulted in nearly quantitative yields of the corresponding hydroquinones.

7-Acetyl- and 4-Acetyl-5-hydroxy-1,3-benzoxathiol-2-ones.—A solution of 7.5 g (0.05 mol) of freshly prepared 2-acetylbenzoquinone[11] in 50 ml of glacial acetic acid and a solution of 5.7 g (0.075 mol) of thiourea in 100 ml of 2 *N* hydrochloric acid were mixed and stirred at room temperature for 30 min. Thin layer chromatographic analysis indicated a mixture of two compounds, one of which fluoresced strongly under a uv lamp. After being heated for 40 min, the fluorescent compound was completely converted into a new product, but the other compound remained unchanged, as indicated by tlc. The mixture was diluted with 50 ml of water and cooled. The solid was collected, washed with water, and dried; it weighed 8.3 g (79%) and had mp 185–187°. Recrystallization from ethanol–water yielded a product, mp 187–188°, which was identified by nmr spectroscopy as the 4-acetyl-5-hydroxy-1,3-benzoxathiol-2-one. The nmr spectrum

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($CDCl_3$) showed a sharp singlet at 2.75 (CH_3, 3 H) and two doublets of an AB quartet centered at 6.99 and 7.28 ppm (aromatic, 2 H, J_{AB} = 9.0 cps).

Anal. Calcd for $C_9H_6O_4S$: C, 51.4; H, 2.9; S, 15.3. Found: C, 51.6; H, 2.9; S, 15.6.

The filtrate was combined with the washings and heated on a steam bath. After 1 hr of heating, no change was detected by tlc. Only upon prolonged heating (3 hr) did a reaction occur. The mixture was poured into 500 ml of water, and the precipitate was collected and recrystallized from ethanol–water to give 1.5 g (11%) of yellow needles, mp 209–210°. This material was identified by nmr spectroscopy as the 7-acetyl isomer. Its nmr spectrum (DMSO-d_6) showed a sharp singlet at 2.64 (CH_3, 3 H) and two doublets of an AB quartet centered at 7.21 and 7.42 ppm (aromatic, 2 H, J_{AB} = 2.5 cps).

Anal. Calcd for $C_9H_6O_4S$: C, 51.4; H, 2.9; S, 15.3. Found: C, 51.5; H, 2.7; S, 15.3.

The product ratio of the crude mixture was analyzed by nmr spectroscopy and vpc to be 83% 4-acetyl isomer and 17% 7-acetyl isomer.

Registry No.—4,7-Dimethyl-5-hydroxy-2-imino-1,3-benzoxathiole hydrochloride, 17630-80-7; **9**, 17631-02-6; **10**, 17631-03-7; **13**, 17631-04-8; **14**, 17631-05-9; **15**, 17630-66-9; **16**, 17630-71-6; 4,7-dichloro-5-hydroxy-2-imino-1,3-benzoxathiol-2-one, 17630-72-[illegible].

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Base-Induced Cyclization of 2-Oximinophosphonium Salts. Synthesis and Spectroscopic Properties of 1,2,5-Oxazaphosph(V)ol-2-ines

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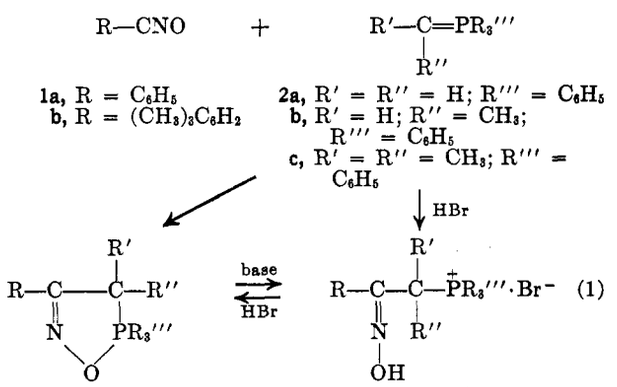
Several 1,2,5-oxazaphosph(V)ol-2-ines (**4**) have been prepared in high yield by basic treatment of 2-oximinophosphonium salts (**3**). These salts were easily obtained either by reaction of α halo ketoximes with triphenyl- or tri-*n*-butylphosphine, by oximation of the corresponding 2-keto phosphonium salts, or finally by reaction of nitrile oxides with phosphonium ylides in dimethyl sulfoxide. The reaction of desyl bromide with triphenylphosphine in benzene gave a mixture of the keto (**8**) and enol phosphonium (**8a**) salts. Treatment of **8** with hydroxylamine gave the corresponding ylide (**9**) instead of the expected oxime. The ring of 1,2,5-oxazaphosph(V)ol-2-ines can be opened by treatment with acids in the cold, affording the corresponding 2-oximinophosphonium salts. Thermal decomposition of 3-(4-bromophenyl)-5,5,5-triphenyl-1,2,5-oxazaphosph(V)-ol-2-ine (**4d**) gave 2H-3-(4-bromophenyl)azirine (**10**) together with triphenylphosphine oxide. The comparison of the mass spectra of 1,2,5-oxazaphosph(V)ol-2-ines with the spectra of the corresponding phosphonium salts confirmed the cyclic structure of the former. ^1H nmr spectra of the title compounds and of the corresponding salts (**3**) were measured in several solvents and discussed. From the chemical-shift and coupling-constant values it can be deduced that the P–O bond in the cycles (**4**) has high covalent character. The effect of substituents on chemical shifts and coupling constants are discussed.

In a recent paper[2] two of us reported the reaction between benzonitrile oxide (**1a**) and a few phosphonium ylides (**2**). The reaction of **1a** with triphenylphosphonium methylide (**2a**) and ethylide (**2b**) in dimethyl sulfoxide (DMSO), after the work-up in acidic medium, gave the 2-oximinophosphonium salts **3a** and **3b** (eq 1). We also reported the successful transformation of **3a** into the corresponding cyclic compound **4a** by means of base, and the reverse reaction which leads from **4a** to **3a** with hydrobromic acid. We pointed out that such a cyclization could be the final step of an easy route to 1,2,5-oxazaphosph(V)ol-2-ines (**4**), starting from α-halo oximes (**5**) and phosphines (**6**), through the phosphonium salts (**3**) (eq 2).



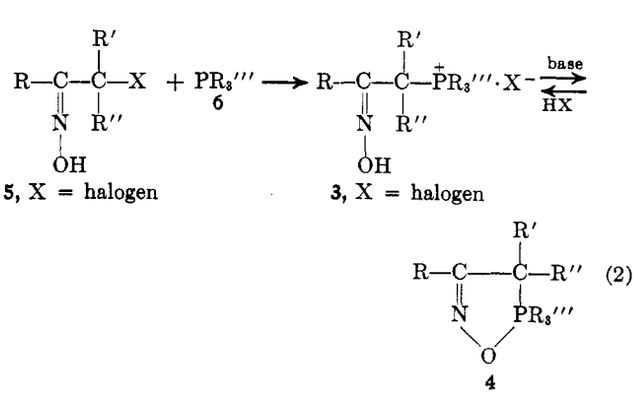
1a, R = C_6H_5
b, R = $(CH_3)_3C_6H_2$

2a, R′ = R″ = H; R‴ = C_6H_5
b, R′ = H; R″ = CH_3; R‴ = C_6H_5
c, R′ = R″ = CH_3; R‴ = C_6H_5

4a, R = R‴ = C_6H_5; R′ = R″ = H
a′, R = $(CH_3)_3C_6H_2$; R′ = R″ = H; R‴ = C_6H_5
d, R = 4-$NO_2C_6H_4$; R′ = R″ = H; R‴ = C_6H_5

3a, R = R‴ = C_6H_5; R′ = R″ = H
b, R = R‴ = C_6H_5; R′ = H; R″ = CH_3
d, R = 4-$NO_2C_6H_4$; R′ = R″ = H; R‴ = C_6H_5

(1)



5, X = halogen

3, X = halogen

(2)

The only members of this class of cyclic compounds **4** so far known are **4a** and its mesityl analog **4a′** obtained by Huisgen and Wulff[3] directly from **1a** and **1b**, respec-

(1) In alphabetical order.

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