support of the acetal structure. Double bond adsorptions were also present at 1600–1650 cm^{-1}. The nmr spectrum showed four singlets of equal intensity at 3.5 ppm which are in agreement for the diketal.

4,7-Methanoindene-1,8-dione. 2,3,3a,4,5,6,7,7a-Octachloro-4,7-dihydro-8-dimethyl Acetal (14).—This compound was isolated from the cycloaddition reaction of the aroyl cyanides with **2a**, or from the pot residue on the distillation of **2a** has mp 228–231°.

Anal. Calcd for $C_{12}H_6O_3Cl_8$: C, 29.90; H, 1.25; Cl, 58.89. Found: C, 29.65; H, 1.18; Cl, 58.75.

The mass spectrum gave an ion at *m/e* 443 and showed the presence of seven chlorines in agreement with the loss of one chlorine from the parent ion. The nmr spectrum ($CDCl_3$) showed two peaks of equal intensity at δ 3.76 and 3.86 ppm. The carbonyl band at 1740 cm^{-1} is consistent with the α,β-unsaturated ketone.

Registry No.—**5b**, 26278-86-4; **5c**, 26278-87-5; **5d**, 26278-88-6; **5e**, 26278-89-7; **5f**, 26278-90-0; **5g**, 26278-91-1; **5h**, 26278-92-2; **5i**, 26278-93-3; **13**, 26278-94-4; **14**, 26322-41-8; **16a**, 26278-95-5; **16b**, 26278-96-6; **16c**, 26278-97-7; **16d**, 26278-98-8; **16e**, 26278-99-9; **16f**, 26279-00-5; methyl 6-(benzoyl)picolinate, 26279-01-6; methyl 6-(4′-toluenesulfonyl)picolinate, 26279-02-7.

Acknowledgments.—The authors are grateful to Mr. G. Kallos and Dr. L. Shadoff for the mass spectral data, to Mr. R. Nyquist for the infrared spectra, to Dr. J. Heeschen and Dr. T. Evans for the nmr data, and to Mr. L. Swim for the elemental analyses.

Rearrangement of Chloroformates of Cyclic Amine–Alcohols

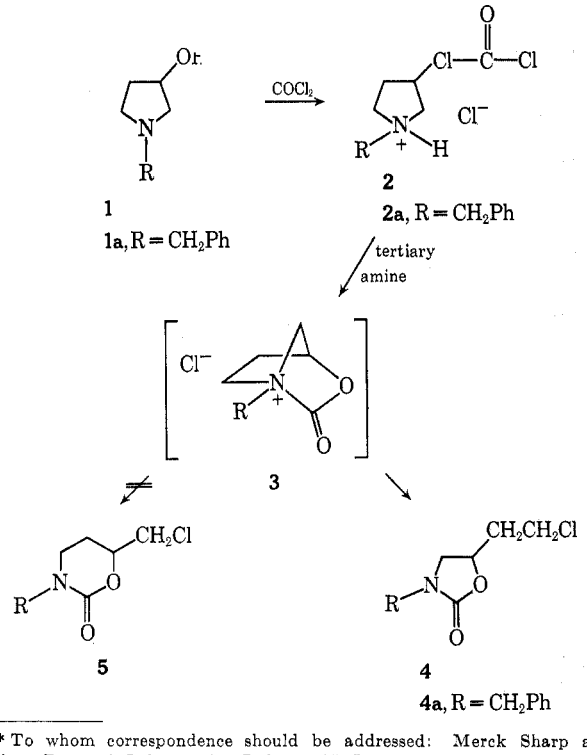
J. PENGMAN LI* AND JOHN H. BIEL

Research Division, Aldrich Chemical Company, Inc., Milwaukee, Wisconsin 53233

Received April 25, 1970

Chloroformates of 3- and 4-piperidinols, 3-pyrrolidinols, and 3-azetidinols undergo facile rearrangements to cyclic carbamates: 2-oxazolidinones and tetrahydro-1,3-oxazin-2-ones. The alkyl substituents on the ring nitrogen atom seem to affect the yields of products. Best yields were obtained with *N*-benzyl derivatives. Bicyclic intermediates are proposed to account for the rearrangements.

An elegant synthesis of 2-oxazolidinones by the rearrangement of chloroformates (**2**) of 3-pyrrolidinols was described by Lunsford, *et al.*[1] They have shown that in the course of rearrangement the pyrrolidine ring opens in a specific manner so that only 5-(2-chloroethyl)-2-oxazolidinones (**4**) are formed. The structure of **4** was verified by pmr and unambiguous synthesis. No isolation of the other possible rearrangement product tetrahydro-1,3-oxazin-2-ones (**5**) was recorded. Yields of **4** varied from 34 to 89% depending on the N substituent. The highest yields were obtained with the *N*-cyclohexyl derivative **4** (R = C_6H_{11}) (see Table I). However, no yield was reported on the *N*-benzyl compound **4a**.[1]



1, 1a, R = CH_2Ph — 2, 2a, R = CH_2Ph — 3 — 5 — 4, 4a, R = CH_2Ph

TABLE I

REARRANGEMENT PRODUCTS OF CHLOROFORMATES OF FOUR-, FIVE-, AND SIX-MEMBERED CYCLIC AMINE ALCOHOLS

Chloroformate	Product	R	Yield, %
2	4	Me	52[a]
		Et	56[a]
		n-Bu	34[a]
		Cyclohexyl	89[a]
		CH_2Ph	94
7	9	Me	0
		Et	0
		CH_2Ph	40
11	13	Me	70–77
		CH_2Ph	Quant
14	16	Me	50[b]
		Cyclohexyl	Quant

[a] Reference 1. [b] Reference 2.

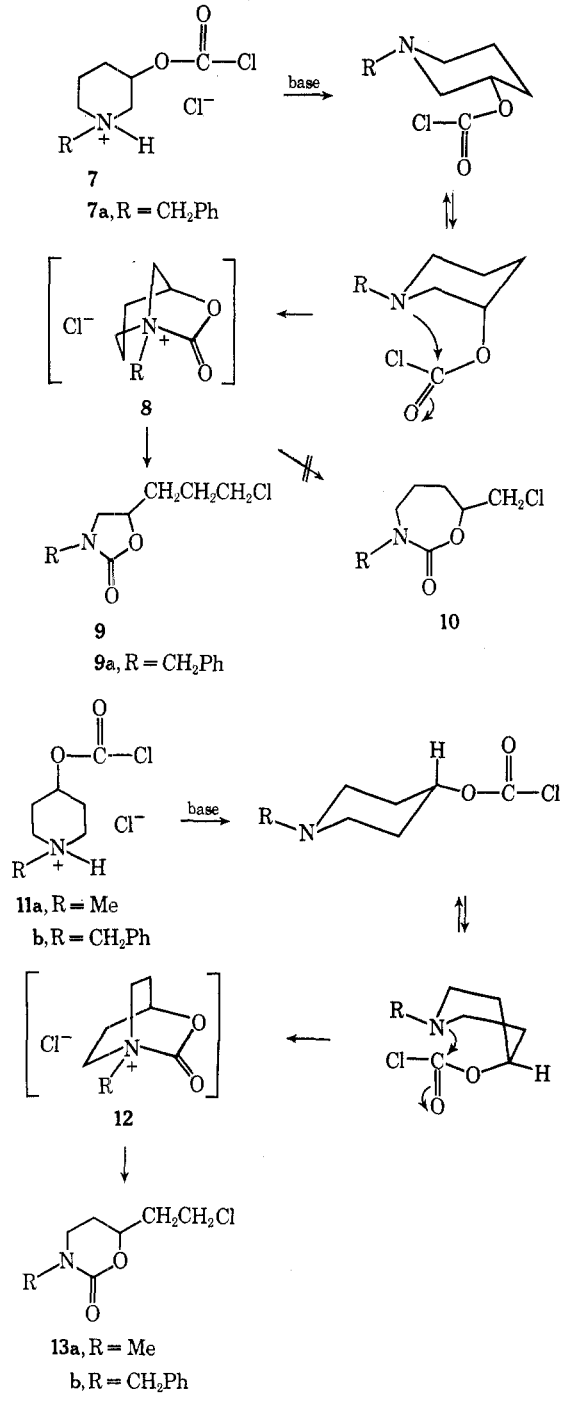
We have repeated this reaction. Thus, **2a** was prepared from the hydrochloride of *N*-benzyl-3-pyrrolidinol (**1a**) and heated with triethylamine in toluene. Compound **4a** was obtained in 94% yield. No attempt was made to detect any **5** which might have formed in the same rearrangement reaction. The results of Lunsford and of ours indicate some effect of the N substituents upon the yields of **4**. Similar substituent effects have been observed in the rearrangement of chloroformates of other cyclic amine–alcohols, which are described below.

* To whom correspondence should be addressed: Merck Sharp and Dohme Research Laboratories, Rahway, N. J. 07065

(1) M. L. Fielden, W. J. Welstead, and C. D. Lunsford, Abstracts, 152nd National Meeting of the American Chemical Society, New York, N. Y., Sept 1966, p P5. We thank Dr. C. D. Lunsford for providing us with a long abstract.

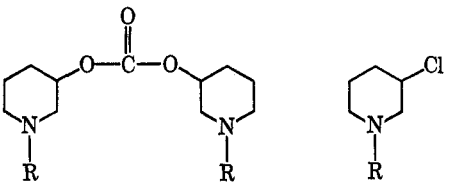
It is conceivable that a [2.2.1]-bicyclic intermediate, such as the ion pair **3**, is involved in the rearrangement of **2** to **4**. It follows that the rearrangement of chloroformates of 3- and 4-piperidinols (**7** and **11**, respectively), and of 3-azetidinols (**14**) *via* [3.2.1]- (**8**), [2.2.2]- (**12**), and [2.1.1]-bicyclic (**15**) intermediates should likewise be feasible (Scheme I). In the rearrangement of

SCHEME I



7, the intermediate **8** is unsymmetrical. Ring opening in two possible ways would lead to two distinctive products, **9** and **10**. In the cases of **11** and **14**, the intermediates **12** and **15** are symmetrical. Therefore, there is only one possible product for each reaction.

When *N*-methyl- and *N*-ethyl-3-piperidinol or the hydrochloride salts were treated with phosgene followed by neutralization with triethylamine, no rearranged products were obtained. The only isolable products from the reactions of **7** (R = Me) were the carbonate **17a** and the chloride **18a**. In the case of **7** (R = Et), the carbonate **17b** was isolated and characterized, but no attempt to isolate the chloride **18b** was made.



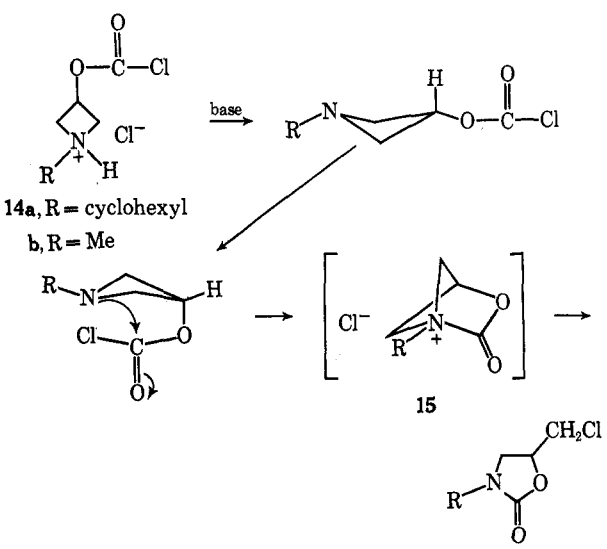
17 **18**

a, R = Me
b, R = Et
c, R = CH_2Ph

Rearrangement occurred when the N substituent was a benzyl group. Thus, treatment of the crude chloroformate hydrochloride **7a** with 1 molar equiv of triethylamine afforded **9a** in 40% yield. This rearrangement product was assigned the structure **9a** on the basis of its infrared and pmr spectra which closely resembled those of **4a** and **16a**. The other product isolated was **18c** (53.5% yield), which might be formed as a result of the breakdown of **7a**, either before or during the rearrangement reaction. However, in no case was the other possible rearrangement product **10** (R = CH_2Ph) or the carbonate **17c** obtained.

The chloroformate hydrochloride **11** readily underwent rearrangement, giving the tetrahydro-1,3-oxazin-2-one **13** in varying yields depending on the N substituent (see Table I). Although only two compounds, **11a** and **11b**, have been investigated, the results are parallel to those observed in the 3-pyrrolidyl chloroformate series.

The chloroformate **14a** also readily rearranged to **16a** in excellent yield according to the speculated course.

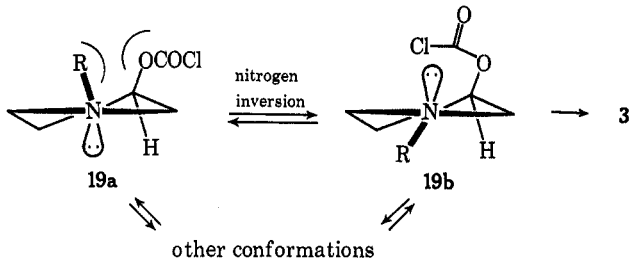


16a, R = cyclohexyl
b, R = Me

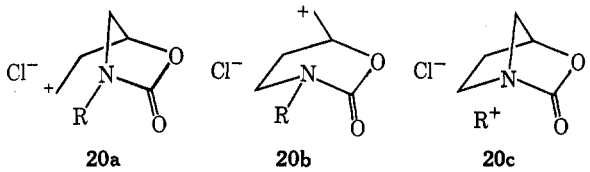
The close proximity of the chlorocarbonyloxy function to the nitrogen atom may facilitate the cyclization step which leads to the formation of **15**. Furthermore, the strain of the bicyclic system possessing a quaternary

nitrogen bridgehead may contribute some driving force for the subsequent ring-opening step. Lunsford[2] had been able to obtain **16b** in 50% yield from 1-methyl-3-azetidinol hydrochloride without isolating the chloroformate **14b**. Thus, a dramatic substituent effect upon the yields of products is also real in the azetidine system.

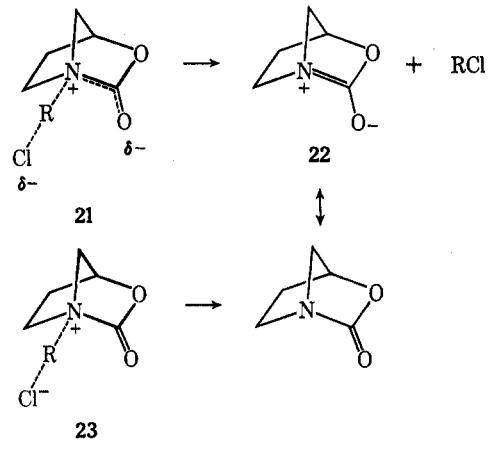
Table I clearly indicates that product yield increases with the bulk of the N substituent in all ring systems. Pyrrolidine has a pseudorotating, puckered ring.[3] For simplicity, the half-chair form with the maximum puckering at carbon atoms 3 and 4 is considered here. The free base derived from **2** by neutralization may exist in forms **19a** and **19b**, among other conformations in equilibrium. Form **19b** is energetically more favorable than **19a** and becomes the predominant conformation when R is a bulky group. With the nitrogen electron lone pair being cis and closest to the chlorocarbonyloxy group, **19b** is also the conformation required for cyclization to **3**. As a consequence, a bulky N substituent facilitates cyclization to the key intermediate **3** by causing a favorable shift of the conformational equilibrium. Analogous arguments apply to the azetidine and piperidine systems.



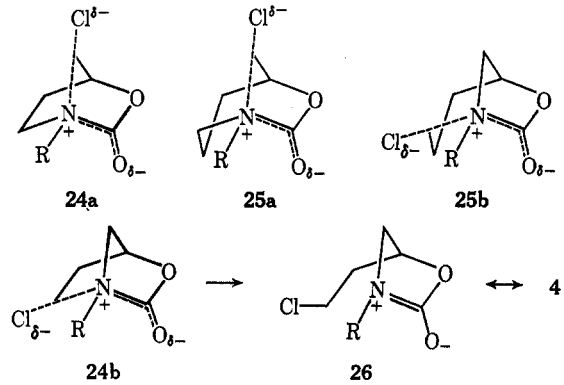
It is unique that, in all of the reactions investigated, none of the N substituents were attacked by the chloride ion. The specificity in product formation requires a "concerted" mechanism and will exclude a mechanism involving the collapse of the ammonium ion into a carbonium ion, such as **20a**, **b**, or **c**, followed by union of the carbonium ion and chloride ion.



In **3**, if Cl^- attacks the R group, the transition state may be depicted as **21**. Since the partial negative charges δ^- are not widely separated spatially, **21** is energetically unfavorable. Furthermore, the primarily formed product **22** has a bridgehead double bond, which violates Bredt's rule. Although anti-Bredt olefin has been postulated,[4] **22** remains a high-energy species. Therefore, both **21** and **22** would preclude chloride ion attack at the R group. Another possibility is an "S_N2" type displacement without involvement of the adjacent carbonyl group in the charge dispersion, as depicted by the transition state **23**. However, **23** is evidently less favorable compared with other transition states, such as **24** and **25**. The same arguments extend to **8**, **12**, and **15**.



In the cases of the unsymmetrical **3** and **8**, Cl^- attack at the C_1 bridge would lead to transition states **24a** and **25a**, whereas Cl^- attack at the C_2 and C_3 bridge, to **24b** and **25b**, respectively. The fact that 2-oxazolidinones are the sole products from **3** and **8** indicates transition states **24b** and **25b** are by far more important. The results are not unexpected when these ring-opening reactions of the bicyclic ammonium ions by chloride ion are compared with solvolysis of norbornyl esters. The conversion of **3** to **26**, a tautomeric form of **4**, *via* **24b** is virtually an example of the retro ring closure of 2-(Δ^3-cyclopentenyl)ethyl arenesulfonates to *exo*-norbornanol derivatives.[5,6]



The 2-oxazolidinones **4a**, **9a**, and **16a** strongly absorbed at 5.72 μ. The carbonyl absorption in this region is characteristic of 2-oxazolidinones.[7-9] In contrast the carbonyl absorption of the tetrahydro-1,3-oxazin-2-ones (**13a** and **13b**) occurred at 5.9–5.92 μ.[9] The pmr spectra of the above compounds have been recorded and conform with their assigned structures, although complete analyses of the spectra are not possible.

All of the chlorides obtained from these rearrangement reactions are useful as intermediates for the preparation of tranquilizing agents. Choosing the appropriate cyclic amine–alcohols, one can easily prepare by

(2) C. D. Lunsford, private communication. We are indebted to Dr. Lunsford for permitting our use of his results before publication.
(3) E. L. Eleel, N. L. Allinger, S. J. Angyal, and G. A. Morrison, "Conformational Analysis," Interscience, New York, N. Y., 1965, pp 202, 244.
(4) S. F. Campbell, R. Stephens, and J. C. Tatlow, *Tetrahedron*, **21**, 2997 (1965).
(5) R. G. Lawton, *J. Amer. Chem. Soc.*, **83**, 2399 (1961).
(6) P. D. Bartlett and S. Bank, *ibid.*, **83**, 2591 (1961).
(7) M. E. Dyen and D. Swern, *Chem. Rev.*, **67**, 197 (1967).
(8) J. E. Herweh, *J. Heterocycl. Chem.*, **5**, 687 (1968).
(9) H. K. Hall, Jr., and R. Zbinden, *J. Amer. Chem. Soc.*, **80**, 6428 (1958).

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

P. T. S. LAU* AND T. E. GOMPF

Research Laboratories, Eastman Kodak Company, Rochester, New York 14650

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).