of as much oil as possible by pressing between filter paper. After three recrystallizations from benzene, the product melted at 53–54°.

Anal. Calcd. for $C_4H_8N_2O$: C, 48.0; H, 8.05; N, 28.0. Found: C, 48.0; H, 7.89; N, 27.8.

For the preparation of N-(5-nitro-2-furfurylidene)-1-amino-2-pyrrolidinone (IV), the clear aqueous solution from the reduction above was treated with an alcoholic solution containing 0.5 g. of 5-nitro-2-furfural per gram of nitrosopyrrolidinone reduced. The crude yellow product separated in a 30–35% yield and melted at 228–230°. Recrystallization from a mixture of one part of nitromethane to two parts of SDA #30 raised the melting point to 233–233.5°; water solubility 89 mg./l.; ϵ_{max} at 3700 and 2700 Å. is 17,200 and 11,800, respectively, in water.

Anal. Calcd. for $C_9H_9N_3O_4$: C, 48.4; H, 4.06; N, 18.8. Found: C, 48.1; H, 4.37; N, 18.6.

NORWICH, N. Y.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF ROCHESTER]

Benzothiophene-4,5-quinones

BY M. MARTIN-SMITH[1] AND MARSHALL GATES

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An investigation of the benzothiophene-4,5-quinones was undertaken. The parent compound or its 2-carboxy derivative could not be prepared by the usual procedures employed in the synthesis of *o*-naphthoquinones. It was possible, however, to synthesize various 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinones. The compounds previously considered as 3,4-dibromo-5-hydroxybenzothiophene and 3-bromobenzothiophene-4,5-quinone are now assigned the structures 4,6-dibromo-5-hydroxybenzothiophene and 6-bromobenzothiophene-4,5-quinone.

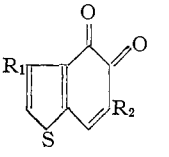
In connection with another problem a 7-(cyanocarbethoxymethyl) - benzothiophene - 4,5 - quinone was required as an intermediate. No such compounds have been reported in the literature. An account of the preparation of several representatives of this class forms the substance of this communication. The method employed was essentially that of condensing ethyl cyanoacetate with a benzothiophene-4,5-quinone under basic conditions, although the intermediate 4,5-quinone was not isolated in all cases.

All the benzothiophene derivatives described were prepared from sodium 5-nitrobenzothiophene-2-carboxylate[2–4] which was converted to 5-hydroxybenzothiophene by a modification of a procedure used previously.[2,3] In this modification which gave slightly better over-all yields the diazotization step was eliminated by making use of the Bucherer reaction.[5] 5-Hydroxybenzothiophene can be converted to its 4-nitroso derivative in excellent yield by sodium nitrite in dilute acetic acid, but all attempts to prepare benzothiophene-4,5-quinone from the nitroso compound failed. Utilization of the modified techniques developed for the preparation of *o*-naphthoquinones in a high state of purity from 1-nitroso-2-naphthols[6] served only to confirm the observations of Fieser and Kennelly[3] on the instability of this quinone. Similarly 5-hydroxy-4-nitrosobenzothiophene-2-carboxylic acid could not be converted into the corresponding 4,5-quinone.

Attempts to prepare benzothiophene-4,5-quinone by the method first extensively investigated by Armstrong and Rossiter[7] and which has been used with success in the preparation of various *o*-naphthoquinones[8–11] also fails, as nitration of 4-bromo-5-hydroxybenzothiophene under the usual experimental conditions yields 4-bromo-5-hydroxy-3-nitrobenzothiophene.[2]

Application to 5-amino-4-bromobenzothiophene-2-carboxylic acid of the diazotization reaction which had been used in two special cases to prepare *o*-naphthoquinones[12,13] also failed to give the 4,5-quinone.

As the parent benzothiophene-4,5-quinone or its 2-carboxy derivative could not be obtained by these procedures, we decided to use a quinone bearing some other substituent capable of subsequent removal. Of the five known benzothiophene-4,5-quinones,[14] only that previously described as the 3-bromo compound Ia,[2] but which the present



Ia, R_1 = Br, R_2 = H
Ib, R_1 = H, R_2 = Br

work would indicate is in reality the 6-bromo compound Ib in accordance with its observed stability by analogy with 3-bromo-1,2-naphthoquinone,[10] would serve as a convenient starting material. It is formed by the action of nitric acid in chloroform on a dibromo compound resulting from the action of two moles of bromine on 5-hydroxybenzothiophene. This dibromo compound was originally assigned the structure of 3,4-dibromo-5-hydroxybenzothiophene,[2] but the recent studies of substitution in the 5-substituted benzothiophene series by Bordwell and Stange[15,16] in which the true 3,4-

(1) Fulbright Exchange Student 1951–1954, Beaunit Mills Fellow 1953–1954.

(2) K. Fries, H. Herring, K. Hemmecke and G. Siebert, *Ann.*, **527**, 83 (1936).

(3) L. F. Fieser and R. G. Kennelly, THIS JOURNAL, **57**, 1611 (1935).

(4) F. G. Bordwell and C. J. Albisetti, Jr., *ibid.*, **70**, 1955 (1948).

(5) H. T. Bucherer, *J. prakt. Chem.*, [2] **69**, 49 (1904).

(6) M. Gates, THIS JOURNAL, **72**, 228 (1950).

(7) H. E. Armstrong and E. L. Rossiter, *Proc. Chem. Soc.*, 89 (1891).

(8) R. Flessa, *Ber.*, **17**, 1481 (1884).

(9) Th. Zincke and O. Kegel, *ibid.*, **21**, 3378 (1888).

(10) K. Fries and K. Schimmelschmidt, *Ann.*, **484**, 245 (1930).

(11) L. F. Fieser and J. L. Hartwell, THIS JOURNAL, **57**, 1479 (1935).

(12) Ad. Claus and O. Jack, *J. prakt. Chem.*, **57**, [2] 15 (1898).

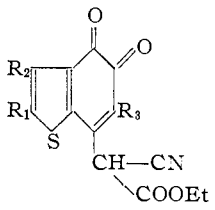
(13) Ad. Claus and O. Philipson, *ibid.*, **43**, [2] 54 (1891).

(14) An excellent review of benzothiophene chemistry is to be found in H. D. Hartough and L. Meisel, "Compounds with Condensed Thiophene Rings," Interscience Publishers, Inc., New York, N. Y., 1954.

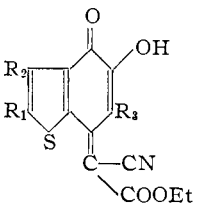
(15) F. G. Bordwell and H. Stange, THIS JOURNAL, **77**, 5939 (1955).

(16) The authors wish to express their appreciation to Professor Bordwell and Dr. Stange for making the results of this research available before publication.

dibromo-5-hydroxybenzothiophene was prepared, suggest that this compound is in all probability 4,6-dibromo-5-hydroxybenzothiophene, and this assignment is supported by the reactions of the 4,5-quinone derived from it. The anilide formed by this quinone was already known to retain bromine,[2] and this fact taken in conjunction with Bordwell's work[15] limits the site of the bromine atom to the 2- or 6-positions. In view of the fact that both *ortho*-positions to the hydroxyl group in 5-hydroxybenzothiophene are reactive[15]—in contrast to its isostere 2-naphthol[17-19]—it seemed probable that the quinone is 6-bromobenzothiophene-4,5-quinone. Further evidence that this assignment is correct was provided by the unexpected course of the condensation of the quinone with ethyl cyanoacetate in the presence of base and potassium ferricyanide. The product was found to have lost bromine and was identical with a specimen of authentic 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone (IIa) prepared from 5-hydroxy-4-nitrosobenzothiophene by the method described later in this communication. This elimination of bromine from the 6-position during substitution at the 7-



II



III

a, $R_1 = R_2 = R_3 = H$ b, $R_1 = COOH$, $R_2 = R_3 = H$
c, $R_1 = R_2 = H$, $R_3 = Br$ d, $R_1 = R_3 = H$, $R_2 = Br$
e, $R_1 = Br$, $R_2 = R_3 = H$

position was found to have an analogy in the naphthalene series. When ethyl cyanoacetate was condensed with 3-bromo-1,2-naphthoquinone in the presence of triethylamine and potassium ferricyanide the only crystalline material that could be isolated was identical with an authentic specimen of 4-cyanocarbethoxymethyl-1,2-naphthoquinone.[20]

However, when 6-bromobenzothiophene-4,5-quinone was condensed with ethyl cyanoacetate in the presence of triethylamine with no potassium ferricyanide present the bromine atom was retained, and the product was 6-bromo-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone (IIc).[21]

It was further found that when the crude 4,5-quinone resulting from the reaction of nitric acid in chloroform on 4,6-dibromo-5-hydroxybenzothiophene was used directly in the condensation with ethyl cyanoacetate in the presence of potassium ferricyanide two products were formed. One was 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone and the other was its 2-bromo derivative IIe. The formation of this latter compound was traced to the presence of 2,6-dibromobenzothiophene-4,5-quinone in the 6-bromobenzothiophene-4,5-quinone. If in the preparation of this quinone the reaction mixture is allowed to stand in a sealed flask rebromination by the bromine displaced from the 4-position occurs, and a good yield of 2,6-dibromobenzothiophene-4,5-quinone can be obtained. This attack at the 2-position is to be expected as 6-bromobenzothiophene-4,5-quinone is essentially a substituted thiophene and not a benzothiophene.

2,6-Dibromobenzothiophene-4,5-quinone on condensation with ethyl cyanoacetate in the presence of triethylamine suffers expulsion of the bromine from the 6-position to give 2-bromo-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone. Attempts to prepare this compound in an alternative manner have failed.

The bromine atom from IIe was readily removed by hydrogenation followed by oxidation of the resulting hydroquinone to give IIa.

A direct method of synthesizing 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinones was developed by modifying the general procedure discussed above so as to avoid isolation of the unstable parent quinones. Thus these compounds result from the oxidation of an unstable 4-amino-5-hydroxybenzothiophene by means of potassium ferricyanide in the presence of triethylamine and ethyl cyanoacetate in an atmosphere of nitrogen. Under these conditions the 4,5-quinone condensed with the ester before decomposition could occur. Both 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone (IIa) and the corresponding 2-carboxy compound IIb were prepared by this method from the 5-hydroxy-4-nitrosobenzothiophenes through the intermediate 4-amino-5-hydroxy compounds. However when the nitroso compounds were employed the reduction stage always proceeded poorly. Better yields of 2-carboxy-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone resulted from the corresponding nitro compound as with it hydrogenation was rapid and went to completion.[22] The 5-hydroxy-4-nitrobenzothiophene-2-carboxylic acid was prepared from 5-acetamidobenzothiophene-2-carboxylic acid by nitration to the 4-nitro compound followed by alkaline hydrolysis, the nitro group *ortho* to the amino group rendering it susceptible to displacement (Fig. 1).

3-Bromo-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone (IId) was prepared by way of the unstable 3,4-dibromo-4,5-dihydro-5-keto-4-nitrobenzothiophene which was obtained from 3,4-dibromo-5-hydroxybenzothiophene prepared by a

(17) T. Zincke, *Ber.*, **21**, 3378, 3540 (1888).

(18) W. Marckwald, *Ann.*, **279**, 1 (1894).

(19) L. F. Fieser and W. C. Lothrop, THIS JOURNAL, **57**, 1459 (1935).

(20) F. Sachs and M. Cravieri, *Ber.*, **38**, 3685 (1905).

(21) The exact manner in which the potassium ferricyanide causes elimination of the bromine atom from the 6-position is by no means clear.

(22) In the preparation of 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinones *via* the 4-amino-5-hydroxybenzothiophenes an interesting effect was noted. The color of the basic reaction mixture upon addition of the oxidizing agent is deep purple, whereas the anion of the purified quinone is deep green. An explanation for this may be that the initial product is the imino-quinone, which has a purple anion, while the true quinone has a green anion. Weight is given to this interpretation by the fact that, to obtain the greatest yield of pure quinone, hydrochloric acid must be added to the solvent from which crystallization is being performed. Furthermore, treatment of an alcoholic solution of the quinone with ammonia gives a green color initially, but upon standing for a few minutes this changes to purple. Acidification with hydrochloric acid gives unchanged quinone. Such a color change from green to purple is not observed under comparable conditions of time with dilute sodium hydroxide solution or triethylamine.

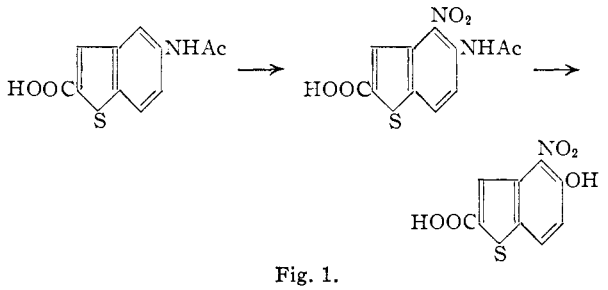


Fig. 1.

slight modification of the method of Bordwell and Stange.[15] The crude 3-bromobenzothiophene-4,5-quinone which results from the decomposition of the 4-bromo-5-keto-4-nitro compound in boiling benzene could not be crystallized without decomposition and was immediately condensed with ethyl cyanoacetate to yield IId.[23]

The phenazines of all the 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinones, in striking contrast to the yellow phenazines formed from the corresponding naphthoquinones,[6] are a very dark blue, and all give a range of colors with various solvents.

Attempts to isolate 7-(cyanomethyl)-benzothiophene-4,5-quinones in a pure state by elimination of the carbethoxy group from the corresponding 7-cyanocarbethoxymethyl compounds failed, although in the case of the 2-bromo compound cleavage was shown to have taken place in the presence of Triton B (benzyltrimethylammonium hydroxide) by the preparation of the stable phenazine of the cleavage product. The free cyanomethylquinone rapidly decomposed on standing. Cleavage with concentrated sodium or lithium hydroxides or with Claisen alkali failed owing to the insolubility of the quinone salts in these media. The utility of Triton B in this cleavage was demonstrated in the known 4 - cyanocarbethoxymethyl - 1,2 - naphthoquinone series,[24] in which the reagent readily yielded 4-cyanomethyl-1,2-naphthoquinone.

Experimental[25,26]

5-Aminobenzothiophene-2-carboxylic Acid.—When this compound was prepared as described by Fries, *et al.*,[2] by reduction of 5-nitrobenzothiophene-2-carboxylic acid with ferrous sulfate and ammonia, it was found that the crude product isolated was not the free amino acid but the sulfate. A sample recrystallized from glacial acetic acid was analyzed, colorless prisms, m.p. > 335°.

Anal. Calcd. for $(C_9H_8O_2NS)_2SO_4$: C, 44.71; H, 3.33. Found: C, 44.62; H, 3.35.

It was more convenient to prepare the amino acid by the Raney nickel–hydrazine hydrate method.[27]

Sodium 5-nitrobenzothiophene-2-carboxylate (15.0 g.) was dissolved in 700 ml. of water by warming. To the warm solution were added *ca.* 2 g. of Raney nickel and 11.0 ml. of hydrazine hydrate (85% in water). There was an immediate vigorous evolution of gas, causing frothing. The solution was heated on the steam-bath for 30 minutes, at the end of which time a little more Raney nickel and a further 3.0 ml. of hydrazine hydrate were added. After a further 30 minutes heating, the solution was filtered free of catalyst and the product precipitated as the sulfate by acidification of the nearly colorless filtrate with dilute sulfuric acid. The solid was collected, dissolved in dilute sodium hydroxide solution, treated with activated carbon and filtered without loss of time, as basic solutions of 5-aminobenzothiophene-2-carboxylic acid show a pronounced tendency to darken on standing. The filtrate was acidified with glacial acetic acid, giving a precipitate of the free amino acid, 10 g. (85%), m.p. 273–275° with decomposition. Several recrystallizations from acetic acid yielded fine colorless needles of m.p. 279–280° with decomposition; reported[2] 278° with decomposition. The crude reaction product, m.p. 273–275°, was pure enough for further work.

5-Hydroxybenzothiophene-2-carboxylic Acid.—Preparation of this compound by the diazotization of 5-aminobenzothiophene-2-carboxylic acid and subsequent decomposition of the diazonium salt as described by Fries, *et al.*,[2] confirmed their reported 10% yield. A more convenient preparation was by means of the Bucherer reaction.[5]

5-Aminobenzothiophene-2-carboxylic acid (10 g.) was refluxed for 48 hr. in 500 ml. of 40% sodium bisulfite solution with stirring to prevent bumping. The amino acid passed into solution after about 3 hr., but as the reaction proceeded solid material separated. On completion of the reaction the solution was diluted to about 800 ml. with water and excess solid sodium hydroxide added. The solution was boiled for 1 hr. with stirring to prevent bumping as some solid material remained. At the end of this time the smell of ammonia could no longer be detected. The cooled solution was filtered, leaving a residue, which on treatment with hydrochloric acid gave 4 g. of a bright yellow compound. This proved very insoluble but could be recrystallized from dilute ethanol to which had been added several drops of pyridine, yellow cubes, m.p. 331–332°. The exact nature of this compound has not yet been determined.

The filtrate from the reaction mixture was acidified with concentrated hydrochloric acid which precipitated 5.5 g. (55%) of crude 5-hydroxybenzothiophene-2-carboxylic acid, m.p. 259–263°. This was recrystallized from dilute ethanol with treatment with activated carbon, 4.8 g. of colorless needles, m.p. 262–263°; reported[2] 264°. There was no mixed m.p. depression with a sample prepared by way of the diazonium salt. Impure samples of the acid have a tendency to gain a yellow tinge.

5-Hydroxybenzothiophene.—5-Hydroxybenzothiophene-2-carboxylic acid (4.25 g.) together with 2 g. of copper bronze powder was heated in 40 ml. of freshly distilled quinoline beneath a current of nitrogen. Carbon dioxide evolution commenced at about 180° and the mixture was kept between 190 and 200° for 30 minutes. The mixture was cooled under nitrogen, diluted with ether and filtered. The residue was washed well with ether and the washings added to the filtrate. The solution was extracted several times with 6 *N* hydrochloric acid to remove all the quinoline. The ether layer was then extracted with dilute sodium hydroxide solution, the aqueous layer treated with activated carbon and filtered. On acidification with 6 *N* hydrochloric acid the product was thrown down as minute colorless plates, 2.40 g. (73%), m.p. 103–105°; reported[2] 103–104°. The product was identical with a specimen prepared from 5-aminobenzothiophene by way of the diazonium salt.

5-Hydroxy-4-nitrosobenzothiophene.—Pure 5-hydroxybenzothiophene (1.0 g.) was dissolved in 7 ml. of glacial acetic acid and 15 ml. of ice-water added. The hydroxy compound was immediately thrown down as a suspension of very fine needles. To the suspension cooled in an ice mixture was added 0.50 g. of solid sodium nitrite and the mixture was swirled for 10 minutes, during which time an orange color developed. A further 0.05 g. of solid sodium nitrite was added (making the total quantity 1 molar proportion) and swirling continued for 20 minutes more. The dark red amorphous solid was collected and washed sparingly with cold methanol. On drying the material turned an ochre color, 1.0 g. (90%). A small sample was submitted for

(23) The infrared spectra in *Nujol mull* of the 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinones show a strong adsorption band just above 3μ at values somewhat higher than the normal positions for phenolic hydroxyl stretching (H. Rosenkrantz, *J. Biol. Chem.*, **173**, 439 (1948)). These peaks are probably due to a highly conjugated enolic hydroxyl group, and it is concluded that in the solid form the 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinones exist in the tautomeric enolic form III. Such tautomerism between keto and enol forms is well established in the similarly constituted 4-dicarbethoxymethyl-1,2-naphthoquinones (L. F. Fieser and C. K. Bradsher, THIS JOURNAL, **61**, 417 (1939)).

(24) M. Gates, R. B. Woodward, W. F. Newhall and R. Künzli, THIS JOURNAL, **72**, 1141 (1950).

(25) All melting points uncorrected.

(26) Microanalyses by Miss V. Williams, Miss A. Smith, H. Seguin. Infrared spectra by C. A. Whiteman.

(27) D. Balcom and A. Furst, THIS JOURNAL, **75**, 4334 (1953).

analysis without recrystallization, although it was later found possible to crystallize the compound, in contrast to the 1-nitroso-2-naphthols,[6] by diluting a methanolic solution with water and allowing it to stand overnight.

Anal. Calcd. for $C_8H_5O_2NS$: C, 53.62; H, 2.81. Found: C, 53.55; H, 2.93.

The amorphous form changed to orange needles at about 110° on slow heating and these melted at 121–123° with decomposition. The compound is soluble in methanol, benzene, ethanol, acetone and chloroform. It is slightly soluble in water and hexane. Its solution in concentrated sulfuric acid is deep green.

5-Hydroxy-4-nitrosobenzothiophene-2-carboxylic Acid.—A suspension of 5-hydroxybenzothiophene-2-carboxylic acid (1.0 g.) in cold 30% acetic acid (35 ml.) was treated with one molar proportion of solid sodium nitrite (0.435 g.), added in two unequal portions, in exactly the same way as for the preparation of 5-hydroxy-4-nitrosobenzothiophene from 5-hydroxybenzothiophene above. The orange product after washing with methanol, 1.0 g. (90%), could not be recrystallized without decomposition. Analysis was performed on the dry reaction product.

Anal. Calcd. for $C_9H_5NO_4S$: C, 48.51; H, 2.24. Found: C, 48.83; H, 2.37.

The compound carbonizes at about 230° without melting. It is soluble in methanol and ethanol. Its solution in concentrated sulfuric acid is bright red. No 4,5-quinone could be isolated from this substance on reduction followed by oxidation.

5-Aminobenzothiophene.—This compound was obtained from 5-nitrobenzothiophene prepared by the method of Fieser and Kennelly.[3] It was found more convenient to reduce the nitro compound by the Raney nickel–hydrazine hydrate procedure[27] and to isolate the amine as its sulfate, as the free amine oxidizes in air.

5-Nitrobenzothiophene (10.0 g.) was suspended in 100 ml. of absolute ethanol and *ca.* 1 g. of Raney nickel added. To the suspension was added 10 ml. of 85% hydrazine hydrate in water, and when the initial vigorous effervescence had subsided, the solution was kept just below its boiling point for 30 minutes. A little activated carbon was added and the solution filtered. As the clear filtrate rapidly darkens, it was poured without loss of time into 100 ml. of 6 *M* sulfuric acid. The insoluble sulfate was collected and dried, 9.8 g. (87%). A sample was recrystallized from water for analysis, fine colorless needles with a tendency to gain a pink tinge decomposing *ca.* 260° and melting 270–272°.

Anal. Calcd. for $(C_8H_8NS)_2SO_4^{--}$: C, 48.48; H, 4.07. Found: C, 48.73; H, 4.19.

4-Bromo-5-hydroxybenzothiophene.—This compound was prepared in 61% yield by the method of Fries, *et al.*[2] It was recrystallized from hexane, colorless needles, m.p. 110.5–112°; reported[2] 112°.

Attempts to convert this compound to benzothiophene-4,5-quinone by shaking with nitric acid in chloroform were unsuccessful. A red gum resulted which did not give a Craven test.[28] Similarly attempts to form 4-bromo-4,5-dihydro-5-keto-4-nitrobenzothiophene with a view to its subsequent decomposition to benzothiophene-4,5-quinone failed. A stable 4-bromo-5-hydroxynitrobenzothiophene of m.p. 173° resulted. This compound has been assigned the structure of the 3-nitro derivative.[2]

4-Bromo-5-hydroxybenzothiophene-2-carboxylic Acid.—5-Hydroxybenzothiophene-2-carboxylic acid (1.0 g.) was dissolved in 25 ml. of glacial acetic acid, and a 5-ml. aliquot of a solution containing 5.44 ml. of bromine per 100 ml. in acetic acid (*i.e.*, 0.82 g. or 1 mole of bromine) was added dropwise to the ice-cold solution. The bromine color was discharged immediately. Careful dilution of the solution with water yielded a colorless solid, 1.3 g. (93%). The crude product was recrystallized from glacial acetic acid for analysis, white feathery needles, m.p. 273–274°.

Anal. Calcd. for $C_9H_5O_3BrS$: C, 39.59; H, 1.81. Found: C, 39.65; H, 1.97.

The compound is soluble in acetic acid, acetone and ethanol. It is somewhat soluble in benzene and insoluble in water. The solid has a tendency to gain a pink tinge.

Attempts to isolate the 4,5-quinone from this compound by way of the 4-bromo-4,5-dihydro-5-keto-4-nitro compound were unsuccessful.

5-Amino-4-bromobenzothiophene-2-carboxylic Acid.—5-Aminobenzothiophene-2-carboxylic acid (2.034 g.) was dissolved in 400 ml. of acetic acid by warming and to the warm solution was added 1.68 g. (1 mole) of bromine in 9 ml. of acetic acid. There was an immediate precipitate of the finely divided hydrobromide of 5-amino-4-bromobenzothiophene-2-carboxylic acid. This material was dissolved in dilute sodium hydroxide solution, treated with activated carbon and filtered. The filtrate on acidification with acetic acid yielded a yellow solid, 2.542 g. (88%). The material exists in two distinct crystalline forms. On recrystallization from ethanol or acetic acid the compound separated as bright yellow needles. On scratching under ethanol the yellow form changed to colorless prisms, which were submitted for analysis, m.p. 273–274°.

Anal. Calcd. for $C_9H_6O_2NSBr$: C, 39.72; H, 2.22. Found: C, 39.70; H, 2.40.

The colorless form also passes into the yellow form on slow heating in the dry state above 200°.

Diazotization of this compound followed by boiling the diazonium salt with water by the method of Claus and Philipson[13] failed to yield the corresponding 4,5-quinone. Instead, a red amorphous material resulted which did not give a Craven test.[28]

4,6-Dibromo-5-hydroxybenzothiophene.—This compound was previously assigned the structure of 3,4-dibromo-5-hydroxybenzothiophene.[2] It was prepared in 75% yield by the method described by the early workers.[2] The purified product melted at 94.5–96°. As a m.p. of 94° is reported for this compound by Bordwell and Stange,[15] it would appear that the originally reported m.p. 103° is in error.

O-Acetyl-4,6-dibromo-5-hydroxybenzothiophene.—4,6-Dibromo-5-hydroxybenzothiophene (700 mg.) was refluxed with 10 ml. of acetic anhydride in 25 ml. of pyridine for 30 minutes. The solvent was removed under reduced pressure, leaving a reddish oil. This was dissolved in chloroform, extracted with dilute aqueous sodium hydroxide solution and the organic layer taken to dryness, yielding a brown oil. This oil was taken up in hexane and run down a column of neutral alumina to remove the colored impurities. The eluent fractions yielded 570 mg. of colorless oil (72%). Crystallization from dilute acetic acid gave white needles, m.p. 76.5–78°.

Anal. Calcd. for $C_{10}H_6SO_2Br_2$: C, 34.31; H, 1.73. Found: C, 34.55; H, 1.89.

Hydrolysis of the acetyl compound with boiling 10% ethanolic sodium hydroxide solution gave a 91% yield of 4,6-dibromo-5-hydroxybenzothiophene. Its melting point either alone or in admixture with the material used in the acylation was 94.5–96°.

6-Bromobenzothiophene-4,5-quinone.—This compound was previously assigned the formula of 3-bromobenzothiophene-4,5-quinone by Fries, *et al.*[2] It was prepared in 74% yield in essentially the same manner as described by these workers except that it was found advantageous to play a stream of air on the reaction mixture to remove the liberated bromine to prevent it substituting in the product. The compound crystallizes in violet-red prisms from ethyl acetate which are red-purple on pulverizing. The melting point is of little use in determining the purity of this compound. Decomposition sets in near 130° and, depending upon the ease with which products of the decomposition can escape, a wide range of melting points is observed. Application of the Craven test[28] gives a deep green color. All attempts to prepare the phenazine of this quinone failed.

2,6-Dibromobenzothiophene-4,5-quinone.—This compound is formed as a secondary product in the preparation of 6-bromobenzothiophene-4,5-quinone and unless the reaction mixture is worked up quickly appreciable amounts are formed. It was obtained in 40% yield by the following procedure. Five hundred milligrams of 4,6-dibromo-5-hydroxybenzothiophene was dissolved in 10 ml. of chloroform and 3 ml. of yellow fuming nitric acid added. The flask was stoppered and shaken vigorously for 2 minutes. Twenty-five milliliters of water was then added, the flask restoppered, and after shaking vigorously for 10 minutes the mixture was allowed to stand for 24 hr. The red chloroform solution was then separated from the aqueous layer, washed twice with water and taken to dryness under re-

(28) R. Craven, *J. Chem. Soc.*, 1605 (1931).

duced pressure. The residue was recrystallized three times from ethyl acetate, 210 mg. of blue-black plates, decomposing *ca.* 130°. On pulverizing the compound appears blue-purple.

Anal. Calcd. for $C_8H_2O_2SBr_2$: C, 30.00; H, 0.63. Found: C, 30.05; H, 0.85.

Condensation of 6-Bromobenzothiophene-4,5-quinone with Ethyl Cyanoacetate in the Presence of Potassium Ferricyanide.—Finely ground 6-bromobenzothiophene-4,5-quinone (160 mg.) was suspended in 10 ml. of ethanol and 2 drops of ethyl cyanoacetate was added, followed by 1 ml. of triethylamine. The mixture, which went deep green, was swirled for four minutes. At the end of this time a previously prepared solution of 1 g. of potassium ferricyanide in 10 ml. of water was added, followed immediately by a solution of 0.5 g. of sodium carbonate in 10 ml. of water to dissolve the insoluble material thrown down on the addition of the oxidizing agent. The contents of the flask were swirled for seven minutes, then carefully acidified with excess dilute sulfuric acid. A tarry precipitate formed, and the mixture was extracted with ether. The orange ethereal solution was taken to dryness and the orange residue recrystallized from dilute acetic acid, 70 mg. of orange microcrystalline material, m.p. 175–180°. A sample was recrystallized from ethyl acetate, orange-red prisms, m.p. 184–186°. Analysis showed this compound to be 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone, bromine having been lost in the reaction.

Anal. Calcd. for $C_{13}H_9O_4NS$: C, 56.71; H, 3.30. Found: C, 56.42; H, 3.27.

This substance was identical with a sample prepared from 4-nitroso-5-hydroxybenzothiophene in a manner analogous to that described below for the preparation of 2-carboxy-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone from 5-hydroxy-4-nitrosobenzothiophene-2-carboxylic acid. Its color in basic solutions is deep green. It is soluble in ethyl acetate, ethanol, methanol and acetic acid.

The phenazine was prepared by boiling molar proportions of the quinone and *o*-phenylenediamine in acetic acid for 15 minutes. The phenazine is a deep navy-blue color, as are all the phenazines of the 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinones. A sample was recrystallized from dilute acetic acid for analysis, blue plates, m.p. 194–196°, going deep green on melting.

Anal. Calcd. for $C_{19}H_{13}O_2N_3S$: C, 65.69; H, 3.75. Found: C, 65.41; H, 3.97.

This compound, like all the phenazines of 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinones, gives a wide range of color reactions in various solvents. In pyridine these phenazines are royal blue; in acetic acid, green; in concentrated sulfuric acid, orange; in acetone or alcohol, turquoise; in ammonia, magenta; and in a mixture of triethylamine and acetic anhydride, purple.

6-Bromo-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone.—This compound resulted when 6-bromobenzothiophene-4,5-quinone, suspended in ethanol, was treated with ethyl cyanoacetate and triethylamine without the addition of potassium ferricyanide. The orange-yellow solid obtained on acidification of the reaction mixture was recrystallized from ethyl acetate, orange-yellow prisms, m.p. 191–192°.

Anal. Calcd. for $C_{13}H_8O_4NSBr$: C, 44.09; H, 2.28. Found: C, 44.25; H, 2.18.

2-Bromo-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone.—Analytically pure 2,6-dibromobenzothiophene-4,5-quinone (70 mg.) was condensed with ethyl cyanoacetate in the presence of potassium ferricyanide in exactly the same manner as described above for 6-bromobenzothiophene-4,5-quinone. On working the reaction up in an analogous manner there resulted 25 mg. of orange-red solid. Recrystallization from ethyl acetate gave orange prisms, m.p. 225–227° with decomposition.

Anal. Calcd. for $C_{13}H_8O_4NBrS$: C, 44.09; H, 2.28. Found: C, 44.12; H, 2.39.

This compound is soluble in ethyl acetate, ethanol, methanol, acetic acid, chloroform, benzene and acetone. It is nearly insoluble in hexane.

The phenazine was prepared in 98% yield by boiling equivalent proportions of the quinone and *o*-phenylenediamine in acetic acid for ten minutes and diluting the solution carefully with water. A sample recrystallized from glacial acetic acid was submitted for analysis, deep purple-black plates, m.p. 203.5–205.5°.

Anal. Calcd. for $C_{19}H_{12}O_2N_3SBr$: C, 53.53; H, 2.84. Found: C, 53.54; H, 3.08.

Reductive Debromination of 2-Bromo-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone.—Four hundred milligrams of 10% palladium chloride on charcoal was prereduced in 20 ml. of ethanol with hydrogen at room temperature and atmospheric pressure. When the uptake of hydrogen was complete, 200 mg. of 2-bromo-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone was introduced into the flask. The adsorption of hydrogen was complete after 45 minutes (94% of 2 moles adsorbed). The solution was filtered under nitrogen. To the filtrate were added a solution of 0.75 g. of potassium ferricyanide in 10 ml. of water and 3 ml. of triethylamine. The solution immediately turned green and by acidification yielded an orange flocculent precipitate. This was crystallized from ethyl acetate, giving 20 mg. of unchanged starting material. The more soluble portion, m.p. 177–184°, was recrystallized further to give 50 mg. (35%) of pure 7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone, identical with authentic material.

Condensation of 3-Bromo-1,2-naphthoquinone with Ethyl Cyanoacetate in the Presence of Potassium Ferricyanide.—3-Bromo-1,2-naphthoquinone[10] (1 g.) was finely ground and suspended in 35 ml. of ethanol. To the suspension were added 0.5 ml. of ethyl cyanoacetate and 1 ml. of triethylamine. The mixture was swirled for five minutes and the quinone went into solution with the development of a deep blue color. A solution of 2.75 g. of potassium ferricyanide in 15 ml. of water was then added, throwing down a dark precipitate. This was taken back into solution by the addition of a solution of 1 g. of sodium carbonate in 80 ml. of water. The solution was swirled for seven minutes and then acidified with 6*M* sulfuric acid. A dark oil separated, which on standing yielded 300 mg. of yellow crystalline material, m.p. 125–128°. This was recrystallized from alcohol, yellow needles, m.p. 127–129°. There was no mixed m.p. depression with authentic 4-carbethoxycyanomethyl-1,2-naphthoquinone, m.p. 129–130°, prepared by the method of Sachs and Cravieri.[20] The infrared spectra of the two specimens were indistinguishable. The remaining tarry material from the reaction was not worked up.

4,6-Dibromo-5-hydroxybenzothiophene-2-carboxylic Acid.—5-Hydroxybenzothiophene-2-carboxylic acid (1.0 g.) together with 2.0 g. of crystalline sodium acetate was dissolved in 35 ml. of acetic acid by warming. To the solution cooled in ice was added 10.3 ml. of bromine–acetic acid solution containing 1.64 g. (2 mole proportion) of bromine. A yellowish solid separated, 1.4 g. (78%), m.p. 295–300°. A sample was recrystallized several times from glacial acetic acid for analysis, m.p. 301–303°, very pale yellow microscopic needles.

Anal. Calcd. for $C_9H_4O_3SBr_2$: C, 30.70; H, 1.15. Found: C, 30.87; H, 1.33.

The acid sublimes unchanged at 1×10^{-2} mm. and 210°. It is not decarboxylated by refluxing in pyridine. No decarboxylated product was isolated when the compound was heated to 330° with finely powdered calcium oxide. When the acid was heated with copper bronze powder in quinoline solution under nitrogen, decarboxylation did not occur below 200°. Above this temperature complete decomposition occurred.

2-Carboxy-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone.—5-Hydroxy-4-nitrosobenzothiophene-2-carboxylic acid (1.0 g.) was hydrogenated over 800 mg. of Raney nickel in 125 ml. of absolute ethanol. Approximately 70% of the theoretical volume (2 moles) of hydrogen was adsorbed. The mixture was filtered under nitrogen into a nitrogen-flushed flask containing a solution of 0.8 ml. of ethyl cyanoacetate and 3 ml. of triethylamine in 25 ml. of ethanol. Without loss of time a solution of 6.0 g. of potassium ferricyanide in 100 ml. of water was added directly and the contents swirled. An immediate deep purple coloration developed and dark material precipitated. This was taken into solution by the addition of a solution of 1 g. of sodium carbonate in 200 ml. of water. The solution was swirled for about 10 minutes and then acidified with 6*M* sulfuric acid. The solution turned brown, and on standing

in the cold for an hour a brown flocculent precipitate was deposited, 300 mg., carbonizing 238–244°.

On recrystallization from glacial acetic acid to which several drops of concentrated hydrochloric acid had been added, 200 mg. of orange microcrystalline material was obtained. The addition of the hydrochloric acid was necessary to obtain a clean product. Treatment of the orange alcoholic solution of the quinone with ammonia causes a color change from green to purple on standing, and this purple solution on acidification yields amorphous brown material once more. This on recrystallization from glacial acetic acid and hydrochloric acid gives unchanged material.

The quinone is soluble in ethanol, methanol, ethyl acetate and acetic acid. A sample was recrystallized several times from acetic acid for analysis, m.p. 268–270° with decomposition.

Anal. Calcd. for $C_{14}H_9O_6NS$: C, 52.66; H, 2.84. Found: C, 52.70; H, 3.04.

The quinone was prepared in better yield (40%) by employing 5-hydroxy-4-nitrobenzothiophene-2-carboxylic acid in place of the 4-nitroso compound. In this case the initial reduction went to completion.

The phenazine was prepared by boiling equivalent proportions of the quinone and *o*-phenylenediamine in glacial acetic acid for 10 minutes. On dilution with water the solution deposited blue plates. A sample was recrystallized twice from dilute acetic acid for analysis. On heating the blue plates change to green needles *ca.* 225–235°, no m.p. observed below 300°.

Anal. Calcd. for $C_{20}H_{13}O_4N_3S$: C, 61.38; H, 3.35. Found: C, 61.34; H, 3.55.

N-Acetyl-5-aminobenzothiophene-2-carboxylic Acid.—Crude 5-aminobenzothiophene-2-carboxylic acid, m.p. 273–275° (10 g.), was refluxed for 2.5 hr. with 175 ml. of acetic anhydride, all the material passing into solution at the end of 2 hr. The brownish solution was allowed to cool somewhat and treated with activated carbon and filtered. The pale yellow filtrate was left standing under 2 l. of water for 48 hr., at the end of which time the acetic anhydride had hydrolyzed away, depositing a colorless solid, 12 g. (98%).

The compound is insoluble in benzene, ethanol and water. It was recrystallized several times from glacial acetic acid, in which it is slightly soluble, for analysis, colorless prisms, m.p. 340°.

Anal. Calcd. for $C_{11}H_9O_3NS$: C, 56.15; H, 3.86. Found: C, 55.89; H, 4.26.

The crude material was suitable for further work.

N-Acetyl-5-amino-4-nitrobenzothiophene-2-carboxylic Acid.—Crude N-acetyl-5-aminobenzothiophene-2-carboxylic acid (4.0 g.) was suspended in 125 ml. of glacial acetic acid, heated to 100°, treated with 5.0 ml. of concentrated nitric acid, and the mixture stirred. The undissolved solid rapidly passed into solution with the development of a bright yellow color. The solution was treated with activated carbon while still hot and filtered. On standing the filtrate deposited yellow needles, 3.1 g. (65%), m.p. 248–250° with decomposition. A sample was recrystallized several times from acetic acid for analysis, bright yellow needles, m.p. 254.5–256° with decomposition.

Anal. Calcd. for $C_{11}H_8O_5N_2S$: C, 47.13; H, 2.88. Found: C, 47.47; H, 3.15.

The crude compound was suitable for further work.

5-Amino-4-nitrobenzothiophene-2-carboxylic Acid.—Crude N-acetyl-5-amino-4-nitrobenzothiophene-2-carboxylic acid (8.0 g.) was heated on a steam-bath together with 300 ml. of water and 40 ml. of 1% sodium hydroxide solution for 25 minutes, yielding a deep red solution. This was treated with activated carbon and filtered. The filtrate was acidified with aqueous chloroacetic acid solution, yielding an orange precipitate, 6.0 g. (88%). A sample was recrystallized several times from acetic acid for analysis, orange needles, m.p. 301–302°.

Anal. Calcd. for $C_9H_6O_4N_2S$: C, 45.37; H, 2.54. Found: C, 45.44; H, 2.52.

The compound is sparingly soluble in acetic acid, dioxane, acetone and ethanol. It is very slightly soluble in water and insoluble in benzene and hexane. The sodium salt is bright orange and gives a red solution in water.

5-Hydroxy-4-nitrobenzothiophene-2-carboxylic Acid.—This compound was obtained by hydrolysis of the 5-amino group in the previous compound, using boiling 10% sodium hydroxide solution followed by acidification. However, it was found convenient to prepare it directly from N-acetyl-5-amino-4-nitrobenzothiophene-2-carboxylic acid by boiling with 10% sodium hydroxide solution for 30 minutes. This method gave a 70% yield. A sample was recrystallized several times from acetic acid for analysis, soft yellow needles, m.p. 269–271°.

Anal. Calcd. for $C_9H_5O_5NS$: C, 45.20; H, 2.11. Found: C, 45.40; H, 2.26.

This compound is soluble in acetic acid, ethanol and acetone. It is sparingly soluble in water and benzene. The aqueous solution of its sodium salt is orange.

O-Acetyl-5-hydroxybenzothiophene.—It was found more satisfactory to prepare this compound by the action of acetyl chloride in pyridine on 5-hydroxybenzothiophene rather than follow the method of Bordwell and Stange.[15] 5-Hydroxybenzothiophene (300 mg.) was dissolved in 10 ml. of pyridine and 167 mg. of acetyl chloride added. An immediate reaction was apparent. After standing 4 hr. the mixture was poured into water and a colorless oil separated, which soon solidified. The product was collected, washed well with water and dried, m.p. 66–68°, reported[15] 70°. This material was used as such to prepare 3-bromo-5-hydroxybenzothiophene by the method of Bordwell and Stange.[15]

3,4-Dibromo-5-hydroxybenzothiophene.—This compound was prepared as described by the previous workers[15] but with the addition of one mole of crystalline sodium acetate to the reaction mixture, as it was found that this procedure raised the yield of pure material to 70%. Recrystallized from hexane, hard white needles, m.p. 147–149°; reported[15] 146–148°.

3-Bromo-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone.—3,4-Dibromo-5-hydroxybenzothiophene (120 mg.) was suspended in 4 ml. of glacial acetic acid and 2 ml. of concentrated nitric acid added. On swirling an orange solution was formed which on careful dilution with water and cooling yielded fluffy yellow needles of 3,4-dibromo-4,5-dihydro-5-keto-4-nitrobenzothiophene. These were collected, washed well with water and dried at the pump. It was dissolved in 10 ml. of benzene and the solution brought to boiling. The color of the solution changed from yellow to red and red fumes were evolved. After ten minutes heating the solvent was removed under reduced pressure and the red-purple residue taken up in 4 ml. of absolute ethanol. As profound decomposition occurred when an attempt was made to recrystallize the compound from ethyl acetate, the ethanolic solution of the crude material (3-bromobenzothiophene-4,5-quinone) was treated in order and with swirling with 0.1 ml. of ethyl cyanoacetate, 0.3 ml. triethylamine, 0.3 g. potassium ferricyanide in 2 ml. of water and 0.15 g. of sodium carbonate in 10 ml. of water. Swirling was continued for five minutes and the solution acidified with dilute sulfuric acid. A red-brown amorphous precipitate was formed. It was collected, dried and crystallized from ethyl acetate, 40 mg. (29%), m.p. 239–240°.

Anal. Calcd. for $C_{13}H_8O_4NSBr$: C, 44.09; H, 2.28. Found: C, 43.99; H, 2.37.

Attempted Hunsdiecker[29] Reaction with 5-Nitrobenzothiophene-2-carboxylic Acid.—Sodium 5-nitrobenzothiophene-2-carboxylate (4 g.) was dissolved in 200 ml. of water by warming and to the solution was added a solution of 5.0 g. of silver nitrate in 50 ml. of water. The gelatinous precipitate was filtered with the aid of a rubber dam and dried over phosphorus pentoxide for 2 days, 4.66 g. (87%). The dry silver salt was refluxed with 40 ml. of carbon tetrachloride distilled from phosphorus pentoxide and over a period of 20 minutes was added a solution of 2.26 g. of anhydrous bromine in 30 ml. of anhydrous carbon tetrachloride. The solution was refluxed for a further 90 minutes. On cooling the solution was filtered free of insoluble silver salts and insoluble organic material. The carbon tetrachloride solution on taking to dryness gave 300 mg. of yellowish material. This was recrystallized from ethanol, pale yellow feathery needles, m.p. 217–218°.

Anal. Calcd. for $C_8H_3O_2NSBr_2$: C, 28.51; H, 0.90. Found: C, 28.80; H, 0.99.

Extraction of the residue from the reaction with absolute

(29) H. Hunsdiecker and A. Hunsdiecker, *Ber.*, **75**, 291 (1942).

ethanol gave 2.6 g. of yellow crystalline material; recrystallized from ethanol, pale yellow needles, m.p. 308–310°.

Anal. Calcd. for $C_9H_4O_4NSBr$: C, 35.78; H, 1.34. Found: C, 36.03; H, 1.35.

This same bromonitro acid resulted on treatment of an aqueous solution of sodium 5-nitrobenzothiophene-2-carboxylate with a molar proportion of bromine in aqueous solution. In all probability it is 7-bromo-5-nitrobenzothiophene-2-carboxylic acid.

4-Cyanomethyl-1,2-naphthoquinone from 4-Cyanocarbethoxymethyl-1,2-naphthoquinone by the Action of Triton B.—4-Cyanocarbethoxymethyl-1,2-naphthoquinone (500 mg.) was dissolved in 80 ml. of Triton B solution. A deep purple color developed immediately. On standing the solution turned a deep red. After 25 minutes the solution was acidified with 6*N* hydrochloric acid, and a bright yellow solid was deposited, 350 mg., m.p. 172–178°. It was recrystallized from dilute acetone, 290 mg. (79%) of fine yellow needles, m.p. 208–211°. The material gave no mixed m.p. depression with a sample of authentic 4-cyanomethyl-1,2-naphthoquinone prepared by the method of Gates, *et al.*[24] Its previously unreported phenazine was prepared by boiling equivalent proportions of the quinone and *o*-phenylenediamine in acetic acid for five minutes and diluting the solution with water. The product was recrystallized from benzene–hexane and then from alcohol, pale yellow needles, m.p. 200–202°.

Anal. Calcd. for $C_{18}H_{11}N_3$: C, 80.28; H, 4.12. Found: C, 80.00; H, 4.35.

The phenazine gives a blood-red coloration with concentrated sulfuric acid. It was identical with the phenazine formed from an authentic sample of 4-cyanomethyl-1,2-naphthoquinone.

2-Bromo-7-(cyanomethyl)-benzothiophene-4,5-quinone.—2-Bromo-7-(cyanocarbethoxymethyl)-benzothiophene-4,5-quinone (400 mg.) was dissolved in 7 ml. of Triton B. The initially green solution went dark and finally a dull red-purple color. After standing for 45 minutes the solution was diluted with about three times its volume of distilled water and filtered. The filtrate was carefully acidified with 6 *N* hydrochloric acid, and on scratching small reddish crystals were deposited. As the compound decomposed on attempts at crystallization, it was converted into its phenazine, which is stable, by boiling equivalent amounts of the crude quinone and *o*-phenylenediamine in acetic acid for 5 minutes and diluting the solution with water. The product was crystallized from dilute acetic acid, deep yellow microscopic needles, m.p. 253–254° with decomposition.

Anal. Calcd. for $C_{16}H_8N_3SBr$: C, 54.26; H, 2.28. Found: C, 54.27; H, 2.39.

With concentrated sulfuric acid the phenazine gives an olive-green color.

ROCHESTER 20, N. Y.

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY, UNIVERSITY OF NORTH CAROLINA]

The Synthesis and Smiles Rearrangement of 2-Hydroxy-5-methyl-2′-nitrodiphenyl Sulfone and Several of its Methyl and Halogen Derivatives[1,2]

BY TOSHIHIKO OKAMOTO[3] AND J. F. BUNNETT

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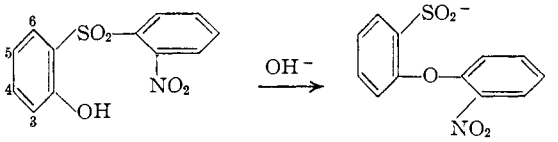
The synthesis of several sulfones of types IV and V is reported. Proof of their structures is presented, and several products and by-products of their alkali-promoted (Smiles) rearrangement are described.

McClement and Smiles[4] reported that the alkali-induced rearrangement of 2-hydroxy-2′-nitrodiphenyl sulfones to 2-(*o*-nitrophenoxy)-benzenesulfinic acids is accelerated by methyl groups in the 6-position. Bunnett and Zahler[5] showed that the



acceleration could be rationally interpreted on steric grounds. However, it seemed desirable to prove by experiment whether or not the acceleration was actually due to the *bulk* of the 6-methyl groups, and to gather good kinetics data on the rearrangement. This paper describes the preparation of several compounds required for the kinetics work, proof of their structures, and careful description of the products and by-products of several typical rearrangements. Our rate measurements are presented and discussed in the following paper.[6]

Our thinking was this: if the acceleration is really due to the bulk of the 6-methyl groups, rather than to their electron-releasing effect as was originally proposed by McClement and Smiles, large 6-substituents of opposite electronic effect ought also to accelerate the reaction. We found that they do.[6] It was necessary, though, to be able to recognize what part of the change in rate caused by the introduction of a 6-substituent might be due to its electronic effect, and for this purpose we chose to compare the rates of rearrangement of isomers of types IV and V. The electronic effect of a 4-substituent (in IV) ought to be similar to that of the same substituent in the 6-position (as in V). The 5-methyl group is a constant factor in all the sulfones prepared in this work; it serves to block the position *para* to the hydroxy group and thereby simplifies problems of synthesis.

The parent sulfone IVa, its rearrangement to sulfinic acid VIa and evidence for the structure of the latter were described by Levy, Rains and Smiles.[7] We have repeated and confirmed much of their work, including particularly the isolation of VIa from the rearrangement, oxidation of VIa to the corresponding sulfonic acid XI and desulfonation of the latter to the ether Xa. Alternatively, we have mercuridesulfinated[8] VIa to form (presumably) VIII (R = H) which in turn was demercu-

(1) Research supported by the Office of Ordnance Research, U. S. Army.

(2) Described in part in a preliminary communication: T. Okamoto and J. F. Bunnett, *J. Org. Chem.*, **21**, 487 (1956).

(3) On leave from the Pharmaceutical Institute, University of Tokyo, 1954–1956; grateful recipient of a Fulbright travel grant.

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