The product in each case is not the expected carbinol, but the olefin that would be formed from it by dehydration. The yields of 1-mesityl-1-phenylethylene and of 1-isoduryl-1-phenylethylene were 64 and 42%, respectively.

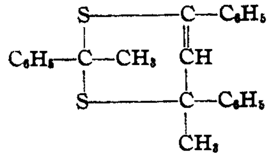
URBANA, ILLINOIS RECEIVED FEBRUARY 9, 1944

[CONTRIBUTION FROM THE M. D. ANDERSON HOSPITAL FOR CANCER RESEARCH, AND THE DEPARTMENT OF PREVENTIVE MEDICINE AND PUBLIC HEALTH OF THE UNIVERSITY OF TEXAS MEDICAL BRANCH]

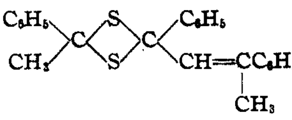
The Synthesis of 2,4-Diarylthiophenes[1]

BY E. CAMPAIGNE

Baumann and Fromm,[2] while investigating thioacetophenone, reported the isolation of a compound, $C_{24}H_{22}S_2$, in good yield from the alcoholic mother liquors of the thioacetophenone preparation. Pyrolysis of this disulfide gave 2,4-diphenylthiophene but no yield was reported. On the basis of analysis and the formation of 2,4-diphenylthiophene, two possible structures were assigned to this compound, which they called "Anhydroacetophenone disulfide"



I

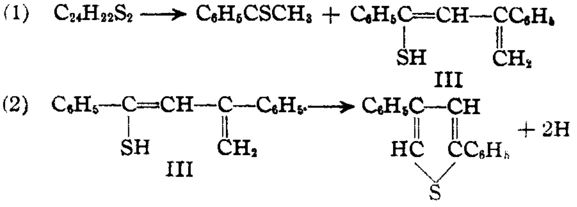


II

Structure I was assumed to be the most probable, since dithioacetophenone had never been isolated.

The synthesis of 2,4-diarylthiophenes has been reviewed by Bogert and Herrera.[3] These compounds are usually prepared by the reaction of phenylethylene or its derivatives with sulfur. This type of reaction gives a possibility of three different isomers, and consequently the yields have been extremely low. Bogert and Herrera[3] reported that by fusing acetophenone anil with sulfur, 2,4-diphenylthiophene was obtained in 28% yield. No 2,5-diphenylthiophene was found. These authors suggest that the formation of thioacetophenone as an intermediate accounts for the higher yield and lack of formation of 2,5-diphenylthiophene. However, Baumann and Fromm[2] reported the isolation of both 2,4- and 2,5-diphenylthiophene from the pyrolysis of thioacetophenone.

It seemed most probable that if either structure, (I) or (II), of "Anhydroacetophenone disulfide" given by Baumann and Fromm[2] were correct, highest yields of pure compounds could be obtained through this intermediate, since only 2,4-diarylthiophene, (IV), could be formed, according to the equations



$$(1)\quad C_{24}H_{22}S_2 \longrightarrow C_6H_5CSCH_3 + C_6H_5\underset{SH}{\underset{|}{C}}=CH-\underset{CH_2}{\underset{\|}{C}}C_6H_5$$

IV

The hypothetical compound III forms 2,4-diphenylthiophene by the loss of two atoms of hydrogen. In the pyrolysis of "Anhydroacetophenone disulfide" apparently acetophenone acts as the hydrogen acceptor, since in addition to the diarylthiophene, styrene and hydrogen sulfide were isolated.[2]

Several experiments were conducted to determine the yield of 2,4-diphenylthiophene from "Anhydroacetophenone disulfide." Pyrolysis of the material at 180° gave a tarry residue from which it was only possible to obtain sufficient pure 2,4-diphenylthiophene for identification. Refluxing the compound for several hours in boiling xylene caused a color change from colorless to deep purple. This would be expected, since the compound is unstable above its melting point, decomposing to give the highly colored thioketone monomers. No diarylthiophene could be isolated from this reaction, but the oily residue contained unsaturated carbon linkages. Apparently the reaction represented by the second equation does not take place readily. When this mixture was treated with copper chromite catalyst, IV was obtained in 83% yield. This reaction might be expected, since this catalyst has been used in the dehydrogenation of alcohols.[4]

A similar experiment with the "Anhydrodisulfide," V, prepared from *p*-methoxypropiophenone gave a 66% yield of 2,4-di-*p*-anisyl-3,5-dimethylthiophene, VI. This reaction was shown to proceed in two steps, as indicated by equations 1 and 2, as follows: the "Anhydrodisulfide" V, was refluxed in xylene, causing decomposition to an unsaturated oil. No thiophene derivative was formed by this treatment. However, when this residual oil was refluxed in alcohol with copper chromite, the dianisylthiophene, VI, was formed in good yield. "Anhydro-*p*-methoxypropiophenone disulfide," V, was not changed by re-

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[1] Presented before the Organic Division at the 106th meeting of the American Chemical Society in Pittsburgh, Pa., September, 1943.

[2] Baumann and Fromm, *Ber.*, **28**, 895 (1895).

[3] Bogert and Herrera, THIS JOURNAL, **45**, 238 (1923).

[4] Lazier, British Patent 301,806, *C. A.*, **23**, 4306 (1929).

fluxing in alcohol alone, or with copper chromite. Therefore, it seems probable that the first step in the reaction is not influenced by copper chromite, but only occurs at high temperatures, near the melting point of the "anhydro-disulfide." The temperature necessary to initiate the second step is dependent on the efficiency of the hydrogen acceptor, because at the temperature of refluxing alcohol copper chromite is active, while it was necessary to heat the compound above 180° for thioacetophenone to be active.

Since compound VI theoretically has no active hydrogens, the usual derivatives were not formed. However, the compound was sufficiently stable, so that the ether linkages could be hydrolyzed to give a di-*p*-hydroxy compound, which was acetylated to the diacetate. In addition to analysis of its derivatives, the identity of the new compound was further clarified by comparison of its ultraviolet absorption curve with that of IV, 2,4-diphenylthiophene. The absorption curves were taken in methanol solutions, using a Hilger Model E-498 spectrograph and a Spekker Photometer. The solutions were approximately 5 × 10^{-5} molar, and the cell thickness was 1 cm. The molar extinction coefficient, *E*, is plotted against the wave length in Fig. 1. It is apparent that the new compound VI, Curve II, and 2,4-diphenylthiophene, IV, Curve I, are very similar in structure, since both show maximum absorption at 250, 265 and 280 millimicrons.

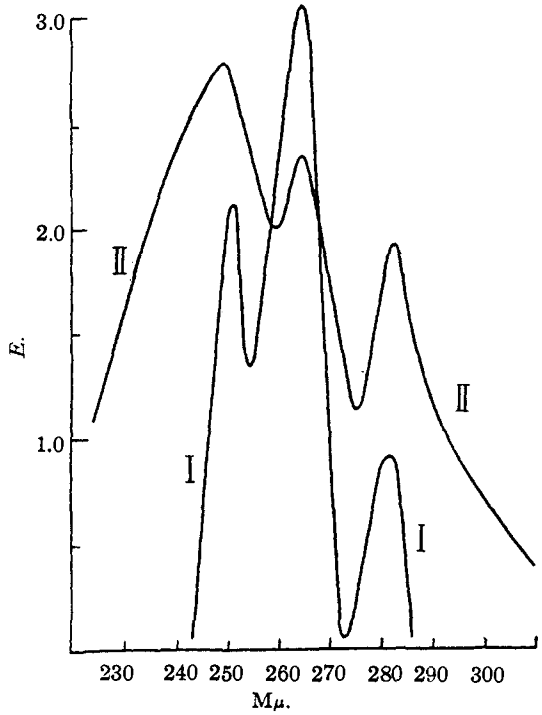

Fig. 1.—Absorption curves taken in methanol of: I, 2,4-diphenylthiophene, and II, 2,4-di-*p*-anisyl-3,5-dimethylthiophene.

Experimental

Preparation of "Anhydroacetophenone Disulfide."—Forty grams of acetophenone was dissolved in 300 ml. of absolute alcohol, and cooled to 0° in an ice-salt bath. Dry hydrogen chloride was passed in for a few minutes, until the rate of gas influx could be regulated, and then hydrogen sulfide also was passed in at a slow rate. Approximately 140 g. of dry hydrogen chloride (the amount calculated to saturate the alcohol) was passed into the solution over a period of six hours. During this time the reaction flask was kept in the ice-salt bath. When all the hydrogen chloride was used, the bath was allowed to come to room temperature while hydrogen sulfide was passed continuously into the flask for eight hours longer. About three hours after starting white crystals began to form in the flask, and a purple resin precipitated. After fourteen hours, the gas-inlet tubes were removed, and the flask was stored in the refrigerator overnight. The white crystals were stirred up and filtered from the mother liquor, leaving the purple resin of thioacetophenone in the flask. The crystals of "Anhydroacetophenone disulfide" were washed once with alcohol and dried. The crude product melted from 106–109°. The yield was 23.5 g. or 57% of theoretical. After two recrystallizations from acetone, the product was obtained in white hexagonal bars, m. p. 107–108° cor.

Anal.[5] Calcd. for $C_{24}H_{22}S_2$: C, 77.00; H, 5.88; S, 17.11. Found: C, 77.04; H, 5.64; S, 17.09.

Reaction of "Anhydroacetophenone Disulfide" with Copper Chromite.—The copper chromite catalyst was prepared according to the directions of Lazier and Arnold.[6] It was finely ground in a mortar before use. Three grams of the sulfur compound was dissolved in 35 ml. of dry xylene, and 10 g. of the copper chromite powder was added. The mixture was brought to reflux and stirred. No hydrogen sulfide was evolved during the course of three hours. At the end of this time the mixture was cooled and filtered. The residual catalyst was washed thoroughly with xylene, and the combined washings and filtrate distilled under water-pump vacuum to remove xylene. The brown residue solidified on cooling. It was dissolved in about 80 ml. of boiling methanol, and treated with norite. Upon cooling, white flaky crystals deposited. These were recrystallized from methanol, and dried. The melting point was 120.6–121.5° cor. The yield was 1.58 g., 83% of theoretical.

Anal. Calcd. for $C_{16}H_{12}S$: C, 81.31; H, 5.08; S, 13.56, Found: C, 81.24; H, 4.89; S, 13.53.

This compound has a reactive hydrogen at position 5, and readily forms a picrate in bright red needles, m. p. 133.1–133.6° cor. Fromm and Fantl[7] give the melting point of the picrate of 2,4-diphenylthiophene as 133–134°. It also gives the 5-chloromercuri- derivative with alcoholic mercuric chloride, white needles, m. p. 222–223° corresponding to the 5-chloromercuri-2,4-diphenylthiophene obtained by Bogert and Herrera.[3]

Preparation of "Anhydro-*p*-methoxypropiophenone Disulfide."—Twenty grams of *p*-methoxypropiophenone, b. p. 124–128° (4 mm.), (from anisole and propionic anhydride with aluminum chloride[8]) was dissolved in 120 ml. of absolute alcohol, and hydrogen chloride and hydrogen sulfide passed in at 0° as in the previous preparation. Approximately 50 g. of dry hydrogen chloride was used. The reaction was allowed to continue for twelve hours. The solution became deep red in color, due to *p*-methoxythiopropiophenone. As the reaction proceeded, white needle-like crystals precipitated. After storing in the refrigerator overnight, the precipitate was filtered off. The red color had faded to a faint pink by this time. The precipitate was recrystallized from a mixture of equal parts

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(5) All analyses are by Mr. H. Morris of this Laboratory.

(6) Lazier and Arnold in Blatt, "Organic Syntheses," Collective Volume II, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 142.

(7) Fromm and Fantl, *Ann.*, **457**, 267 (1927).

(8) Noller and Adams, THIS JOURNAL, **46**, 1889 (1924).

of acetone and alcohol, forming large white needles, which melted to a deep red liquid at 158.1–158.6° cor. The yield was 11 g. or 53.5% of the theoretical.

Anal. Calcd. for $C_{30}H_{34}O_3S_2$: C, 71.2; H, 6.72; S, 12.6. Found: C, 71.8; H, 6.41; S, 12.75.

Reaction of "Anhydro-*p*-methoxypropiophenone Disulfide" with Copper Chromite.—Two grams of the sulfur compound was dissolved in 40 ml. of dry xylene and 10 g. of finely ground copper chromite was added. The mixture was stirred and refluxed for two and one-half hours. After cooling, the mixture was filtered and the xylene removed by vacuum distillation. The residue of brown oil was dissolved in about 10 volumes of hot methanol and cooled, giving yellowish crystals which were recrystallized from methanol in yellow needles, m. p. 112.3–112.8° cor. The yield was 0.85 g., or 66% of the theoretical.

Anal. Calcd. for $C_{20}H_{20}O_2S$: C, 74.1; H, 6.18; S, 9.87. Found: C, 74.5; H, 6.19; S, 9.71.

Demethylation.—The procedure given by Kharasch[9] for demethylation of stilbestrols was used: 1.07 g. of the dianisylthiophene was dissolved in 25 ml. of ethylene glycol, 2.5 g. of potassium hydroxide added, and the mixture sealed in a glass bomb under a pressure of 0.5 mm. of mercury. It was kept at 225° for eighteen hours. When cool it was opened, and the contents diluted with 2 volumes of water and filtered. When 8 ml. of concentrated hydrochloric acid was added, the solution set to a gel immediately. It was digested on a steam-bath, filtered and washed with water and dried. It was recrystallized with difficulty from benzene or toluene. After two recrystallizations from benzene, the gray material darkened at 185°, melted at 194–196°. The yield was 0.61 g., 61% of the theoretical. The compound is a phenol, as the deep yellow color with ferric chloride and the solubility in base indicate.

Anal. Calcd. for $C_{18}H_{16}O_2S$: C, 73.0; H, 5.41; S, 10.81. Found: C, 72.5; H, 5.37; S, 10.83.

Acetylation.—The 2,4-di-*p*-hydroxyphenyl-3,5-dimethylthiophene was readily acetylated by heating 0.1 g. with 0.1 g. of fused sodium acetate in 2.5 ml. of acetic anhydride on a steam-bath for one hour. The mixture was then poured over ice and stirred until the oil had solidified. The amorphous solid was centrifuged out and recrystallized three times from ethyl alcohol, giving fine white needles of the diacetate, which softened at 121°, but melted at 125.9–126.9° cor.

Anal. Calcd. for $C_{22}H_{20}O_4S$: C, 69.5; H, 5.26; S, 8.42. Found: C, 69.7; H, 5.29; S, 8.25.

Formation of the Thiophene in Two Steps.—Approximately 2 g. of "Anhydro-*p*-methoxypropiophenone disulfide" was refluxed in 30 ml. of xylene for three hours. The solution became deep purple in color. The xylene was distilled off under vacuum, and the residual brown oil was taken up in ethanol and stored in the refrigerator. No crystals were obtained in twenty-four hours, although both 2,4-di-*p*-anisyl-3,5-dimethylthiophene and "anhydro-*p*-methoxypropiophenone disulfide" are readily crystallized from alcohol. A few drops of the alcohol solution decolorized an acetone solution of potassium permanganate, indicating unsaturation. The alcohol solution was refluxed for two hours with copper chromite. Upon cooling the filtered alcohol solution, yellow needles were obtained, m. p. 112–113.5°. Mixed with 2,4-di-*p*-anisyl-3,5-dimethylthiophene, the melting point was 112–113°.

Summary

A new method for the synthesis of 2,4-diarylthiophenes, in yields of 65 to 85% based on the reaction of "anhydroketone disulfides" with copper chromite, is described.

The mechanism of this reaction is discussed.

Four new compounds, "Anhydro-*p*-methoxypropiophenone disulfide," 2,4-di-*p*-hydroxyphenyl-3,5-dimethylthiophene, and its dimethyl ether and diacetate, are characterized.

BLOOMINGTON, INDIANA RECEIVED JANUARY 31, 1944

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[9] Kharasch and Kleiman, THIS JOURNAL, **65**, 11 (1943).

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Acetylenic Ethers. IV.[1] Hydration

BY THOMAS L. JACOBS AND SCOTT SEARLES, JR.

It has been shown[2] that acetylenic ethers add water more rapidly than vinyl ethers but less rapidly than ketene acetals. The hydration is acid catalyzed and the rate has been followed quantitatively for several vinyl ethers.[3,4,5] It was of interest to carry out similar experiments with several acetylenic ethers for comparison.

Experimental

A dilatometric method was used to follow the hydration because it has been employed successfully to study the vinyl ethers[3,4,5] and because methods of analysis for acetylenic hydrogen or for the unsaturation of the triple bond are relatively inexact and have not been applied with success to acetylenic ethers. Butyl acetate was isolated[2] in 67% yield by heating butoxyacetylene with distilled water. In dilute solutions containing traces of acid this hydration is the only significant reaction; both the polymerization of the acetylenic ether and the hydrolysis of the ester are slow enough to be neglected. In aqueous alcohol the reaction is accompanied by marked volume contraction. The concentrations of the solutions studied were 0.025 to 0.03 molar.

The acetylenic ethers used in this work were carefully refractionated samples.[2,6] The ethoxyacetylene may have contained a little water and traces of water may have been introduced into all the ethers when samples were being sealed in small bulbs since for this operation the bulbs were embedded in dry-ice and open to the air.

The dilatometer was similar to that described by Leutner[7] and used to study the hydration of vinyl ethers.[3,4,5] The measuring bulb had a volume of 110 ml. and the capillary was 25 cm. long, had a diameter of 0.36 mm. and was uniform within 1% over the calibrated portion.

The acetylenic ethers are not very soluble in water and

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[1] For the third paper of this series see Jacobs and Whitcher, THIS JOURNAL, **64**, 2635 (1942).

[2] Jacobs, Cramer and Hanson, *ibid.*, **64**, 223 (1942).

[3] A. Skrabal and R. Skrabal, *Z. physik. Chem.*, **181A**, 449 (1938).

[4] R. Skrabal, *ibid.*, **185A**, 81 (1939).

[5] Zahorka and Wiemann, *Monatsh.*, **71**, 229 (1938).

[6] Jacobs, Cramer and Weiss, THIS JOURNAL, **62**, 1849 (1940). The ethoxyacetylene was prepared by Mr. John E. Hanson and Mr. Elbert Davis. The phenoxyacetylene was prepared by Mr. William Penn Tuttle, Jr.

[7] Leutner, *Monatsh.*, **66**, 222 (1935).