3. The hydrolysis of α-*d*-glucose phenylhydrazone in the presence of oxalic acid has been found to be pseudo-unimolecular.

4. Increases in the velocity constant toward the end of the hydrolysis have been explained as being due to the adsorption of *d*-glucose from solution by phenylhydrazine oxalate.

5. It is concluded that hydrolytic studies of hydrazones can yield no information of value concerning the structures of the hydrazones or their relationships to the isomers of *d*-glucose.

6. The reactions of the two isomers of *d*-glucose with phenylhydrazine have been followed polarimetrically.

7. The more rapid reaction rate of the alpha form has been explained by assuming a small undetectable amount of catalyst to be present as an impurity in the α-glucose, since the rates in the presence of hydrochloric acid were found to be identical for the alpha and beta forms.

8. It has been shown that strong acids, contrary to general belief, catalyze hydrazone formation, although they fail to catalyze appreciably the formation of osazone.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT AT THE OHIO STATE UNIVERSITY]

The Preparation of Thiophene and its Homologs from 1,3-Diolefins and Sulfur

BY A. F. SHEPARD, A. L. HENNE AND THOS. MIDGLEY, JR.

Thiophene and its homologs can be synthesized from conjugated diolefins and sulfur. The reaction is general and the yields range from 6 to 50%.

The procedure consists in dropping the liquid diolefin into or bubbling the gaseous diolefin through a vessel containing sulfur kept at about 350°, collecting the materials distilling from the vessel and subsequently effecting their separation. The operation is especially smooth with isoprene or dimethylbutadiene and it affords a 47% yield of 3-methylthiophene or a 31% yield of 3,4-dimethylthiophene. Thiophene is obtained from butadiene with a 6% yield, and 2,3-dimethylthiophene from 3-methyl-1,3-pentadiene with a similarly low yield.

The thiophene derivative produced is not contaminated by isomers, nor does it contain a dihydrothiophene, although the formation of the latter compound could have been expected as a primary result of the linking of the sulfur to the diolefin. By-products of the reaction are hydrogen sulfide, carbon bisulfide and non-volatile materials.

Acetylene, mono-olefins[1] and hydroaromatic compounds are not converted by sulfur into thiophene homologs except in traces. Acetylene and heated pyrites[2] give a good yield of thiophene but diolefins[3] and pyrites yield only small quantities of thiophene derivatives.

Experimental

The reaction vessel was a 1.5-liter iron pot with a lid which could be sealed with Wood's metal. An inlet tube and a thermometer extended through this lid. A broad (15 mm.) outlet at the top of the side wall of the pot led through an air condenser to one receiver chilled with ice and to a second kept at −78°. Glass equipment was unsuitable because of the difficulty of removing sulfur residues.

3-Methylthiophene.—After sweeping out the reaction vessel with carbon dioxide, 200 cc. of crude 50% isoprene was dripped into 800 g. of sulfur at 350 ± 10° at a rate of 5–10 cc. per minute. The combined contents of the receivers, after evaporation of the hydrogen sulfide, were then fractionally distilled, a yield of 30 g. (30%) of crude 3-methylthiophene being obtained. The recovered isoprene was immediately and repeatedly re-treated until no more methylthiophene was obtained, the final yield being 46 g. (47%). The low boiling fraction (50 cc.) was carbon disulfide and a mixture of amylenes originally present in the crude isoprene. 3-Methylthiophene possessing the following constants was obtained from the crude in 86% yield by a single fractional distillation: boiling point 114.9–115.4° (corrected) at 748 mm.; freezing point −55.8 to −56.2°; density d_4^{25} 1.009; refractive index n_D^{25} 1.5169; molecular refraction observed 29.4 (calculated 30.1).[4] It gave a pure blue indophenin reaction and formed an iodo compound when treated with iodine and mercuric oxide. From it were prepared chloromercuri-3-methylthiophene melting at 128° (alone and in a mixture with authentic material) and 3-methylthiophene-mercurithiocyanate melting at 167–168° with decomposition;[5] the mother liquor from the chloromercuri compound yielded no 2-methylthiophene-mercurichloride.

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[1] Meyer and Sandmeyer, *Ber.*, **16**, 2176 (1883).

[2] Steinkopf, *Ann.*, **428**, 123 (1922).

[3] Steinkopf, *ibid.*, **403**, 11 (1914).

[4] St. Opolski, *Chem. Centr.*, II, 1797 (1905).

[5] Steinkopf, *Ann.*, **424**, 33 (1921).

The temperature at which the sulfur is kept affects the yields: at 300° the reaction was slow (5% conversion per passage) while at 400° the ultimate yield was 41% and an inconveniently large amount of sulfur distilled over. Dilution of the isoprene with carbon bisulfide (1:1) increased the yield of crude 3-methylthiophene at 350° to 51%.

Thiophene.—Crude 50% butadiene[6] yielded 6% of thiophene when bubbled through molten sulfur at temperatures ranging from 320 to 420°. The same yield was obtained when pure liquid butadiene (from the tetrabromide) was dropped into the apparatus from a chilled separatory funnel. The thiophene boiled at 82–84°, had a density d_{15}^{20} 1.05, gave a blue indophenin reaction, and with mercuric chloride yielded 2-chloro-mercurithiophene which did not depress the melting point of authentic material. Carbon bisulfide was again noted as a by-product.

2,3-Dimethylthiophene.—A distillate fraction boiling at 45–160° was obtained from the pyrolysis products of a mixture of crepe rubber and zinc oxide. This fraction had previously been shown to contain about 4% of 3-methyl-1,3-pentadiene[7] mixed with mono-olefins and hydromatic compounds. One hundred grams of this material was dripped into boiling sulfur and gave 48 g. of crude product. The thiophene homologs were isolated therefrom in a manner similar to that previously described[8] and there were obtained 0.3 g. of 3-methylthiophene and 0.15 g. of 2,3-dimethylthiophene. The 2,3-dimethylthiophene was identified as the mercurichloride, melting at 215° (alone, or mixed with authentic material) and the mercurithiocyanate which blackened but did not melt at 205°.[5]

3,4-Dimethylthiophene.—From 50 cc. of pure dimethylbutadiene which had reacted with sulfur at 400–420° were recovered 10 cc. of unconverted material and 12.5 g. (31% yield) of 3,4-dimethylthiophene, which boiled at 145.5–148.5°, had a density d_{15}^{25} 0.994, a refractive index n_{D}^{25} 1.5187 and gave a blue indophenin reaction. For identification, its mercurichloride (melting at 139–140.5°), mercuriiodide (melting at 140–141°) and *bis*-2-(3,4-dimethylthienyl) mercury (melting at 153–154°) derivatives were prepared.[5]

Summary

A procedure is described for the conversion of diolefins into thiophene homologs by interaction with molten sulfur.

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[6] We are indebted to Dr. B. T. Brooks for a generous supply of this material.

[7] Midgley and Henne, THIS JOURNAL, **53**, 204 (1931); **51**, 1215 (1929).

[8] Midgley, Henne and Shepard, *ibid.*, **54**, 2957 (1932).

[CONTRIBUTION FROM KEDZIE CHEMICAL LABORATORY, MICHIGAN STATE COLLEGE]

Caffeine Derivatives. I. The 8-Ethers of Caffeine

BY RALPH C. HUSTON AND WINSTON F. ALLEN[1]

The extensive investigations and syntheses of compounds in the purine group by Emil Fischer and his associates include the preparation of only two 8-monoethers of caffeine, namely, methoxy- and ethoxycaffeine. Fischer's method,[2] later repeated by W. Wislicenus[3] and H. Biltz,[4] consisted simply in heating 8-chloro- or 8-bromocaffeine in a methyl or ethyl alcohol solution containing an excess of sodium or potassium alcoholate (sodium or potassium added in the form of the metal or hydroxide). Isoamyloxycaffeine was later prepared by the same general procedure.[5] The preparation of fifteen 8-phenyl ethers of caffeine was accomplished by A. Baumann.[6] The methods involved heating 8-chlorocaffeine with a phenol in the presence of an equivalent amount of potassium hydroxide. The reaction took place in an aqueous solution with refluxing, or under pressure at a higher temperature. Xylene was used as the solvent instead of water in some cases.

General Methods of Preparation

Both 8-chloro- and 8-bromocaffeine were used in the preparation of the sixteen ethers described in this paper. The former was used in most cases because of the ease and economy of preparation.[7] Fairly good yields of 8-methoxy- and 8-ethoxycaffeine were obtained by using an excess of metallic sodium or sodium hydroxide, as in Fischer's method. Attempts to prepare the higher alkyl and aryl ethers by the same procedure met with little or no success. A more successful procedure was adopted whereby an exactly equivalent amount of sodium alcoholate or phenylate was used.

In preparing the alkyl ethers, clean metallic sodium was quickly weighed out to 0.02 g. and cut into small pieces.[8]

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[1] Abstract from a thesis presented in partial fulfilment of the requirements for the Ph.D. degree by W. F. Allen, W. K. Kellogg Fellow at Michigan State College, 1932.

[2] E. Fischer, *Ber.*, **17**, 1785 (1884); *ibid.*, **30**, 569 (1897); *Ann.*, **215**, 261 (1882); and "Untersuchungen in der Puringruppe," pp. 38, 95–96, 162.

[3] W. Wislicenus and H. Körber, *Ber.*, **35**, 1992 (1902).

[4] H. Biltz and M. Bergius, *Ann.*, **414**, 59 (1917).

[5] Magnanini, private communication.

[6] A. Baumann, *Arch. Pharm. Inst. Univ. Berlin*, **10**, 127–147 (1913); and *Chem. Zentr.*, II, 2036 (1913).

[7] E. Fischer and Reese, *Ann.*, **221**, 336 (1883).

[8] Sodium in the form of "bird shot" was used sometimes to an advantage when kept in a toluene solution and weighed out as needed.