[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL CORPORATION]

The Redistribution Reaction. XI. Application to the Preparation of Carbon Tetraiodide and Related Halides

BY HAROLD SOROOS AND JAMES B. HINKAMP

Previously reported methods for the synthesis of carbon tetraiodide involve reactions of carbon tetrachloride with aluminum iodide,[1] calcium iodide,[2] boron iodide,[3] or lithium iodide,[4] or of iodoform with alkali hypoiodites.[5] None of these methods is entirely suitable for the preparation of other than small quantities of the compound. Those involving reaction of carbon tetrachloride with a metal iodide require heating the reactants in evacuated sealed tubes for long periods of time, and the reaction of iodoform with alkali hypoiodites yields a product contaminated with iodoform, which is difficult to remove.

Recently, in connection with studies made in this Laboratory for which relatively large amounts of pure carbon tetraiodide were required, it was found that the compound can be prepared simply and in good yield from readily obtainable materials by application of the redistribution reaction.[6]

A mixture of carbon tetrachloride, excess methyl iodide and a catalytic amount of aluminum chloride is heated in a vessel fitted with a distilling column, allowing the methyl chloride produced in the reaction to distill as rapidly as formed. When no more methyl chloride will distill, showing that conversion of the tetrachloride to carbon tetraiodide is complete,[7] the aluminum salts are extracted with water and the crude product is separated from the excess methyl iodide, washed with water, alcohol, and ether and dried *in vacuo*. Except for slight decomposition of the product resulting from the action of light and traces of oxygen, there are no side reactions. The yield is apparently quantitative, apart from handling losses.

The identity and purity of the recrystallized product were determined by hydrolysis with silver nitrate solution and measurement of the gas evolved,[8] and by oxidation with air and titration of the liberated iodine.[9] These analyses established the product to be carbon tetraiodide and showed that its purity was above 99 mole per cent.

By judicious choice of reactants, the procedure described above may be applied to the preparation of other alkyl halides. For example, iodoform and bromoform have been obtained in good yields by interaction of chloroform with methyl iodide and ethyl bromide, respectively.

Experimental

Carbon Tetraiodide.—The apparatus consisted of a 500-ml. two-necked flask, equipped with a vapor-proof mechanical stirrer[10] and a 1 × 40-cm. distilling column packed with glass helices and bearing a low-temperature distillation head. In a typical experiment the flask was charged with 108 g. (0.7 mole) of carbon tetrachloride and 418 g. (2.94 moles) of methyl iodide. Both reagents had previously been distilled from aluminum chloride. Two grams (0.015 mole) of aluminum chloride (Mallinckrodt) was added, stirring was started, and an oil-bath at 40° was raised around the flask. Reaction started immediately, and the methyl chloride produced in the reaction was distilled as rapidly as it formed. After eighty minutes the evolution of methyl chloride ceased, and there remained in the flask a mass of dark red crystals of carbon tetraiodide wet with methyl iodide. After stirring the mixture one hour longer, 100 ml. of air-free water was added, and the mixture was stirred thoroughly to dissolve the aluminum salts. Following this, the crystalline product was filtered under nitrogen, washed successively with 50 ml. of air-free water, two 15-ml. portions of ethyl alcohol, and two 15-ml. portions of ether, and, finally, was dried *in vacuo*. The yield of carbon tetraiodide was 335 g., or 92% based on the carbon tetrachloride charged.

Material for analysis was obtained by recrystallization from benzene *in vacuo*. The purified material was analyzed for iodine by the method of Kharasch, *et al.*[9] *Anal.* Calcd. for CI_4: I, 97.7. Found: I, 97.4. This compares favorably with the best analysis of carbon tetraiodide previously reported, 97.4%.[9]

Samples of 1.8946 g. (3.65 millimoles) and 0.6875 g. (1.32 millimoles) of the purified material were hydrolyzed with 20% aqueous silver nitrate solution, in accordance with the method of Lantenois,[8] and gave 81.5 cc. (3.64 millimoles) and 29.5 cc. (1.32 millimoles) of gas, respectively. Analysis showed the gas to be a mixture of 98.4% carbon monoxide and 1.6% carbon dioxide.

Bromoform.—To the apparatus used for the preparation of carbon tetraiodide were charged 414 g. (3.8 moles) of ethyl bromide, 143 g. (1.2 moles) of chloroform, and 8.5 g. (0.07 mole) of aluminum chloride. Stirring was started and the mixture was heated gently, allowing the ethyl chloride produced in the reaction to distill as rapidly as formed. When no more ethyl chloride would distill, the reaction mixture was washed with water to remove the aluminum salts, and was fractionally distilled. The yield of bromoform distilling at 150–152° was 272 g., or 90% based on the chloroform charged.

Iodoform.—To a 500-ml. flask fitted with a vapor-proof mechanical stirrer and a Hopkins-type reflux condenser were charged 119.4 g. (1.0 mole) of chloroform, 426 g. (3 moles) of methyl iodide, and 5 g. (0.04 mole) of aluminum chloride. Stirring was started, a bath at 40° was raised around the flask, and the reflux condenser was maintained at −25 to −20° by addition of Dry Ice to trichloroethylene. The methyl chloride produced in the reaction was allowed to distill as fast as formed. When no more methyl chloride would distill, the canary-yellow

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(1) Gustavson, *Ann.*, **172**, 173 (1874).

(2) Spindler, *ibid.*, **231**, 264 (1885); Lantenois, *Compt. rend.*, **156**, 1385 (1913).

(3) Moissan, *ibid.*, **113**, 20 (1891).

(4) Lantenois, *J. pharm. chim.*, **10**, 185 (1914).

(5) Robineau and Rollin, *Mon. sci.*, [**4**] **VIII**, 341 (1894).

(6) Calingaert and Beatty, THIS JOURNAL, **61**, 2784 (1939); Calingaert, Soroos, Hnizda and Shapiro, *ibid.*, **62**, 1545 (1940).

(7) As methyl chloride is removed, the composition of the redistribution mixture: $CH_3Cl + CH_3I + CCl_4 + CCl_3I + CCl_2I_2 + CClI_3 + CI_4$, changes in the direction of increasing the concentration of carbon tetraiodide, until, ultimately, a mixture of only carbon tetraiodide and the excess methyl iodide remains.

(8) Lantenois, *Compt. rend.*, **156**, 1029 (1913).

(9) Kharasch, Alsop and Mayo, *J. Org. Chem.*, **2**, 76 (1937).

(10) Calingaert, *Ind. Eng. Chem.*, *Anal. Ed.*, **12**, 51 (1940).

crystalline residue was washed with water, filtered on a Büchner funnel, washed with ethyl alcohol and dried in air. The yield of iodoform was 375 g., or 95%; m. p. 119°.

Summary

Carbon tetraiodide, iodoform and bromoform are prepared readily and in good yield by redistribution reactions between carbon tetrachloride and methyl iodide, chloroform and methyl iodide, and chloroform and ethyl bromide, respectively.

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The Synthesis and Antihemorrhagic Activity of 5-Methyl-4,7-thionaphthenequinone

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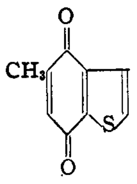
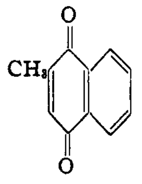
It is well known that the chemical and physiological properties of thiophene compounds are frequently very similar to those of the analogous benzene derivatives. A good deal of attention has been devoted to the synthesis and study of compounds differing from a vitamin or other physiologically active substance by having a sulfur atom instead of a vinyl group, or the converse.[1]

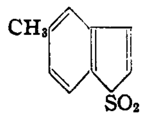
The present paper deals with the synthesis and testing of 5-methyl-4,7-thionaphthenequinone I, which is an isostere of 2-methyl-1,4-naphthoquinone II. It was of special interest to study compound I, since in most other cases in the vitamin K series any substitution in the benzenoid ring of II usually caused an almost complete loss of activity.[2]



I



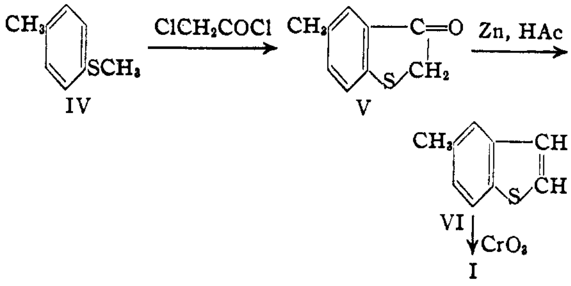
II



III

It was found that the thionaphthenequinone I could be obtained in 10% yield by oxidation of 5-methylthionaphthene with chromic acid in acetic acid solution.[3] When the oxidation was attempted using hydrogen peroxide in acetic acid,[4] which is a useful method of obtaining quinones in some cases, a product was obtained having the composition of the sulfone III.

The 5-methylthionaphthene was obtained by reduction of the corresponding keto compound (V) with zinc and acid[5]; the latter was prepared from methyl p-tolyl sulfide, chloroacetyl chloride and aluminum chloride.[6] In this process, a by-product was isolated in small amount, which was not obtained by Auwers and Arndt.[6]



The structure of compound I was evident from the fact that it formed a diacetate on reductive acetylation, and gave a positive Craven's test[7] for an α-quinone. The ultraviolet absorption spectrum, as shown in the accompanying curves, is similar to that of 2-methyl-1,4-naphthoquinone II, but contains an additional peak at short wave lengths which is usually associated with the presence of sulfur.[8]

The vitamin K activity of compound I was determined in the usual manner,[9] and was found to be approximately 3% of that of 2-methyl-1,4-naphthoquinone, as a result of several runs.

Experimental[10]

Methyl p-tolyl sulfide (IV) was prepared in 94% yield by the action of methyl sulfate and alkali on p-thiocresol; b. p. 94-95° (13 mm.).[11]

5-Methyl-3-keto-1,2-dihydrothionaphthene (V).—To a cold solution of 10 g. of methyl p-tolyl sulfide and 8.5 g. of chloroacetyl chloride in 100 g. of carbon disulfide was added in small portions 12 g. of anhydrous aluminum chloride. After addition of the aluminum chloride, the reaction mixture was slowly brought to refluxing and the bath maintained at 60-65° for five hours. The solvent was re-

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(1) For examples of such "isosteric" compounds, see Erlenmeyer, Berger and Leo, *Helv. Chim. Acta*, **16**, 733 (1933); Tracy and Elderfield, *J. Org. Chem.*, **6**, 54 (1941); Woolley and White, *J. Biol. Chem.*, **149**, 285 (1943); Blicke and Tsao, THIS JOURNAL, **66**, 1645 (1944); English, Clapp, Cole, Halverstadt, Lampen and Roblin, *ibid.*, **67**, 295 (1945).

(2) Doisy, Binkley and Thayer, *Chem. Rev.*, **28**, 501 (1941).

(3) A second method of synthesizing I is described in the accompanying paper by Kitchen and Sandin.

(4) Arnold and Larson, *J. Org. Chem.*, **5**, 250 (1940).

(5) Auwers, *Ann.*, **408**, 282 (1915); according to Auwers and Thies (*Ber.*, **53**, 2285 (1920)) the 3-hydroxythianaphthenes exist principally in the keto form.

(6) Auwers and Arndt, *Ber.*, **42**, 537 (1909).

(7) Craven, *J. Chem. Soc.*, 1605 (1931).

(8) Landolt-Börnstein, "Tabellen," 5 Aufl., Eg. IIb, p. 706, Eg. IIIb, p. 1419. The absorption curve of 2-methyl-1,4-naphthoquinone as previously reported by Ewing, Vandenbelt and Kamm, *J. Biol. Chem.*, **131**, 345 (1939), agrees closely with the curve as we observed it. Our curves were obtained with a Beckman ultraviolet spectrophotometer.

(9) Tarbell, Fukushima and Dam, THIS JOURNAL, **67**, 197 (1945).

(10) All melting points corrected; microanalyses by Dr. Carl Tiedcke, New York City.

(11) The reported value[6] is 94° (31 mm.); the figure of 31 mm. is probably a misprint.