It weighed 790 mg. (97%) and melted at 121–126°. Crystallization from ethanol raised the melting point to 138–140°; $\nu_{max}$ 1725 (C=O), 1550 and 1370 ($NO_2$), 1410, and 960 cm.$^{-1}$. The n.m.r. spectrum in $CCl_4$ shows bands at $\tau$ 5.65 (C-6 H, $W^{1/2}$ 25 c.p.s., axial), 8.94 (C-19, singlet), 9.14 (C-26 and C-27, doublet, $J$ = 6.5 c.p.s.), and 9.32 (C-18, singlet).

*Anal.* Calcd. for $C_{27}H_{45}NO_3$: C, 75.13; H, 10.51; N, 3.25. Found: C, 75.33; H, 10.49; N, 3.42.

Nitro ketone **8a** was also obtained by oxidation of nitro alcohol **7** with 8 $N$ chromic acid in acetone (Jones reagent); it gave a yellow 2,4-dinitrophenylhydrazone, m.p. 184–186° after recrystallization from methanol–acetone.

**6α-Nitroandrostane-3β,17β-diol Diacetate** (**6b**).—Acetylation of 140 mg. of diol **8** in 4 ml. of acetic anhydride and 1 ml. of pyridine at room temperature for 12 hr. gave 120 mg. (68%) of diacetate **6b**, m.p. 183–186°. Two crystallizations from methanol–water furnished the analytical sample, m.p. 187–189°; $\nu_{max}$ 1730 (acetate C=O), 1545 and 1370 ($NO_2$), 1238, 1025, and 900 cm.$^{-1}$.

*Anal.* Calcd. for $C_{23}H_{35}NO_6$: C, 65.53; H, 8.37; N, 3.32. Found: C, 65.43; H, 8.38; N, 3.51.

**6α-Nitroandrostane-3,17-dione** (**8b**).—A solution of 200 mg. of the nitrodiol **7b** in 5 ml. of glacial acetic acid was treated with 200 mg. of chromium trioxide in 5 ml. of 80% aqueous acetic acid. After 12 hr. at room temperature the solution was poured into ice water, made basic with sodium hydroxide, and then just neutralized with 10% hydrochloric acid. The crude dione which precipitated weighed 80 mg. and melted at 235–240°. Two crystallizations from aqueous methanol furnished **8b**, m.p. 244–246°. The infrared spectrum showed peaks at 1740 (C-17, =O), 1712 (C-3, =O), 1560, 1537, 1376, and 778 cm.$^{-1}$ ($NO_2$).

*Anal.* Calcd. for $C_{19}H_{27}NO_4$: C, 68.44; H, 8.16; N, 4.20. Found: C, 68.32; H, 8.29; N, 4.41.

---

# The Preparation of Thiones in the Presence of Anhydrous Hydrogen Fluoride

R. M. ELOFSON, LESLIE A. BAKER, F. F. GADALLAH, AND R. A. SIKSTROM

*Contribution No. 244 from the Research Council of Alberta, Edmonton, Alberta, Canada*

*Received December 9, 1963*

A rapid and facile preparation of aromatic and aliphatic thials and thiones or their polymeric forms is outlined. The method consists of the reaction of the corresponding aldehyde or ketone with hydrogen sulfide in the presence of anhydrous hydrogen fluoride. The scope and limitations of the reaction are described. The results are formulated on the basis of an optimum acid-catalyst concentration in accordance with that demonstrated for many other aldehyde and ketone reactions.

In the course of an electrochemical study on aromatic thiones in this laboratory it became necessary to prepare a number of thiones with a wide range of appended substituents. Thiones have previously been prepared in a number of ways depending on the availability and reactivity of the starting materials. $p,p'$-Dimethoxythiobenzophenone can be prepared from thiophosgene and anisole by the Friedel–Crafts reaction.[1] Michler's thione, $[(CH_3)_2NC_6H_4]_2C{=}S$, has been best prepared by treating auramine with hydrogen sulfide.[2] However, it can also be made by the reaction of Michler's ketone with $P_2S_5$.[3] $p$-Dimethylaminothiobenzophenone has been made by the action of hydrogen sulfide on the corresponding anil.[4] In a few cases sulfur changes a methylene group to a thiocarbonyl[5] as in the preparation of Michler's thione from $p,p'$-dimethylaminodiphenylmethane.

The most widely used method of preparation of thials and thiones depends upon the conversion of an aldehyde or ketone to the corresponding thio compound by hydrogen sulfide in the presence of alcoholic hydrogen chloride.[6] By this method all aliphatic ketones and all aldehydes can be converted to the corresponding thio derivatives which can only be isolated in the form of their dimeric, trimeric, or polymeric derivatives. Aromatic ketones are less reactive but this method has been successfully used to prepare thiobenzophenone, α-naphthylphenylthione, $p$-phenylthiobenzophenone, $p$-methylbenzothione,[7] and thiofluorenone.[8]

$$Ar_2CO + H_2S \xrightleftharpoons{C_2H_5OH,\ HCl} Ar_2C{=}S + H_2O \qquad (1)$$

According to eq. 1 the reaction is reversible and considerable difficulty is encountered in preparing pure materials. In an attempt in this laboratory to force Michler's ketone to react directly with hydrogen sulfide, the ketone was dissolved in liquid anhydrous hydrogen fluoride and the cooled solution was treated with hydrogen sulfide. This resulted in an almost quantitative yield on Michler's thione. The scope and limitations of this reaction is the subject of this paper.

The original selection of liquid anhydrous hydrogen fluoride as a medium for the reaction was based on a number of considerations. This material is a good dehydrating agent, an acidic catalyst, and a good solvent for ketones, all of which would be favorable for thione formation. Unlike some other possible materials, such as sulfuric acid, hydrogen fluoride is neither an oxidizing nor a reducing reagent.

Experimental results with formaldehyde, benzaldehyde, acetone, Michler's ketone, and 3,3′-dinitrobenzophenone fully confirmed expectations. When hydrogen sulfide was passed into chilled solutions of the aldehydes or ketones in anhydrous hydrogen fluoride, quantitative yields of the trimeric thials and of the thiones were obtained.

When the reaction was attempted on benzophenone, much less satisfactory results were obtained. Initially, upon passing hydrogen sulfide into a solution of benzophenone in anhydrous hydrogen fluoride, very little thione was produced. However, if the temperature was allowed to rise and most of the hydrogen fluoride was allowed to evaporate, a blue solution was obtained which was shown by spectrophotometric analysis to contain about 60% thione and 40% ketone. Similar results were obtained with $p$-methylbenzophenone, but with α-naphthylphenyl ketone only about 10% conver-

---

(1) L. Gattermann, *Ber.*, **28**, 2869 (1895).

(2) T. S. Fehrmann, *ibid.*, **20**, 2844 (1887); D. S. Tarbell and V. P. Wystrock, *J. Am. Chem. Soc.*, **68**, 2110 (1946).

(3) Badische Anil-u Sodafabuk, German Patent 3,8074 (1886).

(4) C. Reddelien and H. Danilof, *Ber.*, **54**, 3142 (1921).

(5) R. Mohlen, M. Heinze, and R. Zimmermann, *ibid.*, **35**, 375 (1902).

(6) H. Staüdinger and H. Freudenberger, *ibid.*, **61**, 1576 (1928); *Org. Syn.*, **11**, 94 (1931).

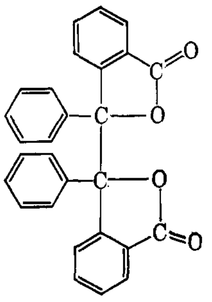
(7) R. W. Bost and B. O. Cosby, *J. Am. Chem. Soc.*, **57**, 1404 (1935).

(8) E. Campaigne and W. B. Reid, Jr., *ibid.*, **68**, 769 (1946).

sion could be demonstrated. In order to get satisfactory yields of pure products from benzophenone and related compounds, it was found necessary to add an alcohol to the reaction mixture. By judicious selection of a suitable ratio of alcohol to hydrogen fluoride, a solution of the ketone could be obtained from which the thione could be precipitated in quite pure form by addition of hydrogen sulfide. Optimum results with benzophenone were obtained with a mixture of 40% hydrogen fluoride and 60% methanol, whereas *n*-butyl alcohol in the same proportions produced the best results with $\alpha$-naphthylphenyl ketone. Detailed directions for reaction of a number of typical carbonyl compounds are given in the Experimental section.

In general, the reaction of carbonyl compounds with hydrogen sulfide in the presence of hydrogen fluoride is much faster than the reaction in ethanolic hydrogen chloride. Only one compound that has been investigated, xanthone, failed to react under at least one of the experimental conditions described, but the products obtained with various other compounds show the limitations of the reaction. Fluorenone reacts rapidly in anhydrous hydrogen fluoride to produce quantitative yields of the dimeric form of thiofluorenone. Little if any of the monomer is produced unless methanol and short reaction times are used. Since the monomer can be isolated quite readily from the reaction in ethanol and hydrogen chloride, the new method is plainly inferior if it is desired to inhibit dimerization.[9]

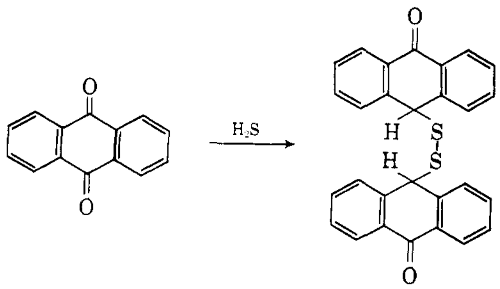
While *p*-carboxybenzophenone was converted without difficulty to the corresponding thione, *o*-carboxybenzophenone was converted in significant yield to the dimeric dilactone I.



I

While no evidence of reduction of nitro groups in nitrobenzophenones by hydrogen sulfide was observed in anhydrous hydrogen fluoride, addition of boron trifluoride to the reaction medium resulted in the production of amines which were not investigated further.

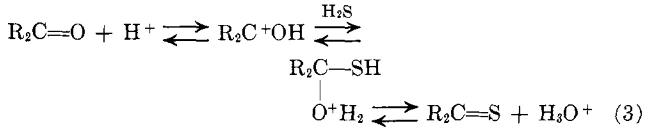
Anthraquinone dissolved in anhydrous hydrogen fluoride reacted rapidly with hydrogen sulfide to produce a yellow material which is believed to be the dianthrone disulfide according to eq. 2. This material has an average sulfur content of about 12% corresponding to a disulfide. All fractions have a carbonyl absorption at 1662 (KBr); anthrone, 1660; and anthraquinone, 1690 cm.$^{-1}$. It dissolves in strong alkali to produce a red solution which is readily oxidized by hydrogen peroxide to anthraquinone and sulfate and by air to anthraquinone and sulfide. Molecular weight measurements in sulfolane[10] gave values up to 450 indicative of dimerization. No reaction between anthraquinone and hydrogen sulfide was observed in ethanolic hydrogen chloride.



(2)

## Discussion

The reaction of hydrogen sulfide with ketones in the presence of hydrogen fluoride involves the nucleophilic attack of hydrogen sulfide on the protonated ketone[11] according to eq. 3.



$$R_2C{=}O + H^+ \rightleftharpoons R_2C^+OH \overset{H_2S}{\rightleftharpoons} \underset{O^+H_2}{R_2C{-}SH} \rightleftharpoons R_2C{=}S + H_3O^+ \quad (3)$$

In the case of aldehydes, aliphatic ketones, Michler's ketone, and 3,3'-dinitrobenzophenone, the reaction goes smoothly indicating that anhydrous hydrogen fluoride is able to protonate ketones such as the latter two which do not react with hydrogen sulfide in alcohol and hydrochloric acid. However, the failure of simple aromatic ketones to react satisfactorily with the reagent without the addition of diluents and of xanthone to react at all, required comment.

According to eq. 3, if the positive charge is delocalized or centered elsewhere in the molecule, reaction would be inhibited. The failure of xanthone to react under all conditions tried is attributed to the predominance of a salt in which the positive charge is centered at the rings instead of at the ketonic carbon.[12]

In the case of benzophenone, another factor may be operating. Benzophenone protonates readily under all conditions described here, but presumably the delocation of charge depletes the positive charge on the carbonyl so that not enough charge persists on this carbon to react with hydrogen sulfide present. Since the hydrogen sulfide would also be largely protonated in anhydrous hydrogen fluoride, addition of methanol should favor the formation of thione by releasing more hydrogen sulfide from its protonated form and thus encourage nucleophilic attack on the protonated carbonyl. The negative substituents in 3,3'-dinitrobenzophenone and Michler's ketone preserve enough charge on the carbonyl carbon of these compounds to react without addition of methanol.

These postulates were checked by the addition of sodium fluoride and boron trifluoride to the reaction medium containing benzophenone and anhydrous hydrogen fluoride. Sodium fluoride, which lowers the acidity of hydrogen fluoride,[13] caused a rapid development of a blue color indicative of thione formation in

---

[9] See also J. H. Wood and R. W. Bost, *J. Am. Chem. Soc.* **59**, 1011 (1937).

[10] J. C. Wood, S. E. Moschopedis, and R. M. Elofson, *Fuel*, **40**, 193 (1961).

[11] Y. Nomura and Y. Takeorich, *J. Chem. Soc. Japan*, 1743 (1960); E. Campaigne, "Organic Sulfur Compounds," N. Kharasch, Ed., Pergamon Press Inc., New York, N. Y., 1961, p. 141.

[12] D. Cook, *Can. J. Chem.*, **39**, 1184 (1961).

[13] E. L. Macken, A. Hofstrau, and J. H. van der Waals, *Trans. Faraday Soc.*, **54**, 66 (1958).

the presence of hydrogen sulfide. Boron trifluoride, in contrast, known to increase the acidity of anhydrous hydrogen fluoride,[13] inhibited development of a blue color until evaporation of most of the hydrogen fluoride. This concept of an optimum acidity for thione formations accords with the findings of Jenek[14] for reaction of ketones with nitrogen bases. The optima were shown to be due to opposing effects of general acid catalysis and decrease in concentration of the attacking free nitrogen base due to conversion to the conjugate acid at low pH. Because of the greater acidity of hydrogen sulfide, the optimum acidity for thione formation is much greater than for semicarbazone formation.

## Experimental

Anhydrous hydrogen fluoride was obtained in cylinders from the Mathieson Co., East Rutherford, N. J., and was used without purification. Hydrogen sulfide was obtained in cylinders from the same source and also was used directly.

Small scale runs of less than 5 g. may be carried out in polyethylene graduates, whereas larger runs are best carried out in polyethylene erlenmeyer flasks. Hydrogen fluoride–methanol mixtures containing crystals can be filtered directly through Whatman No. 1 filter paper using polyethylene Büchner funnels. Anhydrous hydrogen fluoride can be best handled by evaporation of most of the acid before pouring into a solution of bicarbonate. The use of rubber gloves, safety glasses, and shields is mandatory.

More sensitive thiones such as benzothione should be protected from light and air by standard methods. Solvent extracts should be dried as quickly as possible to prevent hydrolysis. Some thiones can be usefully purified by chromatography over Florisil[15] (Floridin Co., Talahassee, Fla.). Some procedures are described briefly below.

**Michler's Thione.**—Michler's ketone (2 g.) was dissolved in 30 ml. of anhydrous hydrogen fluoride cooled in Dry Ice and acetone to about −10 to −20°. Hydrogen sulfide was passed into the solution for 2 hr. while the temperature was allowed to become ambient. The solution was poured with care into 5% sodium bicarbonate; the thione was taken up in chloroform, washed with sodium bicarbonate, and dried over sodium sulfate. The thione was recrystallized either from a small volume of chloroform or from a mixture of chloroform and hexane. The yield of nearly pure material was quantitative. The recrystallized material had m.p. 208–209°, lit.[16] m.p. 202–204° for Michler's thione.

**3,3′-Dinitrobenzothione.**—*p,p′*-Dinitrobenzophenone (5 g.) was dissolved in 40 ml. of anhydrous hydrogen fluoride cooled to −30°. Hydrogen sulfide was passed into the solution for 2 hr. while the temperature was allowed to become ambient. A 4-g. sample of crystals was obtained, m.p. 131.5–132.5°.

*Anal.* Calcd. for $C_{13}H_8N_2O_4S$: S, 11.11. Found: S, 10.85.

**Trithiobenzaldehyde.**—Benzaldehyde (5 g.) was dissolved in 30 ml. of anhydrous hydrogen fluoride cooled to −40°. Hydrogen sulfide was passed through the solution until the temperature became ambient and most of the hydrogen fluoride evaporated. The resulting solution was poured into sodium bicarbonate solution and extracted with hexane. The extract was dried over potassium hydroxide pellets and evaporated to produce a quantitative yield of the B form of trithiobenzaldehyde, m.p. 225–227°, lit.[17] m.p. 226°.

**Trithiane.**—Paraformaldehyde (5 g.) was dissolved in 30 ml. of anhydrous hydrogen fluoride cooled to −40°. Hydrogen sulfide was passed into the solution and the temperature was allowed to rise to room temperature. After most of the hydrogen fluoride had evaporated, the residue was poured into sodium bicarbonate solution and filtered, yielding 6.5 g. of trithiane, m.p. 212–215°, lit.[18] m.p. 216°, without further crystallization.

**Dianthrone Disulfide.**—Anthraquinone (5 g.) was dissolved in 30 ml. of anhydrous hydrogen fluoride cooled to −20°. Hydrogen sulfide was passed into the solution overnight while the temperature was allowed to become ambient. The residue was poured into sodium bicarbonate solution and extracted with chloroform. The chloroform extract was washed with sodium bicarbonate solution and dried over sodium sulfate. Upon evaporation of the chloroform, a yellow to orange solid was produced, m.p. 151–155° (indefinite). The material, crystallized from benzene–hexane mixtures, produced a variety of fractions, some with m.p. 174–175°. The crude material had a sulfur content of about 10–12%. Work is continuing on characterization of this material.

**Benzothione.**—Two grams of benzophenone was dissolved in 20 ml. of anhydrous hydrogen fluoride. A 30-ml. sample of absolute methanol was added to the solution, cooled to −20°, while hydrogen sulfide was passed into the reaction medium. Brilliant blue crystals were formed which, after 1.5 hr. of reaction, were filtered cold, washed with cold methanol, and sealed *in vacuo* in a glass tube, yielding 1.5 g. The nearly pure crystals had m.p. 50–52° and were shown to be free of benzophenone by lack of carbonyl absorption in the infrared. Somewhat higher yields can be obtained by using more concentrated solutions of benzophenone but coprecipitation of benzophenone results in a somewhat impure product.

***p,p′*-Dimethoxybenzothione.**—Five grams of dimethoxybenzophenone was dissolved in 20 ml. of anhydrous hydrogen fluoride and 20 ml. of methanol. The solution was cooled to −30°, and hydrogen sulfide was passed in overnight. The excess hydrogen fluoride was removed at the water pump. The residue was extracted with hexane, washed with sodium bicarbonate, and dried over sodium sulfate. The hexane was removed and the material, recrystallized from absolute ethanol, yielded 4.7 g., m.p. 116–118°, lit.[7] m.p. 115° for dimethoxybenzothione.

***α*-Naphthylphenylthione.**—*α*-Naphthylphenyl ketone (2.6 g.) was dissolved in 15 ml. of anhydrous hydrogen fluoride at −20°. To this solution was added 25 ml. of *n*-butyl alcohol. Hydrogen sulfide was passed into the solution for 1 hr. and the temperature was allowed to rise slowly. A 2.0-g. sample of blue crystals was filtered off, m.p. 112°, lit.[7] m.p. 110° for *α*-naphthylphenylthione.

***p*-Dimethylaminobenzothione.**—*p*-Dimethylaminobenzophenone (10 g.) was dissolved in 100 ml. of anhydrous hydrogen fluoride and 100 ml. of absolute methanol. Hydrogen sulfide was passed into the solution for 4 hr. while the temperature was allowed to become ambient. The reaction mixture was poured into sodium bicarbonate solution, extracted with chloroform, and dried over sodium sulfate. Addition of carbon tetrachloride yielded 9.5 g. of dark red, nearly black crystals, m.p. 86°, lit.[4] m.p. 86° for *p*-dimethylaminobenzothione.

**3,3′-Diphenyl-3,3′-diphthalidyl.**—*o*-Carboxybenzophenone (2 g.) was dissolved in 35 ml. of anhydrous hydrogen fluoride and 18 ml. of methanol. Hydrogen sulfide was passed through the reaction mixture while 30 ml. of additional methanol was added over a period of 2 hr. White crystals formed which were removed by filtration from the slightly blue solution. These crystals weighed 0.5 g. and had a m.p. of 243–247°. The material was recrystallized from benzene, m.p. 258–260°, lit.[19] m.p. 265° for 3,3′-diphenyl-3,3′-diphthalidyl; C=O stretch in carbon tetrachloride, 1782 cm.$^{-1}$.

**Acknowledgment.**—The authors are indebted to Dr. H. W. Habgood of this laboratory for many helpful discussions in preparation of the manuscript and to Dr. J. C. Wood for the molecular weight determinations.

---

(14) W. P. Jenek, *J. Am. Chem. Soc.*, **81**, 475 (1959).

(15) R. H. Abeles, R. F. Hutton, and F. H. Westheimer, *ibid.*, **79**, 712 (1957).

(16) D. S. Tarbell and V. P. Wystrack, *ibid.*, **68**, 2110 (1946).

(17) A. H. Ford-Moore, R. A. Peters, and R. W. Wakelin, *J. Chem. Soc.*, 1754 (1949).

(18) H. Brintzinger, H. Koddebusch, K. E. Kling, and G. Jung, *Ber.*, **85**, 455 (1952).

(19) F. Ullmann, *Ann.*, **291**, 17 (1896).