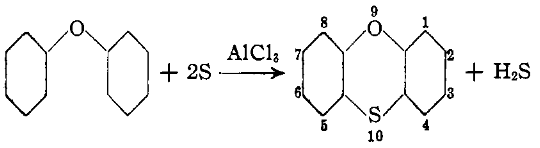
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Phenoxthin. I. A Comparison of the Directive Influences of Oxygen and Sulfur

BY C. M. SUTER, J. P. MCKENZIE AND CHARLES E. MAXWELL

It was claimed some years ago[1] that in the nitration of 2-methoxyphenyl methyl sulfide substitution occurred primarily ortho to the sulfur. This conclusion was subsequently[2] shown to be incorrect, both oxidation and nitration having taken place, the nitro group going para to the ether linkage. Since it was probable that oxidation of the sulfur had occurred before nitration the problem of the relative directive influences of the sulfide and ether groups was left unsettled. To throw more light on this situation a convenient method for the preparation of phenoxthin (phenothioxin) I has been developed and various substitution reactions of this compound have been investigated.

Phenoxthin has been prepared by a series of reactions starting with 3,5-dinitro-4-chlorobenzoic acid and thiocatechol,[3] from phenoxtellurine and sulfur,[4] and by the action of sulfur and aluminum chloride upon phenyl ether.[5] Although Ferrario[5a] claimed practically quantitative yields for this last method, repetition of the reaction according to his directions gave mostly tarry products. However, by the use of an excess of phenyl ether it is possible to obtain 67–72% yields of pure phenoxthin without difficulty. A number of experiments in which the ratio between the reactants was varied indicated that best results are obtained by the use of 1.3 moles of phenyl ether, 1 atom of sulfur and 0.5 mole of aluminum chloride. Since the excess ether apparently functions as a solvent the reaction was also carried out in carbon disulfide and in *sym*-tetrachloroethane. No appreciable change occurred at the boiling point of the carbon disulfide solution while in the tetrachloroethane the yield was 48% at steam-bath temperature.



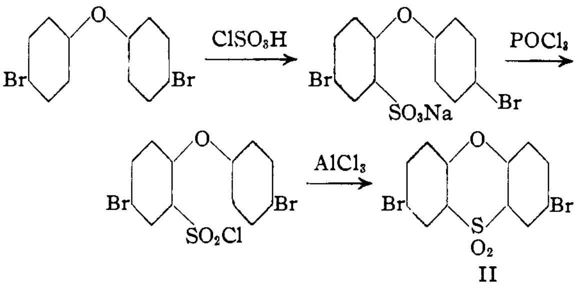
I

Since the preparation of 3-chlorophenoxthin from *p*-chlorophenyl phenyl ether and sulfur has been reported[5b] it seemed probable that the *p*-bromo compound could likewise be converted into a phenoxthin derivative. Numerous attempts to accomplish this were unsuccessful, only tarry reaction products being recovered. Analogous results were obtained with di-(*p*-bromophenyl) ether.

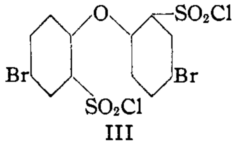
The claim of Ferrario[5a] that heating phenoxthin with metallic copper to 250° yields dibenzofuran could not be verified. Refluxing the phenoxthin (b. p. about 285–290°) with copper bronze or freshly prepared reduced copper gave no evidence of appreciable change. Quite possibly a higher temperature would effect this reaction but this was not investigated.

Apparently no substitution reactions of phenoxthin have been investigated hitherto. It has now been shown definitely that in halogenation, the Friedel–Crafts reaction and sulfonation, substituents enter the phenoxthin nucleus para to oxygen only.

The dibromophenoxthin obtained by direct bromination was demonstrated to be the 3,6-compound[6] by comparing its 10-dioxide (II) with that synthesized as follows



II



III

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[1] Holmes, Ingold and Ingold, *J. Chem. Soc.*, **1684** (1926).

[2] Pollard and Robinson, *ibid.*, 3090 (1926); Ingold and Ingold, *ibid.*, 3092 (1926).

[3] Mauthner, *Ber.*, **39**, 1340 (1906).

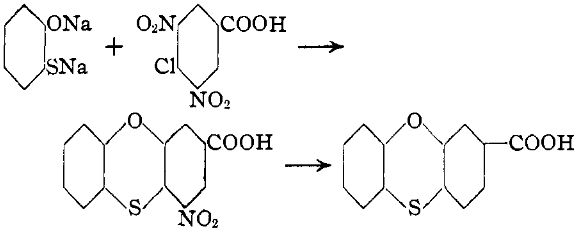
[4] Drew, *J. Chem. Soc.*, 511 (1928).

[5] (a) Ferrario, *Bull. soc. chim.*, [4] **9**, 536 (1911); (b) Ackermann, German Patent 234,743, *Chem. Zentr.*, **82**, I, 1768 (1911); *Frdl.*, **10**, 153.

[6] It has just recently come to our attention that this substance has also been prepared by Stevenson and Smiles, *J. Chem Soc.*, 718 (1931), who obtained it from 2,5,5'-tribromo-2'-hydroxydiphenyl sulfide. In their system of nomenclature it is designated as 2,8-dibromodibenzothioxin.

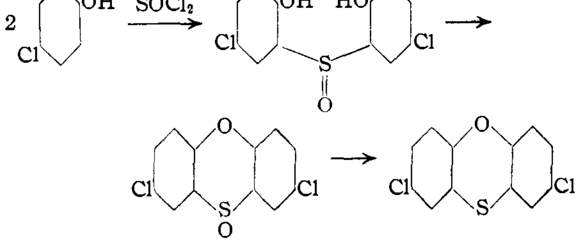
The intermediate 2-(4-bromophenoxy)-5-bromobenzenesulfonyl chloride could not be obtained by the action of excess chlorosulfonic acid upon di-(4-bromophenyl) ether, this reaction giving a disulfonyl chloride (III) in which the second sulfonyl group is probably also ortho to oxygen.

The structure of the acetylphenoxthin obtained by the action of acetyl chloride and aluminum chloride upon phenoxthin was shown to be the 3-compound by oxidation to the corresponding acid with bleaching powder. This acid was found to be not identical with the one obtained by Mauthner[3] by the reactions



Direct evidence for its structure was found in the synthesis from 3-bromophenoxthin through the Grignard reagent. Since the structure of the dibromophenoxthin is known, that of the monobromo compound is also certain. Rather surprisingly the preparation of a Grignard reagent from 3-bromophenoxthin was attended by considerable difficulty. In only one of various attempts did reaction occur and here the yield of acid was low. By analogy it is probable that the mono- and dibenzoylphenoxthins prepared by the Friedel–Crafts method are the 3- and 3,6-compounds, respectively.

Attempts to determine the structure of the phenoxthindisulfonic acid by replacement of the sulfo groups with bromine in aqueous solution were unsuccessful. Upon heating the disulfonyl chloride with phosphorus pentachloride, however, a dichlorophenoxthin, m. p. 134–135°, resulted. This corresponds to the properties of the dichlorophenoxthin described by Hilditch and Smiles[7] who obtained their product by the following reactions



Experimental

Preparation of Phenoxthin.—Various sized runs of this preparation have been made. The best yield so far obtained was from the following procedure. A mixture containing 1700 cc. (10.4 moles) of phenyl ether, 256 g. (8 moles) of sulfur and 512 g. (3.84 moles) of aluminum chloride was heated on a steam-bath in a five liter flask fitted with a reflux condenser until the evolution of hydrogen sulfide was practically complete. This required about four hours. Considerable heat is generated at the start of the reaction but external cooling is usually not necessary. The reflux condenser acts only to condense a small amount of phenyl ether from the hydrogen sulfide evolved. The reaction mixture was hydrolyzed by pouring in ice water and the resulting mixture of phenyl ether and phenoxthin separated and fractionated under reduced pressure. There was obtained 595 g. or a 74% yield of phenoxthin distilling at 185–187° (23 mm.) which after one crystallization from methanol melted at 56–57°. The loss in crystallization is about 3%. Since there are several conflicting reports[3,4] in the literature as to the melting point of phenoxthin, a sample was recrystallized until it was found to be pure when examined with a polarizing microscope. This sample melted[8] at 57.5–58°, confirming the value given by Drew.[4]

Heating 17 g. (0.1 mole) of phenyl ether, 6.4 g. (0.2 mole) of sulfur and 13.5 g. (0.1 mole) of aluminum chloride in 100 cc. of *sym*-tetrachloroethane on the steam-bath in a flask fitted with a reflux condenser for four hours gave 9.5 g. or 48% of the theoretical amount of phenoxthin. There was a considerable amount of tarry residue left in the distilling flask. Attempts to crystallize this material were unsuccessful.

3-Bromophenoxthin.—To a well-stirred solution of 20 g. (0.1 mole) of phenoxthin in 100 cc. of carbon tetrachloride was added gradually 16 g. (0.1 mole) of bromine. After the reaction was complete the solvent was distilled off and the residue crystallized from hot methanol. The yield was 23 g. or 83% of the theoretical amount of material melting at 59–60°.

Anal. Calcd. for $C_{12}H_7OSBr$: S, 11.5. Found: S, 11.8.

3,6-Dibromophenoxthin.—To a solution of 20 g. (0.1 mole) of phenoxthin in 100 cc. of carbon tetrachloride was added 34 g. (11 cc., 0.21 mole) of bromine. The mixture was refluxed until no more hydrogen bromide was evolved, the carbon tetrachloride distilled off and the residue crystallized twice from hot methanol. There was obtained 27 g. or 75% of the theoretical amount of product melting at 92–93°.

Anal. Calcd. for $C_{12}H_6OSBr_2$: Br, 44.65; S, 8.96. Found: Br, 44.61; S, 8.78.

4,4′-Dibromophenoxybenzene-2,2′-disulfonyl Chloride.—To 33 g. (0.1 mole) of di-(4-bromophenyl) ether was added gradually 60 cc. (excess) of chlorosulfonic acid. After standing overnight the mixture was heated on the steam-bath for two hours and then poured into ice water. Addition of acetic acid to the water mixture aided in filtration which was otherwise difficult. There was obtained 38 g. (72%) of a light brown solid which upon recrystalliz-

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(7) Hilditch and Smiles, *J. Chem. Soc.*, **99**, 408 (1911).

(8) All melting points are uncorrected.

ing from chloroform or better from hot acetone to which a few drops of water was added formed colorless crystals melting at 241–243°.

Anal. Calcd. for $C_{12}H_6O_5S_2Cl_2Br_2$: S, 12.20. Found: S, 12.07.

The sodium salt of the corresponding disulfonic acid was obtained by hydrolysis of the sulfonyl chloride or from sulfonation of 33 g. of di-(4-bromophenyl) ether with 60 g. of chlorosulfonic acid at room temperature, pouring into water and adding sodium hydroxide. It was purified by recrystallizing from water–methanol (75:25) in which it is readily soluble when hot. It was dried at 110° before analysis.

Anal. Calcd. for $C_{12}H_6O_7S_2Br_2Na_2$: S, 12.05. Found: S, 11.94.

Sodium 2 - (4 - bromophenoxy) - 5 - bromobenzenesulfonate.—To 16.4 g. (0.05 mole) of di-(4-bromophenyl) ether in 35 cc. of carbon tetrachloride was added slowly 5.8 g. (0.05 mole) of chlorosulfonic acid. The mixture was then refluxed for thirty minutes on the steam-bath, 25 cc. of water added and the carbon tetrachloride layer distilled off. The remaining solution of the sulfonic acid was poured into a saturated solution of sodium chloride. The sodium sulfonate separated as a tan colored oil which solidified upon standing. The yield was about 15 g. The product was recrystallized from water several times and dried.

Anal. Calcd. for $C_{12}H_7O_4Br_2SNa$: Na, 5.35. Found: Na, 5.39.

2 - (4 - bromophenoxy) - 5 - bromobenzenesulfonyl Chloride.—A mixture containing 30 cc. of phosphorus oxychloride and 19 g. of the sodium salt was refluxed on a steam-bath for two hours. The solid remaining after hydrolysis of the excess phosphorus oxychloride amounted to 15 g. (78% yield). After three crystallizations from petroleum ether to which a small percentage of benzene was added it melted at 128–129°.

Anal. Calcd. for $C_{12}H_7O_3Br_2ClS$: S, 7.51. Found: S, 7.54.

3,6-Dibromophenoxthin-10-dioxide. **A.**—To a solution of 8.9 g. (0.025 mole) of 3,6-dibromophenoxthin in 250 cc. of glacial acetic acid was added 20 g. (excess) of 30% hydrogen peroxide. The mixture was warmed for thirty minutes on the steam-bath and then allowed to stand overnight. Dilution with water precipitated a solid which still gave a slight coloration with concentrated sulfuric acid so the above procedure was repeated. This gave 9 g. (92%) of the pure sulfone, m. p. 185–186°.

B.—To a solution of 0.5 g. of 2-(4-bromophenoxy)-5-bromobenzenesulfonyl chloride in 15 cc. of *sym*-tetrachloroethane was added 0.5 g. of aluminum chloride and the whole was heated on the steam-bath for two hours. Hydrolysis and removal of the solvent gave a solid which when recrystallized from acetic acid slightly diluted with water gave crystals of m. p. 183–186°. A mixed m. p. with the material from **A** showed no depression.

Anal. Calcd. for $C_{12}H_6O_3Br_2S$: Br, 40.99. Found: Br, 41.5.

3-Acetylphenoxthin.—To a solution of 20 g. (0.1 mole) of phenoxthin and 8.5 g. (0.11 mole) of acetyl chloride in 100 cc. of carbon disulfide was added in small portions 13.5 g. (0.1 mole) of anhydrous aluminum chloride. After standing for two hours the mixture was refluxed until no more hydrogen chloride was evolved, the solvent distilled off and the residue hydrolyzed with ice. After three crystallizations from ethyl alcohol there was obtained 14 g. or 58% of the theoretical amount of a light yellow powder melting at 111–112°.

Anal. Calcd. for $C_{14}H_{10}O_2S$: S, 13.22. Found: S, 13.15.

The phenylhydrazone melted at 93.5–94.5° and the oxime at 142–143°.

Phenoxthin-3-carboxylic Acid, A.—Five grams of 3-acetylphenoxthin and 25 g. of bleaching powder were mixed with 200 cc. of dilute sodium hydroxide and the whole heated on the steam-bath for five hours. The mixture was then filtered, boiled to remove a trace of chloroform and acidified with dilute hydrochloric acid. The yield of acid was 3 g. or 60% of the theoretical amount. After recrystallizing from hot 50% acetic acid the m. p. was 259–260°. The phenoxthin-2-carboxylic acid obtained by Mauthner[3] melted at 223°.

Anal. Calcd. for $C_{13}H_8O_3S$: neutral equivalent, 244. Found: neutral equivalent, 239.

B.—The only successful preparation of the acid by the Grignard method was carried out as follows. In a 500-cc. three-necked flask fitted with stirrer, condenser and dropping funnel was placed 2.5 g. (0.1 mole) of magnesium turnings and 3 cc. of ethyl iodide in 10 cc. of dry ether. After the reaction was well started there was added over a period of two hours a solution of 21 g. (0.078 mole) of 3-bromophenoxthin (m. p. 59–60°) in 125 cc. of ether. The mixture was refluxed for six hours longer when the reaction appeared to be complete. The mixture was cooled in ice and about 20 g. of solid carbon dioxide added. Working up the mixture in the usual fashion gave 1.5 g. or about 8% of the theoretical amount of material soluble in alkali and a much larger amount of neutral material that was not further investigated. The acid had the m. p. 260–262° and showed no depression when mixed with the acid obtained in **A**.

3-Benzoyl- and 3,6-Dibenzoylphenoxthin.—To a mixture of 20 g. (0.1 mole) of phenoxthin and 14.5 g. (0.1 mole) of benzoyl chloride in 100 cc. of carbon disulfide was added 13.5 g. (0.1 mole) of aluminum chloride. After treatment as in preparation of the acetyl compound the crude product was extracted several times with hot alcohol. Upon cooling there separated 10 g. of a light yellow crystalline substance melting at 96–97°.

Anal. Calcd. for $C_{19}H_{12}O_2S$: S, 10.53. Found: S, 10.53, 10.55.

The alcohol-insoluble residue was recrystallized from glacial acetic acid. There resulted 4.5 g. of yellow leaves melting at 197°.

Anal. Calcd. for $C_{26}H_{16}O_3S$: S, 7.86. Found: S, 7.74, 7.74.

Phenoxthin-3-sulfonic Acid.—To a solution of 20 g. (0.1 mole) of phenoxthin in 30 cc. of carbon tetrachloride was added slowly 11.7 g. (0.1 mole) of chlorosulfonic acid. Reaction was immediate. After the evolution of hydrogen chloride ceased water was added, the carbon tetrachloride layer removed and a saturated solution of salt added to the aqueous layer. About 25 g. of the sodium sulfonate was obtained. The loss in weight of the air-dried salt when heated in an oven at 120° indicated the presence of one molecule of water of hydration. The dry salt was analyzed for sodium.

Anal. Calcd. for $C_{12}H_7O_4S_2Na$: Na, 7.61. Found: Na, 7.66.

Refluxing the dry sodium salt with excess phosphorus oxychloride gave the sulfonyl chloride which separated from petroleum ether as a light yellow solid that melted at 127–128°.

Anal. Calcd. for $C_{12}H_7O_3S_2Cl$: Cl, 11.88. Found: Cl, 11.90.

Warming the sulfonyl chloride with concentrated ammonia for a few minutes gave the amide, obtained as colorless crystals from boiling water. This melted at 177–178°.

Anal. Calcd. for $C_{12}H_9O_3S_2N$: S, 22.96. Found: S, 22.78.

Phenoxthin-3,6-disulfonic Acid.—Sodium phenoxthin-3,6-disulfonate was obtained in exactly the same manner as the monosulfonate except for the use of 46.4 g. (0.4 mole) of chlorosulfonic acid. It is much more soluble in water than the monosulfonation product. Heating the air dried salt at 120° indicated two molecules of water of hydration. The analysis for sodium was made on the dry salt.

Anal. Calcd. for $C_{12}H_6O_7S_3Na_2$: Na, 11.48. Found: Na, 11.39, 11.52.

Addition of silver nitrate to a hot aqueous solution of the sodium salt gave an immediate precipitate of silver phenoxthin-3,6-disulfonate as glistening white crystals.

Anal. Calcd. for $C_{12}H_6O_7S_2Ag_2$: Ag, 37.59. Found: Ag, 37.57.

Refluxing the sodium salt with phosphorus oxychloride for two hours gave the disulfonyl chloride, which separated as light yellow crystals from benzene, m. p. 142–143°. The same compound was obtained from phenoxthin as follows. To 20 g. (0.1 mole of phenoxthin was added slowly 71 g. (0.61 mole) of chlorosulfonic acid. After one and one-half hours of standing at room temperature the mixture was poured on ice and the resulting greenish tar crystallized from benzene. The yield was 9 g. or 23% of the theoretical amount of the same product as was obtained above.

Anal. Calcd. for $C_{12}H_6O_5S_3Cl_2$: Cl, 17.86. Found: Cl, 17.90.

A 2-g. sample of the disulfonyl chloride was heated for thirty minutes with an equal weight of phosphorus pentachloride. The mixture was poured into water and the tarry insoluble material recrystallized from methanol. There was obtained a small amount of crystals, m. p. 134–135°, which when mixed with the original sulfonyl chloride depressed the m. p. to 107–110°. The 3,6-dichlorophenoxthin obtained by another method[7] melted at 135°.

Summary

1. The reaction of sulfur and aluminum chloride upon phenyl ether, *p*-bromophenyl phenyl ether and di-(*p*-bromophenyl) ether has been investigated. The reaction with phenyl ether gives a 74% yield of phenoxthin.

2. In bromination, sulfonation and Friedel–Crafts reactions the directive influence of the oxygen in phenoxthin is dominant over that of the sulfur, substitution invariably occurring para to the ether linkage.

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Electrolysis of Methylmagnesium Halides in Ether Solutions

BY WARD V. EVANS AND EDMUND FIELD

Ether solutions of the Grignard reagent have been shown to possess properties characteristic of electrolytes in low dielectric media. Konduirev[1] has shown that the equivalent conductance of ethylmagnesium iodide goes through a maximum which varies with temperature. Definite and reproducible potentials have been obtained by Evans and Fosdick[2] between hydrogen electrodes and magnesium electrodes immersed in various Grignard solutions. The decomposition potentials of Grignard reagents have been shown by Evans and Lee[3] to be characteristic of the organic radical involved.

On electrolysis of ethylmagnesium bromide Evans and Lee[4] showed that magnesium migrates to both electrodes, with magnesium plating out on the cathode and magnesium bromide, ethane and ethylene forming at the anode. This was evidence for the existence of complex ions in the solution such as Mg^{++} $[Br_2MgEt_2]^{=}$ which must also participate in the equilibrium generally postulated for the Grignard reagent

$$2EtMgBr \rightleftharpoons MgEt_2 + MgBr_2 \text{ (Schlenk)}^5$$

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[1] Konduirev and Ssusi, *Ber.*, **62B**, 1856 (1929).

[2] Fosdick, Ph.D. Dissertation, Northwestern University, 1932.

[3] Evans and Lee, THIS JOURNAL, **57**, 489 (1935).

[4] Evans and Lee, *ibid.*, **56**, 654 (1934).

[5] Schlenk and Schlenk, *Ber.*, **62B**, 920 (1929).