LI.—*A Synthesis of Derivatives of Phenothioxin.*

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DURING the investigation of certain aromatic hydroxysulphoxides (Gazdar and Smiles, *Trans.*, 1910, **97**, 2248), attempts were made to obtain triarylsulphonium bases from them by condensation with a phenolic ether in presence of concentrated sulphuric acid, but the desired result was not obtained. The negative results obtained with these sulphoxides of *p*-cresol and *p*-chlorophenol seemed

remarkable, for the corresponding ethers, *p*-cresetole and *p*-chlorophenetoles sulphoxides, condense readily under the stated conditions, giving good yields of the aromatic sulphonium salt (compare Smiles and Le Rossignol, Trans., 1908, **93**, 709).

The experiments described in this paper were undertaken with the object of ascertaining the cause of the inactivity of these hydroxy-sulphoxides.

The preparation of the latter substances and their chief derivatives has been described in the previous paper (Gazdar and Smiles, *loc. cit.*). In that place, attention was drawn to the fact that all the hydroxy- or alkyloxy-sulphoxides hitherto prepared furnish intensely coloured solutions with concentrated sulphuric acid, and that it is probably the nature of the substances then formed which determines the reactivity of the sulphoxides in this solvent.

It has now been found that the moderately prolonged action of sulphuric acid on the sulphoxides of *p*-cresol and *p*-chlorophenol yields the phenothioxin oxides represented by the following formulæ:

Taking first the dimethyl compound, it is evident that the sulphoxide from which it is prepared has the structure (III),

for the dimethyl ether obtained from it by methylation is identical with the di-*p*-cresol methyl ether sulphoxide which has been previously shown to have this structure (Le Rossignol and Smiles, Trans., *loc. cit.*). The constitution which is now ascribed to the product obtained from this sulphoxide by the interaction with sulphuric acid is shown by the facts:

1. It is produced by loss of the elements of water from the hydroxy-sulphoxide.
2. When reduced, it loses one atomic proportion of oxygen, and
3. When oxidised, it absorbs the same quantity of that element.
4. Neither the substance itself, nor the products of its oxidation or reduction, contain hydroxyl.

It may also be observed that the molecular weight of the reduction product corresponds with this structure.

From this constitution of the substance, those of the reduction and oxidation products follow; these are respectively the phenothioxin itself (V) and the phenothioxin dioxide (VI):

The constitution of the dichloro-compound cannot be said to be based on such rigid proof as that of the dimethyl derivative, for the structure of the *p*-chlorophenol sulphoxide has not been so definitely established. But the product obtained by the action of sulphuric acid with this sulphoxide so closely resembles dimethylphenothioxin oxide in its chemical character, for example, behaviour on oxidation and reduction, with sulphuric acid, and absence of hydroxyl, that no reasonable doubt can be entertained of the cyclic structure (IV) now assigned to it. It follows thence that the sulphoxide has the constitution indicated above (IV).

Further to confirm the phenothioxin structure for these substances, we have examined the naphthathioxin previously obtained by Mauthner (*Ber.*, 1906, **39**, 1345) from the interaction of β -naphthol sulphide and phosphoryl chloride. This substance may be converted into the oxide by interaction with hydrogen dioxide and into the dioxide with permanganate in glacial acetic acid. The behaviour of these substances agrees closely with that of the derivatives under consideration. Experiments have also been made to obtain the phenothioxins directly from the sulphides of *p*-cresol and of *p*-chlorophenol (compare Gazdar and Smiles, *loc. cit.*) by dehydrating agents. It is remarkable that negative results* were obtained even with hot sulphuric acid, zinc chloride at 200°, or boiling phosphoryl chloride. Since dichloro- and dimethylphenothioxin oxides are formed by the action of cold sulphuric acid on the sulphoxide, it appears that this reaction cannot be one of simple dehydration, for, if it were, it is to be expected that the sulphides would behave similarly, at any rate with hot dehydrating agents.

Such considerations lead to the assumption that the thionyl group plays some part in this reaction, and that the phenothioxin oxides are not the first products. This view is justified by the fact that the maximum yields of the cyclic compounds are only obtained by prolonging the reaction. In fact, if the action be stopped at an early period, by mixing the acid solution with water,

* It may be observed that the sulphide of β -naphthol yields the phenothioxin with the last-named of these reagents (Mauthner, *loc. cit.*), but the behaviour of this sulphide profoundly differs from that of other aromatic ortho-dihydroxy-sulphides in other respects, for example, oxidation.

entirely different products are obtained. It is thus evident that, although the phenothioxin oxides do not condense with phenolic ethers to give sulphonium salts, the cause of the inactivity of the parent sulphoxides must be sought in these initial products. The nature of the latter is now under investigation.

It may be observed that the phenothioxin oxides are not the only products of the prolonged action of sulphuric acid with the sulphoxides, for the yields are not good, and sulphonation is extensive.

The phenothioxin series is but little known; indeed, previous knowledge of this group is entirely due to Mauthner (*Ber.*, 1905, **38**, 1411; 1906, **39**, 1340), who synthesised two members of the series from *o*-thiolphenol and picryl chloride or 4-chloro-3:5-dinitrobenzoic acid. From the last-named substance, the parent compound was obtained by eliminating the nitro- and carboxyl groups.

Observations made with the three series of derivatives embraced by the present experiments show that in certain respects these substances resemble the analogous series of thiodiphenylamine. It has been elsewhere shown that the *o*-sulphoxides of diphenylamine yield (Barnett and Smiles, *Trans.*, 1909, **95**, 1253) the intensely coloured azothionium salts with mineral acids, and a similar behaviour has now been observed with the *o*-sulphoxides of diphenyl ether, but in the latter case anhydrous acids of dehydrating power, for example, sulphuric acid, are necessary. Moreover, there is a striking similarity in the action of sulphuric acid on the sulphides of the two series. Thiodiphenylamine is at once oxidised by the cold reagent to the azothionium salt, sulphurous acid being liberated; the phenothioxins are also oxidised by this reagent, giving solutions of an intense blue colour. It may be further observed that these *o*-sulphoxides of diphenyl ether do not contain substituents of strongly acidic character, and they do not yield *S*-aryl derivatives when treated with a phenolic ether in sulphuric acid solution. The same fact has been observed with similar derivatives of diphenylamine *o*-sulphoxide, and it has been shown (Barnett and Smiles, *Trans.*, 1910, **97**, 369) that the disappearance of this characteristic reaction of the thionyl group is due to the immediate conversion of the sulphoxide to the azothionium salt. With sulphoxides of weaker basic power, the rearrangement to azothionium salt proceeds slowly, and the condensation may be effected before this has taken place.

To account for the absence of this characteristic reaction of the thionyl group from the phenothioxin oxides in this solvent, and to display the close analogy between this series and that of thiodiphenylamine, we consider it necessary to represent the products

of interaction of the phenothioxin oxides and sulphuric acid as phenothioxonium salts.

Attempts to isolate these substances have not as yet been successful, for on diluting the acid solution they are hydrolysed, and other substances are formed.

The relations between these series are indicated by the following formulæ:

EXPERIMENTAL.

2: 7-Dimethylphenothioxin, $\text{CH}_3 \cdot \text{C}_6\text{H}_3 \begin{array}{c} \text{O} \\ \diagup \quad \diagdown \\ \text{S} \end{array} \text{C}_6\text{H}_3 \cdot \text{CH}_3$.

p-Cresol *o*-sulphoxide, in quantities of 20 grams at a time, was triturated with cold concentrated sulphuric acid, and the solution thus obtained was set aside at the atmospheric temperature for four hours. It was then carefully poured into cold water, and the muddy precipitate was collected and washed with water until free from sulphuric acid. The solid was triturated with aqueous alkali hydroxide, and a little alcohol was added to the mixture, which was then set aside for sixteen hours. The insoluble portion was then collected, washed until free from alkali, dried, and finally crystallised from dilute alcohol. The product melted indefinitely in the neighbourhood of 65°, and analysis showed that it was a mixture of the phenothioxin and its oxide. To obtain the substance in a pure condition, the product was converted into the oxide, and this was reduced.

Dimethylphenothioxin oxide was reduced in hot glacial acetic acid with zinc dust, and when reduction was complete, the excess of zinc dust was removed, and the filtrate mixed with water. An oil was precipitated, which quickly solidified; it was crystallised from dilute methyl alcohol, from which 2: 7-dimethylphenothioxin separated in colourless leaflets, melting at 74°:

0.1926 gave 0.3224 CO₂ and 0.0930 H₂O. C=73.9; H=5.3.

0.4110, in 16.79 c.c. of benzene gave Δ = -0.547°. M.W.=223.

C₁₄H₁₂OS requires C=73.7; H=5.2 per cent. M.W.=228.

Nitric acid readily attacks the substance, but no definite nitro-derivative could be isolated, for, on modifying the conditions, either the interaction was too violent or none took place.

The substance possesses an odour resembling that of geraniums; it is insoluble in water, and readily soluble in most organic media. It dissolves in concentrated sulphuric acid, the solution rapidly becoming blue, whilst sulphurous acid is evolved.

2: 7-Dimethylphenothioxin Oxide.

The crude product, obtained as described in a previous paragraph from *p*-cresol *o*-sulphoxide and sulphuric acid, was dissolved in cold glacial acetic acid. To this solution an amount of hydrogen dioxide was added slightly in excess of that required to convert all phenothioxin to its oxide. The mixture was set aside at the atmospheric temperature, and after twenty-four hours it was mixed with water. The solid product was recrystallised from dilute alcohol.

2: 7-Dimethylphenothioxin oxide forms colourless needles, which melt at 132—133°. It dissolves in sulphuric acid, the solution being of an intense blue colour:

0.1143 gave 0.2875 CO₂ and 0.0557 H₂O. C=68.7; H=5.4.

C₁₄H₁₂O₂S requires C=68.8; H=4.9 per cent.

2: 7-Dimethylphenothioxin Dioxide.

A solution of the oxide in cold acetic acid was mixed with the calculated quantity of finely powdered potassium permanganate. Solution of the permanganate was assisted by continual shaking, and finally the mixture was set aside for a few hours. Water was then added, and sulphurous acid was passed into the turbid mixture to effect complete decolorisation.

The solid was collected and crystallised from alcohol, when *2: 7-dimethylphenothioxin dioxide* was obtained in colourless prisms, which melted at 172°:

0.1132 gave 0.2693 CO₂ and 0.0485 H₂O. C=64.88; H=4.8.

C₁₄H₁₂O₃S requires C=64.62; H=4.6 per cent.

2: 7-Dichlorophenothioxin Oxide.

p-Chlorophenol *o*-sulphoxide was treated with sulphuric acid in the manner already described with the cresol derivative. Comparative experiments showed that the maximum yields of the phenothioxin derivative (about 25 per cent.) were obtained when the interaction was allowed to proceed for four hours. In this case, however, the product did not appear to contain the phenothioxin, for after it had been recrystallised from alcohol, *2: 7-dichlorophenothioxin oxide* was obtained in shining prisms, which melted at 168°:

0.1005 gave 0.1880 CO₂ and 0.0200 H₂O. C=51.0; H=2.2.

0.1093 „ 0.2035 CO₂ „ 0.0255 H₂O. C=50.7; H=2.5.

C₁₂H₆O₂Cl₂S requires C=50.5; H=2.1 per cent.

The substance gives an intense blue solution with cold sulphuric acid, but no sulphonium base is formed on adding a phenolic ether to this. In one experiment, excess of phenetole was added to the cold solution in sulphuric acid, and after about half an hour had elapsed, this was poured into water. The recrystallised product was found to contain dichlorophenothioxin, and a sample was isolated which melted at 134°. (Found, C=53.2; H=2.7. Calc., C=53.5; H=2.2 per cent.) No sulphonium base could be detected.

Attempts were made to obtain these phenothioxin derivatives by the action of other dehydrating agents with the hydroxy-sulphoxide or sulphide, but with negative results. The reagents employed were fused zinc chloride at 120° and 200°, boiling thionyl chloride, boiling phosphoryl chloride alone or in xylene solution, and boiling phosphorus trichloride. With the latter reagent, the sulphoxide was reduced to sulphide (m. p. 174°). (Found, C=50.3; H=3.1. Calc., C=50.2; H=2.8 per cent.) Warm sulphuric acid acting for one hour also gave negative results with *p*-cresol *o*-sulphide.

This substance was obtained by reducing the phenothioxin oxide with zinc dust in acetic acid, the process being similar to that already described with the dimethyl derivative. It separates from hot alcohol in long, slender needles, which melt at 135°:

0.1163 gave 0.2262 CO₂ and 0.0232 H₂O. C=53.0; H=2.2.

C₁₂H₆OCl₂S requires C=53.5; H=2.2 per cent.

The substance is oxidised by concentrated sulphuric acid.

2: 7-Dichlorophenothioxin Dioxide.

This was prepared from the monoxide by oxidation, as described with the dimethyl derivative. It separates from hot alcohol in small, colourless prisms, which melt at 196°:

0.1310 gave 0.2322 CO₂ and 0.0294 H₂O. C=48.3; H=2.49.

C₁₂H₆O₃Cl₂S requires C=47.8; H=1.99 per cent.

(a) *From Naphthathioxin and Hydrogen Dioxide.*—Naphthathioxin was prepared from β-dihydroxy-α-dinaphthyl sulphide by

interaction with phosphoryl chloride in boiling xylene, as described by Mauthner (*Ber.*, 1906, **39**, 1346). A solution of this substance in a mixture of acetic acid and anhydride, which contained a slight excess of hydrogen dioxide, was set aside at the atmospheric temperature. After four days the mixture was poured into water, and the solid product which then separated was collected and re-crystallised from hot acetic acid. Naphthathioxin oxide, prepared in this manner, forms pale yellow needles, which darken and melt at 221°. (Found, C=75·3; H=4·0. Calc., C=75·9; H=3·8 per cent.)

The solutions in sulphuric acid are of a deep blue colour. This substance has been previously prepared by Mauthner (*loc. cit.*) by the oxidation of naphthathioxin with chromic acid. The product of this method was red, but it melted at the same temperature as that now given.

(b) *From β-Dihydroxy-α-dinaphthyl Sulphide and Sulphuric Acid.*—This substance readily dissolves in sulphuric acid, but oxidation sets in immediately, the solution becoming blue, and sulphurous acid being evolved. In one experiment, the mixture was set aside for twenty-four hours, and then dealt with as described in the preparation of the phenothioxin oxides from the sulphoxides of *p*-cresol and *p*-chlorophenol. The product was repeatedly crystallised from hot acetic acid, and finally naphthathioxin oxide was obtained. It was identified by the melting point of a mixture with that substance obtained from other sources.

Naphthathioxin was oxidised in acetic acid solution with potassium permanganate in the usual manner. The product was crystallised from boiling acetic acid, in which it is sparingly soluble. It forms colourless prisms, which melt at 268°:

0·1043 gave 0·2744 CO₂ and 0·0361 H₂O. C=71·74; H=3·8.

C₂₀H₁₂O₃S requires C=72·3; H=3·6 per cent.

The Ethers of p-Cresol and p-Chlorophenol o-Sulphoxides.

The methyl ether of *p*-cresol *o*-sulphoxide was prepared from the corresponding phenol by interaction with methyl iodide in alkaline solution of methyl alcohol. The product of the reaction was treated in a manner similar to that described in the alkylation of phenol *p*-sulphoxide (*Trans.*, 1907, **91**, 1120). It was purified by crystallisation from ethyl acetate, when it was obtained in colourless prisms, which melted at 134°. A mixture of this substance and the product obtained by direct sulphination of *p*-tolyl methyl

ether melted at the same temperature. The constitution of the latter has been previously discussed (Le Rossignol and Smiles, Trans., 1908, **93**, 745).

The ethyl ether of *p*-chlorophenol *o*-sulphoxide was prepared by direct sulphination of *p*-chlorophenetole, the process being similar to that formerly described (Le Rossignol and Smiles, *loc. cit.*) with *p*-tolyl methyl ether.

The substance crystallises from ethyl acetate in fine needles, which melt at 145°:

0.1130 gave 0.2234 CO₂ and 0.0485 H₂O. C=53.9; H=4.7.

C₁₆H₁₆O₃Cl₂S requires C=53.48; H=4.46 per cent.

Both of these ethers of *p*-cresol and *p*-chlorophenol sulphoxide give blue solutions with sulphuric acid, and condense in that medium with phenetole, when the colour is discharged. The corresponding hydroxy-sulphoxides* do not undergo this condensation under like conditions.

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