CCXXXI.—*The Synthesis of Derivatives of Thioxanthone. Part IV. Synthesis from Aromatic Sulphinic Acids.*

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IN previous communications it has been shown that various types of thioxanthone derivatives may be synthesised from aromatic mercaptans (Trans., 1910, **97**, 1290), from aromatic disulphides (this vol., p. 1353), and from the products obtained by the union of a quinone with *o*-thiolbenzoic acid (this vol., p. 1535). In the two former methods the union of the thio-derivative with the aromatic compound is effected by the condensation of a sulphylic acid which is formed at an intermediate stage in the process, water being eliminated from this substance and the second aromatic nucleus. Since it has been formerly observed (Smiles and Le Rossignol, Trans., 1906, **89**, 700) that aromatic sulphinic acids readily condense with suitable aromatic compounds in the presence of sulphuric acid:

the present experiments were undertaken in order to apply this type of interaction to the production of thioxanthenes.

Both Graebe (*Annalen*, 1891, **263**, 1) and Mayer (*Ber.*, 1909, **42**, 1134, 3046) have shown how easily thioxanthenes are formed by elimination of water from the *o*-carboxylic derivatives of substituted diphenyl sulphides:

so that the synthesis of thioxanthenes by this method is merely a question of choosing suitable aromatic derivatives for condensation with the sulphinic acid. This condensation takes place most readily with hydroxy- and amino-derivatives of benzene, and, since the quadrivalent sulphur grouping then enters the para-position (Smiles and Le Rossignol, *loc. cit.*) with respect to these groups, the *m*-hydroxy- and amino-benzoic acids have been employed in these experiments.

Two methods of effecting the condensation have been investigated, either with warm sulphuric acid or by the aid of heat alone (see Hinsberg, *Ber.*, 1903, **36**, 107); but since the former agent furnishes very poor yields, the latter has been generally adopted. It might be expected that the product furnished by either process would

not be the thioxanthone, but instead the oxide thereof, for example,

but this is not the case, for it appears that at the relatively high temperatures employed the sulphoxide is easily reduced to the sulphide at the expense of the sulphinic acid. In order to obtain the maximum yields of the thioxanthone, it is therefore necessary to employ an excess of sulphinic acid beyond that required by theory, and since even then the yields are not good, the method cannot be recommended for the preparation of the thioxanthenes in large quantities.

Setting out from a sulphinic acid of known constitution, it is evident that the structure to be assigned to the resulting thioxanthone must be chosen from two alternative formulæ which differ in the position taken by the sulphur with respect to the hydroxy- or amino-groups. The alternatives may be illustrated with the case of the condensation of *p*-toluenesulphinic acid with *m*-hydroxybenzoic acid:

From the general results obtained in studying the influences which govern the sulphination of hydroxy-derivatives of benzene, the second type of alternative (II) cannot be entertained as highly probable, for it has been shown that the course of this reaction is susceptible to the influence of "steric" conditions; thus, in forming a substance of type II, not only must ortho-condensation occur in preference to the more general para-condensation, but in forming the parental carboxylic acid (III) it must take place under the more adverse steric conditions. For these reasons we consider that preference must be given to the first type of formula (I), which involves the para-condensation, and the contention is supported in the case of the aminothioxanthone furnished by benzenesulphinic acid and *m*-aminobenzoic acid. The substances possessing the alternative structures in question, 2- and 4-aminothioxanthenes (IV and V), have been prepared by F. Mayer (*Ber.*, 1909, **42**, 3046) with methods which leave no room for doubt as to the constitution of the products. These substances melt respectively at 222° and

203°, whilst that obtained by ourselves melts at the temperature ascribed to the first-named isomeride. We take this opportunity

of expressing our thanks to Dr. Mayer for kindly placing at our disposal a small quantity of the 2-amino-derivative. A close comparison of this substance with that obtained by ourselves finally proved the identity of the latter.

Since there is no reason to suspect that the *o*- and *p*-toluenesulphinic acids should behave differently from benzenesulphinic acid, a corresponding structure has been assigned to other amino- and hydroxy-derivatives of thioxanthone which have been prepared from those substances.

It is evident that the method of synthesis now described may be further varied by changing the situation of the carboxyl group in the components; thus an *o*-carboxy-sulphinic acid may be condensed with a simple aromatic compound:

but no experiments dealing with this method are described in the present paper, for a typical case has already been investigated (Davis and Smiles, *Trans.*, 1910, **97**, 1290), when thioxanthone was prepared from *o*-carboxybenzenesulphinic acid and benzene.

The substances described in the experimental part of this paper are by no means the sole products of the various interactions; in fact, it is not easy with the usual methods to isolate the thioxanthenes from the impure products, and were it not for the help of a method of fractional sublimation (Christopher, *Proc.*, 1911, **27**, 236) it is doubtful whether these experiments could have been brought to a successful conclusion.

EXPERIMENTAL.

An intimate mixture of 10 grams of *m*-aminobenzoic acid with 23 grams of benzenesulphinic acid was heated at 170–190° for four hours. The cold mass was boiled with aqueous sulphuric acid, and then, after being rendered alkaline with alkali hydroxide, the mixture was repeatedly extracted with ether. The united extracts were shaken with diluted sulphuric acid, and the aqueous layer,

which contained the sparingly soluble sulphate, was treated with alkali to liberate the base. The greenish-yellow precipitate was collected, and when dry it was sublimed in a vacuum. The product formed orange needles, which melted at 222° , whether heated alone or mixed with 2-aminothioxanthone obtained from another source (F. Mayer, *loc. cit.*). (Found, C=68.8; H=3.8. Calc., C=68.7; H=3.9 per cent.)

The substance also possessed the other physical properties elsewhere attributed to 2-aminothioxanthone.

2-Amino-7-methylthioxanthone,

The preparation of this substance from *m*-aminobenzoic acid and *p*-toluenesulphinic acid was conducted in the same manner as that described with 2-aminothioxanthone. However, the yields were extremely poor, and unfortunately an accident which occurred during the analysis of the small quantity available rendered invalid the estimation of hydrogen in this substance:

0.1366 gave 0.3506 CO_2 . C=70.0.

$\text{C}_{14}\text{H}_{11}\text{ONS}$ requires C=69.71 per cent.

The substance forms orange needles, which melt at 190° , whilst other physical properties are similar to those of the 2-amino-derivative.

2-Hydroxy-7-methylthioxanthone,

Interaction of 10 grams of *m*-hydroxybenzoic acid with 23 grams of *p*-toluenesulphinic acid was effected by heating the mixture at 190° during four hours. The cold mass was boiled with aqueous sodium hydroxide, and then the phenols were liberated from the solution by saturation with carbonic acid. The semi-solid precipitate was dissolved in ether, and the solution was shaken with excess of aqueous alkali hydroxide. A considerable quantity of material dissolved in the latter medium, forming a deep orange-coloured solution; this was kept for twenty-four hours, when the sparingly soluble sodium salt of the required thioxanthone separated in flocculent masses of needles. The hydroxythioxanthone obtained by treating this sodium salt with dilute mineral acid was almost pure, but it was further purified by sublimation in a vacuum. The

product, 2-hydroxy-7-methylthioxanthone, formed large, lemon-yellow needles, which showed a metallic lustre; these melted at 217° , and dissolved in concentrated sulphuric acid, imparting a brilliant green fluorescence to that medium:

0.1149 gave 0.2910 CO_2 and 0.0426 H_2O . $\text{C}=69.0$; $\text{H}=4.2$.

$\text{C}_{14}\text{H}_{10}\text{O}_2\text{S}$ requires $\text{C}=69.4$; $\text{H}=4.1$ per cent.

The sodium salt of this substance separates in orange needles from an alkaline aqueous solution of the phenol. The latter is sparingly soluble in most cold organic media, but it may be recrystallised from hot acetic acid, in which it is moderately soluble.

2-Hydroxy-5-methylthioxanthone,

The preparation of this hydroxy-derivative was conducted in the manner described in the foregoing paragraph, *m*-hydroxybenzoic and *o*-toluenesulphinic acids being heated together in quantities of 10 and 23 grams respectively. The yields obtained were somewhat poorer than with *p*-toluenesulphinic acid, partly on account of the greater solubility of the sodium salt in the alkaline medium. The product was purified as usual by sublimation in a vacuum, when it was obtained in yellow needles, which melted at 211° :

0.0755 gave 0.1926 CO_2 and 0.029 H_2O . $\text{C}=69.5$; $\text{H}=4.2$.

$\text{C}_{14}\text{H}_{10}\text{O}_2\text{S}$ requires $\text{C}=69.4$; $\text{H}=4.1$ per cent.

Other physical properties of this substance are similar to those of the 7-methyl derivative.

In some previous experiments (Davis and Smiles, *loc. cit.*) a hydroxythioxanthone was obtained by condensation of *o*-thiolbenzoic acid with phenol in the presence of warm concentrated sulphuric acid. Although by heating this substance water could not be expelled from it, the suggestion was offered that it crystallises with water, for repeated fractionation did not appreciably alter the composition. In view of the fact that the methyl derivatives do not crystallise in this manner, it was considered necessary to re-investigate the simpler substance in order to determine the cause of the apparent divergence of properties. It appeared probable that an oxide of the thioxanthone might have been present as an

impurity, for observations from numerous sources have shown that sulphides are apt to be oxidised on prolonged heating with sulphuric acid; but beyond fractional crystallisation, a method of removing substances of this type from the mixture could not be devised until the formation of the methyl derivatives from the sulphinic acids had been investigated. From the alkaline mother liquors whence the sodium salts of these substances had separated, more soluble salts were isolated by adding concentrated alkali hydroxide. The substances obtained from these by mineral acids resisted all attempts at complete purification; but there is little doubt that they are the oxides of the corresponding hydroxythioxanthenes which have escaped reduction by the excess of the sulphinic acid. When heated in a vacuum at 200° they char and furnish a sublimate of the thioxanthone. The solubility of the sodium salts of these substances suggested a means of removing similar impurities from the crude hydroxythioxanthone, and the following method of preparation was adopted.

It was found that the yield of hydroxythioxanthone may be much improved by employing a relatively large quantity of phenol, for much of this substance is removed by sulphonation during the course of the interaction with *o*-thiolbenzoic acid. In other respects the condensation was effected as previously described. The product obtained by adding the mixture to water was dissolved in hot $2N$ -alkali hydroxide, and on cooling the solution the sodium salt of hydroxythioxanthone separated in orange needles. These were collected, and washed with the cold medium, in which they are almost insoluble. The purified phenol was liberated from this sodium salt with mineral acid, and it was eventually sublimed in a vacuum at 200° :

0.1067 gave 0.2655 CO_2 and 0.3569 H_2O . $\text{C}=67.9$; $\text{H}=3.7$.

$\text{C}_{13}\text{H}_8\text{O}_2\text{S}$ requires $\text{C}=68.4$; $\text{H}=3.5$ per cent.

The *hydroxythioxanthone* thus obtained forms large, lemon-yellow needles, which exhibit a metallic lustre, and melt at 243° . The substance is very sparingly soluble in most cold organic media, and its orange-coloured sodium salt is almost insoluble in cold water.

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