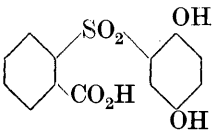
CCCCXVII.—*Hydroxy-derivatives of Thioxanthone Dioxide.*

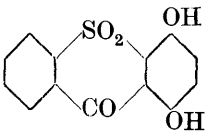
By William Bennett Price and Samuel Smiles.

During an examination of the abnormal properties of 1-methoxy- and 1-hydroxy-thioxanthones a comparison with the corresponding sulphones was desirable. The only method hitherto used for the

preparation of substituted thioxanthone dioxides is the oxidation of the corresponding thioxanthone with hydrogen peroxide or similar agents (Ullmann and Glenck, *Ber.*, 1916, **49**, 2491). This process is generally valuable, but the application to hydroxythioxanthones is not always successful, particularly in the case of 1 : 4-dihydroxy-derivatives. An effective process leading to the 1 : 4-dihydroxythioxanthone dioxide and certain of its derivatives has been found in the action of 2-sulphinobenzoic acid upon *p*-benzoquinones. In accordance with the general behaviour of sulphinic acids with quinones (Hinsberg, *Ber.*, 1894, **27**, 3259) 2 : 5-*dihydroxydiphenylsulphone*-2′-*carboxylic acid* (I) was obtained which by dehydration yielded the thioxanthone dioxide (II).



(I.)



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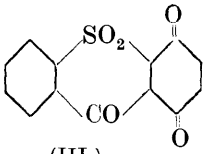
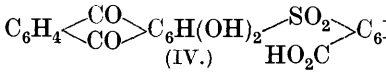
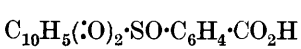


(III.)

The interesting quinone (III) was isolated when this 1 : 4-dihydroxy-derivative was oxidised with lead tetra-acetate. The union of 2-sulphinobenzoic acid with simple *p*-quinones such as toluquinone and chlorobenzoquinone took place easily and even with quinizarinquinone the substituted phenylanthraquinonylsulphone (IV) was obtained, but in this case dehydration yielding the thioxanthone dioxide could not be effected. Union of 1 : 2-naphthaquinone and this sulphinic acid did not take place in the normal manner, but gave an unstable additive product containing an additional molecule of water. Dehydration of this material by heating it alone or in solvents removed water (2 mols.) and gave a product which is to be regarded as the sulphoxide (V) derived from 1 : 2-naphthaquinone, since it yielded a phenylhydrazone and a phenazine and on being heated with acetic anhydride gave the naphthathioxanthonequinone (VI).



(IV.)



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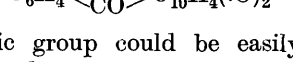
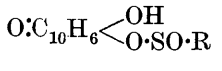


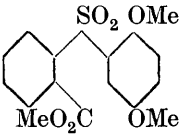
(VI.)

The 2-thiobenzoic group could be easily removed from this primary additive product by reduction, whereas this group in the sulphoxide quinone (V) was relatively stable to mild reducing agents. For these reasons it is suggested that the primary product of reaction between 1 : 2-naphthaquinone and 2-sulphinobenzoic acid is best represented by the structure (VII), the sulphinic acid reacting in the

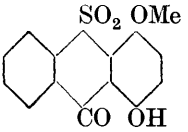
tautomeric hydroxy-form R·SO·OH. This case is evidently similar to that encountered by Hinsberg (*Ber.*, 1919, **52**, 28) in the union of 1 : 4-naphthaquinone with naphthalene-1-sulphinic acid. Hinsberg isolated from these reagents an additive product which under the action of heat lost water and was converted into the sulphoxide (compare V) derived from 1 : 4-naphthaquinone. It was thought that this abnormal behaviour of naphthalene-1-sulphinic acid and of 2-sulphinobenzoic acid might be associated with the ortho-substituent contained by them, but preliminary experiments with other ortho-substituted sulphinic acids and 1 : 2-naphthaquinone have given the usual type of sulphone. Further investigation of the necessary conditions is being made.



(VII.)



(VIII.)



(IX.)

In a study of the methylation of these hydroxythioxanthone dioxides in alkaline media the usual inhibitory effect of the ortho-carbonyl group was observed in the 1-hydroxy-derivatives. For instance, the 2-*methoxy-* and 2 : 3-*dimethoxy-thioxanthone dioxides* were easily obtained from the hydroxy-compounds by this method, but the 1 : 4-dihydroxy-derivative (II) was only slightly attacked even under intense conditions, the chief product being then 1-*hydroxy*-4-*methoxythioxanthone dioxide* (IX). The ortho-sulphonyl group does not exert this inhibitory effect in alkaline methylation. For example, *p*-cresol-*o*-sulphone was rapidly alkylated and 2 : 5-dihydroxydiphenylsulphone-2′-carboxylic acid (I) gave almost theoretical yields of the *ester* (VIII). Similar results were obtained with other hydroxy-sulphones.

Experimental.

When equimolecular quantities of 2-sulphinobenzoic acid and *p*-benzoquinone or its simple derivatives were shaken with water (100 c.c. : 2 g. of reagents) reaction was complete in 1—2 hours. A small quantity of tarry material was usually formed; this was removed and the desired product, which separated from the liquid, was collected. The following are examples of hydroxy-derivatives of diphenylsulphone obtained by this method. 2 : 5-*Dihydroxydiphenylsulphone-2′-carboxylic acid* (I), from *p*-benzoquinone and 2-sulphinobenzoic acid, formed prisms, m. p. 235° (Found : C, 53·0; H, 3·6; S, 10·8. $C_{13}H_{10}O_6S$ requires C, 53·0; H, 3·4; S, 10·8%). The *diacetyl* derivative, needles from acetic acid, had

m. p. 188° (Found: C, 53·9; H, 3·8. $C_{17}H_{14}O_8S$ requires C, 53·9; H, 3·7%). When methyl sulphate (5 mols.) was added to a hot solution of this dihydroxy-acid (1 mol.) in aqueous sodium hydroxide (6 mols.) an almost theoretical yield of *methyl* 2 : 5-*dimethoxydiphenylsulphone*-2′-*carboxylate* (VIII), m. p. 195°, separated (Found: C, 57·1; H, 4·7. $C_{16}H_{16}O_6S$ requires C, 57·1; H, 4·7%). Hydrolysis of this ester yielded 2 : 5-*dimethoxydiphenylsulphone*-2′-*carboxylic acid*, which separated in plates, m. p. 223°, from acetic acid (Found: C, 55·7; H, 4·2. $C_{15}H_{14}O_6S$ requires C, 55·9; H, 4·3%).

Methyl-2 : 5-*dihydroxydiphenylsulphone*-2′-*carboxylic acid*, from 2-sulphinobenzoic acid and *p*-toluquinone, formed needles, m. p. 203° (Found: C, 54·4; H, 3·8. $C_{14}H_{12}O_6S$ requires C, 54·5; H, 3·9%).

Chloro-2 : 5-*dihydroxydiphenylsulphone*-2′-*carboxylic acid*, from chlorobenzoquinone and the sulphinic acid, separated from acetic acid in fine needles, m. p. 210° (Found: C, 47·4; H, 2·8. $C_{13}H_9O_6ClS$ requires C, 47·4; H, 2·7%). Sulphones of this type which form an intermediate stage in the synthesis of thioxanthone dioxides may also be obtained by oxidation of the corresponding sulphides, these being available from the reaction of phenols with the dichloride of 2-sulphinobenzoic acid (this vol., p. 2859). In certain cases this alternative may not be available. For example, when 2 : 4-dihydroxy-2′-carboxydiphenyl sulphide (this vol., p. 2862) was treated in the usual manner with hydrogen peroxide or similar agents the required sulphone could not be isolated, and restricted action of hydrogen peroxide led to 2 : 4-*dihydroxy*-2′-*carboxydiphenyl sulphoxide*, $C_6H_3(OH)_2{\cdot}SO{\cdot}C_6H_4{\cdot}CO_2H$, which gave a purple solution with sulphuric acid and had m. p. 204° (Found: C, 56·3; H, 3·7. $C_{13}H_{10}O_5S$ requires C, 56·1; H, 3·6%). This did not yield the corresponding thioxanthone with the usual dehydrating agents.

2-*Quinizarinphenylsulphone*-2′-*carboxylic Acid* (IV).—Acetic acid (20 c.c.; 1 g. of reagents) containing equal weights of quinizarinquinone and the sulphinic acid was boiled until separation of the products began. The *sulphone* was collected from the cooled liquid and purified from nitrobenzene; it formed red needles, m. p. 263°, and gave a blue solution in aqueous alkali hydroxide (Found: C, 59·2; H, 2·9. $C_{21}H_{12}O_8S$ requires C, 59·4; H, 2·8%).

Derivatives of Thioxanthone Dioxide.—Condensation of the 2-carboxy-derivatives of diphenylsulphone was effected by heating (100°) the solutions in sulphuric acid for varying periods, the progress of the reaction being indicated by the development of the intense red colour due to the thioxanthone dioxide. The products were isolated after addition of ice.

1 : 4-*Dihydroxythioxanthone dioxide* (II) separated from acetic acid in orange needles, m. p. 224°, which gave a crimson solution in

aqueous alkali (Found : C, 56·2; H, 3·0. $C_{13}H_8O_5S$ requires C, 56·5; H, 2·9%). The *diacetyl* derivative separated from alcohol in yellow needles, m. p. 174° (Found : C, 56·7; H, 3·3. $C_{17}H_{12}O_7S$ requires C, 56·6; H, 3·3%).

Methyl-1 : 4-*dihydroxythioxanthone dioxide* formed orange plates, m. p. 175°, from acetic acid (Found : C, 57·5; H, 3·7. $C_{14}H_{10}O_5S$ requires C, 57·9; H, 3·4%).

Chloro-1 : 4-*dihydroxythioxanthone dioxide* was obtained in similar form, m. p. 230° (Found : C, 50·3; H, 2·5. $C_{13}H_7O_5ClS$ requires C, 50·2; H, 2·2%).

Thioxanthone Dioxide 1 : 4-*Quinone* (III).—A thin paste of the 1 : 4-dihydroxy-derivative (2 g.) and acetic acid was triturated with lead tetra-acetate (4 g.). After 4 days the solid was collected and purified from benzene. The desired product was thus obtained in yellow needles, m. p. 185°, which liberated iodine from aqueous potassium iodide (Found : C, 56·7; H, 2·2. $C_{13}H_6O_5S$ requires C, 56·9; H, 2·2%).

1 : 4-*Dimethoxythioxanthone dioxide* was obtained either by oxidation of 1 : 4-dimethoxythioxanthone (Clarke and Smiles, J., 1911, **99**, 1535) with hydrogen peroxide in warm acetic acid or by heating 2 : 5-dimethoxydiphenylsulphone-2′-carboxylic acid or its methyl ester with sulphuric acid. The substance separated from acetic acid in pale yellow needles, m. p. 193° (Found : C, 59·1; H, 4·1. $C_{15}H_{12}O_5S$ requires C, 59·2; H, 3·9%). It is also formed when the dihydroxy-compound is submitted to alkaline methylation, but the yields are poor even under intense conditions. The following experiment is quoted in illustration. The dark red potassium salt of the dihydroxythioxanthone dioxide was heated (130°) for 6 hours with excess of methyl sulphate. After the mixture had been cooled, the excess of the ester was decomposed by aqueous alkali. The dimethyl ether was then obtained (7—8%) from the material unattacked by alkali hydroxide, and from the remainder the 1-hydroxy-4-methoxy-derivative (IX) was isolated by means of the sparingly soluble sodium salt. This monomethyl ether (m. p. 184°) was identified with a sample prepared by another synthesis which will be described in a future communication.

2-*Hydroxythioxanthone Dioxide*.—When phenol and 2-thiolbenzoic acid were dissolved in warm sulphuric acid (Christopher and Smiles, J., 1911, **99**, 2050), or when the product from phenol and the dichloride of 2-sulphinobenzoic acid (this vol., p. 2862) was treated with this solvent, a hydroxythioxanthone was formed which on methylation yielded a methoxythioxanthone identical with the 2-derivative. The constitution of the latter was determined by a synthesis which will be subsequently described.

A solution of this 2-hydroxythioxanthone and excess of hydrogen peroxide in hot acetic acid was kept at 100° during 1 hour. The required *sulphone* then separated in shining yellow needles, m. p. 259° (Found: C, 59·7; H, 3·2. $C_{13}H_8O_4S$ requires C, 60·0; H, 3·0%). 2-*Methoxythioxanthone dioxide*, m. p. 204°, was obtained in good yield by alkaline methylation and formed pale yellow plates from acetic acid (Found: C, 61·0; H, 3·6. $C_{14}H_{10}O_4S$ requires C, 61·3; H, 3·6%).

2 : 3-*Dihydroxythioxanthone Dioxide*.—When pyrocatechol was submitted to the same treatments as phenol in the foregoing case, a dihydroxythioxanthone was obtained. It was identical with a sample of the 2 : 3-derivative prepared by another synthesis. When this substance was oxidised in the usual manner the required *sulphone* was obtained in yellow needles, m. p. 203° (decomp.) (Found: C, 56·2; H, 3·1. $C_{13}H_8O_5S$ requires C, 56·5; H, 2·9%). Aqueous alkaline methylation of this material gave good yields of 2 : 3-*dimethoxythioxanthone dioxide*, which formed long, yellow needles, m. p. 241°, from acetone (Found: C, 59·2; H, 4·2. $C_{15}H_{12}O_5S$ requires C, 59·2; H, 3·9%).

Naphthalene Derivatives.—An aqueous solution (400 c.c.) of 2-sulphinobenzoic acid (3·6 g.) was added to a stirred suspension of 1 : 2-naphthaquinone (2·4 g.) in water (50 c.c.). When the quinone had disappeared, the tarry matter was removed from the clear solution, the latter kept for 2 days, and the crystalline product purified from alcohol–water.

The desired *additive product* (VII) was thus obtained in shining plates, m. p. 156° (decomp.), which were sparingly soluble in water and readily soluble in alcohol (Found: C, 56·2; H, 4·2; S, 8·7. $C_{17}H_{12}O_6S,H_2O$ requires C, 56·3; H, 3·9; S, 8·8%). When a solution of this material in 10 times its weight of acetic acid was boiled for 1 hour, 1 : 2-*naphthaquinone* 2′-*carboxyphenyl sulphoxide* (V) was obtained. This separated from the cooled liquid in red needles, m. p. 236°, which were sparingly soluble in most organic media (Found: C, 62·2; H, 3·3; S, 9·8. $C_{17}H_{10}O_5S$ requires C, 62·6; H, 3·0; S, 9·8%). This quinone yielded, after reaction with phenylhydrazine in acetic acid, a *phenylhydrazone*, m. p. 251° (Found: N, 6·7. $C_{23}H_{16}O_4N_2S$ requires N, 6·7%). Also the *quinoxaline* derivative was obtained by reaction with *o*-phenylenediamine in the usual manner. This formed bright red needles, m. p. 292—293° (Found: C, 69·3; H, 3·8. $C_{23}H_{14}O_3N_2S$ requires C, 69·3; H, 3·5%).

3 : 4-*Naphthathioxanthone*-1 : 2-*quinone* (VI).—When a solution of the naphthaquinone sulphoxide (V) (1 g.) and freshly fused sodium acetate (5 g.) in acetic anhydride (20 c.c.) was boiled (3 hours),

condensation took place. The brown crystalline cake, remaining after the solvent had been decomposed by water, was purified from acetic acid. The *quinone* was then obtained in orange-brown needles with a metallic lustre, m. p. 244—245°, which were insoluble in alkali (Found : C, 69·8; H, 2·9. $C_{17}H_8O_3S$ requires C, 69·8; H, 2·7%).

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