241. *Methoxy-derivatives of Xanthone and Thioxanthone.*

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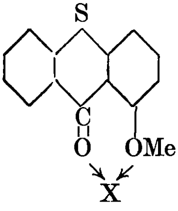
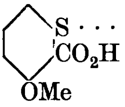
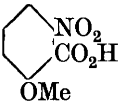
In previous communications (Roberts and Smiles, J., 1929, 863, 1322) it was shown that the salts and stannichlorides of 1-methoxy-derivatives of thioxanthone must be regarded as having a chelate structure (*e.g.*, I where X is H or $SnCl_4$). The data hitherto available have been furnished by derivatives in which methoxy-substitution is homonuclear; the study has now been extended to thioxanthones containing heteronuclear methoxyl groups, the main objects being the examination of a 1 : 8-dimethoxythioxanthone and of the analogue of the dimethyl ether of euxanthone in the thioxanthone series.

(I.)





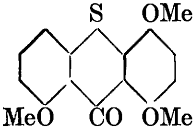
(II.)



(III.)

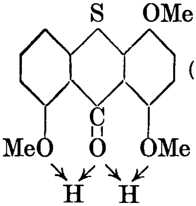
The synthesis of derivatives of these types has involved the preparation of 6-*methoxy*-2-*dithiobenzoic acid* (II). The 2-nitro-6-methoxybenzoic acid (III) which was required is mentioned in the literature, but the properties ascribed to it appear to be indeterminate. Simonsen and Rau (J., 1917, **111**, 227) gave this structure to an acid having m. p. 179—180°, but later it is mentioned (Simonsen, J., 1918, **113**, 782) that an acid of m. p. 159—160° had this constitution. The required material has now been synthesised by oxidation of 2-nitro-6-methoxytoluene, obtained from 2-nitro-6-hydroxytoluene (Ullmann, *Ber.*, 1884, **17**, 1961) by methylation under special conditions. The properties of the acid obtained agreed with those ascribed to it by Simonsen and Rau (*loc. cit.*). The corresponding *amino-acid* readily yielded the diazo-derivative and subsequently the thiocyanate; the latter on alkaline hydrolysis gave the required dithio-acid (II).

When this dithio-acid was condensed with quinol dimethyl ether, 1 : 4 : 8-*trimethoxythioxanthone* (IV) was obtained. This substance yielded a *diperchlorate* having the physical properties characteristic of salts of 1-methoxythioxanthones. Since the saturated anion of perchloric acid does not permit the formation of diacid salts in the manner suggested by Pfeiffer ("Organische Molekül-verbindungen," 1922, 68) in the case of polyhydrochlorides (compare V), it is concluded that the kation of this perchlorate contains quadricovalent oxygen (VI). The existence of oxygen in this condition has already been postulated by Sidgwick (*Nature*, 1923, **111**, 808; J., 1930, 1461; compare also Auger and Robin, *Compt. rend.*, 1924, **178**, 1546). Evidence has also been obtained of the existence of a *distannichloride* of (IV): all thioxanthones hitherto examined containing only one methoxyl in the position indicated have yielded monoperchlorates and monostannichlorides.


(IV.)

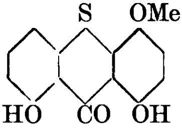
$>C{=}O{\rightarrow}H\}Cl \cdots HCl$

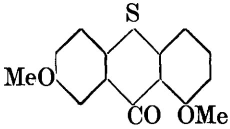
(V.)


(VI.)

Like other derivatives of this series which contain 1-methoxyl groups, the substance (IV) is readily hydrolysed by boiling hydrochloric acid, yielding 1 : 8-*dihydroxy*-4-*methoxythioxanthone* (VII) (compare Levi and Smiles, J., 1931, 530). The latter, like monohydroxy-derivatives of its type, is insoluble in aqueous alkali hydroxide, but the hope thus engendered that a bisdiacetoborate (type VI) would be obtained from it was not fully realised; however, the product obtained by usual methods contained more than 1·5 atoms of boron per molecule of the thioxanthone.

(VII.)




(VIII.)

When 6-methoxy-2-dithiobenzoic acid (II) was condensed with anisole, a *dimethoxythioxanthone* was obtained to which the 1 : 7-

dimethoxy-structure (VIII) is ascribed, since it has been shown (J., 1929, 864) that 2-methoxythioxanthone is obtained from 2-thiolbenzoic acid and anisole in a similar manner. It gave a *monoperchlorate* and a *stannichloride* of the composition B,$SnCl_4$ required by a monochelate structure (I). The corresponding member of the xanthone series, the dimethyl ether of euxanthone, is conveniently obtained from euxanthone by the method of Baker and Robinson (J., 1928, 3116). This substance also yields a *stannichloride* of the composition B,$SnCl_4$ and with dry hydrogen chloride forms a *trihydrochloride* B,3HCl. The basic character of 1-alkyl ethers of euxanthone has been already recorded in the literature; a hydrochloride of the 1-ethyl ether has been observed by Herzig (*Ber.*, 1908, **41**, 3895) and Perkin (J., 1920, **117**, 699) obtained a chloroplatinate and a ferrichloride of 1 : 7-dimethoxyxanthone.

Further investigation of the isomeric monomethyl ethers now recorded supports the structures already assigned to these substances by previous investigators (Ullmann and Panchaud, *Annalen*, 1906, **350**, 108; Herzig, *Monatsh.*, 1912, **33**, 673). Thus the 7-hydroxy-1-methoxyxanthone yields a *stannichloride*, B,$SnCl_4$, and does not give a diacetoborate with the usual reagent and is merely acetylated by it. On the other hand, the 1-hydroxy-7-methoxy-derivative is devoid of basic character and yields a characteristic *diacetoborate*.

A comparison of the basic strengths of these methoxy-derivatives has been made by the method previously described (Roberts and Smiles, *loc. cit.*, p. 866); the data shown in the table represent the relative volumes of alcohol required for complete hydrolysis of equimolecular solutions of the sulphates.

Substance.	C.c.
(1) Xanthone	4
(2) 1 : 7-Dihydroxyxanthone	5
(3) Thioxanthone	7
(4) 1-Hydroxy-7-methoxyxanthone	8
(5) 1-Methoxy-7-acetoxyxanthone	20
(6) 1 : 7-Dimethoxyxanthone	22
(7) 7-Hydroxy-1-methoxyxanthone	30
(8) 1 : 7-Dimethoxythioxanthone	30
(9) 7-Hydroxy-1-methoxythioxanthone	38—40

It is evident that, as previously observed in the thioxanthone series, the stability of the salts of these xanthone derivatives is greatly enhanced by the presence of 1-methoxyl, the comparison of Nos. 2 and 4 with Nos. 5, 6, and 7 being noteworthy. When 1 : 7-dimethoxythioxanthone (VIII) is hydrolysed by 90% sulphuric acid, a *hydroxy-methoxy*-derivative is obtained as in the case of the hydrolysis of 1 : 7-dimethoxyxanthone by this reagent, when 7-hydroxy-1-methoxyxanthone is formed (Herzig, *Monatsh.*, 1891, **12**, 161). An analogous structure is now assigned to the thioxanthone derivative (No. 9), since the substance yields salts of enhanced basic character. In conclusion, attention may be directed to a comparison between Nos. 6 and 8 and between 7 and 9: the evident influence of sulphide sulphur on the stability of the salts is to be expected on theoretical grounds and is of the same kind as that recorded by other observers in comparing *O*- and *S*-analogues (compare Dilthey, *J. pr. Chem.*, 1930, **124**, 81; Behagel and Rollmann, *Ber.*, 1929, **62**, 2693). The increase in basicity associated with the presence in position 7 of the strongly polar hydroxyl is noteworthy.

EXPERIMENTAL.

2-*Nitro*-6-*methoxytoluene*.—2-Nitro-6-hydroxytoluene (20 g.) (Ullmann, *Ber.*, 1884, **17**, 1961) and anhydrous potassium carbonate (55 g.) were treated with methyl sulphate (8·3 g.), and the cooled mixture was treated with water and ether. The methoxy-compound, purified from unchanged cresol, crystallised from aqueous alcohol in long colourless needles, m. p. 53°.

2-*Nitro*-6-*methoxybenzoic Acid* (III).—2-Nitro-6-methoxytoluene (10 g.) and potassium permanganate (23·5 g.) were heated with water (1000 c.c.) until the permanganate was destroyed. After evaporation of the filtered liquid to 50 c.c., the acid was isolated as a colourless crystalline powder, m. p. 180°. It crystallised from water in needles or plates (Found: C, 48·6; H, 3·4. Calc. for $C_8H_7O_5N$: C, 48·7; H, 3·5%).

2-*Amino*-6-*methoxybenzoic Acid*.—The nitro-acid (III) (2·3 g.), dissolved in aqueous ammonia (8·5 c.c.), was added slowly to a well-stirred paste of ferrous hydroxide (from 20 g. of ferrous sulphate). After 30 minutes' boiling, the liquid was filtered from ferric hydroxide and evaporated to 12 c.c. The *amino-acid*, isolated by addition of acetic acid, crystallised from water in needles, m. p. 87° (Found: C, 57·4; H, 5·5. $C_8H_9O_3N$ requires C, 57·4; H, 5·3%).

6-*Methoxy*-2-*dithiobenzoic Acid* (II).—2-Amino-6-methoxybenzoic acid (4·9 g.) in hydrochloric acid (12 c.c.) and water (25 c.c.) was diazotised at 0° with sodium nitrite (2·15 g.) in water (15 c.c.), the solution added to a paste of sodium thiocyanate (6 g.) and cuprous thiocyanate (6 g.) at 70°, the reaction completed at the boiling point, and the resulting thiocyano-acid converted into the corresponding disulphide by evaporation to dryness of its alkaline solution. The *disulphide* crystallised from glacial acetic acid in colourless needles, m. p. 187° [Found: C, 51·9; H, 3·9. $(C_8H_7O_3S)_2$ requires C, 52·4; H, 3·8%].

Derivatives of Thioxanthone.—1 : 4 : 8-*Trimethoxythioxanthone* (IV). The disulphide (II) (3 g.), dissolved in concentrated sulphuric acid

(55 c.c.), was shaken during the gradual addition of a large excess (18 g.) of quinol dimethyl ether. After some hours, the deep red fluorescent liquid was treated in the usual manner. The resulting *thioxanthone*, purified by sublimation under reduced pressure, melted at 208—209° (Found : C, 63·4; H, 4·7. $C_{16}H_{14}O_4S$ requires C, 63·5; H, 4·6%). It was instantly soluble in cold concentrated hydrochloric acid, forming a deep red solution, and gave fluorescent solutions in alcohol and in concentrated sulphuric acid. It absorbed over 2·5 mols. of dry hydrogen chloride at 760 mm. in less than 15 minutes, and was saturated by 2·8 mols. in 1¼ hours (Found : HCl, 25·3. $C_{16}H_{14}O_4S,3HCl$ requires HCl, 26·6%). The deep maroon-red product was unstable.

The *diperchlorate* (compare VI) separated in red needles having a metallic lustre from a solution of the thioxanthone in 60% aqueous perchloric acid (Found : $HClO_4$, 39·9. $C_{16}H_{14}O_4S,2HClO_4$ requires $HClO_4$, 39·9%).

When 1 : 4 : 8-trimethoxythioxanthone (0·5 g.) in dry benzene was added to a solution of stannic chloride (3 g.) in benzene, a deep red substance was formed, the composition of which approximated to that of a *distannichloride* (Found : $C_{16}H_{14}O_4S$, 39·1; SnO_2, 34·2. $C_{16}H_{14}O_4S,2SnCl_4$ requires $C_{16}H_{14}O_4S$, 36·6; SnO_2, 36·6%). When, however, the procedure was reversed by adding the solution of stannic chloride to the thioxanthone solution, a red *monostannichloride* resulted (Found : SnO_2, 27·0. $C_{16}H_{14}O_4S,SnCl_4$ requires SnO_2, 26·8%).

1 : 8-*Dihydroxy*-4-*methoxythioxanthone* (VII). 1 : 4 : 8-Trimethoxythioxanthone was warmed on the water-bath with fuming hydrochloric acid until the liquid was colourless. The insoluble product, which was also insoluble in cold, but slightly soluble in hot 2*N*-caustic soda with a yellow colour, formed an intense purple solution in concentrated sulphuric acid. The small amount of material available was brought to analysis in an impure state (Found : C, 61·7; H, 4·4. $C_{14}H_{10}O_4S$ requires C, 61·3; H, 3·6%).

A small quantity of the *diacetoborate*, prepared in the usual way, was purified by dissolving it in carbon tetrachloride, in which it was readily soluble but which does not dissolve boroacetic anhydride. The weight of the thioxanthone residue obtained on hydrolysing the derivative with boiling water indicated that it was a mixture of mono- and bis-diacetoborates (Found : $C_{14}H_{10}O_4S$, 59·1. $C_{22}H_{20}O_{12}SB_2$ requires 51·6; $C_{18}H_{15}O_8SB$ requires 68·1%).

1 : 7-*Dimethoxythioxanthone* (VIII). When 6-methoxy-2-dithiobenzoic acid in concentrated sulphuric acid was treated with anisole in the usual manner, 1 : 7-*dimethoxythioxanthone* resulted, which crystallised from alcohol as a yellow substance, m. p. 131—132°.

It dissolved in concentrated hydrochloric acid with a bright red colour, and its solutions in alcohol and in concentrated sulphuric acid were notably fluorescent. A specimen sublimed under reduced pressure melted at 136—138° (Found: C, 66·0; H, 4·5. $C_{15}H_{12}O_3S$ requires C, 66·1; H, 4·4%). The substance formed a *monoperchlorate*, which crystallised from the hot aqueous reagent in scarlet cubes having a metallic lustre (Found: $HClO_4$, 27·2. $C_{15}H_{12}O_3S,HClO_4$ requires $HClO_4$, 27·0%). The stannichloride was scarlet.

Initial attempts to obtain 1 : 7-dimethoxythioxanthone involved the use of *p*-thiolanisole, which was readily obtained as follows: Equimolecular quantities of anisole (20 g.) and sulphur chloride (12·7 g.) were warmed together until evolution of hydrogen chloride ceased. The product, when poured into a mixture of acetic acid and 2*N*-sulphuric acid, yielded a solution of *pp'*-dimethoxydiphenyl disulphide, which was forthwith reduced to the mercaptan by boiling it for 1 hour with zinc dust. The substance purified by distillation in steam was a colourless oil, b. p. 227° (Gattermann, *Ber.*, 1899, **32**, 1148, gives 227°), with a mushroom-like smell. No trace of the *o*-isomeride was observed.

7-*Hydroxy*-1-*methoxythioxanthone* was formed when 1 : 7-dimethoxythioxanthone was treated at 100° for 3 hours with 90% sulphuric acid. It crystallised from chloroform in hexagonal plates, m. p. 246° (decomp.) (Found: C, 65·4; H, 3·9. $C_{14}H_{10}O_3S$ requires C, 65·1; H, 3·8%). It formed a strongly yellow solution in aqueous caustic soda, and a green-fluorescent red solution in concentrated hydrochloric acid. The perchlorate was a brick-red solid.

Derivatives of Euxanthone.—1-*Hydroxy*-7-*methoxyxanthone.* The presence of a 1-hydroxyl group was shown by the formation of a *stannichloride* (Found: SnO_2, 31·9. $C_{14}H_{10}O_4,SnCl_4$ requires SnO_2, 32·3%) and of a yellow *diacetoborate* (Found: $C_{14}H_{10}O_4$, 64·9. $C_{18}H_{15}O_8B$ requires $C_{14}H_{10}O_4$, 65·4%).

1 : 7-*Dimethoxyxanthone* (VIII). 1-Hydroxy-7-methoxyxanthone (10 g.) was dissolved in acetone (400 c.c.) containing methyl sulphate (50 c.c.), and 20% aqueous caustic soda solution (50 c.c.) added. The mixture was warmed for a few minutes, further quantities of methyl sulphate and caustic soda added, and the xanthone isolated by the usual methods. A dark brown *trihydrochloride* was formed when the xanthone was saturated with the dry reagent (Found: HCl, 31·2. $C_{15}H_{12}O_4,3HCl$ requires HCl, 30·0%). The dark-coloured *stannichloride* was of the usual type (Found: SnO_2, 29·0. $C_{15}H_{12}O_4,SnCl_4$ requires SnO_2, 29·2%).

7-Hydroxy-1-methoxyxanthone formed a yellow *dihydrochloride* with dry hydrogen chloride (Found : HCl, 23·6. $C_{14}H_{10}O_4,2HCl$ requires HCl, 23·1%). Boroacetic anhydride reagent acetylated the xanthone, the product being 1-methoxy-7-acetoxyxanthone, a colourless substance, m. p. 182°, recently described by Robertson and Waters (J., 1929, 2243) (Found : C, 67·9; H, 4·3. Calc. : C, 67·6; H, 4·2%).

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