CCXXVII.—*A Method of inserting the Thio-aryl Group.*

By Leslie George Scott Brooker and Samuel Smiles.

In previous communications (J., 1924, **125**, 176; 1925, **127**, 224, 1821), the constitution of the disulphoxides was discussed and evidence adduced in favour of the thiolsulphonate structure. It was pointed out that the chief reactions of these substances depend on the fission of the thiosulphonate group, but in many cases the results in their bearing on the structure of the disulphoxides may be ambiguous, since the initial products of fission are liable to further attack by the reagent or to other changes. During a search for reagents which would yield the desired evidence without this complication, it was observed that whilst alkali hydroxide (Otto and Rossing, *Ber.*, 1886, **19**, 1236) or the alkali derivatives of common phenols attack aromatic disulphoxides, giving sulphinic acid and disulphide, the sodium derivatives of certain enolic compounds decompose them smoothly in the simple manner:

$$R'SO_2{\cdot}SR'' + Na[CHX_2] = R'SO_2Na + R''S{\cdot}CHX_2,$$

where X represents acetyl, carbethoxyl, or cyanogen. It is evident that this decomposition clearly indicates the unsymmetrical character of the disulphoxides which has been already claimed on other grounds; but it may be observed that, with the disulphoxides containing different aromatic groups which have been examined, only one sulphinic acid and one thio-aryl derivative are formed. It is also significant that the sulphinic acid isolated has in all cases been found to be the one from which the disulphoxide was synthesised. There is therefore no reason to suppose that intramolecular change such as

$$R'SO_2{\cdot}SR'' \rightleftharpoons R'SO{\cdot}SOR'' \rightleftharpoons R'S{\cdot}SO_2R''$$

takes place and the evidence on this point previously adduced is confirmed. For example, *o*-nitrophenyl *p*-chlorobenzenethiolsulphonate, prepared from silver *p*-chlorobenzenesulphinate and *o*-nitrophenylsulphur chloride, yielded, when treated with the sodium derivative of acetylacetone, sodium *p*-chlorobenzenesulphinate and acetylacetonyl *o*-nitrophenyl sulphide:

$$C_6H_4Cl{\cdot}SO_2{\cdot}S{\cdot}C_6H_4{\cdot}NO_2 + Na[CH(COMe)_2] \rightarrow C_6H_4Cl{\cdot}SO_2Na + (COMe)_2CH{\cdot}S{\cdot}C_6H_4{\cdot}NO_2 \quad (I.)$$

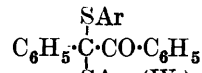
which were isolated in respective yields of 89 and 86% of the theoretical. This behaviour with disulphoxides is exhibited by the sodium derivatives of ethyl malonate, ethyl methylmalonate, acetylacetone, ethyl acetoacetate, and ethyl cyanoacetate. In the experimental part of this paper, twelve examples are quoted and it is

evident that the process may with advantage be applied to the preparation of thio-aryl derivatives of the substances in question.

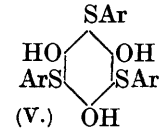
Since it appeared that the capacity of these methylene derivatives to decompose disulphoxides in this manner depends on their tautomeric character, the study was extended to other materials which are known to be capable of tautomeric change or may be suspected of it. Thus phenylacetonitrile gave the very stable disubstituted nitrile (II) and ethyl phenylacetate the corresponding ester (III), deoxybenzoin gave dimercaptols of benzil (IV), whilst phloroglucinol yielded the trithioaryl derivative (V).

(II.) $C_6H_5\cdot C(CN)(SAr)_2$

(III.) $C_6H_5\cdot C(CO_2Et)(SAr)_2$

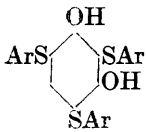


(IV.)

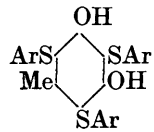


(V.)

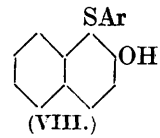
The constitution assigned to the last substance follows from the fact that it furnishes a triacetyl derivative, the structure containing the *gem*-dithioaryl group being thus excluded. Resorcinol yields the trithioaryl derivative (VI) to which the given orientation must be ascribed, since orcinol yields the homologue (VII). The results obtained with the naphthols are equally interesting : β-naphthol yields the mono-derivative (VIII), whilst α-naphthol gave the disubstitution product (IX), and 6- and 8-hydroxyquinolines behave similarly (X and XI).



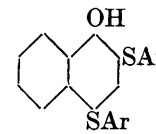
(VI.)



(VII.)



(VIII.)

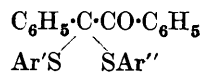


(IX.)

(X.) $C_9H_5N(OH)(SAr)$ $C_9H_4N(OH)(SAr)_2$ (XI.)

One noteworthy feature of these cases is the ease with which complete substitution takes place; even if excess of the sodium derivative be present, the multisubstitution product is formed to the almost complete exclusion of the monothioaryl compound. In fact, it would appear that the later stages of substitution are more easily accomplished than the first, and the conclusion is borne out by the fact that a mixture of deoxybenzoin and its monothioaryl derivative (XII) yielded, when treated with a disulphoxide containing a different thioaryl group, the mixed mercaptol of benzil (XIII) instead of the two individual thioaryl deoxybenzoins (compare XII).

(XII.) 



(XIII.)

The reactivity of phloroglucinol (Herzig and Zeisel, *Monatsh.*, 1888, **9**, 217, 882, etc.) and of the naphthols (Friedländer, *Ber.*, 1921, **54**, 620) might be anticipated from their known character, and the analogous behaviour of resorcinol, orcinol, and the hydroxyquinolines is suggestive. These aromatic hydroxy-derivatives are sharply distinguished from other phenols by this reaction, for it is remarkable that the sodium derivatives of phenol, *p*-cresol, *m*-cresol and others do not behave in this manner; with these substances the disulphoxide merely yields the product of attack by alkali, whilst the phenol remains unsubstituted. Sufficient data are not available at present to permit the mechanism of this reaction to be more fully discussed, but as bearing on the question it is important to note that dibenzoylmethane, anthrone, and resorcinol monomethyl ether do not undergo the reaction. From these facts and others, it appears at the present state of the investigation that the behaviour of sodium enolates with aromatic disulphoxides depends on the mobility of the tautomeric system contained in them.

Experimental.

The interactions were generally conducted as follows: A mixture of the disulphoxide with alcohol was added to a solution of the ester, ketone, or phenol in the same solvent, which contained the requisite quantity of sodium ethoxide. To complete the reaction, the mixture was warmed for a period which varied with the disulphoxide and the type of the other reactant; in most instances, the liquid eventually became neutral or weakly acid, but in either case sufficient alkali carbonate was added to restore alkalinity. The solvent was then evaporated and after the residue had been mixed with water the substituted ester, ketone, or phenol was removed, if necessary, with ether or other suitable solvent. The sulphinic acid was isolated from the aqueous portion in the usual manner, whilst the desired substitution product, sometimes contaminated with a little disulphide, was obtained by evaporating the organic solvent; it was then submitted to a further purification suited to its character. In most cases where esters were under examination, the identity of the product was established by conversion into the acid on hydrolysis.

I.—*Derivatives obtained from Esters and Nitriles.*

p-Tolylthiolacetic acid, $C_7H_7\cdot S\cdot CH_2\cdot CO_2H$, was obtained in colourless plates, m. p. 92·5° (Found: S, 17·3. Calc.: S, 17·6%) by hydrolysis of the liquid esters formed by the interaction of *p*-tolyl disulphoxide with either ethyl malonate, ethyl cyanoacetate or ethyl acetoacetate. In these reactions, *p*-tolylsulphinic acid also was obtained in yields of 80—95%.

p-Chlorophenylthiolacetic acid, $C_6H_4Cl\cdot S\cdot CH_2\cdot CO_2H$, m. p. 104°, was obtained by hydrolysis of the liquid ester formed together with the sulphinic acid (93%) by interaction of *p*-chlorophenyl disulphoxide with ethyl malonate.

α-p-*Tolylthiolpropionic acid*, $C_6H_4Me\cdot S\cdot CHMe\cdot CO_2H$, m. p. 75°, was obtained by hydrolysis of the liquid ester yielded by interaction of *p*-tolyl disulphoxide and ethyl malonate (Found : C, 61·0; H, 6·3; S, 16·0. $C_{10}H_{12}O_2S$ requires C, 61·2; H, 6·2; S, 16·3%).

o-Nitrophenylthiolacetic acid, $O_2N\cdot C_6H_4\cdot S\cdot CH_2\cdot CO_2H$, m. p. 163—164°, was isolated by hydrolysis of the ester produced by the reaction of ethyl malonate with *o*-nitrophenyl 2 : 5-dichlorobenzenethiolsuphonate. In this reaction, the only sulphinic acid formed was the 2 : 5-dichlorophenyl derivative (92%).

Ethyl bis-2 : 5-*dichlorophenylthiolphenylacetate*,

$$C_6H_5\cdot C(S\cdot C_6H_3Cl_2)_2\cdot CO_2Et,$$

obtained (98% yield) from 2 : 5-dichlorophenyl disulphoxide and ethyl phenylacetate, formed colourless needles, m. p. 118°, which were sparingly soluble in alcohol (Found : C, 51·2; H, 3·2. $C_{22}H_{16}O_2Cl_4S_2$ requires C, 51·0; H, 3·1%).

Di-p-*tolylthiolphenylacetonitrile*, $C_6H_5\cdot C(S\cdot C_6H_4Me)_2\cdot CN$, m. p. 89°, obtained (84%) together with *p*-tolylsulphinic acid (90%) from phenylacetonitrile and *p*-tolyl disulphoxide, was sparingly soluble in cold alcohol and was not hydrolysed by boiling concentrated hydrochloric acid (Found : C, 72·9; H, 5·5; S, 17·2. $C_{22}H_{19}NS_2$ requires C, 73·1; H, 5·2; S, 17·7%).

Bis-2 : 5-*dichlorophenylthiolphenylacetonitrile*,

$$C_6H_5\cdot C(S\cdot C_6H_3Cl_2)_2\cdot CN,$$

was prepared in a similar manner. It was purified (m. p. 129°) from acetic acid (Found : C, 51·0; H, 2·5. $C_{20}H_{11}NCl_4S_2$ requires C, 50·9; H, 2·3%).

II.—*Derivatives of Ketones.*

p-*Tolyl acetylacetonyl sulphide*, $C_7H_7\cdot S\cdot CH(COMe)_2$, m. p. 53°, was obtained (85%) from acetylacetone and *p*-tolyl disulphoxide (Found : C, 64·7; H, 6·5; S, 13·9. $C_{12}H_{14}O_2S$ requires C, 64·8; H, 6·35; S, 14·4%). The substance was soluble in aqueous alkali and gave a red coloration with alcoholic ferric chloride.

2 : 5-*Dichlorophenyl acetylacetonyl sulphide*, $C_6H_3Cl_2\cdot S\cdot CH(COMe)_2$, m. p. 97·5°, was obtained in a similar manner (Found : S, 11·3; Cl, 25·6. $C_{11}H_{10}O_2Cl_2S$ requires S, 11·5; Cl, 25·6%).

4-*Chlorophenyl acetylacetonyl sulphide*, $C_6H_4Cl\cdot S\cdot CH(COMe)_2$, obtained from acetylacetone and *p*-chlorophenyl disulphoxide, had m. p. 70° (Found : S, 13·2; Cl, 14·4. $C_{11}H_{11}O_2ClS$ requires S, 13·2; Cl, 14·6%).

o-*Nitrophenyl acetylacetonyl sulphide*, $NO_2 \cdot C_6H_4 \cdot S \cdot CH(COMe)_2$, was obtained from the interaction of acetylacetone and (*a*) *o*-nitrophenyl disulphoxide, (*b*) *o*-nitrophenyl 2 : 5-dichlorobenzenethiolsulphonate, (*c*) *o*-nitrophenyl *p*-chlorobenzenethiolsulphonate, the yield being about 85% in each case. From (*b*) and (*c*) respectively, 2 : 5-dichlorobenzenesulphinic acid (84%) and *p*-chlorobenzenesulphinic acid (89%) also were isolated. The substance, m. p. 136—137° (Found : C, 52·5; H, 4·6; S, 12·5. $C_{11}H_{11}O_4NS$ requires C, 52·1; H, 4·4; S, 12·7%), was further identified by synthesis from *o*-nitrophenylsulphur chloride and acetylacetone in boiling benzene.

Phenyl αα-*bis*-2 : 5-*dichlorophenylthiolbenzyl ketone*,

$$C_6H_5 \cdot CO \cdot C(S \cdot C_6H_3Cl_2)_2 \cdot C_6H_5,$$

was isolated from the interaction of deoxybenzoin and 2 : 5-dichlorophenyl disulphoxide. It separated from acetone and water in colourless prisms, m. p. 138° (Found : C, 56·9; H, 3·1. $C_{26}H_{16}OCl_4S_2$ requires C, 56·7; H, 2·9%). The substance was further identified as a monomercaptol of benzil by synthesis from benzil and 2 : 5-dichlorophenyl mercaptan in alcohol with the aid of hydrogen chloride and zinc chloride; the product melted at 138°, alone or mixed with the preceding specimen.

Phenyl α-5-*chloro*-2-*methoxyphenylthiol*-α-2 : 5-*dichlorophenylthiolbenzyl ketone*, $C_6H_5 \cdot CO \cdot C(S \cdot C_6H_3Cl \cdot OMe)(S \cdot C_6H_3Cl_2) \cdot C_6H_5$, was obtained (95%) from 2 : 5-dichlorophenyl disulphoxide and 5-chloro-2-methoxyphenyl desyl sulphide (XII); it separated from acetic acid in prisms, m. p. 170° (Found : C, 59·0; H, 3·4. $C_{27}H_{19}O_2Cl_3S_2$ requires C, 59·4; H, 3·5%). This product was not identical with the symmetrical mercaptol formed from benzil and 5-chloro-2-methoxyphenyl mercaptan (m. p. 178°). It is also noteworthy that this substance is formed from the reagents mentioned, even if excess of deoxybenzoin be present.

III.—*Derivatives of Aromatic Hydroxy-compounds.*

2 : 4 : 6-*Tri*-p-*chlorophenylthiolphloroglucinol*, $C_6(OH)_3(S \cdot C_6H_4Cl)_3$, formed (73%) by the reaction of phloroglucinol with *p*-chlorophenyl disulphoxide in presence of sodium ethoxide, separated from aqueous alcohol in needles, m. p. 174° (Found : C, 51·6; H, 3·1; Cl, 19·2; S, 17·3. $C_{24}H_{15}O_3Cl_3S_3$ requires C, 52·0; H, 2·7; Cl, 19·2; S, 17·3%).

2 : 4 : 6-*Tri*-p-*tolylthiolphloroglucinol*, $C_6(OH)_3(S \cdot C_6H_4Me)_3$, obtained from phloroglucinol and *p*-tolyl disulphoxide (94%), formed prisms from acetic acid; m. p. 175° (Found : C, 65·6; H, 4·9. $C_{27}H_{24}O_3S_2$ requires C, 65·8; H, 4·8%).

2 : 4 : 6-*Tri*-2′ : 5′-*dichlorophenylthiolphloroglucinol*,

$$C_6(OH)_3(S \cdot C_6H_3Cl_2)_3,$$

prepared in a similar manner, separated from aqueous alcohol in

needles, m. p. 223—224° (Found : C, 43·4; H, 1·9; Cl, 32·5; S, 14·8. $C_{24}H_{12}O_3Cl_6S_3$ requires C, 43·8; H, 1·8; Cl, 32·4; S, 14·6%). The *triacetyl* derivative, m. p. 163°, was obtained in the usual manner (Found : C, 45·8; H, 2·5; Cl, 27·2; S, 12·6. $C_{30}H_{18}O_6Cl_6S_3$ requires C, 46·0; H, 2·3; Cl, 27·2; S, 12·2%).

2 : 4 - *Di* - 4′ - *chlorophenylthiol* - 1 - *naphthol*, $OH{\cdot}C_{10}H_5(S{\cdot}C_6H_4Cl)_2$, obtained from sodium α-naphthoxide and *p*-chlorophenyl disulphoxide, separated from aqueous alcohol in needles, m. p. 135° (Found : C, 61·4; H, 3·4. $C_{22}H_{14}OCl_2S_2$ requires C, 61·5; H, 3·2%). The *acetyl* derivative had m. p. 135° (Found : Cl, 15·1. $C_{24}H_{16}O_2Cl_2S_2$ requires Cl, 15·1%).

2 : 4-*Bis*-2′ : 5′-*dichlorophenylthiol*-1-*naphthol*,

$$OH{\cdot}C_{10}H_5(S{\cdot}C_6H_3Cl_2)_2,$$

m. p. 172°, was prepared in a similar manner (Found : C, 52·5; H, 2·5. $C_{22}H_{12}OCl_4S_2$ requires C, 53·0; H, 2·4%).

Sodium β-naphthoxide with *o*-nitrophenyl *p*-chlorobenzenethiolsulphonate yielded sodium *p*-chlorobenzenesulphinate and 1-*o*-nitrophenylthiol-2-naphthol (formula VIII), m. p. 179—180°, identical with the product obtained by Zincke (*Annalen*, 1912, **391**, 57) from β-naphthol and *o*-nitrophenylsulphur chloride.

1-p-*Tolylthiol*-2-*naphthol*, $C_7H_7{\cdot}S{\cdot}C_{10}H_6{\cdot}OH$, m. p. 84°, was formed by the interaction of sodium β-naphthoxide and *p*-tolyl disulphoxide (Found : C, 76·7; H, 5·5. $C_{17}H_{14}OS$ requires C, 76·7; H, 5·3%), and 1-β-*naphthylthiol*-2-*naphthol*, $C_{10}H_7{\cdot}S{\cdot}C_{10}H_6{\cdot}OH$, m. p. 92°, was obtained from sodium β-naphthoxide and β-naphthyl disulphoxide (Found : C, 79·2; H, 4·9. $C_{20}H_{14}OS$ requires C, 79·4; H, 4·6%). These derivatives of β-naphthol do not couple with diazo-compounds in alkaline solution.

2 : 4 : 6-*Tri*-p-*tolylthiolorcinol*, $C_6Me(OH)_2(S{\cdot}C_6H_4Me)_3$, m. p. 143°, was obtained in the usual manner from orcinol and *p*-tolyl disulphoxide (Found : C, 68·5; H, 5·3; S, 19·1. $C_{28}H_{26}O_2S_3$ requires C, 68·6; H, 5·3; S, 19·6%).

2 : 4 : 6 - *Tri* - p - *chlorophenylthiolresorcinol*, $C_6H(OH)_2(S{\cdot}C_6H_4Cl)_3$, m. p. 158°, was obtained from resorcinol and *p*-chlorophenyl disulphoxide and purified from alcohol (Found : C, 53·6; H, 2·9. $C_{24}H_{15}O_2Cl_3S_3$ requires C, 53·6; H, 2·8%).

2 : 4 : 6-*Tri*-2′ : 5′-*dichlorophenylthiolresorcinol*,

$$C_6H(OH)_2(S{\cdot}C_6H_3Cl_2)_3,$$

m. p. 187°, was obtained in a similar manner (Found : C, 45·0; H, 2·0. $C_{24}H_{12}O_2Cl_6S_3$ requires C, 44·9; H, 1·9%). Alcoholic solutions of these resorcinol derivatives gave no colour when mixed with ferric chloride.

5-p-*Tolylthiol*-6-*hydroxyquinoline*, $C_7H_7{\cdot}S{\cdot}C_9H_5N{\cdot}OH$, obtained from 6-hydroxyquinoline and *p*-tolyl disulphoxide, had m. p.

138° (Found: C, 71·8; H, 5·0. $C_{16}H_{13}ONS$ requires C, 71·9; H, 4·9%).

5 : 7 - *Di* - p - *tolylthiol* - 8 - *hydroxyquinoline*, $(C_7H_7\cdot S)_2C_9H_4N\cdot OH$, formed thin, yellow needles, m. p. 126°, from alcohol. It was obtained from *p*-tolyl disulphoxide and 8-hydroxyquinoline in presence of sodium ethoxide (Found : C, 71·2; H, 5·2. $C_{23}H_{19}ONS_2$ requires C, 71·0; H, 4·9%).

5 : 7-*Bis*-2′ : 5′-*dichlorophenylthiol*-8-*hydroxyquinoline*,

$$(C_6H_3Cl_2\cdot S)_2C_9H_4H\cdot OH,$$

prepared in a similar manner, formed pale orange needles, m. p. 196°, from alcohol (Found : C, 50·2; H, 2·6. $C_{21}H_{11}ONCl_4S_2$ requires C, 50·5; H, 2·2%).

In conclusion, we desire to express our thanks to the Department of Scientific and Industrial Research for a grant which has enabled one of us to take part in these experiments.

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