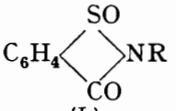
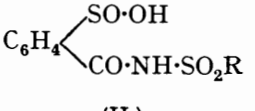
403. *The Chlorination of 2-Thiolbenzoic Acid.*

By L. E. Hart, E. W. McClelland, and (in part) F. S. Fowkes.

Chlorination of 2-thiolbenzoic acid and condensation of the product (IV) with aryl sulphonamides yields benz*iso*thiazolone oxides, the structure of which is deduced from their reactions. When the chlorination is effected in presence of ferric chloride, the product obtained reacts with water to give chlorodithiobenzoic acids and chlorobenzoic acids and condenses with ammonia and acetamide to give chlorobenz*iso*thiazolones. The mechanism of the chlorination of 2-thiolbenzoic acid is discussed.

The product obtained by chlorination of 2-thiol- or 2 : 2′-dithio-benzoic acid (compare Price and Smiles, J., 1928, 2858) reacts with aryl sulphonamides to give benz*iso*thiazolone oxides (I; R = $C_6H_5{\cdot}SO_2$, *p*-$C_6H_4Me{\cdot}SO_2$) and with acetamide to give the corresponding acetyl derivative (I; R = Ac).


(I.)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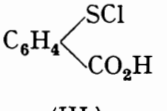
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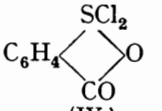
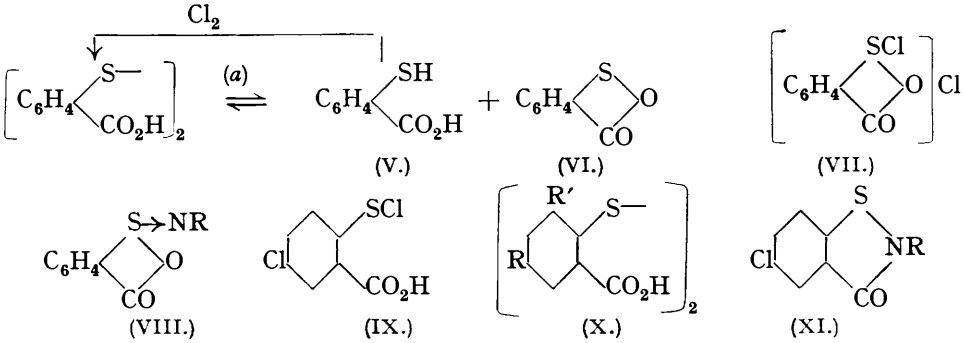

(IV.)

The structure assigned to these compounds is based on the following reactions. Oxidation of the benzenesulphonyl compound (I; R = $C_6H_5{\cdot}SO_2$) gives a small amount of *N*-benzenesulphonyl-*o*-benzoicsulphinide and benzenesulphonamide, and the acetyl derivative (I; R = Ac) yields *o*-benzoicsulphinide. Alkaline hydrolysis of the benzenesulphonyl

compound gives a sulphinic acid, evidently (II; R = C_6H_5), since successive treatment with mercuric chloride and hydrochloric acid eliminates the sulphino-group (Peters, *Ber.*, 1905, **38**, 2567; Kharasch and Chalkley, *J. Amer. Chem. Soc.*, 1921, **43**, 607) and yields *N*-benzoylbenzenesulphonamide. The acetyl compound (I; R = Ac) on hydrolysis with acid or alkali gives a mixture of *o*-carboxybenzenesulphinic acid and 2 : 2′-dithiobenzoic acid. Elimination of the acetyl group by heating with water gives the benz*iso*thiazolone oxide (I; R = H), which on reduction yields 2-thiolbenzamide, identified as the corresponding disulphide.

It has been shown (Price and Smiles, *loc. cit.*) that chlorination of 2-thiol- or 2 : 2′-dithio-benzoic acid gives the *S*-dichloro-anhydride (IV). The formation of this was attributed to loss of hydrogen chloride from the *o*-chlorothiol (III), presumably formed by fission of the disulphide, and subsequent addition of chlorine to the sulphenic anhydride (VI). Recent work on the dismutation of disulphides (McClelland and Warren, J., 1930, 1095; D'Silva and McClelland, J., 1932, 2883; Bartlett and McClelland, J., 1934, 818) suggests a more direct mechanism, not involving the formation of an *o*-chlorothiol; namely dismutation (*a*) of the disulphide and addition of chlorine to the dismutation product (VI), accompanied by oxidation of the thiol (V) to disulphide with consequent completion of the reaction.



The formula (VII) instead of (IV) is suggested for the dichloro-compound. The reaction of such a dichloro-compound with sulphonamides and amides to give the benz*iso*thiazolone oxides (I; R = $ArSO_2$, Ac) can be adequately accounted for by formation of the sulphilimine (VIII) and its subsequent rearrangement (VIII ⟶ I).

Chlorination of 2-thiol- or 2 : 2′-dithio-benzoic acid in presence of ferric chloride and treatment of the product with water yielded a dichloro-2 : 2′-dithiobenzoic acid (X; R = Cl, R′ = H), 3-chlorobenzoic acid, and 3 : 5-dichlorobenzoic acid. The formation of these compounds is attributed to the intramolecular rearrangement of the dichloro-compound (VII) to the chlorothiol (IX). This, reacting with water, gives an unstable sulphenic acid (IX; SCl = S·OH), which yields the dichloro-2 : 2′-dithiobenzoic acid (X; R = Cl, R′ = H) and the sulphinic acid (IX; SCl = SO_2H). The latter by elimination of sulphur dioxide gives 3-chlorobenzoic acid. The formation of 3 : 5-dichlorobenzoic acid indicates that dichlorination takes place to some extent. This was confirmed by the isolation of a tetrachloro-2 : 2′-dithiobenzoic acid (X; R = R′ = Cl) when chlorination was effected at a higher temperature.

The dichloro-2 : 2′-dithiobenzoic acid (X; R = Cl, R′ = H) was oriented by condensing it with ethyl acetoacetate (compare Smiles and McClelland, J., 1921, **119**, 1810). The product was 5-chloro-3-hydroxy-1-thionaphthen, identical with that obtained by cyclisation of 4-chlorothioglycollic acid (compare Auwers and Thies, *Ber.*, 1920, **53**, 2285). The disulphide is thus 5 : 5′-*dichloro*-2 : 2′-*dithiobenzoic acid*. Reduction of the disulphide gave the corresponding thiol (m. p. 193°), evidently 5-*chloro*-2-*thiolbenzoic acid*. Krishna and Singh (*J. Indian Chem. Soc.*, 1927, **4**, 291), by heating 4-chlorothiophenol with carbon tetrachloride, obtained a material which on reduction gave a substance (m. p. 110°) which they suggested was 5-chloro-2-thiolbenzoic acid, but no proof of orientation was given. The isolation of 3 : 5-dichlorobenzoic acid indicates that the tetrachloro-disulphide (X; R = R′ = Cl) is 3 : 5 : 3′ : 5′-*tetrachloro*-2 : 2′-*dithiobenzoic acid*.

When the product of chlorination of 2-thiol- or 2 : 2′-dithio-benzoic acid in presence of ferric chloride was treated with ammonia, the aminothiol (IX; Cl = NH_2) and the benz*iso*thiazolone (XI; R = H) were obtained. The production of the aminothiol is in accord with the formation of the chlorothiol (IX). Substitution of acetamide for ammonia yielded the *N*-acetylbenz*iso*thiazolone (XI; R = Ac) together with the benz*iso*thiazolone (XI; R = H). The former was also obtained by direct acetylation of (XI; R = H). No evidence of the formation of an *O*-acetyl derivative was obtained.

N-*Benzenesulphonyl*-o-*benzoicsulphinide*, which was required for comparison in the foregoing experiments, was obtained by treating the silver salt of *o*-benzoicsulphinide with benzenesulphonyl chloride. When *o*-benzoicsulphinide was treated with benzene- or toluene-sulphonyl chloride in presence of pyridine, the O-*derivatives* were obtained. *N*-Benzenesulphonyl-*o*-benzoicsulphinide undergoes ring fission to 2-*N*-benzenesulphonylcarbamylbenzenesulphonic acid (II; R = C_6H_5, SO_2H = SO_3H) on heating with alkali, whereas the *O*-derivatives yield *o*-benzoicsulphinide.

Experimental.

2-*Keto*-1-*benzenesulphonyl*-1 : 2-*dihydrobenz*iso*thiazole* S-*Oxide* (I; R = $C_6H_5{\cdot}SO_2$).—Chlorine was passed through a suspension of 2-thiolbenzoic acid (15 g.) in carbon tetrachloride (150 c.c.) until solution was complete. After removal of the free chlorine by bubbling nitrogen, the solution was added gradually to a solution of benzenesulphonamide (15 g.) in pyridine (27 c.c.). The product was poured into an excess of hydrochloric acid (2N), and the solid collected. The substance crystallised from acetic acid in colourless plates, m. p. 182°. Yield, 65% (Found: C, 50·6; H, 3·1. $C_{13}H_9O_4NS_2$ requires C, 50·8; H, 3·0%). The substance (4 g.) in acetic acid (40 c.c.) and hydrogen peroxide (2·3 c.c., 90/100 vol.) was heated for 45 minutes at 100°. The solid obtained by addition of water, after crystallisation from alcohol, had m. p. 202° alone or mixed with *N*-benzenesulphonyl-*o*-benzoicsulphinide. The mother-liquor on concentration and neutralisation yielded benzenesulphonamide.

A solution of 2-*keto*-1-*benzenesulphonyl*-1 : 2-*dihydrobenz*iso*thiazole* S-*oxide* (1 g.) in warm sodium hydroxide (2N) was cooled and acidified, and the precipitated material collected and dried. This material gave with anisole in sulphuric acid (Smiles and Le Rossignol, J., 1906, **89**, 696) a blue coloration which faded on addition of an excess of anisole, and was evidently the sulphinic acid (II; R = Ph). It was dissolved in sodium hydroxide (2N), and the solution made faintly acid with sulphuric acid, boiled, and treated with a boiling aqueous solution of mercuric chloride (1 g.). The resulting precipitate was collected and refluxed with alcoholic hydrochloric acid for 30 minutes. The material which separated from the filtered solution on cooling, after purification from alcohol, had m. p. 147° alone or mixed with *N*-benzoylbenzenesulphonamide prepared by Wallach's method (*Annalen*, 1882, **214**, 193).

2-*Keto*-1-p-*toluenesulphonyl*-1 : 2-*dihydrobenz*iso*thiazole* S-*oxide* (I; R = *p*-$C_6H_4Me{\cdot}SO_2$), prepared in a similar way to the benzenesulphonyl analogue, crystallised from acetic acid in colourless plates, m. p. 179° (Found: C, 52·2; H, 3·5; S, 20·5. $C_{14}H_{11}O_4NS_2$ requires C, 52·3; H, 3·5; S, 20·0%).

2-*Keto*-1-*acetyl*-1 : 2-*dihydrobenz*iso*thiazole* S-*oxide* (I; R = Ac), prepared by substituting acetamide for the sulphonamide in the foregoing preparations, crystallised from alcohol in colourless prisms, m. p. 150° (Found: C, 51·3; H, 3·2. $C_9H_7O_3NS$ requires C, 51·6; H, 3·4%). A solution of the substance (0·5 g.) in acetic acid and hydrogen peroxide, heated at 100° for 30 minutes, gave, on dilution with water, *o*-benzoicsulphinide. Hydrolysis of the material by boiling sodium hydroxide (2N) or hydrochloric acid (2N) gave a mixture of 2-carboxybenzenesulphinic acid and 2 : 2′-dithiobenzoic acid. Heated with water at 100° until solution was complete, it gave 2-*keto*-1 : 2-*dihydrobenz*iso*thiazole* S-*oxide* (I; R = H), which crystallised from water in colourless needles, m. p. 159° (Found: C, 50·3; H, 3·3. $C_7H_5O_2NS$ requires C, 50·3; H, 3·0%). 2-Keto-1 : 2-dihydrobenz*iso*thiazole *S*-oxide, on reduction with zinc in acetic acid and hydrochloric acid, gave on standing 2 : 2′-dithiobenzamide.

Chlorination of 2-Thiolbenzoic Acid: 5 : 5′-Dichloro-2 : 2′-dithiobenzoic Acid (X; R = Cl, R′ = H).—An intimate mixture of 2-thiolbenzoic acid (25 g.) and finely powdered anhydrous ferric chloride (1·25 g.) was suspended in carbon tetrachloride (200 c.c.), and chlorine passed until solution was almost complete. After removal of the free chlorine the liquid was filtered and extracted with twice its volume of water. The extract was made alkaline with ammonia, boiled until acidification no longer gave a sticky material, and filtered. The filtrate was acidified, and the precipitated material extracted with boiling water (3 : 5-dichlorobenzoic acid

and 3-chlorobenzoic acid were isolated from the aqueous extract). The residue crystallised from alcohol in colourless prisms (11 g.), m. p. 316—320° (decomp.) (Found: C, 44·9; H, 2·5; Cl, 18·9. $C_{14}H_8O_4Cl_2S_2$ requires C, 44·8; H, 2·1; Cl, 18·9%).

5-Chloro-2-thiolbenzoic Acid.—The above *disulphide* (3 g.) in acetic acid containing a few drops of concentrated hydrochloric acid and zinc dust (3 g.) was refluxed for 1½ hours. The solid precipitated by addition of water to the filtered solution crystallised from benzene in yellow needles, m. p. 193° (Found: S, 16·5. $C_7H_5O_2ClS$ requires S, 17·0%).

Ethyl acetoacetate (0·6 g.) was slowly added with stirring to a suspension of 5 : 5′-dichloro-2 : 2′-dithiobenzoic acid (0·5 g.) in concentrated sulphuric acid (10 g.) kept at 55° for 2 hours. The product was poured on ice, and the solid collected and distilled in steam in presence of sulphuric acid. After crystallisation from alcohol it had m. p. 99—100° alone or mixed with authentic 5-chloro-3-hydroxy-1-thionaphthen, prepared by heating 4-chlorophenylthioglycollic acid (1 mol.) with phosphoric oxide (1 mol.) at 140—150° for 1 hour, boiling the product with sodium hydroxide (2N), filtering and acidifying the solution, and distilling the product in steam.

3 : 5 : 3′ : 5′-Tetrachloro-2 : 2′-dithiobenzoic Acid (X; R = R′ = Cl).—Chlorine was passed into a boiling suspension of 2-thiolbenzoic acid (7 g.) and ferric chloride (0·35 g.) in carbon tetrachloride (70 c.c.) until absorption ceased. The liquid was filtered and evaporated to dryness, and the oily residue heated with water. The resulting solid crystallised from acetic acid in yellow plates (4 g.), m. p. 263° (Found: C, 38·0; H, 1·5; S, 14·6; Cl, 31·7. $C_{14}H_6O_4Cl_4S_2$ requires C, 37·8; H, 1·4; S, 14·4; Cl, 31·9%).

Reactions of the chlorination product. (i) *With ammonia.* Dry ammonia was passed into a solution obtained by chlorinating 2-thiolbenzoic (10 g.) and ferric chloride (0·5 g.) in carbon tetrachloride (80 c.c.). The product was poured into hydrochloric acid (2N), and the solid collected. It was fractionally crystallised from alcohol, the first fractions yielding *4-chloro-2-keto-1 : 2-dihydrobenziso**thiazole* (XI; R = H) (2·3 g.), colourless needles, m. p. 259—261°, giving a purple coloration with alcoholic ferric chloride [Found: C, 45·2; H, 2·2; S, 17·2 (Schoeller); *M*, 190. C_7H_4ONClS requires C, 45·3; H, 2·2; S, 17·3%; *M*, 185], the latter fractions yielding *5-chloro-2-aminothiolbenzoic acid* (IX; SCl = S·NH$_2$) (0·9 g.), colourless needles, m. p. 199° (Found: C, 41·4; H, 2·8. $C_7H_6O_2NClS$ requires C, 41·3; H, 3·0%).

(ii) *With acetamide.* Acetamide (4 g.) in pyridine (18 c.c.) was added gradually to a chlorinated solution of 2-thiolbenzoic acid–ferric chloride prepared in the usual way. The product which separated was collected, washed with hydrochloric acid (2N), and fractionally crystallised from alcohol, yielding from the first fractions 4-chloro-2-keto-1 : 2-dihydrobenz*iso*thiazole and from the latter fractions *4-chloro-2-keto-1-acetyl-1 : 2-dihydrobenziso**thiazole* (XI; R = Ac) (1·75 g.), which was also obtained when 4-chloro-2-keto-1 : 2-dihydrobenz*iso*thiazole (0·5 g.) was refluxed with acetic anhydride (20 c.c.) for 45 minutes. The required material separated on cooling and crystallised from alcohol in colourless plates, m. p. 175—176° [Found: C, 47·4; H, 2·8 (Schoeller). $C_9H_6O_2NClS$ requires C, 47·5; H, 2·7%].

N-Benzenesulphonyl-o-benzoicsulphinide.—The silver salt (5 g.) of *o*-benzoicsulphinide was heated in a sealed tube with benzenesulphonyl chloride (3 c.c.) for 2 hours at 180°. The required *product*, obtained by extraction with hot alcohol, crystallised from alcohol in colourless prisms, m. p. 202° (Found: C, 48·3; H, 3·1. $C_{13}H_9O_5NS_2$ requires C, 48·3; H, 2·8%). The substance (0·5 g.) was boiled with sodium hydroxide (2N) for 1 hour. The material obtained on acidification, after purification by salting-out from an aqueous solution with concentrated hydrochloric acid, formed colourless prisms, m. p. 209—212° [Found: C, 45·5; H, 3·15. $C_{13}H_{11}O_6NS_2$ (II; R = C_6H_5, SO_2H = SO_3H) requires C, 45·7; H, 3·2%].

O-Benzenesulphonyl-o-benzoicsulphinide.—*o*-Benzoicsulphinide (5 g.) in pyridine (20 c.c.) and benzenesulphonyl chloride (4·5 c.c.) were shaken at room temperature for 40 minutes. The mixture was poured into hydrochloric acid (2N); the precipitated solid crystallised from acetic acid in colourless needles, m. p. 249° (Found: C, 48·1; H, 2·7. $C_{13}H_9O_5NS_2$ requires C, 48·3; H, 2·8%). On heating with aqueous sodium hydroxide, it gave *o*-benzoicsulphinide.

O-p-Toluenesulphonyl-o-benzoicsulphinide, prepared in a similar way, crystallised from acetic acid in colourless needles, m. p. 252° (Found: C, 49·5; H, 3·1. $C_{14}H_{11}O_5NS_2$ requires C, 49·8; H, 3·3%). Heating with sodium hydroxide gave *o*-benzoicsulphinide.

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