CCVII.—*The Formation and Stability of the 2-Thio-1 : 2-dihydrobenzisothiazoles.*

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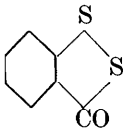
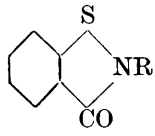
IN a previous communication (McClelland and Longwell, J., 1923, **123**, 3310) it was shown that 2-dithiobenzoyl (I) reacts with ammonia to give 2-keto-1 : 2-dihydrobenz*iso*thiazole (II, R = H), and with primary amines to give disulphides (III) and not cyclic compounds of the type (II). The failure to isolate the cyclic compounds was attributed to their instability towards reducing agents, resulting in their reduction to the disulphides (III) by the hydrogen sulphide liberated during the reaction.



(I.)



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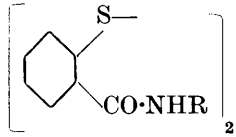

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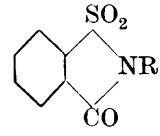
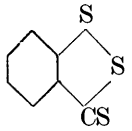


(IV.)

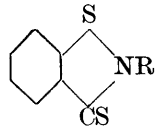
The stability of the S–N link in the corresponding sulphones (IV) appears to be much greater, since it is now found that they are unaffected by hydrogen sulphide or sulphur dioxide, which readily reduce the *iso*thiazoles (II) under the same conditions (compare McClelland and Gait, J., 1926, 921); the increased stability in the sulphone may be attributed to the increased positive character of the sulphur atom. Substitution of another atom or group for the oxygen atom of the ketobenz*iso*thiazoles resulting in an increased stability of the S–N link would indicate that the substituent had brought the sulphur atom into a condition analogous to that in which it exists in the sulphone, *i.e.*, had increased its positive character or utilised the " lone pairs " of electrons. Thus by a study of derivatives of the *iso*thiazole type in which the oxygen atom had been replaced by other atoms or groups information as to the nature of these substituents in comparison with carbonyl oxygen might be obtained.

The effect of replacing oxygen by sulphur in the ketobenz*iso*-thiazoles has now been investigated. On the assumption that this increases the stability of the S–N link towards reducing agents, condensation of primary amines with the thio-analogue (V) of 2-dithiobenzoyl should yield the cyclic type of compound (VI) and not the thioamide disulphide (VII) which by analogy with

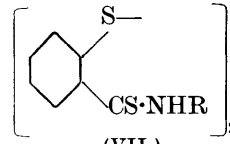
the oxygen compounds (II) would result from the reduction of the thiobenz*iso*thiazole.



(V.)



(VI.)



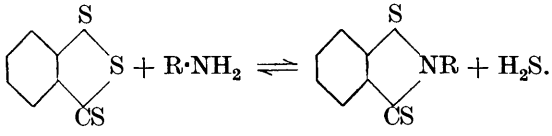
(VII.)

2 : 3-Dithiosulphindene (V) has previously been obtained by Manessier (*Gazzetta*, 1916, **46**, 231) from *o*-benzoic sulphinide. A more convenient source has been found in 2-dithiobenzoyl, which on treatment with phosphorus pentasulphide gave good yields of the required material.

The condensation of 2 : 3-dithiosulphindene with primary amines was carried out as far as possible under conditions similar to those employed with 2-dithiobenzoyl. Reaction with aniline, methylamine, ethylamine, and benzylamine yielded the thiobenz*iso*thiazoles of the type (VI, R = Ph, Me, Et, CH_2Ph). The constitution assigned to these compounds has been confirmed by their oxidation to the corresponding *N*-substituted *o*-benzoic sulphinides (IV).

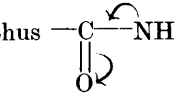
The fact that the thiobenz*iso*thiazoles and not their reduction products (VII) are isolated indicates that the substitution of sulphur for oxygen in the ketobenz*iso*thiazole system increases the stability of the S–N link towards reducing agents.

Further evidence of the stability of the thiobenz*iso*thiazoles, as compared with the oxygen analogues (II), has been obtained in their behaviour towards reducing agents. Thus they react with hydrogen sulphide, which reduces the latter (*loc. cit.*), to give 2 : 3-dithiosulphindene, indicating that the reaction between an amine and 2 : 3-dithiosulphindene is a reversible one :



Further, sulphur dioxide, which was found to reduce the keto-compounds 2-keto-1-methyl-1 : 2-dihydrobenz*iso*thiazole (II, R = Me) and 2-keto-1-phenyl-1 : 2-dihydrobenz*iso*thiazole (II, R = Ph) to the corresponding amide disulphides (III), failed to reduce the thio-compounds, as did other reducing agents such as sodium hydrosulphite and hydrazine, thus supporting the conclusion that the substitution of sulphur for oxygen in the ketobenz*iso*thiazole system increases the stability of the S–N link. On the

assumption that this increase in the stability of the S–N link is due to an increase in the positive character of the *o*-sulphur atom, as suggested, the results indicate that substitution of sulphur for oxygen in the carbonyl group increases the positive character of the sulphur atom in the ortho-position. If this effect is due to an electronic displacement, it is clear that the CS group exerts a greater influence than the CO group.

It seems probable that the acidic character of amides is due to an electronic displacement, which may be represented thus 

(compare Robinson, J., 1925, **127**, 1618). On this hypothesis, since thioamides are more acidic than amides, the CS group evidently exerts a greater influence on the electronic displacement than the CO group. This conclusion is in harmony with that now advanced.

Attempts to prepare 2-thio-1 : 2-dihydrobenz*iso*thiazole (VI, R = H) have not been successful. When 2 : 3-dithiosulphindene was treated with ammonia, a tarry product, consisting chiefly of unchanged dithiosulphindene, resulted, and 2-keto-1 : 2-dihydrobenz*iso*thiazole (II, R = H) reacted with phosphorus pentasulphide to give 2 : 2′-dithiobenzamide (III, R = H), which subsequently yielded 2 : 3-dithiosulphindene. It is noteworthy that the latter is the product of certain reactions which might be expected to yield 2 : 3-dithiothiobenzamide (VII, R = H) : for instance, it is formed when phosphorus pentasulphide and 2 : 2′-dithiobenzamide (III, R = H) interact. Further, 2 : 2-dithiobenzonitrile, prepared by dehydration of the corresponding amide (III, R = H), reacts with hydrogen sulphide, under the conditions described by Kindler (*Annalen*, 1923, **431**, 202) for the preparation of thioamides, to give 2 : 3-dithiosulphindene (V), and not the expected thioamide (VII). The interaction of phosphorus pentasulphide and 2 : 2′-dithiobenzanilide (III, R = Ph), which might be expected to yield the thioanilide, also gave 2 : 3-dithiosulphindene.

A number of *N*-substituted derivatives of *o*-benzoic sulphinide were required for comparison with the oxidation products of the thiobenz*iso*thiazoles in the foregoing experiments. The methods hitherto available for the preparation of these compounds usually involved the treatment of the potassium salt of the imide with aliphatic or aromatic halogen compounds. A more convenient source has been found in the substituted amides of 2 : 2′-dithiobenzoic acid (III), which yield the *N*-substituted *o*-benzoic sulphinides when treated with hydrogen peroxide.

EXPERIMENTAL.

The method previously described [J., 1923, **123**, 172 (b)] for the preparation of 2-dithiobenzoyl has been modified, the 2-thiolbenzoic acid (30 g.) and the thiolacetic acid (40 c.c.) being added simultaneously to cold concentrated sulphuric acid (300 c.c.) with continuous stirring; yield, 85%.

2 : 3-*Dithiosulphindene* (V).—2-Dithiobenzoyl (20 g.), dissolved in xylene (400 c.c.), was refluxed for 6 hours with phosphorus pentasulphide (10 g.). The xylene solution was decanted, the residue extracted with boiling xylene, and the combined xylene solutions distilled in steam. The residual material crystallised from benzene or alcohol in red needles or hexagonal plates, m. p. 94—95° (Found: S, 52·2; *M*, 189. Calc. for $C_7H_4S_3$: S, 52·2%; *M*, 184). The same substance, m. p. 94°, was obtained in very poor yields by Manessier's method (*loc. cit.*; recorded m. p. 98°).

2-*Thio*-1-*methyl*-1 : 2-*dihydrobenz*iso*thiazole* (VI, R = Me).—2 : 3-Dithiosulphindene (2·5 g.) in ethyl alcohol (350 c.c.) was mixed with an aqueous solution of methylamine (10 c.c. of 33%) and kept at room temperature for 4 days. The required material, which crystallised from the concentrated solution, separated from glacial acetic acid and finally from benzene in flat yellow plates, m. p. 138—139° (Found: N, 7·6; S, 35·8; *M*, in naphthalene, 194. $C_8H_7NS_2$ requires S, 35·4; N, 7·7%; *M*, 181). The *substance* is sparingly soluble in ethyl alcohol and benzene. It is feebly basic, being sparingly soluble in dilute (2*N*) hydrochloric acid, and is insoluble in alkali.

2-*Thio*-1-*ethyl*-1 : 2-*dihydrobenz*iso*thiazole* (VI, R = Et) was similarly obtained from 2 : 3-dithiosulphindene (5 g.) in ethyl alcohol (400 c.c.) and aqueous ethylamine (20 c.c. of 30%) in 3 days (yield, including material precipitated by dilution of the mother-liquor, 5·2 g.). It crystallised from benzene–ligroin in colourless plates, m. p. 63—64° (Found: C, 55·1; H, 5·0; N, 7·4; *M*, 194. $C_9H_9NS_2$ requires C, 55·3; H, 4·6; N, 7·2%; *M*, 195). It is much more soluble in organic solvents than the methyl derivative, dissolves in concentrated hydrochloric acid, and is insoluble in alkali.

2-*Thio*-1-*benzyl*-1 : 2-*dihydrobenz*iso*thiazole* (VI, R = CH_2Ph).—A solution of 2 : 3-dithiosulphindene (5 g.) in ethyl alcohol (400 c.c.) and benzylamine (6 c.c.) was boiled for 8 hours. On cooling, the *benzyl* derivative crystallised; a further quantity was obtained on concentration (7·0 g.). The material crystallised from ethyl alcohol in colourless plates, m. p. 122—123° (Found: C, 65·1; H, 4·7; *M*, 261. $C_{14}H_{11}NS_2$ requires C, 65·3; H, 4·3%; *M*, 257).

2-*Thio*-1-*phenyl*-1 : 2-*dihydrobenz*iso*thiazole* (VI, R = Ph).—2 : 3-Dithiosulphindene (5 g.) was boiled with an excess of aniline (5 c.c.)

for 4 hours. The cold solution was extracted with successive quantities of concentrated hydrochloric acid and the extracts were diluted with water and vigorously shaken. The precipitated material was washed with water and dilute alkali solution and dissolved in the minimum quantity of cold ethyl alcohol, and the solution diluted with water. The resulting emulsion crystallised on keeping; m. p. 77° after crystallisation from alcohol (Found: C, 63·9; H, 3·6; S, 26·2; *M*, 239. $C_{13}H_9NS_2$ requires C, 64·1; H, 3·7; S, 26·4%; *M*, 243).

*Action of Hydrogen Sulphide on the Thiobenziso*thiazoles (VI).—A solution of the thiobenz*iso*thiazole (0·5 g.) in ethyl alcohol (20 c.c.) was saturated with hydrogen sulphide and kept for 2 days, gradually developing a red coloration. The material which had crystallised was collected and a further quantity was obtained by dilution of the filtrate. The product was crystallised from ethyl alcohol. All the thiobenz*iso*thiazoles when treated in this way gave 2 : 3-dithiosulphindene. In contrast to the action of hydrogen sulphide on the ketobenz*iso*thiazoles (II), sulphur was not precipitated during the above reactions, indicating that reduction was not taking place.

Action of Sulphur Dioxide.—(a) *On the thiobenziso*thiazoles. A solution of the thio*iso*thiazole (0·5 g.) in ethyl alcohol (20 c.c.) was saturated with sulphur dioxide and after 2 days the sulphur dioxide was boiled off and the solution diluted with water. The thiobenz-*iso*thiazoles were recovered unchanged.

(b) *On the ketobenziso*thiazoles (II). Under similar treatment with sulphur dioxide 2-keto-1-methyl-1 : 2-dihydrobenz*iso*thiazole was reduced. The white needles obtained, m. p. 217°, showed no depression when mixed with an authentic specimen of 2 : 2′-dithiobenzomethylamide (III, R = Me). 2-Keto-1-phenyl-1 : 2-dihydrobenz*iso*thiazole was also reduced by sulphur dioxide under similar conditions to 2 : 2′-dithiobenzanilide, m. p. 243° (III, R = Ph).

o-Benzoic sulphinide, *N*-methyl-*o*-benzoic sulphinide, and *N*-phenyl-*o*-benzoic sulphinide were recovered unchanged after treatment with hydrogen sulphide or sulphur dioxide as in the above experiments.

*Oxidation of the Thiobenziso*thiazoles.—A solution of 2-thio-1-methyl-1 : 2-dihydrobenz*iso*thiazole (VI, R = Me) in glacial acetic acid (150 c.c.) was heated with hydrogen peroxide (40 c.c.) for 1½ hours at 100° and then concentrated by heating on the water-bath. On addition of aqueous potassium hydroxide (50%) to the cold solution a white crystalline material was obtained, which separated from water in colourless needles, and had m. p. 131—133° (Found: N, 7·3. $C_8H_7O_3NS$ requires N, 7·1%), alone or mixed with the oxidation product of 2 : 2′-dithiobenzomethylamide obtained as described below.

In a similar way 2-thio-1-ethyl-1 : 2-dihydrobenz*iso*thiazole (VI, R = Et) yielded a substance, m. p. 93·5—95·5°, which, mixed with an authentic specimen of *N*-ethyl-*o*-benzoic sulphinide (m. p. 94—94·5°), had m. p. 94—95°. 2-Thio-1-phenyl-1 : 2-dihydrobenz*iso*thiazole (VI, R = Ph) on oxidation gave a substance which after purification from aqueous ethyl alcohol had m. p. 190°, alone or mixed with an authentic specimen of *N*-phenyl-*o*-benzoic sulphinide.

Oxidation of 2-thio-1-benzyl-1 : 2-dihydrobenz*iso*thiazole gave a material which after crystallisation from ethyl alcohol had m. p. 111·5—113·5°. According to *Ber.*, 1896, **29**, 1048, *N*-benzyl-*o*-benzoic sulphinide has m. p. 118°. A specimen prepared by this method was found to have m. p. 110·5—112·5° alone and 111·5—113·5° when mixed with the oxidation product described.

N-*Substituted* o-*Benzoic Sulphinides.*—The 2 : 2′-dithiobenzamides were prepared by the action of the corresponding amine either on 2-dithiobenzoyl (J., 1923, **123**, 3310) or on 2 : 2′-dithiobenzoyl chloride. The amide was dissolved in glacial acetic acid, excess of 30% hydrogen peroxide added, and the mixture heated at 100° for 1 hour. It was then diluted with water; the substituted *o*-benzoic sulphinide, which crystallised on cooling, was recrystallised from alcohol or acetic acid. The method seems to be of general application.

N-*Methyl-o-benzoic sulphinide* (IV, R = Me) has m. p. 131°, alone or mixed with the oxidation product of 2-thio-1-methyl-1 : 2-dihydrobenz*iso*thiazole described above. *N*-Ethyl-*o*-benzoic sulphinide was obtained in white needles, m. p. 94—94·5° (recorded m. p., 93—94°; *Ber.*, 1887, **20**, 1598). *N*-Propyl-*o*-benzoic sulphinide has m. p. 75—76°, and 74—75° when mixed with authentic material, m. p. 73—75° (J., 1926, 921). *N*-Phenyl-*o*-benzoic sulphinide has m. p. 191° (Found : N, 5·5. Calc. for $C_{13}H_9O_3NS$: N, 5·4%) (recorded m. p., 190·5°; *Amer. Chem. J.*, 1895, **17**, 320). *N*-*o*-Tolyl-*o*-benzoic sulphinide has m. p. 173° (recorded m. p., 171—173°; *loc. cit.*, p. 327).

2 : 2′-*Dithiobenzonitrile.*—2 : 2′-Dithiobenzamide (10 g.), when boiled in xylene (300 c.c.) for 4 hours in presence of phosphoric oxide (20 g.), gradually dissolved. The solution was then decanted and the xylene removed in steam. The residual oil solidified at 0° and crystallised from ethyl alcohol in pale yellow plates, m. p. 102—103°. 2 : 2′-Dithiobenzonitrile has m. p. 101—102° (*Ber.*, 1926, **59**, 1074).

Action of Hydrogen Sulphide on 2 : 2′-*Dithiobenzonitrile.*—The nitrile (4 g.) was added to a solution of sodium ethoxide (1 g.) in ethyl alcohol (100 c.c.) saturated with hydrogen sulphide at 0°. Hydrogen sulphide was then bubbled through the solution, which

was kept in a freezing mixture, for 2 hours; thereafter the solution was heated under pressure for 2 hours at 95°. On cooling, 2 : 3-dithiosulphindene (2·9 g.) crystallised. A further quantity was obtained from the mother-liquor together with a small amount of a by-product.

The authors desire to express their thanks to Professor Smiles for the interest he has taken in this work and to the Chemical Society for a grant which has defrayed part of the cost.

KING'S COLLEGE, LONDON. [*Received, May 9th,* 1929.]