CXXXVIII.—*The Dismutation of Some Disulphides.*

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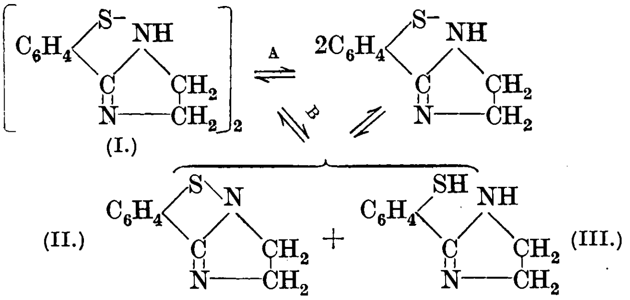
FURTHER investigation of 2 : 2′-*oo*′-dithiodiphenyl-4 : 5-dihydroglyoxaline (I) (McClelland and Warren, J., 1929, 2623) shows that this disulphide exhibits anomalous properties in solution. Molecular-weight determinations of the material in alcohol and benzene by the ebullioscopic method give low values which diminish with dilution (Table I). The low values obtained cannot be ascribed to reaction of solvent and solute, since the latter when recovered is identical with the original and gives values in agreement with those obtained in the initial experiment. Moreover, the apparent molecular weight of the disulphide at a given concentration is constant even on prolonged boiling; it is thus evident that the anomalous results are not due to decomposition but accord with a reversible dissociation of the disulphide.

Solutions of the disulphide are thermochromic, the intensity of the colour increasing with rise of temperature and decreasing on cooling again. This property has previously been observed by Lecher (*Ber.*, 1915, **48**, 524) in certain disulphides and has been attributed to a weakening of the S–S link. The dihydroglyoxaline disulphide, unlike the disulphides investigated by Lecher, shows a marked divergence from Beer's law (Table III).

These unusual properties of the disulphide might be accounted for by dissociation in solution to free radicals (A), or by a reversible change of the type (B) which may be termed reversible dismutation.



It is evident that process (A) may be regarded as the preliminary stage in the formation of the products (II) and (III) and thus any proof of dismutation (B) does not exclude the formation of free radicals as the initial stage of the dismutation. It is noteworthy that tetra-arylhydrazines (Wieland, *Annalen*, 1911, **381**, 200; Wieland and Lecher, *ibid.*, 1912, **392**, 156) and hexaphenylethanes (Schmidlin and Garciá-Banús, *Ber.*, 1912, **45**, 1344) undergo irreversible dismutation which appears to be dependent on the formation of free radicals from these substances.

Since solutions of the dihydroglyoxaline disulphide do not react with oxygen, and no evidence of abnormal reactivity could be obtained, the production of free radicals with anything more than a transitory existence appears to be excluded; indeed their formation although possible is not necessary to an explanation of the phenomena. Evidence proving the formation of the products of dismutation (II and III) is forthcoming from the following independent sources.

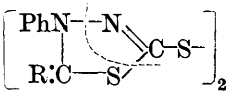
The apparent molecular weight of the disulphide (I) in alcohol to which the free thiol (III) has been added is higher than that in the pure solvent and increases with increasing concentration of the thiol (Table II); this result accords with reversible dismutation of the disulphide to thiol (III) and the tricyclic compound (II). Moreover, the disulphide is formed by treatment of an equimolecular mixture of the tricyclic hydrobromide and the thiol with one equivalent of alkali; the yield of disulphide excludes the possibility of its formation by decomposition of the tricyclic compound and leads to the conclusion that the thiol and the free tricyclic compound react to give the disulphide in equilibrium with these; direct proof of this cannot be obtained, as the tricyclic compound itself has not been isolated.

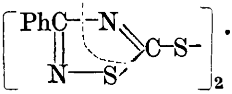
Further evidence of the dismutation process (B) is obtained from the action of methyl iodide on the disulphide, which gave the hydriodide of the *S*-methyl ether of the thiol (III) together with the hydriodide of the tricyclic compound (II); the formation of these products is readily accounted for by dismutation of the disulphide to thiol and tricyclic compound, the hydrogen iodide liberated in the methylation of the thiol forming salts of the *S*-methyl ether and of the tricyclic compound, thus permitting the isolation of the latter salt.

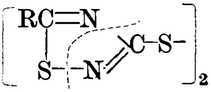
Substitution of the imino-hydrogen of the dihydroglyoxaline disulphide (I) should inhibit dismutation, since cyclisation would be prevented. Unfortunately, attempts to prepare the requisite derivatives have been unsuccessful.

The behaviour of 2 : 2′-mm′- and 2 : 2′-pp′-*dithiodiphenyl*-4 : 5-*dihydroglyoxalines* has been studied in comparison with that of the ortho-compound. These disulphides have now been synthesised from the *amides* of mm′- and pp′-*dithiobenzoic acids*. The *nitriles*, obtained from these, on treatment with ethylenediamine in presence of hydrogen sulphide were readily converted into the dihydroglyoxaline disulphides and thiols; the S-*methyl* ethers of the latter have also been prepared. Normal values for the molecular weight of these disulphides were obtained. Owing to the improbability that the tricyclic system could be formed from the *m*- and *p*-disulphides, it was not anticipated that they would show dismutation in solution, but it was considered that a variation in the stability of the S–S link might exist. The *p*-disulphide, like the *o*-compound, is readily reduced by hydrogen sulphide, but the *m*-compound is not reduced to the thiol. This variation in stability indicates that the dihydroglyoxaline nucleus tends to weaken the S–S link when in the *o*- or *p*-position to it but not in the *m*-, and the effect is probably an electronic one. The instability of the S–N link when in the *o*-position to the $-C{=}N-$ group (McClelland and Warren, *loc. cit.*, p. 2624) appears to be of a similar character.

The authors are not aware of any previously recorded example of reversible dismutation. Irreversible dismutation has been observed in the thiodiazoline series (Busch, *Ber.*, 1895, **28**, 2635); *e.g.*, disulphides of the type (IV, R = H_2) when kept in chloroform yield the corresponding thiols and the endocyclic compounds.


(IV.)


(V.)

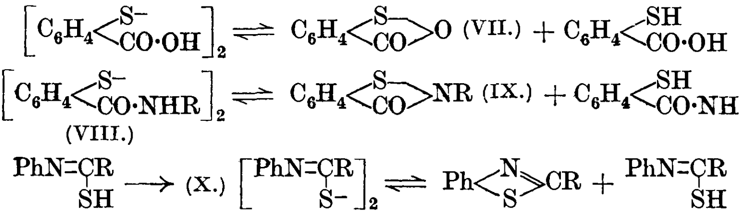

(VI.)

The presence of the $N{=}(C)_n{-}S$ complex in these compounds ($n = 1$) and in the *o*-dihydroglyoxaline disulphide (I, $n = 3$) is significant and suggests that such a complex in a disulphide tends to weaken the S–S link; the reaction of the thioketothiodiazoline disulphides (IV, R = S) with methyl iodide (Busch and Lingenbrink, *J. pr. Chem.*, 1900, **61**, 330) or ammonia (Busch, *Ber.*, 1896, **29**, 2127) to give *S*-methyl ethers or sulphamines confirms this view.

Further evidence is forthcoming from the relative ease of formation of mercaptides from disulphides, which may be taken as an indication of the stability of the S–S link. Many disulphides do not react with mercury (compare Konek, *Ber.*, 1920, **53**, 1666) or do so only under intense conditions (Lecher, *ibid.*, p. 589). On the other hand, the thioketothiodiazoline disulphide (IV, R = S) and disulphides of the types (V and VI, R = Cl, OH) which contain the $N{=}(C)_n{-}S$ complex readily give mercaptides with this metal (Söderbäck, *Annalen*, 1928, **465**, 184). The formation of mercaptides from antipyrine and homoantipyrine disulphides (Konek, *loc. cit.*) suggests that the $O{=}(C)_n{-}S$ complex may have a similar influence; the effect of such groups on the stability of disulphides is being investigated.

Reversible dismutation affords a convenient explanation of many reactions of disulphides. The condensation of 2 : 2′-dithiobenzoic acid with aromatic hydrocarbons (Prescott and Smiles, J., 1911, **99**, 640) to give thioxanthones, in which the intermediate formation of a sulphenic acid has been postulated, may be regarded as the reaction of the dismutation product (VII) with the hydrocarbon and is thus analogous to the formation of anthraquinones from phthalic anhydride (Baeyer and Caro, *Ber.*, 1874, **7**, 968), and the formation of 3-hydroxy-1-thionaphthen and its 2-derivatives

(Hutchinson and Smiles, J., 1912, **101**, 570) may be interpreted on the same basis.



$$\left[C_6H_4<\substack{S-\\ CO\cdot OH}\right]_2 \rightleftharpoons C_6H_4<\substack{S\\ CO}>O\ \text{(VII.)} + C_6H_4<\substack{SH\\ CO\cdot OH}$$

$$\underset{\text{(VIII.)}}{\left[C_6H_4<\substack{S-\\ CO\cdot NHR}\right]_2} \rightleftharpoons C_6H_4<\substack{S\\ CO}>NR\ \text{(IX.)} + C_6H_4<\substack{SH\\ CO\cdot NHR}$$

$$\begin{matrix}PhN{=}CR\\ \quad\ \ |\\ \quad SH\end{matrix} \longrightarrow \text{(X.)}\left[\begin{matrix}PhN{=}CR\\ \qquad |\\ \qquad S-\end{matrix}\right]_2 \rightleftharpoons Ph<\substack{N\\ S}>CR + \begin{matrix}PhN{=}CR\\ \quad\ \ |\\ \quad SH\end{matrix}$$

The oxidation of substituted 2 : 2′-dithiobenzamides (VIII) (McClelland, Warren, and Jackson, J., 1929, 1584) to the *N*-substituted saccharins instead of to the disulphoxides may be ascribed to the dismutation of the amides into ketobenz*iso*thiazoles (IX), which have previously been shown to be readily oxidised to the saccharins (McClelland and Gait, J., 1926, 921). The production of thiazoles by the oxidation of thioanilides and thiourethanes (Jacobson, *Ber.*, 1886, **19**, 1067) may be attributed to the dismutation of an intermediate disulphide (X, R = Ph, OEt) containing the $N{=}(C)_n{-}S$ complex.

EXPERIMENTAL.

The molecular weight of 2 : 2′-*oo*′-dithiodiphenyl-4 : 5-dihydroglyoxaline (I) (J., 1929, 2626) was determined by the Menzies–Wright method (*J. Amer. Chem. Soc.*, 1921, **43**, 2314). Values typical of those obtained are recorded below. Those given under (a) and (b) refer to different specimens, and under (c) the value obtained with material recovered after one of these experiments is given.

TABLE I.

Solvent: ethyl alcohol. *M*, calc., 354.

	(a)		(b)						(c)
Conc. (g./l.) ...	3·19	7·05	0·669	1·58	2·40	3·67	5·15	6·47	4·095
Apparent *M* ...	232	264	168	177	227	236	247	251	243

Solvent : benzene.			
	Conc. (g./l.)	0·649	1·60
	Apparent *M*	303	307

The Effect of the Presence of the Thiol (III) *on the Apparent Molecular Weight of the Disulphide* (I).—The elevation of the boiling point of ethyl alcohol (31·8 c.c.) produced by the disulphide (0·1028 g.) was determined in the usual way; successive quantities of the thiol were added, and the resulting elevations noted. From these values the elevation due to the thiol alone, calculated from the experimental value 185·5, was deducted, whence the apparent molecular weight of the disulphide in presence of the thiol was calculated.

TABLE II.

Apparent M of disulphide	243	304	336	360
Weight (g.) of thiol added	—	0·0694	0·1243	0·1800

The Divergence from Beer's Law of Alcoholic Solutions of the Disulphide (I).—Solutions of the disulphide of different concentrations were matched against a given length of a standard solution of the disulphide in a colorimeter. Three determinations (a, b, c) with different lengths of the standard column were made. Under (C) are given the lengths of columns of a solution of the disulphide of concentration C which matched the standard; under $\frac{1}{2}$C and $\frac{1}{4}$C are given the corresponding lengths for solutions of a half and a quarter of the concentration C. The theoretical values (Beer's law) are given in parentheses.

TABLE III.

	Lengths (cm.) of standard.	C.	$\frac{1}{2}$C.	$\frac{1}{4}$C.
(a)	2·0	3·2	4·8 (6·4)	5·8 (12·8)
(b)	4·0	5·9	8·5 (11·8)	13·2 (23·6)
(c)	6·0	9·8	13·9 (19·6)	16·1 (39·2)

Methylation of the Disulphide (I).—A solution of the disulphide (4 g.) in ethyl alcohol (200 c.c.) and methyl iodide (5 c.c.) was heated on the water-bath till almost colourless (about 10 minutes). Alcohol (100 c.c.) was distilled off; the hydriodide (1·7 g.) which crystallised on cooling was dissolved in hot water and treated with silver nitrate, and the precipitated iodide filtered off. Excess of potassium bromide was added to the filtrate; the hydrobromide which crystallised on cooling, after purification from alcohol, had m. p. 257°, alone or mixed with an authentic specimen of the hydrobromide of the tricyclic compound (II) (J., 1929, 2627). The alcoholic mother-liquor after removal of the hydriodide was diluted with water and concentrated; the material (3·2 g.) which crystallised was purified from water (charcoal). It had m. p. 206—208°, alone or mixed with the hydriodide of 2-*o*-methylthiolphenyl-4 : 5-dihydroglyoxaline (J., 1929, 2626), and on treatment with alkali gave a base, m. p. 98—100° alone or mixed with 2-*o*-methylthiolphenyl-4 : 5-dihydroglyoxaline (picrate, yellow needles, m. p. 207°).

Reaction of 2-o-*Thiolphenyl*-4 : 5-*dihydroglyoxaline* (III) *and the Tricyclic Compound* (II).—A mixture of the tricyclic hydrobromide (1 mol., from 0·45 g. of disulphide I) and the thiol (III) (1 mol.) in boiling alcohol was treated with aqueous potassium hydroxide (1 mol.), and the alcohol removed; the disulphide (I) (0·6 g.) was obtained from the residue.

3 : 3′-*Dithiobenzamide.*—3 : 3′-Dithiobenzoic acid (8 g.) (J., 1921, **119**, 1792) was refluxed for ¼ hour with an excess of thionyl chloride and a trace of ferric chloride. After removal of the thionyl chloride, the product was poured on ice and treated with aqueous ammonia (*d* 0·880); the resulting solid was washed with hydrochloric acid and crystallised from acetic acid (charcoal), giving colourless plates (6·0 g.), m. p. 243° (Found : N, 9·3. $C_{14}H_{12}O_2N_2S_2$ requires 9·2%).

3 : 3′-*Dithiobenzonitrile.*—3 : 3′-Dithiobenzamide (5 g.) was refluxed in xylene (300 c.c.) with phosphoric oxide (5 g.) for 4 hours; the solution was filtered and the xylene removed in steam. The residual material (3·5 g.), purified from alcohol, had m. p. 102—103° (Found : S, 23·6. $C_{14}H_8N_2S_2$ requires S, 23·9%).

2-m-*Thiolphenyl*-4 : 5-*dihydroglyoxaline.*—A solution of 3 : 3′-dithiobenzonitrile (6 g.) and ethylenediamine (6 c.c.) in alcohol (100 c.c.) was saturated with hydrogen sulphide at −10°. The mixture was heated under pressure for 1¼ hours at 90—100°, and the alcohol distilled off. The residual oil was extracted with hydrochloric acid (2*N*) and the extract was treated with charcoal, filtered, and concentrated. The hydrochlorides which separated were treated with excess of sodium hydroxide, the undissolved material (disulphide) was filtered off, and the filtrate treated with carbon dioxide. The precipitated thiol was purified from water, giving yellow needles, m. p. 225—228° after previous softening (Found : S, 17·8; *M*, 190. $C_9H_{10}N_2S$ requires S, 18·0%; *M*, 178). 2-m-*Thiolphenyl*-4 : 5-*dihydroglyoxaline* is sparingly soluble in alcohol and readily soluble in acids and alkalis; it gives a transient red colour with ferric chloride.

2 : 2′-mm′-*Dithiodiphenyl*-4 : 5-*dihydroglyoxaline*, obtained by oxidation of an alkaline solution of the thiol with potassium ferricyanide, crystallised from alcohol (90% aqueous) in pale yellow, hexagonal plates, m. p. 193° (Found : S, 17·9. $C_{18}H_{18}N_4S_2$ requires S, 18·1%). A series of molecular-weight determinations in alcohol at different concentrations gave values from 359 to 370 ($C_{18}H_{18}N_4S_2$ requires *M*, 354), no regular variation in molecular weight with diminishing concentration was observed, and in no case was the observed value less than 354.

2-m-*Methylthiolphenyl*-4 : 5-*dihydroglyoxaline.* — 2-*m*-Thiolphenyl-4 : 5-dihydroglyoxaline (0·46 g.) and methyl iodide (3 c.c.) in alcohol (30 c.c.) were heated on the water-bath till colourless. The *hydriodide* which separated crystallised from aqueous alcohol (charcoal) in pale brown needles, m. p. 262—264° (decomp.) (Found : I, 39·7. $C_{10}H_{12}N_2S,HI$ requires I, 39·7%). The base, obtained in the usual way, crystallised from water in fine colourless needles, m. p. 94—96°.

The following *p*-compounds were prepared in a similar way to the *m*-compounds :

4 : 4′-*Dithiobenzamide* from 4 : 4′-dithiobenzoic acid (J., 1922, **121**, 2024), m. p. 278° (with previous softening) (Found : S, 21·0. $C_{14}H_{12}O_2N_2S_2$ requires S, 21·1%).

4 : 4′-*Dithiobenzonitrile*, pale yellow needles, m. p. 172—173° (Found : S, 23·9. $C_{14}H_8N_2S_2$ requires S, 23·9%).

2-p-*Thiolphenyl*-4 : 5-*dihydroglyoxaline.*—4 : 4′-Dithiobenzonitrile (3 g.) and ethylenediamine (4 c.c.) in alcohol (100 c.c.) were saturated with hydrogen sulphide at −15° and heated under pressure at 100° for 1½ hours. The product, treated as in the preparation of the *m*-compound, gave the disulphide (0·6 g.) and the required material (0·98 g.), which separated from water in pale yellow needles, m. p. 290° (decomp.) (Found : S, 18·1. $C_9H_{10}N_2S$ requires S, 18·0%). The *thiol* gives a green colour with ferric chloride.

2 : 2′-pp′-*Dithiodiphenyl*-4 : 5-*dihydroglyoxaline*, obtained in the previous experiment and by oxidation of the thiol in alkaline solution by potassium ferricyanide, separated from alcohol in very small, colourless crystals, m. p. 213° (Found : S, 18·4. $C_{18}H_{18}N_4S_2$ requires S, 18·1%). Molecular-weight determinations in alcohol at different concentrations gave values from 367 to 381 ($C_{18}H_{18}N_4S_2$ requires *M*, 354), no regular variation in molecular weight with varying concentration was observed, and in no case was the observed value less than 354.

2-*p*-Methylthiolphenyl-4 : 5-dihydroglyoxaline hydriodide, m. p. 237°, gave the base, which separated from water in colourless plates, m. p. 155—156°.

Action of Hydrogen Sulphide on the Dithiodiphenyl-4 : 5-*dihydroglyoxalines.*—Hydrogen sulphide was bubbled through a solution of 2 : 2′-*pp*′-dithiodiphenyl-4 : 5-dihydroglyoxaline (0·5 g.) in warm alcohol (50 c.c.) for 2 hours. The precipitated material was extracted with sulphuric acid (2*N*), and the filtered extract made alkaline; after removal of some unchanged disulphide (0·06 g.) which was precipitated at this stage, the solution was saturated with carbon dioxide; 2-*p*-thiolphenyl-4 : 5-dihydroglyoxaline (0·27 g.) was then obtained, m. p. 290° alone or mixed with an authentic specimen.

2 : 2′-*oo*′-Dithiodiphenyl-4 : 5-dihydroglyoxaline on similar treatment yielded 2-*o*-thiolphenyl-4 : 5-dihydroglyoxaline (0·35 g.), m. p. 242° alone or mixed with an authentic specimen. 2-*m*-Thiolphenyl-4 : 5-dihydroglyoxaline was not obtained when the *m*-disulphide was treated in a similar way with hydrogen sulphide.

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