*Studies with Dithizone. Part VI.** *S-Alkyldithizones.*

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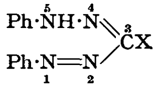
The synthesis of 3-methylthio-1 : 5-diphenylformazan and its identification with the products obtained by methylating silver " keto " dithizonate and the dithizonate ion are discussed in relation to the structure of the metal dithizonates.

The structure (II*a*) for the analytical reagent " dithizone " is supported by a recent synthesis (Irving and Bell, *J.*, 1953, 3538) from 3-chloro-1 : 5-diphenylformazan (I; X = Cl) and sodium hydrogen sulphide, but the possibility of its solutions containing the thiol (II*a*) and the thione form (II*b*) in tautomeric equilibrium is strongly supported by studies of absorption spectra which will be reported later.



(I)

(II*a*) (II*b*)

Despite the extensive use in analysis of the chelate compounds which dithizone forms with metals, their structures have not been elucidated. Absorptiometric studies by " reversion " procedures (cf. Irving, Risdon, and Andrew, *J.*, 1949, 537, 541; Irving and Bell, *loc. cit.* and refs. therein), or by Job's method of continuous variations (Irving, Bell,

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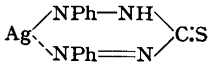
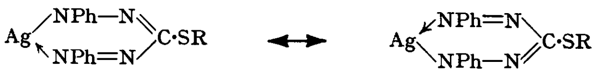
* Part V, *J.*, 1953, 3538.

and Williams, *J.*, 1952, 357; Cooper and Hibbits, *J. Amer. Chem. Soc.*, 1953, **75**, 5084), only established the number of molecules of dithizone which have reacted with each metal ion. The actual displacement of hydrogen by metal during complex formation has been demonstrated experimentally in certain cases (cf. Irving, Cooke, Woodger, and Williams, *J.*, 1949, 1847) and inferred in others, but the number of hydrogen atoms replaced per atom of metal has rarely been established by precise analysis of a pure, solid complex, and in one case only by a complete study of partition equilibria (Irving, Bell, and Williams, *loc. cit.*).

Fischer (*Angew. Chem.*, 1934, **47**, 685; 1937, **50**, 919) postulated that the so-called metal " keto " dithizonates were derived from the thione form (II*b*) by replacement of the hydrogen of the phenylamino-group. Silver " keto " dithizonate was formulated as (III). However, since the grouping –NH·C(S)– is still present it would be more likely to exist in the tautomeric form (IV; R = H) since this would be stabilised by resonance. In that event the presence of the 3-thiol group should confer acidic properties which have not, in fact, been observed.


(III)


(IV)

Dithizone is a monobasic acid (Irving, Cooke, and Woodger, *loc. cit.*) and dissolves in aqueous alkali. The action of methyl sulphate on such a solution gives a monomethyl derivative of dithizone as an almost black solid with a bronze reflex, m. p. 119—120°. That the methyl group is attached to sulphur and not to nitrogen is established by its identity with 3-methylthio-1 : 5-diphenylformazan (I; X = MeS) prepared by the action of sodium methyl sulphide on 3-chloro-1 : 5-diphenylformazan (I; X = Cl). We also find that the same *S*-methyldithizone is produced by the action of methyl iodide on a hot chloroform solution of silver " keto " dithizonate, an observation which is difficult to reconcile with its formulation as (III) or (IV). 3-Methylthio-1 : 5-diphenylformazan was purified most conveniently chromatographically on a column of alumina, and the identity of the substances prepared by the three routes was established by analyses and mixed melting points, and by their giving identical absorption spectra in carbon tetrachloride. 3-Ethylthio-1 : 5-diphenylformazan, m. p. 70° (as I; X = EtS), closely resembles its lower homologue.

Since 3-methylthioformazan still possesses a potentially ionisable hydrogen atom in position 5, it ought to form complexes of the " keto " type if Fischer's hypothesis were correct. It is, however, insoluble in aqueous alkali as expected. But even when its solution in chloroform was shaken with aqueous solutions of copper, silver, mercury, zinc, or cadmium salts at various pH, no evidence of complex formation could be obtained under conditions where metal dithizonates are very readily produced. Although red crystals, m. p. 144°, separate on mixing of a solution of mercuric acetate in acetone with one molecular equivalent of *S*-methyldithizone, this loose adduct has a metal : ligand ratio of 0·6 : 1 and after dissolution in chloroform it gives the absorption spectrum appropriate to its content of *S*-methyldithizone. Copper and palladium gave similar addition compounds to which no definite molecular formulæ could be ascribed.

Since its ability to dissolve in aqueous alkali and to form metal dithizonates is lost on *S*-alkylation, it seems certain that the acidic properties of dithizone are derived from the thiol form (II*a*) and that the " keto " complexes are to be formulated as thiol derivatives as suggested previously (Irving, Cooke, Woodger, and Williams, *loc. cit.*). Studies of *N*-alkylated and deuterated dithizones designed to confirm this hypothesis and to elucidate the structure of the so-called " enol " complexes will be reported later.

Freshly prepared *S*-methyldithizone gives permanganate-pink solutions in a number of organic solvents, *e.g.*, light petroleum, but when they are kept for some hours in the dark or in diffused daylight the colour changes to yellow. The original colour is restored by exposure to bright sunlight or by irradiation of light of short wave-length. An examination of these changes will be reported later. The absorption spectra of *S*-methyl- and

S-ethyl-dithizone are very similar, as shown by the tabulated data for " pink " solutions in acetone, although they differ appreciably from that of dithizone itself.

Absorption spectra in acetone.

Dithizone	λ (mu)	610 *	524	445 *	—
	$10^{-4}\,\varepsilon$	3·26	0·61	1·93	—
3-Methylthio-1 : 5-diphenylformazan	λ (mu)	540 *	448	418 *	376
	$10^{-4}\,\varepsilon$	1·19	0·58	0·65	0·45
3-Ethylthio-1 : 5-diphenylformazan	λ (mu)	538 *	462	418 *	368
	$10^{-4}\,\varepsilon$	0·96	0·56	0·68	0·43

* Indicates a maximum; otherwise minimum.

EXPERIMENTAL

Preparation of 3-*Methylthio*-1 : 5-*diphenylformazan* (I; X = MeS).—(a) *From sodium methyl sulphide and* 3-*chloro*-1 : 5-*diphenylformazan.* Methanethiol, generated by the action of a solution of sodium hydroxide on *S*-methyl*iso*thiourea, was absorbed in ethyl alcohol (50 ml.) containing sodium (0·3 g.), and the resulting solution of sodium methyl sulphide was refluxed on the water-bath for 20 min. with 3-chloro-1 : 5-diphenylformazan (3·45 g.), then poured into chloroform (300 ml.) and water (300 ml.). The chloroform layer was removed and after being washed several times with water (25 ml.) was dried (Na_2SO_4). Removal of the solvent at 20° under reduced pressure gave crude *S*-methyldithizone as a black solid which was taken up in the smallest volume of carbon tetrachloride and transferred to a column (3·8 × 35 cm.) of alumina (type " A," 100—200 mesh). Elution with benzene gave in succession a faint pink, a dark brown (which contained most of the desired product), and a small, paler brown band. The main product was further purified chromatographically and gave finally 3-*methylthio*-1 : 5-*diphenylformazan* as a black powder with a bronze reflex, m. p. 119—120° (Found : C, 62·55; H, 5·5; N, 20·3; S, 11·7. $C_{14}H_{14}N_4S$ requires C, 62·2; H, 5·2; N, 20·7; S, 11·9%).

(b) *By the action of methyl sulphate on an alkaline solution of dithizone.* A solution of dithizone (5 g.) in 2N-sodium hydroxide (15 ml.) and water (50 ml.) was vigorously shaken with methyl sulphate (2·6 g.); the initial yellow colour rapidly disappeared and a black solid separated. Excess of methyl sulphate was destroyed by 2N-sodium hydroxide (15 ml.) at 100° during 20 min. After being cooled, crude *S*-methyldithizone was extracted with successive quantities of chloroform. The combined extracts were washed with dilute aqueous sodium hydroxide until free from unmethylated dithizone, then with water, and dried (Na_2SO_4). Removal of the solvent and chromatographic purification of the black residue as previously described gave 3-methylthio-1 : 5-diphenylformazan, m. p. 119°, which did not depress the m. p. of the previous specimen (Found : N, 20·6%).

(c) *From silver dithizonate and methyl iodide.* Silver " keto " dithizonate was prepared by introducing a solution of silver nitrate (1 mol.) in 0·1N-nitric acid into a stirred solution of dithizone (1 mol.) in chloroform. The organic layer was evaporated at room temperature and the reddish-brown solid residue of silver " keto " dithizonate was purified by precipitation from dry chloroform with ethanol. It melted over the range 204—208°. A solution of this product (3·9 g.) in chloroform (30 ml.) was heated under reflux with a slight excess of methyl iodide for 1 hr. Chloroform (50 ml.) was added and the mixture extracted repeatedly with aqueous sodium thiosulphate to remove silver iodide. Removal of the solvent from the (dried) chloroform extract gave a small yield of crude *S*-methyldithizone which, after chromatography as previously described, formed a black powder, m. p. 118—119°, alone or mixed with the previous specimens (Found : N, 20·8%). The absorption spectra of the three samples in carbon tetrachloride were identical: with $\lambda_{max.}$ 415 ($\varepsilon = 1·50 \times 10^4$), $\lambda_{min.}$ 482 ($\varepsilon = 0·42 \times 10^4$), and $\lambda_{max.}$ 540 ($\varepsilon = 0·61 \times 10^4$).

3-*Ethylthio*-1 : 5-*diphenylformazan.*—A solution of sodium ethyl sulphide, prepared from sodium (0·3 g.) and ethanethiol (0·8 g.) in ethyl alcohol (50 ml.), was shaken for 2 hr. with 3-chloro-1 : 5-diphenylformazan (2·5 g.). The solvent was then removed under reduced pressure and the residue taken up in chloroform, and washed with dilute aqueous sodium hydroxide and then with water. After being dried, the organic solvent was removed under reduced pressure and the viscous black material which remained was purified chromatographically on alumina (see above). 3-*Ethylthio*-1 : 5-*diphenylformazan* formed a black solid, m. p. 70° (Found : N, 19·6. $C_{15}H_{16}N_4S$ requires N, 19·7%).

Addition Compound of S-*Methyldithizone and Mercury.*—When solutions of *S*-methyldithizone

(1 mol.) in acetone and mercuric acetate (1 mol.) in aqueous alcohol were mixed, red crystals, m. p. 144°, separated (Found: C, 43·1; H, 3·6; N, 14·4; Hg, 30·5%). The spectrum of a solution of this substance in chloroform (100 mg./l.) rapidly changed to that characteristic of *S*-methyldithizone in this solvent showing a strong maximum at 415 mμ and a subsidiary peak at 540 mμ. The measured absorbancy of 0·487 at 415 mμ corresponds to a concentration of 70 mg./l. of pure *S*-methyldithizone and thence a ligand : metal ratio of 1 : 0·58 in agreement with the data for ultimate analysis.

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