

### 133. The Associating Effect of the Hydrogen Atom. Part XI. Hydrogen Bonds involving the Sulphur Atom. The S-H-N Bond.

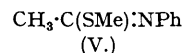
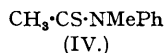
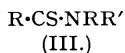
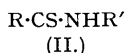
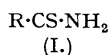
By GORDON HOPKINS and LOUIS HUNTER.

By an examination of the molecular condition of 35 organic sulphur compounds, it is shown that thioamides possessing the group  $\text{-NH}\cdot\text{CS-}$  are associated by virtue of intermolecular S-H-N bonds. Replacement of the imino-hydrogen atom, or its engagement in chelate ring formation, prevents association by rendering such bonds impossible. The unimolecular state of thiodiphenylamine compared with the high molecular association shown by thioacridone supports the view that only hydrogen capable of tautomeric transfer will take part in S-H-N bonds, and a common cause for both association and tautomeric character is suggested. Derivatives of thioformamide show abnormal association not necessarily dependent on hydrogen bonds.

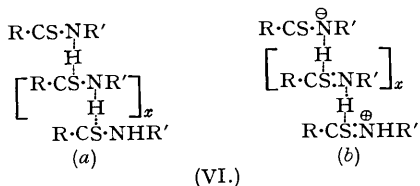
ALTHOUGH there is no lack of evidence that the sulphur atom can donate electrons to form a co-ordinate bond with a great variety of other atoms, it has been generally assumed (see, *inter alia*, Sidgwick, "The Covalent Link," Cornell, 1933, p. 164; Lassettre, *Chem. Reviews*, 1937, 20, 267; Pauling, "The Nature of the Chemical Bond," Cornell, 1940, p. 290) that it is reluctant to share electrons with the hydrogen atom to form a hydrogen bond. This conclusion has been reached mainly by a consideration of the abnormal physical properties of water when compared with those of hydrogen sulphide, and of the absence of molecular association in thioalcohols and thiophenols (v. Auwers, *Z. physikal. Chem.*, 1899, 30, 529). Such evidence is obviously only valid against the S-H-S bond.

On the other hand, there are various indications that the sulphur atom can form hydrogen bonds of the type S-H-O and S-H-N possessing considerable stability; e.g., compounds formed between quinones and mercaptans or thiophenols (Beilstein's Handbuch, 4th Edn., Vol. VII, pp. 615, 616, 646) have long been known, whose quinhydrone-like character is strongly suggestive of a S-H-O structure. The molecular association of thioacetic acid (v. Auwers, *loc. cit.*) and the tautomeric behaviour of the thioacids, if attributable to a cause similar to that which prevails in the carboxylic acids, must denote a S-H-O structure in these compounds. Contemporary American workers have recently attributed the anomalous behaviour of mercaptans in certain donor solvents in regard to heats of mixing (Copley, Marvel, and Ginsberg, *J. Amer. Chem. Soc.*, 1939, 61, 3161), and infra-red absorption (Gordy and Stanford, *ibid.*, 1940, 62, 497), to the formation of weak S-H-N and S-H-O bonds. It is difficult, without further evidence, to interpret the Raman spectroscopic work of Saunders, Murray, and Cleveland (*ibid.*, 1942, 64, 1230) on solutions of thiophenol in donor solvents, but it seems clear that some kind of interaction is indicated between thiophenol and dioxan.

In previous parts of this series numerous examples have been given of the parallel between tautomeric character and molecular association, and have indicated that a factor contributing more than any other to hydrogen-bond stability is the condition that the hydrogen atom constituting the bond should be tautomeric. We have, therefore, sought evidence of hydrogen-bond formation in the thioamides and the thioanilides, the tautomeric behaviour of which is formally represented by the equilibrium  $\text{R}\cdot\text{CS}\cdot\text{NHR}' \rightleftharpoons \text{R}\cdot\text{C}(\text{SH})\cdot\text{NR}'$ . An examination has been made of the molecular condition of a large number of thioamides by cryoscopic measurement of molecular weight in naphthalene solution. The results clearly show that, provided one or both of the hydrogen atoms of the thioamido-group remain unsubstituted (as in I and II), the compounds exhibit a marked degree of association, but that replacement of both amide-hydrogen atoms by alkyl or aryl groups (as in III) results in loss of associated character. Whether the replacement of the second (imino-)



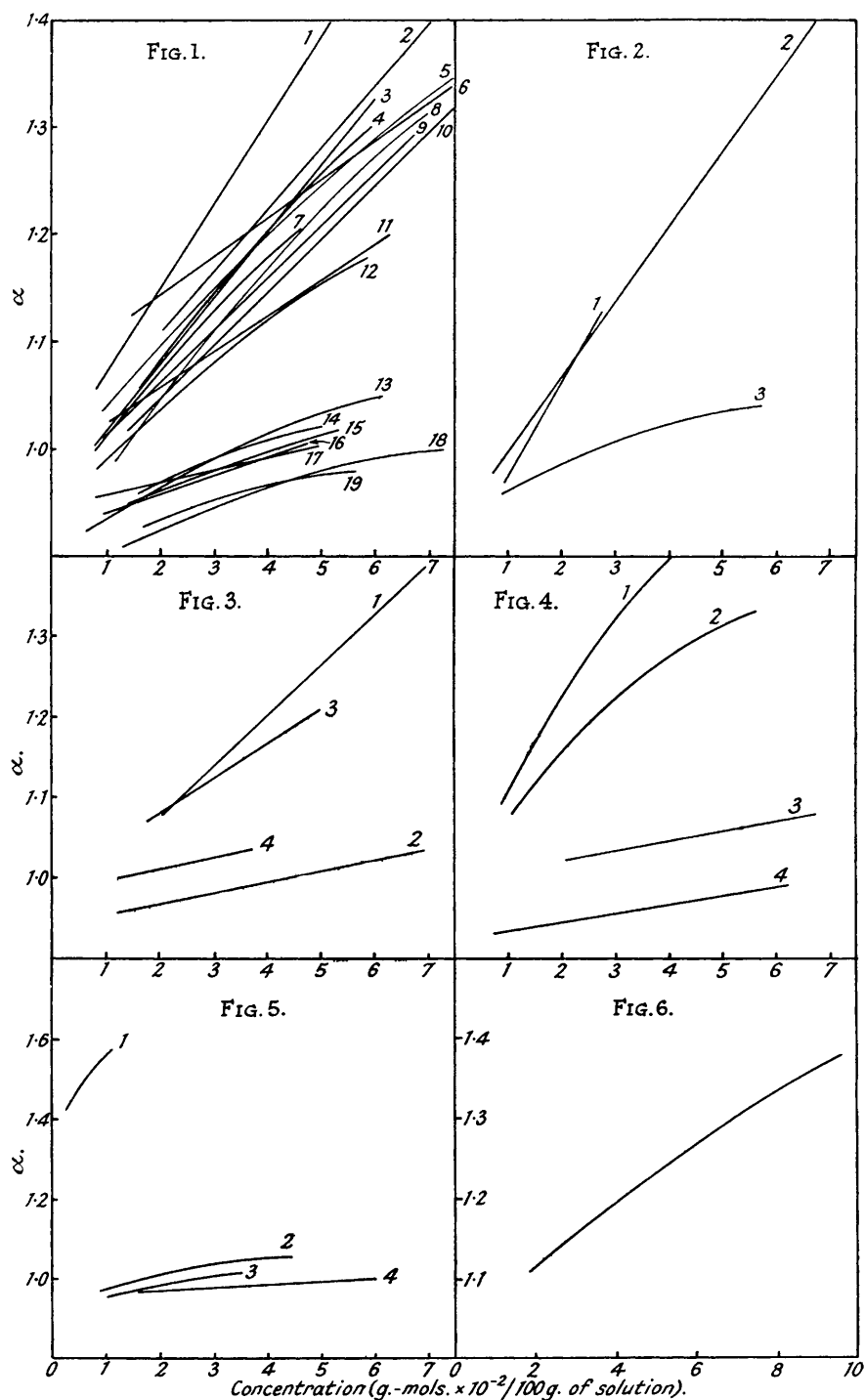
hydrogen atom is effected in the thioanilide (as in IV) or in its mercapto-imide tautomer (as in V), the resulting check in association is the same in both cases. As in previous parts of this series, molecular association is inferred from the molecular weight measurements in all cases where the factor of association ( $\alpha$ ) rises steeply with increasing concentration: a steep association-concentration curve is taken to indicate molecular association, whereas a flat or gently sloping curve (in the region,  $\alpha = 1$ ) is interpreted as absence of association. Fig. 1 shows that the thioamides fall sharply into two classes, those possessing a free imino-group being highly associated, and those in which the imino-hydrogen atom has been replaced being unimolecular. The suggestion is therefore made that the association of thioamides of the former class is a consequence of intermolecular union through hydrogen bonds, the imino-group of one molecule sharing its hydrogen atom with the sulphur atom of a second, and resulting in polymers united through S-H-N bonds, of a type similar to those previously postulated for amides and sulphonamides (Chaplin and Hunter, *J.*, 1937, 1114). A chain polymer containing  $x + 2$  molecules connected by S-H-N bonds is shown in (VI), in which (a) and (b) are unperturbed structures of the resonance hybrid. Such a polymer



will show the properties usually attributed to the tautomeric equilibrium  $\text{R}\cdot\text{CS}\cdot\text{NHR}' \rightleftharpoons \text{R}\cdot\text{C}(\text{SH})\cdot\text{NR}'$ .

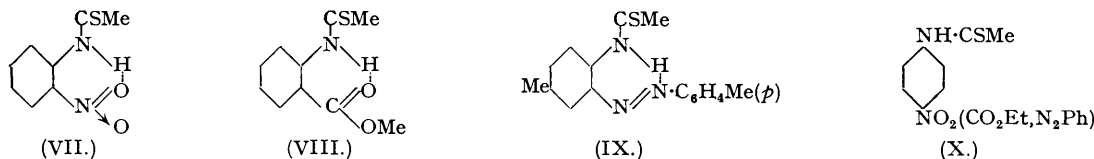
Further confirmation that the imino-hydrogen atom is responsible for the association of thioamides has been obtained by the synthesis of a number of thioanilides in which the anilido-hydrogen atom is engaged

in chelate ring formation with suitably constituted ortho-substituents. Thus, although thioacetanilide (II; R = Me, R' = Ph) shows a high degree of association, *thioacet-o-nitroanilide* (VII), *methyl thioacetanthranilate* (VIII), and *2-thioacetamido-5:4'-dimethylazobenzene* (IX) are all substantially unimolecular (Figs. 2 and 3).

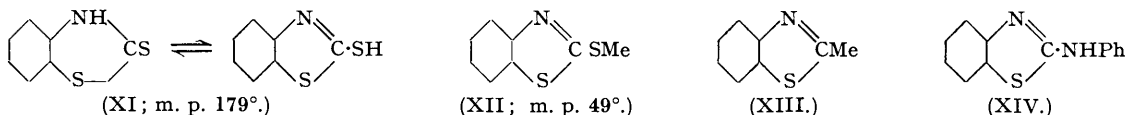


In these compounds it is evident that *intra*-molecular co-ordination of the anilido-hydrogen atom renders it no longer available for *inter*-molecular co-ordination of the type postulated for thioacetanilide. On the other hand, isomers (or close analogues) of these compounds having *m*- or *p*-substituents (*e.g.*, X), in which the donor

groups are too far removed to involve the anilido-hydrogen atom in chelate ring formation, prove to be as highly associated as the parent thioacetanilide (Figs. 2 and 3).



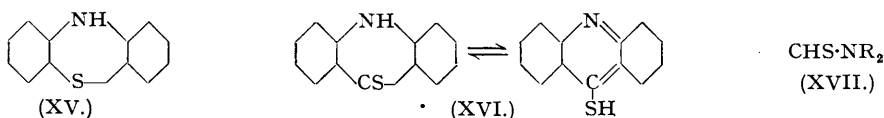
Observations have also been extended to thioamides whose  $\text{-NH}\cdot\text{CS-}$  group forms part of a cyclic system. Attention was particularly directed to 1-thiolbenzthiazole (XI) partly on account of its tautomeric character, and partly because of the remarkable reduction ( $130^\circ$ ) in melting point brought about by its methylation to 1-methylthiobenzthiazole (XII). This contrasting behaviour strongly suggests molecular complexity in the



former compound, and molecular weight measurements show it to be highly associated, whereas the latter is substantially unimolecular (Fig. 4). Confirmation of the divergent character of (XI) and (XII) is also indicated in their widely differing dipole moments (Oesper, Lewis, and Smyth, *J. Amer. Chem. Soc.*, 1942, 64, 1130).

In accordance with expectations, 1-methylbenzthiazole (XIII) is completely unassociated. This compound, though possessing nitrogen and sulphur atoms, has no tautomeric hydrogen atom to provide the bridge necessary for molecular association, and indeed may legitimately be regarded as a cyclic analogue of (V), the *o*-phenylene (or benz) group providing the substituent attached to both nitrogen and sulphur atoms. In this connexion, examination was made of 1-phenylaminobenzthiazole (XIV) in the expectation that it would prove similar to (XIII) in regard to molecular association. Fig. 4 shows, on the contrary, that it is strongly associated, and there seems little doubt that this is due to amidine association (Part VIII, J., 1941, 777), especially as this compound has been shown (R. F. Hunter and Wali, J., 1937, 1513) to possess the character of a semicyclic amidine; it is therefore clearly a case of association by N-H-N bonds.

The belief, previously expressed, that tautomeric character predisposes a hydrogen atom to hydrogen-bond formation, receives striking support from a comparison between thiodiphenylamine (XV) and thioacridone (XVI). The former, though possessing all the atoms necessary to form a S-H-N bond, does not, in fact, do so, as is amply evident from its flat association-concentration curve (Fig. 5, curve 4). On the other hand, thioacridone, which contains sulphur, nitrogen, and hydrogen atoms combined in a manner such that the latter is markedly tautomeric, has properties consistent with high molecular complexity; e.g., it is very sparingly soluble in hydrocarbon solvents, and its high melting point ( $275^\circ$ ) is very greatly reduced by replacement of its tautomeric hydrogen atom (e.g., *S*-methyl ether, m. p.  $114^\circ$ ; *S*-ethyl ether, m. p.  $65^\circ$ ; *S*-benzoyl



derivative, m. p.  $209^\circ$ ). Although insufficiently soluble in hydrocarbons to permit of molecular weight determination in naphthalene, thioacridone shows high association in nitrobenzene solution, whereas its *S*-methyl and *S*-benzoyl derivatives are unassociated (in naphthalene solution) (Fig. 5). Association in nitrobenzene solution may be taken to indicate a marked degree of stability in the associated molecules, for a solvent with such strong donor properties will tend rather to simplify the solute molecules. In view of these facts, thioacridone is considered to have a chain-polymeric structure in which the molecular units are held together by S-H-N bonds formed between CS and NH groups in adjacent molecules. We may legitimately conclude from the divergent behaviour of thiodiphenylamine and thioacridone that bivalent sulphur when a member of a cyclic system does not form hydrogen bonds, and that, for example, the cyclic sulphur atom in 1-thiolbenzthiazole (XI) plays no part in the molecular association of that compound.

In considering the molecular association of the thioamides, the case of thioformyl derivatives deserves particular mention. A review of the properties of thioformamide and its *N*-substituted derivatives, many of which are described by Willstätter and Wirth (*Ber.*, 1909, 42, 1908), reveals that they are in many respects abnormal. The dialkyl compounds (XVII) are liquids of particularly high boiling point showing many of the characteristics of high molecular complexity. The simplest member, thioformdimethylamide (XVII; R = Me), has been the subject of preliminary study, and proves to be highly associated in benzene solution (Fig. 6). The cause of this association is at present obscure, for there can be no possibility of S-H-N bonds; but it is



FIG. 2.

Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>
Thioacet- <i>p</i> -nitroanilide (196). (Curve 1.)			Thioacet- <i>m</i> -nitroanilide. (Curve 2.)			Thioacet- <i>o</i> -nitroanilide. (Curve 3.)					
0.95	191	0.97	0.67	191	0.98	0.92	188	0.96			
2.11	210	1.07	2.81	220	1.12	2.16	194	0.99			
2.72	220	1.125	4.05	236	1.21	3.47	199	1.015			
			5.61	259	1.32	4.52	202	1.03			
			6.70	274	1.40	5.69	204	1.04			

FIG. 3.

Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>
Ethyl <i>p</i> -thioacetamido- benzoate (223). (Curve 1.)			Methyl thioacetanthranil- ate (209). (Curve 2.)			<i>p</i> -Thioacetamidoazo- benzene (255). (Curve 3.)			2-Thioacetamido-5 : 4'-di- methylazobenzene (283). (Curve 4.)		
2.11	241	1.08	1.22	201	0.955	1.84	272	1.07	1.23	284	1.00
3.42	261	1.17	2.75	203	0.975	2.77	284	1.11	2.50	289	1.02
4.94	282	1.26	4.55	210	1.005	3.42	291	1.14	3.72	293	1.035
6.36	301	1.35	5.77	213	1.015	4.23	300	1.175			
6.98	307	1.38	6.92	216	1.03	4.98	307	1.21			

FIG. 4.

Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>
1-Thiolbenzthiazole (167). (Curve 1.)			1-Phenylaminobenz- thiazole (226). (Curve 2.)			1-Methylthiobenzthiazole (181). (Curve 3.)			1-Methylbenzthiazole (149). (Curve 4.)		
0.92	183	1.095	1.09	244	1.08	2.10	185	1.02	0.75	137	0.92
1.84	202	1.21	2.02	262	1.16	3.69	187	1.035	2.17	141	0.95
2.87	218	1.305	2.92	274	1.215	5.20	192	1.06	3.12	142	0.95
3.78	229	1.375	3.73	285	1.265	6.75	195	1.08	4.08	145	0.97
4.42	237	1.42	4.75	294	1.30				5.05	146	0.98
			5.53	300	1.33				6.31	147	0.99

FIG. 5.

Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>
Thioacridone (211). (Curve 1.)			S-Methylthioacridone (225). (Curve 2.)			S-Benzoylthioacridone (315). (Curve 3.)			Thiodiphenylamine (199). (Curve 4.)		
0.31 *	299	1.42	0.90	219	0.97	1.02	301	0.955	1.61	193	0.97
0.79 *	325	1.54	1.72	225	1.00	2.01	310	0.985	2.64	192	0.97
1.01 *	331	1.57	2.78	230	1.025	2.59	311	0.99	4.00	193	0.97
			3.59	234	1.04	3.54	320	1.015	4.93	195	0.98
			4.46	236	1.05				6.10	198	1.00

FIG. 6.

Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>	Concn.	<i>M.</i>	<i>a.</i>
Thioformdimethylamide (89).											
1.92 †	98	1.11	6.09 †	113	1.27	7.96 †	118	1.33	9.66 †	123	1.38
4.12 †	107	1.20									

\* Concentrations in nitrobenzene.

† Concentrations in benzene.

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