Hydrogen Bonding Abilities and Self-association of Some Potentially Bifunctional Catalysts. Part 2.[1] Mercaptoazole Derivatives

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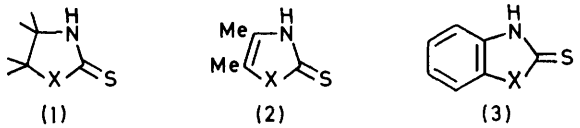
Hydrogen bonding abilities of 2-mercaptoazoles (1)—(3) towards dimethyl sulphoxide (K_A) or 4-chlorophenol (K_B) have been studied quantitatively in CCl_4 by i.r. spectroscopy at 25 °C. The N–H proton of mercaptoazoles exhibits a high tendency to hydrogen bonding ($40 < K_A < 3\,000$ l mol^{-1}) which is correlated with the basicity of the 2-alkylazole analogues. The C=S sulphur atom shows good hydrogen bonding ability ($20 < K_B < 250$ l mol^{-1}) which roughly parallels its nucleophilic reactivity towards methyl iodide. Knowledge of the K_A and K_B constants allows a better understanding of the factors which affect the self-association constants of mercaptoazoles ($100 < K_D < 4\,700$ l mol^{-1}).

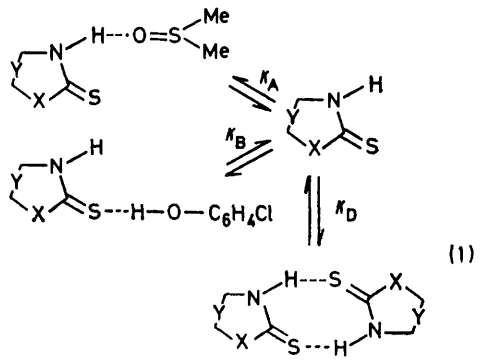
MERCAPTOAZOLE derivatives (1)—(3) are potentially bifunctional catalysts of the ' tautomeric ' type.[2] Conceptually, the simplest model which involves the concerted action of both electrophilic and nucleophilic centres can be found in the self-association of these compounds [equation (1)]. Since homoassociation in-



(1) (2) (3)

a; X = O
b; X = S
c; X = NMe

volves both the N–H proton and the C=S sulphur atom respectively, it was of interest, in order to have a better understanding of the factors which affect the self-association of these compounds, to measure directly the substituent and structural effects on the electrophilicity of the N–H proton on one hand and on the nucleophilicity of the C=S sulphur atom on the other. This paper reports a quantitative i.r. study of the self-association of mercaptoazoles (1)—(3) and of their complexation with a proton acceptor [dimethyl sulphoxide (DMSO) or hexamethylphosphoramide (HMPA)] (K_B) and with a proton donor (4-chlorophenol) (K_B) respectively in CCl_4 [equation (1)].



(1)

RESULTS AND DISCUSSION

The self-association of mercaptoazoles in solution has been reported several times;[3-5] however, quantitative

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[3] (*a*) P. Sohar, J. Nyitrai, K. Zauer, and K. Lempert, *Acta Chem.*, 1968, **58** (1), 31; (*b*) R. S. Lebedev, *Izvest. Vyssh. Ucked. Zaved. Fiz.*, 1972, **15** (5), 148, 159.
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data are scarce.[6] I.r. spectra of mercaptoazoles in CCl_4 feature two absorption bands in the region 2 900—3 500 cm^{-1}, a sharp peak (3 409—3 470 cm^{-1} depending on the structure) attributed to the free N–H bond stretching and a broad one (*ca.* 3 200—2 900 cm^{-1}) which corresponds to associated N–H stretching.[3] In some cases, the associated N–H stretching appears together with the C–H absorptions. In all the compounds studied, however, $\Delta\nu = \nu_{free} - \nu_{ass}$ is large enough to avoid any overlap of the two absorptions. Self-association has been followed by the change in free N–H absorbance as a function of concentration C_0 at 25 °C. As previously shown,[1] the best fit of the experimental curve $C_0 = f(d)$ is obtained for the monomer–cyclic dimer model [equation (1)].

Results are reported in Tables 1 and 2 together with the number of experimental points, the free and associated N–H frequencies, and the concentration range. The complexation constants (K_A and K_B) of mercaptoazoles with a proton acceptor (C = DMSO or HMPA) or with a proton donor (C = 4-chlorophenol) are also given in Tables 1 and 2. They were obtained as described in the Experimental section. Most of the mercaptoazoles are so highly associated that even at

Self-association $2M \rightleftharpoons M_2$ K_D (2)

Complexation $M + C \rightleftharpoons MC$ K_A or K_B (3)

very low concentration, the simultaneous equilibria (2) and (3) must be considered (M = concentration of mercaptoazole monomer, M_2 = concentration of cyclic dimer, C = concentration of complexing species, MC = concentration of the complex). Calculation shows that the error in K_A comes mainly from the error in B in the determination of $K_D = A/2B^2$ (see Experimental section). Thus the errors on K_A and K_D are rather similar.

Determinations of K_B are rendered difficult by the very low solubility of the mercaptoazoles in CCl_4. It results that the change in the absorbance $(d_0 - d)$ of the free O–H stretching of the 4-chlorophenol is often low. The error in K_B comes from the error in K_D and on the $(d_0 - d)$ term. It has been calculated as *ca.* 40%. It must be pointed out, however, that separate measurements with different initial concentrations lead to good convergence of the K_B values. We discuss the results in terms of proton donating ability (K_A values) [equation (1)], proton accepting ability (K_B values) [equation (1)], and their application to the self-association constants.

Proton Donating Ability.—Large changes are observed in the proton donating ability of mercaptoazoles (Tables 1 and 2). Thus, the complexation constants with DMSO show a *ca.* 70 fold decrease on going from (3a) to (1c). Two general trends are clearly evident. (i) In each series, azolidines, azolines, or benzazolines, the order of proton donating ability obtained from the association constant with DMSO is oxazole (X = O) >

TABLE 1

Auto-association (K_D) and complexation constants with DMSO (K_A) or 4-chlorophenol (K_B) of mercaptoazoles in CCl_4

Compounds	ν(NH free)/ cm^{-1}	ν(NH ass.)/ cm^{-1}	ε/ l mol^{-1} cm^{-1}	l/ cm	10^3C_0/ M [a]	No [b]	10^2A [c]	10^2B [c]	K_D [d]/l mol^{-1} ($\Delta K/K$%)	K_A [e]/l mol^{-1} ($\Delta K/K$%)	K_B [f] ($\Delta K/K$%)
(1a)	3 470	3 175	255	1.8	0.3—2	15	0.272 ±0.036	0.217 ±0.014	290 (25)	500 (25)	35 (40)
(2a)	3 461	≃3 000	180	5.0	0.4—3.3	15	0.984 ±0.112	0.111 ±0.025	4 000 (50)	1 200 (50)	100 (50)
(3a)	3 458	≃3 000	270	1.8	0.5—3	15	0.527 ±0.120	0.207 ±0.035	620 (50)	3 000 (50)	25
(1b)	3 420	3 145	300	1.8	0.3—2	15	0.119 ±0.032	0.185 ±0.016	170 (40)	200 (40)	30 (40)
(2b)	3 408	≃3 000	260	5.0	0.1—2.5	30	0.544 ±0.046	0.077 ±0.02	4 700 (50)	1 100 (40)	100 (50)
(3b)	3 409	≃3 000	285	1.8	0.5—3	15	0.552 ±0.056	0.195 ±0.024	730 (35)	2 000 (30)	20
(1c)	3 468	3 218	240	1.0	0.8—4.5	12	0.364 ±0.10	0.411 ±0.055	100 (50)	42 (40)	120 (20)
(2c)	3 469	≃3 000	220	5.0	0.3—3	15	0.356 ±0.024	0.089 ±0.013	2 250 (35)	300 (30)	245 (40)
(3c)	3 467	≃3 000	195	5.0	0.3—1.5	20	0.072 ±0.022	0.103 ±0.014	340 (50)	400 (35)	50

[a] Concentration range. [b] Number of experimental points; all points taken. [c] A and B are the coefficients of the equation $C_0 = Ad^2 + Bd$ where d is the absorbance of free NH. The quoted errors are random errors calculated from statistical analysis (0.9 confidence level). [d] Obtained from $K = A\varepsilon^2l^2/2$ and $\varepsilon = 1/Bl$. [e] Obtained from relation (7). [f] Obtained from relation (9).

TABLE 2

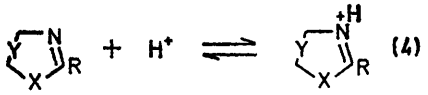
Auto-association (K_D) and complexation constants with DMSO (K_A) or 4-chlorophenol (K_B) of Δ^4-thiazoline-thiones (4a—i)

Compounds	K_D [a]	K_A DMSO	K_A HMPA	$\Delta K_A/K_A$ [b]	K_B	$\Delta K_B/K_B$ [b]
(4a)	1 200	1 000	4 500	30	30	50
(4b)	2 200	1 100	2 700	25	45	50
(4c)	1 500	1 050	2 650	40	37	50
(4d)	1 700	800	1 800	40	35	60
(4e)	1 000	1 150	1 700	20	50	35
(4f)≡(2b)	4 700	1 100	2 200	40	100	50
(4g)	2 900	700	1 500	35	60	60
(4h)	1 000	800	650	20	80	30
(4i)	120	175	175	20	60	25

[a] Taken from ref. 1. [b] Estimated.

[6] P. J. F. Griffiths, G. D. Morgan, and B. Ellis, *Spectrochim. Acta*, 1972, **28A**, 1899.

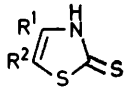
thiazole (X = S) > imidazole (X = N–Me). (ii) In each series, oxazole, thiazole, or imidazole, the order of proton donating ability towards DMSO is benzazoline > azoline > azolidine. It is noteworthy that



(4)

the effect of structural changes on the proton donating ability of 2-mercaptoazole derivatives towards DMSO parallels the effect of these changes on the basicity of 2-alkylazole derivatives [equation (4); Table 3]. This may be of some help in the design of the electrophilic part of bifunctional catalysts.

Steric effects on both partners involved in complexation may be also important in the design of these catalysts. The steric effect of substituents *ortho* to the N–H bond in compounds (4) decreases the complexation



(4)

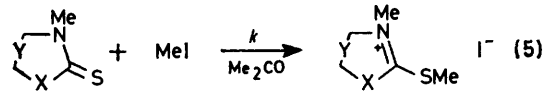
a; $R^1 = R^2 = H$ f; $R^1 = R^2 = Me$ [≡(2b)]
b; $R^1 = Me$, $R^2 = H$ g; $R^1 = Et$, $R^2 = Me$
c; $R^1 = Et$, $R^2 = H$ h; $R^1 = Pr^i$, $R^2 = Me$
d; $R^1 = Pr^i$, $R^2 = H$ i; $R^1 = Bu^t$, $R^2 = Me$
e; $R^1 = Bu^t$, $R^2 = H$

constant with DMSO (Table 2). The importance of the steric contribution of R^1 is clearly evident in the series (4f—i) for which the complexation constant decreases by a factor of 5 on going from $R^1 = Me$ to $R^1 = Bu^t$. In compound (4i) the t-butyl group is related to the 5-methyl group such that a methyl lies in the plane of the heterocyclic skeleton and is directed towards the N–H bond.[1] This conformational effect increases the effective size of a t-butyl group.[1,7]

Further clear evidence of the importance of steric effects is given by the relative changes in the ratio $K_{A(HMPA)}/K_{A(DMSO)}$ (Table 2) for the series (4a—i). In the absence of steric effects, several examples are known [8] in which this ratio is *ca.* 4.5; it falls to 1 in the case of (4i). This can be explained in terms of the higher hydrogen bonding ability of HMPA and of its larger size.

Complexation constants ($dm^3\ mol^{-1}$) with DMSO are known for CCl_4 solution for some other compounds, *e.g.* alkynes (K_A 0.3),[9] 4-bromoaniline (K_A 4.5),[8] rhodanine (K_A 170),[10] phenol (K_A 188),[11] water (K_A 200),[12] 2-methylimidazole (K_A 410),[13] 4-chlorophenol (K_A 476),[11] and 2-methylbenzimidazole (K 590).[13] When compared with these compounds, it is clear that mercaptoazoles exhibit good to very good proton donating ability towards DMSO, due to conjugation of the nitrogen lone pair with π electrons (azolidine < azoline < benzazoline).

Proton Accepting Ability.—Large changes are observed in the hydrogen bonding ability of the thiocarbonyl group of mercaptoazoles (Table 1) towards 4-chlorophenol. Two general trends are again clearly evident. (i) In each series, azolidine, azoline, or benzazoline, the



(5)

order of proton accepting ability towards 4-chlorophenol is imidazole (X = NMe) > thiazole (X = S) ≃ oxazole (X = O). (ii) In each series, oxazole, thiazole, and imidazole, the proton accepting ability is in the order azoline > azolidine > benzazoline.

The same order has been already observed for the alkylation by methyl iodide of the NMe analogues [equation (5)] [14] (Table 3). Since it has been shown that

TABLE 3

Comparison of proton donating ability (log K_A) of 2-mercaptoazoles with the basicity (pK) of analogous 2-alkylazoles and comparison of proton accepting ability (K_B) with nucleophilicity (k_N) of the C=S sulphur atom

Compounds	log K_A	pK [a]	K_B	$10^6 k$ [b] (25 °C)
(1c)	1.62	11.30	120	335
(2c)	2.48	8.92	245	3 200 [d]
(3c)	2.60	6.55	50	144
(1a)	2.70	5.5	35	Unknown
(1b)	2.30	5.37	30	160
(2b)	3.04	3.70	100	440
(2a)	3.08	2.85	100	140
(3b)	3.30	1.00	20	17
(3a)	3.48	~0.4 [c]	25	4.00

[a] From ref. 20. [b] Ref. 14, solvent acetone. [c] Estimated from ref. 16. [d] Rate constant for 1,3-dimethylimidazoline-2-thione.

the rate constants for alkylation are correlated with the ionisation potential obtained from photoelectron spectroscopy of the unpaired *n* electrons of the sulphur atom,[15] it can be assumed that the same unpaired *n* doublet is involved in the hydrogen bond formation with 4-chlorophenol. It must be pointed out, however, that oxazoles have higher hydrogen bonding ability towards 4-chlorophenol than expected from its nucleophilic reactivity. A discussion of this tendency in terms of donating effects

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[9] J. P. Paugam and J. Lauransan, *Bull. Soc. chim. belges*, 1976, **85**, 179.
[10] L. Le Gall, A. Le Narvor, J. Lauransan, and P. Saumagne, *Canad. J. Chem.*, 1973, **51**, 433.
[11] J. P. Leicknam, Thesis, Paris, 1966.
[12] A. Le Narvor, E. Gentric, J. Lauransan, and P. Saumagne, *J.C.S. Faraday I*, 1976, 1329.
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[14] M. Arbelot, R. Gallo, M. Chanon, and J. Metzger, *Internat. J. Sulfur Chem.*, 1974, 201.
[15] M. Arbelot, J. Metzger, M. Chanon, C. Guimon, and G. Pfister-Guillouzo, *J. Amer. Chem. Soc.*, 1974, **96**, 6217.

of sulphur compared with oxygen in different electron-demanding situations [16,17] such as hydrogen bonded complexes and S_N2 transition states, is unfortunately not soundly based because of the low precision of the K_B values. Hydrogen bonding abilities of some other nucleophilic species towards 4-chlorophenol in CCl_4 are: 5-phenyl-1,2-dithiole-3-thione (K_B 2),[18] dibutyl ether (K_B 8),[11] camphor (K_B 11),[19] acetone (K_B 20),[11] pyridine (K_B 83),[11] triethylamine (K_B 132),[11] HMPA (K_B 6 100).[9] Mercaptoazoles which are soft nucleophiles with very low basicities [20] are involved in hydrogen bonded systems with 4-chlorophenol of similar or higher stability than the much more basic nucleophiles such as pyridine or triethylamine.

Auto-association.—Auto-association [equation (1)] involves the hydrogen bonding tendencies of both the N–H proton and of the C=S sulphur atom. In each series, azolidine, azoline, or benzazoline, the auto-association constants are in the order oxazole (X = O) ≥ thiazole (X = S) > imidazole (X = NMe). The lower stability of the auto-associated species in the imidazole series compared to the oxazole or thiazole analogues, in spite of a good proton accepting ability (towards 4-chlorophenol), is explained by their poor proton donating ability (towards DMSO). In each series, oxazole, thiazole, or imidazole, the auto-association constants are in the order azoline > benzazoline > azolidine. This order has been already shown for the thiazole series.[6] Azolidines which exhibits a medium proton accepting and a poor proton donating ability are the least associated compounds. Azolines on the other hand show a good proton accepting and a good proton donating ability which result in a high tendency to give associated species. The quite high proton donating ability of benzazoline derivatives partially compensates for their poor proton accepting ability.

Knowledge of the K_A and K_B constants of Δ^4-thiazoline-2-thione derivatives (4a—i) allows interpretation of the substituent effect on the auto-association of these compounds. From the point of view of proton accepting ability, compounds (4) can be divided in three families: K_B *ca.* 30 for (4a), K_B *ca.* 45 for (4b—e), and K_B *ca.* 80 for (4f—i). This substituent effect is well accounted for by the electronic effect of the alkyl group on going from the unsubstituted (4a) to the 4-mono- (4b) and 4,5-di-substituted compounds (2b) = (4f). Thus, for the unhindered compounds (4a, b, and f) the increase of the auto-association constant is governed by the increase in the proton accepting ability of the sulphur atom, since they have a very similar proton donating ability. The steric effect of R^1 affects mainly the proton donating ability of the N–H bond; thus the large difference in K_D between (4f and i) is essentially governed by the observed change in the proton donating ability. This interpretation fits well with our previous proposal on the change in K_D of these compounds.[1]

In summary, structural factors affect specifically the proton donating and/or accepting ability of mercaptoazoles, which in turn affect the auto-association constants. Large auto-association constants are found when proton donating and accepting abilities are both high. The next step is to apply the general trends found in this study to the optimization of the formation of heteroassociated species involving two suitable mercaptoazoles. This work is in progress.[21]

EXPERIMENTAL

Materials.—Thiazolidine-2-thione (1b), benzothiazoline-2-thione (3b), benzoxazoline-2-thione (3a), and oxazolidine-2-thione (1a) are commercially available. They were purified by preparative column chromatography (silica; eluant ethyl acetate–benzene 20 : 80). Preparation of thiazoline-2-thiones (2b) and (4a—i) has already been reported; [1] they were purified twice by crystallisation from ethanol–water. 1-Methylbenzimidazoline-2-thione (3c) was prepared by S–N transposition from 2-methylthiobenzimidazole.[22] The latter compound (5 g) was heated with 3% I_2 at 180 °C in a sealed tube for 72 h. The product was purified by column chromatography and crystallized from ethanol, m.p. 120 °C, δ ($CDCl_3$) 3.80 (NMe) and 7.20br (ArH). 1,4,5-Trimethylimidazoline-2-thione (2c) and 4,5-dimethyloxazoline-2-thione (2a) were prepared according to Kjellin and Sandstrom [23] and were purified by column chromatography after crystallization in ethanol. 1-Methylimidazolidine-2-thione (1c) was prepared by Kyster and Assef [24] and purified by column chromatography.

I.r. Measurements.—All spectra were obtained with a Beckman IR9 spectrophotometer at 25°. The spectral slit width was *ca.* 1 cm^{-1}. For each compound, three or four solutions were prepared by weighing and dilution.

Auto-association and Complexation Constant Determinations.—Auto-association was studied as previously described.[1] The absorbance d can be expressed by relation (6) in which l is the cell length and C_M the concentration in

$$d = \varepsilon l C_M \qquad (6)$$

monomer. K_A, the complexation constant with DMSO or HMPA, is expressed by relation (7) in which C_0 and C_A^0

$$K_A = \frac{C_0 - Bd - Ad^2}{Bd(C_A^0 - C_0 + Bd + Ad^2)} \qquad (7)$$

are the initial concentrations of mercaptoazole and proton acceptor (DMSO or HMPA), respectively. A and B in

$$\frac{\Delta K_A}{K_A} = \Delta B\left[\frac{1}{B} + \left(\frac{1}{D} + \frac{1}{D'}\right)d\right] + \Delta A\left[d^2\left(\frac{1}{D} + \frac{1}{D'}\right)\right] + \Delta d\left[\frac{1}{d} + \left(\frac{1}{D} + \frac{1}{D'}\right)(B + 2Ad)\right] \qquad (8)$$

[16] L. W. Deady, *Austral. J. Chem.*, 1973, **26**, 1949.
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relation (7) come from the separate determination of K_D given in ref. 1. Thus $\Delta K_A/K_A$ is given by relation (8) in which $D = C_0 - Bd - Ad^2$ and $D' = C_A^0 - D$. Complexation with a proton donor is followed by the change in absorbance of the free O–H bond stretching of 4-chlorophenol (3 610 cm^{-1}). The concentration range is chosen

$$K_B = \frac{4K_D\,(d_0 - d_i)}{d_i\left[\left\{1 + 8K_D\left(C_i^0 - \frac{d_0 - d_i}{d_0}C_D^0\right)\right\}^{1/2} - 1\right]} \quad (9)$$

in such a manner that 4-chlorophenol is not auto-associated. After calibration, the concentration of free 4-chlorophenol is determined and the complexation constant K_B obtained by relation (9) where d_i is the absorbance of $\nu(O{-}H_{free})$ for a known initial concentration of mercaptoazole C_{0i} ($d_i = d_0$ for $C_{0i} = 0$) and C_D^0 is the initial concentration of 4-chlorophenol. Derivation of relation (9) gives (10) in which Z is given by relation (11). Δd was taken as *ca.* 0.01, ΔA, ΔB, and ΔK_D were determined during the auto-association constant determination and are given in Table 1.

$$\frac{\Delta K_B}{K_B} = \Delta K_D\left[\frac{1}{K_D} - \frac{4\left(C_i^0 - \frac{d_0 - d_i}{d_0}C_D^0\right)}{Z(Z-1)}\right] + \Delta d\left[\frac{2}{d_0 - d_i} - \frac{1}{d_i} + \frac{4K_D C_D^0\,\frac{d_0 + d_i}{d_0^2}}{Z(Z-1)}\right] \quad (10)$$

$$Z = \left\{1 + 8K_D\left(C_0 - \frac{d_0 - d_i}{d_0}C_D^0\right)\right\}^{1/2} \quad (11)$$

[6/1107 *Received*, 11*th June*, 1976]