atoms at the 2,6 positions. The splittings, 7.84, 7.96, and 8.07 gauss, respectively, are very similar to splittings reported by Geske, *et al.*, for the anions of pentamethylnitrobenzene (8.4 gauss),[54] nitrodurene (7.6 gauss),[27] 2,4,6-tri-*t*-butylnitrobenzene (9.4 gauss),[54] 2,6-tri-*t*-butyl-4-amino-nitrobenzene (9.8 gauss),[27] and 2,3,5,6-tetraisopropylnitrobenzene (9.3 and 7.7 gauss).[54,55] Since the spin density at the 3,5 positions (*meta* to the nitro group) is undoubtedly very small, it is probable that the splitting arises from the ring carbon atoms or the methyl (or isopropyl or *t*-butyl) carbon atoms at the 2,6 positions. As has been pointed out by Geske,[27] the procedure of Karplus and Fraenkel[56] is incapable of explaining a splitting of more than about 1 gauss at the ring carbon atoms, even for rather generous estimates of spin densities. The methyl carbon splitting would be expected to be even less.[57]

A number of unusual mechanisms for the origin of this splitting can be imagined. If the methyl groups *ortho* to the nitro group are pushed out of the plane of the ring, as suggested above, it is conceivable that the parameter $Q_{CC'}{}^{C}$ would increase sufficiently through rehybridization of the ring carbon atom to account for the observed splitting. However, studies of orbital following have suggested that rehybridization occurs only to a very limited degree.[58] Similarly, as the methyl group is moved above or below the plane of the ring, some degree of overlap of the methyl carbon 2s orbital with the π system is expected to occur. Sample calculations of this effect, however, indicate that the expected splitting is far smaller than that observed. Estimates of the splitting due to nitrogen and oxygen π-orbital density at the methyl and ring carbon nuclei are likewise far smaller than the observed splittings.

The most probable mechanism of the splitting, and also the most difficult to estimate quantitatively, involves delocalization of the unpaired electron density from the "π" system of the nitro group into the "σ" system of the benzene ring. In these molecules, the nitrogen and oxygen 2p orbitals have appreciable overlap with the $2p_x$ orbitals of the ring carbon atoms at positions 1 and 2,6. Very crude estimates suggest that such a resonance interaction is responsible for the observed splittings. A fuller study of this interaction is of some interest, but should be postponed until an experimental basis for the assignment is available.

Acknowledgments. We thank Professor G. K. Fraenkel for samples of dinitrodurene, dinitromesitylene, and nitromesitylene, and for a number of discussions. We thank Professor D. H. Geske for allowing us to see a manuscript prior to publication and for a number of helpful comments.

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Hydrogen Bonding in Thiols[1]

Sheldon H. Marcus[2] and Sidney I. Miller

Contribution from the Department of Chemistry, Illinois Institute of Technology, Chicago, Illinois 60616.
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Abstract: Dilution shifts of the sulfhydryl proton magnetic resonance signal have been used to obtain hydrogen-bonding association constants of several thiols. The dimerization constants (K_2) in M^{-1} of thiols in carbon tetrachloride are: ethyl, 0.0056; *n*-propyl, 0.011; isopropyl, 0.0126; *n*-butyl, 0.0132; *t*-butyl, 0.0067; cyclohexyl, 0.093. Since K_2 ($= 0.0182$) for 1-butanethiol in cyclohexane is close to K_2 in carbon tetrachloride, this suggests that at least for these solvents, no specific or peculiar medium effects on the thiols are present. Structural effects on the magnitude of K_2 are consistent with the known polar and steric effects of the groups involved. A comparison of our K_2 values with those previously determined indicates rough agreement. In carbon tetrachloride, our data for thiophenol indicated an apparent monomer–tetramer association ($K_4 = 10^{-4}\ M^{-3}$), but in chlorobenzene, the thiophenol data were consistent with a monomer–dimer equilibrium ($K_2 = 0.011\ M^{-1}$). Because the medium anisotropy in carbon tetrachloride changes drastically with thiophenol concentration, an effect which is largely absent in chlorobenzene, we believe that the existence of tetramer is illusory.

At one time, it was claimed that thiols do not self-associate through hydrogen bonds.[3] Evidence against such bonding was adduced through studies using such techniques as cryoscopy,[4] dipole moment,[5] solubility,[6] proton magnetic resonance (pmr),[7] and infrared spectroscopy.[8] As recently as 1958 at a conference whose theme was "Sulfur in Proteins," the possibility of S···H—S bonds could only be con-

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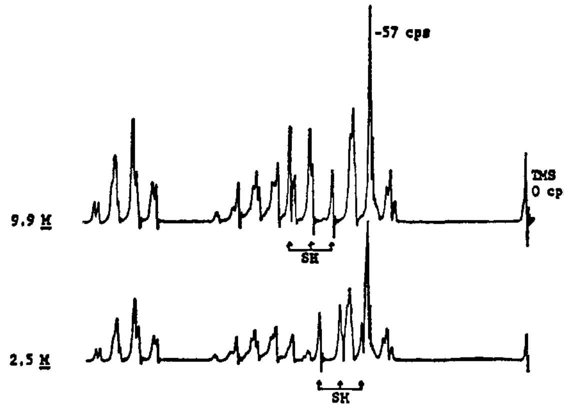

Figure 1. 60-Mc/sec pmr spectra of 1-propanethiol in carbon tetrachloride.

sidered briefly and tentatively.[9] The sulfhydryl group does in fact form hydrogen bonds with oxygen, nitrogen, carbon, and sulfur atoms, and possibly with aromatic π electrons.[10-16] In this work, we report on the self-association of several thiols.

Specific infrared evidence for S···H—S hydrogen bonding has been given by several groups.[11-14] From the spectra of increasingly concentrated solutions of thiophenol in carbon tetrachloride, Josien, *et al.*, made assignments of the monomer, dimer, and polymer S—H stretching frequencies.[11] Subsequently, other workers measured both band frequencies and intensities in the 3.8-μ region.[12-14] Some of the equilibrium constants extracted from such data are discussed below.

Support for hydrogen bonding has also come from pmr spectroscopy.[15,16] The formation of such a bond generally results in a downfield shift of the proton resonance of the hydrogen atom involved in the association.[17] This proton deshielding can be ascribed to two phenomena: (a) partial withdrawal of the proton from its electronic environment by the electronegative acceptor atom; (b) inhibition of electronic circulation about the proton by the electric field of the electronegative atom. At higher temperatures or in a more dilute inert solvent, more of the hydrogen bonds will be broken. The chemical shift (ν) of the proton moves upfield, and a dilution curve (ν *vs.* C) relating the chemical shift of the hydrogen-bonded proton to the gross concentration may be obtained. These dilution shifts arise in part from the changing medium and in part from the changing proportions of monomeric and hydrogen bonded, *i.e.*, dimeric, trimeric, etc., species.

A linear dilution curve of ethanethiol in carbon tetrachloride was reported by Forsén.[16] The limiting slope (LS) method,[18] to be described below, was applied to the data and a dimerization equilibrium constant was obtained. Colebrook and Tarbell reported dilution shifts for *n*-propanethiol, benzylthiol, and thiophenol in carbon tetrachloride, but made no attempt to extract association constants from the data.[15] Murthy, *et al.*, obtained a dilution curve for thiolbenzoic acid in benzene, but ascribed this variation to a concentration-dependent aromatic ring effect; the same workers found a small dilution shift with thiophenol in carbon tetrachloride.[7] In our work, pmr dilution shift data were used to obtain association constants for several thiols by the method of Saunders and Hyne (S.H.).[19]

Experimental Section

Detailed procedures of our work with thiols have been published elsewhere.[20] All proton chemical shifts reported are averages of three determinations. The range of deviation of individual from average values is 0.01–0.3 cps. The mean deviation is 0.1 cps. Thus, proton chemical shifts in this study can reasonably be accepted as precise to ±0.2 cps.

The sulfhydryl proton exhibits a very sharp magnetic resonance signal. *No foreign additives are necessary to promote rapid exchange and produce a sharpened signal.* In the aromatic thiols, the ring proton signals are shifted far downfield from that of the sulfhydryl group owing to the ring current effect. In aliphatic thiols, however, alkyl and sulfhydryl proton signals overlap. The sulfhydryl signal, usually a doublet or triplet, can be identified from spectra obtained at different concentrations in an inert solvent. In carbon tetrachloride, the sulfhydryl proton signal is shifted owing to changes in hydrogen-bonding equilibria, while the alkyl proton signals remain unchanged; this is illustrated in Figure 1 which shows spectra of 1-propanethiol at two concentrations in carbon tetrachloride.

Dilution shift data for thiophenol, and *n*-propyl, isopropyl, *n*-butyl, *t*-butyl, and cyclohexyl thiols are given in Table I in the units cps from tetramethylsilane (TMS), the internal standard, at an applied radiofrequency of 60 Mc/sec. The deviations listed are average deviations of the individual from the average chemical shifts at each concentration. The solvents, carbon tetrachloride, cyclohexane, and chlorobenzene, were reagent grade.

Analysis of Dilution Shift Data. For a hydrogen-bonding association involving *n* monomer units

$$nX\text{-}H \rightleftharpoons (X\text{-}H)_n \qquad (1)$$

$$K_n = M_n/M_1^n \qquad (2)$$

where M_1 and M_n are the molar concentrations of monomer and *n*-mer of X-H, respectively. Three approaches to the evaluation of association constants are available. We shall begin with the most general method and obtain the other two by suitable approximations. Incidentally, we hope to resolve a standing controversy[18,19] in the course of this discussion.

The analysis of Saunders and Hyne (S.H.) begins with the assumptions: (a) the dilution shift is due exclusively to hydrogen bonding; (b) there is only one hydrogen-bonding equilibrium throughout the concentration range; (c) the observed proton resonance frequency (ν) is a weighted average of monomer (ν_1) and polymer (ν_n) frequencies; (d) the monomer and polymer frequencies ν_1 and ν_n are constant throughout the concentration range.[19] As Crook and Schug point out in their work on the hydrazines,[21]

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Table I. Dilution Shift Data for Thiols at 28 ± 1°

	Concn, *M*	$-\nu$, cps	Av dev		Concn, *M*	$-\nu$, cps	Av dev
n-C_3H_7SH	10.99	74.9	0.03	$C_6H_{11}SH$	8.43	88.4	0.03
in CCl_4	9.89	74.2	0.1	in CCl_4	7.59	87.7	0.1
	8.79	73.1	0.1		6.75	86.3	0.1
	7.03	70.7	0.1		5.40	84.0	0.1
	4.94	66.5	0.1		3.79	81.4	0.1
	3.52	64.5	0.01		2.70	79.6	0.03
	2.47	62.9	0.03		1.90	78.2	0.01
	1.76	61.8	0.2		1.35	77.4	0.1
	1.24	61.1	0.1		0.95	76.9	0.03
	0.62	60.2	0.1		0.47	76.1	0.1
					0.09	75.5	0.1
i-C_3H_7SH	11.03	94.9	0.2	C_6H_5SH	9.78	202.9	0.1
in CCl_4	9.92	94.3	0.1	in CCl_4	7.83	200.7	0.2
	8.82	93.3	0.03		4.89	197.1	0.2
	7.06	91.0	0.1		3.91	197.0	0.2
	4.96	88.1	0.1		2.45	195.7	0.1
	3.53	86.3	0.1		1.22	195.5	0.1
	2.48	84.8	0.1		0.61	195.5	0.1
	1.76	84.0	0.03		0.12	195.4	0.1
	1.24	83.2	0.03				
	0.61	82.4	0.03				
	0.12	81.8	0.03				
n-C_4H_9SH	9.28	78.4	0.1	C_6H_5SH	8.82	201.6	0.1
in CCl_4	7.42	76.3	0.2	in	7.84	200.3	0.1
	6.70	75.4	0.3	C_6H_5Cl	6.26	198.6	0.1
	5.57	73.5	0.2		4.41	196.5	0.1
	4.70	72.2	0.03		3.13	195.3	0.03
	3.71	70.7	0.1		2.21	194.3	0.1
	2.78	69.3	0.1		1.56	193.6	0.1
	1.86	67.9	0.03		1.10	193.0	0.1
	1.39	67.1	0.2		0.55	192.4	0.03
	0.93	66.3	0.2		0.11	191.7	...
	0.46	65.4	0.2				
	0.09	64.8	...				
n-C_4H_9SH	9.28	78.6	0.03	t-C_4H_9SH	8.81	108.3	0.1
in C_6H_{12}	8.35	78.1	0.1	in CCl_4	7.93	107.7	0.1
	7.42	76.5	0.1		7.05	106.5	0.01
	5.94	74.0	0.1		5.64	104.6	0.1
	4.17	71.0	0.01		3.97	102.3	0.03
	2.97	68.6	0.03		2.82	100.7	0.01
	2.09	67.0	0.03		1.98	99.5	0.03
	1.48	65.7	0.1		1.41	98.9	0.03
	1.04	64.6	0.03		0.99	98.3	0.1
	0.52	63.2	0.1		0.50	97.8	0.1

ν_n is characteristic of protons in the polymer whether they are hydrogen bonded or not. If the total solute concentration is taken as C

$$C = M_1 + nK_nM_1^n \tag{3}$$

$$\nu = (\nu_1M_1 + nK_nM_1^n\nu_n)/C \tag{4a}$$

$$\nu = [(\nu_1 - \nu_n)M_1/C] + \nu_n \tag{4b}$$

$$dM_1/dC = 1/(1 + n^2K_nM_1^{n-1}) \tag{5}$$

$$-\frac{d\nu}{dC} = \frac{(\nu_1 - \nu_n)n(n-1)K_nM_1^{n-2}}{(1 + nK_nM_1^{n-1})^2(1 + n^2K_nM_1^{n-1})} \tag{6}$$

In the general S.H. analysis, it is convenient to use the dilution curve in the form ν *vs.* log C. Although Saunders and Hyne used this form to full advantage,[19] it is necessary to have the following analytical expressions.

$$\frac{d\nu}{d\log C} = 2.303(\nu_n - \nu_1)\left[\frac{1}{1 + n^2K_nM_1^{n-1}} - \frac{1}{1 + nK_nM_1^{n-1}}\right] \tag{7}$$

$$\frac{d^2\nu}{d(\log C)^2} = \frac{d}{dM_1}\left(\frac{d\nu}{d\log C}\right)\frac{dM_1}{dC}\frac{dC}{d\log C} \tag{8}$$

At the point of inflection $d^2\nu/d(\log C)^2 = 0$. Since neither dM_1/dC nor $dC/d\log C$ can be zero, the inflection point (ip) condition is given by

$$\frac{d}{dM_1}\left(\frac{d\nu}{d\log C}\right)_{ip} = 0 \text{ and } (M_1^{n-1}K_n)_{ip} = n^{-3/2} \tag{9}$$

$$\left(\frac{d\nu}{d\log C}\right)_{ip} = 2.303(\nu_1 - \nu_n)\left[\frac{n^{-1/2} - n^{1/2}}{n^{-1/2} + n^{1/2} + 2}\right] \tag{10}$$

If all frequencies are measured from ν_1, then the slope of the ν *vs.* log C curve is proportional to ν_n at the inflection point, and the proportionality constant is a function of n only. Thus, for each n a value of ν_n can be obtained from eq 10 and the observed slope. Now, K_n is set equal to unity and plots of ν *vs.* log C are constructed for n = 2, 3, 4, etc. The displacement of the calculated from the observed curve is equal to (log K)/(n − 1). The n value giving the best fit of the theoretical curve to the experimental data is accepted as the degree of association.

For weakly hydrogen-bonding systems such as the thiols, the S.H. treatment must be modified: the inflection point in the dilution curve is reached about the time that the concentration is that of pure liquid. Thus, the slope at the inflection point is uncertain. One may fit eq 4 to the experimental data by trial and error, but the labor involved is prohibitive. Or one may guess $(d\nu/d\log C)_{ip}$, obtain a value of ν_n in eq 10, and by iteration converge on consistent values of ν_n and K_n.

We used the second approach and proceeded as follows: (a) ν_1 was obtained by extrapolation of the dilution curve to infinite dilution; (b) ν_n was obtained from eq 10, and a value of the $(\text{slope})_{ip}$ estimated from our experimental curve; (c) insertion of these values into eq 4b generated pairs of values of C and M_1; (d) K_n was calculated from eq 2; (e) at another point on the curve the appropriate C, M_1, and K_n were used in eq 4b to produce a new value of ν_n. This cycle was repeated, usually from two to five times, until ν_n and K_n remained constant. The two points used in our analysis were defined by C = 1.0 *M* and M_1 = 3.0 *M*, respectively. These lay in the region which is very sensitive to the choice of ν_n, K_n, and n.

The system 1-butanethiol in carbon tetrachloride serves as an example. The monomeric proton resonance frequency was determined by extrapolation to infinite dilution: $\nu_1 = -64.7$ cps. The slope of the ν_{SH} *vs.* log C curve at high concentration was 23.8 cps. Application of eq 10 for n = 2 gave $\nu_2 = -125.0$ cps. Three iterations were necessary for convergence. The values of K_2 in the three cycles were 0.0154, 0.0132, and 0.0132 M^{-1}; the values of $-\nu_2$ were 125.0, 135.7, and 137.0 cps. In this way, the values of ν_2 and K_2 were determined. The same analysis was performed for the n = 3 case and the following values were obtained: $K_3 = 0.0419\ M^{-2}$; $\nu_3 = -83.9$ cps. The experimental points and theoretical curves are shown in Figure 2. The parameters resulting from the n = 2 analysis fit the experimental data throughout most of the concentration range, including the sensitive bend region. Apart from the low concentration range, where the curve for *any* polymer will match experiment, the parameters for an n = 3 analysis do not fit the data. Thus, it is concluded that the experimental data fit a monomer–dimer model within the S.H. method. The inability of the derived parameters to fit the data at very high concentrations is in accord with the breakdown in this region of the basic assumption of a single hydrogen-bonding equilibrium.

We note that an error in ν_n would result in an incorrect slope at high concentration. If errors are considered to be additive, then from eq 4b, $|\Delta\nu| \approx 2|\Delta\nu_n|$. In order to distinguish between n values, the theoretical curve must fit the experimental points to within ±1 cps (Figure 2): the maximum allowable $\Delta\nu = \pm 1$ cps. Therefore, the maximum allowable $\Delta\nu_n = \pm 0.5$ cps. Such an error causes an error in K_2 of $10^{-4}\ M^{-1}$ or *ca.* 1%. An error in K_n would result in a displacement of the theoretical curve along the log C axis equal to the error in $[1/(n-1)]$ log K_n. The theoretical curve fits the experimental data to within ±0.02 unit along the log C axis. For n = 2 and $K \approx 0.01$, the theoretical curve fits the experimental data to within $\pm 0.0004\ M^{-1}$ in K_2, or ±4%.

Thus far, the LS treatment of hydrogen bonding has been ignored.[18] It turns out that if we impose restrictions on eq 6, namely

$$(d\nu/dC)_{C\to 0} = (d\nu/dC)_{M_1\to 0} = -(\nu_1 - \nu_n)n(n-1)K_nM_1^{n-2} \tag{11}$$

Table II. Hydrogen-Bonding Data for Thiols, RSH, at 28 ± 1° [a,b]

R	Solvent	n	ν_1	$\nu_1 - \nu_{RSH}$	$\nu_1 - \nu_n$	K_n (pmr)	$\nu_1 - \nu_2'$	K_2' (pmr)	K_2' (infrared)[c]
C_2H_5[d]	CCl_4	2	62.4	22.8	165.6	0.0056	∞	0	0.021
n-C_3H_7	CCl_4	2	59.2	15.3	72.5	0.0110	200	0.022	0.053
i-C_3H_7	CCl_4	2	80.2	13.3	57.7	0.0126	220	0.018	0.018
n-C_4H_9	CCl_4	2	64.7	13.7	72.3	0.0132	400	0.0089	0.016
n-C_4H_9	CCl_4	3	64.7	13.7	19.2	0.0419			
n-C_4H_9	C_6H_{12}	2	62.1	16.6	74.2	0.0182	280	0.016	
t-C_4H_9	CCl_4	2	97.5	11.1	95.0	0.0067	400	0.0069	0.016
C_6H_{11}	CCl_4	2	75.7	13.0	83.8	0.0093	∞	0	
C_6H_5	CCl_4	4	195.4	7.5	44.6	0.0001	∞	0	
C_6H_5	C_6H_5Cl	2	192.2	11.2	57.5	0.0110	∞	0	0.019

[a] Our "best" association constants are in the column under K_n (pmr); their precision is *ca.* 4%. [b] n = degree of association; ν in cps at 60 Mcps; ν_{RSH}, shift for pure liquid; ν_n, the S–H frequency of eq 4; ν_2', shift for dimer from eq 15; K_n in units M^{1-n}; K_2', from eq 15 for process 16. [c] The infrared data are from ref 13; the precision claimed in the constants is 30%. [d] Pmr data from ref 16: Forsén finds K_2 = 0.012 M^{-1} by the LS method.

and consider only $n = 2$, we obtain the LS expression

$$(d\nu/dC)_{C\to 0} = 2K_2(\nu_2 - \nu_1) \qquad (12)$$

In a real sense this "explains" the controversy and removes apparent inconsistencies in the two approaches; the LS approach is included in the S.H. analysis as a rather special case at infinite dilution. For strongly hydrogen-bonded systems, *e.g.*, alcohols, it is possible that a dimer may be indicated by LS, but a higher polymer required by S.H.;[18,19] perhaps both approaches should be used in such a case. For any hydrogen-bonded system, the important deficiency in the LS approach is that the value of ν_2 is normally not available, and must be guessed, or estimated, if K_2 is to be obtained from eq 12.[16] Therefore, we did not use the LS method.

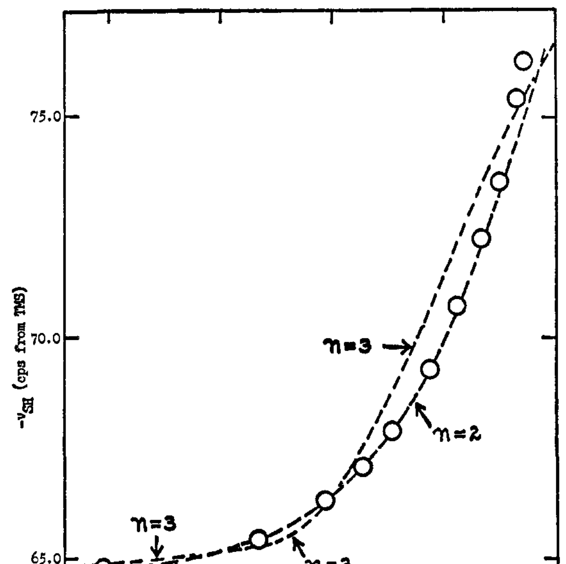
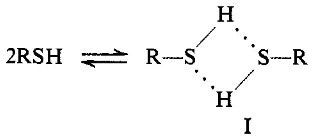


Figure 2. Dependence of sulfhydryl proton chemical shift on log concentration for n-C_4H_9SH in CCl_4: O, experimental; ----, theoretical.

A third method of treating dilution shift data is similar to that of Spurr and Byers,[13] and Li, *et al.*[10a,b] As applied to the thiols, the assumption is made that only dimerization need be considered, and that the degree of association is low over the whole range of solute concentrations.[13] We derive the expression

$$\frac{1}{\nu - \nu_1} = \frac{1}{(\nu_2' - \nu_1)}\left(\frac{1}{2K_2'C} + 2\right) \qquad (13)$$

for the process in which the dimer contributes only to ν_2

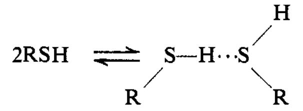


(14)

Another expression

$$\frac{1}{\nu - \nu_1} = \frac{1}{(\nu_2' - \nu_1)}\left(\frac{1}{K_2'C} + 4\right) \qquad (15)$$

applies to the process in which the open dimer contributes to ν_1 and ν_2



$$2RSH \rightleftharpoons \underset{R}{S}\text{—H}\cdots\underset{R}{\overset{H}{S}} \qquad (16)$$

According to eq 13 and 15, plots of $1/(\nu - \nu_1)$ *vs.* $1/C$ yield different values of ν_2' and the same constant, K_2', provided ν_1 is known. This rather simple approach to association data turns out to be unreliable for several reasons; we shall discuss them later.

Results and Discussion

Equilibrium constants for the self-association of several thiols are listed in Table II. Our "best" constants were obtained by the S.H. analysis and are listed as K_n (pmr). Based on these data, dimerization generally appears to be favored over other associations. The possible trimerization of 1-butanethiol, for example, was disposed of in our discussion of Figure 2.

Since the type of thiol self-association could depend on the solvent, *e.g.*, hydrogen bonding to the chlorine atoms of carbon tetrachloride, we checked 1-butanethiol in cyclohexane. Hydrogen bonding to the hydrocarbon solvent should be minimal. The data obtained fit a dimerization equilibrium, and the association constants, K_2 = 0.0182 in cyclohexane and 0.0132 M^{-1} in carbon tetrachloride, agree reasonably well (Table II). This constitutes support for the assumption that a hydrogen-bonding association, dimerization, is involved.

As we have used it, the pmr technique is vulnerable to several criticisms, which, in fact, are not peculiar to it alone. The S.H. treatment does not apply to simultaneous equilibriums involving several polymeric species. (It is true, however, that if only two equilibriums were involved, a plot such as that of Figure 2 could be helpful in bracketing the experimental curve; then one could fit the data by the appropriate complex equilibrium expressions.) A more serious problem is that there is little assurance that K_n, ν_1, or ν_n are unaffected by the medium over the whole concentration range.[22,23] Now, it does appear that the alkyl protons of our thiols exhibit essentially no dilution shifts (Figure 1); this indicates that the changing medium has almost no effect on inactive alkyl hydrogens. While it cannot be stated with certainty that ν_1 and ν_n must also remain constant, it is probable that the change in ν_2 will parallel (roughly) that in ν_1 so that the over-all effect will be reduced.[24] Since it is not apparent how this medium effect on K_n, ν_1, and ν_n should be treated, we have lumped all of the uncertainty into ν_n in order to estimate the uncertainty of *ca.* 4% in our K_2 (pmr) values.

Inspection of the dimerization constants of the alkyl thiols (Table II) reveals differences which seem to depend both on the experimental technique and its interpretation. Spurr and Byers considered the association process 14 and used appropriate integrated absorption coefficients in the infrared region 3.8–3.9 μ to obtain K_2' (infrared).[13] They recognized several possible sources of errror: the overlap of monomer–dimer bands, the failure of the Beer–Lambert law, and the inapplicability of the equilibrium expressions at the higher thiol concentrations. In another critical study, Bulanin, *et al.*, used the same infrared technique on selected thiols and thioethers.[12] They concluded that process 14, which involved the cyclic dimer (I), was inappropriate, and that an unassociated proton of the dimer does contribute to the band intensity of the monomer: eq 16 is more appropriate for thiols.[12] In addition, Bulanin, *et al.*, were not satisfied with the Spurr and Byers method of calculation of K_2.[25] We find that the Spurr and Byers constants do not give the trends one might expect on the basis of known inductive and steric effects, but we find it remarkable that K_2 (pmr) and K_2' (infrared) agree as well as they do!

It is quite another matter to apply the Spurr and Byers approach to pmr data. The necessary extrapolation $1/C \rightarrow 0$ in eq 14 or 16, which presupposes that monomer and dimer are the only species, is highly questionable. As noted earlier, Josien, *et al.*, have presented infrared evidence for polymeric species in concentrated solutions of thiols.[11] In principle, this problem can be dealt with in the infrared technique, but may be inaccessible in this pmr method. As a further practical problem, we found that appropriate plots of eq 15 (or 13) were often curved in the region of high thiol concentration. This led to uncertainties in the evaluation of the slope and intercept, which in turn enter additively into the evaluation of K_2'. The uncertainty in K_2' for isopropyl mercaptan in carbon tetrachloride is *ca.* 25%. In a few cases, the intercept appeared to be zero (or negative) so that we obtained $\nu_2 = \infty$ and $K_2' = 0$. Because of these objections, we can have little confidence in the constants, given as K_2' (pmr) in Table II.

Our pmr dilution shift data for thiophenol in carbon tetrachloride were best fitted by a monomer–tetramer equilibrium (Figure 3). This result is inconsistent both with the infrared data for thiophenol[11,13] and our pmr data for the alkanethiols. We believe that this apparent anomaly is caused by a medium anisotropy effect.[7,22] As the thiophenol concentration increases, the deshielding effect of hydrogen-bond formation is counteracted by the shielding ring current effect of aromatic molecules in solution; the result is a reduced total dilution shift. Thus, the observed ν_1–ν_{RSH} for thiophenol in carbon tetrachloride, 7.5 cps, can be compared with the lowest alkanethiol value of 11.1 cps for *t*-butylthiol (Table II).

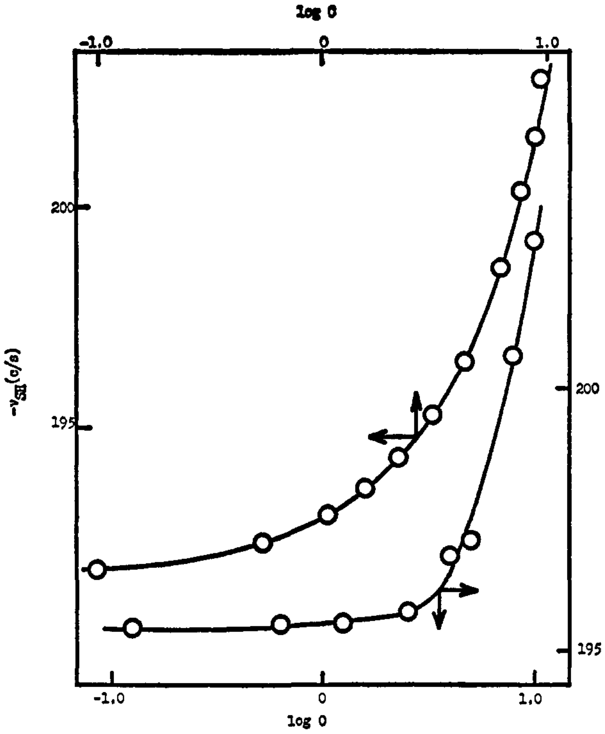


Figure 3. Dependence of ν_{SH} on the concentration of thiophenol: upper curve for the "dimer" ($n = 2$) in chlorobenzene; lower curve for the "tetramer" ($n = 4$) in carbon tetrachloride (see text).

We believe that this medium anisotropy effect could be minimized by a judicious choice of aromatic solvent. Such a solvent should have a molecular weight and density similar to that of the solute, so that the "aromatic" concentration remains essentially constant throughout the entire concentration range. Further, the substituent effect on the induced ring currents should be small. The solvent chlorobenzene seems to fit these requirements for thiophenol. The concentrations of pure thiophenol and chlorobenzene are 9.76 and 9.83 *M*, respectively; thus, there is less than 1% change in aromatic concentration throughout the dilution range. The thiophenol–chlorobenzene data fit a monomer–dimer model (Figure 3). The total dilution shift of 11.2 cps is now within the range observed for the alkyl thiols. It is assumed that the use of chlorobenzene as a solvent for hydrogen-bonding studies of thiophenol effectively eliminates the medium anisotropy effect and that the entire dilution shift is the result of hydrogen-bond formation.

The hydrogen-bonding shifts (ν_1–ν_2) obtained for the thiols are spread over a range of *ca.* 145 cps. As we have noted earlier, ν_2 is a peculiar chemical shift which averages contributions from all sulfhydryl protons in the dimer,[21] and perhaps higher polymers as well; the

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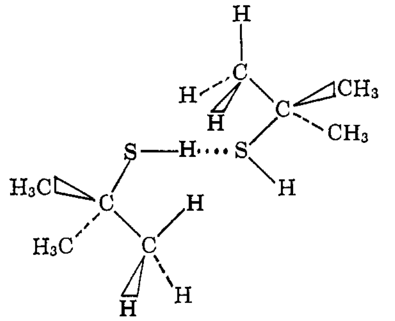
absence of systematic variations with structure is reasonable. On the other hand, a correlation between ν_1 and Taft substituent constants was reported previously.[20]

The equilibrium constants, K_2 (pmr), show distinct substituent effects. For the unbranched alkyl mercaptans, the trend in K_2 is ethyl < *n*-propyl < *n*-butyl. As the electron-releasing power of the alkyl group increases or the electron density at the sulfur atom increases, K_2 increases. The effect of branching on K_2 is ethyl < isopropyl > *t*-butyl. If it is granted that the unbranched series establishes the trend for polar effects, then the reversal in the branched series suggests the incursion of another effect. In all probability, this is a steric effect arising from spatial restrictions on some conformations of the hydrogen-bonded complex, *e.g.*, II.



II

In concluding this paper, it seems important to stress that thiols self-associate. We shall not attempt to "rate" or "grade" the infrared and pmr techniques in general; indeed, either has specific advantages in particular hydrogen-bonding applications. For thiols, infrared evidence may be uniquely useful in identifying monomeric, dimeric, and higher polymeric structures, and in distinquishing between cyclic and open dimers. However, it is difficult to obtain "correct" thiol association contants from infrared data. On the other hand, pmr thiol data, while "blind" to structure and subject to assorted medium effects, are particularly suitable for generating association constants. According to the S.H. analysis, such constants apply with high precision over the dilute to medium concentration range of the thiols and should be superior on this score. Therefore, although we cannot claim to have determined thiol association constants in an absolute sense, we believe that our values are the best available.

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Molecular Complex Equilibria. Solution Ideality, Solvent Interactions, and Concentration-Scale Dependence[1]

Philip J. Trotter and Melvin W. Hanna[2]

Contribution from the Department of Chemistry, University of Colorado, Boulder, Colorado. Received January 8, 1966

Abstract: Two-parameter physical methods of the Benesi–Hildebrand (BH) type used in determining complex equilibria have been analyzed to determine the effect of concentration-scale ideality and solvent interactions. This analysis shows that excellent linear plots obtained in BH-type treatments fail to provide justification either for the validity of the ideal mixture of species assumption or for the assumption that the solvent is not a reactant. Results of BH analyses of weak complexes have been shown to be strongly dependent on the concentration scale used. Examples from optical and nmr spectroscopic studies of molecular complexes have been given to illustrate ambiguities in the results obtained from simple BH treatments. Experimental approaches designed to overcome some difficulties of the BH method are suggested. Physical studies of other weak complexes in solution, such as hydrogen-bonded complexes, should also be subject to many of the considerations given here.

Molecular complexes of many types have received a great deal of attention in the past 15 years, and some of the books[3,4] and reviews[5–9] which summarize this work are listed below. In the process of treating complex equilibria, one obtains such quantities as the equilibrium quotient for association and the molar absorbancy index[3,4,10] or nuclear magnetic resonance (nmr) proton shifts[11–14] of the complex.

The most widely used method for determining formation constants of 1:1 complexes in solution is that of

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(2) Alfred P. Sloan Fellow.

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