The Effect of Structure on Mercaptan Dissociation Constants[1]

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In a previous paper[2] the acid dissociation constants, K_A, of a number of mercaptans in water were reported and a linear relation was noted between log K_A and the Taft inductive parameters,[3] σ^*, for most of the compounds studied. Thiophenol, however, deviated from this correlation by 1.6 log units. The deviation was attributed to resonance stabilization of the anion. No Baker–Nathan effect was noted in the two alkyl mercaptans studied having other than two α-hydrogen atoms.

While that paper was in press another value for the K_A of thiophenol appeared[4] differing by over a power of ten from ours and fitting the correlation moderately well.[4] The present note reports a redetermination of the K_A for thiophenol and also a number of other K_A values, some of which are new and some redetermined. Four of these bear on the question of a Baker–Nathan effect. It is concluded that there is no Baker–Nathan effect but that there is a resonance exaltation of mercaptan dissociation constants of ~1.3 log units for conjugated mercaptans.

Results

Dissociation constants were measured by pH titration, by a spectrophotometric method, and a gas solubility method, all of which have been previously described.[2] Dissociation constants were evaluated from eq. 1, in which the mean ion activity coefficient, $f_\pm$, was evaluated from the Debeye–Hückel limiting law, eq. 2.[5] (The symbols are those of our earlier

$$K_A = \frac{(\mathrm{H}^+)(\mathrm{RS}^-)f_\pm{}^2}{(\mathrm{RSH})} \qquad (1)$$

$$\log f_\pm = -\frac{S_f\sqrt{\Gamma}}{1 + A\sqrt{\Gamma}} \qquad (2)$$

paper[2] and of Harned and Owen.[5]) In no case did the total electrolyte concentration exceed 0.1 *M*. For the pH titrations and the spectrophotometric determinations, the solutions also contained 1% ethanol, which was used as a solvent for stock solutions of the mercaptans, but this is not thought to change the dissociation constants by more than a few per cent.[2] The resulting acid dissociation constants are shown in Table I. They are not thought to differ from their thermodynamic values in pure water by more than their experimental uncertainty, ~10%. The K_A values reported here are the average of at least four determinations and the uncertainty given is the average deviation from the mean value. Better precision is precluded by the unavoidable presence of traces of oxygen, which results in the oxidation of a small, irreproducible, fraction of the mercaptide ions.

TABLE I

ACID DISSOCIATION CONSTANTS OF MERCAPTANS, RSH

R	K_a	Method[g]
CH_3CO	$3.85 \pm 0.32 \times 10^{-4}$	pH tit.
	4.69×10^{-4} [a]	
C_6H_5	$2.97 \pm 0.33 \times 10^{-7}$	pH tit.
	3.0×10^{-7} [b]	
	1.66×10^{-8} [c]	
	3.2×10^{-7} [d]	
	2.0×10^{-7} [e]	
(2-Pyridyl)CH_2	$1.52 \pm 0.16 \times 10^{-9}$	pH tit.
$C_2H_5OCOCH_2CH_2$	$3.25 \pm 0.39 \times 10^{-10}$	pH tit.
$HOCH_2C(CH_3)_2$	$1.42 \pm 0.13 \times 10^{-10}$	pH tit.
CH_3	$4.7 \pm 0.8 \times 10^{-11}$	Gas sol.
t-C_4H_9	$9.0 \pm 0.6 \times 10^{-12}$	Spec.
	8.9×10^{-12} [f]	
t-C_5H_{11}	$4.5 \pm 0.6 \times 10^{-12}$	Spec.
	6.2×10^{-12} [f]	

[a] Ref. 9. [b] Ref. 2. [c] Ref. 4. [d] Ref. 6. [e] Ref. 7. [f] Ref. 10. [g] pH tit. = pH titration, gas sol. = gas solubility, spec. = spectrophotometric.

Discussion

The redetermined value of K_A for thiophenol is in excellent agreement with our previous value, which had been determined by an entirely different method (spectrophotometric) so that similar, systematic errors are quite unlikely. In addition, our values are in substantial agreement with those reported by De-Deken and co-workers[6] and by Albert and Barlin.[7] The Calvin value,[8] cited by Danehy and Noel[4] as similar to their own, was actually obtained in partially alcoholic solution, and so is not directly comparable with values in aqueous solutions. Accordingly, a value around 3×10^{-7} must be considered correct.

The agreement between the present K_A of thiolacetic acid and a very old value determined conductimetrically by Ostwald[9] is surprisingly good. For *t*-butyl and *t*-amyl mercaptans the present values are in good agreement with those of Yabroff,[10] obtained by a solvent extraction method.

In order to test more rigorously the possibility of a Baker–Nathan effect,[11] the parameters of eq. 3,[3] ρ^* and α, were redetermined using only K_A values for compounds, XCH_2SH. (Equation 3 appears in ref. 2 with a sign error but the value of α later given pertains to the correct equation.) Using the nine such K_A

$$\log K_A = \sigma^*\rho^* + \alpha \qquad (3)$$

values previously available[2] and also that for ethyl β-mercaptopropionate, a value of 3.50 is obtained for

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[1] This work was supported by the U. S. Army, Surgeon General's Office, through Contract DA-49-193-MD-2027.

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ρ^* and -10.22 for α by the method of least squares.[12] (A σ^* was estimated for $C_2H_5OCOCH_2CH_2$– by dividing that for CH_3OCO– by 2.8^2.)[3] As the 50% confidence limits[12] on ρ^* are about ± 0.15 in each case, these are not appreciably different from the values of 3.40 and -10.17 obtained using all the data previously available.[2] These parameters were then used in eq. 3 to calculate K_A for mercaptans having other than two α-hydrogen atoms. If there is a significant Baker–Nathan effect, K_A for methyl mercaptan should be higher than calculated and K_A values for mercaptans having less than two α-hydrogen atoms should be systematically lower.[11] It is plain from Table II that this is not so. The large deviation for hydrogen sulfide has been discussed previously.[2] It is in the wrong direction for a Baker–Nathan effect. The other deviations, averaging 0.17 log units, are not much larger than those of values used to obtain the correlation and are also in the wrong direction for a Baker–Nathan effect. It seems likely, therefore, that the Baker–Nathan effect is not larger than 0.05 log units per α-hydrogen atom. Steric effects would also appear to be small, apart from the possibility that the H_2S anomaly is to be explained in that way.[2] In fact, as also shown in Table II, the new data seem to be excellently correlated by eq. 3 using the old parameters.

TABLE II

DEVIATIONS FROM EQUATION 3 WITH OTHER THAN TWO α-HYDROGEN ATOMS

Compound	$\log K_A^{\text{obsd}} - \log K_A^{\text{calcd}\,a}$	$\log K_A^{\text{obsd}} - \log K_A^{\text{calcd}\,b}$
H_2S^c	+1.49	+1.48
$HOCH_2C(CH_3)_2SH$	+0.35	+0.17
CH_3SH	0.00	−0.05
t-C_4H_9SH	+0.22	+0.13
	+0.12	+0.03

[a] Calculated using the parameters obtained with groups having two α-hydrogen atoms. [b] Calculated using the parameters of ref. 2. [c] Corrected by a symmetry factor of two.

As previously noted[2] thiophenol deviates from eq. 3 by ~1.6 log units. This deviation has been attributed to enhanced resonance stabilization in the anion, and designated $\Delta pK\psi$. For thiolacetic acid $\Delta pK\psi$ is ~1.1 log units. Unfortunately this value is not so reliable as it might be, as the correlation with σ^* is being used well outside of the range in which it was experimentally verified. Nevertheless, these results tend to support the idea[13] that resonance stabilization due to a neighboring unsaturated group is roughly independent of the nature of that group.

The absence of a Baker–Nathan effect, in spite of the presence of a resonance effect due to conjugation, is interesting, since, at least in Hückel approximation, the former is usually predicted to be proportional to the latter.[11] The proportionality constant has been variously estimated as ~1/10[13] and 1/13.[11] The only model which avoids this prediction is one in which *both* the carbon sp^3-orbital holding the α-hydrogen atom *and* the α-hydrogen 1s-orbital have nonzero resonance integrals with a neighboring p-orbital. This model predicts a much larger magnitude for Baker–Nathan effects in electron-deficient systems than in electron-surplus systems, such as the mercaptide ions. Although more data would be very desirable before reaching a final conclusion, this model should probably receive more attention than it has in the past.

Experimental

Dissociation Constants.—The pH titration, spectrophotometric, and gas solubility methods for determining dissociation constants have been previously described.[2] In determining the dissociation constant of methyl mercaptan it was found desirable to have more basic buffer solutions than those previously used. These were provided by phenol–phenoxide ion buffers. The hydrogen ion concentration of these was estimated using 1.00×10^{-10} as the acid dissociation constant of phenol.[14] In a simple buffer system of this sort the activity coefficients cancel, to a first approximation, and the dissociation constant of the mercaptan is given by eq. 5.

$$K_A^{CH_3SH} = K_A^{C_6H_5OH} \frac{(C_6H_6OH)(CH_3S^-)}{(C_6H_5O^-)(CH_3SH)} \qquad (5)$$

Materials.[15]—Thiolacetic acid (Eastman Kodak Co., practical grade) was redistilled and the center cut, b.p. 84–85°, was used. Thiophenol (Mathieson Co., reagent grade) was redistilled under vacuum to give b.p. 55–56° at 10 mm. (2-Pyridyl)methyl mercaptan was a gift of the Walter Reed Army Institute of Research through Dr. T. R. Sweeney and was used as supplied. Ethyl β-mercaptopropionate was prepared by the method of Karrer and Schmid[16] from β-mercaptopropionic acid (gift of Evans Chemetics, Inc.) and purified by vacuum distillation to give b.p. 54° at 6 mm. 2-Mercapto-2-methyl-1-propanol was prepared from isobutylene oxide by the method of Davies and Savige[17] and had b.p. 68° at 29 mm. Methyl mercaptan was purchased from Eastman Kodak Co. and was not further purified except that it was distilled into the gas solubility apparatus. t-Amyl mercaptan was prepared from t-amyl bromide by the method of Backer[18] and had b.p. 104°. t-Butyl mercaptan was prepared in essentially the same way from t-butyl chloride and had b.p. 63°.

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Nucleophilic Heteroaromatic Substitution. I. Pyridazines

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In contrast to the numerous studies of nucleophilic homoaromatic substitutions,[2] kinetic studies of nucleophilic heteroaromatic substitutions have been few. Such studies have been confined mainly to pyridines[3] and pyrimidines[4] where annular nitrogen α and/or γ to the group displaced, generally halogen, facilitates reaction through electron withdrawal.

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