

Mechanism of Dissolution II: Experimental Determination of Surface Tension of a Solid

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Abstract □ A graphical method for determining solid surface tension is presented. The method is based on the Ostwald-Freundlich equation for the solubility dependence on particle size and on the Fowkes geometrical mean relationship. The solid surface tension, γ_s , and the particle size in equilibrium with saturated solution are both determined graphically. For the solid *m*-acetotoluide, γ_s was calculated to be 34.4 ergs/cm.². The calculated particle size in equilibrium with saturated solution was in agreement with electron microscopic determinations. It is proposed that the method is applicable to the determination of γ_s for any solid for which a particle size-solubility relationship can be determined.

Keyphrases □ Surface tension, solids—graphical determination, *m*-acetotoluide □ *m*-Acetotoluide—graphical determination of surface tension and particle size in equilibrium with saturated solution □ Solid surface tension—graphical determination □ Dissolution, mechanisms—experimental determination of surface tension of a solid

It has, in general, been difficult to measure experimentally the surface tension of both low (<100 ergs/cm.²) and high energy solid surfaces. A number of theoretical approaches have been investigated, particularly with high energy surfaces (1), while heats of adsorption and immersion have provided the most successful experimental approach (2). Zisman (3) utilized contact angle measurements to study low energy macromolecular surfaces. However, the vast majority of pharmaceutically active drugs are low energy micromolecular solids for which very little has been accomplished with regard to the determination of solid surface tension. It is the micromolecular low energy solid that is involved in the numerous problems arising in the development of various dosage forms. This study describes a general method for experimentally determining the surface tension of low energy micromolecular solids. Subsequent investigations will utilize this method in studying the mechanism of the dissolution of solids.

THEORETICAL

The development of surface theory from contact angle measurements by Zisman (3) and the postulation of the geometrical mean relationship by Girifalco and Good (4) and Fowkes (2) to predict intermolecular forces at interfaces lead to an experimental method of determining the surface tension of a solid.

Consider the Ostwald-Freundlich equation (5) relating particle size to solubility:

$$\log \frac{S_1}{S_2} = \frac{2\bar{V}\gamma_{SL}}{2.3RT} \left(\frac{1}{r_1} - \frac{1}{r_2} \right) \quad (\text{Eq. 1})$$

where S_1 is the solubility¹ of particles of radius r_1 , S_2 is the solubility of particles of radius r_2 , \bar{V} is the molar volume of the solid, and

¹ It is assumed that S_1 and S_2 are sufficiently similar so that the ratio of activity coefficients which should appear in Eq. 1 is equal to unity.

γ_{SL} is the solid-liquid interfacial tension. When r_2 is much greater than r_1 , Eq. 1 reduces to:

$$\log \frac{S_1}{S_2} = \frac{2\bar{V}\gamma_{SL}}{2.3RT r_1} \quad (\text{Eq. 2})$$

Substitution of the geometrical mean relationship (2):

$$\gamma_{SL} = \gamma_s + \gamma_L - 2\sqrt{\gamma_s^d \gamma_L^d} \quad (\text{Eq. 3})$$

where γ^d 's are the dispersion force components of the solid and liquid, into Eq. 2 yields:

$$\log \frac{S_1}{S_2} = \frac{2\bar{V}}{2.3RT r_1} \gamma_L + \left(\frac{2\bar{V}\gamma_s}{2.3RT r_1} - \frac{4\bar{V}\sqrt{\gamma_s^d \gamma_L^d}}{2.3RT r_1} \right) \quad (\text{Eq. 4})$$

The solubility dependence on particle size for a given solid may then be determined in various solvents, and a plot of $\log(S_1/S_2)$ versus γ_L may be constructed. The slope of this line will be $2\bar{V}/2.3RT r_1$, from which r_1 may be calculated, and the intercept will contain γ_s , the surface tension of the solid, as well as γ_s^d and γ_L^d . Both γ_s^d and γ_L^d may be determined experimentally, γ_s^d from contact angle measurements and γ_L^d from interfacial tension measurements or, in the case of pure hydrocarbon liquids, $\gamma_L^d = \gamma_L$.

The assumption that Eq. 3 is linear is in reality incorrect. The dispersion force component of the liquid, γ_L^d , is not independent of its surface tension, and Eq. 3 shows some deviation from linearity. The deviation is, however, minimized by the square root relationship and can be further controlled through the proper selection of solvent. As will be seen, the present study justified the assumption of linearity for Eq. 3.

EXPERIMENTAL

Particle Preparation—Reagent grade *m*-acetotoluide was sieved on a nest of sieves (ASTM). The 30/60 sieve cut was taken as particles having radius r_2 . The greater than 100-mesh portion was micronized using a fluid energy mill (Gem T) using dry nitrogen at 80 lb./in.². The micronized material was used as particles with radius r_1 . A particle-size analysis of the micronized *m*-acetotoluide using an electron microscope (Philips EM 300) showed a particle-size range of 43.4–348 Å. A comparison of particle size for r_1 and r_2 ($r_2 = 125 \mu$) is ample justification for disregarding $1/r_2$ in Eq. 1.

Determination of Solubility Ratio, S_1/S_2 —An oven (model 1206 Hotpack) was modified to function as a glove box in which the temperature was set to $30 \pm 0.05^\circ$ with a thermometer (NBS) and controlled to $\pm 0.003^\circ$ with a thermostat (Sargent). Five hundred milligrams of the micronized *m*-acetotoluide was placed in a flask containing 25.0 ml. of hydrocarbon solvent. A 500.0-mg. sample of nonmicronized large crystals of *m*-acetotoluide was treated in the same manner. They were stirred until the assay indicated equilibrium was obtained. All operations of sampling and dilution of sample were carried out inside the glove box with temperature-equilibrated equipment and solvent to assure accurate temperature control of both solid samples. The solubility ratios, S_1/S_2 , are shown in Table I.

Measurement of Liquid Hydrocarbon Surface Tension—Spectrograde hydrocarbon solvents were used for all solubility and contact angle determinations. The surface tension of the hydrocarbon solvents was determined at 30° inside the glove box using a tensiometer (Fisher DuNouy). The corrected values of the surface tension are shown in Table I. There was apparently no discernible difference between pure solvent surface tensions and surface tensions of *m*-acetotoluide-saturated solutions.

Table I—Solubility and Surface Tension Data

Solvent	$\frac{S_1}{S_2}$	$\left(\log \frac{S_1}{S_2}\right) \times 10^3$	γ_L , ergs/cm. ²	Per- cent Solid Dis- solved
Cyclohexane	1.08	3.34	23.7 ± 0.1	5.2
<i>m</i> -Heptane	1.06	2.53	19.5 ± 0.1	3.2
<i>m</i> -Hexane	1.03	1.28	17.9 ± 0.0	3.0

Determination of γ_s^d by Contact Angle Measurement—The *m*-acetotoluide surface was prepared for contact angle measurement by casting the melted solid against a highly polished steel die positioned in a die holder. The contact angle was then measured on the solid surface with a goniometer (Ramé-Hart) with the environmental chamber at 30°.

X-ray diffraction patterns were obtained from McGreery mounts of crystalline, micronized, and cast and reground *m*-acetotoluide. The X-ray data showed all three samples to have identical crystalline structure.

RESULTS

Figure 1 is a plot of the Fowkes equation:

$$\cos \theta = -1 + 2\sqrt{\gamma_s^d} \frac{\sqrt{\gamma_L^d}}{\gamma_L} \quad (\text{Eq. 5})$$

for decahydronaphthalene on the solid *m*-acetotoluide. As pointed out by Fowkes (2), one contact angle measurement is sufficient to determine the dispersion force component of the solid. The dispersion force component, γ_s^d , of *m*-acetotoluide evaluated from the slope of Fig. 1 is 28.0 ergs/cm.².

A graph of Eq. 4 for the solid *m*-acetotoluide in the hydrocarbon solvents hexane, heptane, and cyclohexane is shown in Fig. 2. The method of least squares was used to calculate the slope and the intercept. From the slope a value for r_1 of 141 Å was calculated. The surface tension of *m*-acetotoluide was calculated from the intercept. By using the dispersion force component of the solid equal to 28.0 ergs/cm.² and the particle radius, r_1 , equal to 141 Å, the surface tension of *m*-acetotoluide was calculated to be 34.4 ergs/cm.².

DISCUSSION

The calculation of the solid surface tension is dependent upon the last two terms of Eq. 4 remaining constant. An examination of these terms reveals that γ_s , γ_s^d , and \bar{V} are characteristics of the solid and are, therefore, constant. R is the gas constant and T is held constant by experimental design. By choosing the solvents cyclohexane, *n*-heptane, and *n*-hexane, $(\gamma_L^d)^{1/2}$ varies by only about 5% (4.51 ± 0.24 ergs^{1/2}/cm.). Thus, the last two terms in Eq. 4 remain practically constant, certainly within the limits of the experimental design.

The calculated value of the solid surface tension is also dependent upon the value of r_1 determined graphically from Eq. 4. Variation in r_1 from solvent to solvent was minimized by using relatively massive amounts of *m*-acetotoluide in determining the solubility ratios (S_1/S_2). Table I shows that 94.8-97% of the solid remained undissolved. The graphically determined value for r_1 (141 Å) is greater than the smallest value determined with the electron microscope (43.5 Å). The graphical value of r_1 from Eq. 4 is, however, the radius of the smallest particles in equilibrium with the saturated solution and should be greater than the smallest particles of the micronized solid determined microscopically. The smaller particles in a population will dissolve first (6), thus causing a natural increase in the size of the smallest particle present in solution. Indirect support for the graphical value of r_1 is found in the work of Enustun and Turkovich (6), who observed a change in the smallest size particles from 190 to 250 Å during solution of SrSO₄.

The fact that the microscopic particle size and the graphical size for r_1 are of essentially the same magnitude is strong evidence that the graphical value is really an accurate particle-size value. These two methods for particle-size measurement are completely indepen-

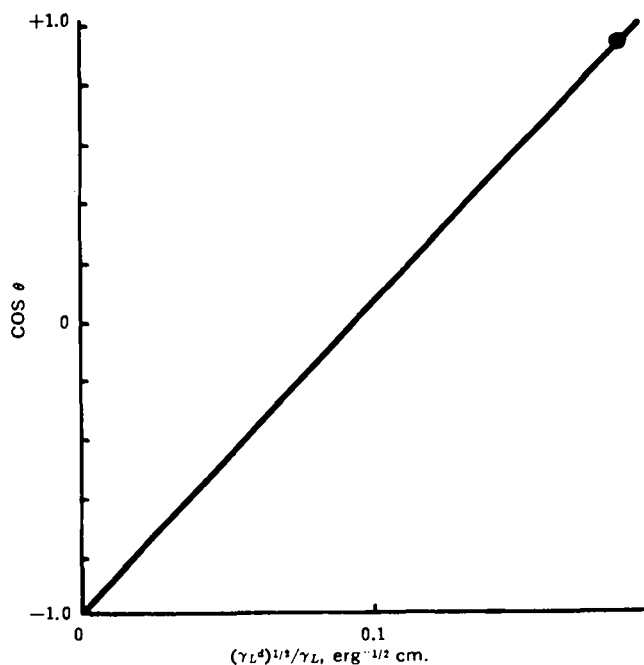


Figure 1—Contact angle of decahydronaphthalene on *m*-acetotoluide plotted according to Eq. 5 for determination of $(\gamma_s^d)^{1/2}$.

dent of each other, yet they yield particle sizes that are remarkably close. This makes the calculated solid surface tension of *m*-acetotoluide, based on the graphically determined value of r_1 , extremely reliable.

Additional evidence for the reliability of γ_s lies in comparing the calculated value of 34.4 ergs/cm.² with literature values of γ_s for similar materials. Gorskii (7) published surface energies for antipyrine and β -naphthylsalicylate of 41 and 39 ergs/cm.², respectively. These values appear to correlate well with the greater polar character of antipyrine as compared to β -naphthylsalicylate. The presence of polar interactions contribute to an increase in the surface energy because these polar interactions are in addition to the dispersion force contributions. Water, for example, has a total surface energy of 72.9 ergs/cm.² Of this amount, 21.8 ergs/cm.² is derived from dispersion forces (2) and the remainder is derived from polar interactions. The nonpolar hydrocarbon liquids, on the other hand, have much lower surface energies. The surface energies of solids

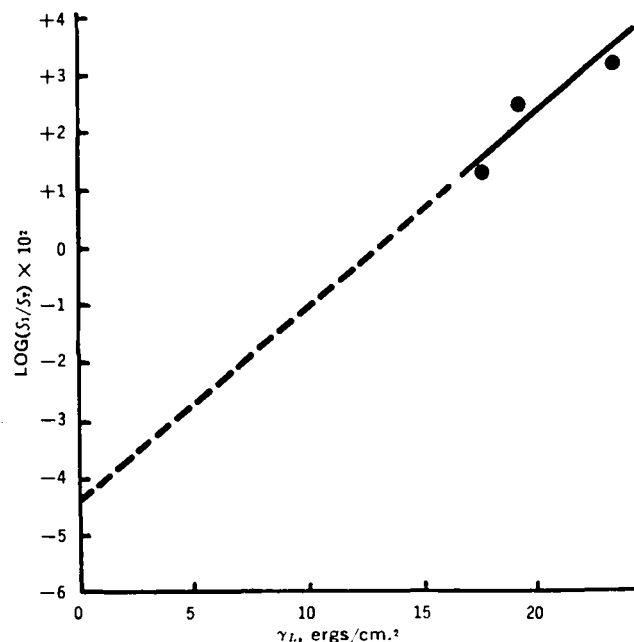


Figure 2—Plot of Eq. 4 for determination of r_1 and γ_s .

Table II—Contact Angles and Spreading Coefficients

Solvent	Contact Angle, Degrees	Spreading Coefficient, ergs/cm. ²
Decahydronaphthalene	19 ± 1	-7.4
Cyclohexane	0	0.6
<i>m</i> -Heptane	0	7.3
<i>m</i> -Hexane	0	10.6

may also be expected to be influenced by their polar character, increasing as the polarity of the molecular structure increases. On a molecular basis, *m*-acetotoluide is closer in polarity to β -naphthylsalicylate than antipyrine. Therefore, in relation to Gorskii's results (7), the value of 34.4 ergs/cm.² would appear to be an accurate value of the solid surface energy of *m*-acetotoluide.

Further confirmation of the reliability of γ_s equal to 34.4 ergs/cm.² for *m*-acetotoluide is found in the calculated spreading coefficients. The spreading coefficient is given by:

$$S = \gamma_s - (\gamma_L + \gamma_{LS}) \quad (\text{Eq. 6})$$

The spreading coefficient is the difference between the work of adhesion, W_a , for liquid-solid interactions and the work of cohesion, W_c , for liquid-liquid interactions, or:

$$S = W_a - W_c \quad (\text{Eq. 7})$$

It is easily seen that negative spreading coefficients indicate that the cohesive forces between liquid molecules are stronger than the adhesive forces between the solid-liquid molecules and predict that the liquid forms an angle of contact on the solid. Positive spreading coefficients indicate spreading of the liquid over the solid. Spreading coefficients were calculated, and the values are tabulated in Table II. The calculated values of S , based on γ_s equal to 34.4 ergs/cm.², are in perfect agreement with the observed contact angle behavior.

The ability to calculate both γ_s and γ_s^d now makes it possible to calculate the polar contribution to the surface tension of *m*-acetotoluide. For *m*-acetotoluide the polar contribution to the surface tension, taken as the difference $\gamma_s - \gamma_s^d$, is 6.4 ergs/cm.². This is due to the substituted amide group and may involve a π -bonding interaction with adjacent phenyl groups. Data for the contribution of dipole-dipole interactions of various polar functional groups to the surface tension of solids are lacking, so it is difficult to evaluate the relative magnitude of the 6.4 ergs/cm.² for *m*-acetotoluide. For the liquid formamide, a polar contribution can be determined from reported values of γ_L and γ_L^d (2) equal to 18.7 ± 7 ergs/cm.². The deviation is quite large, and the value is difficult to evaluate relative to *m*-acetotoluide; it may, however, be considered in fairly good agreement with the 6.4 ergs/cm.² for *m*-acetotoluide when considering relative molecular size and the greater degree of interaction possible with formamide.

The solubility dependence on particle size previously was used to calculate the surface energy of a solid. Using differences in heats of solution between fine and coarse powders, Benson and coworkers (8, 9) and Lipsett *et al.* (10) calculated the surface energy of sodium chloride. This method is limited, in general, to solid-liquid systems in which dissolution is rapid. The method proposed in this study, however, is applicable to any solid for which a solubility dependence on particle size can be determined, regardless of the solid's dissolution properties. In addition, it is now possible to evaluate the contribution of polar interactions of the various polar groups to solid surface tension and to determine the effect of the polar interaction on dissolution and other physical and chemical properties of solids.

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