quantities to be extracted from solubility data. Both these are
difficult to achieve in many cases because of a lack of experimental or
theoretical information concerning activity coefficients. Where
thermodynamic quantities can be found, they are not evaluated critically,
since this task would involve critical evaluation of a large body of
data that is not directly relevant to solubility. The following
is an outline of the principal thermodynamic relations encountered in
discussions of solubility. For more extensive discussions and references,
see books on thermodynamics, e.g., (7-14).

   Activity Coefficients (1)

      (a) *Mixtures*. The activity coefficient f_B of a substance B is given
by

$$RT \ln (f_B x_B) = \mu_B - \mu_B{}^* \qquad [7]$$

where $\mu_B{}^*$ is the chemical potential of pure B at the same temperature and
pressure. For any substance B in the mixture,

$$\lim_{x_B \to 1} f_B = 1 \qquad [8]$$

   (b) *Solutions*.

      (i) *Solute B*. The molal activity coefficient γ_B is given by

$$RT \ln(\gamma_B m_B) = \mu_B - (\mu_B - RT \ln m_B)^\infty \qquad [9]$$

where the superscript ∞ indicates an infinitely dilute solution. For any
solute B,

$$\gamma_B{}^\infty = 1 \qquad [10]$$

   Activity coefficients y_B connected with concentrations c_B, and $f_{x,B}$
(called the *rational activity coefficient*) connected with mole fractions
x_B, are defined in analogous ways. The relations among them (1, 9) are,
where ρ^* is the density of the pure solvent:

$$f_B = (1 + M_A \sum_s m_s)\gamma_B = [\rho + \sum_s(M_A - M_s)c_s]y_B/\rho^* \qquad [11]$$

$$\gamma_B = (1 - \sum_s x_s)f_{x,B} = (\rho - \sum_s M_s c_s)y_B/\rho^* \qquad [12]$$

$$y_B = \rho^* f_{x,B}[1 + \sum_s(M_s/M_A - 1)x_B]/\rho = \rho^*(1 + \sum_s M_s m_s)\gamma_B/\rho \qquad [13]$$

   For an electrolyte solute $B \equiv C_{\nu_+}A_{\nu_-}$, the activity on the molality
scale is replaced by (11):

$$\gamma_B m_B = \gamma_\pm{}^\nu m_B{}^\nu Q^\nu \qquad [14]$$

where $\nu = \nu_+ + \nu_-$, $Q = (\nu_+{}^{\nu_+}\nu_-{}^{\nu_-})^{1/\nu}$, and $\gamma_\pm$ is the mean ionic activity
coefficient on the molality scale. A similar relation holds for the
concentration activity, $y_B c_B$. For the mole fractional activity,

$$f_{x,B} x_B = Q^\nu f_\pm{}^\nu x_\pm{}^\nu \qquad [15]$$

where $x_\pm = (x_+ x_-)^{1/\nu}$. The quantities x_+ and x_- are the ionic mole
fractions (11), which are:

$$x_+ = \nu_+ x_B/[1 + \sum_s(\nu_s - 1)x_s]; \quad x_- = \nu_- x_B[1 + \sum_s(\nu_s - 1)x_s] \qquad [16]$$

where ν_s is the sum of the stoichiometric coefficients for the ions in a
salt with mole fraction x_s. Note that the mole fraction of solvent is now

$$x_A{}' = (1 - \sum_s \nu_s x_s)/[1 + \sum_s(\nu_s - 1)x_s] \qquad [17]$$

so that

$$x_A{}' + \sum_s \nu_s x_s = 1 \qquad [18]$$

   The relations among the various mean ionic activity coefficients are:

$$f_\pm = (1 + M_A \sum_s \nu_s m s)\gamma_\pm = [\rho + \sum_s(\nu_s M_A - M_s)c_s]y_\pm/\rho^* \qquad [19]$$

$$\gamma_\pm = \frac{(1 - \sum_s x_s)f_\pm}{1 + \sum_s(\nu_s - 1)x_s} = (\rho - \sum_s M_s c_s)y_\pm/\rho^* \qquad [20]$$

$$y_\pm = \frac{\rho^*[1 + \sum_s(M_s/M_A - 1)x s]f_\pm}{\rho[1 + \sum_s(\nu_s - 1)x_s]} = \rho^*(1 + \sum_s M_s m_s)\gamma_\pm/\rho \qquad [21]$$

(ii) *Solvent, A:*

The *osmotic coefficient*, ϕ , of a solvent A is defined as (1):

$$\phi \; = \; (\mu_A{}^* - \mu_A)/RT \, M_A \sum_s m_s \qquad [22]$$

where $\mu_A{}^*$ is the chemical potential of the pure solvent.

The *rational osmotic coefficient*, ϕ_x, is defined as (1):

$$\phi_x \; = \; (\mu_A - \mu_A{}^*)/RT\ln x_A \; = \; \phi M_A \sum_s m_s / \ln(1 + M_A \sum_s m_s) \qquad [23]$$

The activity, a_A, or the activity coefficient, f_A, is sometimes used for the solvent rather than the osmotic coefficient. The activity coefficient is defined relative to pure A, just as for a mixture.

For a mixed solvent, the molar mass in the above equations is replaced by the average molar mass; i.e., for a two-component solvent with components J, K, M_A becomes

$$M_A \; = \; M_J + (M_K - M_J)x_{v,K} \qquad [24]$$

where $x_{v,K}$ is the solvent mole fraction of component K.

The osmotic coefficient is related directly to the vapor pressure, p, of a solution in equilibrium with vapor containing A only by (14, p.306):

$$\phi M_A \sum_s \nu_s m_s \; = \; - \ln(p/p_A{}^*) + (V_{m,A}^* - B_{AA})(p - p_A{}^*)/RT \qquad [25]$$

where $p_A{}^*$ is the vapor pressure of pure solvent A, $V_{m,A}^*$ is the molar volume of pure A in the liquid phase, and B_{AA} is the second virial coefficient of the vapor.

The Liquid Phase

A general thermodynamic differential equation which gives solubility as a function of temperature, pressure and composition can be derived. The approach is similar to that of Kirkwood and Oppenheim (9); see also (13, 14). Consider a solid mixture containing c thermodynamic components i. The Gibbs-Duhem equation for this mixture is:

$$\sum_{i=1}^{c} x_i{}'(S_i{}'dT - V_i{}'dp + d\mu_i{}') \; = \; 0 \qquad [26]$$

A liquid mixture in equilibrium with this solid phase contains c' thermodynamic components i, where $c' \geqslant c$. The Gibbs-Duhem equation for the liquid mixture is:

$$\sum_{i=1}^{c} x_i(S_i dT - V_i dp + d\mu_i{}') + \sum_{i=c+1}^{c'} x_i(S_i dT - V_i dp + d\mu_i) \; = \; 0 \qquad [27]$$

Subtract [26] from [27] and use the equation

$$d\mu_i \; = \; (d\mu_i)_{T,p} - S_i dT + V_i dp \qquad [28]$$

and the Gibbs-Duhem equation at constant temperature and pressure:

$$\sum_{i=1}^{c} x_i(d\mu_i{}')_{T,p} + \sum_{i=c+1}^{c'} x_i(d\mu_i)_{T,p} \; = \; 0 \qquad [29]$$

The resulting equation is:

$$RT \sum_{i=1}^{c} x_i{}'(d\ln a_i)_{T,p} \; = \; \sum_{i=1}^{c} x_i{}'(H_i - H_i{}')dT/T - \sum_{i=1}^{c} x_i{}'(V_i - V_i{}')dp \qquad [30]$$

where

$$H_i - H_i{}' \; = \; T(S_i - S_i{}') \qquad [31]$$

is the enthalpy of transfer of component i from the solid to the liquid phase at a given temperature, pressure and composition, with H_i and S_i the partial molar enthalpy and entropy of component i.

Use of the equations

$$H_i - H_i{}^0 \; = \; -RT^2(\partial \ln a_i/\partial T)_{x,p} \qquad [32]$$

and

$$V_i - V_i{}^0 \; = \; RT(\partial \ln a_i/\partial p)_{x,T} \qquad [33]$$

where superscript o indicates an arbitrary reference state gives:

$$RT \sum_{i=1}^{c} x_i{}'d\ln a_i \; = \; \sum_{i=1}^{c} x_i{}'(H_i{}^0 - H_i{}')dT/T - \sum_{i=1}^{c} x_i{}'(V_i{}^0 - V_i{}')dp \qquad [34]$$

where

$$d\ln a_i = (d\ln a_i)_{T,p} + (\partial\ln a_i/\partial T)_{x,p} + (\partial\ln a_i/\partial p)_{x,T} \qquad [35]$$

The terms involving enthalpies and volumes in the solid phase can be written as:

$$\sum_{i=1}^{c} x_i'H_i' = H_s^* \qquad\qquad \sum_{i=1}^{c} x_i'V_i' = V_s^* \qquad [36]$$

With eqn [36], the final general solubility equation may then be written:

$$R\sum_{i=1}^{c} x_i'd\ln a_i = (H_s^* - \sum_{i=1}^{c} x_i'H_i^0)d(1/T) - (V_s^* - \sum_{i=1}^{c} x_i'V_i^0)dp/T \quad [37]$$

Note that those components which are not present in both phases do not appear in the solubility equation. However, they do affect the solubility through their effect on the activities of the solutes.

Several applications of eqn [37] (all with pressure held constant) will be discussed below. Other cases will be discussed in individual evaluations.

(a) *Solubility as a function of temperature.*

Consider a binary solid compound A_nB in a single solvent A. There is no fundamental thermodynamic distinction between a binary compound of A and B which dissociates completely or partially on melting and a solid mixture of A and B; the binary compound can be regarded as a solid mixture of constant composition. Thus, with $c = 2$, $x_A' = n/(n + 1)$, $x_B' = 1/(n + 1)$, eqn [37] becomes:

$$d\ln(a_A^n a_B) = -\Delta H_{AB}^0 d(1/RT) \qquad [38]$$

where

$$\Delta H_{AB}^0 = nH_A + H_B -(n + 1)H_s^* \qquad [39]$$

is the molar enthalpy of melting and dissociation of pure solid A_nB to form A and B in their reference states. Integration between T and T_0, the melting point of the pure binary compound A_nB, gives:

$$\ln(a_A^n a_B) = \ln(a_A^n a_B)_{T=T_0} - \int_{T_0}^{T}\Delta H_{AB}^0 d(1/RT) \qquad [40]$$

(1) Non-electrolytes

In eqn [32], introduce the pure liquids as reference states. Then, using a simple first-order dependence of ΔH_{AB}^* on temperature, and assuming that the activity coefficients conform to those for a simple mixture (8):

$$RT \ln f_A = wx_B^2 \qquad\qquad RT \ln f_B = wx_A^2 \qquad [41]$$

then, if w is independent of temperature, eqn [32] and [33] give:

$$\ln\{x_B(1-x_B)^n\} + \ln\left\{\frac{n^n}{(1 + n)^{n+1}}\right\} = G(T) \qquad [42]$$

where

$$G(T) = - \left[\frac{\Delta H_{AB}^* - T^*\Delta C_p^*}{R}\right]\left\{\frac{1}{T} - \frac{1}{T^*}\right\}$$

$$+ \frac{\Delta C_p^*}{R} \ln(T/T^*) - \frac{w}{R}\left[\frac{x_A^2 + nx_B^2}{T} - \frac{n}{(n + 1)T^*}\right] \qquad [43]$$

where ΔC_p^* is the change in molar heat capacity accompanying fusion plus decomposition of the pure compound to pure liquid A and B at temperature T^*, (assumed here to be independent of temperature and composition), and ΔH_{AB}^* is the corresponding change in enthalpy at $T = T^*$. Equation [42] has the general form:

$$\ln\{x_B(1-x_B)^n\} = A_1 + A_2/(T/K) + A_3\ln(T/K) + A_4(x_A^2 + nx_B^2)/(T/K) \quad [44]$$

If the solid contains only component B, then $n = 0$ in eqn [42] to [44].

If the infinite dilution reference state is used, then:

$$RT \ln f_{x,B} = w(x_A{}^2 - 1)$$ [45]

and [39] becomes

$$\Delta H_{AB}{}^{\infty} = nH_A{}^* + H_B{}^{\infty} - (n + 1)H_S{}^*$$ [46]

where $\Delta H_{AB}{}^{\infty}$ is the enthalpy of melting and dissociation of solid compound A_nB to the infinitely dilute reference state of solute B in solvent A; $H_A{}^*$ and $H_B{}^{\infty}$ are the partial molar enthalpies of the solute and solvent at infinite dilution. Clearly, the integral of eqn [32] will have the same form as eqn [35], with $\Delta H_{AB}{}^{\infty}$ replacing $\Delta H_{AB}{}^*$, $\Delta C_p{}^{\infty}$ replacing $\Delta C_p{}^*$, and $x_A{}^2 - 1$ replacing $x_A{}^2$ in the last term.

See (7) and (13) for applications of these equations to experimental data.

(ii) Electrolytes

   (a) Mole fraction scale

If the liquid phase is an aqueous electrolyte solution, and the solid is a salt hydrate, the above treatment needs slight modification. Using rational mean activity coefficients, eqn [34] becomes:

$$\ln\left\{\frac{x_B{}^{\nu}(1 - x_B)^n}{[1 + (\nu - 1)x_B]^{n+\nu}}\right\} - \ln\left\{\frac{n^n}{(n + \nu)^{n+\nu}}\right\} + \ln\left\{\left[\frac{f_B{}_*}{f_B{}^*}\right]^{\nu}\left[\frac{f_A{}_*}{f_A}\right]^n\right\}$$
$$= -\left[\frac{\Delta H_{AB}{}^* - T^*\Delta C_p{}^*}{R}\right]\left\{\frac{1}{T} - \frac{1}{T^*}\right\} + \frac{\Delta C_p{}^*}{R}\ln(T/T^*)$$ [47]

where superscript * indicates the pure salt hydrate. If it is assumed that the activity coefficients follow the same temperature dependence as the right-hand side of eqn [47] (15-17), the thermochemical quantities on the right-hand side of eqn [47] are not rigorous thermodynamic enthalpies and heat capacities, but are apparent quantities only. Data on activity coefficients (11) in concentrated solutions indicate that the terms involving these quantities are not negligible, and their dependence on temperature and composition along the solubility-temperature curve is a subject of current research.

A similar equation (with $\nu = 2$ and without the heat capacity terms) or activity coefficients) has been used to fit solubility data for some $MOH-H_2O$ systems, where M is an alkali metal (15); enthalpy values obtained agreed well with known values. The full equation has been deduced by another method in (16) and applied to MCl_2-H_2O systems in (16) and (17). For a summary of the use of equation [47] and similar equations, see (18).

      (2) Molality scale

Substitution of the mean activities on the molality scale in eqn [40] gives:

$$\nu\ln\left[\frac{\gamma_{\pm}m_B}{\gamma_{\pm}{}^*m_B{}^*}\right] - \nu(m_B/m_B{}^* - 1) - \nu\{m_B(\phi - 1)/m_B{}^* - \phi^* + 1\}$$
$$= G(T)$$ [48]

where $G(T)$ is the same as in eqn [47], $m_B{}^* = 1/nM_A$ is the molality of the anhydrous salt in the pure salt hydrate and $\gamma_{\pm}$ and ϕ are the mean activity coefficient and the osmotic coefficient, respectively. Use of the osmotic coefficient for the activity of the solvent leads, therefore, to an equation that has a different appearance to [47]; the content is identical. However, while eqn [47] can be used over the whole range of composition ($0 < x_B < 1$), the molality in eqn [48] becomes infinite at $x_B = 1$; use of eqn [48] is therefore confined to solutions sufficiently dilute that the molality is a useful measure of composition. The essentials of eqn [48] were deduced by Williamson (19); however, the form used here appears first in the Solubility Data Series. For typical applications (where activity and osmotic coefficients are not considered explicitly, so that the enthalpies and heat capacities are apparent values, as explained above), see (20).

The above analysis shows clearly that a rational thermodynamic basis exists for functional representation of solubility-temperature curves in two-component systems, but may be difficult to apply because of lack of experimental or theoretical knowledge of activity coefficients and partial molar enthalpies. Other phenomena which are related ultimately to the stoichiometric activity coefficients and which complicate interpretation

include ion pairing, formation of complex ions, and hydrolysis. Similar considerations hold for the variation of solubility with pressure, except that the effects are relatively smaller at the pressures used in many investigations of solubility (7).

    (b) *Solubility as a function of composition.*

    At constant temperature and pressure, the chemical potential of a saturating solid phase is constant:

$$\mu_{A_nB}^* = \mu_{A_nB}(\text{sln}) = n\mu_A + \mu_B \qquad [49]$$

$$= (n\mu_A^* + \nu_+\mu_+^\infty + \nu_-\mu_-^\infty) + nRT \ln f_A x_A$$

$$+ \nu RT \ln(\gamma_\pm m_\pm Q)$$

for a salt hydrate A_nB which dissociates to water (A), and a salt (B), one mole of which ionizes to give ν_+ cations and ν_- anions in a solution in which other substances (ionized or not) may be present. If the saturated solution is sufficiently dilute, $f_A = x_A = 1$, and the quantity K_B in

$$\Delta G^\infty = (\nu_+\mu_+^\infty + \nu_-\mu_-^\infty + n\mu_A^* - \mu_{AB}^*)$$

$$= -RT \ln K_B$$

$$= -\nu RT \ln(Q\gamma_\pm m_B) \qquad [50]$$

is called the *solubility product* of the salt. (It should be noted that it is not customary to extend this definition to hydrated salts, but there is no reason why they should be excluded.) Values of the solubility product are often given on mole fraction or concentration scales. In dilute solutions, the theoretical behavior of the activity coefficients as a function of ionic strength is often sufficiently well known that reliable extrapolations to infinite dilution can be made, and values of K_B can be determined. In more concentrated solutions, the same problems with activity coefficients that were outlined in the section on variation of solubility with temperature still occur. If these complications do not arise, the solubility of a hydrate salt $C_\nu A_\nu \cdot nH_2O$ in the presence of other solutes is given by eqn [50] as

$$\nu \ln\{m_B/m_B(0)\} = -\nu \ln\{\gamma_\pm/\gamma_\pm(0)\} - n \ln\{a_A/a_A(0)\} \qquad [51]$$

where a_A is the activity of water in the saturated solution, m_B is the molality of the salt in the saturated solution, and (0) indicates absence of other solutes. Similar considerations hold for non-electrolytes.

    Consideration of *complex mixed ligand equilibria* in the solution phase is also frequently of importance in the interpretation of solubility equilibria. For nomenclature connected with these equilibria (and solubility equilibria as well) see (21, 22).

(c) *Alteration of the dissolution medium for pharmaceuticals*

    Many substances which are only slightly soluble in water may be made more soluble by the addition of a cosolvent, surface-active agents, or complexing agents.

      (i) Addition of a cosolvent. It is frequently necessary to dissolve a quantity of drug in a small volume of liquid so that it may be administered parenterally by injection. If the drug is not sufficiently soluble in water because of its hydrophobicity, the addition of a quantity of water-miscible, but less polar solvent may render the drug soluble in a small quantity of the mixed solvent. Solvents used for this purpose have included propylene glycol, glycerol, ethanol, polyethylene glycol and glycofural. Solubilities of many drug substances in water-organic solvent mixtures have been tabulated by Yalkowsky and Roseman (23).

      (ii) Surface-active agents. Another approach to increasing the solubility and rate of dissolution of drug substances is to add a surface-active agent. There is an extensive literature on the application of surfactants and micellar dissolution, which has been summarized recently by Florence (24). Cationic, anionic or neutral surfactants are available. In choosing a surfactant, the possibility of charge-charge interactions between the drug and the surfactant must be considered, as well as the degree of ionization of each species as a function of pH. Micellar dissolution of drugs or additives may protect the dissolved species from hydrolytic degradation by the aqueous solvent. The stability of drugs may therefore be enhanced considerably by the addition of a surfactant. Surfactants may also facilitate the transport of drugs across biological

membranes. Examples of substantially improved bioavailability of drugs
under the influence of micellar dissolution have been reported (24).
       (iii) Other modifications of the dissolution medium. The solubility
of weak acid and weak base drugs will usually depend on the pH of the
medium. Within reasonable limits for pharmaceutical preparations, pH may
be adjusted to obtain the drug in the charged (and usually more soluble)
form. The addition of complexing agents such as chelating agents, organic
salts, cyclodextrins, or ion-pairing agents may be used to enhance
solubility and rate of dissolution. Examples are given in the chapter by
A.J. Repta in (3).

The Solid Phase

   The definition of solubility permits the occurrence of a single solid
phase which may be a pure anhydrous compound, a salt hydrate, a non-
stoichiometric compound, or a solid mixture (or solid solution, or
"mixed crystals"), and may be stable or metastable. As well, any
number of solid phases consistent with the requirements of the phase
rule may be present. Metastable solid phases are of widespread
occurrence, and may appear as polymorphic (or allotropic) forms or
crystal solvates whose rate of transition to more stable forms is very
slow. Surface heterogeneity may also give rise to metastability, either
when one solid precipitates on the surface of another, or if the size of
the solid particles is sufficiently small that surface effects become
important. In either case, the solid is not in stable equilibrium
with the solution. See (25) for the modern formulation of the effect of
particle size on solubility. The stability of a solid may also be
affected by the atmosphere in which the system is equilibrated.

   Many of these phenomena require very careful, and often prolonged,
equilibration for their investigation and elimination. A very general
analytical method, the "wet residues" method of Schreinemakers (26),
is often used to investigate the composition of solid phases in
equilibrium with salt solutions. This method has been reviewed in (27),
where [see also (28)] least-squares methods for evaluating the composition
of the solid phase from wet residue data (or initial composition data)
and solubilities are described. In principle, the same method can be used
with systems of other types. Many other techniques for examination of
solids, in particular X-ray, optical, and thermal analysis methods, are
used in conjunction with chemical analyses (including the wet residues
method).

Solid State Manipulation in Pharmaceuticals

   (i) Polymorphism. Many drug substances may crystallize in more than
one form, a phenomenon called *polymorphism*. The different modifications
(polymorphs) arise because of the relative positions and bonding of the
molecules in their crystal lattices; true polymorphs do not differ in
chemical composition. Polymorphs of the same substance frequently have
different physical properties such as solubility and rate of dissolution.
Ultimately, the solubility of all forms will revert to that of the form
with the lowest Gibbs energy; the solubility of a less-stable form will
thus be an initial solubility. The rate of reversion to the most stable
form is often very slow, and a form with higher Gibbs energy may exhibit
its higher solubility for hours. This phenomenon may be used to advantage
by choosing the polymorph with the desired solubility or rate of
dissolution. Examples of polymorphism and methods of characterization
have been reviewed by Haleblian (29) and Burger (30).
   (ii) Crystallinity. In many cases, drug substances may occur in the
solid state as amorphous or partly crystalline forms. This is a special
case of polymorphism, and may result from rapid precipitation or from
freeze-drying. These amorphous or partly crystalline materials are
unstable relative to the crystalline form. However, reversion to the
crystalline form may be slow, and the less stable forms may be used to
enhance solubility and rate of dissolution (31).
   (iii) Choice of salt form. Many drug substances are organic salts. In
most cases the drug moiety is the organic cation or anion, such as a
quaternary ammonium cation or a carboxylate or sulfonate anion. The
counterion is frequently an inorganic ion such as sodium or chloride. It
is possible to obtain large variations in initial solubility depending on
the choice of the salt form of the drug.

COMPILATIONS AND EVALUATIONS

   The formats for the compilations and critical evaluations have been
standardized for all volumes. A brief description of the data sheets

has been given in the FOREWORD; additional explanation is given below.

Guide to the Compilations

The format used for the compilations is, for the most part, self-explanatory. The details presented below are those which are not found in the FOREWORD or which are not self-evident.

Components. Each component is listed according to IUPAC or Chemical Abstracts (CA) name and CA Registry Number. The formula is given either in terms of the IUPAC or Hill (32) system and the choice of formula is governed by what is usual for most current users: i.e., IUPAC for inorganic compounds, and Hill system for organic compounds. Components are ordered according to:
   (a) saturating components;
   (b) non-saturating components in alphanumerical order;
   (c) solvents in alphanumerical order.
The saturating components are arranged in order according to a 18-column periodic table with two additional rows:
   Columns 1 and 2: H, alkali elements, ammonium, alkaline earth elements
         3 to 12: transition elements
        13 to 17: boron, carbon, nitrogen groups; chalcogenides, halogens
              18: noble gases
          Row 1: Ce to Lu
          Row 2: Th to the end of the known elements, in order of
                 atomic number.

Salt hydrates are generally not considered to be saturating components since most solubilities are expressed in terms of the anhydrous salt. The existence of hydrates or solvates is carefully noted in the text, and CA Registry Numbers are given where available, usually in the critical evaluation. Mineralogical names are also quoted, along with their CA Registry Numbers, again usually in the critical evaluation.

Original Measurements. References are abbreviated in the forms given by *Chemical Abstracts Service Source Index* (CASSI). Names originally in other than Roman alphabets are given as transliterated by *Chemical Abstracts*.

Experimental Values. Data are reported in the units used in the original publication, with the exception that modern *names* for units and quantities are used; e.g., mass per cent for weight per cent; mol dm^{-3} for molar; etc. Both mass and molar values are given. Usually, only one type of value (e.g., mass per cent) is found in the original paper, and the compiler has added the other type of value (e.g., mole per cent) from computer calculations based on 1983 atomic weights (33).

Errors in calculations and fitting equations in original papers have been noted and corrected, by computer calculations where necessary.

Method. Source and Purity of Materials. Abbreviations used in *Chemical Abstracts* are often used here to save space.

Estimated Error. If these data were omitted by the original authors, and if relevant information is available, the compilers have attempted to estimate errors from the internal consistency of data and type of apparatus used. Methods used by the compilers for estimating and and reporting errors are based on the papers by Ku and Eisenhart (34).

Comments and/or Additional Data. Many compilations include this section which provides short comments relevant to the general nature of the work or additional experimental and thermodynamic data which are judged by the compiler to be of value to the reader.

References. See the above description for Original Measurements.

Guide to the Evaluations

The evaluator's task is to check whether the compiled data are correct, to assess the reliability and quality of the data, to estimate errors where necessary, and to recommend "best" values. The evaluation takes the form of a summary in which all the data supplied by the compiler have been critically reviewed. A brief description of the evaluation sheets is given below.

Components. See the description for the Compilations.

Evaluator. Name and date up to which the literature was checked.

Critical Evaluation

(a) Critical text. The evaluator produces text evaluating all the published data for each given system. Thus, in this section the evaluator reviews the merits or shortcomings of the various data. Only published data are considered; even published data can be considered only if the experimental data permit an assessment of reliability.

(b) Fitting equations. If the use of a smoothing equation is justifiable the evaluator may provide an equation representing the solubility as a function of the variables reported on all the compilation sheets.

(c) Graphical summary. In addition to (b) above, graphical summaries are often given.

(d) Recommended values. Data are *recommended* if the results of at least two independent groups are available and they are in good agreement, and if the evaluator has no doubt as to the adequacy and reliability of the applied experimental and computational procedures. Data are considered as *tentative* if only one set of measurements is available, or if the evaluator considers some aspect of the computational or experimental method as mildly undesirable but estimates that it should cause only minor errors. Data are considered as *doubtful* if the evaluator considers some aspect of the computational or experimental method as undesirable but still considers the data to have some value in those instances where the order of magnitude of the solubility is needed. Data determined by an inadequate method or under ill-defined conditions are *rejected*. However references to these data are included in the evaluation together with a comment by the evaluator as to the reason for their rejection.

(e) References. All pertinent references are given here. References to those data which, by virtue of their poor precision, have been rejected and not compiled are also listed in this section.

(f) Units. While the original data may be reported in the units used by the investigators, the final recommended values are reported in S.I. units (1, 35) when the data can be accurately converted.

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September, 1986   R. Cohen-Adad,
                                            Villeurbanne, France

                                         S. Lindenbaum,
                                            Lawrence, Kansas, U.S.A.

                                         J.W. Lorimer,
                                            London, Ontario, Canada

                                         A.N. Paruta,
                                            Kingston, R.I., U.S.A.

                                         R. Piekos,
                                            Gdansk, Poland

                                         M. Salomon,
                                            Fair Haven, New Jersey, U.S.A.

Table I-1

Quantities Used as Measures of Solubility
Conversion Table for 2-Component Systems
Containing Solvent A and Solute B

	mole fraction $x_B =$	mass fraction $w_B =$	molality $m_B =$	concentration $c_B =$
x_B	x_B	$\dfrac{1}{1 - M_A(1 - 1/x_B)/M_B}$	$\dfrac{1}{M_A(1/x_B - 1)}$	$\dfrac{\rho}{M_B + M_A(1/x_B - 1)}$
w_B	$\dfrac{1}{1 + M_B(1/w_B - 1)}$	w_B	$\dfrac{1}{M_B(1/w_B - 1)}$	$\rho w_B/M_B$
m_B	$\dfrac{1}{1 + 1/m_B M_A}$	$\dfrac{1}{1 + 1/M_B m_B}$	m_B	$\dfrac{\rho}{M_B + 1/m_B}$
c_B	$\dfrac{1}{1 + (\rho/c_B - M_B)/M_A}$	$M_B c_B/\rho$	$\dfrac{1}{\rho/c_B - M_B}$	c_B

ρ = density of solution
M_A, M_B = molar masses of solvent, solute
Formulas are given in forms suitable for rapid computation; all
calculations should be made using SI base units.

STRUCTURES

H₂N—⟨⟩—SO₂NH—⟨⟩—SO₂NH₂ [547-52-4] M.W.=327.38	H₂N—⟨⟩—SO₂NH—⟨⟩—SO₂N(CH₃)₂ [515-67-3] M.W.=355.44
HCl·H₂N—⟨⟩—SO₂NH—⟨⟩—SO₂NH₂ [77400-69-2] M.W.=363.84	H₂N—⟨⟩—SO₂NH—⟨pyridine⟩ [144-83-2] M.W.=249.29
SO₂NH₂ H₂N—⟨⟩—SO₂N(Na)—⟨⟩ [77400-68-1] M.W.=349.36	H₂N—⟨⟩—SO₂NH—⟨pyridine⟩ [599-81-5] M.W.=249.29
SO₂NH₂·H₂O H₂N—⟨⟩—SO₂N(Na)—⟨⟩ [81815-35-2] M.W.=367.38	H₂N—⟨⟩—SO₂N(CaOH)—⟨pyridine⟩ [77400-70-5] M.W.=305.37
CH₃CONH—⟨⟩—SO₂NH—⟨⟩—SO₂NH₂ [56444-82-7] M.W.=369.42	·2H₂O H₂N—⟨⟩—SO₂N(CaOH)—⟨pyridine⟩ [77400-71-6] M.W.=341.40
H₂N—⟨⟩—SO₂NH—⟨⟩—SO₂NHCH₃ [547-53-5] M.W.=341.41	H₂N—⟨⟩—SO₂N(Na)—⟨pyridine⟩ [127-57-1] M.W.=271.27
H₂N—⟨⟩—SO₂NH—⟨⟩—SO₂NHCH₃ [71119-14-7] M.W.=383.44	H₂N—⟨⟩—SO₂N(Zn½)—⟨pyridine⟩ [71261-89-7] M.W.=561.94

H$_2$N— —SO$_2$N— (pyridine)
|
Ag

[24342-38-9]   M.W.= 356.16

H$_2$N— —SO$_2$NH— (pyridine)—Cl

[34392-82-0]   M.W.=283.73

CH$_3$CONH— —SO$_2$NH— (pyridine)

[19077-98-6]   M.W.=291.33

H$_2$N— —SO$_2$NH— (pyridine)—Br

[17103-43-4]   M.W.=328.19

H$_2$N— —SO$_2$NH— (pyridine)—Br

[16805-99-5]   M.W.=328.19

H$_2$N— —SO$_2$NH— (pyridine)—OH

[71119-20-5]   M.W.=265.29

H$_2$N— —SO$_2$NH— (pyridine)—I

[71119-21-6]   M.W.=375.19

H$_2$N— —SO$_2$NH— (pyridine)—NH$_2$

[17103-45-6]   M.W.=264.30

H$_2$N— —SO$_2$NH— (pyridine)—NO$_2$

[39588-36-8]   M.W.=294.29

H$_2$N— —SO$_2$NH— (pyridine)—OC$_2$H$_5$

[71720-65-5]   M.W.=293.34

H$_2$N— —SO$_2$NH— (pyridine)—NH$_2$

[16840-28-1]   M.W.=264.30

H$_2$N— —SO$_2$N— (pyridine)
|
CH$_3$

[51543-29-4]   M.W.=263.32

OC$_2$H$_5$
H$_2$N— —SO$_2$NH— (pyridine)

[71119-19-2]   M.W.=293.34

H$_2$N— —SO$_2$N— (pyridine)
|
CH$_3$

[51543-30-7]   M.W.=265.33

H$_2$N— —SO$_2$NH— (pyridine)
|
CH$_2$CH$_2$OH

[71119-27-2]   M.W.=294.35

H$_2$N— —SO$_2$NH— (pyridine)—NHSO$_2$— —NH$_2$

[71119-18-1]   M.W.=419.48

H$_2$N— —SO$_2$NH— (pyridine)
|
COOCH$_3$

[71119-28-3]   M.W.=297.33

H$_2$N— —SO$_2$NH— (pyridazine)

[515-62-8]   M.W.=250.28

H_2N—C$_6$H$_4$—SO_2NH—(pyridazine)—Cl [80-32-0] M.W.=284.72	H_2N—C$_6$H$_4$—SO_2NH—(pyrimidine) [68-35-9] M.W.=250.28
H_2N—C$_6$H$_4$—SO_2NH—(pyridazine)—CH_3 [5433-63-6] M.W.=264.31	H_2N—C$_6$H$_4$—SO_2NH—(pyrimidine) [599-82-6] M.W.=250.28
H_2N—C$_6$H$_4$—SO_2NH—(pyridazine)—OCH_3 [80-35-3] M.W.=280.31	H_2N—C$_6$H$_4$—SO_2NH—(pyrazine) [17103-48-9] M.W.=250.28
H_2N—C$_6$H$_4$—SO_2N(Co$_{1/2}$)—(pyridazine)—OCH_3 · $2H_2O$ [72384-11-3] M.W.=653.57	H_2N—C$_6$H$_4$—SO_2N(Al$_{1/3}$)—(pyrimidine) [71280-76-7] M.W.=774.80
H_2N—C$_6$H$_4$—SO_2N(Mg$_{1/2}$)—(pyridazine)—OCH_3 · nH_2O [84812-83-9] M.W.=UNSPECIFIED	H_2N—C$_6$H$_4$—SO_2N(Ce$_{1/3}$)—(pyrimidine) [66269-03-2] M.W.=887.94
H_2N—C$_6$H$_4$—SO_2N(Mn$_{1/2}$)—(pyridazine)—OCH_3 · nH_2O [84812-82-8] M.W.=UNSPECIFIED	H_2N—C$_6$H$_4$—SO_2N(Cr$_{1/2}$)—(pyrimidine) [71262-84-2] M.W.=550.54
H_2N—C$_6$H$_4$—SO_2N(Ni$_{1/2}$)—(pyridazine)—OCH_3 · nH_2O [84825-01-4] M.W.=UNSPECIFIED	H_2N—C$_6$H$_4$—SO_2N(Cu)—(pyrimidine) [71261-85-3] M.W.=312.82
CH_3CONH—C$_6$H$_4$—SO_2NH—(pyridazine)—OCH_3 [127-75-3] M.W.=322.34	H_2N—C$_6$H$_4$—SO_2N(Cu$_{1/2}$)—(pyrimidine) [12171-53-8] M.W.=562.09
H_2N—C$_6$H$_4$—SO_2NH—(pyridazine)—SCH_3 [7758-81-8] M.W.=296.37	H_2N—C$_6$H$_4$—SO_2N(Co$_{1/2}$)—(pyrimidine) [71280-79-0] M.W.=557.48

H_2N—...—SO_2N—pyrimidine—$Fe_{1/3}$

[71261-86-4]   M.W.=803.66

H_2N—...—SO_2N—pyrimidine-CH_3—$Zn_{1/2}$

[71496-63-4]   M.W.=591.98

H_2N—...—SO_2N—pyrimidine—Ag

[22199-08-2]   M.W.=357.14

CH_3CONH—...—SO_2NH—pyrimidine-CH_3

[127-73-1]   M.W.=306.34

[76634-39-4]   M.W.=493.29

H_2N—...—SO_2NH—pyrimidine-OCH_3

[3213-22-7]   M.W.=280.31

$AgOOCCH_2CH_2CONH$—...—SO_2N—pyrimidine—Ag

[76619-75-5]   M.W.=564.07

H_2N—...—SO_2NH—pyrimidine-OCH_3

[651-06-9]   M.W.=280.31

H_2N—...—SO_2N—pyrimidine—Na

[547-32-0]   M.W.=272.26

H_2N—...—SO_2NH—pyrimidine-OCH_3

[71119-37-4]   M.W.=280.31

H_2N—...—SO_2N—pyrimidine—$Zn_{1/2}$

[66219-86-1]   M.W.=563.92

H_2N—...—SO_2NH—pyrimidine-OCH_3

[1220-83-3]   M.W.=280.31

CH_3CONH—...—SO_2NH—pyrimidine

[127-74-2]   M.W.=292.32

H_2N—...—SO_2NH—pyrimidine-OCH_3 · crown ether

[65177-18-6]   M.W.=544.62

H_2N—...—SO_2NH—pyrimidine-CH_3

[127-79-7]   M.W.=264.31

H_2N—...—SO_2NH—pyrimidine-OC_2H_5

[71138-72-7]   M.W.=294.34

H_2N—〇—SO_2NH—(pyrimidine)—Cl [4482-46-6] M.W.=284.72	H_2N—〇—SO_2N(Cu½)—(pyrimidine, 4,6-di-CH_3) · nH_2O [86729-23-9] M.W.=UNSPECIFIED
H_2N—〇—SO_2NH—(pyrimidine)—Cl [17103-49-0] M.W.=284.72	H_2N—〇—SO_2N(Mn½)—(pyrimidine, 4,6-di-CH_3) · nH_2O [84812-75-9] M.W.-UNSPECIFIED
H_2N—〇—SO_2NH—(pyrimidine)—NH_2 [16806-00-1] M.W.=265.29	H_2N—〇—SO_2N(Ni½)—(pyrimidine, 4,6-di-CH_3) · nH_2O [84812-74-8] M.W.=UNSPECIFIED
H_2N—〇—SO_2NH—(pyrimidine)—NH_2 [71119-38-5] M.W.=265.29	H_2N—〇—SO_2N(Ag)—(pyrimidine, 4,6-di-CH_3) [53081-02-0] M.W.=385.19
H_2N—〇—SO_2NH—(pyrimidine)—$N(C_2H_5)_2$ [71119-24-9] M.W.=321.40	H_2N—〇—SO_2N(Zn½)—(pyrimidine, 4,6-di-CH_3) [71261-83-1] M.W.=620.02
H_2N—〇—SO_2NH—(pyrimidine, 4,5-di-CH_3) [4462-43-5] M.W.=278.33	CH_3CONH—〇—SO_2NH—(pyrimidine, 4,6-di-CH_3) [100-90-3] M.W.=320.37
H_2N—〇—SO_2NH—(pyrimidine, 4,6-di-CH_3) [57-68-1] M.W.=278.33	CH_3CONH—〇—SO_2N($COCH_3$)—(pyrimidine, 4,6-di-CH_3) [59224-69-0] M.W.=362.41
H_2N—〇—SO_2NH—(pyrimidine, 4,6-di-CH_3) · 1/2H_2O [82537-68-6] M.W.=287.34	H_2N—〇—SO_2NH—(pyrimidine, 4-CH_3, 5-$CH_2CH_2CH_2CH_2CH_3$) [71119-35-2] M.W.=334.44
H_2N—〇—SO_2N(Co½)—(pyrimidine, 4,6-di-CH_3) · nH_2O [86729-24-0] M.W.=UNSPECIFIED	H_2N—〇—SO_2NH—(pyrimidine, 4,6-di-OCH_3) [155-91-9] M.W.=310.34

[599-84-8] M.W.=264.31	[84812-79-3] M.W.=UNSPECIFIED
[515-64-0] M.W.=278.33	[2447-57-6] M.W.=310.34
[71261-88-6] M.W.=620.02	[5018-54-2] M.W.=352.38
[3136-31-3] M.W.=320.37	[40016-88-4] M.W.=459.44
[122-11-2] M.W.=310.34	[71119-39-6] M.W.=420.47
[86729-20-6] M.W.=UNSPECIFIED	[6912-98-7] M.W.=282.28
[86729-19-3] M.W.=UNSPECIFIED	[116-44-9] M.W.=250.28
[84812-81-7] M.W.=UNSPECIFIED	[547-31-9] M.W.=272.26
[84812-80-6] M.W.=UNSPECIFIED	[152-47-6] M.W.=280.31

CH₃CONH—⟨benzene⟩—SO₂NH—⟨pyrazine, OCH₃⟩ [655-78-7] M.W.=322.35	H₂N—⟨benzene⟩—SO₂NH—⟨quinazoline, CH(CH₃)₂, CH₃⟩ [71119-36-3] M.W.=360.47
H₂N—⟨benzene⟩—SO₂NH—⟨pyrimidine, NH₂, NH₂⟩ [51249-11-7] M.W.=281.29	H₂N—⟨benzene⟩—SO₂NH—⟨quinoxaline, tetrahydro⟩ [71119-34-1] M.W.=304.37
H₂N—⟨benzene⟩—SO₂NH—⟨quinoline⟩ [59-40-5] M.W.=286.32	H₂N—⟨benzene⟩—SO₂NH—⟨pyrimidine, CH₃, CH₃CH₃⟩ [71720-66-6] M.W.=358.46