

## Construction of solid–liquid phase diagrams in ternary systems by titration calorimetry

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### Abstract

Titration calorimetry was used to construct the solid–liquid equilibrium line in ternary systems containing the solute and an aqueous mixed solvent by measuring the heat of dissolution of the solid solute during successive additions of the liquid solvent. The plot of cumulated heats versus the mole ratio,  $n_{\text{solvent}}/n_{\text{solute}}$ , yields two (almost) linear increases of different slopes. These two lines represent successively the enthalpy of dissolution then the enthalpy of dilution of the medium; their intersection gives the solubility and the enthalpy of dissolution of the solute. Phase diagrams have been established over the whole concentration range for *o*-anisaldehyde, 1,3,5-trimethoxybenzene and vanillin, in water + methanol, +ethanol, or +*n*-propanol at 303, 313 and 318 K.

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### 1. Introduction

The present study develops a method useful for the acquisition of thermodynamic data on phase equilibria in crystallization engineering. Crystallization is of particular interest since it very often constitutes the final step in the purification of solids. Several methods have been used to obtain phase diagrams of a solid solute in a liquid medium acting as crystallization solvent. Such methods were often optical ones in which appearance of a crystal phase (or disappearance), due to temperature or concentration changes was observed. Besides the advantage of observing the type of crystallinity, such methods are rather qualitative. More recently, more precise quantitative techniques have been used to detect the solubility limit through the disappearance of the last crystal. In such dissolution techniques the solution concentration is observed continuously by following the change with temperature of a physical property of the solution, spectroscopic signal, density, vapor pressure, conductivity, etc. (see for exam-

ple the automatic method based on conductivity measurements by Berthet and Counieux [1]). However, since rigorous control of temperature is essential in solubility phenomena, isothermal experimental techniques should be favoured. The construction of a phase diagram containing a solid solute and a liquid solvent is simply based on the determination of the solubility of the solid solute in the solvent. The solvent can be a pure liquid component or a liquid mixture for efficient solvent–antisolvent selective capability. In such ternary systems the crystallization of the solute can be obtained by adding the antisolvent to a concentrated solution of the solute in the other (“good”) solvent. Thus, the choice of solvents in crystallization processes rests on the knowledge of the solid phase contour of the precipitate in the presence of the solvent–antisolvent mixture. When the solute is organic, the solvent is generally a binary mixture of water + a hydrophilic organic component. The aqueous mixed solvent behaves as a homogeneous phase over its entire mole fraction range. Determination of the maximum solubility of the solid solute at points along the solid–liquid line of the ternary system provides data from which the locus of the maximum solubility is readily obtained.

The solubility limit was determined by slowly adding (to remain at thermodynamic equilibrium) successive small incre-

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ments of the binary solvent to a known amount of the solid solute until solubilisation of the solid crystals was complete. Titration calorimetry was used to detect the dissolution of the solid in the binary solvent through the heat effect during each addition. Titration calorimetry has been traditionally used for titration or acid–base reactions [3]. Isothermal titration calorimetry, ITC, is also currently used to study complex formation and numerous examples of such investigations can be found in recent publications where different calorimeters have been used [4–6]. However, titration calorimetry has been very rarely used to measure solubilisation or dissolution of solid compounds.

In this work the “target” molecule was vanillin; it represents a class of important molecules where the three functional groups, hydroxyl, aldehyde, methoxy, are present on an aromatic ring. Vanillin is a product of technological importance produced industrially in large amounts. The ultimate step in the production line is crystallisation in an appropriate solvent in order to obtain an end-product of pure small crystals. Water–alcohol binary mixtures are the most suitable solvents in terms of cost and recycling. Phase diagrams have been established over the whole concentration range for *o*-anisaldehyde, 1,3,5-trimethoxybenzene and vanillin in water + methanol, +ethanol, or +*n*-propanol. The effect of temperature was examined through measurements in the temperature range of 303–318 K.

## 2. Experimental

### 2.1. Chemicals

4-Hydroxy-3-methoxybenzaldehyde (vanillin) with 99 mol% purity, *o*-anisaldehyde with 98 mol% purity and 1,3,5-trimethoxybenzene with 99 mol% purity were provided by (Fine Chemicals) Acros Organics, France; methyl alcohol with purity >99.8 mol% was provided by Fluka Chemika, France; ethyl alcohol absolute RE was provided by Carlo Erba, France; *n*-propanol p.a. with purity >99.5 mol% was provided by (Fine Chemicals) Acros Organics, France. All chemicals were used without further purification. Solutions were prepared by weight with freshly bidistilled water.

### 2.2. Instrumentation

The titration calorimeter, Titrys by Setaram, was used to perform the measurements. The calorimetric block temperature is regulated to  $\pm 20$  mK; it houses two thermopiles in which are placed the measuring and reference cells. The detection limit is  $0.1 \mu\text{W}$ . The instrument can be operated in the temperature range from 303.15 to 318.15 K. Each cell has an active volume from 1 to  $12 \text{ cm}^3$  and the contents of each cell can be stirred by a small magnetic bar activated by a single motor which ensures the same (adjustable) stirring speed in both cells. The injection system is a Dual Syringe Pump Model 33 from Harvard Instruments, that delivers identical volumes through stainless capillaries at the same rate in both cells. To ensure control of the volumes delivered by the pumps, the whole assembly was placed in a small air bath thermostatted to  $\pm 50$  mK. Before injection into

the calorimetric cells, liquids coming from the pumps are further thermostatted as the capillary tubes are coiled in two small thermostats placed inside the calorimetric block on top of each cell.

### 2.3. Experimental procedure

An initial mass, 0.05–2.50 g depending on the type of solid, of finely hand-ground (in a mortar) crystallized powder, is placed in the measuring cell. The two syringe pumps are filled with the same water–alcohol solution of known composition. A dissolution run consists in adding the same volume of the solution simultaneously in both cells. The heat repeatedly evolved during each addition is due to the heat of dissolution of part of the solid in the added solution. Typically, each injection consists in adding  $0.20 \text{ cm}^3$  of solution at the rate of  $0.10 \text{ cm}^3 \text{ min}^{-1}$  and a complete run is achieved after an average of 10 successive additions. The volume for an injection may vary from 0.04 to  $2.00 \text{ cm}^3$  at a rate between 0.02 and  $0.70 \text{ cm}^3 \text{ min}^{-1}$ . Each run yields a series of peaks of heat rate versus time. The cumulative sums  $\Delta H$  of peak areas divided by  $n_1$  ( $n_1 = n_{\text{solute}}$ , initial number of moles of solute), are plotted versus  $\alpha = n_{\text{solvent}}/n_{\text{solute}}$  which represents the ratio of the number of moles of solvent to the number of moles of solute. Each run yields the type of plot shown in Fig. 1. Typically each plot is composed of two parts. First an approximately linear increase of  $\Delta H/n_{\text{solute}}$  represented by

$$\Delta H/n_1 = A_1\alpha \quad (1)$$

When all the solid has dissolved, the second part, which is simply related to the heat of dilution of the medium, is generally well

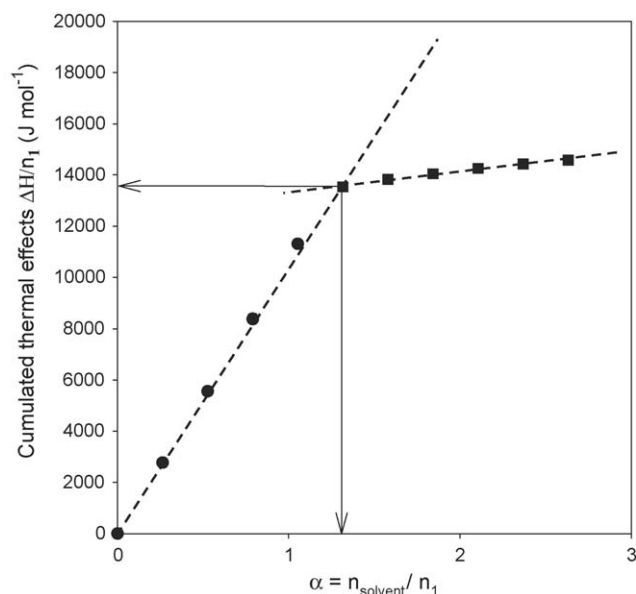


Fig. 1. Plot of cumulated thermal effects,  $\Delta H/n_1$  (in  $\text{J mol}^{-1}$ ), vs.  $\alpha = n_{\text{solvent}}/n_1$ , obtained during a run, showing the initial dissolution (●) of the solid solute followed by the dilution (■) of the solution. The intersection gives the enthalpy of dissolution and the ratio  $\alpha_S$  at saturation;  $n_1$  is the initial number of moles of solute  $n_{\text{solute}}$  placed in the measuring cell.

represented by a quadratic polynomial:

$$\Delta H/n_1 = A'_0 + A'_1\alpha + A'_2\alpha^2 \quad (2)$$

The coefficients  $A_1$ ,  $A'_0$ ,  $A'_1$ ,  $A'_2$  were determined by linear regression. The intersection of Eqs. (1) and (2) gives the enthalpy of dissolution for a given ratio  $\alpha_S$  at saturation:

$$A_1\alpha_S = A'_0 + A'_1 + \alpha_S + A'_2\alpha_S^2 \quad (3)$$

From  $\alpha_S$  the composition of the ternary system at saturation can be determined as follows, where  $n_i$  and  $x_i$  are the numbers of moles and the corresponding mole fractions of components 1 (solute), 2 (water) and 3 (alcohol), respectively, in the solution:

$$\alpha_S = n_{\text{solvent}}/n_1 = (n_2 + n_3)/n_1 = (x_2 + x_3)/x_1 \quad (4)$$

Since  $x_1 + x_2 + x_3 = 1$

$$\alpha_S = (1 - x_1)/x_1 \quad (5)$$

and

$$x_1 = 1/(\alpha_S + 1) \quad (6a)$$

$$x_2 = x_{2,S}(1 - x_1) \quad (6b)$$

$$x_3 = x_{3,S}(1 - x_1) \quad (6c)$$

where  $x_{2,S}$  and  $x_{3,S}$  are respectively the mole fractions of components 2 and 3 in the water + alcohol binary mixture.

It is worth noting that one can also obtain the enthalpy of solution at saturation (e.g. the heat of dissolution in the mixed solvent) from Eq. (1) with  $\alpha = \alpha_S$ .

The dissolution runs are made so as to cover the whole concentration of the binary aqueous mixture. Then a ternary plot ( $x_1$ ,  $x_2$ ,  $x_3$ ) can be constructed where the three mole fractions are the actual experimental mole fractions corresponding to the individual coordinates of the different intersections.

### 3. Results and data treatment

The experimental mole fractions  $x_1$ ,  $x_2$  and  $x_3$  are listed in Table 1 in the supplementary data file. Graphical representations are shown in Figs. 2–5. In these figures the smoothed curves were obtained by the following procedure. The original raw data are the amount (in weight  $w_1$ ) of solute 1, the volume of the aqueous mixed solvent (water + alcohol) in which the amount  $w_2$  of water is known as well as the amount  $w_3$  of alcohol. Densities of water–alcohol mixtures were taken from [2] to evaluate the respective quantities of water and alcohol in the injected volumes of solvent. From the different weights  $w_i$  the corresponding mole fractions were calculated. To represent the solid–liquid equilibrium lines for the different systems, firstly, a plot of  $x_1$  versus  $x_2$  was fitted by least squares with polynomial  $y$  which actually represents the mole fraction  $x_1$  as a function of  $x_2$ :

$$y = x_1 = f(x_2) = \sum_{i=0}^n a_i(1 - x_2)^i \quad (7)$$

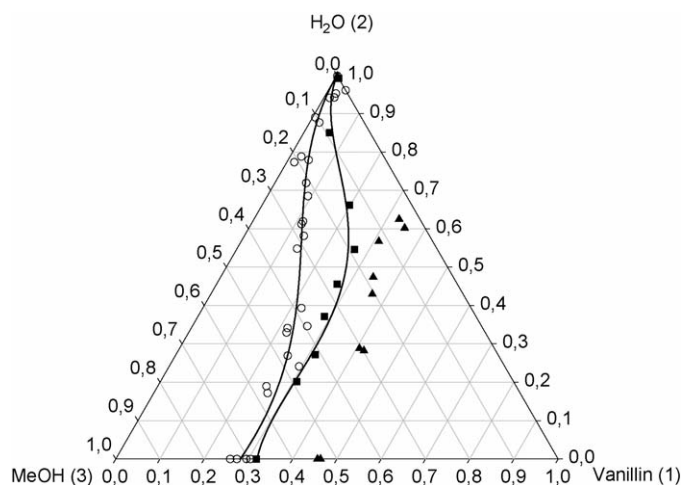


Fig. 2. Ternary plot for the system vanillin (1)+H<sub>2</sub>O (2)+methanol (3) at 303.15 K, ○, this work; ternary plot for the system vanillin (1)+H<sub>2</sub>O (2)+methanol (3) at 313.15 K, ■, this work; ▲, data at 318.15 K [7].

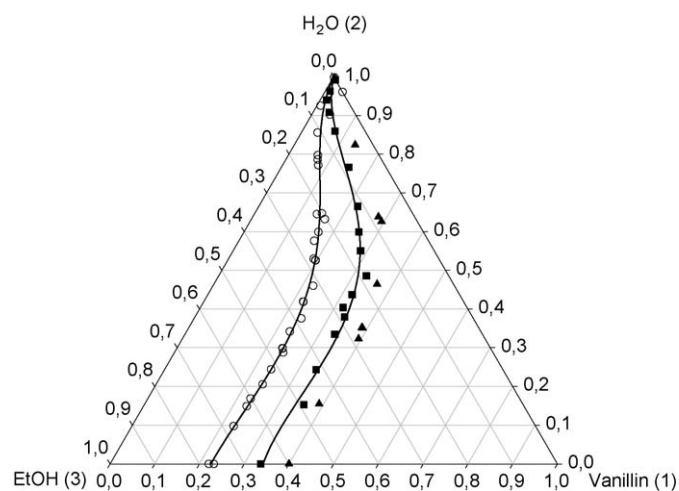


Fig. 3. Ternary plot for the system vanillin (1)+H<sub>2</sub>O (2)+ethanol (3) at 303.15 K, ○, this work; ternary plot for the system vanillin (1)+H<sub>2</sub>O (2)+ethanol (3) at 313.15 K, ■, this work; ▲, data at 318.15 K [7].

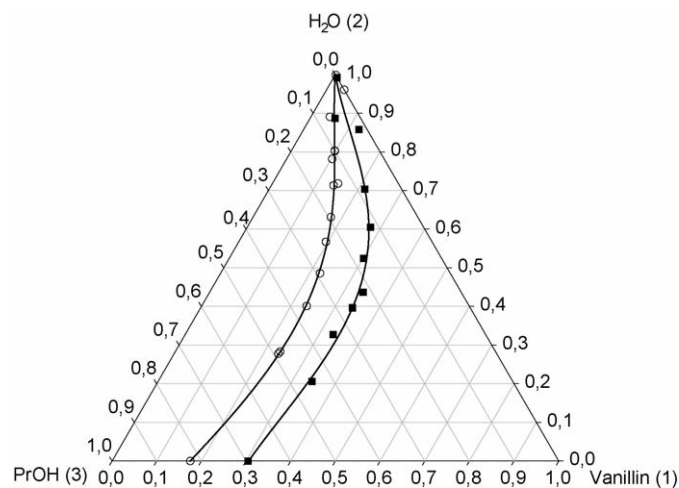


Fig. 4. Ternary plot for the system vanillin (1)+H<sub>2</sub>O (2)+propanol (3) at 303.15 K, ○, this work; ternary plot for the system vanillin (1)+H<sub>2</sub>O (2)+propanol (3) at 313.15 K, ■, this work.

Table 1

Coefficients of the fitting Eq. (7) and corresponding standard deviations  $\sigma$  used to represent the smoothed curves in Figs. 2–5

Systems	$a_0$	$a_1$	$a_2$	$a_3$	$a_4$	$\sigma$
Vanillin + H <sub>2</sub> O + MeOH 303.15 K	–	0.0060	1.1346	–1.0615	0.2023	0.0189
Vanillin + H <sub>2</sub> O + MeOH 313.15 K	–	0.1654	2.3974	–4.3348	2.0916	0.0119
Vanillin + H <sub>2</sub> O + EtOH 303.15 K	–	0.1037	1.7322	–2.8849	1.2743	0.0087
Vanillin + H <sub>2</sub> O + EtOH 313.15 K	–	0.3027	2.1692	–4.0721	1.9423	0.0102
Vanillin + H <sub>2</sub> O + PrOH 303.15 K	–	0.4354	0.5372	–1.3635	0.5659	0.0080
Vanillin + H <sub>2</sub> O + PrOH 313.15 K	–	0.6449	0.8499	–2.3078	1.1189	0.0145
<i>o</i> -Anisaldehyde + H <sub>2</sub> O + EtOH 303.15 K	0.0292	0.4758	0.4811	0.7530	–0.9381	0.0097
Trimeth + H <sub>2</sub> O + EtOH 303.15 K	$a_1$ : 1.5758	$a_2$ : –8.8622	$a_3$ : 19.429	$a_4$ : –18.480	$a_5$ : 6.4261	0.0139

Secondly, polynomial  $y$  was used to generate a table of numerical values  $X_3$  as a function of  $X_2$ ,  $X_3 = f(X_2)$ , at rounded values of  $X_2$  (e.g.  $0 \leq X_2 \leq 1$  at 0.02 increments) using the relation:

$$X_3 = 1 - x_1 - X_2 \quad (8)$$

where  $x_1 = y = f(X_2)$ , as given by Eq. (7), and  $x_1 + X_2 + X_3 = 1$ ;  $X_2$  and  $X_3$  are calculated values, at rounded values  $X_2$ , of mole fractions of components 2 and 3 corresponding to the experimental mole fraction  $x_1$  of solute 1.

This “normalization” step allows drawing the smoothed curves in Figs. 2–5. Eq. (7) is the actual fitting equation of the experimental data points. The best fit has been obtained by least squares which gives the solubility maximum of the solid in the

Table 2

Mole fractions of the three components in each ternary system corresponding to the maximum of solubility of the solid solute in the optimal composition of the binary aqueous mixture

Systems	$x_1$ (maximum)	$X_2$ (H <sub>2</sub> O)	$X_3$ (ROH)
Vanillin + H <sub>2</sub> O + MeOH 303.15 K	0.2852	0.0600	0.6548
Vanillin + H <sub>2</sub> O + MeOH 313.15 K	0.3196	0.0000	0.6804
Vanillin + H <sub>2</sub> O + EtOH 303.15 K	0.2383	0.2600	0.5017
Vanillin + H <sub>2</sub> O + EtOH 313.15 K	0.3446	0.2800	0.3754
Vanillin + H <sub>2</sub> O + PrOH 303.15 K	0.2375	0.3200	0.4425
Vanillin + H <sub>2</sub> O + PrOH 313.15 K	0.3451	0.3200	0.3349
<i>o</i> -Anisaldehyde + H <sub>2</sub> O + EtOH 303.15 K	0.8012	0.0100	0.1888
1,3,5-Trimeth + H <sub>2</sub> O + EtOH 303.15 K	0.0935	0.8600	0.0465

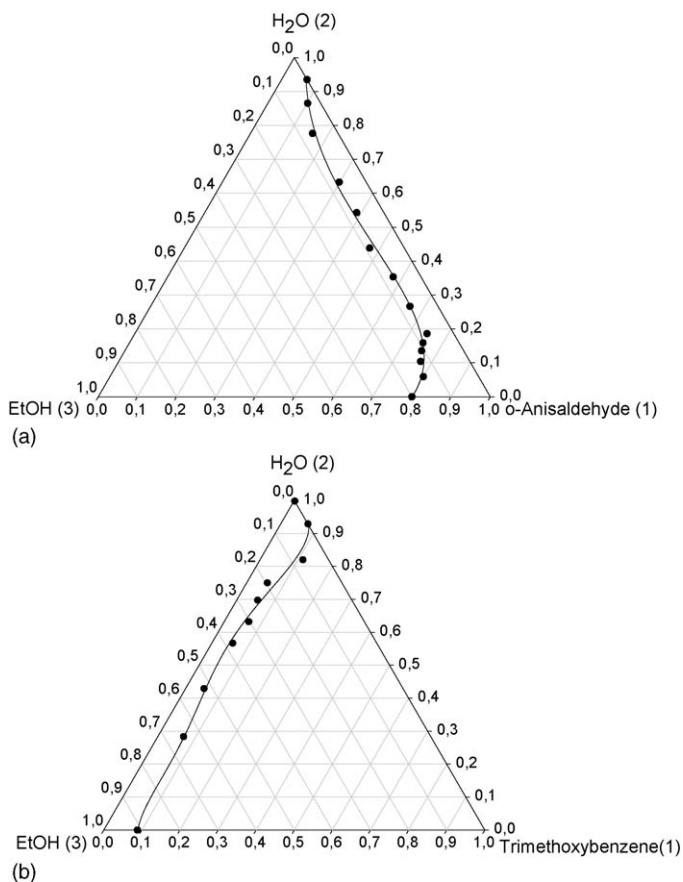


Fig. 5. (a) Ternary plot for the system *o*-anisaldehyde (1) + H<sub>2</sub>O (2) + ethanol (3) at 303.15 K, ●, this work; (b) ternary plot for the system 1,3,5-trimethoxybenzene (1) + H<sub>2</sub>O (2) + ethanol (3) at 313.15 K, ●, this work.

optimal composition of the aqueous mixture. The coefficients  $\alpha_i$  and corresponding standard deviations  $\sigma$  are listed in Table 1.

#### 4. Discussion

General conclusions can be drawn from the ternary phase diagrams (Figs. 2–5) and the data at saturation given in Table 2. At 303.15 K vanillin is more easily solubilized in methanol than in ethanol and propanol. Temperature has a distinct influence on the solubility. At 313.15 K the increase of solubility is about 30%. At 318.15 K in presence of methanol and ethanol, Laurent [7], see Figs. 2 and 3, has shown that solubility is substantially increased and less alcohol is necessary.

The chemical structure of the solute influences its solubility. As shown in Fig. 5a and b and in Table 2, at a given temperature (303.15 K) and in water–ethanol binary solvent *o*-anisaldehyde is much more soluble than 1,3,5-trimethoxybenzene.

In conclusion, titration calorimetry can be recommended as a convenient technique to obtain precise concentrations of the components along the solid–liquid line. The fitting equations developed to represent this line can be used for engineering calculations.

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**Appendix A. Supplementary data**

Supplementary data associated with this article can be found, in the online version, at [doi:10.1016/j.tca.2006.02.017](https://doi.org/10.1016/j.tca.2006.02.017).

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