Experimental Methods for Phase Equilibria at High Pressures

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Abstract

Knowledge of high-pressure phase equilibria is crucial in many fields, e.g., for the design and optimization of high-pressure chemical and separation processes, carbon capture and storage, hydrate formation, applications of ionic liquids, and geological processes. This review presents the variety of methods to measure phase equilibria at high pressures and, following a classification, discusses the measurement principles, advantages, challenges, and error sources. Examples of application areas are given. A detailed knowledge and understanding of the different methods is fundamental not only for choosing the most suitable method for a certain task but also for the evaluation of experimental data. The discrepancy between the (sometimes low) true accuracy of published experimental data and the (high) accuracy claimed by authors is addressed. Some essential requirements for the generation of valuable experimental results are summarized.

INTRODUCTION

Many technical and natural processes occur at high pressures, and knowledge of the phase behavior is essential to understanding them. Pressure is one of the state variables that determine thermodynamic equilibrium and thereby strongly influences the composition of the coexisting phases. A pressure increase may induce a phase transition, e.g., from vapor to liquid or from liquid to solid. High pressure favors phases of lower volume. At high pressures substantial quantities of a gas can be dissolved in a liquid, thereby changing its properties toward a gas-expanded liquid with different solvent power. Pressure increases the ability of gases to dissolve high-boiling substances; high-density supercritical fluids have a solvent power similar to that of a light hydrocarbon for most solutes. Knowledge of pressure effects on phase equilibria is crucial for the design and optimization of high-pressure chemical and separation processes such as high-pressure reactions, gas processing, supercritical fluid applications, and polymer processing. Other examples of areas that need high-pressure phase equilibrium data include petroleum reservoir simulation, enhanced oil recovery, carbon capture and storage, transportation and storage of natural gas, hydrate formation, refrigeration and heat-pump cycles, applications of ionic liquids, and the study of geological processes. Established (1, 2) and new (3) applications of supercritical fluids include extraction; particle formation; impregnation (wood preservation, polymers, catalysts, textiles); leather, paper, and textile treatment; dyeing; cleaning; reaction in supercritical fluids (4), at near-critical conditions (5), or in gas-expanded liquids (6); chromatography; drying of aerogels; injection molding and extrusion; electronic chip manufacturing; and design of drug delivery systems (7).

Today, process design is based on process simulations that require precise thermophysical property data. Particularly for difficult separations, small uncertainties in phase equilibrium data can have a huge impact on the design of separation equipment, e.g., an underestimation by only 2% of the correct value of the separation factor $\alpha = 1.1$ leads to a calculated distillation column height that is more than 27% too high (8). Accurate phase equilibrium data are important for reactor design as well. For example, debottlenecking of a high-pressure reaction to produce an aromatic compound in the presence of a by-product (water) requires reduction of the amount of solvent (isopropanol) while avoiding a phase split into an aqueous and an organic liquid phase. Correct experimental determination of the liquid-liquid phase boundary leads to a significant reactor capacity increase that could be implemented immediately without any additional investment (e.g., 10 wt% less solvent leads to a 20% higher capacity; initial solvent ratio 1:1).

Even though computational methods for the prediction of phase equilibria have made considerable progress in the past decades, the experimental determination of phase equilibrium remains an indispensable source of data. Deviations from ideality are stronger at high pressures than at ambient or low-pressure conditions, and the phase behavior is often more complex and difficult to predict with thermodynamic models. For model development and model application, experimental high-pressure phase equilibrium data are valuable both for the theoretician, as a severe test of theoretical concepts (e.g., equations of state, pair potentials, mixing rules) (9), as well as for the chemical engineer, as an input for process design, because many models such as equations of state need at least some experimental data points in order to adjust the interaction parameters of the model.

Experimental investigation of the high-pressure phase behavior of fluids has a long history. In 1822, Charles Cagniard de la Tour (10) discovered the critical point of a substance by using a synthetic-nonvisual method. He studied the behavior of a liquid when heated in a closed vessel by listening to the sound of a ball rolling inside a sealed gun barrel, which no longer exhibited a discontinuity when the temperature in the barrel reached the critical temperature. In the Bakerian

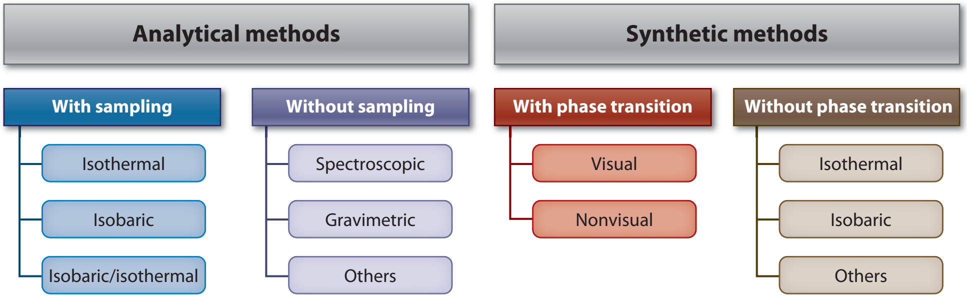

Figure 1

Classification of experimental methods for phase equilibria at high pressures. Reprinted with modification from Dohrn et al. (16), copyright © 2010, with permission from Elsevier.

lecture of 1869, Thomas Andrews (11) reported the first quantitative determination of the critical point of a substance. By using a synthetic-visual method he discovered that above 31°C, carbon dioxide (CO_2) cannot be liquefied under pressurization. Inspired by findings about the continuity of the gaseous and the liquid states of matter, many researchers, such as Kuenen (12), Kamerlingh Onnes (13), and Roozeboom (14), carried out extensive experimental investigations of fluid phase behavior. P.W. Bridgeman pioneered experimental work at very high pressures in the first half of the twentieth century. Increasing performance and commercial availability of high-pressure equipment paired with rising interest in applications of supercritical fluids and ionic liquids at high pressures as well as interest in hydrate formation, polymer foaming processes, and new solvents for CO_2 capture, have led to a steady increase in publications on high-pressure phase equilibria during the past 30 years (15).

A wide variety of methods and techniques is currently available for experimental studies of phase equilibria at high pressures (9, 15–24). Which method is suitable in each individual case depends on both the properties of the components and the phenomena to be investigated. Because each method has advantages and disadvantages as well as specific error sources, a detailed knowledge and understanding of the different methods is necessary for the validation of experimental data (25). A classification focused on characteristic error sources has been developed (15–18); it consists of two main classes that depend on whether the compositions of the equilibrium phases are determined (analytically) or the mixture has been prepared (synthesized) with precisely known composition. These are known as analytical methods and synthetic methods (**Figure 1**). The characteristic error sources of all analytical methods are related to the precise determination (analysis) of the compositions of the coexisting phases, either by sampling or by composition determination under equilibrium pressure. The main challenges of all synthetic methods are the precise preparation of the investigated mixture, detection of a phase transition, and determination of additional properties needed for the evaluation of the raw data. In this classification we avoid expressions such as static or dynamic that have no clear reference to characteristic error sources. For example, a static method can be an analytical-isothermal method with sampling, a synthetic method with visual or nonvisual phase detection, or even a synthetic-isothermal method without phase change that is based on a mass balance, e.g., to calculate gas solubilities. These methods are based on different principles and have different requirements in terms of experimental procedure and error minimization.

In this review we present experimental methods for the study of phase equilibria at high pressures, and—following the classification outlined above—we examine the measurement principles and give examples of areas of application. For each method, we describe advantages

Analytical method: phase equilibria are determined by analysis of the equilibrium phases

Synthetic method: mixtures are prepared precisely (synthesized), and phase equilibria are determined without analysis of the phases and disadvantages, the most common sources of errors that can affect the quality of the results, and techniques to circumvent problems.

ANALYTICAL METHODS

Analytical methods to determine high-pressure phase equilibria involve the determination of the compositions of the coexisting phases. This can be done by taking samples from each phase and then analyzing them outside the equilibrium cell at ambient pressure (analytical methods with sampling) or by using physicochemical analysis methods with the substances under pressure inside the equilibrium cell (analytical methods without sampling). When the compositions of all phases in equilibrium are analyzed, analytical methods yield complete information on the tie line(s). These methods can be used for systems with more than two components without significant complications, and they are applicable where synthetic methods are disadvantageous, i.e., when phase boundaries depend strongly on composition. The main challenge of analytical methods is the accurate analysis of the compositions of the coexisting phases. **Figure 2** compiles the advantages and challenges of analytical methods and contains information on the frequency of use. Although during the 1980s and 1990s the number of systems measured with analytical and with synthetic methods were almost equally high (17, 18), the relative use of analytical methods has declined over the past decade (15, 16).

Analytical-Isothermal Methods

When isothermal methods are used, equilibration is attained at a constant temperature, whereas the other equilibrium properties such as pressure and phase composition adjust themselves depending on the temperature, the total composition, and the volume of the equilibrium cell. **Figure 3** shows the three fundamental steps of analytical-isothermal methods: (*a*) preparation of the mixture, (*b*) equilibration, and (*c*) sampling and analysis of the phase compositions. The third step is the most critical. Sampling from a closed high-pressure vessel leads to a pressure drop and to a change in the total composition. As a consequence, a new equilibration is initiated that results in changed compositions of the equilibrated phases as well as a changed level of the phase boundaries in the cell. Both must be carefully considered if more than one sample is taken. A case study (26) showed that the pressure drop owing to sampling is smaller than the relative sample volume because the system reacts by evaporating part of the liquid phase until a new equilibrium pressure has been reached. This effect is stronger when a large quantity of gaseous components such as CO_2 is dissolved in the liquid phase, which means that less significant pressure drops occur at high pressures than at low pressures. Furthermore, higher liquid levels in the equilibrium cell lead to lower pressure drops because a larger reservoir of dissolved gaseous components is available in the cell. There are several technical options to avoid negative feedback of sampling on the state in the equilibrium cell (26). Using a large equilibrium cell or taking small samples through capillaries (27, 28) or special valves (29–32) reduces the pressure drop. Alternatively, the pressure in the equilibrium cell can be kept constant during sampling by reducing the cell volume using a piston (33–35) or a bellows (25), by blocking off the content of the cell from the sample before withdrawing it (36–39), or by adding one or more components to the equilibrium cell during sampling (40–42).

Figure 2

Analytical methods for high-pressure phase equilibria: advantages, challenges and frequency of use in the periods 2000–2004 (15) and 2005–2008 (16). Arrows indicate a significant change in the frequency of use.

Analytical methods		Use			Advantages	Challenges
		2000–4	2005–8			
Analytical methods Total composition not exactly known, analysis of phases		**45.6%**	**37.0%**	↘	Information on tie lines; multicomponent systems; strongly composition-dependent phase boundaries	Effort of analyzing phase compositions
Analytical methods with sampling					**Sampling and analysis are separated; analysis at ambient pressure**	**Labor intensive; problems at similar phase densities, e.g., critical region**
AnT	Analytical isothermal method	**27.6%**	**19.7%**	↘	Time for equilibration can be extended	Compensation for pressure drop due to sampling is needed
Stir	Equilibration promoted with stirrer				Effective mixing; fast equilibration	Temperature inhomogeneities; dead corners
Rock	Equilibration promoted by rocking				Simple mixing; good for hydrates	Connecting tubes must be movable; vibrations
Vcir	Vapor-phase recirculation				Sampling volume can be filled isobarically; density measurement in recirculation loop	Additional pumps; partial condensation of recirculated (saturated) phases
Lcir	Liquid-phase recirculation					
Cap	Sampling through capillaries				Place of sampling within cell can be chosen	Partial condensation due to pressure loss in capillary
Val	Sampling using a special valve				Small samples possible; direct coupling to analysis	Less flexible concerning analytical methods
Blo	Blocking off a large sampling volume				Large samples possible	Reequilibration for each sample
Ins	In situ sampling				No valves needed	Complicated handling; careful expansion is crucial
Mla	Material loss analysis				Solubilities in very low-volatile substances, e.g., polymers	Extrapolation of raw data; multicomponent systems
AnP	Analytical isobaric method	**0.0%**	**0.0%**	—	Recirculation without pumps; ebulliometer-like heat pipe	Limited to lower pressures; very rarely used
AnPT	Analytical isobaric-isothermal method	**15.4%**	**11.2%**	↘	Large samples can be accumulated without disturbing the equilibrium	Sampling remains complicated; good flow control is essential
Con	Continuous-flow method				Short residence time in apparatus; thermolabile substances	Short equilibration time; large amount of chemicals needed
Sem	Semiflow method				Solubilities of solids in gases (SemY) or gases in liquids (SemX)	Difficult for multicomponent systems (composition change)
Chro	Chromatographic method				Diffusivities and infinite dilution partition coefficients, e.g., fluid and ionic liquid or polymer	Limited applicability; interactions with substrate of stationary phase possible
Analytical methods without sampling					**Prevention of errors associated with sampling procedure**	**Analytical method under high pressure is required; calibration at high pressure**
AnSpec	Analytical spectroscopic method	**1.5%**	**1.1%**	—	Fast analysis; suitable for reacting systems	Time-consuming calibration and signal evaluation of spectra
AnGrav	Analytical gravimetric method	**1.1%**	**5.0%**	↗	Low solubilities and diffusivities of volatiles in polymers or ionic liquids	Buoyancy due to swelling of sample; expensive equipment
AnOth	Other analytical method	**1.1%**	**0.6%**	—	For special applications	Few opportunities to share experience with other groups

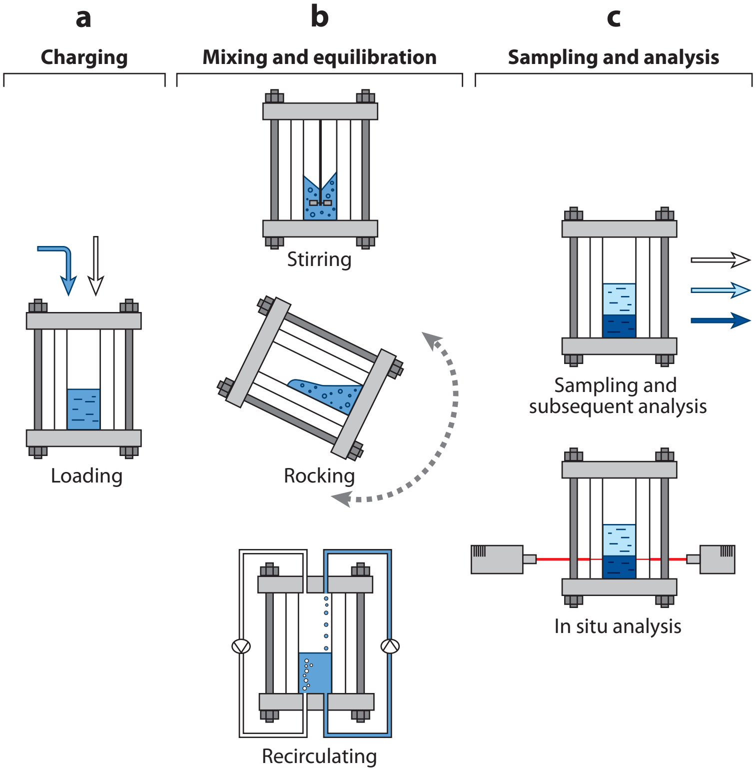

Figure 3

Fundamental steps of the analytical-isothermal method. (*a*) An equilibrium cell is charged with the substances of interest. The pressure is adjusted above or below the desired equilibrium value, depending on how equilibration will change the pressure. (*b*) At the desired temperature, equilibration of the phases is promoted by stirring the mixture, rocking the autoclave, or recirculating one or more phases. After some time, the pressure reaches a plateau. The pressure can be readjusted by adding or withdrawing material or by changing the volume of the equilibrium cell. Usually, the equilibration is continued for at least 30 min after the pressure plateau is sufficiently close to the desired value. (*c*) After a good separation of the phases (at least 30 min after the mixing has stopped), a sample is withdrawn, followed by depressurization and further sample preparation steps for analysis, or the phase compositions are determined without sampling.

When special valves are used, such as high-pressure liquid chromatography (HPLC) multiport valves or systems such as the rapid on-line sample injector (ROLSI^{TM}) valves (43), the equilibrium cell can be directly coupled to analytical equipment, usually using chromatographic methods such as HPLC (44), supercritical-fluid chromatography (SFC) (29), or gas chromatography (GC) (31, 32, 45). This direct coupling can prevent contact of the sample with potentially reactive substances or gases in the atmosphere. Furthermore, the extremely low dead volumes, low sample volumes, and immediate flushing with a (preheated) inert fluid counteract the incomplete removal of the sample from the valve.

SFC: supercritical-fluid chromatography

Sampling through capillaries can cause differential vaporization, which, especially for mixtures composed of both light and heavy components, leads to a scattering of the results caused by a pressure drop along the length of the capillary (28). This problem can be circumvented by an adequate experimental design that ensures that most of the pressure drop occurs at the end of the capillary, close to the subsequent sample-preparation or analysis step. Isobaric sampling

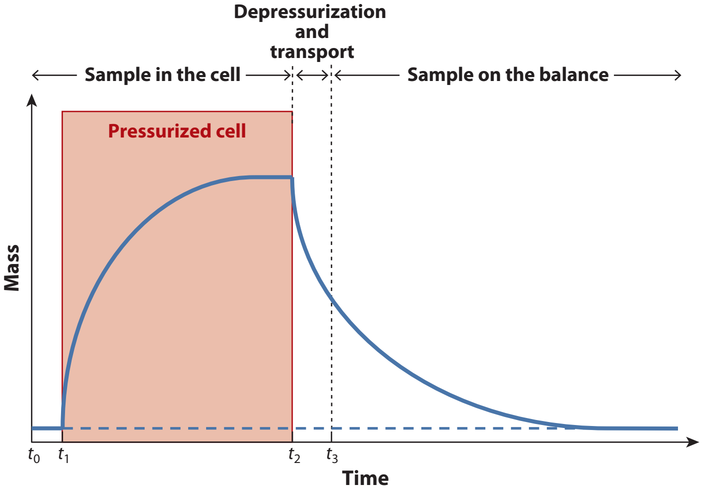

Figure 4

Analytical-isothermal method with sampling after depressurization, known as material-loss analysis. After the equilibrium cell has been pressurized at time t_1, the mass of the polymer sample increases with the dissolution of the volatile component up to an equilibrium value. Equilibration is followed by a fast depressurization procedure at t_2 and quick transport of the sample to an analytical balance. The mass decrease of the polymer sample owing to desorption of the volatile component is recorded from t_3 onward. The initial sorbate mass can be determined by extrapolation of the desorption curve to the initial depressurization time t_2.

from a recirculation line (39) can prevent errors related to the pressure drop during sampling, such as differential vaporization. Sampling can also occur after complete depressurization of the equilibrium cell such as when in situ sampling methods (46, 47) or material-loss analysis methods (48, 49) are applied. In situ sampling methods are often used to determine the solubility of solids in supercritical fluids. Material-loss analysis can be used to determine the solubility and diffusivity of volatile components (often CO_2) in polymers, as depicted schematically in **Figure 4**.

Analytical-Isobaric-Isothermal Methods

In analytical-isobaric-isothermal methods one or more fluid streams are continuously pumped into a thermostatic equilibrium cell. The pressure is kept constant during the experiment by controlling an effluent stream, most commonly the vapor-phase stream, with a backpressure regulator. Isothermal-isobaric methods can be divided into continuous-flow methods, semiflow methods, and chromatographic methods.

In a typical continuous-flow method design, shown schematically in **Figure 5*a***, high-pressure metering pumps are used to supply a constant flow of the components, which after a preheating stage enter a mixer kept at the desired temperature in which phase equilibrium is attained. Often, static mixers are used (50). The stream from the mixer is then separated in an equilibrium cell into a vapor and a liquid phase. To facilitate phase separation, a cyclone separator can be used (50). Effluents from both phases are continually withdrawn, depressurized, and accumulated; they are usually analyzed after the experiment. The interface level between the fluid phases in the equilibrium cell can be adjusted with a bottom-phase expansion valve; typically the interface level is determined visually (51). For example, Hurst et al. (52) describe a sophisticated continuous-flow

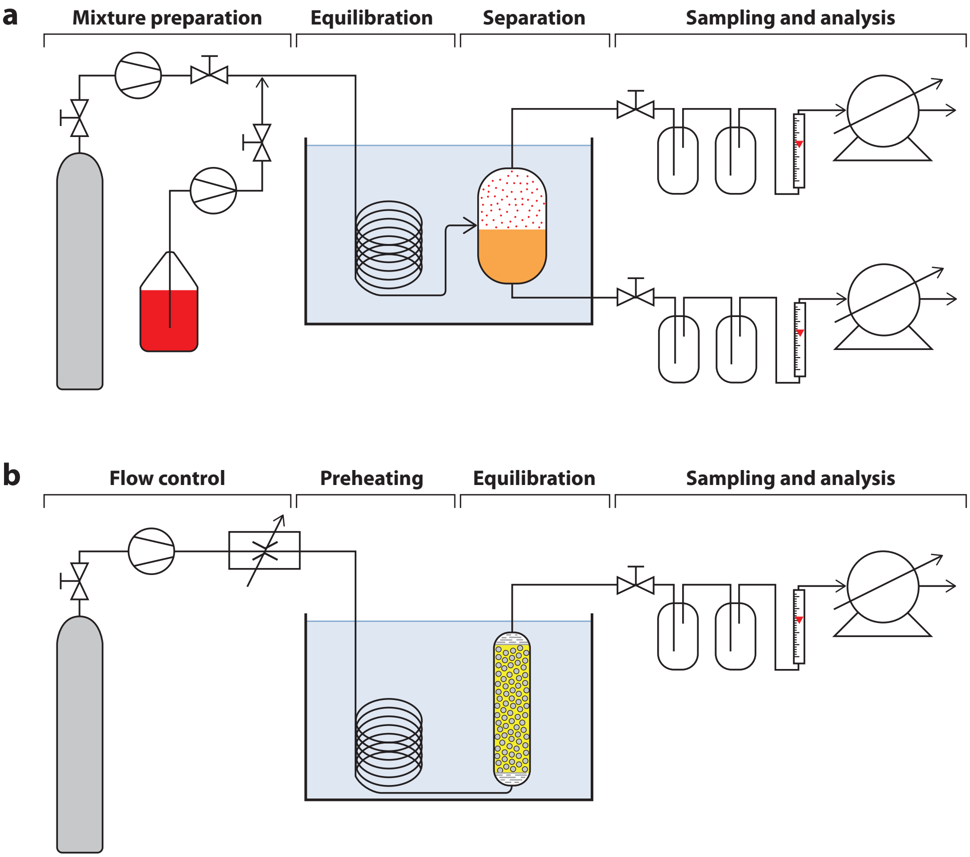

Figure 5

Fundamental steps of analytical-isothermal-isobaric methods: (*a*) continuous flow method and (*b*) semiflow method.

apparatus allowing visual observation and Raman spectroscopic studies of aqueous solutions at temperatures up to 770 K. Continuous-flow methods allow measurements with temperature-sensitive compounds at higher temperatures without thermal decomposition or polymerization reactions owing to the short residence time of the components in the apparatus (53).

In semiflow methods, only one of the phases is flowing; the other is stationary in an equilibrium cell. A high-pressure fluid stream is passed through one cell or two cells in series that contain the solute, which is either a liquid or a solid (**Figure 5*b***). When two cells are used, the first cell serves as a presaturator and the second as the equilibrium cell. Often, a syringe pump is used because it operates at constant pressure and enables a pulse-free constant fluid flow (54). Upon equilibration, the vapor phase effluent is reduced in pressure and introduced into a cold trap, in which the condensed component is collected. The quantity of gas can be determined volumetrically by a gas meter or a flow meter such as a wet test meter (55, 56).

In most applications, only the composition of the vapor phase is analyzed, for example, when measuring the solubility of a low-boiling (liquid or solid) substance in a supercritical fluid (56, 57). Many techniques are suitable for the determination of the vapor-phase effluent composition, such as online spectroscopic methods (58, 59), multiport sampling valves coupled with chromatographic equipment (60), or depressurization of the sample followed by diverse other analysis methods. Loss of volatile components can be prevented by a single or series of cold traps (61), absorption baths (62), or an adsorber in which the solute under study can be retained (63). When the composition of the liquid phase is analyzed, the semiflow method can be used to measure vapor-liquid equilibria (VLE) and gas-liquid equilibria (64, 65). Alternatively, the amount of gas dissolved in a liquid can be calculated from the variation over time of the amount of gas in the effluent vapor stream during an absorption experiment (66).

VLE: vapor-liquid equilibrium

Continuous-flow methods and semiflow methods have the advantage that sampling does not disturb the equilibrium. If larger samples are needed for analysis, the run time of the experiment can be extended to accumulate more material. Flow methods can be used only for systems in which the time needed to attain phase equilibrium is sufficiently short, e.g., a few minutes.

In chromatographic methods, the retention of a solute in a chromatographic column is measured and related to the Gibbs energy of solute transfer between the stationary and the mobile phase. Roth (67) reviewed applications of SFC for the determination of the relative solute solubilities in supercritical fluids and of solute partition coefficients between a supercritical fluid and the stationary phase. In SFC, the thermodynamic analysis of solute retention is more challenging than in common GC because the uptake of the mobile phase by the stationary phase is no longer negligible. The main advantage of chromatographic methods is the ability to determine equilibrium properties and diffusion coefficients simultaneously (68).

Analytical-Isobaric Methods

One of the most common methods for the measurement of vapor pressures in the range from 1 kPa to 100 kPa is ebulliometry (from Latin *ebullio* “to boil, to bubble up”). This method can be extended to high pressures (69). The boiling temperature of a mixture is measured under isobaric conditions, and the phase compositions are determined through sampling and analysis.

Analytical-Spectroscopic Methods

Spectroscopic methods allow fast analysis of phase compositions at high pressures without the need to withdraw samples. They are particularly suitable for the study of phase equilibria of reacting systems. Several spectroscopic techniques can be used, such as infrared spectroscopy (70, 71) or the ^{2}H NMR technique combined with light microscopy that Francisco et al. (72) used in the study of the phase behavior of lecithin + water + hydrocarbon + CO_2 mixtures. Pasquali et al. (73) used attenuated total reflection infrared (ATR-IR) spectroscopy to simultaneously measure the sorption of CO_2 in polyethylene glycol and the polymer swelling.

Aizawa et al. (74) developed a high-pressure optical cell for the investigation of absorption and fluorescence phenomena using a totsu (denoting the shape) type of window. The protruding part of the window acts as a light guide and enhances the laser power on the sample. Shieh et al. (75) studied the effect of CO_2 on the morphological structure of compatible crystalline/amorphous polymer blends by measuring absolute scattering intensity using small-angle X-ray scattering.

The advantage of avoiding sampling is often offset by the need for time-consuming calibrations at different pressures and compositions for signal evaluation of the spectra. A further disadvantage is that spectroscopic methods do not always allow the accurate determination of the concentrations of all components, which is a limiting factor, particularly in multicomponent systems. Less than 2% of all systems investigated in the past decade have been measured with a spectroscopic method (15, 16).

Analytical-Gravimetric Methods

Gravimetric methods are based on the monitoring of the mass of a nonvolatile condensed phase, such as a polymer (76–80) or an ionic liquid (81), in phase equilibrium with a fluid phase. Using additional information, such as the density of the phases, the phase compositions can be determined. Although quartz spring balances are progressively less used, commercially available electrobalances are becoming more widespread. More than 25 years ago, Kleinrahm & Wagner (82) developed a unique balance, known as magnetic suspension balance, intended for accurate measurements of fluid densities; its main advantage is that the sample and the balance are spatially separated from each other. Several researchers have used a magnetic suspension balance to measure the solubility and diffusivity of volatile components in polymers (83). Gravimetric methods require corrections for buoyancy effects, particularly at high pressures. Therefore, exact information on the density of the fluid phase and on the density and the volume of the condensed phase is essential.

Other Analytical Methods

For special applications, other analytical methods can be used to determine the composition of the phases without sampling. Some of these have been described in earlier reviews (15, 16). An example is the use of quartz crystal microbalances to determine the solubility of a gas in a polymer. From the basic principle, this is not a gravimetric measurement, so buoyancy effects play a different role. Guigard et al. (84) applied a quartz crystal technique for the measurement of low solubilities of metal chelates in supercritical fluids. A small mass of solute is deposited on the crystal, and the solubility is measured by observing the change in the frequency of the crystal as the solute dissolves in the supercritical fluid.

When compared with conventional methods, a quartz crystal microbalance provides a much higher sensitivity for the determination of mass changes, which means that smaller amounts of components are necessary to perform the experiments. This in turn yields a faster equilibration process and faster experiments (85) because equilibration time is inversely proportional to the square of the film thickness. However, the quartz crystal microbalance technique also has some drawbacks. Preparation and loading of the sample onto the crystal can be challenging, and the system tends to be highly sensitive to small changes in electrical current, air flow or motion in the surroundings, or any other interference occurring in the same room or even next door (86). Furthermore, errors rise with temperature and pressure owing to dampening and viscous dissipation upon entering the glass transition and rubbery state (76, 87).

Synthetic Methods

The basic principle of synthetic methods is to prepare a mixture of precisely known composition and then to observe the phase behavior in an equilibrium cell and to measure properties, such as pressure and temperature, in the equilibrium state. As no sampling is necessary, synthetic methods can be applied in situations in which analytical methods fail, for example, if the phase separation is difficult owing to similar densities of coexisting phases, e.g., near or even at critical points. However, the problem of analyzing fluid mixtures is replaced by the problem of synthesizing them.

Because no sampling is necessary, the experimental equipment requires few components, and the volume of the equilibrium cell can be smaller. Equilibrium cells for synthetic methods can be designed for extreme conditions of temperature and pressure. For example, in a recent review,

		Use 2000–4	Use 2005–8		Advantages	Challenges
Synthetic methods Total composition exactly known, no analysis of phases		**53.3%**	**62.4%**	↗	No sampling; no analysis; applicable when phase densities are similar; small equipment (expensive or dangerous chemicals, very high pressures)	No tie-line information; careful preparation (synthesis) of mixture; less accurate when phase boundaries are strongly composition dependent
Synthetic methods with a phase transition					**Direct determination of a point on a phase boundary**	**Detection of phase transition difficult; use of variable-volume cell is advisable**
SynVis	Synthetic-visual method	**36.4%**	**36.0%**	–	Visual observation provides additional information, e.g., phase volumes, foam	Visual observation of phase transition is dependent on ability of observer
SynNon	Synthetic-nonvisual method	**8.4%**	**13.4%**	↗	Applicable where visual methods fail, e.g., in porous media	Technical requirements for nonvisual detection of phase transition
Synthetic methods without a phase transition					**No need to detect a phase transition**	**Additional property data are needed, e.g., phase densities**
SynT	Synthetic-isothermal method	**6.1%**	**11.8%**	↗	Few error sources at lower pressures; combinable with other methods	Phase densities need to be known; vapor-phase composition calculated
SynP	Synthetic-isobaric method	**0.2%**	**0.5%**	–	Fluids are degassed by boiling; ebulliometer acts as a heat pipe	Essentially limited to measurement of vapor pressures of pure substance
SynOth	Other synthetic method	**2.2%**	**0.7%**	↘	For special applications	Few opportunities to share experience with other groups

Figure 6

Synthetic methods for high-pressure phase equilibria: advantages, challenges and frequency of use in the periods 2000–2004 (15) and 2005–2008 (16). Arrows indicate a significant change in the frequency of use.

Smith & Fang (22) gave examples of the use of diamond-anvil cells at high pressures, particularly for hydrothermal systems. In addition, Cohen-Adad (88) describes a diamond-anvil cell that can be used for pressures up to 135 GPa. For multicomponent systems, experiments with synthetic methods yield less information than those with analytical methods because the tie lines cannot be determined without additional experiments. Therefore, synthetic methods are used mainly for binary systems (15, 16). **Figure 6** describes the advantages and challenges of synthetic methods.

In synthetic methods with a phase transition, the conditions (pressure, temperature, or composition) in the equilibrium cell are altered until a new phase appears or one of the existing phases disappears. The composition of the large phase can be set to the known overall composition, whereas the composition of the small (appearing or disappearing) phase is not known. Each experiment yields one point of the *pTx* phase envelope. Usually pressure or temperature is varied to cause a phase transition; alternatively, the overall composition can be changed. For example, to determine phase boundaries for a precipitation with a compressed antisolvent process, Fusaro et al. (89) changed the overall concentration in a variable-volume view cell by adding an antisolvent (CO_2) to a clear solution (DMSO + lysozyme) at isobaric conditions; the volume of the cell was increased when CO_2 was added. Depending on how the phase transition is detected, synthetic methods with a phase transition can be divided into synthetic-visual and synthetic-nonvisual methods.

Diamond-anvil cell: a cell of tiny volume, made of two diamonds pressed around one gasket, that allows measurements at extremely high pressures

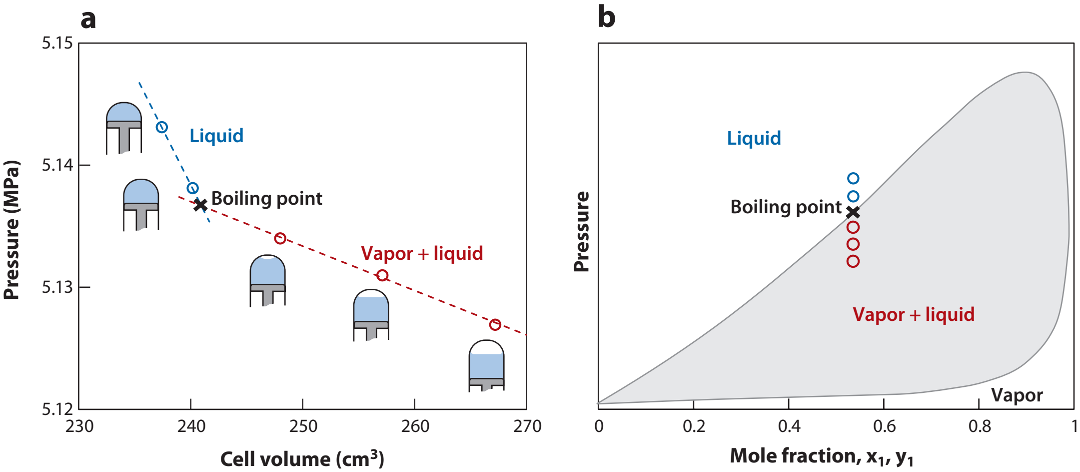

Figure 7

A boiling-point determination with a synthetic-visual and a synthetic-nonvisual method. (*a*) The pressure is measured as the volume of the cell increases. The phase transition is detected visually by observing at what pressure the vapor phase appears. The phase transition is detected nonvisually by observing the change in the slope of the *pV* curve. (*b*) Graphical representation of a boiling-point determination (panel *a*) in a pressure-composition diagram: pressure versus mole fraction of component 1 in the liquid phase (x_1) and in the vapor phase (y_1).

In synthetic methods without a phase transition, equilibrium properties such as pressure, temperature, phase volumes, and phase densities are measured, and phase compositions are calculated using a material balance. These methods can be divided into isothermal, isobaric, and other synthetic methods.

Synthetic-Visual Methods

Phase transitions are detected by visual observation, for example, the appearance or disappearance of a meniscus or turbidity (**Figure 7**). Visual observation is not feasible in isooptic systems in which the coexisting phases have approximately the same refractive index. Synthetic-visual methods have a wide range of application, from the determination of simple VLE to the study of more complex phase behavior such as multiphase equilibria (90), solid-liquid equilibria (91), critical curves of mixtures (92), gas hydrate formation (93), cloud-point determinations of ionic liquid systems (94), or phase equilibria in polymer-solvent systems (95).

The Cailletet apparatus (41) is based on a more than 140-year-old design. It consists mainly of a thick-walled glass tube with the open end immersed in mercury and was used by Thomas Andrews (11) for his investigations of the critical point. Many valuable phase equilibrium data for numerous systems have been determined with this apparatus. Today, however, most laboratories avoid the handling of mercury and use variable-volume view cells for the synthetic-visual method. To reduce the effective volume when only small quantities of a sample are available for observation of solid-liquid-gas equilibria, a glass capillary can be placed inside a high-pressure view cell (96, 97).

Equivalent to analytical-continuous-flow methods, synthetic-visual-continuous-feed methods have the advantage that the substances are kept at the desired temperature only for a short time, which reduces thermal degradation when critical points are measured at high temperatures. Soo et al. (98) describe a flow apparatus that is suitable for the measurement of critical points of pure components and of binary mixtures. Pressure and temperature are adjusted until critical opalescence is observed.

Synthetic-Nonvisual Methods

As an alternative to visual inspection, other physical properties can be monitored to detect the occurrence of phase transitions, e.g., by analyzing the slope of pressure-volume curves of mixtures (99, 100), as depicted in **Figure 7**. As an alternative, $pVTx$ measurements can be performed, and the intersection of isochors can be used to determine points on the coexistence curve; a sharp change in the (dp/dT) slope occurs at the phase boundary (101, 102). This is one of the most frequently used methods for the determination of hydrate formation conditions. In a variation of this method, the temperature is lowered to promote a faster appearance of the hydrate phase and subsequently increased in small steps to record the pT curves (103, 104).

$pVTx$: pressure, volume, temperature, mole fraction

Pyrometry: noncontact technique based on the measurement of thermal radiation; particularly used for the measurement of high temperatures

Minicucci et al. (105) used transmitted X rays instead of visible light as the basis for phase detection, whereas Drozd-Rzoska et al. (106) used measurements of the relative dielectric permittivity for liquid-liquid equilibrium experiments at high, low, and negative pressures. May et al. (107) used a microwave reentrant resonator in the detection of dew and bubble points in hydrocarbon systems, whereas Takagi et al. (108) measured bubble point pressures using an ultrasonic speed apparatus. Valyashko et al. (109) used jumps of the isochoric heat capacity to detect the appearance of a vapor phase or a second liquid phase. Würflinger & Urban (110) studied the phase behavior of liquid crystals with high-pressure differential thermal analysis. Ke et al. (23) describe several novel nonvisual methods for detecting phase transitions, particularly to follow chemical reactions, e.g., a shear-mode quartz sensor, a speed-of-sound sensor, a fiber-optic reflectometer, an ATR-IR crystal, and pressure-drop measurements of fluid flow through a packed bed.

Diamond-anvil cells are particularly suitable for nonvisual measurements at very high pressures (88). The selective transparency of diamond for IR to X-ray and γ-ray radiation allows in situ measurements during experiments. Manara et al. (111) investigated the melting point of uranium dioxide at high pressures using helium as a pressurizing medium. Temperatures of almost 3,200 K were needed for the measurements. Such high temperatures can be measured optically by pyrometry.

Ngo et al. (112) used a synthetic-nonvisual method for the determination of the solubility of solids in CO_2. The cell is initially charged with the solid and subsequently pressurized with CO_2 under permanent stirring. By periodically taking spectra (UV absorbance) of the solution, the equilibrium state is identified in situ. The pressure is then raised stepwise until no further significant increase in the peak absorbance is observed, which means that the entire solid has dissolved in the fluid phase.

Randzio et al. (113) presented a transitiometric method for the investigation of solid-phase behavior in asymmetric binary systems. Transitiometry is based on a simultaneous recording of both mechanical and thermal variables of a thermodynamic transition induced by scanning one independent variable, either pressure, temperature, or volume, whereas the other independent variable is kept constant.

Nonvisual methods can be particularly advantageous in studies of phase behavior in porous media. For example, Zatsepina & Buffett (114) used electrical resistance measurements to monitor the appearance and growth of CO_2 hydrate crystals in the pore fluid. Omi et al. (115) used a high-pressure NMR probe to investigate the pressure and pore size dependence of the critical behavior of xenon in mesopores.

Synthetic-Isothermal Methods

Experiments using synthetic-isothermal methods are performed by measuring the pressure of a synthesized multiphase mixture at isothermal conditions. The experimental procedure is shown

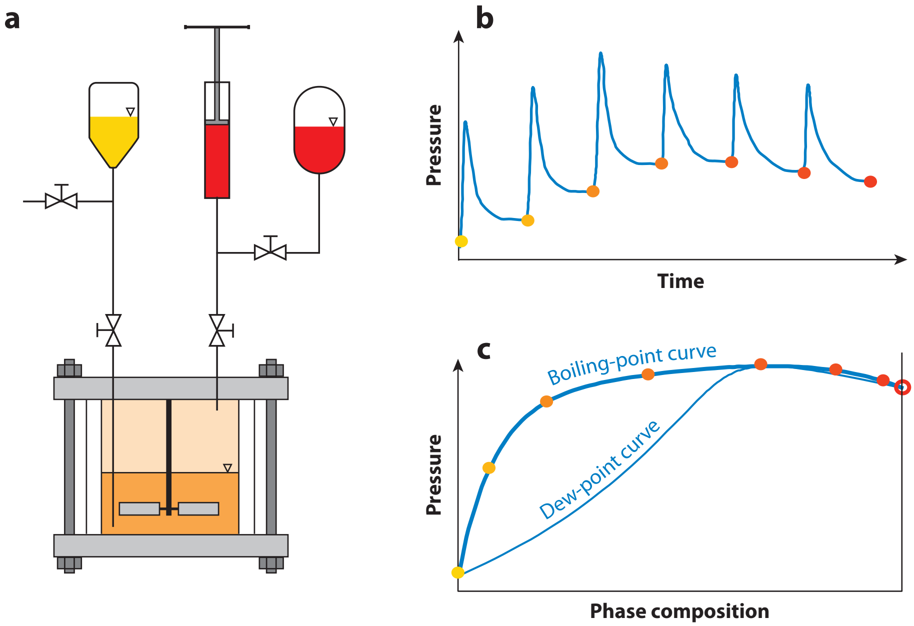

Figure 8

Experimental procedure for the synthetic-isothermal method. (*a*) Experimental apparatus. (*b*) Pressure change with time during the experiment, which includes several additions of the light compound. (*c*) The resulting pressure-composition diagram. Thick blue line: boiling-point curve with pressures taken from panel *b* and liquid-phase compositions calculated using the mass balance. Thin blue line: dew-point curve calculated with a thermodynamic model using the experimental data of the boiling-point line.

in **Figure 8**. An evacuated equilibrium cell is charged with an exactly known amount of the first component before setting the system to the desired temperature. Subsequently, a precisely known amount of the second component is added to the cell, which leads to an increase in the pressure of the system. As the second component dissolves into the liquid phase, the pressure inside the equilibrium cell decreases, eventually reaching an equilibrium value. For this reason, this method is often referred to as the pressure decay method. After equilibration of the system, the pressure and temperature are registered, and the composition of the vapor phase is calculated with a phase equilibrium model. The composition of the liquid phase is calculated using the material balance from the known total composition, the composition of the vapor phase, and the phase densities and volumes (116). More experimental points along the boiling-point line can be measured by repeating the experiment with a different amount of the second component or just by repeating the addition of the second component into the cell.

Synthetic-isothermal methods are commonly used (8, 117), particularly at high pressures, e.g., to determine the solubility of low-boiling substances in polymers (118, 119) or of gases in ionic liquids (120–123), oils (124), or electrolyte solutions (125). Krüger et al. (126) compared the results of the synthetic-isothermal method for VLE of the *n*-pentane + poly(dimethylsiloxane) system with those of the gravimetric sorption method and inverse GC. These methods differ in their underlying experimental principles as well as in the complexity of data analysis. Despite these differences, the agreement of the measured VLE data is excellent.

Synthetic-Isobaric Methods

The boiling temperature of a synthesized mixture is measured at isobaric conditions, and the phase compositions are calculated by means of a material balance. In contrast to the analytical-isobaric methods described above, no sampling or analysis is performed. Ewing & Ochoa (127) used comparative ebulliometry to precisely determine the vapor pressure of pure components at high pressures. The sample and a reference fluid are boiled in separate ebulliometers under a common pressure of a gas such as helium or nitrogen, and the condensation temperatures of the sample and the reference fluid are measured.

Ebulliometer: one-stage total-reflux boiler equipped with a vapor-lift pump to spray slugs of equilibrated liquid and vapor onto a thermometer well

Other Synthetic Methods

Properties measured in the homogeneous or heterogeneous region are used for the calculation of phase boundaries. For example, Abdulagatov et al. (128) performed two-phase isochoric heat-capacity measurements to determine the critical pressure and slope of the vapor pressure curve at the critical point of 18 pure components. In addition, Di Nicola et al. (129) used results of isochoric *pVTx* measurements in the single-phase region to fit the binary interaction parameters of an equation of state. Subsequently, the compositions of the coexisting phases were calculated using the equation of state.

IMPORTANT POINTS FOR PHASE EQUILIBRIUM MEASUREMENTS

Although most of the experimental methods have been used for decades, the knowledge of how to obtain accurate results with a certain method and how to avoid mistakes is not widespread because, in general, experimental difficulties and errors are not published. In some cases, the true accuracy of published experimental data is much less than the accuracy claimed by the authors for the apparatus used. For example, the data sets from Byun & Shin (130) and Stevens et al. (131) for the determination of the dew and boiling points of the system CO_2 + vinyl acetate using the synthetic-visual method differ by up to 23 mol% even though Byun & Shin estimated an accumulated error for the solubility isotherms of less than ±1 mol%. A further example is the discrepancy between the data from Cheng & Chen (132) and that of Kodama et al. (133). Both determined VLE data for the system CO_2 + isopropyl acetate using the analytical-isothermal method with liquid-phase recirculation and online sampling. The data sets differ by 7.9 mol%, whereas Cheng & Chen estimated the accuracy of their measured equilibrium compositions as ±0.2 mol%. The observed discrepancies can be explained by the researchers overlooking error sources of the experimental procedure and eventual deficiencies of the apparatus. In the following section, some essential characteristics for the generation of valuable experimental results are summarized.

Mixture Preparation

All parts of the apparatus must be clean at the beginning of the experiment. Dead zones, which are difficult to clean, should be minimized. The substances under investigation must be pure and should be degassed, particularly if synthetic methods are applied. For synthetic methods, the precise preparation of the mixture is essential. Independent of the applied method, the components must be stable during the entire experiment, particularly when investigations are performed at high temperatures.

Equilibration

The system under investigation must be in a state of true equilibrium, which requires that the equilibration time is sufficiently long and that no zones of inhomogeneity exist owing to temperature gradients, incomplete mixing, or accumulation of dirt in the equilibrium cell. If isothermal methods are applied, the equilibrium state generally can be identified by a constant pressure. However, when investigating vapor-liquid-liquid equilibria of complex multicomponent mixtures, an apparently constant pressure is not a clear indicator of complete equilibration because changes in the distribution of a particular component between the liquid phases do not interfere significantly with the total pressure of the system. The equilibrium state of such systems, particularly concerning the concentrations of minor components, should be confirmed by subsequent analysis of the composition of the liquid phases, e.g., by sampling at different points in time.

Time-consuming equilibration can be accelerated by intensifying contact between the phases to improve the mass transfer efficiency. This can be realized by stirring, rocking, or recirculating one or more of the phases. Most commonly the mixture is stirred with a motor-driven rotating axis passing through the wall of the cell (134) or with a magnetic stirring system. The first technique is susceptible to leaks owing to the wearing of the seals, which is a problem because the leak-induced pressure drop makes complete equilibration impossible. In comparison, magnetic stirring systems have simpler equipment and do not interfere with cell tightness (33, 41). The efficiency of magnetic stirring can be inadequate if the phases to be mixed have a high viscosity or, in the case of high-temperature applications, the magnet loses its strength with increasing temperature. Use of a cooled magnetic stirring system can minimize this problem but may have a negative impact on the homogeneity of the equilibrium cell temperature. For low-temperature applications, care should be taken that the heat produced by the stirring motor does not interfere with the equilibrium cell temperature. When investigating systems with gas hydrates, rocking the equilibrium cell can promote fast achievement of equilibrium (40). Here, all connections to the cell need to be flexible.

Another common mixing technique is recirculating one or more phases by means of pumps, continuously bubbling the gas phase through the liquid phase (135, 136) or pumping the liquid phase to the top of the cell, where it reenters through the gas phase (137, 138). Recirculation is an effective mixing method; however, it can disturb the phase equilibrium owing to cavitation or a pressure drop across the pump. Furthermore, small temperature gradients can lead to partial condensation or vaporization in the recirculation line. Consequently, recirculation methods are not recommended for studies in the region close to the critical point, where small changes in temperature and pressure strongly influence the phase behavior (139). The complexity in terms of connections and tubing also can present a problem owing to pressure leaks. Furthermore, high-quality pumps characterized by small pressure drops have high investment costs. Nevertheless, recirculation methods allow isobaric sampling from the recirculation line and easy, simultaneous measurement of the density of the phase(s) through the inclusion of a vibrating-tube densitometer in the recirculation loop(s) (30, 140). To avoid errors owing to pulsation, the pumps should be turned off during the density measurements (141).

Continuous-flow and semiflow methods require special care regarding the time needed for complete equilibration because these methods usually imply comparatively short retention times. Therefore, they are suitable only for systems in which the time needed to attain phase equilibrium is sufficiently short. To ensure complete equilibration, often two or more cells connected in series are used. The first cell(s) is used as a premixer or presaturator; only the last operates as an equilibrium cell. The accuracy of the results depends on the choice of the flow rate. Low flow rates lead to long experiment times during which experimental conditions such as pressure, temperature, and flow rate must be kept constant. If the rate is too high, other errors occur that partly cancel each other out: On one hand, a high flow rate reduces the time available for equilibration, and, for example, a too-small solubility is measured. On the other hand, entrainment is a serious concern, particularly when the solute is a liquid, and results in an apparent too-high solubility. Chen et al. (54) used a long vertical tube above the equilibrium cell as a buffer zone to avoid entrainment.

To obtain reliable phase equilibrium data, in addition to complete equilibration, a complete phase separation of the equilibrated phases is required, particularly if samples are withdrawn from the different phases. Thus, before taking samples from the coexisting phases, the mixture must be given sufficient time without stirring, rocking, or recirculation for the phases to separate, particularly if the density difference is small; otherwise, inhomogeneous samples in which the sampled phase still contains material from another phase(s), such as droplets, bubbles, or solid particles, are withdrawn (142). In addition, for methods in which no samples are withdrawn and the phase equilibria are calculated from mass balances, a good phase separation is essential to correctly identify the position of the interface between the phases to determine their volumes.

Visual observation of the content of the equilibrium cell helps to reduce error sources, e.g., by the detection of sufficient phase separation; of the position of phase interfaces; or of the formation of emulsions, solids, foam, or corrosion products. For the synthetic-isothermal method, visual observation is extremely useful for the visual determination of the volumes of the liquid and the vapor phase (122, 123). Windows can be made of thick glass (39, 41) or quartz (143), but most commonly sapphire is used (111, 137). Equilibrium cells can incorporate a single window (111, 143), two small parallel windows (144), or even a 360° window encompassing a whole section of the equilibrium cell (33, 40, 41). Secuianu et al. (142) used a variable-volume cell with two sapphire windows in which one of the windows also serves as the piston.

Independent of the applied method, the pressure and temperature should be measured precisely, which requires careful calibration of the sensors. The calibration must always be done for the entire measurement range. Furthermore, the relative error of pressure measurements is higher at lower pressures and dependent on the maximum pressure of the transducer. Temperature also may change a signal used for measurement, e.g., Raman and infrared spectra or the signal of a pressure transducer.

Sampling and Analysis/Phase Transition

All experimental procedures and analytical tools are worthless if the sample fails to effectively represent the actual composition of the analyzed mixture. Therefore, to obtain reliable and representative samples, several issues must be considered carefully. This particularly concerns sampling from high-pressure fluid mixtures because the sampling affects not only the sample itself but also the remaining system (26).

The major challenge in sampling by pressure drop is handling the abrupt change in the properties of the sample, which ranges from solid precipitation to an increase in viscosity, to the loss of highly volatile components. Solid formation and an increased viscosity may result in incomplete sample transport through the valves and lines, which in turn makes a reliable determination of the sample composition impossible and leads to misinterpretations of the composition of the actual sample as well as those of following samples. Therefore, it has to be ensured that no residues from the current system under investigation, from earlier experiments or impurities such as corrosion products, are left in the sampling line.

Incomplete sample transfer as a consequence of solid precipitation or viscosity increase can be prevented by a late pressure drop in the sampling line such that the phase split, viscosity increase, and other property changes occur close to the outlet and the two-phase system can be flushed out. Another countermeasure is sampling with counterpressure generated, for example, using a piston, mercury (145), or an inert gas such as nitrogen. Furthermore, special care must be taken to avoid adsorption inside transfer lines and sealings because quantitative desorption of the adsorbed components is often difficult or impossible. This is even more important when working in the trace region of many compounds, such as water, hydrogen sulfide, or methanol.

In general, more than one sample is withdrawn, as often the first sample serves to flush the transfer line. Therefore, consideration of the influence of sampling on the equilibrium state of the remaining system is crucial, as the induced pressure drop and the changed total composition lead to a new equilibrium state with phase compositions that differ from the originals. The change in the composition and its error owing to sampling can be kept low if the relative sampling volume is low. This can be achieved by utilizing large cell volumes. On one hand, large cells are expensive and, compared with small equilibrium cells, require more effort and time to achieve the desired temperature because the system reacts more slowly. On the other hand, once the desired equilibrium has been reached, this inertia toward perturbations makes systems in large-volume equilibrium cells rather stable.

If the substances to be investigated are expensive, dangerous, or available only in small quantities, small equilibrium cells are preferred. Here special attention must be paid to the sampling volume, which must be kept as small as possible. This can be achieved by using capillaries and special sampling valves as well as minimizing dead volumes.

Another way to prevent distortion of cell equilibrium is to keep the pressure of the cell constant during sampling by changing the volume of the cell or by adding one or more components during sampling. The variation of the cell volume is usually accomplished by using a bellows (25) or a moveable piston; their position is regulated either by direct mechanical actuation (140) or through a pressure-transmitting medium and a syringe pump (34). This last technique can be especially efficient and practical if an electronic syringe pump is used (146). Special care should be taken so that the piston is leak free. When a pressure-transmitting fluid is used, leaks often are not noticed because both sides of the piston are at similar pressures and no significant pressure drop is observed. To improve the leak tightness of the piston, it can be made to fit precisely in the body of the cell. However, this might lead to an increase of friction, which makes an exact and stepless pressure adjustment impossible because the piston can be moved only if a certain pressure differential is present. Concerning the analysis of the samples, the careful calibration of all analytical instruments used is essential.

CONCLUSIONS

Knowledge of high-pressure phase equilibria is crucial in many fields, from the scientific understanding of natural processes to the optimization of industrial processes that results in lower manufacturing costs. High-pressure phase equilibria are essential for the design of new environmentally compatible and profitable processes and for many health, safety, environment, and quality issues. A survey by the European Federation of Chemical Engineering on industrial needs for thermodynamic and transport properties (147) indicated a clear need for qualified laboratories with experienced staff to provide high-quality experimental data. Reliable and precise measurements are often expensive and time consuming; the investment is not only in acquisition of equipment or the development of custom-made experimental setups, but also in developing qualified and experienced personnel. Good measurements are not easy to perform; many experimental challenges must be overcome. The scope of the errors made with the different experimental methods generally cannot be quantified because many different sources of error exist and the error itself is often strongly dependent on the experimenter, e.g., when synthetic-visual methods are used.

The discrepancies between data sets and given accuracies can be explained by researchers overlooking error sources in the experimental procedure or eventual apparatus deficiencies. Often a new apparatus is evaluated by comparing experimental results with results documented in the literature, and this comparison often covers selected conditions rather than the entire range of $pTxy$ conditions. Good agreement at low temperatures gives no information about problems that may arise in the high-temperature range, such as possible temperature gradients owing to inadequate temperature control or insufficient thermal insulation, as can occur at the windows of view cells or owing to heat dissipation via holders.

The more data points are available for a system, the more reliable the evaluation of the data sets' quality is. A consistency check of the data is possible if sufficient points on various isotherms are available and when a theoretically derived temperature dependence exists with which the experimental data can be compared. Often, too few data points for a system are published, which makes an examination of consistency difficult; sometimes one suspects that apparently inconsistent data points were excluded.

A wide variety of methods and techniques is available for experimental studies of phase equilibria at high pressures. The best method for a particular case depends both on the properties of the components and on the phenomena to be investigated. For example, an analytical-isothermal-isobaric method does not lead to reliable values in the critical region, whereas a synthetic-visual method does; the opposite is true when the solubility of a low-volatility substance is measured in a supercritical fluid. A detailed understanding of the different methods is fundamental not only for the choice of the method most suitable for a certain measurement task but also for the evaluation of experimental data and for the development of new methods using modern techniques.

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LITERATURE CITED

1. Brunner G. 2004. *Supercritical Fluids as Solvents and Reaction Media*. Amsterdam: Elsevier Sci.
2. Knox DE. 2005. Solubilities in supercritical fluids. *Pure Appl. Chem.* 77:513–30
3. Brunner G. 2010. Applications of supercritical fluids. *Annu. Rev. Chem. Biomol. Eng.* 1:321–42
4. Nunes da Ponte M. 2009. Phase equilibrium–controlled chemical reaction kinetics in high pressure carbon dioxide. *J. Supercrit. Fluids* 47:344–50
5. Pereda S, Brignole EA, Bottini SB. 2009. Advances in phase equilibrium engineering of supercritical reactors. *J. Supercrit. Fluids* 47:336–43
6. Akien GR, Poliakoff M. 2009. A critical look at reactions in class I and II gas-expanded liquids using CO_2 and other gases. *Green Chem.* 11:1083–100
7. Thakkar FMVT, Soni TG, Gohel MC, Gandhi TR. 2009. Supercritical fluid technology: a promising approach to enhance the drug solubility. *J. Pharm. Sci. Res.* 1:1–14
8. Dohrn R, Pfohl O. 2002. Thermophysical properties–industrial directions. *Fluid Phase Equilib.* 194–197:15–29
9. Deiters UK, Schneider GM. 1986. High pressure phase equilibria: experimental methods. *Fluid Phase Equilib.* 29:145–60
10. Cagniard de la Tour C. 1822. Exposé de quelques résultats obtenu par l'action combinée de la chaleur et de la compression sur certains liquides, tels que l'eau, l'alcool, l'ether sulfurique et l'essence de pétrole rectifiée. *Ann. Chim. Phys.* 21:127–32
11. **Andrews T. 1869. Bakerian lecture: on the continuity of the gaseous and liquid states of matter. *Philos. Trans. R. Soc. Lond.* 159:575–90**
12. Kuenen JP. 1906. *Theorie der Verdampfung und Verflüssigung von Gemischen*. Leipzig: Barth Verlag

11. Bakerian Lecture in 1869 of Thomas Andrews; full of experimental details.

13. Kammerlingh Onnes H. 1991. *Through Measurement to Knowledge: The Selected Papers of Heike Kamerlingh Onnes (1853–1926)*. Boston: Kluwer Acad.
14. Roozeboom HWB. 1904. *Die heterogenen Gleichgewichte vom Standpunkte der Phasenlehre. Zweites Heft. Systeme aus zwei Komponenten.* Braunschweig: Vieweg Verlag
15. **Fonseca JMS, Dohrn R, Peper S. 2011. High-pressure fluid-phase equilibria: experimental methods and systems investigated (2005–2008). *Fluid Phase Equilib.* 300:1–69**
16. Dohrn R, Peper S, Fonseca JMS. 2010. High-pressure fluid-phase equilibria: experimental methods and systems investigated (2000–2004). *Fluid Phase Equilib.* 288:1–54
17. Christov M, Dohrn R. 2002. High-pressure fluid phase equilibria: experimental methods and systems investigated (1994–1999). *Fluid Phase Equilib.* 202:153–218
18. Dohrn R, Brunner G. 1995. High-pressure fluid-phase equilibria: experimental methods and systems investigated (1988–1993). *Fluid Phase Equilib.* 106:213–82
19. Raal JD, Muehlbauer AL. 1998. *Phase Equilibria: Measurement and Computation*. Washington, D.C.: Taylor & Francis
20. Tsiklis DS. 1968. *Handbook of Techniques in High-Pressure Research and Engineering*. New York: Plenum
21. Richon D. 2009. Experimental techniques for the determination of thermophysical properties to enhance chemical processes. *Pure Appl. Chem.* 81:1769–82
22. Smith J, Fang Z. 2009. Techniques, applications and future prospects of diamond anvil cells for studying supercritical water systems. *J. Supercrit. Fluids* 47:431–46
23. **Ke J, Sánchez-Vicente Y, Akien GR, Novitskiy AA, Comak G, et al. 2010. Detecting phase transitions in supercritical mixtures: an enabling tool for greener chemical reactions. *Proc. R. Soc. A* 466:2799–818**
24. Richon D, de Loos T. 2005. Vapor-liquid equilibrium at high-pressures. In *Measurement of the Thermodynamic Properties of Multiple Phases*, ed. RD Weir, T de Loos, pp. 89–136. Amsterdam: Elsevier
25. Peper S, Haverkamp V, Dohrn R. 2010. Measurement of phase equilibria of the systems CO_2 + styrene and CO_2 + vinyl acetate using different experimental methods. *J. Supercrit. Fluids* 55:537–44
26. Peper S, Dohrn R. 2012. Sampling from fluid mixtures under high pressure: review, case study and evaluation. *J. Supercrit. Fluids* 66:2–15
27. Lu C, Tian Y, Xu W, Li D, Zhu R. 2008. High-pressure phase equilibrium for the binary systems of {carbon dioxide (1) + dimethyl carbonate (2)} and {carbon dioxide (1) + diethyl carbonate (2)} at temperatures of 273 K, 283 K, and 293 K. *J. Chem. Thermodyn.* 40:321–29
28. Brunner G, Teich J, Dohrn R. 1994. Phase equilibria in systems containing hydrogen, carbon dioxide, water and hydrocarbons. *Fluid Phase Equilib.* 100:253–68
29. Duarte CMM, Crew M, Casimiro T, Aguiar-Ricardo A, Nunes da Ponte MN. 2002. Phase equilibrium for capsaicin + water + ethanol + supercritical carbon dioxide. *J. Supercrit. Fluids* 22:87–92
30. Tsivintzelis I, Missopolinou D, Kalogiannis K, Panayiotou C. 2004. Phase compositions and saturated densities for the binary systems of carbon dioxide with ethanol and dichloromethane. *Fluid Phase Equilib.* 224:89–96
31. Madani H, Valtz A, Coquelet C, Meniai AH, Richon D. 2008. (Vapor + liquid) equilibrium data for (carbon dioxide + 1,1-difluoroethane) system at temperatures from (258 to 343) K and pressures up to about 8 MPa. *J. Chem. Thermodyn.* 40:1490–94
32. Valtz A, Coquelet C, Richon D. 2007. Vapor-liquid equilibrium data for the hexafluoroethane + carbon dioxide system at temperatures from 253 to 297 K and pressures up to 6.5 MPa. *Fluid Phase Equilib.* 258:179–85
33. **Folas GK, Berg OJ, Solbraa E, Fredheim AO, Kontogeorgis GM, et al. 2007. High-pressure vapor-liquid equilibria of systems containing ethylene glycol, water and methane: experimental measurements and modeling. *Fluid Phase Equilib.* 251:52–58**
34. Sawamura S, Egoshi N, Setoguchi Y, Matsuo H. 2007. Solubility of sodium chloride in water under high pressure. *Fluid Phase Equilib.* 254:158–62
35. Secuianu C, Feroiu V, Geana D. 2007. Investigation of phase equilibria in the ternary system carbon dioxide + 1-heptanol + *n*-pentadecane. *Fluid Phase Equilib.* 261:337–42
36. Bünz AP, Zitko-Stemberger N, Dohrn R. 1994. Phase equilibria of ternary and quaternary systems containing carbon dioxide, water, isopropanol, and glucose. *J. Supercrit. Fluids* 7:43–50

15–18. Reviews that cover high-pressure phase-equilibrium data and experimental methods published between 1988 and 2008.

23. Describes the newest developments in synthetic-nonvisual methods.

33. Interesting apparatus equipped with two automated pistons for volume variation and a 360° sapphire window.

37. Pfohl O, Timm J, Dohrn R, Brunner G. 1996. Measurement and correlation of vapor-liquid-liquid equilibria in the glucose + acetone + water + carbon dioxide system. *Fluid Phase Equilib.* 124:221–33
38. Raabe G, Janisch J, Koehler J. 2001. Experimental studies of phase equilibria in mixtures relevant for the description of natural gases. *Fluid Phase Equilib.* 185:199–208
39. Kim CN, Lee EH, Park YM, Yoo J, Kim KH, et al. 2000. Vapor-liquid equilibria for the 1,1,1-trifluoroethane (HFC-143a) + 1,1,1,2-tetrafluoroethane (HFC-134a) system. *Int. J. Thermophys.* 21:871–81
40. Ostergaard KK, Tohidi B, Danesh A, Burgass RW, Todd AC. 2000. Equilibrium data and thermodynamic modelling of isopentane and 2,2-dimethylpentane hydrates. *Fluid Phase Equilib.* 169:101–15
41. Shariati A, Peters CJ. 2002. Measurements and modeling of the phase behavior of ternary systems of interest for the GAS process: I. The system carbon dioxide + 1-propanol + salicylic acid. *J. Supercrit. Fluids* 23:195–208
42. Pfohl O, Petersen J, Dohrn R, Brunner G. 1997. Partitioning of carbohydrates in the vapor-liquid-liquid region of the 2-propanol + water + carbon dioxide system. *J. Supercrit. Fluids* 10:95–103
43. **Guilbot P, Valtz A, Legendre H, Richon D. 2000. Rapid on-line sampler-injector: a reliable tool for HT-HP sampling and on-line GC analysis. *Analusis* 28:426–31**
44. Wagner K-D, Dahmen N, Dinjus E. 2000. Solubility of triphenylphosphine, tris(*p*-fluorophenyl)phosphine, tris(pentafluorophenyl)phosphine, and tris(*p*-trifluoromethylphenyl) phosphine in liquid and supercritical carbon dioxide. *J. Chem. Eng. Data* 45:672–77
45. Grigiante M, Stringari P, Scalabrin G, Ihmels EC, Fischer K, Gmehling J. 2008. (Vapour + liquid + liquid) equilibria and excess molar enthalpies of binary and ternary mixtures of isopropanol, water, and propylene. *J. Chem. Thermodyn.* 40:537–48
46. Galia A, Argentino A, Scialdone O, Filardo G. 2002. A new simple static method for the determination of solubilities of condensed compounds in supercritical fluids. *J. Supercrit. Fluids* 24:7–17
47. Sherman G, Shenoy S, Weiss RA, Erkey C. 2000. A static method coupled with gravimetric analysis for the determination of solubilities of solids in supercritical carbon dioxide. *Ind. Eng. Chem. Res.* 39:846–48
48. Nikitin LN, Gallyamov MO, Vinokur RA, Nikolaev AY, Said-Galiyev EE, et al. 2003. Erratum to "Swelling and impregnation of polystyrene using supercritical carbon dioxide": [J. of Supercritical Fluids 26 (2003) 263–273]. *J. Supercrit. Fluids* 27:131
49. Nikitin LN, Gallyamov MO, Vinokur RA, Nikolaev AY, Said-Galiyev EE, et al. 2003. Swelling and impregnation of polystyrene using supercritical carbon dioxide. *J. Supercrit. Fluids* 26:263–73
50. Fonseca J, Simoes PC, Nunes da Ponte MN. 2003. An apparatus for high-pressure VLE measurements using a static mixer. Results for (CO_2 + limonene + citral) and (CO_2 + limonene + linalool). *J. Supercrit. Fluids* 25:7–17
51. Bamberger A, Sieder G, Maurer G. 2000. High-pressure (vapor + liquid) equilibrium in binary mixtures of (carbon dioxide + water or acetic acid) at temperatures from 313 to 353 K. *J. Supercrit. Fluids* 17:97–110
52. Hurst WS, Hodes MS, Bowers WJ, Bean VE, Maslar JE, et al. 2002. Optical flow cell and apparatus for solubility, salt deposition and Raman spectroscopic studies in aqueous solutions near the water critical point. *J. Supercrit. Fluids* 22:157–66
53. Mahmood S, Zhao Q, Kabadi VN. 2001. High-temperature VLE for the tetralin-quinoline system. *J. Chem. Eng. Data* 46:994–99
54. Chen P-Y, Chen W-H, Lai S-M, Chang C-MJ. 2011. Solubility of *Jatropha* and *Aquilaria* oils in supercritical carbon dioxide at elevated pressures. *J. Supercrit. Fluids* 55:893–97
55. Cheng KW, Tang M, Chen YP. 2001. Vapor-liquid equilibria of carbon dioxide with diethyl oxalate, ethyl laurate, and dibutyl phthalate binary mixtures at elevated pressures. *Fluid Phase Equilib.* 181:1–16
56. Eustaquio-Rincón R, Trejo A. 2001. Solubility of *n*-octadecane in supercritical carbon dioxide at 310, 313, 333, and 353 K, in the range 10–20 MPa. *Fluid Phase Equilib.* 185:231–39
57. Berna A, Chafer A, Montón JB, Subirats S. 2001. High-pressure solubility data of system ethanol (1) + catechin (2) + CO_2 (3). *J. Supercrit. Fluids* 20:157–62
58. Fu D, Sun X, Qiu Y, Jiang X, Zhao S. 2007. High-pressure phase behavior of the ternary system CO_2 + ionic liquid [bmim][PF_6] + naphthalene. *Fluid Phase Equilib.* 251:114–20
59. Kordikowski A, Siddiqi M, Palakodaty S. 2002. Phase equilibria for the CO_2 + methanol + sulfathiazole system at high pressure. *Fluid Phase Equilib.* 194–197:905–17

43. Description of the ROLSI^{TM} sampling valve.

60. Goodarznia I, Esmaeilzadeh F. 2002. Solubility of an anthracene, phenanthrene, and carbazole mixture in supercritical carbon dioxide. *J. Chem. Eng. Data* 47:333–38

61. Sovová H, Stateva RP, Galushko AA. 2007. High-pressure equilibrium of menthol + CO_2. *J. Supercrit. Fluids* 41:1–9

62. Banchero M, Ferri A, Manna L, Sicardi S. 2006. Solubility of disperse dyes in supercritical carbon dioxide and ethanol. *Fluid Phase Equilib.* 243:107–14

63. Alessi P, Kikic I, Cortesi A, Fogar A, Moneghini M. 2003. Polydimethylsiloxanes in supercritical solvent impregnation (SSI) of polymers. *J. Supercrit. Fluids* 27:309–15

64. Cheng KW, Kuo SJ, Tang M, Chen YP. 2000. Vapor-liquid equilibria at elevated pressures of binary mixtures of carbon dioxide with methyl salicylate, eugenol, and diethyl phthalate. *J. Supercrit. Fluids* 18:87–99

65. Tan ZQ, Gao GH, Yu YX, Gu C. 2001. Solubility of oxygen in aqueous sodium carbonate solution at pressures up to 10 MPa. *Fluid Phase Equilib.* 180:375–82

66. Lerche BM, Stenby EH, Thomsen K. 2009. CO_2 capture from flue gas using amino acid salt solutions. *Proc. Risø Int. Energy Conf., 2009, Roskilde, Denmark*, Sept. 14–16, pp. 232–41

67. Roth M. 2004. Determination of thermodynamic properties by supercritical fluid chromatography. *J. Chromatogr. A* 1037:369–91

68. Funazukuri T, Kong CY, Murooka N, Kagei S. 2000. Measurements of binary diffusion coefficients and partition ratios for acetone, phenol, α-tocopherol, and β-carotene in supercritical carbon dioxide with a poly(ethylene glycol)-coated capillary column. *Ind. Eng. Chem. Res.* 39:4462–69

69. Susial P, Rios-Santana R, Sosa-Rosario A. 2010. VLE data of methyl acetate + methanol at 1.0, 3.0 and 7.0 bar with a new ebulliometer. *J. Chem. Eng. Jpn.* 43:650–56

70. Andersen WC, Sievers RE, Lagalante AF, Bruno TJ. 2001. Solubilities of cerium(IV), terbium(III), and iron(III) β-diketonates in supercritical carbon dioxide. *J. Chem. Eng. Data* 46:1045–49

71. Haines AH, Steytler DC, Rivett C. 2008. Solubility dependence of peracylated D-glucopyranoses in supercritical carbon dioxide on the structure of their acyl moieties. *J. Supercrit. Fluids* 44:21–24

72. Francisco JdC, Topgaard D, Sivik B, Bergenståhl B. 2004. Phase behavior of the system lecithin-water: the effects of addition of the hydrocarbon 1,8-cineole and supercritical carbon dioxide. *J. Supercrit. Fluids* 31:255–62

73. Pasquali I, Andanson JM, Kazarian SG, Bettini R. 2008. Measurement of CO_2 sorption and PEG 1500 swelling by ATR-IR spectroscopy. *J. Supercrit. Fluids* 45:384–90

74. Aizawa T, Kanakubo M, Ikushima Y, Saitoh N, Arai K, Smith RL. 2004. "Totsu"-window optical cell for absorption and emission studies of high-pressure liquids and supercritical fluids. *J. Supercrit. Fluids* 29:313–17

75. Shieh YT, Liu KH, Lin TL. 2004. Effect of supercritical CO_2 on morphology of compatible crystalline/amorphous PEO/PMMA blends. *J. Supercrit. Fluids* 28:101–12

76. Pantoula M, Panayiotou CG. 2006. Sorption and swelling in glassy polymer/carbon dioxide systems: Part I. Sorption. *J. Supercrit. Fluids* 37:254–62

77. Pantoula M, von Schnitzler J, Eggers R, Panayiotou CG. 2007. Sorption and swelling in glassy polymer/carbon dioxide systems: Part II. Swelling. *J. Supercrit. Fluids* 39:426–34

78. Sato Y, Takikawa T, Sorakubo A, Takishima S, Masuoka H, Imaizumi M. 2000. Solubility and diffusion coefficient of carbon dioxide in biodegradable polymers. *Ind. Eng. Chem. Res.* 39:4813–19

79. von Solms N, Rubin A, Andersen SI, Stenby EH. 2005. Direct measurement of high temperature/high pressure solubility of methane and carbon dioxide in polyamide (PA-11) using a high-pressure microbalance. *Int. J. Thermophys.* 26:115–25

80. von Solms N, Zecchin N, Rubin A, Andersen SI, Stenby EH. 2005. Direct measurement of gas solubility and diffusivity in poly(vinylidene fluoride) with a high-pressure microbalance. *Eur. Polym. J.* 41:341–48

81. Anthony JL, Maginn EJ, Brennecke JF. 2002. Solubilities and thermodynamic properties of gases in the ionic liquid 1-*n*-butyl-3-methylimidazolium hexafluorophosphate. *J. Phys. Chem. B* 106:7315–20

82. Kleinrahm R, Wagner W. 1986. Measurement and correlation of the equilibrium liquid and vapour densities and the vapour pressure along the coexistence curve of methane. *J. Chem. Thermodyn.* 18:739–60

82. Original article describing the principles of the magnetic suspension balance.

83. Sato Y, Takikawa T, Takishima S, Masuoka H. 2001. Solubilities and diffusion coefficients of carbon dioxide in poly(vinyl acetate) and polystyrene. *J. Supercrit. Fluids* 19:187–98
84. Guigard SE, Hayward GL, Zytner RG, Stiver WH. 2001. Measurement of solubilities in supercritical fluids using a piezoelectric quartz crystal. *Fluid Phase Equilib.* 187–188:233–46
85. Oliveira NS, Oliveira J, Gomes T, Ferreira A, Dorgan J, Marrucho IM. 2004. Gas sorption in poly(lactic acid) and packaging materials. *Fluid Phase Equilib.* 222–223:317–24
86. Saldaña MDA, Sun L, Guigard SE, Temelli F. 2006. Comparison of the solubility of β-carotene in supercritical CO_2 based on a binary and a multicomponent complex system. *J. Supercrit. Fluids* 37:342–49
87. Park K, Koh M, Yoon C, Kim H, Kim H. 2004. The behavior of quartz crystal microbalance in high pressure CO_2. *J. Supercrit. Fluids* 29:203–12
88. **Cohen-Adad MTh. 2001. Phase diagrams at high temperature and high pressure. Determination and consequent developments. *Pure Appl. Chem.* 5:771–83**
89. Fusaro F, Kluge J, Mazzotti M, Muhrer G. 2009. Compressed CO_2 antisolvent precipitation of lysozyme. *J. Supercrit. Fluids* 49:79–92
90. Franceschi E, Grings MB, Frizzo CD, Oliveira JV, Dariva C. 2004. Phase behavior of lemon and bergamot peel oils in supercritical CO_2. *Fluid Phase Equilib.* 226:1–8
91. Yang M, Terakawa E, Tanaka Y, Sotani T, Matsuo S. 2002. Solid-liquid phase equilibria in binary (1-octanol + *n*-alkane) mixtures under high pressure: Part 1. (1-octanol + *n*-tetradecane or *n*-hexadecane) systems. *Fluid Phase Equilib.* 194–197:1119–29
92. Diefenbacher A, Türk M. 2001. Critical properties (p_c, T_c, and ρ_c) and phase equilibria of binary mixtures of CO_2, CHF_3, CH_2F_2, and SF_6. *Fluid Phase Equilib.* 182:121–31
93. Link DD, Ladner EP, Elsen HA, Taylor CE. 2003. Formation and dissociation studies for optimizing the uptake of methane by methane hydrates. *Fluid Phase Equilib.* 211:1–10
94. Najdanovic-Visak V, Esperanca JMSS, Rebelo LPN, Nunes da Ponte MN, Guedes HJR, et al. 2003. Pressure, isotope, and water co-solvent effects in liquid−liquid equilibria of (ionic liquid + alcohol) systems. *J. Phys. Chem. B* 107:12797–807
95. Byun HS, McHugh MA. 2000. Impact of "free" monomer concentration on the phase behavior of supercritical carbon dioxide-polymer mixtures. *Ind. Eng. Chem. Res.* 39:4658–62
96. Dohrn R, Bertakis E, Behrend O, Voutsas E, Tassios D. 2007. Melting point depression by using supercritical CO_2 for a novel melt dispersion micronization process. *J. Mol. Liq.* 131–132:53–59
97. Knez Z, Skerget M, Mandzuka Z. 2010. Determination of S-L phase transitions under gas pressure. *J. Supercrit. Fluids* 55:648–52
98. Soo CB, Théveneau P, Coquelet C, Ramjugernath D, Richon D. 2010. Determination of critical properties of pure and multi-component mixtures using a "dynamic-synthetic" apparatus. *J. Supercrit. Fluids* 55:545–53
99. Domanska U, Morawski P. 2002. High pressure investigations of (*n*-alkanes + ether) mixtures. *Phys. Chem. Chem. Phys.* 4:2264–68
100. **Kodama D, Miyazaki J, Kato M, Sako T. 2004. High pressure phase equilibrium for ethylene + 1-propanol system at 283.65 K. *Fluid Phase Equilib.* 219:19–23**
101. Ivanic J, Huo Z, Sloan ED Jr. 2004. Improved hydrate equilibrium measurements in ternary gas and black oil systems. *Fluid Phase Equilib.* 222–223:303–10
102. Mohammadi AH, Afzal W, Richon D. 2008. Gas hydrates of methane, ethane, propane, and carbon dioxide in the presence of single NaCl, KCl, and $CaCl_2$ aqueous solutions: experimental measurements and predictions of dissociation conditions. *J. Chem. Thermodyn.* 40:1693–97
103. Gnanendran N, Amin R. 2004. Equilibrium hydrate formation conditions for hydrotrope-water-natural gas systems. *Fluid Phase Equilib.* 221:175–87
104. Masoudi R, Tohidi B, Anderson R, Burgass RW, Yang J. 2004. Experimental measurement and thermodynamic modelling of clathrate hydrate equilibria and salt solubility in aqueous ethylene glycol and electrolyte solutions. *Fluid Phase Equilib.* 219:157–63
105. Minicucci D, Zou X-Y, Shaw JM. 2002. The impact of liquid-liquid-vapour phase behaviour on coke formation from model coke precursors. *Fluid Phase Equilib.* 194–197:353–60

88. Description of a diamond-anvil cell for high pressures.

100. Uses an interesting apparatus in which density measurements are made in the recirculation loops.

106. Drozd-Rzoska A, Rzoska SJ, Imre AR. 2004. Liquid-liquid phase equilibria in nitrobenzene-hexane critical mixture under negative pressure. *Phys. Chem. Chem. Phys.* 6:2291–94

107. May EF, Edwards TJ, Mann AG, Edwards C, Miller RC. 2001. Development of an automated phase behaviour measurement system for lean hydrocarbon fluid mixtures, using re-entrant rf/microwave resonant cavities. *Fluid Phase Equilib.* 185:339–47

108. Takagi T, Fujita K, Furuta D, Tsuji T. 2003. Bubble point pressure for binary mixtures of propane and pentafluoroethane. *Fluid Phase Equilib.* 212:279–83

109. Valyashko VM, Abdulagatov IM, Levelt Sengers JMH. 2000. Vapor-liquid-solid phase transitions in aqueous sodium sulfate and sodium carbonate from heat capacity measurements near the first critical end point. 2. Phase boundaries. *J. Chem. Eng. Data* 45:1139–49

110. Würflinger A, Urban S. 2001. Thermodynamic measurements on three 5-*n*-alkyl-2-(4′-isothiocyanatophenyl)-1,3-dioxanes (6DBT, 8DBT, 10DBT) at elevated pressures. *Phys. Chem. Chem. Phys.* 3:3727–31

111. Manara D, Ronchi C, Sheindlin M. 2002. Pressure dependence of UO_2 melting measured by double-pulse laser heating. *Int. J. Thermophys.* 23:1147–56

112. Ngo TT, Bush D, Eckert CA, Liotta CL. 2001. Spectroscopic measurement of solid solubility in supercritical fluids. *AIChE J.* 47:2566–72

113. Randzio SL, Stachowiak C, Grolier JPE. 2003. Transitiometric determination of the three-phase curve in asymmetric binary systems. *J. Chem. Thermodyn.* 35:639–48

114. Zatsepina OY, Buffett BA. 2001. Experimental study of the stability of CO_2-hydrate in a porous medium. *Fluid Phase Equilib.* 192:85–102

115. Omi H, Nagasaka B, Miyakubo K, Ueda T, Eguchi T. 2004. High-pressure ^{129}Xe NMR study of supercritical xenon confined in the mesopores of FSM-16. *Phys. Chem. Chem. Phys.* 6:1299–303

116. Fischer K, Wilken M. 2001. Experimental determination of oxygen and nitrogen solubility in organic solvents up to 10 MPa at temperatures between 298 K and 398 K. *J. Chem. Thermodyn.* 33:1285–308

117. Pfohl O, Dohrn R. 2004. Provision of thermodynamic properties of polymer systems for industrial applications. *Fluid Phase Equilib.* 217:189–99

118. Pfohl O, Riebesell C, Dohrn R. 2002. Measurement and calculation of phase equilibria in the system *n*-pentane + poly(dimethylsiloxane) at 308.15–423.15 K. *Fluid Phase Equilib.* 202:289–306

119. Sato Y, Takikawa T, Yamane M, Takishima S, Masuoka H. 2002. Solubility of carbon dioxide in PPO and PPO/PS blends. *Fluid Phase Equilib.* 194–197:847–58

120. Blanchard LA, Gu Z, Brennecke JF. 2001. High-pressure phase behavior of ionic liquid/CO_2 systems. *J. Phys. Chem. B* 105:2437–44

121. Kumelan J, Kamps ÁP-S, Tuma D, Yokozeki A, Shiflett MB, Maurer G. 2008. Solubility of tetrafluoromethane in the ionic liquid [hmim][Tf_2N]. *J. Phys. Chem. B* 112:3040–47

122. Yuan X, Zhang S, Liu J, Lu X. 2007. Solubilities of CO_2 in hydroxyl ammonium ionic liquids at elevated pressures. *Fluid Phase Equilib.* 257:195–200

123. Zhang S, Chen Y, Ren RXF, Zhang Y, Zhang J, Zhang X. 2005. Solubility of CO_2 in sulfonate ionic liquids at high pressure. *J. Chem. Eng. Data* 50:230–33

124. Bobbo S, Fedele L, Scattolini M, Camporese R, Stryjek R. 2007. Solubility of carbon dioxide in 2-methylbutyric, 2-methylvaleric and 2-methylhexanoic ester oils. *Fluid Phase Equilib.* 256:81–85

125. Kiepe J, Horstmann S, Fischer K, Gmehling J. 2002. Experimental determination and prediction of gas solubility data for $CO_2 + H_2O$ mixtures containing NaCl or KCl at temperatures between 313 and 393 K and pressures up to 10 MPa. *Ind. Eng. Chem. Res.* 41:4393–98

126. Krüger KM, Pfohl O, Dohrn R, Sadowski G. 2006. Phase equilibria and diffusion coefficients in the poly(dimethylsiloxane) + *n*-pentane system. *Fluid Phase Equilib.* 241:138–46

127. Ewing MB, Ochoa JCS. 2004. Vapor pressures of acetonitrile determined by comparative ebulliometry. *J. Chem. Eng. Data* 49:486–91

128. Abdulagatov AI, Stepanov GV, Abdulagatov IM. 2003. Vapor-pressure for the pure fluids from calorimetric measurements near the critical point. *Fluid Phase Equilib.* 209:55–79

129. Di Nicola G, Giuliani G, Polonara F, Stryjek R. 2003. Isochoric measurements of the R23 + CO_2 binary system. *Fluid Phase Equilib.* 210:33–43

130. Byun HS, Shin JS. 2003. Bubble-point measurement for CO_2 + vinyl acetate and CO_2 + vinyl acrylate systems at high pressures. *J. Chem. Eng. Data* 48:97–101
131. Stevens RMM, van Roermund JC, Jager MD, de Loos TW, de Swaan Arons J. 1997. High-pressure vapour-liquid equilibria in the systems carbon dioxide + 2-butanol, + 2-butyl acetate, + vinyl acetate and calculations with three EOS methods. *Fluid Phase Equilib.* 138:159–78
132. Cheng C-H, Chen YP. 2005. Vapor-liquid equilibria of carbon dioxide with isopropyl acetate, diethyl carbonate and ethyl butyrate at elevated pressures. *Fluid Phase Equilib.* 234:77–83
133. Kodama D, Sugiyama K, Ono T, Kato M. 2008. Volumetric properties of carbon dioxide + isopropyl ethanoate mixtures at 308.15 and 313.15 K. *J. Supercrit. Fluids* 47:128–34
134. Laursen T, Rasmussen P, Andersen SI. 2002. VLE and VLLE measurements of dimethyl ether containing systems. *J. Chem. Eng. Data* 47:198–202
135. Fedele L, Bobbo S, Camporese R, Scattolini M. 2007. Isothermal vapour + liquid equilibrium measurements and correlation for the pentafluoroethane + cyclopropane and the cyclopropane + 1,1,1,2-tetrafluoroethane binary systems. *Fluid Phase Equilib.* 251:41–46
136. Jou FY, Mather A. 2007. Solubility of hydrogen sulfide in [bmim][PF_6]. *Int. J. Thermophys.* 28:490–95
137. Brass M, Pritzel T, Schulte E, Keller JU. 2000. Measurements of vapor-liquid equilibria in the systems NH_3-H_2O-NaOH and NH_3-H_2O-KOH at temperatures of 303 and 318 K and pressures 0.1 MPa $< p <$ 1.3 MPa. *Int. J. Thermophys.* 21:883–98
138. Marcelino Neto MA, Barbosa JR Jr. 2008. Solubility, density and viscosity of a mixture of R-600a and polyol ester oil. *Int. J. Refrig.* 31:34–44
139. Nagahama K. 1996. VLE measurements at elevated pressures for process development. *Fluid Phase Equilib.* 116:361–72
140. Kato M, Sugiyama K, Sato M, Kodama D. 2007. Volumetric property for carbon dioxide + methyl acetate system at 313.15 K. *Fluid Phase Equilib.* 257:207–11
141. Freitag J, Díez MTS, Tuma D, Ulanova TV, Maurer G. 2004. High-pressure multiphase behavior of the ternary systems (ethene + water + 1-propanol) and (ethene + water + 2-propanol): Part I: Experimental investigation. *J. Supercrit. Fluids* 32:1–13
142. Secuianu C, Feroiu V, Geana D. 2003. High-pressure vapor-liquid equilibria in the system carbon dioxide and 2-propanol at temperatures from 293.25 K to 323.15 K. *J. Chem. Eng. Data* 48:1384–86
143. Tian Y, Zhu HG, Xue Y, Liu ZH, Yin L. 2004. Vapor-liquid equilibria of the carbon dioxide + ethyl propanoate and carbon dioxide + ethyl acetate systems at pressure from 2.96 MPa to 11.79 MPa and temperature from 313 K to 393 K. *J. Chem. Eng. Data* 49:1554–59
144. Kang SP, Lee H, Lee CS, Sung WM. 2001. Hydrate phase equilibria of the guest mixtures containing CO_2, N_2 and tetrahydrofuran. *Fluid Phase Equilib.* 185:101–9
145. Pauchon V, Cissé Z, Chavret M, Jose J. 2004. A new apparatus for the dynamic determination of solid compounds solubility in supercritical carbon dioxide: solubility determination of triphenylmethane. *J. Supercrit. Fluids* 32:115–21
146. Sane A, Taylor S, Sun YP, Thies MC. 2004. A semicontinuous flow apparatus for measuring the solubility of opaque solids in supercritical solutions. *J. Supercrit. Fluids* 28:277–85
147. Hendriks E, Kontogeorgis G, Dohrn R, de Hemptinne J-C, Economou IG, Fele Žilnik L, Vesovic V. 2010. Industrial requirements for thermodynamics and transport properties. *Ind. Eng. Chem. Res.* 49:11131–41

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