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# Solubility of iodopropynyl butylcarbamate in supercritical carbon dioxide

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ABSTRACT

Supercritical carbon dioxide has been considered an appropriate alternative for extraction and purification process of cosmetics, pharmaceuticals, food supplements and natural products. Solubility information of biological compounds is essential for choosing supercritical fluid (SCF) processes. The solubility of iodopropynyl butylcarbamate (IPBC), a fungicide and anti-dandruff agent, was measured in supercritical carbon dioxide with a high pressure apparatus equipped with a variable volume view cell at 313.15, 323.15, and 333.15 K and at pressure between 80 and 35 MPa. The experimental data were correlated well with Peng–Robinson equation of state (PR EOS) and quasi-chemical nonrandom lattice fluid model.



## 1. Introduction

The important applications of supercritical fluid (SCF) technology are the extraction and purification of cosmetics, pharmaceuticals, food supplements and natural products [1]. In particular, supercritical carbon dioxide ($scCO_2$) offers a nonflammable, nontoxic process that possesses low critical temperature of 304.21 K. Therefore, $scCO_2$ is often used as a clean medium and has replaced traditional organic solvents for various industrial applications. Although $scCO_2$ has many desirable features for separations of pharmaceutical compounds, the development of new processes has been delayed by lack of engineering data and thermodynamic models. Solubility information of biological compounds is crucial for choosing supercritical fluid processes for extraction, purification, and particle design.

The solubility of solid in supercritical carbon dioxide has been measured by static [2], flow-through [3] and recirculation systems [4]. Flow systems involve the dynamic flow of carbon dioxide over packed bed of the solid. This method can often difficult to ensure the accurate sampling during depressurization [5]. Recirculation systems use a fixed fluid volume that is continuously recirculated through them until equilibrium is reached. All recirculation units usually include on on-line coupled UV–vis detector, an injection and a recirculation pump. Static solubility determinations are performed in cells filled with a preset amount of solute by varying the pressure or temperature until the cloud point was observed. Since cloud point measurements are made by visible observation, at low solubility with the order $10^{-6}$ or $10^{-7}$ mole fraction, it is often difficult to observe when the solid fully dissolves. However, cloud point can successfully be measured at relatively high solubility with over the order $10^{-5}$ mole fraction [5].

Iodopropynyl butylcarbamate (IPBC) is a halogenated unsaturated carbamate with significant widespread cosmetic and pharmaceutical applications such as fungicide [6] and anti-dandruff agent [7,8]. IPBC has been shown to be active against Malassezia strains, yeasts that cause some skin disorders (dermatitis, pruritis). IPBC is white crystalline powder and has poor solubility in water.

The present status of studies on the thermodynamic modeling of SCF phase equilibria has been reviewed by Brennecke and Eckert [9]. Correlations of solid solubility containing biological compounds in supercritical carbon dioxide were presented using Peng–Robinson equation of state (PR EOS) [10], solution model [11], and lattice model [12]. Most recently, the present authors presented a quasi-chemical nonrandom lattice fluid (QLF) model [13,14] and found that the model EOS successfully modeled the phase behavior of classical pure fluids and mixtures containing nonassociating and associating molecules.

In this study, the equilibrium solubility of IPBC was measured in supercritical carbon dioxide with static method in the pressure range from 8 to 35 MPa and at temperatures of 313.15, 323.15, and 333.15 K. The experimental data were correlated by the PR EOS [15] and the QLF EOS.

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**Nomenclature**

*List of symbols*

| | |
|---|---|
| $A$ | Helmholtz free energy |
| $c$ | number of the component |
| $f$ | fugacity |
| $k$ | Boltzmann's constant |
| $N$ | number of molecule |
| $N_q$ | defined by Eq. (10) |
| $N_r$ | defined by Eq. (10) |
| $q$ | surface area parameter |
| $r$ | number of segments per molecule |
| $T$ | temperature |
| $V$ | volume |
| $v$ | molar volume |
| $v^*$ | close packed volume of a mer |
| $y$ | vapor mole fraction |
| $z$ | lattice coordination number |
| $Z$ | compressibility factor |

*Greek letters*

| | |
|---|---|
| $\beta$ | reciprocal temperature ($1/kT$) |
| $\varepsilon_{ii}$ | energy parameter of pure system |
| $\varepsilon_M$ | defined by Eq. (13) |
| $\varphi$ | fugacity coefficient |
| $\rho$ | molar density |
| $\rho^*$ | close packed molar density |
| $\theta$ | surface area fraction |
| $\omega$ | acentric factor |

*Superscript*

| | |
|---|---|
| $r$ | residual properties |
| $\sim$ | reduced properties |
| $*$ | characteristic properties |

## 2. Experimental

### 2.1. Materials

Carbon dioxide (min. 99.5%) was supplied from Korea Industrial Gases. IPBC (min. 97.0%) was supplied by SPC Co., Ltd. Phenanthrene has a stated purity of 98.0% and was supplied by Aldrich. These materials were used without further purification.

### 2.2. Solubility measurement

The cloud point of IPBC in $scCO_2$ was measured using a high-pressure apparatus installed a variable volume view cell. In our previous studies, this apparatus was used and published in phase behavior of polymer + monomer + carbon dioxide [16] and fluoroalcohol + carbon dioxide systems [17]. The viewcell is constructed with high nickel-content austenitic steel (5.7 cm o.d., 1.59 cm i.d., ~25 $cm^3$ working volume). As shown in Fig. 1, the cell is equipped with a sapphire window to enable observation of the turbidity of the solution as pressure is reduced, a movable piston to change pressure, a magnetic stirring bar and a pressure generator (High Pressure Equipment Co., 50-6-15). The pressure of the system was determined by measuring the pressure of the water with a digital pressure transducer (Paroscientific Inc., Model 43KR-HHT-101, accurate to 0.01% of reading) and pressure indicator (Paroscientific Inc., Model No. 730). The temperature was measured with a PRT type thermometer (Hart Scientific, Inc., Model 5622-32SR, accuracy of ±0.045 K) fixed to the surface of the cell and displayed by an indicator (Hart Scientific, Inc., Model 1502). The temperature of the cell was maintained and measured both to within ±0.1 K.

The experiment was performed as follows: after the addition of a fixed amount of IPBC into the cell, the cell was purged with $CO_2$ gas to remove trapped air and known volumes of $CO_2$ were then charged into the cell. The solution in the cell was agitated by the magnetic bar and heated to the desired temperature. After the solution reached and was maintained as a single phase, the pressure was slowly reduced by moving the piston located within the cell using the pressure generator until the solution became cloudy. The inside of the cell was projected onto a computer monitor using a camera (Veltek International, Inc., Model CVC5520) with a boroscope (Olympus Corp., Model R100-038-000-50) set toward the sapphire window. The solubility of IPBC in $scCO_2$ was determined by observing the cloud point which is defined as the pressure at which it is no longer possible to observe the magnetic bar [17]. When the cloud point was observed, the solubility was calculated using the known amount of solid loaded into the vessel along with the amount of carbon dioxide present in the vessel. After each cloud point observation, the view cell was vent, thoroughly cleaned, and dried. This procedure was repeated several times until the fluctuation of phase transition pressure was minimized to within ±0.05 MPa.

## 3. Correlation

In this work, the experimental data for the $CO_2$ + IPBC system were correlated with the PR EOS and the QLF EOS.

The PR EOS is expressed as follows

$$P = \frac{RT}{V-b} - \frac{a(T)}{V(V+b)+b(V-b)} \tag{1}$$

$$a(T) = 0.45724\frac{R^2T_c^2}{P_c}\alpha(T) \tag{2}$$

$$b = 0.07780\frac{RT_c}{P_c} \tag{3}$$

$$\alpha(T) = \left[1+\kappa\left(1-\sqrt{\frac{T}{T_c}}\right)\right]^2 \tag{4}$$

$$\kappa = 0.37464 + 1.54226\omega - 0.26992\omega^2 \tag{5}$$

where $T_c$ and $P_c$ are the critical temperature and the critical pressure of the pure substance, respectively, and $\omega$ is the acentric factor. The van der Waals one fluid mixing rules used in this study are given by

$$a = \sum_i\sum_j x_i x_j a_{ij} \tag{6}$$

$$b = \sum_i x_i b_i \tag{7}$$

$$a_{ij} = \sqrt{a_i a_j}(1-k_{ij}) \tag{8}$$

where $k_{ij}$ is the binary interaction parameter.

The QLF model has three molecular parameters; close packed volumes of a mer ($v_i^*$), segment numbers ($r_i$), and energy parameter ($\varepsilon_{ii}$) of pure systems. The QLF EOS and the fugacity coefficient of a component in mixture are expressed as follows,

$$\frac{\tilde{P}}{\tilde{T}} = -\ln(1-\tilde{\rho}) + \frac{z}{2}\ln\left[1+\left(\frac{q}{r}-1\right)\tilde{\rho}\right] - \frac{\theta^2}{\tilde{T}} \tag{9}$$