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# Solubility of climbazole in various alcohols at different temperatures

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## ARTICLE INFO

## ABSTRACT

(Solid + liquid) equilibria for climbazole in various alcohols (ethanol, 1-propanol, 1-butanol, 1-pentanol, 1-hexanol, and 1-heptanol) were investigated. The solubility data for climbazole in pure alcohols were obtained at temperatures ranging from (278.15 to 318.15) K. The melting temperature and fusion enthalpy of climbazole were measured using a differential scanning calorimeter (TA instrument Q100) and the experimental solubility was determined by the gravimetric method. The experimental solubility data were correlated by the equation for solubility of a solid in a liquid, and the activity coefficients were estimated by a non-random two liquid (NRTL), universal quasi-chemical (UNIQUAC), and Wilson models.

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## 1. Introduction

Climbazole (1-(4-chlorophenoxy)-1-(1H-imidazol-1-yl)-3,3-dimethyl-2-butanone, Chemical abstract Service Registry Number 33083-17-9) is an anti-fungal agent that mitigates skin disorders caused by fungal infections. Climbazole is usually added to anti-dandruff and anti-fungal products, including shampoos and conditioners. Climbazole has been widely used in cosmetic and pharmaceutical applications such as anti-itching agents [1] and biocides [2,3].

The (solid + liquid) equilibrium data are important in many fields of chemical engineering such as crystallization, extraction, and purification. The difference between the concentration of a super-saturated solid solution and the saturation solubility is the main factor of nucleation, growth, and agglomeration, which influence the crystal size distribution and morphology. Therefore, the solubility data are the essential to the crystallization process. Also, impurities in a solid can be eliminated by crystallization with several solvents. However, solubility data for climbazole in pure alcohols has not been investigated yet.

In general, three methods are used to measure the concentration of saturated solution. They are a laser technique method [4,5], an instrumental analytical method [6], and a gravimetric method [7]. The laser technique method can obtain solubility data quickly, but it is hard to identify the (solid + liquid) equilibrium. The instrumental analytical method is used for the systems with very low solubility and it includes the high performance liquid chromatographic (HPLC) and the ultraviolet (UV) spectrophotometric methods. With high solubility, however, the gravimetric method is the most appropriate and the simplest method among the three methods. Because of the high solubility of climbazole in pure alcohols, the gravimetric method was implemented in this work.

The solubility of climbazole in ethanol, 1-propanol, 1-butanol, 1-pentanol, 1-hexanol, and 1-heptanol was measured at temperatures ranging from (278.15 to 318.15) K at atmospheric pressure. The reliability of the experimental apparatus was investigated in previous work [8]. The experimental data were correlated by a non-random two liquid (NRTL) model [9], universal quasi-chemical (UNIQUAC) model [10] and Wilson model [11].

## 2. Experimental

### 2.1. Materials

Ethanol, 1-propanol, 1-butanol, 1-pentanol, and 1-hexanol were supplied by Sigma Aldrich (St. Louis, MO, USA). 1-Heptanol and climbazole were purchased from Tokyo Chemical Industry (Tokyo, Japan). All chemicals were used without further purification. The provenance and purity of chemicals used are reported in table 1.

### 2.2. Apparatus and procedures

The solubility of climbazole was measured at several temperatures ranging from (278.15 to 318.15) K at atmospheric pressure. A (solid + liquid) equilibrium measurement apparatus with an

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**List of symbols**

| | |
|---|---|
| $m_1$ | molality expressed in moles of solute per kg of solvent, equation (1) |
| $x_1$ | solute mole fraction, equation (2) solubility of a solid in a liquid phase, equation (6) |
| $W_1$ | mass of solute, equation (1) |
| $W_2$ | mass of solvent, equation (1) |
| $M_1$ | molar mass of solute, equation (1) |
| $M_2$ | molar mass of solvent, equation (2) |
| $N_i$ | occurrences of the type $i$ group in a molecule, equations (3)–(5) |
| $M_j$ | occurrences of the type $j$ group in a molecule, equation (5) |
| $v_{1i}$ | contribution of the type $i$ groups to liquid molar volume, equation (5) |
| $v_{2j}$ | contribution of the type $j$ groups to liquid molar volume, equation (5) |
| $R_i$ | contribution of the type $i$ groups to UNIQUAC volume parameter, equation (3) |
| $Q_i$ | contribution of the type $i$ groups to UNIQUAC area parameter, equation (4) |
| $\Delta_{fus}H$ | molar enthalpy of fusion of the solid, equation (6) |
| $T_m$ | melting temperature of the solid, equation (6) |
| $\Delta g_{12}, \Delta g_{21}$ | adjustable parameters contained in the NRTL model, equation (A.2) |

| | |
|---|---|
| $\Delta u_{12}, \Delta u_{21}$ | adjustable parameters contained in the UNIQUAC model, equation (A.5) |
| $z$ | coordination number, equation (A.4) |
| $N$ | number of experimental points, equation (8) |
| $x_{1,j}^{calc}$ | correlated solubility value, equation (8) |
| $x_{1,j}^{exp}$ | experimental solubility value, equation (8) |

*Greek letters*

| | |
|---|---|
| $\gamma_1$ | activity coefficient of the solid, equation (6) |
| $\alpha_{12}$ | adjustable parameters contained in the NRTL model (related to the non-randomness in the mixture), equation (A.2) |
| $\Delta\lambda_{12}, \Delta\lambda_{21}$ | adjustable parameters contained in the Wilson model, equation (A.9) |

*Superscripts*

| | |
|---|---|
| calc | calculation |
| exp | experiment |

*Subscripts*

| | |
|---|---|
| fus | fusion |
| m | melting |

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external thermostat was used for measuring the solubility. The experimental temperature was controlled by an external thermostat within ±0.05 K. The temperatures were measured by a digital thermometer (Hart Scientific, Inc., Model 5618B) with an accuracy of ±0.066 K and displayed by an indicator (Hart Scientific, Inc., Model 1502A). The excess amounts of climbazole were added to ethanol in 50 ml glass tube. The solution was stirred by a magnetic stirrer for at least 48 h to ensure the (solid + liquid) equilibrium was reached. After the suspension was settled down, the upper clear solution was extracted by a syringe (10 ml) and filtered using a disposable syringe filter (PTFE, 0.2 μm). The mass of the sample (filtered solution) was recorded. The sample was dried and evaporated in a vacuum oven. Throughout the drying process, the sample was repeatedly weighed until the constant weight is obtained in order to certify that no solvent remained. The rest of solvents followed the similar procedure. All of the mass was measured by an analytical balance (EPG 214) (Ohaus Corp., Model EPG 214) with an accuracy of ±0.0001 g. For all data points, experiments were conducted more than three times to increase the reliability of the experimental results.

The molality, $m_1$, and mole fraction, $x_1$, were obtained with the following equation:

$$m_1/(mol/kg) = \frac{1000(W_1/M_1)}{W_2}, \tag{1}$$

$$x_1 = \frac{W_1/M_1}{W_1/M_1 + W_2/M_2}, \tag{2}$$

where $W_1$ and $W_2$ are the mass of the solute and solvent, and $M_1$ and $M_2$ represent the molar mass of the solute and solvent, respectively.

### 2.3. Determination of the thermochemical properties

The thermochemical properties (UNIQUAC volume parameter, UNIQUAC area parameter, and liquid molar volume) of the climbazole were estimated by the group contribution methods [12,13]. In the group contribution method, a molecule is regarded as an aggregation of functional groups and a property of a molecule is the sum of contributions made by the molecule's functional groups.

UNIQUAC parameters of climbazole were calculated by the following equations: [12]

$$r = \sum_i N_i R_i, \tag{3}$$

$$q = \sum_i N_i Q_i, \tag{4}$$

where $N_i$ is the number of the type $i$ groups in a molecule. $R_i$ and $Q_i$ are the contributions of the type $i$ groups. The group contribution

**TABLE 1**
The source and mass fraction purity of chemicals.

| Chemical name | Source | Mass fraction purity |
|---|---|---|
| Ethanol | Sigma Aldrich | ⩾0.999 |
| 1-Propanol | Sigma Aldrich | ⩾0.999 |
| 1-Butanol | Sigma Aldrich | ⩾0.997 |
| 1-Pentanol | Sigma Aldrich | ⩾0.990 |
| 1-Hexanol | Sigma Aldrich | ⩾0.990 |
| 1-Heptanol | TCI[a] | >0.980 |
| Climbazole | TCI[a] | >0.980 |

[a] Tokyo Chemical Industry.

**TABLE 2**
Group contribution information on the climbazole for the UNIQUAC volume and area parameters.

| Group (type $i$) | Volume $R_i$ | Surface area $Q_i$ | Occurrences $N_i$ |
|---|---|---|---|
| ACCl | 1.1562 | 0.844 | 1 |
| ACH | 0.5313 | 0.400 | 7 |
| AC | 0.3652 | 0.120 | 1 |
| CH₃ | 0.9011 | 0.848 | 3 |
| C | 0.2195 | 0.000 | 1 |