Available online at www.sciencedirect.com
ScienceDirect
Fluid Phase Equilibria 249 (2006) 61–66
FLUID PHASE EQUILIBRIA
www.elsevier.com/locate/fluid

Activity coefficients of the species in the methanol solutions of acetaminophen and two silylated derivatives at 298.15 K

Jaber Jahanbin Sardroodi *, Mohammad Ghaleh Assadi, Mehrdad Mahkam, Yahya Kazemi

Department of Chemistry, Faculty of Basic Sciences, Azarbaijan University of Tarbiat Moallem, Tabriz, Iran

Received 20 June 2006; received in revised form 21 August 2006; accepted 26 August 2006
Available online 30 August 2006

Abstract

An isopiestic method was used to measure the solvent osmotic coefficients in solutions of acetaminophen, triethylsilylacetaminophen and tertiarybuthyldimethylsilylacetaminophen in methanol at 298.15 K. The experimental data for osmotic coefficients have been correlated and solute unsymmetric convention activity coefficients have been calculated using the nonrandom factor (NRF) model, the nonrandom, two-liquid (NRTL) model, a three-parameter Margules equation, and a fourth-order polynomial equation in terms of molality. Standard deviations are least for the models with more parameters, but all models describe the data within experimental uncertainty. The solute activity coefficients are greater than unity, increasing with molecular size.

Keywords: Silylated acetaminophen; Methanol; Activity coefficient; Isopiestic; NRF model; NRTL model

1. Introduction

Thermodynamic properties of the solutions of pharmaceutical materials and their derivatives are useful in understanding their behavior in various media and in the body. Acetaminophen is a widely used pharmaceutical and its silyl ether and other derivatives of it used as prodrugs. Because of the solute–solvent interactions in the solutions of the silicon-containing compounds are not the same as those in the solutions of their carbon analogues, silicon-containing compounds are generally more lipophilic than their carbon analogues. The enhanced lipophilicity of these compounds is expected to improve their therapeutic properties.

We expect that the thermodynamic properties of the solutions of silicon-containing compounds to show different behavior compared to the solutions of their carbon analogues. A survey of the literature reveals some reports on the thermodynamic properties of acetaminophen and its derivatives in various solvents or solvent mixtures [1–8]. However, these studies are limited to the solubility of the acetaminophen in various solvents and there are no reports on solute activity coefficients of acetaminophen or its derivatives as a function of composition.

In this work we measured the osmotic coefficients of the solutions of acetaminophen and its two silyl derivatives in methanol by an isopiestic method at 298.15 K. The method used here has been employed previously for studying of a wide variety of mixtures including aqueous and nonaqueous solutions of electrolytes, nonelectrolytes and polymers [9–16]. The experimental data for osmotic coefficients have been correlated and solute unsymmetric convention activity coefficients have been calculated using well-known thermodynamic models. These models are nonelectrolyte version of nonrandom factor (NRF) model [16,17], the nonrandom two-liquid (NRTL) model [18], a three-parameter Margules equation [19], and a fourth-order polynomial equation in terms of the molality. The standard deviation of the fitting obtained by considered models has been used in order to comparison the capability of the models. The overall results show that the models express the data within experimental uncertainty, but models with more parameters provide better fittings. In other words, the standard deviations of the polynomial and Margules equations with three and four fitting parameters respectively, are least.

At the next step of this work, we evaluated the activity coefficients of the solutes in the studied solutions. Unsymmetrical activity coefficients of the solutes have been evaluated via model equations with the help of parameters obtained from the fitting of the osmotic coefficients.

* Corresponding author. Tel.: +98 412 4524991; fax: +98 412 4524991.
E-mail address: jsardroodi@azaruniv.edu (J. Jahanbin Sardroodi).

0378-3812/$ – see front matter © 2006 Published by Elsevier B.V.
doi:10.1016/j.fluid.2006.08.020

2. Experimental

2.1. Materials

Methanol and NaI (solute of the isopiestic reference standard solution) used in this work were obtained from Merck. They were analytical pure grade reagent (absolute methanol, GR, minimum 99.8% by mass; NaI, GR, minimum 99.5% by mass). NaI was used without further purification, however was dried in vacuum with the help of a convection oven at about 55–70 °C for 3–5 h prior to use. Methanol was dried by the method described by Vogel [20]. The density, d_0, of pure, dried methanol was measured with a vibrating-tube densimeter as 787.50 kg m^{-3}, which is in reasonable agreement with the literature value [21] of 787.36 kg m^{-3}. The silyl derivatives of acetaminophen used in this work have been prepared in our laboratory following the procedure published in details elsewhere [22].

2.2. Apparatus and procedure

The isopiestic apparatus employed is essentially the same as the one used previously [9–16]. This apparatus consisted of a five-leg manifold attached to round-bottom flasks. The five flasks were typically used as follows. Two flasks contained the standard NaI solutions, two flasks contained investigated solutions, and the central flask was used as a methanol reservoir. The apparatus was held in a constant-temperature bath at least 120 h for equilibration at 298.15 K. The temperature was controlled to within ±0.005 °C with a Heto temperature controller (Hetotherm PF, Heto Lab Equipment, Denmark). After equilibrium had been reached, the manifold assembly was removed from the bath and each flask was weighed with a high precision (10^{-7} kg) analytical balance (Shimadzu, 321-34553, Shimadzu Co., Japan). It was assumed that the equilibrium condition was reached when the differences between the molalities of each duplicate were less than 1%. The equilibrium was reached in a time interval between 5 and 7 days depending on the concentration of the solutions. This interval in which the weights of the samples are reached a constant value, has been determined primarily by continues weighting of a concentrated ($m \approx 7$ mol kg^{-1}) and a dilute sample ($m \approx 0.09$ mol kg^{-1}). In all cases, averages of the duplicates are reported as the final isopiestic molalities. The uncertainty in the measurement of solvent activity as estimated to be ±0.0002.

3. Results and discussions

3.1. Experimental results

At the isopiestic equilibrium, the osmotic coefficient of the investigated solution can be obtained by the help of the relation

$$\Phi = \frac{2m^*}{m}\Phi^* \quad (1)$$

where m and Φ stand for the molality and osmotic coefficient, respectively and the superscript * refers to the reference NaI solution.

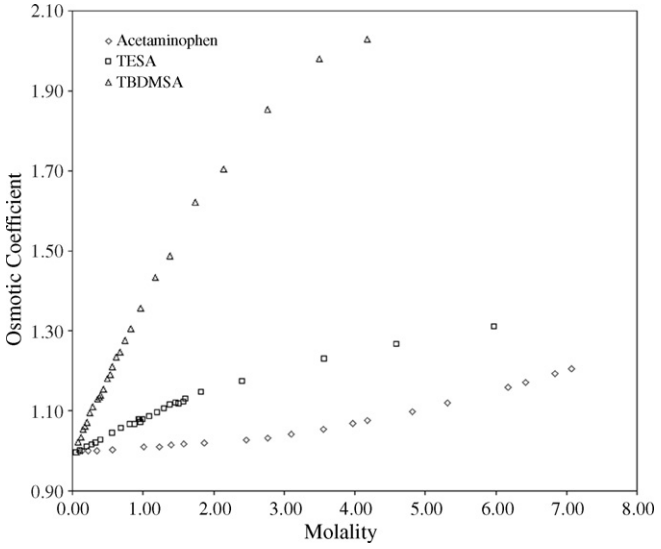

Fig. 1. Isopiestic osmotic coefficients of the studied solutions vs. molality at 298.15 K (TESA: triethylsilylacetaminophen and TBDMSA: tertiarybuthyldimethylsilylacetaminophen).

The osmotic coefficients of the isopiestic reference solution, Φ^*, at the isopiestic equilibrium molalities, m^*, have been evaluated by the Pitzer equation using the parameters reported by Zafarani-Moattar and Nasirzadeh [23]. The osmotic coefficients obtained in this manner are tabulated in Table 1

. This table is also contained the activity coefficients for the solvent and solute. The solvent activity coefficient (γ_1) has been calculated from the experimental osmotic coefficients using the equations:

$$\Phi = -\frac{\ln a_1}{mM_1} \quad (2)$$

$$\ln(\gamma_1) = \ln(a_1) - \ln(x_1) \quad (3)$$

where a_1, M_1 and x_1 are respectively the activity, the molar mass (in kg mol^{-1}) and the mole fraction of methanol. Figs. 1 and 2 are contained osmotic coefficients and activity coefficients of the methanol in the studied solutions versus molality of the solute.

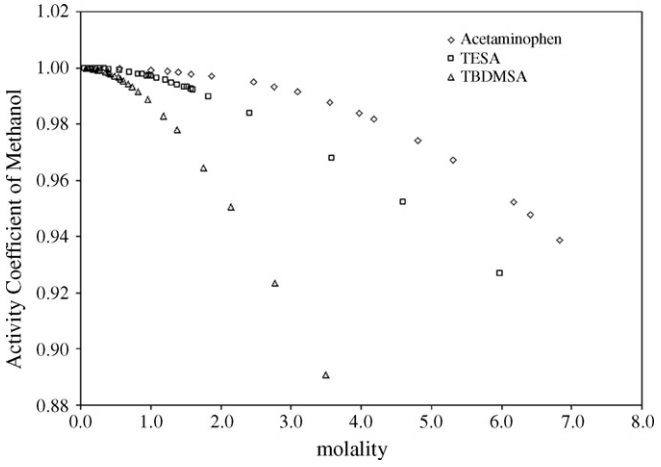

Fig. 2. Molality dependence of the activity coefficient of methanol for the studied solutions at 298.15 K (TESA: triethylsilylacetaminophen and TBDMSA: tertiarybuthyldimethylsilylacetaminophen).