Solubility of *p*-Toluenesulfonamide in Pure and Modified Supercritical Carbon Dioxide

Jia-lin Li, Jun-su Jin,* Ze-ting Zhang, and Xue-mei Pei

College of Chemical Engineering, Beijing University of Chemical Technology, Beijing 100029, China

The experimental equilibrium solubilities of *p*-toluenesulfonamide (*p*-TSA) in supercritical carbon dioxide were measured at temperatures between (308.15 and 328.15) K and for pressures from (8.0 to 21.0) MPa using a dynamic flow method. The solubility ranged from a *p*-TSA mole fraction of $0.97 \cdot 10^{-5}$ (308.15 K, 8.0 MPa) to $5.12 \cdot 10^{-5}$ (328.15 K, 21.0 MPa). The effects of two cosolvents, ethanol and glycol, were investigated at a cosolvent mole concentration of 3.5 %. The results showed that the solubility was greatly enhanced by the presence of both the cosolvents, and ethanol exhibited a higher cosolvent effect. The Peng−Robinson EOS with van der Waals (VDW2) mixing rules was employed to calculate the density of the supercritical carbon dioxide (SC CO_2) + ethanol mixture. The solubility data in the absence and presence of cosolvents were correlated by the Chrastil equation and the modified Mendez-Santiago and Teja equation, respectively. Both the correlations yielded satisfactory results, with average absolute relative deviation (AARD) values less than 6 %.

Introduction

Supercritical fluid (SCF) technology has a great application potential in many industrial processes, such as pharmaceutical, food, dyeing, and polymer processing. For most of the supercritical fluid processes, solubility is the most important criterion affecting the efficacy. A major difficulty in utilizing supercritical fluid technology is the difficulty in measurement and prediction of the solubilities of compounds in supercritical solvents at various pressures and temperatures. The measurement methods of solubility can be divided into two major categories: static and dynamic. The dynamic method has been widely employed in the measurement of solubility. In the method, a supercritical fluid continuously flows through the vessel, which is filled with a solute. A mild flow rate is used so that the outlet stream is assumed to reach equilibrium, which is then analyzed for the solute concentration. Supercritical carbon dioxide (SC CO_2) has been well applied because it is environmentally benign, inexpensive, nontoxic, nonflammable, and has a near-ambient critical temperature. Ram B. Gupta and Jae-Jin Shim have compiled the solubility data in SC CO_2 with and without cosolvents for a variety of compounds.[1]

In this work, the experimental equilibrium solubilities of *p*-toluenesulfonamide (*p*-TSA) in SC CO_2 were measured using a dynamic apparatus. *p*-TSA is used as an intermediate for a number of organic syntheses for the fields of pharmaceuticals, pesticides, dyes, pigments, resins, and other organic target compound preparations.[2] However, the solubility data of *p*-TSA in SC CO_2 has not been reported in the literature. In this work, saturated solubility data of *p*-TSA in supercritical carbon dioxide were measured from (8.0 to 21.0) MPa at (308.15, 318.15, and 328.15) K. As evidenced from experimental results, the SC CO_2 modified by the addition of a small amount of cosolvents can effectively enhance the solubilities;[3] therefore, the cosolvent effects of ethanol and glycol were also studied and compared.

Many developed semiempirical models are often used to correlate solid solubility in SC CO_2. The most common semiempirical models are based upon providing a correlation between solubility and density. In this study, two density-based equations, the Chrastil equation[4] and the modified Mendez-Santiago and Teja equation,[5] were employed to correlate the solubility data.

The present work is a part of our long-term objective to predict the solubility behavior of solutes in supercritical fluids by analyzing the contribution of different classes of functional groups.[6] The solubility determination of *p*-TSA is essential to know the property of the functional group SO_2NH_2, which is a typical functional group in some antibiotic drugs.

Experimental Section

Materials. High-purity CO_2 (a purity of more than 99.9 %) was supplied by Beijing Praxair Industrial Gas Co. Ltd. *p*-TSA (CAS 70-55-3) was obtained from Beijing Chemical Reagent Factory with a minimum purity of 99.0 %. Ethanol and glycol, both analytical grade, were also purchased from Beijing Chemical Reagent Factory with a purity of more than 99.7 % and 99.9 %, respectively. No purification was made for all chemicals before use.

Apparatus and Procedure. The dynamic apparatus for solubility measurements is shown schematically in Figure 1. A detailed description of the apparatus and operating procedure has been reported previously.[7] Liquid CO_2 was directed from a cylinder into a high-pressure syringe pump (Nova, model, 5542121) where it was compressed to the desired operating pressure. After leaving the pump, the pressurized CO_2 entered into the preheating and mixing cell wrapped with a heating coil, thus enabling the CO_2 to reach the desired operating temperature and to be SCF.

The pump used for cosolvents was a high-pressure pump (Beijing Weixing Factory, model LB-10C) that controlled the flow rate. The cosolvent and pure CO_2 mixed sufficiently in the preheating cell and the long coil. Both the coil and the

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* To whom correspondence should be addressed. Tel.: +86-10-64434788. Fax: +86-10-64436781. E-mail: jinjs@mail.buct.edu.cn.

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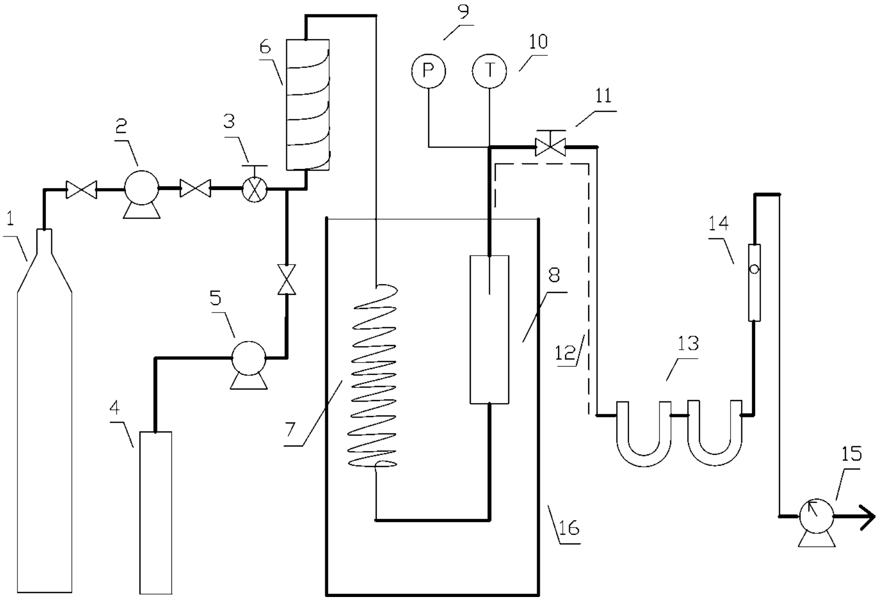

Figure 1. Schematic diagram of the experimental apparatus: 1, CO_2 cylinder; 2, syringe pump; 3, pressure regulating valve; 4, cosolvent vessel; 5, high-pressure pump; 6, preheating and mixing cell; 7, preheating coil; 8, high-pressure equilibrium cell; 9, pressure gauge; 10, thermometer; 11, decompression sampling valve; 12, heating coil; 13, U-shape tube; 14, rotated flow meter; 15, wet-gas flow meter; 16, constant-temperature stirred water bath.

equilibrium cell were immersed in a constant-temperature stirred water bath (Chongqing Yinhe Experimental Instrument Corporation, model CS-530) that maintained a constant temperature to within ± 0.01 K. The temperature and pressure in the cell were measured using an internal platinum resistance thermometer (Beijing Chaoyang Automatic Instrument Factory, model, XMT) at the top of the space above the solute and a calibrated pressure gauge (Heise, Newtown CONN). The accuracy of the temperature measurement is ± 0.1 K, and that for pressure is ± 0.05 MPa.

After achievement of equilibrium in the cell, the saturated SCF stream was depressurized through a metering valve that was wrapped with a heating coil to prevent clogging with dry ice or precipitation of solid solute in the flow line. The solute finally precipitated in the two connected U-shape tubes, and the total volume of CO_2 released during the experiment was measured by the calibrated wet gas flow meter (Changchun Instrument Factory, model LML-2) with an accuracy of ± 0.1 % at room temperature and atmospheric pressure. The solid solute in the U-shape tubes was dissolved in a prepared solvent. An ultrasonic bath was used to ensure a complete dissolution. A model 2100 Unico UV−vis spectrophotometer was used to determine the mass of the solute in the solution. Experiments were performed to establish a calibration curve, and the regression coefficient of the calibration curve is better than 0.9998. The solubility of *p*-TSA was determined from the mass of the solute and the corresponding volume of CO_2 released.

Before each run, about 40 g of *p*-TSA mixed with glass beads was packed into the equilibrium cell. The equilibrium time needed for all the systems studied was found to be within 30 min. Flow rate experiments were carried out to establish the conditions under which equilibrium would be maintained. Measurements were made at various flow rates ranging from (0.2 to 0.6) L·min^{-1}, and the variation of the flow rate in this range was found to have no effect on the observed solubilities. Thus, the flow rate in the range of (0.3 to 0.5) L·min^{-1} was adopted in this work. Each reported datum was an average of at least three replicated sample measurements. The solubility data obtained were found to be reproducible within ± 5 %.

Table 1. Solubilities of *p*-TSA in SC CO_2: SC CO_2 Density ρ, Mole Fraction y, and Concentration S

T/K	P/MPa	ρ/kg·m^{-3}	10^5y	10^4S/g·L^{-1}
308.15	8.0	436.24	0.97	0.75
	11.0	745.54	2.54	1.94
	13.0	786.89	2.81	2.15
	17.0	838.96	3.09	2.36
	21.0	874.40	3.64	2.78
318.15	8.0	241.86	0.56	0.43
	11.0	605.92	2.42	1.85
	13.0	695.25	3.14	2.40
	17.0	776.53	3.69	2.82
	21.0	823.71	4.38	3.35
328.15	8.0	204.05	0.54	0.41
	11.0	417.06	2.22	1.70
	13.0	573.33	3.24	2.48
	17.0	704.97	4.45	3.40
	21.0	768.74	5.12	3.91

Results and Discussion

Solubility of Solid in Pure SC CO_2. The experimental equilibrium solubility data for *p*-TSA in pure SC CO_2 together with the density of carbon dioxide at each operating condition are shown in Table 1. The density data of carbon dioxide were obtained from the National Institute of Standards and Technology Web site. The solubility is expressed in terms of *p*-TSA mole fraction (y) and in terms of mass of the solute per unity of volume of SC CO_2 (S). The relationship between y, the equilibrium mole fraction of the solute in SC CO_2, and P, the total pressure of the system, is illustrated in Figure 2.

Over the entire experimental conditions, the mole fractions of *p*-TSA are in the range of 10^{-5} to 10^{-4}. Since carbon dioxide is nonpolar, the solid−gas equilibrium behavior was governed mainly by the physical interactions. The effect of pressure on the solute solubility follows the expected trends that the solubilities increase with the increase of pressure for all three temperatures investigated. Raising the pressure at constant temperature increases the density of SC CO_2, thereby increasing the specific interaction between the solute and solvent molecules.

The solubility isotherms have a crossover region at pressures around (11.5 to 13.0) MPa as shown in Figure 2, where the three isotherms seem to intercept and cross over each other.

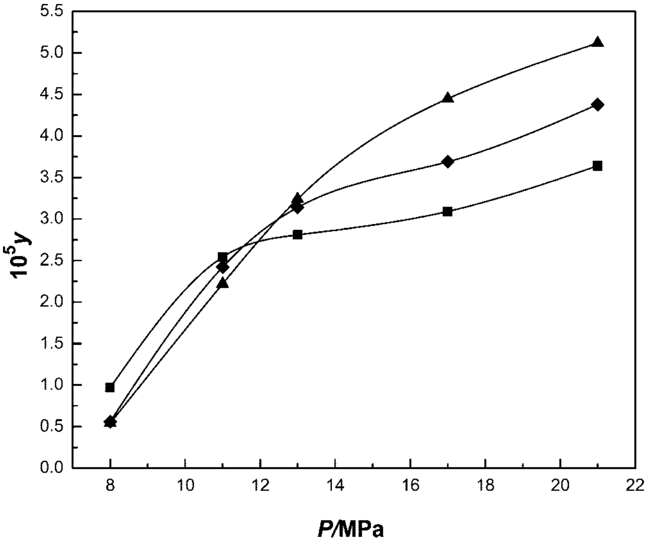

Figure 2. Solubility isotherms of *p*-TSA in SC CO_2 as a function of pressure: ■, $T = 308.15$ K; ◆, $T = 318.15$ K; ▲, $T = 328.15$ K.

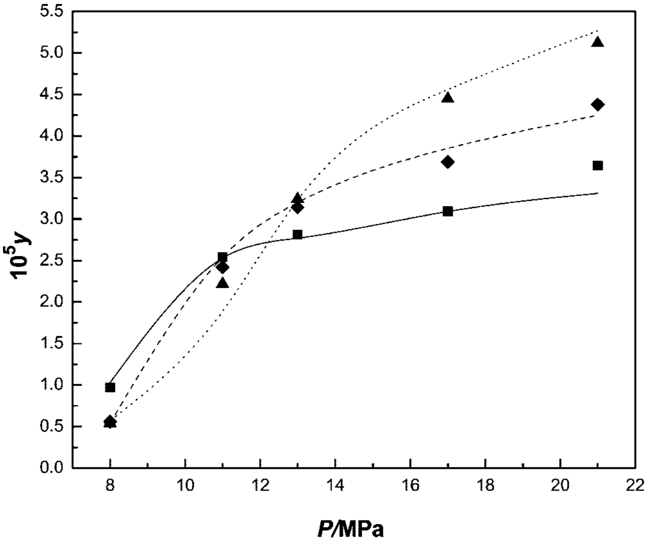

Figure 3. Comparison of experimental solubility of *p*-TSA in SC CO_2 and the calculated results using the Chrastil equation. Experimental data: ■, $T = 308.15$ K; ◆, $T = 318.15$ K; ▲, $T = 328.15$ K. Calculated results: —, 308.15 K; ---, 318.15 K; and •••, 328.15 K.

The solute vapor pressure, solvent density, and intermolecular interactions in the fluid phase are influenced by the system temperature, and their contributions to the solubility of *p*-TSA vary with the temperature. The crossover phenomena could be mainly attributed to the combined effects of increasing solute's vapor pressure and decreasing solvent's density as an increase of temperature.[8]

The results were correlated by the following density-based equation proposed by Chrastil

$$\ln S = k \ln \rho + a/T + b \tag{1}$$

where S ($g \cdot L^{-1}$) is the solubility of the solute in the supercritical fluid; ρ ($kg \cdot m^{-3}$) is the density of the supercritical fluid; k is an association number; a is a function of the heat of solvation and heat of vaporization; b is a function of the molecular weights of the solute and supercritical fluid; and T (K) is temperature.

The quality of all data correlations is quantified by the average absolute relative deviation (AARD), defined as follows

$$\text{AARD}\,(\%) = \frac{100}{n}\sum_{1}^{n}\frac{|S_{\text{cal}} - S_{\text{exp}}|}{S_{\text{exp}}} \tag{2}$$

The Chrastil equation was successfully correlated, with an AARD of 4.2 % and a regression coefficient r_2 of 0.9929 (r_2 = ssreg/sstotal). The values for a, b, and k regressed from the experimental solubility data were determined to be −3464, −8.444, and 1.685, respectively. Figure 3 shows the comparison of experimental solubility data of *p*-TSA in SC CO_2 and the calculated results using the Chrastil equation.

Table 2. Solubilities of *p*-TSA in Modified SC CO_2: Modified SC CO_2 Density ρ_f, Mole Fraction y', and Enhancement Factor e

T/K	cosolvent	P/MPa	$10^5y'$	e	$\rho_f/kg \cdot m^{-3}$
308.15	ethanol	8.0	1.69	1.74	675.0
		11.0	4.65	1.83	763.5
		13.0	5.98	2.13	800.5
		17.0	8.41	2.72	854.7
		21.0	9.89	2.72	895.0
318.15	ethanol	8.0	0.94	1.68	343.0
		11.0	3.96	1.64	655.4
		13.0	5.87	1.87	713.9
		17.0	9.78	2.65	788.2
		1.0	13.17	3.01	838.9
328.15	ethanol	8.0	0.78	1.44	236.7
		11.0	3.34	1.50	513.7
		13.0	5.44	1.68	612.2
		17.0	10.51	2.36	715.8
		21.0	15.15	2.96	779.5
308.15	glycol	8.0	1.07	1.10	
		11.0	2.91	1.15	
		13.0	3.44	1.22	
		17.0	4.65	1.50	
		21.0	6.22	1.71	

Solubility of Solid in Modified SC CO_2. The addition of small amounts of cosolvents can greatly increase the solubilities of solutes in the SCF, which is an effective method to expand the application of SCF. Since CO_2 is nonpolar, some polar cosolvents, such as ethanol and methanol, have been widely used to improve the solubility of polar organic compounds in SC CO_2. In this study, the effects of two cosolvents, ethanol and glycol, were investigated at a cosolvent mole concentration of 3.5 %. Table 2 presents the experimental saturated solubility data, at temperatures between (308.15 and 328.15) K and pressures ranging from (8.0 to 21.0) MPa. For comparison of the effects, the enhancement factors of the two cosolvents are also shown. The enhancement factor e was defined as the ratio of the solubility obtained with cosolvents, $y'(P, T, y_3 = 0.035)$, to that obtained without cosolvents at the same temperature and pressure, y $(P, T, y_3 = 0)$, and was depicted as

$$e = \frac{y'(P, T, y_3 = 0.035)}{y(P, T, y_3 = 0)} \tag{3}$$

As seen from the tabulated values, the magnitudes of equilibrium solubility are effectively enhanced by the presence of both the cosolvents. Specific hydrogen bonds are expected to be formed between the group SO_2NH_2 of *p*-TSA and the hydroxyl group of ethanol or glycol. The solubility enhancement obtained for ethanol is much more pronounced than that for glycol at 308.15 K. The difference of the solubility enhancement between ethanol and glycol is probably due to the stronger hydrogen bond property of ethanol. Though glycol has a higher solvent polarity value, the β-scale of solvent hydrogen-bond acceptor basicity for ethanol, $\beta = 0.77$, is greater than that of glycol, for which $\beta = 0.51$, which results in a higher capacity of ethanol to form hydrogen bonds with *p*-TSA.[9,10]

The relationship between y', the equilibrium mole fraction of the solute in the ethanol modified SC CO_2, and P, the total

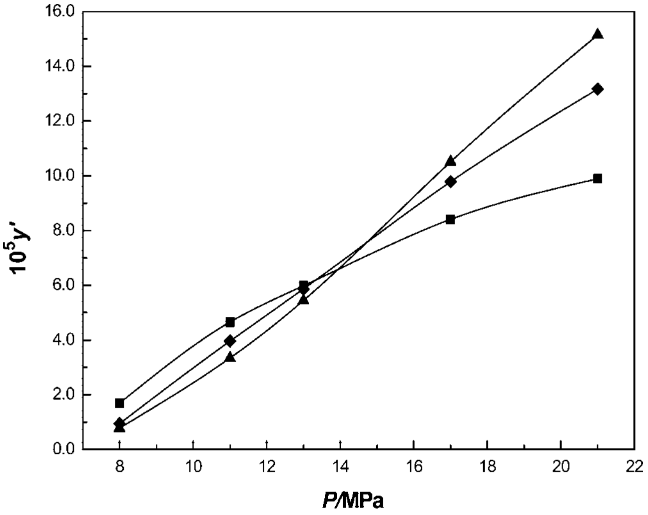

Figure 4. Solubility isotherms of *p*-TSA in ethanol modified SC CO_2 as a function of pressure: ■, $T = 308.15$ K; ◆, $T = 318.15$ K; ▲, $T = 328.15$ K.

pressure of the system, was illustrated in Figure 4. *p*-TSA in the SC CO_2 + ethanol mixture exhibited "crossover" behavior similar to that seen in pure CO_2. The addition of ethanol results in a crossover region at pressures around (13.5 to 15.0) MPa as shown in Figure 4, higher than that in pure SC CO_2. Similar shifts of the crossover pressure have been observed by other researchers.[11,12]

Mendez-Santiago and Teja have presented a semiempirical density-based model for ternary cosolvent systems.[13] An equation that follows a simple relationship for the solubility of solids in modified supercritical fluids was expressed as

$$T \ln\left(\frac{y' \cdot P}{P^{\mathrm{sub}}}\right) = A + B\rho + Cx$$

where y' is the solubility of solute in the fluid (solvent + cosolvent mixture); P^{sub} (Pa) is the sublimation pressure of the solid at temperature T (K); ρ (kg·m^{-3}) is the pure solvent density (cosolvent and solute free); x is the mole fraction of cosolvent; and A, B, and C are adjustable parameters independent of T and P.

Because the sublimation pressures of the solid are not often available, a modified Mendez-Santiago and Teja equation was proposed by Sauceau et al.,[5] which was expressed as

$$T \ln\left(\frac{y' \cdot P}{P^{\mathrm{std}}}\right) = A + B\rho_{\mathrm{f}} + Cx + DT \quad (4)$$

where P^{std} is the standard pressure; ρ_{f} (kg·m^{-3}) is the density of the fluid (solvent + cosolvent mixture); and A, B, C, and D are adjustable parameters.

The solubility data of *p*-TSA with an ethanol cosolvent was correlated with the modified Mendez-Santiago and Teja equation. In the present work, x is a constant of 0.035, thereby leading to the following equation with three adjustable parameters

$$T \ln\left(\frac{y' \cdot P}{P^{\mathrm{std}}}\right) = A' + B\rho_{\mathrm{f}} + DT \quad (5)$$

where $A' = A + Cx$.

The density of the fluid, ρ_{f}, which is shown in Table 2, is calculated by using the Peng–Robinson equation of state[14] with the van der Waals mixing rules (VDW2) with two binary interaction parameters.[15]

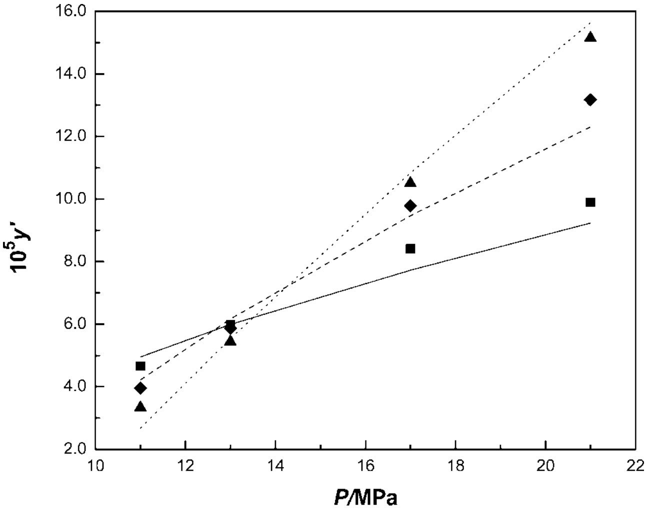

Figure 5. Comparison of experimental solubility data of *p*-TSA in ethanol modified SC CO_2 and the calculated data using the modified Mendez-Santiago and Teja equation. Experimental data: ■, $T = 308.15$ K; ◆, $T = 318.15$ K; ▲, $T = 328.15$ K. Calculated results: —, 308.15 K; ---, 318.15 K; and ···, 328.15 K.

In a first attempt, all the solubility data with ethanol cosolvent were treated. The correlation received an AARD of 21.3 %. Furthermore, in the next correlation, the solubility data except the ones at 8.0 MPa were well fit with an AARD of 5.9 % and a regression coefficient r_2 of 0.9878. The second multiple linear regression yielded $A' = -10623$ K, $B = 2.9774$ K·m^3·kg^{-1}, and $D = 21.882$ (with units for T in K, P in Pa, and ρ_{f} in kg·m^{-3}). As an illustrative case, Figure 5 compares the calculated results with the experimental solubility values of the CO_2 + ethanol solvent with the exception of the ones at 8.0 MPa. Mendez-Santiago and Teja noticed a low density limit of about 0.5 ρ_c (critical density) of solvent for the models in their works.[15,16] Therefore, the relative low density of the CO_2 + ethanol mixture at 8.0 MPa may contribute to the difference of the two correlations.

Conclusion

The solubilities of *p*-TSA in supercritical CO_2 with and without cosolvents were measured at (308.15, 318.15, and 328.15) K between (8.0 and 21.0) MPa. The crossover behavior was also found both in the SC CO_2 + *p*-TSA binary system [(11.5 to 13.0) MPa] and in the SC CO_2 + *p*-TSA + ethanol ternary system [(13.5 to 15.0) MPa]. Ethanol exhibited a higher cosolvent effect than glycol. The experimental data in pure SC CO_2 was successfully correlated by the Chrastil equation, with an AARD of 4.2 %. The modified Mendez-Santiago and Teja equation was used to correlate the solubility data in ethanol-modified SC CO_2, and the correlation of the data with the exception of the ones at 8.0 MPa yielded satisfactory results, with an AARD of 5.9 %.

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