Solvent Effects on Esterification Equilibria

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DOI 10.1002/aic.14873

Solvents are known to have strong impacts on the yields of equilibrium reactions. This work focuses on the thermodynamic investigation of these solvent effects on esterification reactions of acetic acid and propionic acid with ethanol. Esterification of acetic acid was performed in the solvents acetone, acetonitrile (ACN), dimethylformamide (DMF), and tetrahydrofurane as well as in mixtures thereof. ACN promotes the esterification of acetic acid, whereas it is strongly suppressed by DMF. The esterification of propionic acid was investigated with various reactant concentrations in acetone. The experimental equilibrium data in pure solvents and solvent mixtures were modeled using the thermodynamic equilibrium constant K_a and the reactant/product activity coefficients predicted by the perturbed chain-statistical associating fluid theory (PC-SAFT). For a given K_a, PC-SAFT is able to predict the influence of the solvent and even solvent mixtures on the equilibrium concentrations of esterification in almost quantitative agreement with the experimental data.

Keywords: reaction equilibrium, perturbed chain-statistical associating fluid theory, esterification

Introduction

Solvents create the reaction environment for liquid-phase reactions. Therefore, solvents have a strong influence on reaction kinetics and yields.[1] The selection of the solvent also affects the succeeding purification steps and, therefore, is quite important for the efficiency of a reaction process. In addition to the application of pure solvents, solvent mixtures are also used to facilitate catalyst recycling or to provide specific properties to reaction media.

Solvent effects were first described by Berthelot and Péan de Saint-Gilles[2] in 1862. They reported a suppressive effect of solvents on the esterification reaction of ethanol and acetic acid. Today, solvent effects are described in the literature for a variety of equilibrium reactions,[1–4] including tautomerizations, other isomerizations, electron-transfer reactions, host/guest complexations, and acid/base equilibria.[1] Solvent effects can support or suppress reaction kinetics, reaction equilibria, and consequently, yields.[1–5] Moreover, a strong impact of solvents on the selectivity in complex reaction systems is described in the literature.[3–5]

The state-of-the-art modeling of solvent effects on reaction equilibria is so far mainly based on considering the solubilities of the reactants or other properties, such as Gibbs energies of solvation. A comprehensive overview of this topic is given by Reichardt and Welton.[1] Solvent effects on esterification reactions have not yet been modeled.

Moreover, the reactants themselves can act as solvents and affect the reaction equilibria, resulting in concentration-dependent apparent equilibrium constants.[6,7] This was investigated for the ethanol/acetic acid[6] and butanol/acetic acid[7] reactions, where the vapor-liquid equilibria (VLE) and reaction equilibria were considered simultaneously in the context of reactive distillation. Several thermodynamic models (NRTL, UNIQUAC, PC-SAFT, and COSMO-RS) were applied to describe the activity coefficients of the reactants and products and, thus, the temperature dependence and concentration dependence of the equilibrium concentrations in the solvent-free butanol/acetic acid esterification[7]; PC-SAFT was shown to describe the temperature dependence of the equilibrium concentrations qualitatively correct.[7] Moreover, ePC-SAFT was recently used to predict CO_2 solubility in aqueous, amine-containing systems with simultaneous calculation of the complexation reaction.[8]

In this work, the influence of the solvents and solvent mixtures on the equilibrium concentrations of various esterification reactions was investigated. Esterification reactions were chosen as model reaction for liquid-phase reactions. The equilibrium concentrations in various solvents and solvent mixtures were measured for the esterification of acetic acid and propionic acid and compared with those obtained from

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This article was submitted in honor of John M. Prausnitz.

Thank you, John for your ongoing interest in our work, for your support, and for all that you did for the entire thermodynamics community. You always taught us that thermodynamics is not just "gray theory" but is a favorable combination of both theory and experiments. This article perfectly demonstrates that you are completely right!

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(solvent-independent) thermodynamic equilibrium constants and reactants'/products' activity coefficients. The latter were again obtained using PC-SAFT, which specifically accounts for association among the components involved in esterification reactions. Only binary VLE data were used to determine the model parameters.

Theory

The standard Gibbs energy of reaction $\Delta^{\mathrm{R}} g^{+}$ can be obtained from Eq. 1

$$\Delta^{\mathrm{R}} g^{+}(T,p) = \sum_i v_i \Delta^{\mathrm{F}} g_{0i}^{+} = \; -RT \cdot \ln K_a \tag{1}$$

Here, T is the temperature, R is the universal gas constant, $\Delta^{\mathrm{F}} g_{0i}^{+}$ are standard Gibbs energies of formation and the v_i are the stoichiometric coefficients of the reactants and products. K_a is the thermodynamic equilibrium constant based on the activities a_i of the reactants and products according to Eq. 2

$$K_a = \prod\nolimits_i a_i^{v_i} = \underbrace{\prod_i \mathrm{x}_i^{v_i}}_{K_x} \cdot \underbrace{\prod_i \gamma_i^{v_i}}_{K_\gamma} \tag{2}$$

The thermodynamic equilibrium constant results from the product of the mole-fraction-based apparent equilibrium constant K_x and an activity-coefficient-based contribution K_γ.

K_a only depends on temperature. It does not depend on the concentrations of the reactants and products or on the solvents. In contrast, K_γ depends on both the concentration and the type of solvents, as does K_x. For a given K_a, K_x can be calculated using Eq. 2 once K_γ is known. The latter can be calculated from the activity coefficients of the reactants and products obtained using an appropriate thermodynamic model.

In this work, the activity coefficients were calculated from the fugacity coefficients using Eq. 3

$$\gamma_i = \frac{\varphi_i}{\varphi_{0i}} \tag{3}$$

where φ_i is the fugacity coefficient of component i in the reaction mixture and φ_{0i} is the fugacity coefficient of the pure component i. The fugacity coefficients were derived from the residual Helmholtz energy A^{residual} according to

$$\ln \varphi_i = \frac{1}{RT}\left(\frac{\partial A^{\mathrm{residual}}}{\partial n_i}\right)_{T,V,n_{j\neq i}} - \ln\left(\frac{pv}{RT}\right) \tag{4}$$

where n_i is the mole number of component i, p is the pressure, and v is the molar volume of the system. The residual Helmholtz energy was calculated from PC-SAFT[9,10]

$$A^{\mathrm{residual}} = A^{\mathrm{hard-chain}} + A^{\mathrm{dispersion}} + A^{\mathrm{association}} \tag{5}$$

According to PC-SAFT, the residual Helmholtz energy is calculated from a repulsive (hard-chain) contribution and attractive contributions, which separately account for dispersion (van der Waals attraction) and association (formation of hydrogen bonds).

Within PC-SAFT, a molecule i is described as a chain of m_i segments, where each segment has a segment diameter σ_i. The dispersive interaction is characterized by the dispersion-energy parameter $\frac{u_i}{k_B^{-1}}$. Associative interactions are described by two parameters, the association volume $\kappa_{A_iB_i}$ and the association energy $\frac{\varepsilon_{A_iB_i}}{k_B^{-1}}$ between N_i association sites. Associating molecules, such as water, alcohols, or acids, require five parameters for a description with PC-SAFT, whereas non-associating molecules, such as ethyl acetate or the solvents considered within this work, require only three parameters. These parameters are usually obtained from regression to vapor pressures and liquid density data of the pure components.

Table 1. Chemicals Used Within This Study

Chemical	Supplier	Purity (%)
Acetic acid	Merck KGaA	99.8
Acetone	Merck KGaA	99.0
Acetonitrile	Prolabo	99.9
H_2SO_4	Merck KGaA	98.0
Dimethylformamide	Prolabo	99.8
Ethanol	Merck KGaA	99.9
Ethyl acetate	Acros Organics	99.9
Ethyl propionate	Sigma Aldrich	99.0
Propionic acid	Sigma Aldrich	99.5
Tetrahydrofurane	Prolabo	99.7

Berthelot–Lorenz combining rules are applied to model mixtures of components i and j as described in Eqs. 6 and 7

$$\sigma_{ij} = \frac{\left(\sigma_i + \sigma_j\right)}{2} \tag{6}$$

$$u_{ij} = \; \sqrt{u_i u_j}\left(1 - k_{ij}\right) \tag{7}$$

k_{ij} in Eq. 7 is a binary interaction parameter, which is usually fitted to binary phase-equilibrium data to correct the dispersion energy in a binary system of unlike species. Cross-association is calculated using combining rules as suggested by Wolbach and Sandler[11] without further parameter fitting according to Eqs. 8 and 9

$$\varepsilon^{A_iB_j} = \frac{\left(\varepsilon^{A_iB_i} + \varepsilon^{A_jB_j}\right)}{2} \tag{8}$$

$$\kappa^{A_iB_j} = \sqrt{\kappa^{A_iB_i}\kappa^{A_jB_j}}\left(\frac{\sqrt{\sigma_i\sigma_j}}{\frac{1}{2}\left(\sigma_i + \sigma_j\right)}\right)^3 \tag{9}$$

Materials

Information on the purities and suppliers of all of the chemicals used in this work is reported in Table 1. All chemicals were applied without further purification. Deionized water was used in the preparation of the standards for gas chromatography (GC).

Reaction Experiments

Reaction mixtures were prepared in 25-mL Erlenmeyer flasks using a balance with an accuracy of ±0.1 mg. All reaction mixtures initially contained 0.4 mol of the reactants and solvents. Then, 0.1 g of 98% H_2SO_4 $(\cong x_{\mathrm{H_2SO_4}} = 0.003)$ was added as a catalyst. The initial concentrations of the carboxylic acid and ethanol were chosen according to the mole-fraction ratios of $\frac{x_{\mathrm{carboxylic\ \ acid}}}{x_{\mathrm{ethanol}}} = \frac{3}{1}; \frac{1}{1}; \frac{1}{3}$

The reaction experiments were performed in an oil bath. The oil bath was placed on an electrical-heating plate combined with a magnetic stirrer (RCT classic IKAMAG® safety control, IKA, Staufen, Germany). The temperature was controlled within ±0.5 K. All reactions were performed at 313.15 K and atmospheric pressure.

The progress of the reaction was monitored by the water content, which was measured using Karl–Fisher titration in triplicate (Metrohm 915 KF Ti-Touch, Metrohm, Herisau,

Table 2. Equilibrium Concentrations of the Esterification Reaction of Acetic Acid and Ethanol at 313.15 K and Activity Coefficients of Reactants and Products Obtained with PC-SAFT Using Parameters from Tables 3 and 4

Initial Mole-Fraction Ratio Ethanol/Acetic Acid	$^1/_3$		$^1/_1$		$^1/_1$		$^3/_1$	
	x	$\gamma_{\text{PC-SAFT}}$	x	$\gamma_{\text{PC-SAFT}}$	x	$\gamma_{\text{PC-SAFT}}$	x	$\gamma_{\text{PC-SAFT}}$
Ethanol	0.014	1.2554	0.146	1.2558	0.172	1.2227	0.542	1.0540
Acetic acid	0.512	0.7663	0.190	0.5326	0.181	0.5198	0.035	0.5172
Water	0.241	1.7668	0.382	1.8423	0.33	1.9741	0.228	2.1466
Ethyl acetate	0.234	1.2680	0.283	1.9598	0.317	1.8586	0.196	2.0888
K_x/K_γ	7.7 ± 0.2	2.33	3.9 ± 0.1	5.40	3.4 ± 0.1	5.77	2.32 ± 0.05	8.23
K_a	17.95		21.05		19.32		19.09	

Switzerland). After the water content was constant for at least 1 h, the reaction was assumed to be in equilibrium and the concentrations were analyzed using a gas chromatograph Agilent 7890A equipped with an Agilent INNOWax (30 m, 0.32 mm, 0.5 µm) column and a thermal-conductivity detector.

GC measurements were calibrated separately for each reaction system and quantification of the components was performed in triplicate. The uncertainties in the K_x values were determined from the maximum of the standard deviations of the resulting K_x values and via uncertainty propagation from the GC measurements; these values are given in Tables 2, 7, and A1–A10.

Results and Discussion

Esterification of acetic acid

Equilibrium Concentrations in the Solvent-Free System. The reaction equilibria were experimentally investigated for the esterification of acetic acid and ethanol (Eq. 10) at varying reactant starting concentrations and 313.15 K.

$$C_2H_5OH + CH_3COOH \leftrightarrow H_2O + CH_3COOC_2H_5 \qquad (10)$$

Experimental data on the equilibrium concentrations of reactants and products are reported in Table 2 and depicted in Figure 1.

As expected, an initial excess of acetic acid (low ethanol concentrations) shifts the equilibrium to the product side. High K_x values of 7.7–7.8 were observed. However, an excess of ethanol suppresses the esterification reaction, leading to low K_x values of 2.3. This observation agrees with the results from the literature, where high alcohol concentrations that result in low K_x values for butanol esterification are described.[7]

The activity coefficients of the reactants (ethanol and acetic acid) and products (ethyl acetate and water) were calculated with PC-SAFT using the pure-component parameters summarized in Table 3 and binary interaction parameters as reported in Table 4. The binary interaction parameters were fitted to the binary VLE data[12–16] only at different temperatures than the reaction. In addition to the binary interaction parameters, the average absolute deviations (AAD) and average relative deviations (ARD) to referenced literature data are reported in Table 4. The resulting activity coefficients of the four components of the reaction system are listed in Table 2.

Based on the activity coefficients, K_γ was calculated to finally obtain the thermodynamic equilibrium constant K_a according to Eq. 2. The resulting thermodynamic equilibrium constants are given in Table 2 and are depicted in Figure 2.

Following from Eq. 1, K_a should be constant over the entire concentration range. The average thermodynamic equilibrium constant K_a obtained using PC-SAFT from Table 2 is 19.4 ± 1.3. The corresponding standard Gibbs energy of reaction calculated using Eq. 1 is $\Delta^R g^+_{\text{this work}} = -7.7 \pm 0.2\,\frac{\text{kJ}}{\text{mol}}$, which is in the order of the literature data obtained from the Gibbs energies of formation[27–32] ($\Delta^R g^+ = -6.2 \pm 1.4\,\frac{\text{kJ}}{\text{mol}}$) and the value reported by Essex and Clark[28,33] ($\Delta^R g^+ = -6.5\,\frac{\text{kJ}}{\text{mol}}$).

Using the average value of $K_a = 19.4$ and the K_γ values from PC-SAFT, the K_x values can almost quantitatively be described with an AAD of 0.15 and a corresponding ARD of 3.37% (Figure 1).

For comparison, the activity coefficients at the concentrations given in Table 2 were also predicted using the state-of-the-art g^E-models UNIFAC (Dortmund),[34] NRTL-SAC,[35] and COSMO-RS.[36] The calculations using UNIFAC (Dortmund) and NRTL-SAC were performed with ASPEN® Properties V8.4; the COSMO-RS calculations were kindly performed by Kai Leonhard from Aachen, Germany. The results for K_a obtained from these models (K_γ) and the experimental K_x (Table 2) obtained in this work are also shown in Figure 2.

A strong scattering of K_a values is observed, which is much larger than the scattering of the K_a values obtained based on PC-SAFT. The resulting thermodynamic equilibrium constants scatter around their mean value by 5.5 for UNIFAC (Dortmund), 6.0 for NRTL-SAC, 4.2 for COSMO-RS, and 1.3 for PC-SAFT, which might be explained by the more accurate description of the association interactions within PC-SAFT. The SAFT-based models explicitly consider cross association between different molecules. As three (alcohol, acids, and water) out of the four reacting molecules interact via cross-

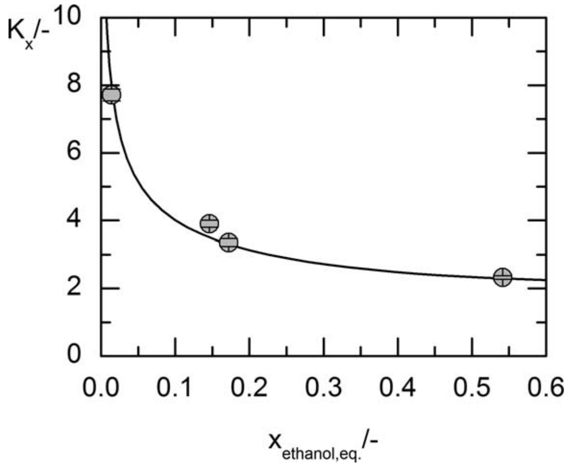

Figure 1. K_x of the esterification of acetic acid and ethanol at 313.15 K and atmospheric pressure as a function of the equilibrium mole fraction of ethanol $x_{\text{ethanol,eq}}$.

The symbols are experimental data as reported in Table 2. The line is the PC-SAFT model with the parameters from Tables 3 and 4 and $K_a = 19.4$.

Table 3. PC-SAFT Pure-Component Parameters Used Within This Study

Substance	m	σ(Å)	u/k_B (K)	N_i	$\varepsilon_{A_iB_i}/k_B$ (K)	$\kappa_{A_iB_i}$	Reference
Acetic acid	1.3403	3.8582	211.59	2	3044.4	0.07555	10
Acetone	2.8287	3.2497	250.26	–	–	–	17
Acetonitrile	2.3290	3.1898	311.31	–	–	–	17
Dimethylformamide	2.3880	3.6580	363.77	–	–	–	17
Ethanol	2.3827	3.1771	198.24	2	2653.4	0.03238	10
Ethyl acetate	3.5375	3.3079	230.80	–	–	–	9
Ethyl propionate	3.8371	3.4031	232.78	–	–	–	9
Propionic acid	3.7069	2.9937	200.73	2	2173.4	0.3205	18
Tetrahydrofurane	2.4250	3.4966	280.41	–	–	–	This study[a]
Water	1.0656	3.0007	366.51	2	2500.7	0.03487	10

[a] Ref. VLE data: 19–24.

association, this model leads to a superior description of the four-component system compared with the other models. The larger deviations obtained for the g^E-models are even more surprising because the accuracies of these models are quite comparable to PC-SAFT when calculating the VLE of the binary subsystems (Table 5). The average ARDs for the six binary subsystems are 3.33% for UNIFAC (Dortmund), 2.35% for NRTL-SAC, and 2.21% for PC-SAFT, which means that the VLE modeling with PC-SAFT is not significantly better for the VLE of the binary systems but provides a better description of the four-component reaction equilibrium.

To understand the influence of ethanol on K_γ and, thus, on K_x, the activity coefficients of the reactants and products as calculated by PC-SAFT are shown as functions of the ethanol mole fraction at equilibrium in Figure 3. While the activity coefficients of the reactants (acetic acid and ethanol) are almost constant, the activity coefficients of the products (water and ethyl acetate) increase with increasing ethanol concentration, as is already known from the respective binary systems.[37–39] According to Eq. 11, the fact that K_a is a constant is the reason for the lower K_x values at high ethanol concentrations.

$$K_x = K_a \cdot \frac{\prod \gamma_{\text{reactants}}^{\nu_i}}{\prod \gamma_{\text{products}}^{\nu_i}} \tag{11}$$

Pure-Solvent Effects on Acetic Acid Esterification. To evaluate the effects of different solvents, the esterification of acetic acid was performed in acetone, acetonitrile (ACN), dimethylformamide (DMF), and tetrahydrofurane (THF). The broad variety of different types of solvents allows for a general evaluation of the presented approach. These solvents were chosen to assure complete miscibility of all involved substances (reactants and products) and to avoid the formation of a second liquid phase. To predict the effects of these solvents on the esterification equilibrium, the binary interaction parameters between the reactants and products on one side and each of the solvents on the other side were fitted to the binary VLE data using the pure-component parameters from Table 3. The resulting binary parameters are reported in Table 6.

Using these parameters, the activity coefficients of the reactants and products in the mixtures with the respective solvents and, thus, the K_γ values for esterification in these solvents were predicted. Figure 4 shows the K_x values finally obtained from Eq. 11 for solvent mole fractions of 0.5 compared with the experimental data. The initial reactant ratios were chosen as in the solvent-free investigations (Table 5). The corresponding experimentally obtained equilibrium concentrations are reported in Appendix (Tables A1–A4).

As shown in the experimental data in Figure 4, ACN promotes the esterification reaction, leading to higher K_x values than in the solvent-free system. In contrast, DMF strongly suppresses the reaction resulting in K_x values below unity, as described earlier by Berthelot and Péan de Saint-Gilles.[2] Acetone suppresses the esterification reaction at low ethanol concentrations but promotes it in conditions with excess ethanol, where higher K_x values were found than in the solvent-free reaction system. THF suppresses the reaction resulting in K_x values between those of the solvent-free system and the DMF system.

Using the above-determined K_a of 19.4 and applying the binary interaction parameters from Tables 4 and 6 together with the pure-component parameters from Table 3, PC-SAFT predicts K_x values that are comparable to the experimental data with AADs and ARDs of 0.35 and 6.64% for acetone, 0.22 and 3.63% for ACN, 0.09 and 28.62% for DMF, and 0.39 and 25.22% for THF. The high ARD for DMF results from the K_x values between 0.08 and 0.63, which are much smaller than for the other systems. The effect of THF is also well predicted with the exception of only one data point in the excess ethanol conditions, where the solvent effect is underestimated by PC-

Table 4. Binary Interaction Parameters for PC-SAFT Between Reactants and Products Used Within This Study

Substance i	Substance j	k_{ij}	AAD	ARD (%)	Reference for Phase Equilibrium Data
Acetic acid	Ethanol	−0.03	473 Pa	2.86	12
Acetic acid	Ethyl acetate	−0.15	3.16 K	0.86	16
Acetic acid	Water	−0.13	559 Pa	2.41	12
Ethanol	Ethyl acetate	−0.02	1.64 K	0.47	13
Ethanol	Water	−0.02	700 Pa	2.87	25
Ethyl acetate	Water	−0.08	13.31 K	3.78	15
Ethyl Propionate	Water	−0.15	–	–	26
Propionic acid	Ethanol	0	674 Pa	5.43	12
Propionic acid	Ethyl propionate	−0.05	627 Pa	9.03	12,16
Propionic acid	Water	−0.01	1993 Pa	10.98	12

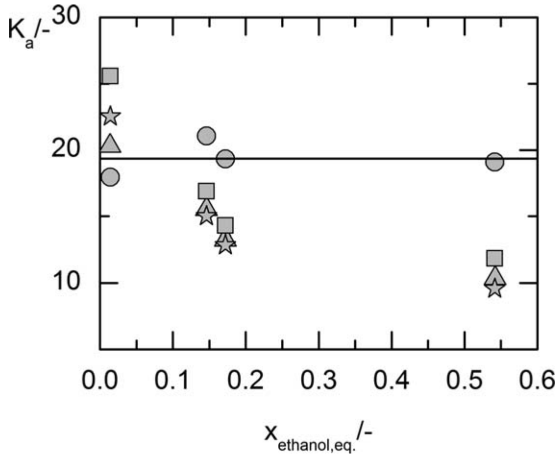

Figure 2. Thermodynamic equilibrium constants (K_a) for the esterification of acetic acid and ethanol at 313.15 K obtained at various equilibrium concentrations shown in Table 2 as functions of the equilibrium mole fractions of ethanol.

The K_γ values were obtained from different models: PC-SAFT (circles), UNIFAC (Dortmund) (stars), NRTL-SAC (squares), and COSMO-RS (triangles). The solid line corresponds to $K_a = 19.4$.

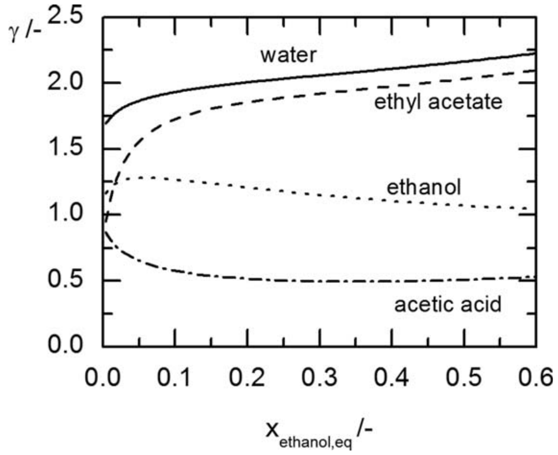

Figure 3. Activity coefficients of ethanol (dotted line), acetic acid (dashed-dotted line), water (solid line), and ethyl acetate (dashed line) as functions of the mole fraction of ethanol in equilibrium at 313.15 K, as predicted by PC-SAFT using the parameters in Tables 3 and 4 and $K_a = 19.4$.

SAFT. It should be mentioned that all binary PC-SAFT parameters were fitted to VLE data only, and none of the experimentally found K_x data were used for parameter estimation. Therefore, the predictions of the pure-solvent effects on the reaction equilibrium are in remarkably good agreement with the experimental data.

An explanation for the solvent influence on K_x can again be obtained by looking at the influence of the solvents on the activity coefficients of the reactants and products. As ACN and DMF had the greatest impact, the activity coefficients in the reaction mixtures containing ACN (Figure 5) and DMF (Figure 6) were considered in more detail.

The activity coefficient of acetic acid in the ACN system is quite similar to that in the solvent-free system, whereas the activity coefficient of ethanol increases significantly when dissolved in ACN (Figure 5a). This result most likely occurs because the number of hydrogen bonds formed by ethanol molecules decreases considerably when diluted in ACN because the latter is not able to interact via hydrogen bonds. The product activity coefficients are differently affected by ACN (Figure 5b): the water activity coefficient increases in ACN compared with the solvent-free system (most likely for the same reason as ethanol), whereas the ethyl acetate activity coefficient decreases in the presence of ACN. Assuming that the latter effects cancel out in Eq. 11, the increase in the ethanol activity coefficient in ACN ultimately leads to the increase in K_x when the esterification is performed in ACN compared with the solvent-free system.

For the esterification in DMF, the reactant activity coefficients both decrease compared with the solvent-free system (Figure 6a), whereas higher activity coefficients for both products were obtained in mixtures with DMF compared with the solvent-free system (Figure 6b). According to Eq. 11, the two effects add up, leading to the very low K_x values observed for the reaction in DMF.

Mixed-Solvent Effects on Acetic Acid Esterification. Finally, the ability of PC-SAFT to predict the effects in solvent mixtures was examined. Binary interaction parameters between the previously investigated solvents were fitted for that purpose to binary VLE data and are reported in Table 6.

As before, the above-determined K_a of 19.4 was used, and the activity coefficients of the reactants and product in the mixed-solvent reaction mixture were predicted without any additional parameter fitting. K_x for the esterification in mixed solvents (overall solvent concentration $x_{\text{solvents}} = 0.5$) were predicted for the solvent mixtures of ACN mixed with acetone or THF (Figure 7a) and for DMF mixed with ACN, acetone, or THF (Figure 7b). The corresponding experimental data are reported in Appendix (Tables A5–A9).

In the case of acetone/ACN, an almost linear increase of K_x as a function of the ACN mole fraction was observed in the experiments (Figure 7a). The model also predicts an almost

Table 5. Comparison of the Phase-Equilibrium Calculations for the Binary Subsystems

		PC-SAFT		UNIFAC (DORTMUND)		NRTL-SAC	
Substance *i*	Substance *j*	AAD	ARD (%)	AAD	ARD (%)	AAD	ARD (%)
Acetic acid	Ethanol	473 Pa	2.86	1590 Pa	10.67	702 Pa	4.41
Acetic acid	Ethyl acetate	3.16 K	0.86	1.01 K	0.27	2.04 K	0.56
Acetic acid	Water	559 Pa	2.41	1693 Pa	6.21	630 Pa	2.54
Ethanol	Ethyl acetate	1.64 K	0.47	0.47 K	0.14	0.65 K	0.19
Ethanol	Water	700 Pa	2.87	127 Pa	0.45	832 Pa	2.96
Ethyl acetate	Water	13.31 K	3.78	7.74 K	2.23	12.18 K	3.45
Average			2.21		3.33		2.35

Calculations were performed using ASPEN® Properties V8.4.

Table 6. PC-SAFT Binary Interaction Parameters Between Reactants/Products and Solvents Used Within This Study

Substance i	Substance j	k_{ij}	Reference for VLE Data
Acetone	Acetic acid	−0.155	40
Acetone	Acetonitrile	−0.005	41
Acetone	Dimethylformamide	0.01	42
Acetone	Ethanol	−0.05	43
Acetone	Ethyl acetate	0	44
Acetone	Ethyl propionate	−0.045	[a]
Acetone	Propionic acid	−0.1125	[a]
Acetone	Water	−0.171	45
Acetonitrile	Acetic acid	−0.15	46
Acetonitrile	Dimethylformamide	0	47
Acetonitrile	Ethanol	0.035	48
Acetonitrile	ethyl acetate	0.0025	49
Acetonitrile	Tetrahydrofurane	0.0175	50
Acetonitrile	Water	−0.02	51
Dimethylformamide	Acetic acid	−0.35	52
Dimethylformamide	Ethanol	−0.08	53
Dimethylformamide	Ethyl acetate	0.01	54
Dimethylformamide	Water	0	55
Tetrahydrofurane	Acetic acid	−0.125	56
Tetrahydrofurane	Ethanol	−0.08	57
Tetrahydrofurane	Ethyl acetate	0.005	58
Tetrahydrofurane	Water	−0.11	59

[a] VLE data of the binary systems were not available in the literature. k_{ij} was fitted to predictions using UNIFAC.[60]

linear increase of K_x as a function of the ACN mole fraction with an AAD of only 0.41. However, at this particular ethanol to acetic acid ratio (1:1) shown in Figure 7, the effect of ACN is underestimated by the model (Figure 4). This limits the accuracy of the predictions in ACN/acetone mixtures. The increase in K_x with increasing ACN concentration in the solvent system THF/ACN is predicted by PC-SAFT and is in excellent agreement with the experimental data (AAD of 0.21) (Figure 7a).

In solvent mixtures with DMF (Figure 7b), the suppressive effect of DMF on K_x is more pronounced than the supporting effects of the other solvents. With increasing DMF mole fraction, the K_x values strongly decrease, which is also predicted by PC-SAFT with AADs of 0.29, 0.25, and 0.21 for the mixtures of DMF with acetone, ACN, and THF, respectively. Although the predicted K_x values for acetone-containing systems (Figures 7) are less accurate than for the other solvent mixtures, the predictions are at least in qualitative agreement with the predicted K_x values and are in the correct order compared with the other solvent systems.

Esterification of propionic acid

Equilibrium Concentrations in the Solvent-Free System. The reaction equilibria for the esterification of propionic acid and ethanol (Eq. 12) were experimentally investigated at 313.15 K and varying reactant starting concentrations.

$$C_2H_5OH+C_2H_5COOH \leftrightarrow H_2O+C_2H_5COOC_2H_5 \qquad (12)$$

The experimental results are listed in Table 7 and illustrated in Figure 8.

As for the esterification of acetic acid,[7] high acid concentrations (low ethanol mole fraction) support the esterification reaction, leading to a high K_x value of 4.6. A low K_x value of 2.9 was obtained at high ethanol concentrations. The reaction set-up with equal initial amounts of propionic acid and ethanol is found at a medium K_x of 3.8.

To determine the thermodynamic equilibrium constant K_a and the corresponding standard Gibbs energy of reaction, PC-SAFT was again used to predict the activity coefficients of the reactants and products using the pure-component parameters from Table 3 and binary interaction parameters given in Table 4. The latter were again fitted to binary phase equilibria data (AADs and ARDs given in Table 4). Using these activity coefficients and the experimentally determined K_x values (Table 7), K_a was found to be 9.6 ± 0.8. This result leads to a standard Gibbs energy of reaction $\Delta^R g^+_{\text{this work}} = -5.8 \pm 0.2 \frac{\text{kJ}}{\text{mol}}$. This value is in the range of the literature data calculated from the standard Gibbs energies of formation[27–29,61–67] ($\Delta^R g^+ = -8.7 \pm 2.8 \frac{\text{kJ}}{\text{mol}}$) and the value reported by Essex and Sandholzer[28,68] ($\Delta^R g^+ = -5.1 \frac{\text{kJ}}{\text{mol}}$). Modeling K_x with PC-SAFT and a K_a of 9.6 describes the experimental equilibrium data of the esterification of propionic acid in very good agreement with the experimental data (AAD 0.22 and ARD 5.55%, see also Figure 8).

Solvent Effect of Acetone on the Propionic Acid Esterification. Because acetone showed interesting effects in the study with acetic acid (Figure 4), it was also investigated for its effect on the esterification of propionic acid. The esterification was performed at acetone mole fractions of approximately 0.2, 0.5, and 0.8, whereas the reactant ratios were varied as before in the solvent-free system.

Figure 9 depicts the equilibrium concentrations in the reaction mixture at 313.15 K as reported in Table A10. At an acetone mole fraction of 0.2 and high ethanol concentrations (equimolar and with excess ethanol), acetone suppresses the esterification, which leads to K_x values from 2.35 to 3.59 compared with 2.94 and 3.80 in the solvent free system (Table 7). At low ethanol concentrations, no effect of acetone on K_x can be observed as the two K_x values in the solvent-free system and at an acetone mole fraction of 0.2 differ only within experimental uncertainty. At an acetone mole fraction of 0.5, the esterification is suppressed compared with the solvent-free system over the entire ethanol concentration range with K_x

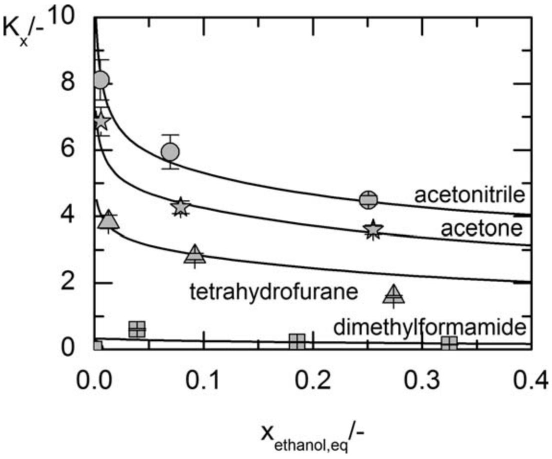

Figure 4. K_x of the esterification of acetic acid and ethanol at 313.15 K and atmospheric pressure as functions of the equilibrium ethanol mole fraction.

The solvent concentration is $x_{\text{solvent}} = 0.5$ in all cases. The symbols are the experimental data as reported in Tables A1–A4 of Appendix. The solvents are acetone (stars), ACN (circles), DMF (squares), and THF (triangles). The solid lines are the PC-SAFT predictions using the parameters from Tables 3, 4, and 6 and $K_a = 19.4$. The dashed-dotted line is the PC-SAFT prediction for the solvent-free system.

Table 7. Equilibrium Concentrations of the Esterification Reaction of Propionic Acid and Ethanol at 313.15 K and Activity Coefficients of Reactants and Products Obtained from PC-SAFT Using the Parameters in Tables 3 and 4

Initial Mole-Fraction Ratio Ethanol/Propionic Acid	$^1/_3$		$^1/_1$		$^3/_1$	
	x	$\gamma_{\text{PC-SAFT}}$	x	$\gamma_{\text{PC-SAFT}}$	x	$\gamma_{\text{PC-SAFT}}$
Ethanol	0.0320	1.2189	0.2319	1.1576	0.5935	1.0496
Propionic acid	0.4504	0.9057	0.1192	0.7946	0.0207	0.8767
Water	0.2579	1.8018	0.3266	1.617	0.2225	1.8433
Ethyl propionate	0.2594	1.2087	0.3220	1.5663	0.1631	1.5472
K_x/K_γ	4.62 ± 0.08	1.97	3.80 ± 0.10	2.75	2.94 ± 0.06	3.10
K_a	9.17		10.47		9.09	

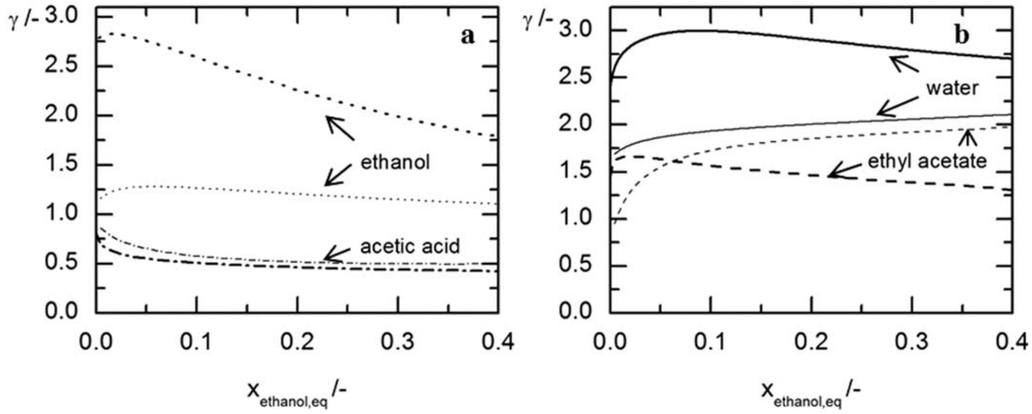

Figure 5. Activity coefficients of reactants and products of the esterification of acetic acid and ethanol in the reaction mixture as functions of the mole fraction of ethanol at equilibrium at 313.15 K and atmospheric pressure predicted by PC-SAFT using the parameters in Tables 3, 4, and 6 and $K_a = 19.4$ for the solvent-free system (thin lines) and in ACN ($x_{ACN} = 0.5$) (bold lines).

(a) Ethanol (dotted lines) and acetic acid (dashed-dotted lines) and (b) water (solid lines) and ethyl acetate (dashed lines).

values between 2.35 and 4.36. At high acetone mole fractions of 0.8, the reaction is significantly supported by acetone, which leads to K_x values between 3.8 and 6.3.

To predict the solvent effect of acetone, the binary PC-SAFT parameters were determined between the reactants/products and acetone. The binary interaction parameters for acetone/ethanol and acetone/water were already determined for the esterification of acetic acid (Table 6). The binary phase-equilibrium data for the acetone/propionic acid and acetone/ethyl propionate systems are not available in the literature. Therefore, the UNIFAC predictions for the VLE of these binary systems were used for PC-SAFT parameter estimation. The resulting parameters and the AADs and ARDs of the modeling are reported in Table 6.

Using these binary parameters and K_a of 9.6, PC-SAFT describes the experimental data for the propionic acid esterification with an AAD of 0.44 and an ARD of 11.14%. An interesting observation is the strong increase in the predicted K_x

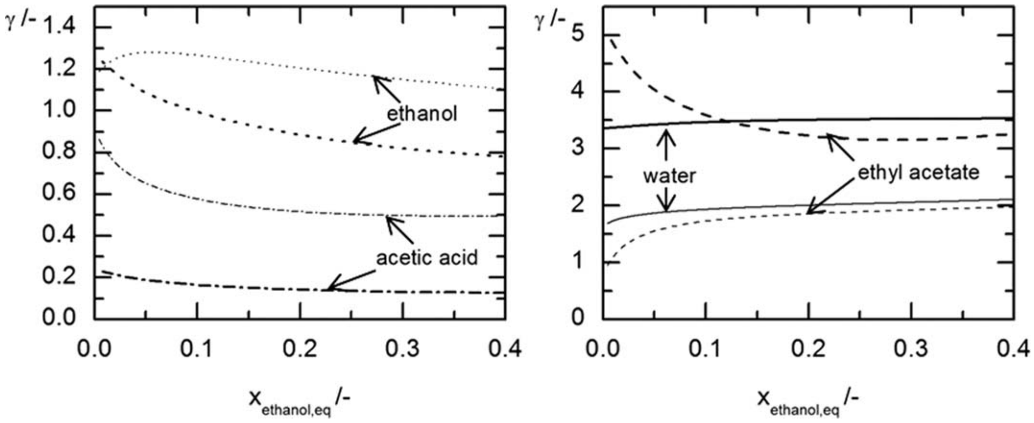

Figure 6. Activity coefficients of the reactants and products of the esterification of acetic acid and ethanol in the reaction mixture as functions of the mole fraction of ethanol at equilibrium at 313.15 K and atmospheric pressure predicted by PC-SAFT using parameters of Tables 3, 4, and 6 and $K_a = 19.4$ for the solvent-free system (thin lines) and in DMF ($x_{DMF} = 0.5$) (bold lines).

(a) Ethanol (dotted lines) and acetic acid (dashed-dotted lines) and (b) water (solid lines) and ethyl acetate (dashed lines).

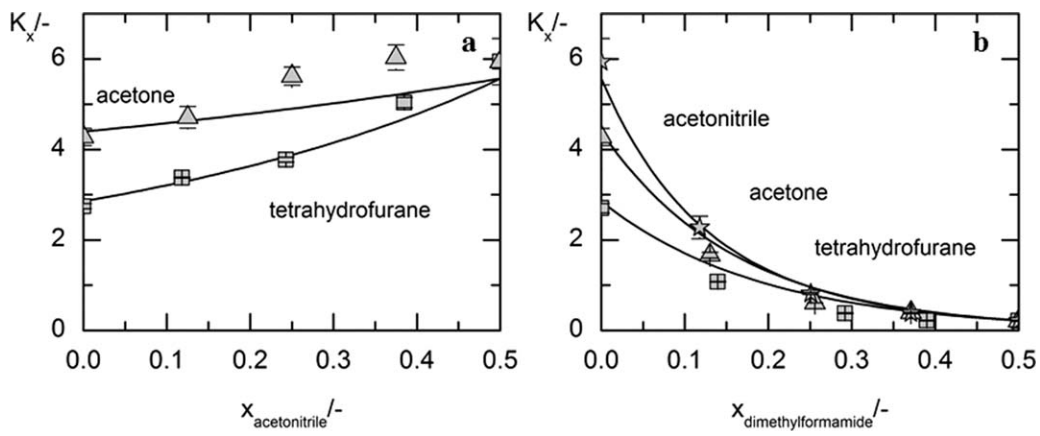

Figure 7. K_x of the esterification of ethanol and acetic acid with an equimolar initial mole-fraction ratio at 313.15 K and atmospheric pressure.

The effects of the mixed solvents ($x_{\text{solvents}} = 0.5$) as functions of the mole fraction of one solvent in the reaction mixture. The lines are PC-SAFT predictions (pure-component parameters as reported in Table 3, k_{ij}'s as reported in Tables 4 and 6, and $K_a = 19.4$). The symbols are experimental data as reported in Tables A5–A9 of Appendix; (a) ACN-containing solvent mixtures. The symbols are experimental data for solvent mixtures composed of ACN/acetone (triangles) and ACN/THF (squares) and (b) DMF-containing solvent mixtures. The symbols are experimental data for solvent mixtures composed of DMF/acetone (triangles), DMF/ACN (stars), and DMF/THF (squares).

values at high acetone concentrations up to about $K_x = 20$, which fits to the fact that most chemical reactions are performed at high dilution rates.

An explanation for this behavior can again be obtained by looking at the reactants'/products' activity coefficients as shown for $x_{\text{ethanol,eq}} = 0.02$ in Figure 10. The activity coefficient of ethanol increases with increasing acetone concentration, which promotes esterification. The activity coefficient of propionic acid is below unity for any acetone concentration, which hinders the esterification reaction. At higher acetone concentrations, the activity coefficient of propionic acid shows a minimum and increases again, which is explained by Eq. 11, that is, the supporting effect at high acetone concentrations. Although the water activity coefficient shows an unfavorable maximum at high acetone concentrations, the ethyl propionate activity coefficient dramatically decreases at high acetone excess, finally leading to the extremely high K_x values at high dilution in acetone.

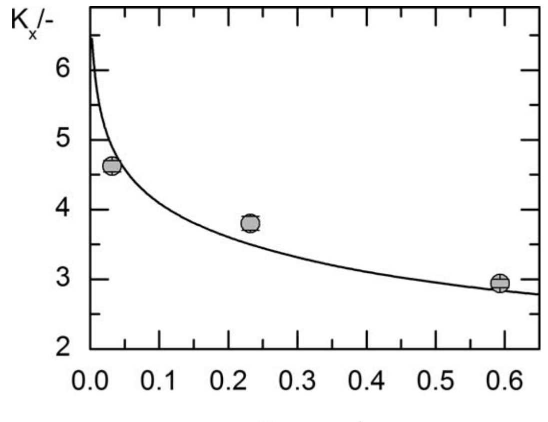

Figure 8. K_x of the esterification of propionic acid and ethanol at 313.15 K and atmospheric pressure as a function of the equilibrium mole fraction of ethanol $x_{\text{ethanol,eq}}$.

The symbols are experimental data as reported in Table 7. The line is the PC-SAFT model after applying the parameters from Tables 3 and 4 and $K_a = 9.6$.

Therefore, the activity coefficients of both reactants and products at infinite dilution may be used for solvent screening in chemical synthesis under excess solvent conditions. However, a rigorous modeling of the complex reaction system is essential for a comprehensive understanding and optimization of the reaction media.

Conclusion

A comprehensive thermodynamic investigation of pure-solvent and mixed-solvent effects on esterification reactions was presented.

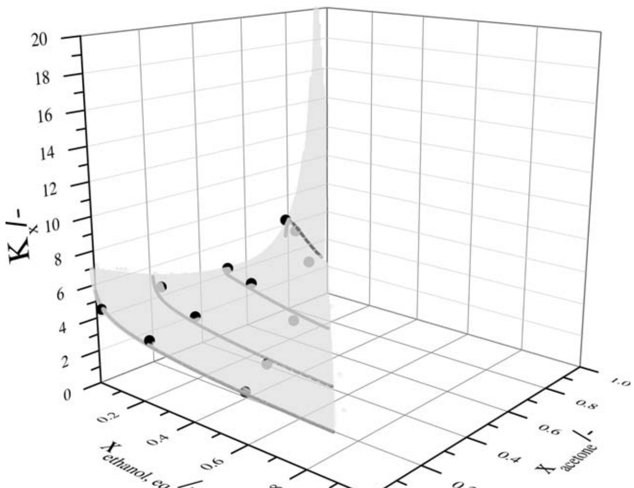

Figure 9. K_x of the esterification of propionic acid and ethanol at 313.15 K and atmospheric pressure as a function of the ethanol mole fraction at equilibrium and the mole fraction of acetone.

The symbols are experimental data as reported in Table A10. The gray lines and the light gray surfaces are predictions from PC-SAFT using the parameters from Tables 3, 4, and 6 and $K_a = 9.6$.

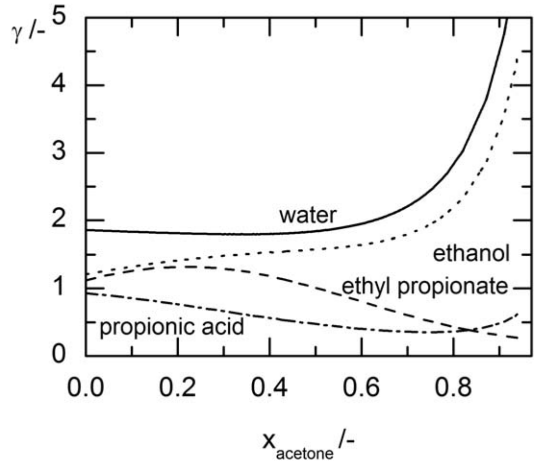

Figure 10. Activity coefficients of the reactants and products of the esterification of propionic acid and ethanol in the reaction mixture as functions of the acetone mole fraction.

This result was obtained using PC-SAFT and the parameters in Tables 3, 4, and 6 and $K_a = 9.6$ for the reactants and products of the propionic acid esterification at $x_{ethanol,eq} = 0.02$ and 313.15 K.

Based on experimentally determined equilibrium concentrations and the activity coefficients of the reactants (alcohol and acids) and products (esters and water) predicted using PC-SAFT, the thermodynamic equilibrium constants for the esterifications of acetic acid and propionic acid with ethanol were determined and found to be in good agreement with the values obtained based on the Gibbs energies of formation of the reactants and products. Using these thermodynamic equilibrium constants, the equilibrium concentrations could be modeled almost quantitatively as functions of the reactant concentrations in the solvent-free systems.

Furthermore, this approach was successfully applied to predict the influence of pure and mixed solvents on the reactant/product activity coefficients therewith on K_x of the esterification of acetic acid. A variety of solvents, including ACN, DMF, acetone, and THF, was examined. The investigated solvents showed different impacts on the reaction equilibrium: ACN promotes the esterification reaction, whereas DMF and THF suppress the reaction, leading to lower product mole fractions (yields) than the solvent-free system.

These effects could be predicted by PC-SAFT in excellent agreement with the experimental data. The binary PC-SAFT interaction parameters between the solvents and the reactants/products used for that purpose were fitted to the VLE data of the binary systems only. Based on the PC-SAFT predictions of the activity coefficients in the reaction mixture, it was found that the solvents that support the esterification (ACN and acetone) cause increasing activity coefficients of the reactants and decreasing activity coefficients of the esters. In contrast, suppressive-solvent effects (DMF and THF) could be explained by decreased activity coefficients of the reactants and increased activity coefficients of the esters in the presence of the solvents.

This approach is also applicable to solvent mixtures, where the influence of the solvent composition on the equilibrium concentrations of the acetic acid esterification could again be predicted by PC-SAFT in almost quantitative agreement with the experimental findings.

Finally, the concept is also applicable to other esterification reactions as shown here for the esterification of propionic acid. Therefore, it will also be transferable to other equilibrium reactions. Because this approach is able to consider the physics of the reactants/products and solvents (e.g., association, polar interactions), it allows for rigorous modeling of the solvent influence on the reaction equilibria and, therefore, is a valuable tool for finding the right solvent for equilibrium-limited reactions.

Acknowledgments

This work is part of the Collaborative Research Centre Transregio 63 "Integrated Chemical Processes in Liquid Multiphase Systems." Financial support from the Deutsche Forschungsgemeinschaft (DFG) is gratefully acknowledged. The authors gratefully acknowledge Prof. Dr. Kai Leonhard from the Institute of Technical Thermodynamics of RWTH Aachen University for performing the COSMO-RS calculations.

Notation

Abbreviations

AAD = average absolute deviation, unit of the corresponding value
ACN = acetonitrile
ARD = average relative deviation, %
COSMO-RS = conductor-like screening model for real solvents
DMF = dimethylformamide
GC = gas chromatography
NRTL = nonrandom two liquid
NRTL-SAC = NRTL-segment activity coefficient
PC-SAFT = perturbed chain-statistical associating fluid theory
THF = tetrahydrofurane
UNIFAC = universal quasichemical functional group activity coefficients
VLE = vapor-liquid equilibrium

Symbols

a = activity
A = Helmholtz energy, J
$\frac{\varepsilon_{A_iB_j}}{k_B}$ = association-energy parameter, K^{-1}
$\Delta^F g_i^+$ = standard Gibbs energy of formation, kJ/mol
$\Delta^R g^+$ = standard Gibbs energy of reaction, kJ/mol
N_i = association sites
$\frac{u_i}{k_B}$ = dispersion-energy parameter, K^{-1}
$\kappa_{A_iB_j}$ = association-volume parameter
v_i = stoichiometric factor
g^E = excess Gibbs energy, kJ/mol
Index i = component i
Index j = component j
K_a = activity-based thermodynamic equilibrium constant
K_γ = activity coefficient contribution to the equilibrium constant
k_{ij} = binary interaction parameter of the dispersion energy between component i and j
K_x = mole-fraction-based apparent equilibrium constant
m_i = segment number
p = pressure, mbar
R = ideal gas constant, J/mol/K
T = temperature, K
x = mole fraction
γ = activity coefficient
σ_i = segment diameter, Å
φ_i = fugacity coefficient

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Appendix

Table A1. Equilibrium Concentrations of the Esterification Reaction of Acetic Acid and Ethanol at 313.15 K with $x_{\mathrm{acetone}} = 0.5$

Initial Mole-Fraction Ratio Ethanol/Acetic Acid	x		
	$^1/_3$	$^1/_1$	$^3/_1$
Ethanol	0.008	0.081	0.251
Acetic acid	0.255	0.082	0.015
Water	0.127	0.168	0.125
Ethyl acetate	0.110	0.169	0.109
K_x	6.9± 0.4	4.3± 0.2	3.6± 0.1

Table A2. Equilibrium Concentrations of the Esterification Reaction of Acetic Acid and Ethanol at 313.15 K with $x_{\mathrm{acetonitrile}} = 0.5$

Initial Mole-Fraction Ratio Ethanol/Acetic Acid	x		
	$^1/_3$	$^1/_1$	$^3/_1$
Ethanol	0.007	0.071	0.253
Acetic acid	0.255	0.075	0.012
Water	0.128	0.186	0.126
Ethyl acetate	0.111	0.168	0.109
K_x	8.1 ± 0.6	5.9 ± 0.5	4.5 ± 0.1

Table A3. Equilibrium Concentrations of the Esterification Reaction of Acetic Acid and Ethanol at 313.15 K with $x_{\mathrm{dimethylformamide}} = 0.5$

Initial Mole-Fraction Ratio Ethanol/Acetic Acid	x		
	$^1/_3$	$^1/_1$	$^3/_1$
Ethanol	0.039	0.161	0.312
Acetic acid	0.294	0.169	0.073
Water	0.080	0.124	0.048
Ethyl acetate	0.087	0.047	0.068
K_x	0.60 ± 0.03	0.21 ± 0.01	0.14 ± 0.01

Table A4. Equilibrium Concentrations of the Esterification Reaction of Acetic Acid and Ethanol at 313.15 K with $x_{\mathrm{tetrahydrofurane}} = 0.5$

Initial Mole-Fraction Ratio Ethanol/Acetic Acid	x		
	$^1/_3$	$^1/_1$	$^3/_1$
Ethanol	0.013	0.092	0.262
Acetic acid	0.260	0.096	0.027
Water	0.119	0.159	0.111
Ethyl acetate	0.108	0.152	0.100
K_x	3.82 ± 0.05	2.7 ± 0.1	1.59 ± 0.03

Table A5. Equilibrium Concentrations of the Esterification Reaction of Acetic Acid and Ethanol at 313.15 K in the Solvent Mixture of Acetone and Acetonitrile with $x_{\text{solvents}} = 0.5$

	x		
Acetone	0.129	0.249	0.372
Acetonitrile	0.371	0.251	0.128
Ethanol	0.073	0.076	0.082
Acetic acid	0.072	0.072	0.076
Water	0.184	0.180	0.167
Ethyl acetate	0.171	0.172	0.175
K_x	6.0 ± 0.5	5.6 ± 0.4	4.7 ± 0.2

Table A6. Equilibrium Concentrations of the Esterification Reaction of Acetic Acid and Ethanol at 313.15 K in the Solvent Mixture of Tetrahydrofurane and Acetonitrile with $x_{\text{solvents}} = 0.5$

	x		
Acetonitrile	0.120	0.256	0.379
Tetrahydrofurane	0.380	0.244	0.121
Ethanol	0.087	0.084	0.078
Acetic acid	0.090	0.086	0.076
Water	0.159	0.164	0.172
Ethyl acetate	0.165	0.166	0.174
K_x	3.38 ± 0.05	3.76 ± 0.04	5.0 ± 0.1

Table A7. Equilibrium Concentrations of the Esterification Reaction of Acetic Acid and Ethanol at 313.15 K in the Solvent Mixture of Acetone and Dimethylformamide with $x_{\text{solvents}} = 0.5$

	x		
Acetone	0.127	0.244	0.374
Dimethylformamide	0.373	0.256	0.126
Ethanol	0.145	0.136	0.108
Acetic acid	0.162	0.145	0.110
Water	0.098	0.111	0.144
Ethyl acetate	0.095	0.109	0.137
K_x	0.40 ± 0.01	0.61 ± 0.01	1.7 ± 0.1

Table A8. Equilibrium Concentrations of the Esterification Reaction of Acetic Acid and Ethanol at 313.15 K in the Solvent Mixture of Acetonitrile and Dimethylformamide with $x_{\text{solvents}} = 0.5$

	x		
Acetonitrile	0.132	0.247	0.380
Dimethylformamide	0.368	0.253	0.120
Ethanol	0.154	0.128	0.102
Acetic acid	0.154	0.134	0.097
Water	0.098	0.120	0.149
Ethyl acetate	0.093	0.118	0.151
K_x	0.38 ± 0.03	0.82 ± 0.02	2.3 ± 0.2

Table A9. Equilibrium Concentrations of the Esterification Reaction of Acetic Acid and Ethanol at 313.15 K in the Solvent Mixture of Tetrahydrofurane and Dimethylformamide with $x_{\text{solvents}} = 0.5$

	x		
Tetrahydrofurane	0.121	0.212	0.368
Dimethylformamide	0.379	0.288	0.132
Ethanol	0.166	0.142	0.123
Acetic acid	0.175	0.167	0.122
Water	0.081	0.099	0.124
Ethyl acetate	0.078	0.091	0.131
K_x	0.22 ± 0.01	0.38 ± 0.01	1.08 ± 0.02

Table A10. Equilibrium Concentrations of the Esterification Reaction of Propionic Acid and Ethanol at 313.15 K with Acetone

x_{ethanol}	$x_{\text{propionic acid}}$	x_{water}	$x_{\text{ethyl propionate}}$	x_{acetone}	K_x
0.0251	0.3439	0.2023	0.2000	0.2282	4.7 ± 0.1
0.1739	0.1006	0.2548	0.2464	0.2224	3.59 ± 0.09
0.4665	0.0205	0.1546	0.1449	0.2116	2.35 ± 0.02
0.0129	0.2403	0.1138	0.1191	0.5139	4.36 ± 0.05
0.1085	0.0606	0.1589	0.1551	0.5219	3.75 ± 0.05
0.3020	0.0118	0.0911	0.0918	0.5034	2.35 ± 0.08
0.0064	0.0826	0.0716	0.0467	0.7927	6.3 ± 0.2
0.0387	0.0212	0.0740	0.0607	0.8043	5.6 ± 0.1
0.1086	0.0051	0.0560	0.0374	0.7926	3.80 ± 0.08

Manuscript received Dec. 3, 2014, and revision received Mar. 23, 2015.