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Phase Equilibria with Supercritical Carbon Dioxide for the Enzymatic Production of an Enantiopure Pyrethroid Component. Part 2. Ternary and Five-Component Systems

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(*S*)-α-Cyano-*m*-phenoxybenzyl alcohol is an important synthon for pyrethroid insecticides. It is obtained by the lipase-catalyzed kinetic resolution of racemic α-cyano-*m*-phenoxybenzyl acetate, with 1-octanol acting as an acyl acceptor and thus being converted to 1-octyl acetate. Supercritical carbon dioxide is used as a unique solvent for the reaction and the subsequent product recovery by extraction. Phase equilibria of the ternary systems CO_2 + α-cyano-*m*-phenoxybenzyl alcohol + α-cyano-*m*-phenoxybenzyl acetate and CO_2 + 1-octanol + 1-octyl acetate were measured at 313.15 K and at respective pressures of 20 MPa and 8 MPa. The latter ternary exhibits alyotropic behavior. Phase equilibria of the ternary CO_2 + 1-octanol + α-cyano-*m*-phenoxybenzyl acetate and the five-component system CO_2 + 1-octanol + 1-octyl acetate + α-cyano-*m*-phenoxybenzyl alcohol + α-cyano-*m*-phenoxybenzyl acetate were determined at 313.15 K and at various pressures of up to 17 MPa. The Soave−Redlich−Kwong equation of state with the mixing rules due to Huron and Vidal was checked for its ability to reproduce the measured equilibrium data. Whereas model predictions match experimental data of the ternary systems within the estimated accuracy of the measurements, larger deviations exist for the five-component systems.

Introduction

In a lipase-catalyzed kinetic resolution racemic α-cyano-*m*-phenoxybenzyl acetate (CPBAc) and 1-octanol (OAl) are converted by about 50%, yielding the desired product (*S*)-α-cyano-*m*-phenoxybenzyl alcohol (CPBAl) and 1-octyl acetate (OAc):

$$\mathrm{CPBAc} + \mathrm{OAl} \rightarrow \mathrm{CPBAl} + \mathrm{OAc} \qquad (1)$$

The reaction can be carried out in supercritical CO_2 (Stephan et al., 1995; Chrisochoou et al., 1995). Thus, a five-component system has to be dealt with in the chemical conversion and in the following separation process, where CO_2 can be used as the solvent in supercritical fluid extraction (SFE).

As was explained in the first part of this work (Chrisochoou et al., 1997), a knowledge of the phase equilibria is essential for both the enzymatic catalyzed reaction and the SFE process. There, we presented phase equilibrium data of the four binary systems of one of the reactants plus CO_2.

In this part, we want to treat the whole five-component system and important ternary subsystems: (1) Due to the thermolability of CPBAl, the reaction temperature is not to be increased much beyond 313.15 K. On the contrary, the reaction pressure can be varied widely. In the reaction, the ternary system of CO_2 and the two substrates CPBAc and OAl is transformed into a five-component system whose composition depends on the effected conversion. Therefore, the ternary CO_2 + OAl + CPBAc and different five-component systems will be investigated at 313.15 K and at various pressures. (2) As the components CPBAl and CPBAc show much lower solubilities in CO_2 than OAl and OAc, it seems most reasonable to separate in the SFE process these two fractions first. The components of each fraction have to be isolated afterward. As a consequence, the phase equilibria of the ternary systems CO_2 + CPBAl + CPBAc and CO_2 + OAl + OAc are essential to be known. They each will be explored at 313.15 K and at a constant pressure.

Table 1. Oven Temperature Programs Used for the Systems Investigated: CO_2 + CPBAl + CPBAc (System I), CO_2 + OAl + OAc (System II), CO_2 + OAl + CPBAc (System III), and CO_2 + OAl + OAc + CPBAl + CPBAc (System IV)

	K				min				K/min		
system	T_{ini}	$T_{\mathrm{fin},1}$	$T_{\mathrm{fin},2}$	$T_{\mathrm{fin},3}$	τ_{ini}	$\tau_{\mathrm{fin},1}$	$\tau_{\mathrm{fin},2}$	$\tau_{\mathrm{fin},3}$	r_1	r_2	r_3
I	323.15	503.15	513.15		1.5	2.0	4.0		30	30	
II	343.15	408.15			1.5	3.5			30		
III, IV	323.15	408.15	503.15	513.15	1.5	2.5	1.5	2.5	30	30	30

Experimental Section

Materials. The substances used for the experiments were of the same origin and purity as specified in the first part of our work. Here, only the purities are given: CO_2 >99.995%, OAl >99%, OAc ≈98%, CPBAl ≈92%, CPBAc ≈97%.

Apparatus and Procedure. All measurements were performed using a high-pressure apparatus based on drawing samples from a visual equilibrium cell and analyzing them online by gas chromatography (GC). As both the experimental setup and procedure were described in detail in the first part of our work only the most important items are briefly repeated.

Accuracies of the temperature and pressure measurements are estimated to be ±0.1 K and ±0.03 MPa, respectively. For analyzing samples, a gas chromatograph with a thermal conductivity detector (HP 5890A) and an electronic integrator (HP 3396A) were used. The injector was operated at 513.15 K, and the detector

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Table 2. Estimated Accuracies in Mole Fraction x or y

x, y	absolute error	rel error, %
0.5	±0.01	2
0.1	±0.01	10
0.01	±0.002	20
0.001	±0.0005	50
0.0001	±0.0002	200

Table 3. Pure Component Parameters for the SRK Equation

component	p_c/MPa	T_c/K	m	n
CO_2	7.39	304.2	0.660 48	0.205 37
OAl	2.86	652.5	0.527 63	0.782 07
OAc	2.13	656.3	1.213 76	0.34 10
CPBAl	2.90	844.0	1.10	0.55
CPBAc	2.19	853.0	1.088 41	0.528 53

temperature was 543.13 K. A packed column (6 ft. × 1/8 in., UCW-982) was employed and different multiple-step programs were used for adjusting oven temperature. Table 1 contains the oven temperature programs used for the different systems investigated. GC analysis was calibrated with different quantities of the pure substances to yield calibration functions of the second-order polynomial type.

The values of all phase equilibrium data were calculated as mean values of the results for up to ten single measurements. Table 2 gives an overview of the concentration accuracies as estimated on the basis of the standard deviation of measured values.

Results

In the following, the experimental phase equilibrium data are presented and compared to the model predictions of the cubic equation of state proposed by Redlich and Kwong (1949) and modified by Soave (1972, 1979), referred to as the SRK equation. To account for interactions between the mixture components, the mixing rules developed by Huron and Vidal (1979) are applied (HV mixing rules).

In the first part of our work, we explained at full length about the model structure. It can be summarized as follows:

$$p = \frac{RT}{\bar{V} - b} - \frac{a}{\bar{V}(\bar{V} + b)} \tag{2}$$

with

$$a = a(x_i \text{ or } y_i,\ T,\ T_{c,i},\ p_{c,i}, m_i,\ n_i,\ \alpha_{ij},\ C_{ij}) \tag{3}$$

$$b = b(x_i \text{ or } y_i,\ T_{c,i},\ p_{c,i}) \tag{4}$$

The critical data $T_{c,i}$ and $p_{c,i}$ and the Soave parameters m_i and n_i were derived in part one of our work. So were the binary interaction parameters due to Huron and Vidal, α_{ij}, C_{ij}, and C_{ji} for the four binary pairs with CO_2. In order to describe the phase equilibria of the complete five-component system, interaction parameters are also required for the six binaries excluding CO_2. For these binaries, the literature holds no phase equilibrium data that could serve for fitting the missing parameters. Avoiding time-consuming measurements, we calculated a set of phase equilibrium data for each binary at a temperature of 313.15 K using the UNIFAC model. These data were then employed for the fitting procedures. In Tables 3 and 4 all the parameters of the SRK model are given.

Table 4. Binary Interaction Parameters due to Huron and Vidal

binary $i + j$	α_{ij}	C_{ij}/[(kPa·m^3)/mol^{-1}]	C_{ji}/[(kPa·m^3)/mol^{-1}
CO_2 + OAl	−0.008 018 3	27.003	−3.5994
CO_2 + OAc	−0.002 887 8	26.958	−2.0886
CO_2 + CPBAl	0.000 219 3	49.007	−5.4978
CO_2 + CPBAc	−0.003 760 2	50.127	−4.5031
OAl + OAc	0.375 19	0.19935	2.0955
OAl + CPBAl	0.022 911	15.962	−7.6498
OAl + CPBAc	0.010 650	17.824	−5.8610
OAc + CPBAl	0.064 656	17.709	−7.7899
OAc + CPBAc	0.031 027	17.743	−7.8401
CPBAl + CPBAc	−0.092 598	0.44987	0.36226

Table 5. Phase Equilibrium of CO_2 + CPBAl + CPBAc at 313.15 K and 20.0 MPa

		experimental				SRK model			
no.	comp	x	y	x^*	y^*	x	y	x^*	y^*
1	CO_2	0.556	0.9970			0.549	0.9974		
	CPBAl	0.422	0.0021	0.950	0.700	0.421	0.0018	0.934	0.699
	CPBAc	0.022	0.0009	0.050	0.300	0.030	0.0008	0.066	0.301
2	CO_2	0.574	0.9969			0.586	0.9958		
	CPBAl	0.340	0.0014	0.798	0.452	0.332	0.0018	0.802	0.416
	CPBAc	0.086	0.0017	0.202	0.548	0.082	0.0024	0.198	0.584
3	CO_2	0.653	0.9939			0.657	0.9921		
	CPBAl	0.184	0.0017	0.530	0.279	0.182	0.0015	0.529	0.196
	CPBAc	0.163	0.0044	0.470	0.721	0.161	0.0064	0.471	0.804
4	CO_2	0.694	0.9908			0.689	0.9899		
	CPBAl	0.123	0.0012	0.402	0.131	0.124	0.0014	0.399	0.136
	CPBAc	0.183	0.0080	0.598	0.869	0.187	0.0087	0.601	0.864
5	CO_2	0.742	0.9875			0.713	0.9879		
	CPBAl	0.076	0.0014	0.295	0.112	0.085	0.0012	0.297	0.098
	CPBAc	0.182	0.0111	0.705	0.888	0.202	0.0109	0.703	0.902

When a SFE process for fractionating components is being designed, molar fractions on a solvent-free basis are very useful to be considered. They are defined as

$$z_i^* = \frac{n_i}{\sum\limits_{j \neq CO_2} n_j} = \frac{z_i}{1 - z_{CO_2}} \qquad i \neq CO_2 \tag{5}$$

and will be given for the results in addition to normal mole fractions.

Ternary Systems

Phase equilibria of the ternary CO_2 + CPBAl + CPBAc were determined at a temperature of 313.15 K and a pressure of 20.0 MPa. Numerical results appear in Table 5 together with the predictions of the SRK model. In Figures 1 and 2 the comparison is illustrated by means of mole fractions (triangular diagram) and solvent-free concentrations (equilibrium selectivity diagram). Deviations of the calculated data from experimental results are within the estimated accuracies of the measurements.

As can be seen, the ternary is of the 3/2-type. CPBAc always shows a higher solubility in the extract phase than CPBAl, causing the equilibrium curve in the selectivity diagram to run entirely above the diagram diagonal. This implies that the two components CPBAl and CPBAc are to be completely separated using a fractional extraction column operated at these conditions (Pratt, 1991).

The system CO_2 + OAl + OAc was investigated at 313.15 K and 8.0 MPa. Experimental results and model calculations are listed in Table 6. In Figures 3 and 4, measured phase equilibria are compared to calculated equilibrium curves. Here, the maximum difference of measured and correlated data slightly exceeds experimental accuracies.

Once again, the ternary is of the 3/2-type. It can be seen from Figure 4 that the equilibrium curve first extends above and then below the diagram diagonal. This means

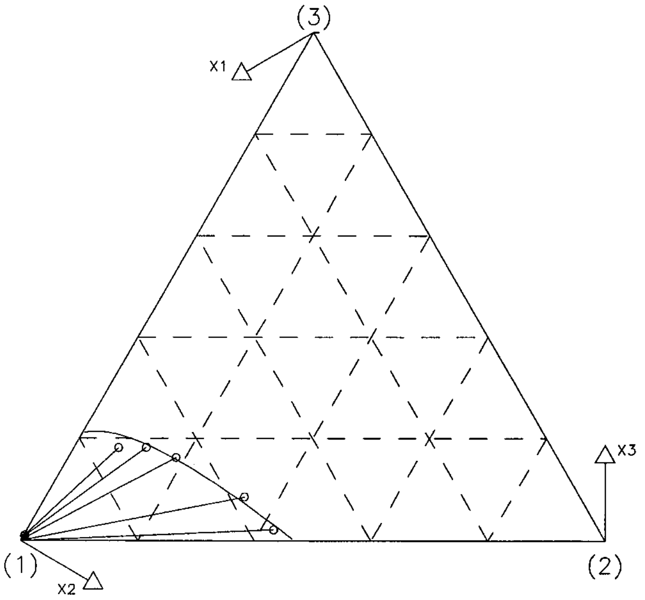

Figure 1. Phase equilibrium of CO_2 (1) + CPBAl (2) + CPBAc (3) at 313.15 K and 20.0 MPa: (○) experimental this work; (—) SRK model.

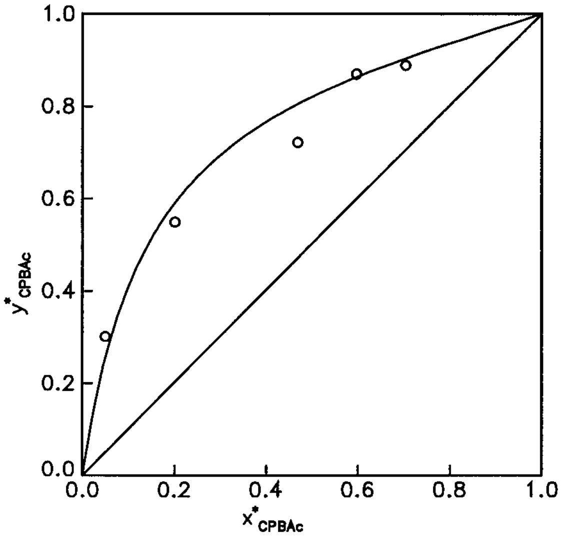

Figure 2. Phase equilibrium on a solvent-free basis of CO_2 + CPBAl + CPBAc at 313.15 K and 20.0 MPa: (○) experimental this work; (—) SRK model.

that OAc drops its role as the component of higher solubility to become the lower soluble component; OAl behaves vice versa. The point where the equilibrium curve and diagram diagonal intersect is called an alyotrope (Schuberth, 1972). It corresponds to a tie line in the triangular diagram whose extension meets the corner of the solvent (CO_2). This implies that the quantity ratios of both components (OAl and OAc) are equal in both extract and raffinate phase. Thus an alyotrope poses a limit to any fractional extraction process aiming at completely separating a binary mixture—just as does an azeotrope in distillation. Here, it can be concluded that OAl and OAc are not to be fractionated by a SFE process operating at 313.15 K and 8.0 MPa.

Phase equilibria of the system CO_2 + OAl + CPBAc were measured at a temperature of 313.15 K and at various pressures. The quantities of OAl and CPBAc in the total mixture employed were equal—as they are in possible substrate mixtures of the enzymatic reaction (before conversion).

Table 6. Phase Equilibrium of CO_2 + OAl + OAc at 313.15 K and 8.0 MPa

		experimental				SRK model			
no.	comp	*x*	*y*	*x**	*y**	*x*	*y*	*x**	*y**
1	CO_2	0.6459	0.99889			0.6408	0.99907		
	OAl	0.3014	0.00079	0.851	0.712	0.3057	0.00054	0.851	0.585
	OAc	0.0527	0.00032	0.149	0.288	0.0535	0.00039	0.149	0.415
2	CO_2	0.6863	0.99887			0.6426	0.99906		
	OAl	0.2645	0.00076	0.843	0.673	0.3006	0.00054	0.841	0.573
	OAc	0.0492	0.00037	0.157	0.327	0.0568	0.00040	0.159	0.427
3	CO_2	0.7137	0.99900			0.6743	0.998 92		
	OAl	0.2001	0.00049	0.699	0.490	0.2285	0.00049	0.701	0.459
	OAc	0.0862	0.00051	0.301	0.510	0.0972	0.00059	0.299	0.541
4	CO_2	0.7346	0.99880			0.7101	0.99886		
	OAl	0.1532	0.00054	0.577	0.450	0.1685	0.00046	0.581	0.404
	OAc	0.1122	0.00066	0.423	0.550	0.1214	0.00068	0.419	0.596
5	CO_2	0.7476	0.99877			0.7375	0.99884		
	OAl	0.1263	0.00048	0.501	0.390	0.1315	0.00044	0.501	0.375
	OAc	0.1261	0.00075	0.499	0.610	0.1310	0.00072	0.499	0.625
6	CO_2	0.8093	0.99885			0.7970	0.99881		
	OAl	0.0618	0.00033	0.324	0.287	0.0650	0.00036	0.320	0.300
	OAc	0.1289	0.00082	0.676	0.713	0.1380	0.00083	0.680	0.700
7	CO_2	0.8127	0.99870			0.8089	0.99880		
	OAl	0.0522	0.00040	0.278	0.308	0.0517	0.00033	0.270	0.272
	OAc	0.1351	0.00090	0.722	0.692	0.1394	0.00087	0.730	0.728
8	CO_2	0.8177	0.99868			0.8144	0.99881		
	OAl	0.0449	0.00037	0.246	0.280	0.0446	0.00030	0.240	0.253
	OAc	0.1374	0.00095	0.754	0.720	0.1410	0.00089	0.760	0.747
9	CO_2	0.8176	0.99794			0.8202	0.99881		
	OAl	0.0364	0.00046	0.199	0.223	0.0360	0.00027	0.200	0.224
	OAc	0.1460	0.00160	0.801	0.777	0.1438	0.00092	0.800	0.776

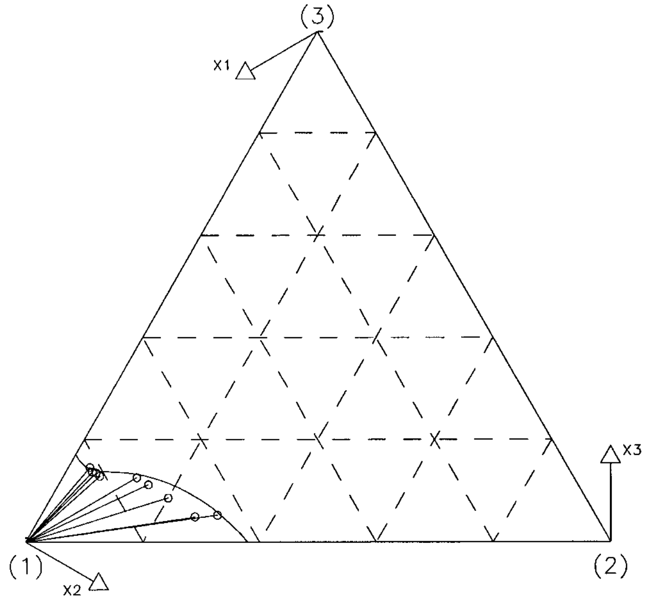

Figure 3. Phase equilibrium of CO_2 (1) + OAl (2) + OAc (3) at 313.15 K and 8.0 MPa: (○) experimental this work; (—) SRK model.

Results are listed in Table 7, which contains also the predictions of the SRK model. They match experimental values within the error tolerances estimated for the measurements.

Five-Component Systems

Finally, the five-component system CO_2 + OAl + OAc + CPBAl + CPBAc was investigated at 313.15 K and at different pressures. The mixtures used in the experiments were prepared to contain quantities of the four reactants corresponding to a 25% and a 50% conversion of an equimolar substrate mixture.

Experimental and correlated data are summarized in Table 8. Here, deviations of both data sets are encoun-

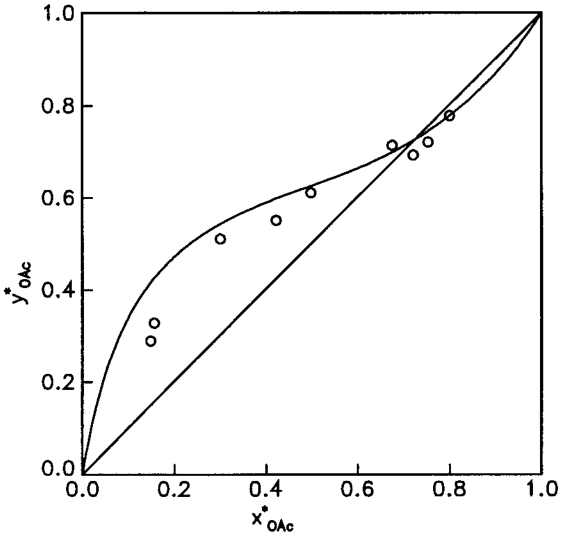

Figure 4. Phase equilibrium on a solvent-free basis of CO_2 + OAl + OAc at 313.15 K and 8.0 MPa: (○) experimental this work; (—) SRK model.

Table 7. Phase Equilibria of CO_2 + OAl + CPBAc at 313.15 K

		experimental				SRK model			
p/MPa	comp	x	y	x^*	y^*	x	y	x^*	y^*
9.4	CO_2	0.735	0.9928			0.741	0.9908		
	OAl	0.123	0.0062	0.462	0.861	0.118	0.0081	0.456	0.886
	CPBAc	0.142	0.0010	0.538	0.139	0.141	0.0011	0.544	0.114
12.9	CO_2	0.802	0.9621			0.796	0.9576		
	OAl	0.083	0.0278	0.419	0.734	0.088	0.0289	0.431	0.682
	CPBAc	0.115	0.0101	0.581	0.266	0.116	0.0134	0.569	0.318
16.2	CO_2	0.827	0.9385			0.826	0.9346		
	OAl	0.066	0.0335	0.382	0.545	0.069	0.0369	0.397	0.564
	CPBAc	0.107	0.0280	0.618	0.455	0.105	0.0285	0.603	0.436

tered, being beyond the assumed accuracies of the experimental procedure.

Conclusions

In this second part of our work, phase equilibria of the five-component reaction system and three of its ternary subsystems were determined. Together with the measurements of binary subsystems presented in the first part of our work, a comprehensive set of equilibrium data is available. They can serve as engineering data in designing a supercritical fluid process consisting of the enzymatic conversion and the subsequent separation by extraction.

Table 8. Phase Equilibria of CO_2 + OAl + OAc + CPBAl + CPBAc at 313.15 K

		experimental				SRK model			
p/MPa	comp	x	y	x^*	y^*	x	y	x^*	y^*
9.2	CO_2	0.694	0.9845			0.693	0.9848		
	OAl	0.110	0.0076	0.360	0.491	0.113	0.0085	0.370	0.558
	OAc	0.030	0.0056	0.098	0.361	0.030	0.0055	0.097	0.360
	CPBAl	0.040	0.0005	0.130	0.032	0.036	0.0001	0.117	0.006
	CPBAc	0.126	0.0018	0.412	0.116	0.128	0.0011	0.416	0.076
12.0	CO_2	0.736	0.9621			0.724	0.9615		
	OAl	0.092	0.0177	0.348	0.467	0.098	0.0212	0.354	0.552
	OAc	0.025	0.0101	0.095	0.266	0.025	0.0097	0.090	0.252
	CPBAl	0.041	0.0009	0.155	0.024	0.035	0.0006	0.125	0.016
	CPBAc	0.106	0.0092	0.402	0.243	0.118	0.0070	0.431	0.180
9.8	CO_2	0.658	0.9563			0.655	0.9609		
	OAl	0.085	0.0122	0.248	0.279	0.091	0.0130	0.265	0.333
	OAc	0.073	0.0229	0.213	0.523	0.066	0.0224	0.191	0.572
	CPBAl	0.084	0.0036	0.246	0.082	0.083	0.0006	0.239	0.016
	CPBAc	0.100	0.0050	0.293	0.116	0.105	0.0031	0.305	0.077
15.1	CO_2	0.738	0.9167			0.697	0.9218		
	OAl	0.066	0.0243	0.251	0.291	0.081	0.0260	0.266	0.333
	OAc	0.055	0.0398	0.209	0.478	0.063	0.0380	0.207	0.486
	CPBAl	0.066	0.0077	0.251	0.092	0.070	0.0033	0.232	0.041
	CPBAc	0.075	0.0115	0.289	0.139	0.089	0.0109	0.295	0.140

The SRK equation with the mixing rules due to Huron and Vidal was used for correlating the measured results. Although model parameters were fitted to experimental data of the binary subsystems only, predicted phase equilibria of ternary subsystems match experimental results almost within the estimated accuracies of the measurements. Especially, the alyotropic behavior of the ternary CO_2 + OAl + OAc is calculated both qualitatively and quantitatively well. In modeling phase equilibria of the complete five-component system, somewhat greater deviations from measured data are incurred.

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