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Measurements of Binary Diffusion Coefficient and Partition Ratio at Infinite Dilution for Linoleic Acid and Arachidonic Acid in Supercritical Carbon Dioxide

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The binary diffusion coefficient D_{12} and partition ratio k were measured for two ω6 group compounds, linoleic acid and arachidonic acid, at infinite dilution in carbon dioxide at temperatures from 308.15 K to 343.15 K and pressures from 9 MPa to 30 MPa by a tracer response technique with a poly(ethylene glycol)-coated capillary column. The measured D_{12} values were well represented by a correlation of D_{12}/T versus CO_2 viscosity and by the Schmidt number correlation for each solute, and the k values were well represented as a function of temperature and CO_2 density. Partial molar volumes were also obtained from the k values.

Introduction

Unsaturated fatty acids are important fat-soluble compounds in the food and pharmaceutical industries as healthy ingredients and supplements.[1] The compounds are widely distributed in various natural products such as fish oils, vegetable oils, nuts, seeds, and so forth. Unsaturated fatty acids are sometimes classified with respect to the position of carbons having unsaturated bonds such as ω3 and ω6 groups, which designate the compounds as having an unsaturated carbon in the third and the sixth position, respectively, from the methyl end. Since these are heat- and light-labile compounds, supercritical fluid extraction/chromatography has an advantage over the conventional liquid extraction process with organic solvents. In fact, many studies on extraction/fractionation of these unsaturated fatty acids and their derivatives with supercritical fluids have been made.[2−10] Due to nontoxicity and nonflammability, carbon dioxide is often employed as a supercritical solvent. To estimate mass transfer rates in these processes, the binary diffusion coefficients are required as well as other transport properties. Binary diffusion coefficient data for unsaturated fatty acids and their derivatives in supercritical carbon dioxide are limited: those for free fatty acids[11−14] and the methyl and the ethyl esters[14−18] are available.

The measurements of binary diffusion coefficients in supercritical fluids have been made mostly by the Taylor dispersion method since Swaid and Schneider[19] applied it. While this method is adequate for non- or less viscous liquid solutes, it is not easy to inject a constant amount of solid or highly viscous solute in the absence of a dissolving organic solvent over a wide pressure range. We have developed the tracer response technique with a poly(ethylene glycol)-coated capillary column,[13,20−22] instead of an uncoated capillary column as used in the Taylor dispersion. This method is capable of measuring simultaneously binary diffusion coefficient D_{12} and partition ratio k by a single solute injection by fitting the response curve calculated to that measured experimentally. We have applied this method to measure diffusion coefficients for ω3 compounds such as docosahexaenoic acid,[13] eicosapentaenoic acid,[13] and α-linolenic acid,[13] as well as other human-active compounds such as α-tocopherol,[20,21] β-carotene,[20,21] and ubiquinone CoQ10.[22] The authors[23] have also measured binary diffusion coefficients for phenol, α-tocopherol, β-carotene, ubiquinone CoQ10, and vitamin K_3 in supercritical carbon dioxide by the modified Taylor dispersion method with a polymer-coated and an uncoated capillary column connected in series. So far, binary diffusion coefficients for the ω6 group compounds and the derivatives in supercritical fluids are scarce. In this study, binary diffusion coefficient and partition ratio for two ω6 group compounds, *cis*-9,12-octadecadienoic acid (linoleic acid, molecular weight (MW) = 280.4) and *cis*-5,8,11,14- eicosatetraenoic acid (arachidonic acid, MW = 304.5), in supercritical carbon dioxide were measured by a tracer response technique with a poly(ethylene glycol)-coated capillary column. Infinite dilution partial molar volumes for both the solutes were derived from the k values. Correlations for D_{12} and for k values were developed.

Theory

The theoretical background was described elsewhere.[20−22] Let $C_a(x,t)$ be the average concentration of the local tracer concentration of $C(r,x,t)$ on the cross section of the capillary column coated with a polymer film in eq 1.

$$C_a(x,t) = \frac{2}{R^2}\int_0^R C(r,x,t)r\,dr \qquad (1)$$

The analytical solution C_a is given in eqs 2 and 3:[13,20−22]

$$C_a(x,t) \approx \left(\frac{m}{\pi R^2}\right)\frac{1}{(1+k)\sqrt{4\pi a t}}\exp\left[-\frac{\{x - u_a t/(1+k)\}^2}{4at}\right] \qquad (2)$$

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$$a = \frac{D_{12}}{1+k} + \frac{1+6k+11k^2}{(1+k)^3}\frac{{u_a}^2R^2}{48D_{12}} \tag{2a}$$

where t is time, x and r are axial and radial distances, respectively, R is the tubing radius, m is the injected amount of the tracer, k is the partition ratio of the tracer in the polymer phase to the supercritical phase, D_{12} is the binary diffusion coefficient of the tracer, and u_a is an average solvent velocity. A parameter set of binary diffusion coefficient D_{12} and partition ratio k was determined so as to minimize the fitting error ϵ, defined in eq 3, where t_1 and t_2 are the frontal and the latter times at 10% of the maximum peak height, and $C_{a,meas}(L,t)$ and $C_{a,calc}(L,t)$ are the concentration measured experimentally at an axial distance L from the injection point and that calculated by assuming the values of D_{12} and k, respectively.

$$\epsilon = \left[\frac{\int_{t_1}^{t_2}\{C_{a,meas}(L,t) - C_{a,calc}(L,t)\}^2\,dt}{\int_{t_1}^{t_2}\{C_{a,meas}(L,t)\}^2\,dt}\right]^{1/2} \tag{3}$$

Experimental Section

The experimental apparatus and the procedures were almost identical to those described elsewhere.[21,22] A 0.2-μL quantity of hexane (95%, Aldrich) solution of linoleic acid (99%, Sigma) at a concentration of 4.7 mg/mL or arachidonic acid (99%, Aldrich) at a concentration of 5.0 mg/mL was injected to a polymer-coated column (UACW-15W-1.0F, 0.515 mm i.d. ×15.86 m long, bonded poly(ethylene glycol), film thickness of 1 μm and coil diameter of 270 mm, Frontier Laboratories Ltd., Japan). The diffusion column was immersed horizontally in a water bath whose temperature was maintained at the prescribed value with the fluctuation within 0.01 K. The pressure was regulated at an intended pressure within 0.002 MPa by a back pressure controller equipped with a high-frequency open−shut valve operated electromagnetically. The pressure drop between the inlet and the outlet of the diffusion column was less than 0.01 MPa. The pressures were calibrated with two Heise pressure gauges. The response curves were obtained by scanning from 195 nm to 250 nm at every 1.6 s and increments of 1 nm. Prior to the parameter determination, the effects of wavelength measuring on D_{12} and k values, linearity of peak area, and fitting error were examined. Consequently, the response curves measured at a wavelength of 210 nm were used to determine D_{12} and k values. All measurements were made at low flow rates so that the effect of secondary flow on D_{12} and k values was negligible as described in the previous studies.[20−22] The $De\cdot Sc^{1/2}$ values as a criterion of the secondary flow effect are listed in Table 1; mostly $De\cdot Sc^{1/2} < 8$, 11.4 at the maximum, where De and Sc are the Dean number and the Schmidt number, respectively. The Reynolds and the Schmidt numbers ranged from 21 to 75 and from 7 to 22 for linoleic acid, and from 20 to 96 and from 7 to 22 for arachidonic acid, respectively.

Results and Discussion

The D_{12} and k values for both solutes are listed in Table 1, together with the fitting error ϵ and the $De\cdot Sc^{1/2}$ values. Each data set of D_{12} and k values was obtained by a single injection. Figure 1 shows the response curves measured and calculated at 333.15 K and 20.05 MPa for linoleic acid. Note that $C_a^* = C_a/\int_{t_1}^{t_2}C_a\,dt$. The calculated response curves were obtained by assuming various D_{12} values at $k = 0.780$, corresponding to $\epsilon = 0.0256$, 0.03, and 0.05. The best fit was at $\epsilon = 0.0256$, and the calculated curve was fitted well to that measured experimentally. As mentioned in the previous studies[20−22] and shown in Figure 1, the fit was acceptably good at fitting errors less than 0.03. In this study, fitting errors were mainly less than 0.03, except those at lower pressures. The accuracies of D_{12} and k values for the solutes measured in this study were as good as those for β-carotene[20] and α-tocopherol,[20] measured by the same apparatus employed in this study: the uncertainty in the D_{12} value was less than ±4.3%, corresponding to a fitting error less than 0.03, and that in the k value was less than ±0.1%. The reproducibilities of D_{12} and k values for both solutes were less than 2%, mainly 1%, in comparison with the values at almost the same pressures listed in Table 1.

Figure 2 plots D_{12}/T versus CO_2 viscosity for linoleic acid and arachidonic acid. The D_{12} data for both solutes were well correlated by eq 4, as has been observed for various solutes.[13,20−26]

$$D_{12}/T = \alpha\eta^{\beta} \tag{4}$$

where D_{12} is in $m^2\cdot s^{-1}$, T is temperature in Kelvin, η is solvent viscosity in Pa·s, and α and β are constants, which are specific to the solute and solvent system. The α and β values for both solutes together with average absolute deviation AAD% are presented in Table 2. The CO_2 viscosities were estimated by the equation of Vesovic et al.[27]

The original Schmidt number correlation[28] given by eq 5 was also found to be effective for correlating D_{12} values for various solutes in supercritical fluids.[13,20−24,26]

$$Sc^+ = \frac{Sc}{Sc^*} = 1 + \exp\left[\sum_{i=0}^{5} a_i\left(\frac{\nu_0}{\nu}\right)^i\right] \tag{5}$$

where

$$Sc^* = \frac{5}{6}\left[\frac{\sigma_1+\sigma_2}{2\sigma_2}\right]^2\left[\frac{2M_1}{M_1+M_2}\right]^{1/2} \quad \text{for binary diffusion} \tag{5a}$$

The coefficients a_i for $i = 0$ to 5 are -4.92519817, 5.45529385×10^1, -2.45231443×10^2, 6.07893924×10^2, -7.08884016×10^2, and 3.29611433×10^2, respectively. Sc and Sc^* are the Schmidt numbers at high pressure and at atmospheric pressure at the same temperature, respectively, v is the molar volume of the solvent, v_0 is the hard-sphere closest-packed volume of solvent molecules, and σ_1 and σ_2 are the hard-sphere diameters for the solute and solvent, respectively. The σ_2 value is obtained from the v_0 correlation with temperature.[28] Figure 3 illustrates the plots for linoleic acid and arachidonic acid, when hard-sphere diameters of the solutes were chosen as to minimize the deviations of the measured data from those predicted by the correlation. Unfortunately, since the hard-sphere diameters for both solutes were unknown, the van der Waals diameters, σ_{vw}, estimated by the method of Bondi,[29] were employed. The correlations represented well the data for both solutes: AAD% = 3.70% ($\sigma_{vw} = 0.843$ nm) and 4.76% ($\sigma_{vw} = 0.863$ nm) for linoleic acid and arachidonic acid, respectively. Note that the original Schmidt number correlation[28] does not have any adjustable parameters. When hard-sphere diameters were adjusted, as has been seen for other solutes,[13,20] the accuracies slightly improved: AAD% = 3.42% ($\sigma = 0.854$ nm) and AAD% =

Table 1. Measured D_{12} and k Values, Together with Fitting Errors ϵ, Defined by Equation 3, and the $De\cdot Sc^{1/2}$ Value for Each Solute

solute	T/K	P/MPa	$10^8 D_{12}$/m$^2\cdot$s^{-1}	k	$10^2\epsilon$	$De\cdot Sc^{1/2}$
linoleic acid	308.15	8.50	0.870	4.969	1.42	7.4
		8.97	0.831	3.275	1.70	7.0
		10.00	0.753	1.963	0.98	5.9
		11.02	0.733	1.519	1.64	5.5
		12.00	0.689	1.276	1.76	5.6
		14.00	0.645	0.981	1.69	5.6
		16.01	0.613	0.817	1.47	5.6
		17.47	0.602	0.751	1.80	5.3
		18.02	0.590	0.719	1.98	5.6
		20.00	0.585	0.633	2.78	5.8
		21.00	0.571	0.632	1.82	5.1
		22.03	0.569	0.603	2.03	5.1
		25.00	0.526	0.535	1.86	4.3
		26.00	0.520	0.522	2.15	4.3
		28.05	0.505	0.496	1.89	4.1
		30.30	0.496	0.466	1.25	4.4
	313.21	9.49	0.947	5.826	1.20	9.1
		10.04	0.874	3.377	0.77	7.2
		10.99	0.803	2.116	1.30	7.8
		12.00	0.770	1.596	1.60	6.6
		14.02	0.717	1.101	1.72	5.6
		15.98	0.675	0.865	1.18	5.0
		17.98	0.647	0.741	2.24	5.4
		20.00	0.613	0.640	2.23	4.4
		21.99	0.597	0.581	1.65	4.4
		24.00	0.577	0.532	2.23	4.1
		26.01	0.563	0.497	2.09	4.0
		27.99	0.546	0.471	1.63	4.1
		30.04	0.549	0.459	2.57	3.9
		30.11	0.539	0.453	2.07	4.0
	323.15	12.02	0.890	3.730	3.58	9.3
		12.51	0.915	2.814	3.28	7.4
		13.00	0.886	2.261	2.14	6.8
		14.00	0.858	1.616	2.19	5.8
		16.00	0.776	1.059	1.76	5.1
		18.00	0.739	0.807	2.10	4.7
		20.01	0.706	0.669	2.08	4.5
		22.00	0.683	0.581	2.15	4.4
		24.00	0.657	0.519	2.57	4.2
		26.00	0.637	0.473	2.57	4.0
		28.02	0.612	0.433	2.43	3.7
		30.29	0.590	0.407	2.45	3.9
	333.15	13.89	0.959	3.556	3.34	7.0
		14.48	0.999	2.648	2.37	6.7
		15.00	0.967	2.175	2.11	5.7
		15.98	0.933	1.587	2.67	4.9
		18.00	0.866	1.025	2.43	4.6
		20.00	0.828	0.777	2.69	4.2
		20.05	0.817	0.780	2.56	4.2
		22.00	0.782	0.629	2.45	4.4
		24.02	0.758	0.537	2.85	3.8
		26.06	0.721	0.480	2.78	3.9
		27.02	0.714	0.450	2.81	3.8
		28.02	0.703	0.414	2.61	3.8
		29.04	0.699	0.410	2.53	3.8
		30.07	0.682	0.382	2.46	3.7
	343.15	16.20	1.017	2.508	3.40	7.4
		16.21	1.039	2.539	3.05	6.0
		16.99	1.019	1.903	2.86	5.7
		17.99	0.985	1.410	2.97	5.6
		18.00	0.984	1.426	1.95	4.8
		18.99	0.943	1.157	2.97	5.3
		20.00	0.901	0.962	3.07	4.3
		20.04	0.918	0.942	2.49	4.5
		22.00	0.871	0.701	2.90	3.9
		24.00	0.837	0.568	2.27	3.8
		26.01	0.811	0.484	2.87	3.6
		26.99	0.788	0.457	1.83	4.2
		28.01	0.777	0.426	2.78	3.5
		29.05	0.781	0.397	2.77	3.8
		30.03	0.764	0.387	3.13	3.4
arachidonic acid	308.15	9.50	0.750	4.253	1.88	8.1
		10.00	0.717	3.307	1.73	7.7
		10.52	0.703	2.837	1.88	7.1
		10.87	0.675	2.587	1.66	7.2
		11.00	0.658	2.494	1.34	6.4
		11.50	0.657	2.247	1.91	5.6
		12.01	0.670	2.042	2.00	5.7
		12.02	0.648	2.049	1.95	6.1
		12.49	0.627	1.889	1.56	6.2
		12.99	0.618	1.774	1.80	5.8
		14.00	0.617	1.547	1.89	5.6
		15.99	0.590	1.277	1.59	5.5
		17.99	0.563	1.097	1.98	5.2
		20.01	0.548	0.975	1.88	5.0
		22.00	0.538	0.888	1.71	5.1
		24.00	0.525	0.816	1.74	5.2
		26.00	0.511	0.765	1.77	5.1
		28.01	0.502	0.716	1.59	5.0
		30.24	0.499	0.683	2.23	4.5
		30.49	0.485	0.671	2.10	4.2
	313.21	9.50	0.904	10.248	3.75	9.4
		10.00	0.841	6.252	1.18	11.4
		11.01	0.776	3.587	1.68	8.2
		12.01	0.710	2.598	1.56	6.6
		14.00	0.666	1.755	2.25	5.4
		16.00	0.629	1.354	2.37	4.8
		18.00	0.606	1.123	2.42	4.7
		20.00	0.578	0.972	2.31	4.5
		22.01	0.564	0.861	2.03	4.4
		24.01	0.553	0.788	2.37	4.2
		26.01	0.536	0.725	2.10	4.3
		28.02	0.524	0.676	2.09	4.3
		30.04	0.510	0.646	2.20	4.1
		30.13	0.510	0.640	1.78	4.1
	323.15	12.01	0.902	6.589	1.89	9.7
		12.50	0.907	4.904	1.87	9.4
		13.02	0.866	3.799	1.73	8.6
		13.48	0.828	3.205	1.51	7.8
		14.01	0.815	2.690	2.39	6.9
		15.99	0.744	1.713	2.60	6.0
		18.00	0.703	1.267	2.40	5.0
		20.02	0.678	1.025	2.56	5.1
		21.99	0.642	0.868	2.37	4.6
		24.00	0.621	0.763	2.29	4.4
		26.00	0.602	0.689	2.26	4.4
		28.02	0.588	0.629	2.34	4.2
		30.05	0.564	0.584	1.72	4.2
		30.06	0.582	0.586	2.41	4.1
	333.15	13.89	1.053	6.254	2.51	11.2
		15.03	0.916	3.630	2.57	7.3
		15.50	0.904	3.036	2.42	7.6
		16.98	0.847	2.023	1.95	5.6
		17.50	0.832	1.790	2.43	5.5
		19.01	0.791	1.371	2.31	5.0
		19.99	0.767	1.192	2.27	4.8
		22.01	0.726	0.945	2.33	4.5
		24.00	0.701	0.803	2.59	4.4
		26.01	0.681	0.703	2.08	4.7
		26.06	0.678	0.679	1.80	4.4
		28.03	0.668	0.604	2.55	4.4
		30.16	0.649	0.549	2.32	4.0
	343.15	16.20	1.005	4.262	2.48	9.0
		16.99	0.957	3.147	2.49	6.9
		17.49	0.945	2.685	2.57	7.0
		18.01	0.914	2.299	2.79	5.9
		18.99	0.893	1.827	2.77	5.9
		19.99	0.861	1.486	2.78	5.3
		21.00	0.846	1.242	2.73	4.8
		22.01	0.832	1.073	2.15	4.6
		22.98	0.787	0.952	2.12	4.7
		23.99	0.779	0.862	3.09	4.3
		26.00	0.758	0.710	2.96	3.9
		28.00	0.712	0.610	2.89	3.7
		28.05	0.730	0.602	2.16	3.9
		30.26	0.713	0.539	2.82	3.7

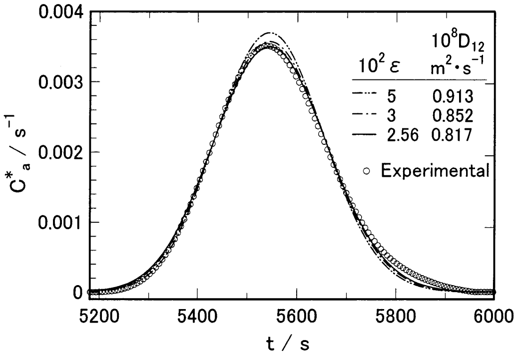

Figure 1. Response curves measured and calculated by assuming D_{12} values at fixed $k = 0.780$ for linoleic acid at 333.15 K and 20.05 MPa.

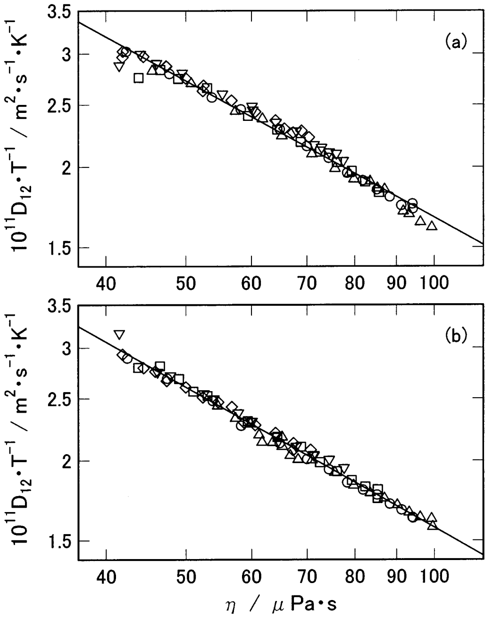

Figure 2. D_{12}/T vs CO_2 viscosity for (a) linoleic acid and (b) arachidonic acid: △, 308.15 K; ○, 313.21 K; □, 323.15 K; ▽, 333.15 K; ◇, 343.15 K.

Table 2. Determined α and *β* Values in Equation 4

solute	α	*β*	AAD%	*N*[a]
linoleic acid	2.513×10^{-14}	−0.706	1.91	71
arachidonic acid	1.949×10^{-14}	−0.727	1.33	75

[a] *N* = number of data points.

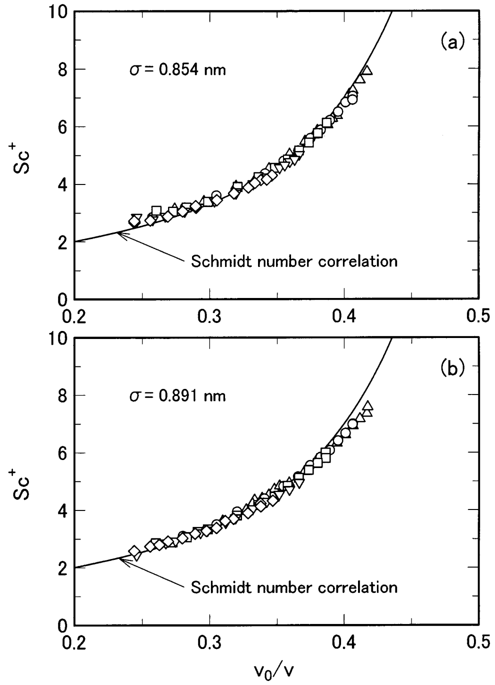

Figure 3. Schmidt number correlation for (a) linoleic acid and (b) arachidonic acid. The key is the same as in Figure 2. Sc^+ is defined by eq 5.

Table 3. Determined c_1, c_2, c_3, and c_4 Values in Equation 6

solute	c_1	c_2	c_3	c_4	AAD%	*N*[a]
linoleic acid	0.006 54	−7.703	−0.0756	61.33	2.83	71
arachidonic acid	0.004 36	−7.488	−0.0640	61.27	2.34	75

[a] *N* = number of data points.

3.06% (σ = 0.891 nm) for linoleic acid and arachidonic acid, respectively.

As has been shown for various solutes,[13,20,22] *k* values were well expressed by eq 6 with AAD% of 2.83% and 2.34% for linoleic acid and arachidonic acid, respectively.

$$\ln(k) = (c_1(T/\mathrm{K}) + c_2)\ln(\rho/\mathrm{kg{\cdot}m^{-3}}) + c_3(T/\mathrm{K}) + c_4 \qquad (6)$$

where *k* is the partition ratio with no dimension, *T* is absolute temperature, ρ is the density, and c_1−c_4 are constants for each solute, as listed in Table 3. The CO_2 density was estimated by the equation of state of Pitzer and Schreiber.[30]

Figure 4 plots $\bar{v}_1^\infty$ values calculated from the *k* value versus pressure for (a) linoleic acid and (b) arachidonic acid, where the partial molar volume was obtained through eq 7, by assuming $\bar{v}_{s,1}^\infty$ to be negligible,[31] as compared with $\bar{v}_1^\infty$.

$$\left(\frac{\partial(\ln k)}{\partial(\ln \rho)}\right)_T = \frac{\bar{v}_1^\infty - \bar{v}_{s,1}^\infty}{R_g T \beta_T} - 1 \qquad (7)$$

where $\bar{v}_1^\infty$ and $\bar{v}_{s,1}^\infty$ are the solute partial molar volumes for the supercritical and the stationary (polymer) phase, respectively, R_g is the gas constant, and β_T is isothermal compressibility. As has been seen for ubiquinone CoQ10[22], α-tocopherol,[20,23] *β*-carotene,[20,23] eicosapentaenoic acid,[13] docosahexaenoic acid,[13] and α-linolenic acid,[13] large negative partial molar volumes showed near 9 MPa in the temperature range studied. The large negative values caused by excess local density of the supercritical solvent in the near critical region have been discussed.[32] As the pressure increases away from the critical pressure, the values increase up to 20 MPa, and then those nearly leveled off. Unfortunately, the interaction parameters k_{ij} and the critical properties for both the solutes are unknown or the prediction is less reliable, and the prediction was not made by an equation of state.

Conclusions

At infinite dilution, binary diffusion coefficient and partition ratio for two ω6 compounds were determined at temperatures from 308.15 K to 343.15 K and pressures from 9 MPa to 30 MPa by a tracer response technique with a poly(ethylene glycol)-coated capillary column. Solute partial molar volume at infinite dilution was also obtained from the *k* value. The D_{12} values were well

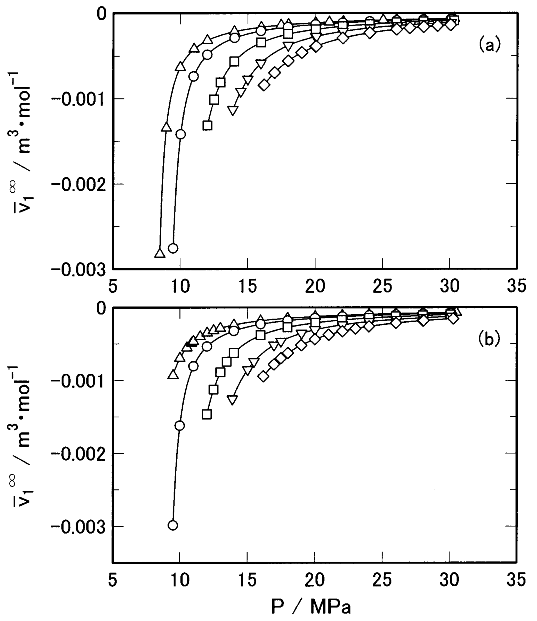

Figure 4. $\bar{v}_1^\infty$ value vs pressure for (a) linoleic acid and (b) arachidonic acid. The key is the same as in Figure 2, and the lines drawn in the figure were obtained from eq 7. The temperature and the pressure designated with the key in the figures correspond to those at which each datum was measured.

expressed by two correlations: D_{12}/T versus CO_2 viscosity and the Schmidt number correlation. The k values were well represented with a function of temperature and CO_2 density.

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