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Liquid−Liquid Equilibria for Systems Containing 2-methoxyphenol or 2-ethoxyphenol and Selected Alkanes

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1. Introduction

For several years ago, we have been interested on the investigation of intramolecular effects between the phenyl ring (C_6H_5-group) and a polar group, X, more or less directly attached to aromatic ring, as these effects are very different to those between the same groups when they belong to different molecules. For example, the upper critical solution temperature (UCST) of the phenol + decane mixtures is 336,50 K [1], while the excess molar enthalpy, H_m^E, of decan-1-ol + benzene system at equimolar composition and 298.15 K is 1050 J. mol^{-1}, extrapolated value [2]. That is, intramolecular effects lead to enhanced interactions between like polar molecules, while intermolecular effects make usually more favourable in interactions between unlike molecules. For this purpose, we have studied, experimental and theoretically, intramolecular effects, also termed proximity effects, in mixtures containing aromatic amines [3-11] (anilines, 2-amino-1-methylbenzene, 1-phenylmethanamine, 2-ethoxy-benzenamine, 4-ethoxy-benzenamine, 1H-pyrrole, quinoline or imizadoles); phenylmethanal, 1-phenylethanone, 4-phenyl-2-butanone, benzyl ethanoate [12-15], benzonitrile, phenylacetonitrile, 3-phenylpropionitrile [16], 2-phenoxyethanol or aromatic alkanols (phenol, phenylmethanol, 2-phenylethan-1-ol) [17-19]. As a continuation, we provide now liquid-liquid equilibria data for alkane systems involving 2-methoxyphenol (guaiacol) or 2-ethoxyphenol. Alkoxyphenol molecules exhibit unique structural characteristics, wherein two distinct polar groups (-OH and -O-) are attached to the phenyl ring at different positions. It is anticipated that intramolecular interactions between these two groups play a significant role. In a previous study conducted by our research group, we investigated the phenoxyethanol + alkane systems [17]. However, this case presents a slight deviation, as the -O- and -OH groups are situated within the same linear chain that is connected to the phenyl ring. Phenol derivatives play a crucial role as intermediates in the synthesis of various specialty chemicals. Understanding the phase behaviour of these product mixtures is of utmost importance for the development of manufacturing processes. Alcoxyphenols exhibit diverse applications. For instance, 2-methoxyphenol serves as an expectorant and finds utility as an antioxidant and anti-skinning agent in the context of paints. It also serves as a precursor for flavourings such as eugenol and vanillin, and is employed as an intermediate in the chemical synthesis of active pharmaceuticals, flavouring agents, and perfumery products. Additionally, it acts as an indicator in chemical reactions that generate oxygen. In studies focused on phenolic compounds' ability to inhibit oral bacteria, 2-ethoxyphenol is employed. 2-ethoxyphenol is also investigated for its potential as a cyclooxygenase inhibitor for prostaglandins. Moreover, it serves as a reagent for the stereoselective preparation of (arylthiomethyl)morpholines, which are selective inhibitors of norepinephrine reuptake and dual inhibitors of serotonin/norepinephrine reuptake.

2. Materials

All the information related to the source, purity, water content and density (ρ) of the pure compounds used in the present experimental research is collected in Table 1. The chemicals were used as received. Prior to use, the liquids are stored in containers with molecular sieve (Union Carbide Type 4D, Fluka). Density measurements were conducted by means of a vibrating-tube densimeter, Anton Paar model DSA-5000. The repeatability and the relative standard uncertainty of the ρ values are 5 10^{-3} kg·m^{-3}. Density values listed in Table 1 show that our results for n-alkanes are in good agreement with values from the literature. A careful survey of literature data showed that no ρ value has been previously reported for the 2-ethoxyphenol. 2-methoxyphenol presents subcooling effect at room temperature and its purity was tested thought the melting point. A TA Instruments Q2000 modulated differential scanning calorimeter (MDSC) was used to measure melting temperature. Tzero aluminum pans and lids purchased from TA instruments were filled with ∼7 mg of sample, and hermetically sealed. The seal prevented loss of mass from volatilization of the sample or operator error. A Sartorius MSE125P microbalance with a reproducibility of 0.015 mg was used to weigh the sealed pans. Water contents were determined by the Karl-Fischer method. The relative standard uncertainty of the corresponding measurements is estimated to be 0.02.

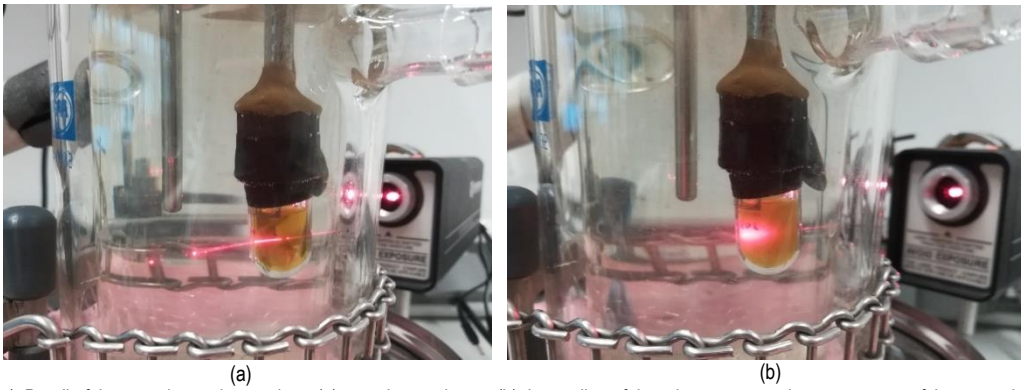
The mixtures are prepared by weighing with a measurement precision of 0.0001 g, inside Pyrex tubes with an internal diameter of 0.9 cm and a length of 4 dm. These tubes are immediately sealed at atmospheric temperature and pressure. The conversion to molar magnitudes is based on the 2013 Relative Atomic Mass Table published by the IUPAC Commission of Isotopes Abundances and Atomic Weights (CIAAW) [22] . The uncertainty in the calculation of the mole fractions is less than 0.0005. The weighing precision is 0.0001, but due that the most volatile component partially evaporates in the free volume of the ampoule (≅ 1.17 ×10^{-6} m^3) this value is slightly lower.

Table 1: Properties of pure compound at 0.1 MPa and 298.15 K[a]

Compound	CAS	Suplier	Reported purity[b]	M.P (exp)/K	M.P (Lit)/K	Water content[c]
2-methoxyphenol	90-05-1	Sigma-Aldrich	≥98%	299.01	300.65 [20]	128 ppm
Compound	CAS	Suplier	reported purity[b]	ρ^a /kgm^{-3} Exp.	ρ/kgm^{-3} Lit.	Water content
2-ethoxyphenol	94-71-3	Sigma-Aldrich	≥98%	995.93	-----	32 ppm
n-Octane	111-65-9	Sigma-Aldrich	≥99%	698.68	698.62 [21]	38 ppm
n-Decane	24-18-5	Fluka	≥99%	726.35	726.35 [21]	20 ppm
n-N-dodecane	112-40-3	Fluka	≥98%	745.51	745.32 [21]	25 ppm
n-Tetradecane	629-59-4	Fluka	≥99%	759.27	759.32 [21]	25 ppm
n-Hexadecane	544-76-3	Fluka	≥99%	770.221	770.06 [21]	33 ppm

[a] Standard uncertainties are: u(T) = 0.01 K; u(P) = 0.5 kPa; the relative standard uncertainty for density is $u_r(\rho)$ = 0.002 and 0.02 for water content.
[b] Provides by the supplier by gas chromatography; [c] In mass fraction

The LLE curves were determined by means of the observation of the turbidity produced on cooling (1.2 K h-1) when a second phase takes place. Details on the experimental method applied and on the apparatus calibration can be found elsewhere [19, 23]. Figure 1 shows the change in the appearance of the mixture when the phase separation occurs. The equilibrium temperatures were measured using a Pt-1000 resistance. Two or three runs are conducted for a better assessment of these temperatures. The thermometer was calibrated according to the ITS-90 scale of temperature using the triple point of the water and the fusion point of Ga as fixed points. The precision of the equilibrium temperature measurements is ± 0.001 K. The corresponding estimated standard uncertainty depends on the region where measurements are conducted. In the flat region of the LLE curves (top of the curves), the uncertainty of the temperature is 0.1 K. Outside from this region (tails of the curves), it is 0.2 K. For the equilibrium mole fractions, the standard uncertainty is 0.0005. This value is estimated taking into account that the more volatile component is partially evaporated to the mentioned free volume of the ampoule.



(a) (b)

Figure 1. Detail of the experimental procedure: (a) one phase mixture; (b) the cooling of the mixture causes the appearance of the second phase.

3. Results

The directly measured liquid-liquid equilibrium temperatures, T, vs. x_1, the mole fraction of the alkoxyphenol, for the systems 2-methoxyphenol + n-C10, or + n-C12, or + n-C14, or + n-C16 and for 2-ethoxyphenol + n-C8, or + n-C12, or + n-C14, or + n-C16 are collected in Figs. 2, 3. Values of liquid-liquid equilibria for systems alkoxyphenol + n-alkane are not available in the literature. As in many systems previously investigated [6-8, 12-16, 18, 19, 24] the LLE curves if mixtures under study are characterized by some typical features: (i) they show a rather flat maximum (Figs. 1-a, 1-b); (ii) the curves become progressively shifted towards higher x_1 values when the chain length of the alkane increases, (iii) the upper critical solution temperature, UCST, increases linearly with the number of C atoms of the n-alkane (Table 2).

The experimental (x_1, T) data of each system were correlated by means of the equation 1 [25, 26]:

$$T = T_c + k|y - y_c|^m \quad (1),$$

where

$$y = (\alpha \cdot x_1)/(1 + x_1 \cdot (\alpha - 1)) \quad (2),$$

$$y_c = (\alpha \cdot x_c)/(1 + x_{1c} \cdot (\alpha - 1)) \quad (3).$$

In eqs. 1 to 3, m, k, α, T_c, and $x_{1,c}$,are the coefficients to be fitted to the experimental results. The coordinates of the critical point are denoted by (x_{1c}, T_c). When $\alpha = 1$, eq. 1 is similar to the well-known equation [27-29]

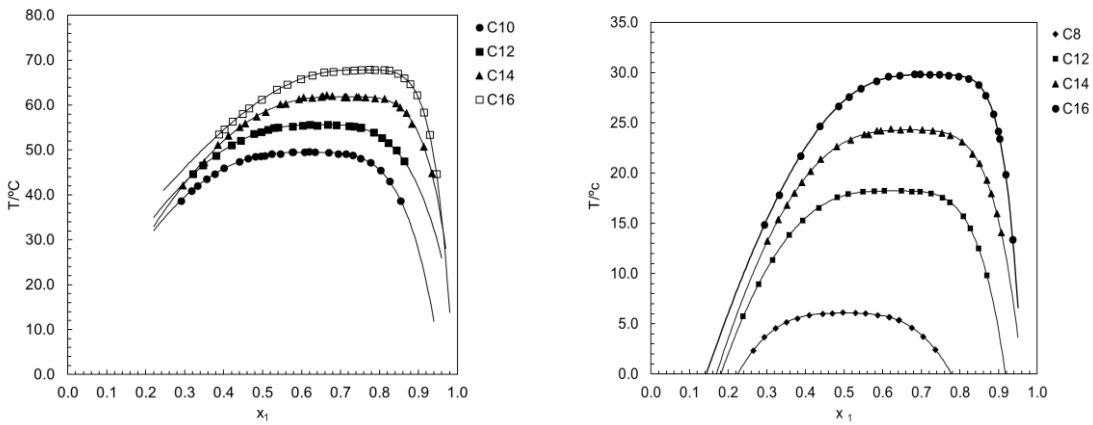
$$\Delta\lambda = \mathrm{B}\tau^{\beta} \quad (4).$$

In this equation, $\Delta\lambda_1 = \lambda_1' - \lambda_2''$ is any order parameter, that is, any density variable in the conjugate phase (along this research, $\lambda_1 = x_1$) On the other hand, $= T_C - T/T_C$, is the reduced temperature, β the critical exponent related to $\Delta\lambda_1$and B stands for the amplitude. The critical exponent, β, depends on the theory applied to its determination [23, 28].

The parameters m, k, α, T_c, and $x_{1,c}$ were obtained from an adjustment on a Marquardt algorithm [30] with all the points weighted equally. Results are collected in Table 2. Also listed is the standard deviation, defined by:

$$\sigma(T) = \sqrt{\sum\left(T_{exp} - T_{calc}\right)^2/(N-n)} \qquad (5)$$

where N and n stand for the number of data points and the number of fitted parameters, respectively. Results listed in Table 3 show that Eq. (1) correctly fits the experimental results.



a) b)

Figure 2: LLE for a) 2-methoxyphenol (1) + n-alkane (2) mixtures; b) 2-ethoxyphenol (1) + n-alkane (2). Points, experimental results. Solid lines are the result of the fitting of the experimental data by means of equation (1) using the parameters collected in Table 2.

Table 2: Coefficients in eq. (1) for the fitting of the (x_1, T) pairs for 2-methoxyphenol or 2-ethoxyphenol (1) + n-alkane (2) mixtures; $\sigma(T)$ is the Standard Deviation Defined by eq. (5).

N [a]	m	k	α	T_c/K	x_{1c}	$\sigma(T)$/K
		2-methoxyphenol (1) +n-decane (2)				
27	3.2225	-585.32	0.5182	322.63	0.6252	0.07
		2-methoxyphenol (1) + n-dodecane (2)				
25	2.9390	-377.98	0.5389	328.75	0.6523	0.13
		2-methoxyphenol (1) + n-tetradecane (2)				
32	3.3945	-627.75	0.4050	335.02	0.7169	0.13
		2-methoxyphenol (1) + n-hexadecane (2)				
26	3.3648	-692.23	0.2676	340.99	0.7614	0.06
		2-ethoxyphenol (1) + n-octane (2)				
19	3.1438	-343.54	1.0112	279.20	0.5006	0.04
		2-ethoxyphenol (1) + n-dodecane (2)				
25	3.4908	-557.07	0.5428	291.37	0.6320	0.04
		2-ethoxyphenol (1) + n-tetradecane (2)				
27	3.3927	-476.88	0.5091	297.43	0.6713	0.06
		2-ethoxyphenol (1) + n-hexadecane (2)				
24	3.9204	-917.07	0.3246	302.95	0.7311	0.05

[a] number of experimental points

4. Discussion

For a given alkoxyphenol, the UCST of the studied systems increases with the length chain of the n-alkane (Figure 3) and the curves become progressively shifted towards higher x_1 values when the chain length of the n-alkane increases (Figure 4). The same behaviour is observed in mixtures formed by n-alkane with linear and aromatic alkanone [15], linear organic carbonate [31], acetic anhydride [32], alkoxyethanol [23, 33] and alkoxybenzenamine [8]. For a fixed n-alkane, the UCST of mixtures of methoxyphenol are higher than those with ethoxyphenol. The intramolecular interaction (hydrogen bonds) between the hidroxil group (-OH) and the alkoxyalkane group (-O-R, R=CH_3 or CH_2-CH_3) are stronger the shorter the length of the alkane (-R). Comparison with other systems in which two functional groups are included to the aromatic ring, jointly or separately, is mandatory. In previous works, the LLE of phenylamine [11], phenol [17], and 2-ethoxybenzenamine [8] mixtures with n-alkanes has been studied. For a given n-alkane, the UCTS of phenylamine (C_6H_5-NH_2) >phenol (C_6H_5-OH) > 2-ethoxybenzenamine (C_2H_5-O-C_6H_4-NH_2) > 2-ethoxyphenol (C_2H_5-O-C_6H_4-OH). On the behaviour of the molecule with a single X group (X= phenol or aniline) the steric (size) effects exerted by the addition of a second Y functional group (alkoxyalkane group) are weakened. It appears that the steric effects exerted by the new Y

group at position 2 are predominant over the new intramolecuar XY effect leading to the decrease in UCTS. These interactions become smaller as the alkoxy chain length increases.

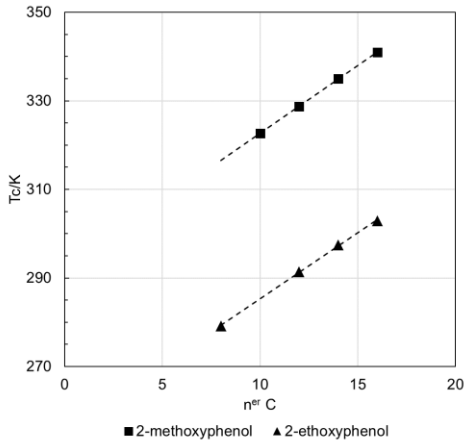


Figure 3. T_C vs n^{er} of carbons in the n-alkane

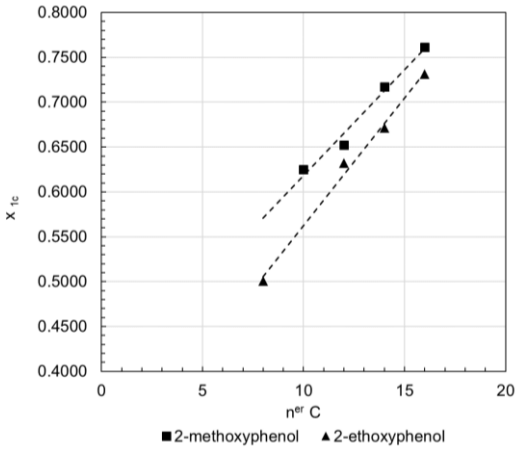


Figure 4. x_{1C} vs n^{er} of carbons in the n-alkane

5. Conclusions

Thermophysical properties of binary liquid mixtures have been very useful in obtaining information on the intermolecular interactions and geometrical effects in the systems. The liquid−liquid equilibrium (LLE) curves for 2-methoxyphenol or 2-ethoxyphenol+ n-alkane mixtures have been obtained by the critical opalescence method using a laser scattering technique. All of the systems show an upper critical solution temperature (UCST). In addition, the LLE curves have a rather horizontal top, and their symmetry depends on the alkane size. The UCST increases almost linearly with the number of carbons in the n-alkane. The strong intermolecular interactions that occur due to hydrogen bonding in mixtures with phenol and aniline are drastically reduced when a second alkoxy functional group is included in the aromatic molecule, and this reduction is greater the larger the size of the alkoxy group.

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