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Aqueous Solubilities of Alkylphenols and Methoxyphenols at 25 °C

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The aqueous solubilities of 25 phenolic substances (2-methylphenol; 3-methylphenol; 4-methylphenol; 2,3-dimethylphenol; 2,4-dimethylphenol; 2,5-dimethylphenol; 2,6-dimethylphenol; 3,4-dimethylphenol; 3,5-dimethylphenol; 2-ethylphenol; 4-ethylphenol; 2,3,5-trimethylphenol; 2,4,6-trimethylphenol; 3,4,5-trimethylphenol; 4-propylphenol; 2-isopropylphenol; 4-isopropylphenol; 4-butylphenol; 3-*tert*-butylphenol; 4-*tert*-butylphenol; 4-hexylphenol; 3,5-di-*tert*-butylphenol; 4-octylphenol; 3-methoxyphenol; and 4-methoxyphenol) were determined at 25 °C, by a conventional shake-flask, batch contacting method with analysis by high-pressure liquid chromatography with UV detection. Satisfactory agreement was obtained between measured and previously reported solubilities for 10 of these substances. The liquid or supercooled liquid solubilities are satisfactorily correlated with the solute's LeBas molar volume and with first-order valence molecular connectivity, yielding structure–property relationships that may be useful for predictive purposes.

Introduction

The lethality and bioconcentration of alkylphenols are sufficiently high to warrant a more detailed study of their sources, environmental fate, and effects. Alkylphenols are widely used or formed industrially. Methylphenols (cresols) are present in waste water from wood pulping, metal manufacturing, and refining industries; 2,4-dimethylphenol may be released during its use in the manufacture of plastic and resins, pharmaceuticals, insecticides and fungicides, disinfectants, and solvents; 4-*tert*-butylphenol is used for the production of a variety of resins and as a stabilizer. Octyl- and nonylphenols are employed as nonionic surfactants.

In a review of phenolic and chlorophenolic compounds Suntio et al. (*1*) noted the lack of physical–chemical property data of many compounds, rendering an adequate understanding of their fate in the environment difficult and incomplete. Aqueous solubility is an important parameter for assessing environmental partitioning because it influences air–water partitioning, evaporation, and partitioning or sorption to biotic and abiotic phases. There is thus a need to obtain experimental solubility data for these substances and establish structure–property relationships using appropriate molecular descriptors. Solubility is also of interest because it can be used to estimate the fundamental thermodynamic property, namely the chemical's activity coefficient in the aqueous phase.

Experimental Section

The following materials were used, the purities being given in parentheses.

Alkylphenols. 2-Methylphenol (98%), 3-methylphenol (97%), 4-methylphenol (99%), 2,3-dimethylphenol (97%), 2,4-dimethylphenol (97%), 2,5-dimethylphenol (99+%), 2,6-dimethylphenol (97%), 3,4-dimethylphenol (99%), 3,5-dimethylphenol (99+%), 2-ethylphenol (99%), 4-ethylphenol (99%), 2,3,5-trimethylphenol (99%), 2,4,6-trimethylphenol (99%), 3,4,5-trimethylphenol (99%), 4-propylphenol (98%), 2-isopropylphenol (98%), 4-isopropylphenol (98%), 3-*tert*-butylphenol (99%); 4-*tert*-butylphenol (99%), 3,5-di-*tert*-butylphenol (99%), 3-methoxyphenol (97%), and 4-methoxyphenol (99%) were purchased from Aldrich Chemical Co.; 4-octylphenol (99%), 4-butylphenol (99%), and 4-hexylphenol (99%) were purchased from Eastman Kodak Co. The chemicals were used as purchased and were not purified. Double-distilled water was used for all saturated solutions preparation. Methanol (HPLC grade) was obtained from Caledon Laboratories, Ontario. Milli-Q ultrapure deionized water was used with methanol as the mobile phase for the HPLC system.

Preparation of Saturated Solutions. Excess amounts of alkylphenols were added to 25 or 50 mL Erlenmeyer flasks containing double-distilled water. They were stirred or shaken gently for 24 h and allowed to settle at 25 °C for at least 24 h before analysis. pH values were measured by a Canlab Model 607 pH meter. There was no pH adjustment or buffering. The pH of the double-distilled water was 7.05.

Equipment. A Waters Associates (Milford, MA) liquid chromatograph (HPLC system) consisting of a Model 6000 solvent delivery system, a Model M45 solvent delivery system, a Model 440 UV absorbance detector with 254 and 280 nm kits, and a Model 721 system flow controller was used for analysis. It was operated in isocratic mode with methanol–water mixture (the ratio varied from 85:15 to 95:5 by volume) as the mobile phase. The analytical column was a Waters 3.9 mm o.d. × 300 mm long μBondapak C_{18} column. Aqueous samples were directly injected onto the column. Peak areas were integrated and recorded by a Waters Model 730 data module. Calibration standards were prepared by dissolving measured masses of the phenolic substances in methanol.

Results and Discussion

Table 1 gives the measured aqueous solubilities of the compounds at 25 °C and previously reported values. The present solubility data have a precision (standard deviation) varying from 2 to 7%. Also given is the molar volume $V_M/(\mathrm{cm^3 \cdot mol^{-1}})$ as calculated using the simple, additive LeBas method (*2*) which for mono-, di- and tri-methylphenols reduces to the equation below, where n is the number of methyl groups and 22.2 represents the difference in molar volume between a methyl group and hydrogen

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Table 1. Aqueous Solubilities, Supercooled Liquid Solubilities (C_L), and Related Properties Including First-Order Valence Molecular Connectivity Index (MCI) ($^1\chi^v$) of Alkylphenols and Methoxyphenols at 25 °C

compound	MP/°C	MW	pK_a (ref 13)	LeBas mol vol/ $cm^3 \cdot mol^{-1}$	solubility/ $g \cdot m^{-3}$	C_L/ $mol \cdot m^{-3}$	at pH	lit. value ($g \cdot m^{-3}$)	method[a]	ref	MCI $^1\chi^v$
phenol	41	94.11	9.92	103.4	nm[b]	1352	nm	88360	SF-UV spec	5	2.134
o-cresol	31	108.13	10.26	125.6	26800 ± 2500	284.1	3.6	25950	SF-UV spec	5	2.551
m-cresol	12	108.13	10.0	125.6	19600 ± 300	181.3	4.45				2.545
p-cresol	34.8	108.13	10.26	125.6	22000 ± 300	254.3	3.9	19000	SF-UV spec	5	2.545
2,3-dimethyl-	75	122.17	10.4[c]	147.8	6480 ± 40	165.6	6.0				2.968
2,4-dimethyl-	26	122.17	10.6	147.8	8200 ± 100	68.67	6.5	6200 7870	SF-UV spec LSC	5 6	2.962
2,5-dimethyl-	75	122.17	10.3	147.8	3760 ± 60	96.11	4.5	3176	SF-UV spec	5	2.962
2,6-dimethyl-	49	122.17	10.6	147.8	6150 ± 110	86.95	6.3	6230	SF-UV spec	5	2.968
3,4-dimethyl-	66−68	122.17	10.4	147.8	7250 ± 90	154.4	6.25	5100	SF-UV spec	5	2.962
3,5-dimethyl-	68	122.17	10.2	147.8	6710 ± 50	146.2	6.15	4886	SF-UV spec		2.957
2-ethylphenol	−3.4	122.17	10.2	170	14042 ± 213	114.9	5.2				3.112
4-ethylphenol	42−45	122.17	10.0	170	7980 ± 120	99.54	nm				3.106
2,3,5-trimethyl-	57−59	136.1	10.6	170	855 ± 16	13.32	5.95	762	SF-UV spec	5	3.378
2,4,6-trimethyl-	64−66	136.1	10.9	170	1420 ± 23	25.94	4.85	1007	SF-UV spec	5	3.378
3,4,5-trimethyl-	108−110	136.1	10.5[c]	170	1540 ± 40	76.64	5.75				3.378
4-propylphenol	22	136.1	10.3[c]	170	1278 ± 25	9.39	5.55				3.606
2-isopropylphenol	15−16	136.1	10.3[c]	170	4423 ± 99	32.5	nm				3.494
4-isopropylphenol	59−61	136.1	10.3[c]	170	3263 ± 48	53.2	5.1				3.488
4-butylphenol	22	150.22	10.3[c]	192.2	617 ± 20	4.11	5.25				4.106
3-*tert*-butylphenol	44−46	150.22	10.1[c]	192.2	2070 ± 30	21.73	5.95				3.798
4-*tert*-butylphenol	101	150.22	9.9	192.2	1850 ± 40	69.52	6.05	580	SF-UV spec	7	3.798
4-hexylphenol	32	178.28		236.6	391 ± 6	2.572	4.3				5.106
3,5-di-*tert*-butyl-	87−89	206.33	10.3[c]	281	14.0 ± 2	0.278	5.95				5.456
4-octylphenol	41−42	206.33		281	14.1 ± 0.6	0.0995	nm	12.6	GC-Fluo	6	6.106
4-nonylphenol		220.36		303.2	nm		nm	5.43	GC-Fluo	6	6.606
2-methoxyphenol	28	124.14	9.98	134.7	nm		nm	24800		8	2.663
3-methoxyphenol	<−17.5	124.14	9.65	134.7	67800 ± 1200	546	3.55				2.657
4-methoxyphenol	55−57	124.14	10.21	134.7	19500 ± 1100	318	nm				2.657

[a] SF, shake flask; UV spec, UV spectrophotometry; LSC, liquid scintillation counting; GC-Fluo, generator column, spectrofluorometry. [b] nm, not measured. [c] Estimated value, ref 10.

$$V_M = 103.4 + 22.2n$$

For correlating solubilities as a function of molar volume, the solubilities of solid solutes should be "corrected" to those of the supercooled liquid values. For this correction the fugacity ratio (i.e., ratio of solid to supercooled liquid solubilities) was calculated using either reported values of the enthalpy change $\Delta_{fus}H$ or entropy change $\Delta_{fus}S$ of fusion. $\Delta_{fus}S$ was found to be 36.6 $J \cdot mol^{-1} \cdot K^{-1}$ for phenol, 52.0 $J \cdot mol^{-1} \cdot K^{-1}$ for *o*-cresol, 37.5 $J \cdot mol^{-1} \cdot K^{-1}$ for *m*-cresol, and 41.3 $J \cdot mol^{-1} \cdot K^{-1}$ for *p*-cresol (*9*). The fugacity ratios were estimated by the expression

$$f_S/f_L = \exp[\Delta_{fus}H(1/T_M - 1/T)/R] = \exp[\Delta_{fus}S\,(1 - T_M/T)/R]$$

or in the absence of reported values estimated values of $\Delta_{fus}S$ were used by employing the expression suggested by Yalkowsky (*3*)

$$f_S/f_L = \exp[-6.79\,(T_M/T - 1)]$$

which implies that $\Delta_{fus}S/R$ is 6.79 or $\Delta_{fus}S$ is 56 $J \cdot mol^{-1} \cdot K^{-1}$. For liquids (i.e., melting point below 25 °C) no fugacity ratio correction is needed. The supercooled liquid solubilities C_L ($mol \cdot m^{-3}$) are also reported in Table 1.

When dissociation affects the measured solubility, a correction may be applied to account for the presence of ionized phenols in solution. Reported pK_a values are given in Table 1. For compounds for which no measured pK_a is available, this quantity can be estimated from the Hammett equation, as discussed by Perrin et al. (*10*).

$$pK_a = pK_a^0 - \varrho(\sum\sigma)$$

where σ is a constant assigned to a particular substituent, ϱ is a constant for a specific series, and pK_a^0 refers to the parent compound. For each substituent a different σ value applies for each position (ortho, meta, and para). The pK_a values of alkylphenols can be calculated from the equation for phenolic compounds

$$pK_a = 9.92 - 2.23\sum\sigma$$

The estimated values of pK_a are shown with a superscript *c* in Table 1. No estimate was made for hexyl-, octyl-, isooctyl-, and nonylphenols. The relatively low values of −0.06 for σ_{meta} and −0.14 for σ_{para} for methyl substituent indicate that alkylphenols have pK_a values similar to that of phenol.

A structure−property relationship, for example, relating solubility to molar volume, is likely to apply to the nonionized or neutral form. The ratio of concentrations of ionized and nonionized forms can be estimated as

$$(\text{ionized})/(\text{nonionized}) = 10^{(pH - pK_a)}$$

All the alkylphenols measured have relatively high pK_a values, and the difference between pK_a and pH values of the measurements always exceeds 3.8; therefore, the dissociation does not significantly affect the solubility at the pH values used here, and no correction is necessary.

Some discrepancies between measured and previously reported values are apparent. In all such cases the determination was repeated to confirm the measured value, but a possibility of systematic error remains. Thus, the value should be used with caution. Specifically, 2,4-dimethylphenol has a higher solubility than reported (*5*, *6*). It has a higher solubility than the 2,3-, 2,5-, and 2,6-isomers, but this is attributable to its lower melting point; indeed, its supercooled liquid solubility is less than that of

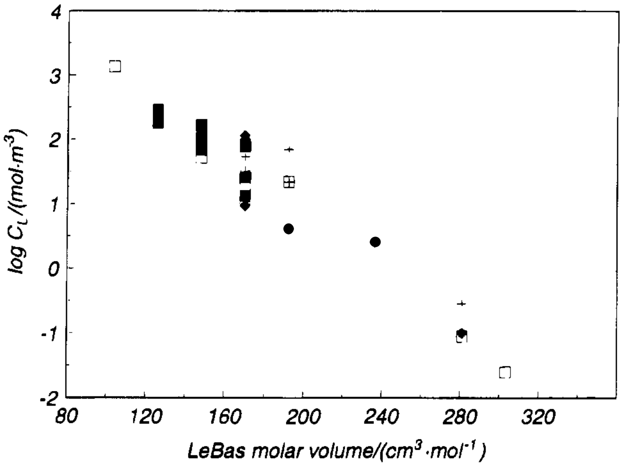

Figure 1. Aqueous solubilities of alkylphenols as a function of LeBas molar volume. Substituent: (◆) straight chain; (+) branched chain; (■) methyl group; (□) literature values.

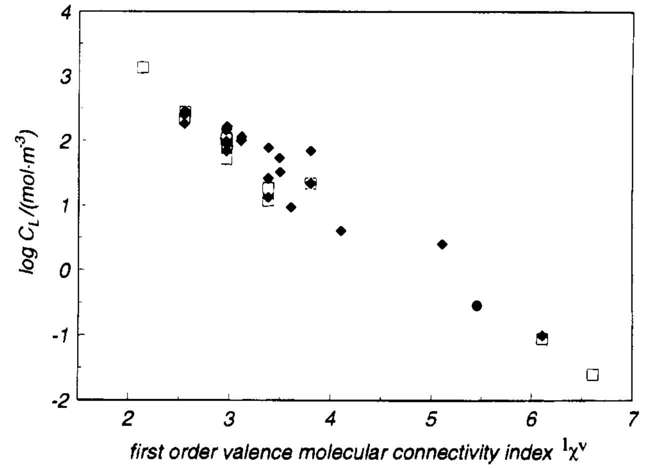

Figure 2. Aqueous solubilities of alkylphenols as a function of first-order valence molecular connectivity index: (□) literature values.

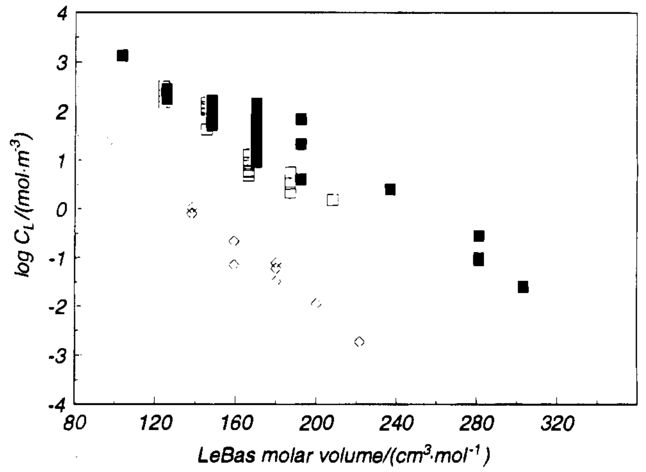

Figure 3. Aqueous solubilities of alkylphenols, chlorophenols, and chlorobenzenes as a function of LeBas molar volume: (■) alkylphenols; (□) chlorophenols; (◇) chlorobenzenes.

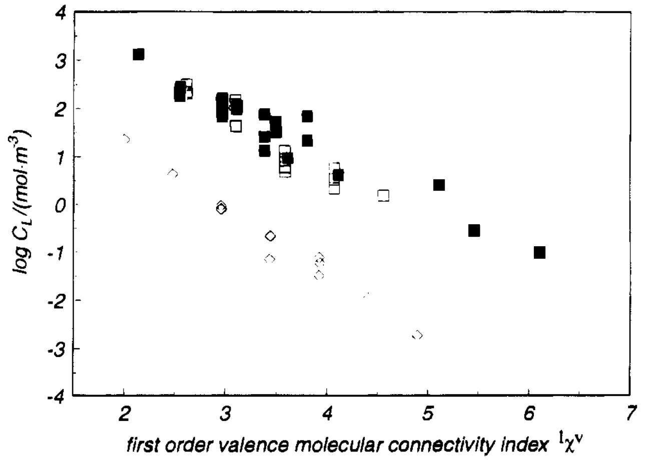

Figure 4. Aqueous solubilities of alkylphenols, chlorophenols, and chlorobenzenes as a function of first-order valence molecular connectivity index: (■) alkylphenols; (□) chlorophenols; (◇) chlorobenzenes.

those isomers. The measured solubility of 4-*tert*-butylphenol is also higher than reported (*7*) by a factor of 3.2, and surprisingly its supercooled liquid solubility exceeds that of 4-isopropylphenol. The branched isomers (e.g., isopropylphenols) are consistently more soluble than the polymethyl isomers (e.g., trimethylphenols), although part of this is attributable to generally lower melting points of the less symmetric branched isomers. Further interpretation is confounded by the possibility that the entropies of fusion are in error for the higher molecular weight substances.

Figure 1 is a plot of supercooled liquid solubility of alkylphenols versus molar volume which shows log–linear behavior with addition of methyl or methylene groups. The two methoxyphenols are not included because they constitute a different series. Both monomethoxy derivatives have the same molar volume; thus, no structure–property relationship can be established. The increase in molar volume with alkylation decreases the solubility in water, generally by a factor of 2.78, i.e. 0.44 log unit/methylene group. Alternatively, the slope is about 2.1 log units/100 cm^3·mol^{-1}. Examination of the data shows that substituting a methyl group for hydrogen on the aromatic ring causes less of a reduction in solubility than adding a methylene group to a side chain, despite the identical LeBas molar volume increase. The use of molecular connectivity was tested as an alternative molecular descriptor. The first-order valence molecular connectivity indices calculated according to the method of Kier and Hall (*4*) are dependent on the structure of the molecule and allow for differences between polymethyl derivatives and isomeric phenols with long alkyl chains. Specifically, the index includes an allowance for branching which generally results in an isomer that is more compact and offers less surface area to the water matrix, thus resulting in a higher solubility. The scatter is reduced as shown in Figure 2. The correlation coefficient for molar volume as a molecular descriptor is 0.93, while for this molecular connectivity index it is 0.95.

Figure 3 is a compilation of data for chloro- and alkylphenols from a number of sources (*11*, *12*, *14*) and includes for comparison chlorobenzene data. The phenols generally display a slope of about 2.8 log units/100 cm^3·mol^{-1}, whereas the chlorobenzenes show a slope corresponding to a decrease in log solubility by 3.5 units (a factor of 4.5). The chlorophenols are generally less soluble than the alkylphenols at the same molar volume.

Figure 4 shows the same data as in Figure 3, but using first-order valence molecular connectivity as the molecular descriptor, and gives a better overall correlation than molar volume. Apparently there is no profound difference in solubility or aqueous phase activity coefficient between chloro- and alkylphenols. The primary determinant of solubility is molar volume as best expressed by this molecular connectivity index. The chlorobenzenes are also well correlated, displaying solubilities which range from

1.5 to 3.0 log units (factors of 30−1000) larger. It is hoped that these data will be of value for assessing the environmental fate and effects and the fundamental thermodynamics for this class of compounds.

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