Partition Coefficients and Structures of Monohydric Phenols by the Technique of Countercurrent Distribution

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Partition coefficients of 40 monohydric phenols have been determined between cyclohexane and 0.1% aqueous sodium chloride by the technique of countercurrent distribution. Factors that affect the value of partition coefficient such as size, position, and nature of alkyl substituents, have been discussed. A graphical method has been proposed for predicting the partition coefficient of a phenol from its structure. This investigation will facilitate systematic study of phenols in systems such as tars from low temperature carbonization of coals, by the technique of countercurrent distribution.

THE PARTITION coefficient, k, of a solute is its preferential solubility between a pair of immiscible solvents. The underlying causes for the value of k are unquestionably related to those forces which determine solubility. According to Pearson and Levine (*6*) these forces are presumably hydrogen bonding ability of the solvent, dipole attraction, and van der Waal's attraction forces. But the precise contribution of these forces to the partition coefficient of a solute is not known. Nevertheless, there are valuable correlations between k and the structure of homologs and isomers of a class of compounds such as the monohydric phenols, because the forces controlling solubility are intimately associated with the structural characteristics of a molecule.

Obviously, the partition coefficient of a solute should be determined with accuracy. The usual method of single or double partition (*1*) in a separating funnel is not very reliable, particularly for solutes having high or low k values.

PROPOSED METHOD

In this laboratory k has been accurately determined by multiple extractions (*7*) in Craig's (*2*) countercurrent distribution apparatus. A small amount of solute (5 to 25 mg.) is subjected to few transfers (15 to 25) by the fundamental procedure between a properly chosen pair of immiscible solvents. The equation:

$$\frac{T_r}{T_{r+1}} = \frac{1}{k} \times \frac{r+1}{n-r} \qquad (1)$$

is plotted. Tr is the fractional amount of solute in the mobile phase (or any other property proportional to the amount of solute) in the rth tube and n is the transfer number. (T_{r+1}) is the fractional amount of solute in the mobile phase of tube number $(r+1)$.

The reciprocal of the slope of the resultant straight line passing through the origin gives k. Advantages of this method are: the solute need not be very pure or accurately weighed. Small amount of an impurity does not generally interfere unless its partition coefficient is close to that of the solute. The method is applicable for high as well as low values of k. The partition coefficients thus determined can be reliably used for the identification and estimation of a solute by the CCD technique.

Partition coefficients of 40 pure phenols (Table I) have been determined by the above method between spectroscopically pure cyclohexane (*7*) and 0.1% aqueous sodium chloride. The plot of the ratio of the absorbances (at a suitable wavelength determined in a Unicam ultraviolet spectrophotometer) of the solute in the cyclohexane layer in two adjacent tubes, $(r+1)/(n-r,)$ for all the tubes in the distribution band fell exactly on or very close to a straight line for all the phenols, showing that k had been very accurately determined.

BOILING POINT, STERIC HINDRANCE, and PARTITION COEFFICIENT

Table I gives the boiling points (*3, 9, 10*) and partition coefficients of monohydric phenols between cyclohexane and 0.1% aqueous sodium chloride. From the boiling points a rough idea of steric hindrance of the groups present in phenols may be visualized, on the assumption that intermolecular attraction will be less in the case of phenols whose substituents hinder one another sterically and hence possess a lower boiling point. Among isomers, the lowest boiling one would be the least solube in the aqueous phase, that is, it would have the highest partition coefficient, because the lowest boiling isomer has the greatest steric effect which prevents hydrogen bonding with water. The solubility of phenols in the aqueous phase is due mainly to their ability to form hydrogen bonding with water (*11*). Consequently ortho-substituted phenols, which are likely to have greater steric hindrance, will be less soluble in the aqueous solvent than the corresponding meta and para isomers. For the same reason if the alkyl side chains increase in size, the steric effect will be predominant, more so in the case of ortho-substituted phenols. In the case of ortho-substituted and other alkyl-substituted phenols, the solubility in the aqueous phase will decrease and hence the partition coefficients will increase as the size of the alkyl group increases. The partition coefficients of the alkyl phenols will further increase owing to the increase in their solubility in the cyclohexane phase with an increase in the

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size of the alkyl groups. As these two factors operate simultaneously, the partition coefficients of alkyl phenols are likely to increase very rapidly as the size of the alkyl group increases. These expectations are largely confirmed by the experimental results described. Thus, in the case of homologous phenols, the partition coefficient will be decided by the solubility in cyclohexane as well as in the aqueous phase, while in the case of isomeric phenols water solubility will be the deciding factor.

EFFECT OF SUBSTITUENTS ON PARTITION COEFFICIENTS

Size of Alkyl Substituents.—A larger alkyl group in any position—ortho, meta, or para—with respect to the phenolic hydroxyl gives a higher value of k, owing to decreased water solubility and increased cyclohexane solubility, associated with increased molecular weight. The ratio of partition coefficients of two adjacent homologs is approximately equal for ortho, para, or meta substituents (Table II). Thus the increase in the size of alkyl substituent will affect k of phenols nearly to the same extent whether they are ortho, para, or meta substituted.

Position of Alkyl Substituents.—As meta and para positions are nearly equidistant from the phenolic group, their values of k will be close. Yet p-phenols have invariably higher k values than the corresponding m-phenols; this is in keeping

Table I. Boiling Points and Partition Coefficients of Phenols

Compound	Boiling Point (at 760 mm.), ° C.	Refs.	Partition Coefficient
Phenol	181.7	(*9*)	0.17
o-Cresol	190.6	(*9*)	1.25
2,6-Xylenol	200.6	(*10*)	8.47
p-Cresol	201.5	(*9*)	0.645
m-Cresol	202.1	(*9*)	0.625
o-Ethylphenol	207.5	(*9*)	4.76
2,4-Xylenol	211.3	(*10*)	3.57
2,5-Xylenol	211.5	(*10*)	3.70
o-Isopropylphenol	214.5	(*9*)	. . .
2,3-Xylenol	217.1	(*9*)	3.21
2,6-Diethylphenol	218.0	(*10*)	. . .
p-Ethylphenol	218.2	(*10*)	2.35
m-Ethylphenol	218.5	(*9*)	2.27
o-Propyl phenol	219.4	(*10*)	15.0
2,4,6-Trimethylphenol	220.6	(*10*)	17.20
o-*tert*-Butylphenol	221.0	(*9*)	. . .
3,5-Xylenol	221.7	(*10*)	1.86
2-Ethyl-4-methylphenol	222.3	(*10*)	. . .
2-Ethyl-5-methylphenol	224.2	(*10*)	11.36
4-Methyl-2-isopropylphenol	225.0	(*10*)	. . .
p-Isopropylphenol	225.0	(*10*)	5.88
3,4-Xylenol	226.9	(*9*)	1.57
3-Ethyl-2-methylphenol	227.0	(*3*)	9.33
2-Methyl-4-ethylphenol	227.3	(*9*)	10.20
2-Methyl-5-ethylphenol	227.7	(*10*)	10.57
m-Isopropylphenol	228.0	(*9*)	. . .
m-Propylphenol	228.0	(*9*)	6.81
p-Propylphenol	234.5	(*9*)	7.20
o-Butylphenol	235.0	(*9*)	. . .
2,4,5-Trimethylphenol	235.2	(*9*)	8.70
3-Methyl-5-ethylphenol	235.9	(*10*)	5.41
2,3,5-Trimethylphenol	236.0	(*3*)	9.35
2,3,4-Trimethylphenol	237.0	(*3*)	. . .
p-*tert*-Butylphenol	239.0	(*9*)	13.1
3-Methyl-4-ethylphenol	240.0	(*3*)	. . .
4-Methyl-3-ethylphenol	240.0	(*3*)	5.50
4-Indanol	244.0	(*3*)	4.07
p-*n*-Butylphenol	246.0	(*9*)	19.40
m-Butylphenol	248.0	(*9*)	. . .
3,5-Diethylphenol	248.0	(*3*)	. . .
3,4,5-Trimethylphenol	251.9	(*10*)	4.25
5-Methyl-4-indanol	250.0	(*3*)	16.25
3-Methyl-4-indanol	250.0	(*3*)	. . .
5-Indanol	251.0	(*3*)	3.02
6-Methyl-4-indanol	257.0	(*3*)	9.98
3-Methyl-5-indanol	257.0	(*3*)	. . .
6-Methyl-5-indanol	257.0	(*3*)	. . .
4-Methyl-5-indanol	257–258.0	(*3*)	. . .
1-Methyl-5-indanol	258.0	(*3*)	. . .
7-Methyl-4-indanol	262.0	(*3*)	11.60
7-Methyl-5-indanol	268–270	(*3*)	7.38
2-Phenylphenol	275.0	(*3*)	. . .
1-Naphthol	284.4	(*10*)	3.31
2-Naphthol	296.0	(*10*)	1.96
1-Methyl-4-indanol	. . .		9.40
2-Methyl-5-isopropylphenol	. . .		20.0

Table II. Effects of Size of Side Chain of Partition Coefficient

Compound	Partition Coefficient	Ratio
A. In Para Position		
Phenol	0.17	3.78
p-Cresol	0.645	3.64
p-Ethylphenol	2.35	3.64
p-*n*-Propylphenol	7.2	3.06
p-*n*-Butylphenol	19.4	2.72
B. In Meta Position		
m-Cresol	0.625	3.63
m-Ethylphenol	2.27	3.00
m-*n*-Propylphenol	6.81	
C. In Ortho Position		
o-Cresol	1.25	3.80
o-Ethylphenol	4.76	3.15
o-Propylphenol	15.0	

Table III. Effect of Position of Side Chain on Partition Coefficient

Isomer		Partition Coefficient	Boiling Point, ° C.
A. Cresols			
m-Cresol		0.625	202.1
p-Cresol		0.645	201.5
o-Cresol		1.25	190.6
B. Ethylphenols			
m-Ethylphenol		2.27	218.5
p-Ethylphenol		2.35	218.2
o-Ethylphenol		4.76	207.5
C. Xylenols			
Group I.	3,4-Xylenol	1.57	226.9
	3,5-Xylenol	1.86	221.7
Group II.	2,3-Xylenol	3.21	217.1
	2,4-Xylenol	3.65	211.3
	2,5-Xylenol	3.70	211.5
Group III.	2,6-Xylenol	8.47	200.6
D. Trimethylphenols			
3.4,5-Trimethylphenol		4.25	251.9
2,4,5-Trimethylphenol		8.70	235.2
2,3,5-Trimethylphenol		9.35	236.0
2,4,6-Trimethylphenol		17.20	220.6
E. Indanols			
6-Methyl-4-indanol		9.98	257.0
7-Methyl-4-indanol		11.61	262.0
5-Methyl-4-indanol		16.25	250.0

with the slightly lower boiling point of the para isomer and is also supported by the infrared spectra of phenols. According to Friedel (*4*), alkyl substitution in the para position causes more intense OH bands than substitution in the corresponding meta position. Greater intensity of the OH band indicates greater steric hindrance of the compound. The remarkably higher *k* of *o*-phenols can be explained by the very strong steric hindrance associated with the so-called "ortho" effect (*11*).

Table III shows for cresols, xylenols, and ethylphenols that the higher boiling isomer has the lower partition coefficient. The 6- and 7-methyl-4-indanols, and 2,3,5- and 2,4,5-trimethylphenols appear to be exceptions, but both cases are understandable from a consideration of the relative meta-para effects.

In the case of 7-methyl-4-indanol, the methyl group in the 7 position, being para to hydroxyl, has a greater partition coefficient than 6-methyl-4-indanol, where the methyl group is meta with respect to the solubilizing hydroxyl group. In the other cases, the two trimethylphenols differ in the position of the second methyl group in the 3 or 4 position; probably the 3-methyl confers a greater "ortho" effect on the existing methyl group in the 2 position. In fact, according to Sears and Kitchen (*8*), a methyl group forces an adjacent *o*-methyl group closer to the hydroxyl, increasing the steric hindrance. Similarly 2,3,4-trimethylphenol will have a higher partition coefficient than 2,4,5-trimethylphenol, and 2,3,6-trimethylphenol will have greater *k* than 2,4,6-trimethylphenol. The "hydrogen bonding index" of Sears and Kitchen (*8*) (zero for completely hindered and unity for unhindered phenols) is 0.29 for 2,3,6-trimethylphenol and 0.33 for 2,4,6-trimethylphenol.

The partition coefficients of methyl-ethyl phenols may be similarly interpreted as those of the xylenols. In other words, they can be classified in order of increasing *k* as follows:

Group I.
3-Methyl-4-ethylphenol
3-Methyl-5-ethylphenol
2-Methyl-3-ethylphenol
3-Ethyl-4-methylphenol
3-Ethyl-5-methylphenol
2-Ethyl-3-methylphenol

Group II.
2-Methyl-4-ethylphenol
2-Methyl-5-ethylphenol
2-Ethyl-4-methylphenol
2-Ethyl-5-methylphenol

Group III.
2-Methyl-6-ethylphenol

The values of *k* determined for some of the methylethyl phenols (Table I) also confirms the above classification. Isomers of other alkyl phenols can be similarly classified.

Nature of Alkyl Substituents.—Branching in the alkyl substituents lowers the value of *k* (Table IV).

Table IV. Effect of Nature of Substituents on Partition Coefficient[a]

Compound	Partition Coefficient	pH of Aqueous Buffer
4-Indanol	0.68	11.20
4-Indenol	0.13	11.20
5-Indanol	0.79	11.20
5-Indenol	0.31	11.20
2-Phenylphenol	51	10.28
2-Cyclohexylphenol	2100	10.10
2-Naphthol	0.59	10.28
5,6,7,8-Tetrahydro 2-naphthol	6.7	10.28

[a] Data taken from Karr *et al.* (*5*).

The data of Karr *et al.* (*5*) (Table IV) show that unsaturation in the substituent reduces the value of *k*. Although Karr *et al.* used a different solvent pair, namely, cyclohexane and aqueous phosphate buffer, the same observation will be generally true for the solvent system, cyclohexane–aqueous sodium chloride.

Nature of Nucleus.—The partition coefficients of phenol, two naphthols, and two indanols in Table V show a variation with the nature of nucleus of phenols. High partition coefficients of the naphthols compared to that of phenol can be explained from increased steric effect and molecular weight of the naphthols. The higher partition coefficients of 4-indanol over 1-naphthol and of 5-indanol over 2-naphthol, although the indanols are of smaller molecular weights, are due to the alicyclic nature of the 5-membered ring of the indanols. The "ring" not containing the hydroxyl is in the ortho position in both 1-naphthol and 4-indanol, and in the meta position in 2-naphthol and 5-indanol. This explains the greater partition coefficient of 1-naphthol over 2-naphthol and of 4-indanol over 5-indanol. Karr *et al.* (*5*), however, obtained a greater *k* value for 5-indanol than 4-indanol, in the solvent system cyclohexane–phosphate buffer.

Table V. Effect of Nature of Nucleus on Partition Coefficient

Compound	Partition Coefficient
Phenol	0.18
2-Naphthol	1.96
1-Naphthol	3.31
5-Indanol	3.02
4-Indanol	4.07

Substitution in Binuclear Phenols.—The partition coefficients of the phenols in Table VI, *A* and *B*, have been reproduced from the work of Karr *et al.* (*5*). The higher *k* value of 1-methyl-2-naphthol over 3-methyl-2-naphthol is due to the increased steric hindrance conferred on the 1 position by the second ring, even though the methyl substituent in both the cases is ortho to the phenolic hydroxyl. Table VI, *B*, shows that alkyl substitution in the ring not containing the hydroxyl group increases the value of *k* when in the 6, 7, or 8 position. This can be seen from a consideration of relative ortho, meta, and para effects in phenols. 5-Methyl-2-naphthol is expected to have a partition coefficient close to that of 7-methyl-2-naphthol as the methyl group in both the compounds is equidistant from the phenolic group.

Prediction of *k* of Homologous Phenols.—Even an approximate knowledge of partition coefficients is very helpful in

Table VI. Effect of Alkyl Substitution in Double-Ringed Phenols on Partition Coefficient[a]

Isomer	Partition Coefficient	pH
A. Substitution in the Ring Containing Phenolic Group		
4-Methyl-2-naphthol	2.5	9.94
3-Methyl-2-naphthol	6.6	9.94
1-Methyl-2-naphthol	7.4	9.94
B. Substitution in the Ring not Containing Phenolic Group		
6-Methyl-2-naphthol	0.14	11.85
7-Methyl-2-naphthol	0.59	11.85
8-Methyl-2-naphthol	2.3	11.85

[a] Data taken from Karr *et al.* (*5*).

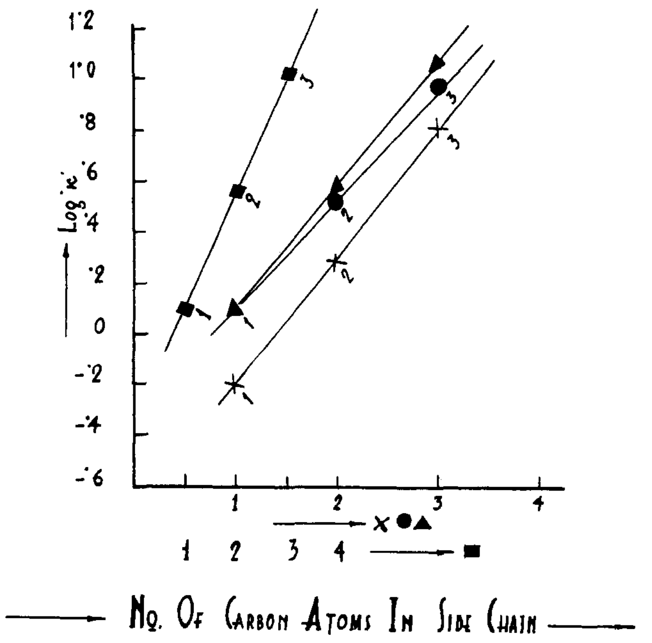

Figure 1. Prediction of partition coefficient of monoalkyl phenols

● *p*-Phenols
  1. Phenol 2. *p*-Cresol 3. *p*-Ethylphenol
  4. *p*-Propylphenol 5. *p*-n-Butylphenol

■ *m*-Phenols
  1. Phenol 2. *m*-Cresol
  3. *m*-Ethylphenol 4. *m*-Propylphenol

▲ o-Phenols
  1. o-Cresol 2. o-Ethylphenol 3. o-Propylphenol

the identification of a class of compounds (like the phenols) by the CCD technique. The importance of a reliable method of prediction of *k* from the structure is, therefore, obvious. A plot of the number of carbon atoms in alkyl side chains against the logarithm of *k* (between cyclohexane and 0.1% aqueous sodium chloride) of homologous phenols, gives a straight line. This has been shown for monoalkyl phenols (Figure 1) and for dialkylphenols (Figure 2). Other alkyl substituted phenol homologs can be similarly classified into various groups. This graphical method of finding partition coefficients will facilitate systematic investigation (qualitative and quantitative) of coal tar phenols by the technique of countercurrent distribution. The *k* values for isomeric phenols can be easily determined. From the linear relationship of log *k* against carbon atoms in side chain of phenol (k = 0.17), *p*-cresol (k = 0.645) and *p*-ethylphenol (k = 2.35), the partition coefficients of other higher *p*-phenols, namely *p*-propylphenol (k = 7.20), *p*-*n*-butylphenol (k = 19.40) can be determined.

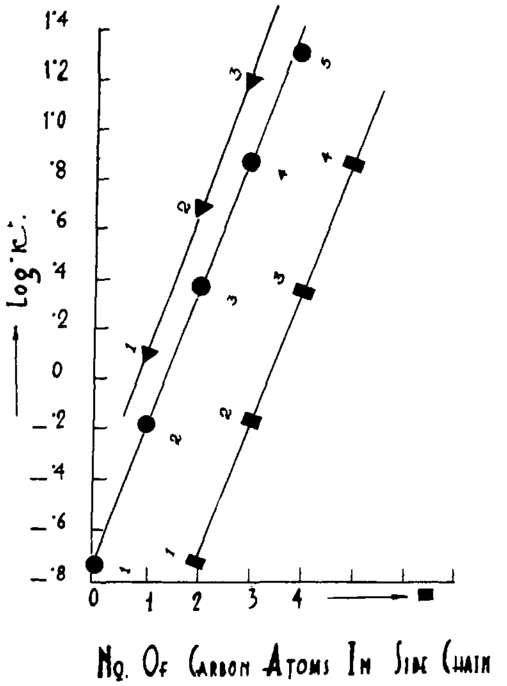

Figure 2. Prediction of partition coefficients of dialkylphenols

	1. 3-Methylphenol	2. 3,5-Dimethylphenol	3. 3-Methyl-5-ethylphenol
●	1. 2-Methylphenol	2. 2,3-Dimethylphenol	3. 2-Methyl-3-ethylphenol
▲	1. 2-Methylphenol	2. 2,5-Dimethylphenol	3. 2-Methyl-5-ethylphenol
■	1. 2-Methylphenol	2. 2,4-Dimethtyphenol	3. 2-Methyl-4-ethylphenol

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