

RELATIVE PARTITION COEFFICIENT MEASUREMENTS BY HPLC

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Partition coefficients, used in structure-activity studies to characterise hydrophobicity, are often determined by the 'shake-flask' method, but this method is encumbered with many problems (Mirrlees et al 1975). Consequently, other methods, especially using chromatography, have been developed.

Good agreement has been shown in t.l.c. between R_m values ($\log \frac{1}{R_f} - 1$) and the logarithm of the partition coefficient ($\log P$) (Tomlinson 1975). Several attempts have been made using hplc (Mirrlees et al 1975). Partition data from such hplc studies is obtained from the observed linear relationship between $\log P$ and $\log k'$ (the capacity factor) where $k' = (R_T - R_0)/R_0$ and R_T , R_0 are the retention times of the solute and unretained solute peak respectively. As lipophilicity often varies widely within a congeneric series, difficulty may be encountered in selecting a chromatographic condition which allows analysis of all compounds. A potential solution is to use varying compositions of a suitable binary mobile-phase and by extrapolation of a plot of k' or $\log k'$ vs mobile phase composition, estimate a k' value for each compound at a single mobile-phase composition. Unfortunately, such plots are rarely linear and thus do not lend themselves to extrapolation. We have found that plots of R_{mLC} [$\log((R_T - R_0)/R_T)$], however, are linear.

Fig.1 shows such a plot for some barbiturates. The analytical system employed was based on that by Clark (1978), using Hypersil ODS (5 μ m; 30m x 0.5 cms) with the mobile-phase, (acetonitrile-water) delivered at a flow-rate of 1.0 ml min⁻¹. The R_{mLC} values for various barbiturates were calculated at different concentrations of acetonitrile. Back extrapolation of the linear plots (Fig.1) gave R_{mLC} values for all of the congeners at a mobile phase composition of 0% v/v acetonitrile (100% v/v water); as seen in Fig.2 these values correlated extremely well ($r^2 = 0.989$) with literature values of $\log P$ (Yih, 1977). We believe that the above rapid and easy method to obtain partition data has application to other congeneric series.

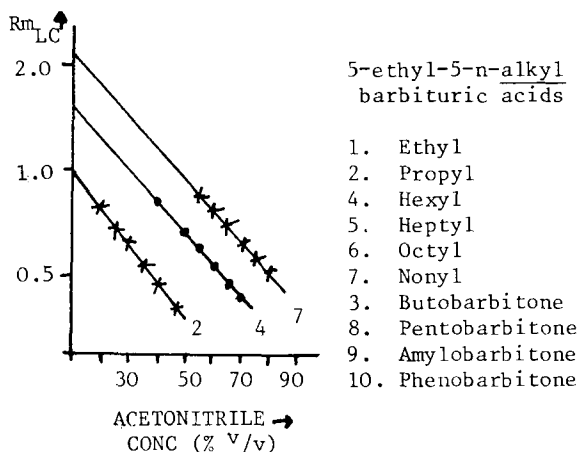


Fig.1. Plot of R_{mLC} vs Percent Acetonitrile.

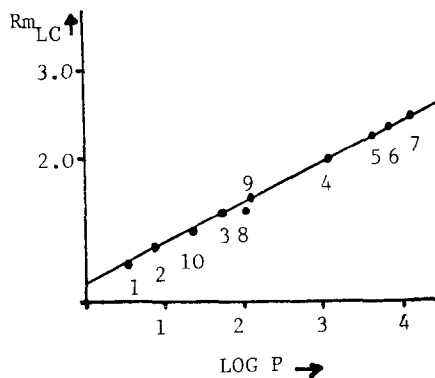


Fig.2. Showing linear relationship between R_{mLC} and $\log P$.

Clark, C.R., Chan, J.L. (1978) *Analyt.Chem.* 50: 635

Mirrlees, M.S. et al. (1976) *J.Med.Chem.* 19: 615

Tomlinson, E. (1975) *J.Chromat.* 113: 1

Yih, T.D. (1977) Ph.D. Thesis, University of Nijmegen, Netherlands