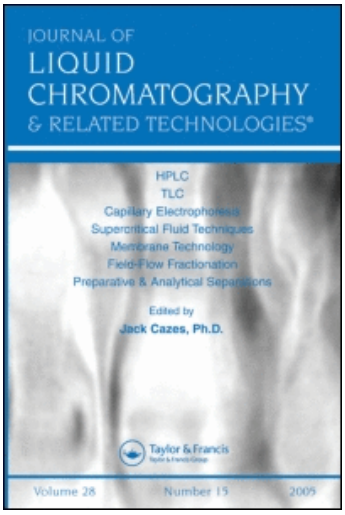

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Application of Topological Index and the R_F Parameter to the Estimation of Lipophilic Properties of Selected Porphyrins

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Application of Topological Index and the R_F Parameter to the Estimation of Lipophilic Properties of Selected Porphyrins

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Abstract: This work refers to using the chosen topological index A—to the assessment of the lipophilic porphyrin properties. Porphyrin and alkyloxy porphyrin derivatives were separated by thin-layer chromatography. RP-18 as the stationary phase and CH_2Cl_2:MeOH 6:4 (v/v) as the mobile phase were applied. A topological index A and log P were calculated on the basis of computer programs and the Rekker equation, and log P was appointed experimentally. We were suggested the way of calculating the W parameter, which describes lipophilic properties of investigated compounds.

Keywords: Porphyrins, TLC, log P, Topological index

INTRODUCTION

Porphyrins and their metal derivatives, owing to their specific physicochemical, biochemical, and biological properties, are the subject of numerous scientific investigations. The porphyrin ring appears, among others, in vitamin B and chlorophyll.[1–3] Simultaneously, porphyrins and their derivatives are applied as antitumour medicaments.[4–9]

Lipophilic properties are among the most fundamental physicochemical properties of the above mentioned compounds. Lipophilic properties are determined by log P. This coefficient characterizes partition of substances in the n-octanol-water system.[10] The following methods are used for the determination and comparison of the lipophilic properties of chemical substances:

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- the Rekker's method;[11,12]
- experimental methods;[13,14]
- theoretical and computational methods;[15,16] and
- methods of liquid chromatography in the reverse phase system and combination of chromatographic data with the Rekker's method.[17–20]

The above listed methods, in many cases, yield varying numerical values of log P. Therefore, there is still need for new methods of determination of this important physicochemical parameter.

The aim of this study is to apply the selected topological index and R_F parameters to the estimation of the lipophilic properties of the studied porphyrins. The present work is a continuation of the studies on physicochemical properties of selected porphyrins.[21,22]

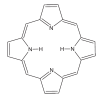
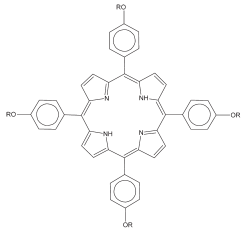
EXPERIMENTAL

The subject of these studies were porphine and alkyloxy tetraphenylporphyrins. The chemical structures of the compounds are presented in Table 1.

TLC

TLC was performed on commercially available and RP $18F_{254s}$ (Merck, Darmstadt, Germany, #1.15389). RP-18 plates were used without preliminary treatment. Standard solutions of the analyzed compounds (0.1%) were prepared in chloroform and 2 μL volumes were spotted onto the plates. Chromatograms were developed to a distance of 10 cm with the mobile phase, CH_2Cl_2:MeOH 6:4 (v/v). The time of chamber saturation

Table 1. The porphyrins investigated

Basic structural formula	-R	Abbreviation	Name
	—	P1	Porphine
	$-CH_3$	P2	5,10,15,20-Tetra-(4-methoxyphenyl)porphyrin
	$-C_5H_{11}$	P3	5,10,15,20-Tetra-(4-pentyloxyphenyl)porphyrin
	$-C_{10}H_{21}$	P4	5,10,15,20-Tetra-(4-decyloxyphenyl)porphyrin
	$-C_{16}H_{33}$	P5	5,10,15,20-Tetra-(4-hexadecyloxyphenyl)porphyrin

with pairs of solvents amounted to about 30 min. After development, the plates were dried at room temperature and the spots were detected visually. Each experiment was repeated three times.

Calculation of the Topological Index A

We used the topological index A which was taken from the paper by Pyka,[23] which has been calculated according to Equation (1).

$$A = \sqrt{\sum_{i} (S_i)^2} \tag{1}$$

where S_i is the sum of the values from i-th row of the distance matrix; the d_{ii} and d_{ij} are entries to the distance matrix, and are given by the following formula:

$$d_{ii} = 1 - \frac{6}{Z_i}$$

$$d_{ij} = \sum_{r} k_r$$

$$k_r = \frac{36}{b_r Z_i Z_j}$$

$b_r = 3/2$ for the bond in the aromatic ring; $b_r = 1$ for the single bonds, and Z_i, Z_j are atomic numbers of the atoms i, j, respectively.

Calculation of log P

Log P was computed by the following computer programs:[15,16] A log P, C log P, KOWWIN, and X log P.

Log P was computed from the Rekkeŕs equation[11,12] (Equation (2)):

$$\log P = \sum_{n} a_n f_n \tag{2}$$

where, f is the constant for the fragment, denoting the lipophilic contribution of the structural fragment to the lipophilicity of the whole compound, n is the number of fragments in the molecule, a–factor indication how many times the given fragment occurs in the molecule.

Experimental Appointment of log P

Experimentally, the distribution rate log P in the octanol–water system was appointed according to the description given at work.[24]

Water which was saturated with n-octanol and n-octanol which was saturated with water (25 mL of each) were placed in a separatory funnel. The contents of the funnel were well shaken for 30 min. The mixture was then left for 24 hours at 22°C to achieve thermodynamic equilibrium. The concentrations of the porphyrin derivatives were then determined by RP-HPLC (column 150 mm × 3.3 mm i.d. Separon SixC18, chromatograph Knauer, detector UV 254 nm).

Calculation of Parameter W

The W parameter was appointed on the basis of the R_F value and the topological index A (Eq. (3)).

RESULTS AND DISCUSSION

The studied compounds were separated by partition thin layer chromatography. RP-18 was used as the stationary phase, while the experimentally chosen CH_2Cl_2 at the 6:4 (v/v) ratio was used as the mobile phase.

Table 2 presents the R_F values and the calculated topological indices A for the studied porphyrins.

Taking into account the obtained R_F values and the values of the topological index A, we propose to calculate the value of the W parameter (Eqs. (3), 4)) describing the lipophilic properties of the studied substances as:

$$W = K \cdot A \tag{3}$$

$$K = \frac{R_{F1} + R_{F2}}{R_{F1} \cdot 1000} \tag{4}$$

where, $R_{F1} > R_{F2}$, and A is the topological index of Pyka.

The calculated W values are presented in Table 3. Experimental data–the R_F values–obtained in the system: RP-18 as the stationary phase, CH_2Cl_2 at

Table 2. R_F values and topological index A values of investigated porphyrins

Compound	R_F stationary phase: RP-18 mobile phase: CH_2Cl_2:MeOH 6:4 (v/v)	Topological index A
P1	0,76	324
P2	0,70	2230
P3	0,60	4682
P4	0,48	9930
P5	0,31	19908

Table 3. Log P values calculated by the computer programs, and by the Rekker equation, appointed experimentally and the parameter W of investigated porphyrins

Compound	A log P_s	IA log P	C log P	KOWWIN	X log P	$LogP_{Rekkera}$	log $P_{exp.}$	W
P1	3,04	0,33	6,47	6,01	2,04	0,83	1,58	0,62
P2	7,50	3,12	14,18	13,75	9,13	2,64	3,50	4,14
P3	10,29	7,33	22,65	21,60	16,80	10,95	9,00	8,43
P4	11,03	9,60	33,23	31,43	25,23	21,33	20,01	16,34
P5	10,64	—	45,92	43,21	—	33,78	—	32,77

the 6:4 (v/v) ratio as the mobile phase, were used for the calculation of the W value.

Table 3 contains log P values calculated by the computer programs and by the Rekker's equation, appointed experimentally, and the W parameter.

Reverse phase chromatography with the CH_2Cl_2:MeOH 6:4 (v/v) mobile phase was used to separate the studied porphyrins. Then, from a variety of topological indices, the A index was chosen for further calculations concerning the comparison of lipophilicities of the studied porhyrins. The obtained values of the topological index A are displayed in Table 2. The relationship between the R_F values and the topological index A, for the calculation of the W parameter characterizing the lipophilic properties of the studied compounds, is proposed (Equation (3)).

The calculated W parameter correlates rather well with log P, according to Rekker. This fact verifies the data presented in Table 3.

Log P values obtained from the computer programs: A log P_s, IA log P, C log P, KOWWIN, X log P, log P_{Rekker} differ markedly among themselves.

The proposed new method of the W parameter determination will be used for the estimation of lipophilicities of other organic species of biological relevance.

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