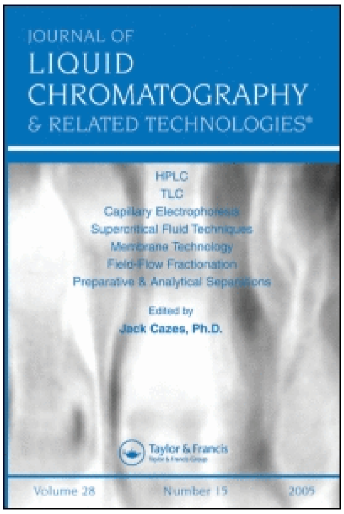

Journal of Liquid Chromatography & Related Technologies
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597273

Correlation Between the Chemical Structures of Dialkyl Peroxides and Their Retention in Reversed-Phase High-Performance Liquid Chromatography

Stefan Baj[a]; Małgorzata Dawid[a]
[a] Institute of Organic Chemistry and Technology Silesian Technical University ul, Gliwice, Poland

To cite this Article Baj, Stefan and Dawid, Małgorzata(1994) 'Correlation Between the Chemical Structures of Dialkyl Peroxides and Their Retention in Reversed-Phase High-Performance Liquid Chromatography', Journal of Liquid Chromatography & Related Technologies, 17: 18, 3933 — 3949

To link to this Article: DOI: 10.1080/10826079408016164

URL: http://dx.doi.org/10.1080/10826079408016164

JOURNAL OF LIQUID CHROMATOGRAPHY, 17(18), 3933-3949 (1994)

CORRELATION BETWEEN THE CHEMICAL STRUCTURES OF DIALKYL PEROXIDES AND THEIR RETENTION IN REVERSED-PHASE HIGH-PERFORMANCE LIQUID CHROMATOGRAPHY

STEFAN BAJ AND MAŁGORZATA DAWID
Institute of Organic Chemistry and Technology
Silesian Technical University
ul. Krzywoustego 4
44-101 Gliwice, Poland

ABSTRACT

High-performance liquid chromatographic capacity factors were determined on LiChrosorb RP 18 10 μm stationary phase for various organic peroxides. Studies of the quantitative structure-retention relationship (QSRR) employing non-empirical structural descriptors for the investigated compounds were performed by means of multiple regression analysis. Semi-empirical methods MINDO/3, MNDO, AM1, PM3 were employed to determine the structural descriptors which may influence the retention in a reversed-phase chromatographic system. Informative values of non-empirical structural descriptors determined with various semi-empirical methods have been compared.

INTRODUCTION

Organic peroxides are a group of organic compounds of considerable practical and theoretical importance [1-4]. Mixtures which contain organic peroxy substances are on the whole difficult to analyse by means of conventional techniques.

High-performance liquid chromatography (HPLC) is a versatile, efficient and relatively rapid method of separating non-volatile, thermally labile compounds, and it is ideal for the separation and study of mixtures containing peroxy compounds [5-9]. The importance of HPLC in the analysis of peroxy compounds seems to be quite obvious.

The study of the relationship between retention indices and parameters describing the structure of molecules of the solute is one of the most intensively investigated question in modern chromatography [10]. These studies concern a set of various chemical compounds and various sets of structural parameters have been employed; no investigations of this type, however, have been carried out as far as organic peroxy compounds are concerne. Using this approach, it is possible to identify the dominant factors which define the interaction of solute molecules with chemical entities forming the chromatographic system. The assignment of retention factors for various substituents was suggested by Martin [11] and validated by Bate-Smith and Westall [12]. Horwath and co-workers [13.14] and others [15,16] have determined the quantitative structure-retention relationship (QSRR) for a variety of compounds and demonstrated the value of contribution of the functional group for both the prediction of retention and structural elucidation. Most QSRR reported in chromatographic literature were derived by means of multiple regression analysis. The dependent variable formed a set of retention data, while various empirical, semi-empirical and non-empirical structural parameters were assumed as independent variables. The selection of independent variables (structural descriptors) depends on numerous factors, among them the chromatographic techniques applied in the investigations. Retention differences related to the chemical structure have been discussed in adsorption liquid chromatography, where hydrogen bonding and $\pi-\pi$ interaction are dominant as well as in reversed-phase and ion-exchange liquid chromatography, where the molecular interaction is probably related to solubility. One method of measuring this solubility in terms of the hydrophobic fragmental constant (log P) has been proposed by Rekker [17]. These QSRR have been discussed in detail by Kaliszan [18-20] who listed over 100 studies relating the partition coefficient (log P) factor to retention in HPLC.

Recent studies in reversed-phase chromatography have shown that both electrostatic and hydrophobic interactions make important contributions to retention [21-23]. The former is directly related to the solute charges and the latter to solute hydrophobicity.

In our study, the QSRR analysis a the variety of organic peroxides on RP HPLC was established through the simultaneous solution of a set of linear equations. As independent variables (structural descriptors) non-empirical parameters of the molecules were chosen which can be related to the hydrophobic or electrostatic properties of the molecules. These descriptors were calculated by means of semi-empirical methods of quantum chemistry: PM3, AM1, MNDO i MINDO/3. Such an approach makes it possible to investigate also the application of this type of method for the prediction of retention.

The experiments described in this paper were designed to obtain some insight into the molecular mechanism of retention under reversed phase conditions and to evaluate the informative value of structural descriptors most often used in QSRR studies by means of different semi-empirical methods.

EXPERIMENTAL

Materials

Ethyl cumyl peroxide, n-propyl cumyl peroxide, iso-propyl cumyl peroxide, n-butyl cumyl peroxide, iso-butyl cumyl peroxide, sec-butyl cumyl peroxide, tert-butyl cumyl peroxide, n-hexyl cumyl peroxide, n-heptyl cumyl peroxide, n-oktyl cumyl peroxide , n-nonyl cumyl peroxide, allyl cumyl peroxide and benzyl cumyl peroxide were synthetized in the Institute of Organic Chemistry and Technology according to the method presented in reference [24].

Methyl alcohol, HPLC grade; Merck Darmstadt.

Instrumentation

The chromatographic system consists of a Philips LC XPD Chromatograph, a Reodyne Model 7125 syringe-loading injector with a 20 μl loop and a standard Cartrige Glass Column LiChrosorb RP 18 (10 μm). The mobile phase were methanol-water mixtures at a flow rate of 1.0 cm3/min. The compounds were detected at 257 nm with LC XPD UV-VIS Detector and integrated with a CDP4 integrator.

Determination of retention parameters

Chromatography was carried out using eluents with the following proportions (v/v) of methanol to water: 95 :5, 90 :10, 85 : 15, 80 : 20, 75 :25, 70 : 30. The capacity factors k' were calculated assuming a constant dead volume of the column, taking the signal of water as the dead time marker. Logarithms of capacity factors (log *k'*) for the respective compounds were plotted against the volume of methanol concentration.

Determination of structural descriptors

For each investigated peroxide the individual structural parameters which may influence retention, are: the total energy (E_{TOTAL}), the heat of formation, the net electron charges on individual atoms (O1, O2), the dipole moment, the square of the dipole moment (DIP^2), the torsion angle between some of the atoms in a molecule (C1-O1-O2-C2) (see Fig. 1.), the energy of LUMO (E_{LUMO}) and HOMO (E_{HOMO}) molecular orbitals. Molecular geometries were optimized and all the parameters mentioned above were calculated by means of the appropriate orbital package MOPAC procedures according to the methods PM3 [25], AM1 [26], MNDO [27] and MINDO/3 [28]. The structure of a methyl cumyl peroxide molecule, optimised according to the MNDO method is presented in Figure 1.

The values of structural descriptors obtained by means of all the applied methods are listed in tables I-IV.

RESULTS AND DISCUSSION

Logarithms of the capacity factors (log *k'*) for the respective organic peroxides were plotted against the volume fraction of methanol in the eluent. The parameters derived from least squares regression for the investigated systems are given in Table V. Excellent linear relationships were obtained.

From the regression equations obtained (log k' = a*x + b), the log k' coefficients were calculated for all investigated compounds at the point corresponding to the proportion (v/v) 82 : 12 methanol : water as eluent. The calculated values of log k' were then subjected to a correlated analysis with parameters describing the structure of the molecules of the organic peroxides.

In order to describe the relation between the retention indices of organic peroxides and the calculated structural parameters, a multiparameter regression analysis was performed. The QSRR equations were solved first by a stepwise regression analysis taking into consideration the significance of the respective descriptors. The setting up of such a preliminary correlation made it possible to

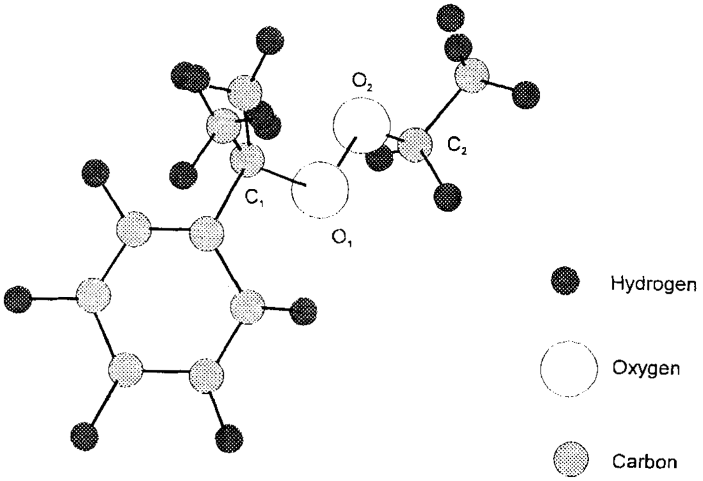

FIGURE 1. Molecular structure of ethyl cumyl peroxide calculated with MNDO semi-empirical method.

eliminate from them those descriptors which did not indicate a good correlation with log k'. Based on these calculations the following descriptors were eliminated: the heat of formation, the net charge on the atoms O1 and O2, the torsion angle between the atoms C1-O1-O2-C2, and the dipole moment. Multiple regression analysis, applying log k' as a dependent variable and the total energy (E_{TOTAL}), the values of LUMO and HOMO energy (E_{HOMO} and E_{LUMO}) and the square of dipole moment $(DIP)^2$ as dependent variables, was performed for each set of structural descriptors (MINDO/3, MNDO, AM1, PM3 results). The obtained QSRR equation are presented below:

MINDO3:

$$\log k' = -49.6814 - 0.0026\,(\pm 0.0002) E_{TOTAL} - 4.5693(\pm 1.65418) E_{HOMO} + 3.0164(\pm 0.92318) E_{LUMO} + 0.6366(\pm 0.13483)(DIP)^2 \quad \textbf{(1)}$$

$$R = 0.9900, \qquad F = 89.386, \qquad p < 1\ 10^{-5}$$

MNDO:

$$\log k' = -159.490 - 0.003\,(\pm 0.00035) E_{TOTAL} - 16.091(\pm 8.33871) E_{HOMO} + 11.512(\pm 4.21971) E_{LUMO} + 0.738(\pm 0.59894)(DIP)^2 \quad \textbf{(2)}$$

$$R = 0.9620, \qquad F = 24.801, \qquad p < 1.5\ 10^{-4}$$

TABLE I
MOLECULAR STRUCTURE DESCRIPTORS DERIVED FROM OPTIMISED GEOMETRIC STRUCTURES OF ORGANIC PEROXIDES USING MINDO/3 METHOD.

Peroxide	E_{TOTAL} [eV]	Heat of formation [kcal/mol]	Torsion angle [deg]	Net Charge at O2 atom [*e*]	Net Charge at O1 atom	E_{HOMO} [eV]	E_{LUMO} [eV]	$(DIP)^2$ [Debye]
Ethyl cumyl peroxide	-2251.71	3.142	-130.792	-0.2272	-0.2376	-9.1755	0.6025	1.3456
***n*-Propyl cumyl peroxide**	-2408.40	-17.886	-129.044	-0.2290	-0.2366	-9.1755	0.5834	1.5092
***iso*-Propyl cumyl peroxide**	-2408.31	-15.644	-129.817	-0.2431	-0.2414	-9.1568	0.6102	1.0899
***n*-Butyl cumyl peroxide**	-2564.99	-22.089	-131.981	-0.2180	-0.2388	-9.0437	0.8365	0.7772
***iso*-Butyl cumyl peroxide**	-2564.60	-12.962	-132.167	-0.2393	-0.2162	-8.9996	0.9544	0.7807
***sec*-Butyl cumyl peroxide**	-2564.97	-21.447	-130.218	-0.2450	-0.2417	-9.1586	0.5990	1.0829
***tert*-Butyl cumyl peroxide**	-2564.50	-10.676	-177.302	-0.2682	-0.2576	-9.1319	0.6319	0.2642
***n*-Hexyl cumyl peroxide**	-2878.42	-36.004	-131.266	-0.2253	-0.2371	-9.1714	0.5840	1.3675
***n*-Heptyl cumyl peroxide**	-3034.99	-39.871	-132.438	-0.2255	-0.2375	-9.1726	0.5896	1.3718
***n*-Octyl cumyl peroxide**	-3191.78	-48.526	-131.719	-0.2373	-0.2255	-9.1713	0.5840	2.7386
***n*-Nonyl cumyl peroxide**	-3348.28	-50.743	-132.529	-0.2258	-0.2375	-9.1795	0.5815	1.4195
Allil cumyl peroxide	-2377.56	14.063	-130.700	-0.2257	-0.2417	-9.1447	0.5889	1.1881
Benzyl cumyl peroxide	-2913.85	29.983	-139.372	-0.2220	-0.2488	-8.9623	0.7062	0.4019

TABLE 2

MOLECULAR STRUCTURE DESCRIPTORS DERIVED FROM OPTIMISED GEOMETRIC STRUCTURES OF ORGANIC PEROXIDES USING MNDO METHOD.

Peroxide	E_{TOTAL} [eV]	Heat of formation [kcal/mol]	Torsion angle	Net Charge at O2 atom	Net Charge at O1 atom	E_{HOMO} [eV]	E_{LUMO} [eV]	$(DIP)^2$ [Debye]
Ethyl cumyl peroxide	-2274.55	0.611	-177.120	-0.1917	-0.1871	-9.3717	0.1823	0.3490
***n*-Propyl cumyl peroxide**	-2430.97	-3.606	-146.937	-0.1902	-0.1877	-9.3479	0.1946	0.5461
***iso*-Propyl cumyl peroxide**	-2430.85	-0.892	-207.634	-0.1926	-0.1865	-9.3403	0.2013	0.4879
***n*-Butyl cumyl peroxide**	-2587.42	-8.421	-147.855	-0.1893	-0.1908	-9.3413	0.1991	0.4529
***iso*-Butyl cumyl peroxide**	-2587.27	-4.982	-148.691	-0.1868	-0.193	-9.3736	0.1801	0.3181
***sec*-Butyl cumyl peroxide**	-2587.26	-4.779	-190.138	-0.1896	-0.1959	-9.3416	0.1992	0.0678
***tert*-Butyl cumyl peroxide**	-2586.98	26.877	-172.058	-0.1904	-0.1947	-9.3279	0.2112	0.0371
***n*-Hexyl cumyl peroxide**	-2900.31	-17.809	-140.786	-0.1888	-0.1901	-9.3430	0.1972	0.5255
***n*-Heptyl cumyl peroxide**	-3056.76	-22.038	-146.875	-0.1888	-0.19	-9.3446	0.1991	0.5423
***n*-Octyl cumyl peroxide**	-3213.21	-25.25	-145.042	-0.1882	-0.1896	-9.3420	0.1957	0.5844
***n*-Nonyl cumyl peroxide**	-3369.65	-31.928	-145.299	-0.1882	-0.1897	-9.3441	0.1968	0.5668
Allil cumyl peroxide	-2401.35	26.129	-150.207	-0.1870	-0.1929	-9.3336	0.2053	0.6439
Benzyl cumyl peroxide	-2940.95	34.859	-151.704	-0.1870	-0.1938	-9.3333	0.1075	0.3628

TABLE 3

MOLECULAR STRUCTURE DESCRIPTORS DERIVED FROM OPTIMISED GEOMETRIC STRUCTURES OF ORGANIC PEROXIDES USING AM1 METHOD.

Peroxide	E_{TOTAL} [eV]	**Heat of formation** [kcal/mol]	**Torsion angle**	**Net Charge at O1 atom**	**Net Charge at O2 atom**	E_{HOMO} [eV]	E_{LUMO} [eV]	**$(DIP)^2$** [Debye]
Ethyl cumyl peroxide	-2266.68	-7.742	-113.369	-0.1524	-0.1504	-9.4725	0.4520	2.6050
***n*-Propyl cumyl peroxide**	-2422.49	-13.989	-113.224	-0.1527	-0.1498	-9.4721	0.4520	2.3104
***iso*-Propyl cumyl peroxide**	-2422.49	-12.258	-111.164	-0.1495	-0.1484	-9.4675	0.4568	2.7914
***n*-Butyl cumyl peroxide**	-2578.34	-21.309	-113.214	-0.1517	-0.1497	-9.4710	0.4530	2.7390
***iso*-Butyl cumyl peroxide**	-2578.24	-18.983	-113.249	-0.1524	-0.1499	-9.4709	0.4535	2.3482
***sec*-Butyl cumyl peroxide**	-2578.23	-18.717	-111.188	-0.1498	-0.1474	-9.4591	0.4650	2.7192
***tert*-Butyl cumyl peroxide**	-2578.00	-13.282	-177.268	-0.1623	-1.6130	-9.4460	0.4725	1.5409
***n*-Hexyl cumyl peroxide**	-2889.95	-33.558	-113.105	-0.1516	-0.1498	-9.4710	0.4541	2.8800
***n*-Heptyl cumyl peroxide**	-3045.75	-39.675	-113.086	-0.1516	-0.1498	-9.4715	0.4539	2.8900
n-Oktyl cumyl peroxide	-3201.68	-48.687	-113.172	-0.1517	-0.1498	-9.4720	0.4524	2.7822
n-Nonyl cumyl peroxide	-3357.36	-51.935	-110.773	-0.1496	-0.1475	-9.4744	0.4510	3.3966
Allil cumyl peroxide	-2393.80	17.673	-113.236	-0.1514	-0.147	-9.4290	0.4290	2.4766
Benzyl cumyl peroxide	-2933.63	26.555	-113.379	-0.1526	-0.1443	-9.4971	0.3419	2.0781

TABLE 4
MOLECULAR STRUCTURE DESCRIPTORS DERIVED FROM OPTIMISED GEOMETRIC STRUCTURES OF ORGANIC PEROXIDES USING PM3 METHOD.

Peroxide	E_{TOTAL} [eV]	Heat of formation [kcal/mol]	Torsion angle	Net Charge at O2 atom	Net Charge at O1 atom	E_{HOMO} [eV]	E_{LUMO} [eV]	$(DIP)^2$ [Debye]
Ethyl cumyl peroxide	-2134.92	-16.333	-216.187	-0.1498	-0.1594	-9.6393	0.1937	1.0323
n-Propyl cumyl peroxide	-2284.29	-17.744	-215.464	-0.1471	-0.1528	-9.6236	0.2777	0.9819
iso-Propyl cumyl peroxide	-2284.37	-19.59	-147.267	-0.1469	-0.1533	-9.6575	0.1890	0.6777
n-Butyl cumyl peroxide	-2434.01	-27.211	-216.247	-0.1623	-0.1623	-9.6405	0.1949	1.1077
iso-Butyl cumyl peroxide	-2434.04	-27.897	-211.134	-0.1641	-0.1641	-9.6394	0.1939	0.7428
sec-Butyl cumyl peroxide	-2433.92	-25.263	-135.076	-0.1512	-0.1512	-9.6421	0.2123	1.1396
tert-Butyl cumyl peroxide	-2433.89	-24.533	-144.481	-0.1475	-0.1475	-9.6432	0.2120	0.6338
n-Hexyl cumyl peroxide	-2732.95	-34.924	-166.252	-0.1555	-0.1517	-9.6597	0.1777	0.0912
n-Heptyl cumyl peroxide	-2882.49	-39.939	-156.688	-0.155	-0.151	-9.6687	0.1768	0.2414
n-Oktyl cumyl peroxide	-3032.02	-45.761	-157.918	-0.1548	-0.1515	-9.6610	0.1778	0.1840
n-Nonyl cumyl peroxide	-3181.54	-50.313	-145.067	-0.149	-0.1514	-9.6204	0.2706	0.7812
Allil cumyl peroxide	-2252.46	9.033	-212.289	-0.1604	-0.1604	-9.1769	0.3945	0.5293
Benzyl cumyl peroxide	-2757.19	20.607	-181.048	-0.1564	-0.1564	-9.6625	0.0178	0.0495

TABLE 5

STATISTICAL PARAMETERS OF LINEAR FIT OF LOG k' *VERSUS* METHANOL CONCENTRATION IN MOBILE PHASE

Number of calibration points for each compounds, n=5; number of replicates of each injection, m=7

Compounds	Intercept *b*	Slope *a*	R[a]	S.E[b]
Ethyl cumyl peroxide	7.291±0.205	-0.079±0.003	0.998	0.0405
n-Propyl cumyl peroxide	9.219±0.303	-0.098±0.004	0.998	0.0597
iso-propyl cumyl peroxide	9.912±0.402	-0.110±0.005	0.997	0.0792
n-Butyl cumyl peroxide	10.810±0.610	-0.076±0.008	0.993	0.1203
iso-Butyl cumyl peroxide	10.725±0.508	-0.113±0.006	0.995	0.0999
sec-Butyl cumyl peroxide	10.794±0.500	-0.115±0.006	0.996	0.0979
tert-Butyl cumyl peroxide	8.872±0.091	-0.097±0.001	0.999	0.0179
n-Hexyl cumyl peroxide	12.352±0.766	-0.124±0.087	0.995	0.0978
n-Heptyl cumyl peroxide	14.076±1.047	-0.147±0.012	0.993	0.1345
n-Oktyl cumyl peroxide	101.780±1.241	-6.596±0.534	0.993	0.9000
n-Nonyl cumyl peroxide	102.288±1.352	-5.794±0.496	0.993	0.9500
Allil cumyl peroxide	6.651±0.442	-0.071±0.006	0.991	0.0868
Benzyl cumyl peroxide	10.345±0.274	-0.111±0.003	0.998	0.0540

[a] R = correlation coefficient

[b] S.E. = standard error of regresion

AM1:

$$\log k' = -27.4426 - 0.0028\,(\pm 0.00045)E_{TOTAL} - 1.7695(\pm 9.77508)E_{HOMO} + 8.7019(\pm 4.71280)E_{LUMO} + 0.3789(\pm 0.33524)(DIP)^2 \qquad \mathbf{(3)}$$

$$R = 0.9492, \qquad F = 18.203, \qquad p < 4\ 10^{-4}$$

PM3:

$$\log k' = -37.4557 - 0.0028\,(\pm 0.00059)E_{TOTAL} - 3.2411(\pm 2.01671)E_{HOMO} + 6.5051(\pm 3.23314)E_{HOMO} - 0.5614(\pm 0.58134)(DIP)^2 \qquad \mathbf{(4)}$$

$$R = 0.9355, \qquad F = 14.041, \qquad p < 1\ 10^{-3}$$

TABLE 6

PARTIAL CORRELATION COEFFICIENTS DERIVED FROM MULTIPARAMETER REGRESSION OF LOG K' *VERSUS* STRUCTURAL DESCRIPTORS CALCULATED WITH MINDO/3, MNDO, AM1 AND PM3 METHODS.

Structural descriptor	**Partial Correlation Coefficient**			
	MINDO/3	**MNDO**	**AM1**	**PM3**
E_{TOTAL}	-0.9778	-0.9532	-0.9126	-0.8551
E_{HOMO}	-0.6987	-0.5637	-0.1201	-0.4940
E_{LUMO}	0.7661	0.6942	0.2056	0.5794
$(DIP)^2$	0.8578	0.4992	0.1574	0.3730

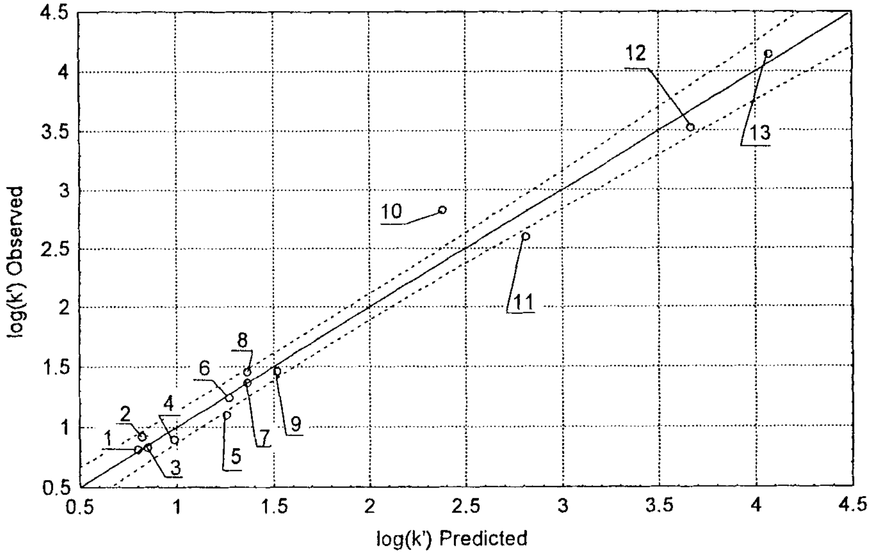

FIGURE 2. Relationship between the retention parameters of organic peroxide (log k') determined experimentally by RP HPLC (stationary phase: LiChrosorb RP 18 10 μm; mobile phase: methanol : water = 82 : 18 v/v) and calculated using eqn. 1 (MINDO/3). 1 - Ethyl cumyl peroxide; 2 - allyl cumyl peroxide; 3 - *iso*-propyl cumyl peroxide; 4 - *tert*-butyl cymyl peroxide; 5 - *n*-propyl peroxide; 6 - benzyl cumyl peroxide; 7 - *sec*-butyl cumyl peroxide; 8 - *n*-butyl cumyl peroxide; 9 - *iso*-butyl cumyl peroxide; 10 - hexyl cumyl peroxide; 11 - heptyl cumyl peroxide; 12 - octyl cumyl peroxide; 13 - nonyl cumyl peroxide.

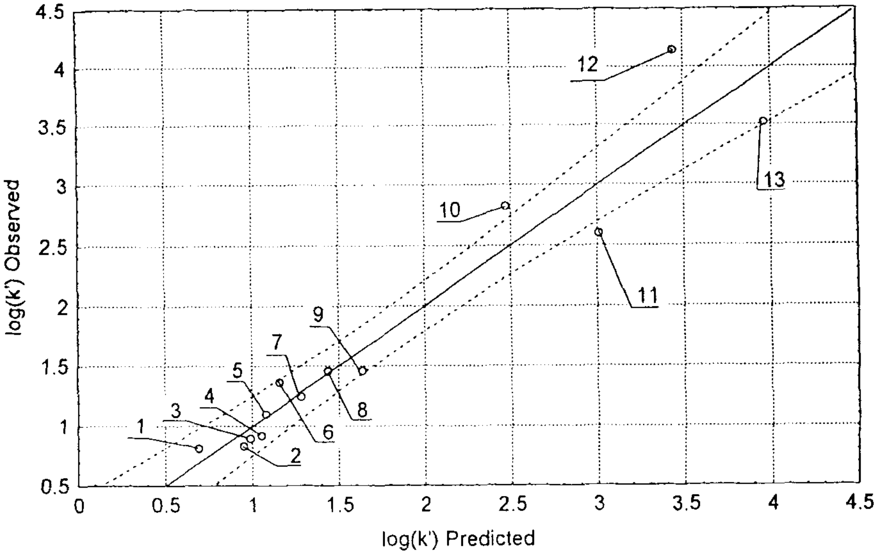

FIGURE 3. Relationship between the retention parameters of organic peroxide (log k') determined experimentally by RP HPLC (stationary phase: LiChrosorb RP 18 10 μm; mobile phase: methanol : water = 82 : 18 v/v) and calculated using eqn. 1 (MNDO). 1 - Ethyl cumyl peroxide; 2 - allyl cumyl peroxide; 3 - *iso*-propyl cumyl peroxide; 4 - *tert*-butyl cymyl peroxide; 5 - *n*-propyl peroxide; 6 - benzyl cumyl peroxide; 7 - *sec*-butyl cumyl peroxide; 8 - *n*-butyl cumyl peroxide; 9 - *iso*-butyl cumyl peroxide; 10 - hexyl cumyl peroxide; 11 - heptyl cumyl peroxide; 12 - octyl cumyl peroxide; 13 - nonyl cumyl peroxide.

The values in parentheses are the standard deviations of regression coefficients, *R* is the correlation coefficient, *F* is the *f*-test value, *p* is the significance level of the whole equation.

The correlation coefficients *R* obtained in all the calculation methods, applied to determine the structural descriptors, are good. The correlation coefficient R derived from equation (1) (MINDO/3 results) is excellent. The partial correlation coefficients between the respective variable and the dependent variable (log k') after controlling for all other independent variables in the equation are presented in Table VI. Negative values of these coefficients in the case of E_{TOTAL} and E_{HOMO} are the consequence of the fact thet relationship between dependent variable and structural descriptors mentioned above is described by a decreasing function. These coefficients indicate the

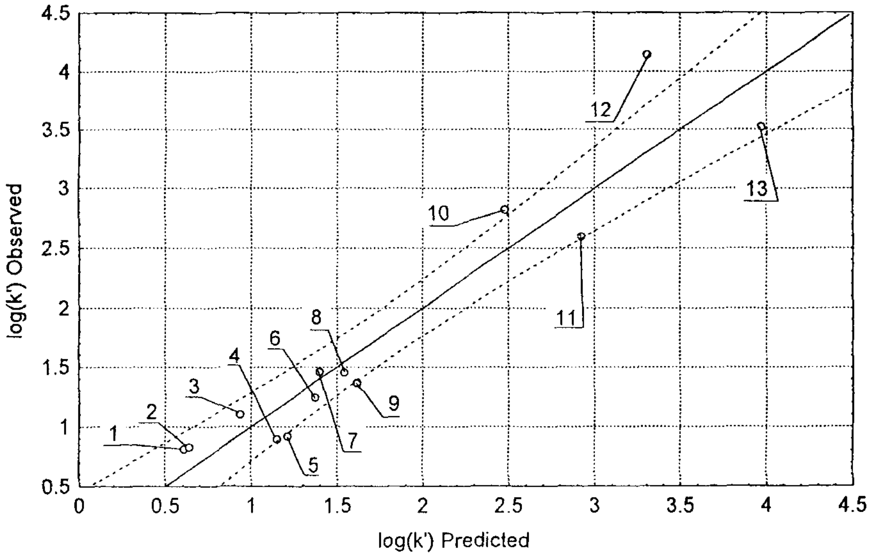

FIGURE 4. Relationship between the retention parameters of organic peroxide (log k') determined experimentally by RP HPLC (stationary phase: LiChrosorb RP 18 10 μm; mobile phase: methanol : water = 82 : 18 v/v) and calculated using eqn. 1 (AM1). 1 - Ethyl cumyl peroxide; 2 - allyl cumyl peroxide; 3 - *iso*-propyl cumyl peroxide; 4 - *tert*-butyl cymyl peroxide; 5 - *n*-propyl peroxide; 6 - benzyl cumyl peroxide; 7 - *sec*-butyl cumyl peroxide; 8 - *n*-butyl cumyl peroxide; 9 - *iso*-butyl cumyl peroxide; 10 - hexyl cumyl peroxide; 11 - heptyl cumyl peroxide; 12 - octyl cumyl peroxide; 13 - nonyl cumyl peroxide.

descriptor E_{TOTAL} as the most significant in each equation. The total molecular energy provides information about the bulkiness of the solute. This size-related descriptor may be related to the interaction between the solute molecule and the stationary phase occurring in reversed-phase liquid chromatography. The larger the solute molecule, the stronger the solute-adsorbent interaction. E_{HOMO} and E_{LUMO} descriptors are related to the ability of the solutes to participate in electron pair donor-acceptor interactions with eluent molecules. As may be concluded from the partial correlation coefficients, this kind of interaction is rather less importance for retention.

The last principal component $(DIP)^2$ determines the ability of the solute to participate in intermolecular interactions with the stationary and/or mobile phase of the dipole-dipole and dipole-induced dipole type. Their participation in the correlation equation is rather similar to E_{HOMO} and E_{LUMO}.

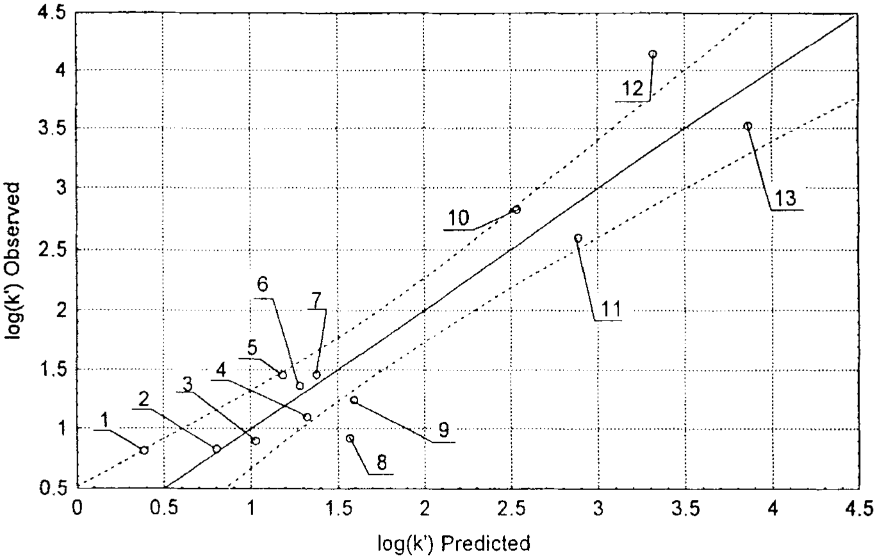

FIGURE 5. Relationship between the retention parameters of organic peroxide (log k') determined experimentally by RP HPLC (stationary phase: LiChrosorb RP 18 10 μm; mobile phase: methanol : water = 82 : 18 v/v) and calculated using eqn. 1 (PM3). 1 - Ethyl cumyl peroxide; 2 - allyl cumyl peroxide; 3 - *iso*-propyl cumyl peroxide; 4 - *tert*-butyl cymyl peroxide; 5 - *n*-propyl peroxide; 6 - benzyl cumyl peroxide; 7 - *sec*-butyl cumyl peroxide; 8 - *n*-butyl cumyl peroxide; 9 - *iso*-butyl cumyl peroxide; 10 - hexyl cumyl peroxide; 11 - heptyl cumyl peroxide; 12 - octyl cumyl peroxide; 13 - nonyl cumyl peroxide.

The remaining factors, i.e. torsion angle C1-O1-O2-C2, net charges at O1 and O2 atoms, the heat of formation and dipole moment are not essential for retention of organic peroxides in reversed phase liquid chromatography.

The correlation coefficient ***R*** is excellent in equation (1), where the structural descriptors were calculated according to the MINDO/3 method. The remaining equations do not provide such good results. The correlation between retention log *k'* and structural descriptors calculated according to the PM3 method is the worst one. The conclusion may be drawn that QSRR equations have different form depending on the method applied for calculating the structural descriptors. The best results were obtained using the MINDO/3 method to describe molecule parameters. The MINDO/3 method, applied to calculate the molecular parameter of organic peroxides, can in fact yield more accurate results than much more recent semi-empirical methods like AM1 or PM3. One of the major assets of MINDO/3 was its demonstrated ability to reproduce *all* ground-state properties [29] of molecules of *all* kinds. Problems arise, however, in the case of molecules containing heteroatoms, such as nitrogen or sulphur, conjugated molecules, overcrowded molecules (e.g. neopentane) or molecules containing four-membered rings. This method can not be used to estimate activation energy, which tends to be too large. After several years of efforts these errors have been gradually corrected by means of the new methods MNDO, AM1 and PM3.

In the case of the organic peroxide molecules investigated in this paper, the ground-state parameters calculated with MINDO/3 methods are satisfactory and give the best correlation with the retention indices. The predictive potencies of eqns. 1 - 4 are illustrated in Figs 2-5.

CONCLUSIONS

The results of this study identify the structural factors which affect retention, and provide a quantitative estimation of the importance of these structural factors. Retention in reversed-phase chromatography was found to be a net effect of non-specific, dispersive, bulkiness-dependent interactions and electrostatic interactions involving solute molecules and molecules of both mobile and stationary phases. The E_{TOTAL} descriptors related to the first kind of interaction seem to be dominant in the retention mechanism. The correlation obtained between the selected set of structural descriptors and the retention indices for a variety of organic peroxides is very good and may be used to predict the retention properties of the investigated system of molecules.

Additionally, the present paper illustrates the applicability of semi-empirical calculations to investigations and to the understanding of the retention mechanism. This method can be used to predict the chromatographic properties of the investigated molecules. The relationship between log *k'* and the structural descriptors is different in the case of the semi-empirical methods employed. For organic peroxide molecules MINDO/3 method gives the most reliable values of E_{TOTAL}, E_{HOMO} and E_{HOMO} and $(DIP)^2$ parameters.

REFERENCES

1. H. Kropf, Organische Peroxo-Verbinddungen in Methoden de Organischen Chemie (Houben-Weyl), Band E 13, Teil 1-2, Georg Thieme Verlag, Stuttgart, 1988.

2. J. K. Kochi, Free Radicals Vol.1, John Wiley & Sons, New York 1973.
3. R. Hiatt, Organic Peroxides Vol. 3, Ed.: Swern, D. J., Wiley & Sons, New York 1983
4. R. A. Sheldon, "Synthesis and Uses of Alkyl Hydroperoxides and Dialkyl Peroxides" in Chem. Peroxides ,161 Ed.;Patai, S., John Wiley & Sons, New York, 1983.
5. L. Topolova, K. Dimitrov, and M. Aleksandrova, Izv. Akad. Nauk SSSR, Ser. Khim., 19: 520 (1986)
6. C. P. Patel, and V. Lilly, LC-GC, 6: 424 (1988)
7. J. B. Beltra, and B. de Havedia, Afinidad, 46: 185 (1989)
8. W. van Tilborg, J. Chromatogr., 115: 616 (1975)
9. S. Baj, and Z. Kulicki, J. Chromatogr., 588: 33 (1991)
10. T. Hanai, J. Chromatogr., 550: 313 (1991)
11. A. J. P. Martin, Biochem. Soc. Symp., 3: 4 (1949)
12. E. C. Bate-Smith, and R. G. Westall, Biochem. Biophys. Acta, 4: 427 (1950)
13. I. Molnar, and Cs. Horvath, J. Chromatogr., 145: 371 (1978)
14. B. K. Chen, and Cs. Horvath, J. Chromatogr., 171: 15 (1979)
15. C. M. Riley, E. Tomlinson, and T. M. Jefferies, J. Chromatogr., 185: 197 (1979)
16. E. Tomlinson, H. Poppe, and J. C. Kraak, Int. J. Pharmacol., 7: 225 (1981)
17. R. F. Rekker, The Hydrophobic Fragmental Constant, Elsevier, Amsterdam, 1977.
18. R. Kaliszan, Quantitative Structure-Chromatographic Retenrion Relationships (Chemical Analysis, Vol. 93), Ed. J. D. Winefordner, Wiley, New York, 1987.
19. R. Kaliszan, and K. Osmiałowski, J. Chromatogr., 506: 3 (1990)
20. R. Kaliszan, A. Kaliszan, T. A. G. Noctor, W. P. Purcell, and I. W. Wainer, J.Chromatogr., 609: 68 (1992)
21. H. Zou, Y. Zhang, and P. Lu, J. Chromatogr., 265: 171 (1983)
22. P. Zou, H. Lu, and Y. Zhang, Microchim. Acta Part III, 35 (1990)
23. H. Liu, and F. F. Cantwell, Anal. Chem., 63: 2032(1991)
24. S. Baj, Pol. J. App. Chem., 35: 137 (1991)
25. J. J. P. Stewart, J. Comp. Chem., 10: 209 (1989)
26. M. J. S. Dewar, E. G. Zoebisch, E. F. Heal, and J. J. P. Stewart, J. Am. Chem. Soc., 107: 3902 (1985)
27. M. J. S. Dewar, and W. Thiel, J. Am. Chem. Soc., 99: 4899 (1977)

28. R. C. Bingham, M. J. S. Dewar, and D. H. Lo, J. Am. Chem. Soc., 97: 1285, 1294, 1302, 1307 (1975)

29. M. J. S. Dewar, and H. S. Rzepa, J. Am. Chem. Soc., 99: 7432 (1977)

Received: January 29, 1994
Accepted: June 27, 1994