

CHROMSYMP. 288

RETENTION *VERSUS* VAN DER WAALS VOLUME AND π ENERGY IN LIQUID CHROMATOGRAPHY

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SUMMARY

A system in which only the size and the π energy of the molecules may be involved, is examined by reversed-phase liquid chromatography using octadecyl bonded silica gels as the packing. If hydrogen bonding and Coulombic forces are negligible, the retention of molecules depends upon their size, and the presence of π electrons enhances the selectivity. Therefore, the difference between the logarithm of the capacity ratios of alkanes and polycyclic aromatic hydrocarbons (PAH) was defined as the π energy effect and $\log k'(\text{PAH}) = \log k'(\text{Van der Waals volume}) - \log k'(\pi \text{ energy effect})$.

The π energy effect calculated for alkylbenzenes and chlorobenzenes from the capacity ratios obtained on different packings in acetonitrile-water mixtures was constant. Therefore, the prediction of the retention time of these compounds was also possible from their Van der Waals volumes and π energy. The solvent effects of tetrahydrofuran and *n*-hexane are also discussed.

INTRODUCTION

The optimization of liquid chromatography by quantitative analysis of weak molecular interactions inside a column is an important topic in chemistry. In reversed-phase liquid chromatography, the retention of solutes can be explained by the solvation of solutes in the liquid phase formed on the surface of packings. Therefore, if the components of an eluent are homogeneously distributed on the surface, the partition coefficient, like $\log P$ derived from an octanol-water system, can be used for the optimization of liquid chromatography¹⁻⁶. The accuracy of the optimization, however, decreases in eluents with a high concentration of either organic modifier or water owing to heterogeneous solvation on the surface of the packings and selective solvation of the solutes. This phenomenon is manifested as a change of the elution volume of the components of eluents. The basic phenomenon in liquid chromatography is not like a liquid phase reaction where all components are well homogenized, rather it is similar to a solid phase reaction where the solutes and the components of the solvent are localized on a suitable site, depending on the nature of the components. Therefore, electronic and/or Coulombic effects will enhance the selectivity. The introduction of Hammett's equation in the above system made it possible to

predict the retention time for ionic compounds⁴. However, the partition coefficients that are widely used by medicinal chemists, and which are obtained by a summation of weak interactions of molecules, do not provide the flexibility to account for different solvations.

The solubility is qualitatively explained as a combination of Van der Waals volume, repulsion, dipole-dipole interaction, charge-transfer interaction, hydrogen bonding and Coulombic forces. The typical size exclusion liquid chromatography can be analysed in terms of the Van der Waals volume of solutes, and simple reversed-phase liquid chromatography can be explained as a function of the hydrophobicity of solutes. Generally, molecules become more hydrophobic when their size increases because solvation takes longer. The elution order due to hydrophobicity can be reversed when a non-aqueous eluent is substituted for an aqueous eluent, but one group of compounds, polycyclic aromatic hydrocarbons (PAH), does not fit the above pattern. In a non-aqueous phase system their retentions are related to resonance⁷⁻⁹, delocalization⁸, π electron energy⁹ and the number of π electrons⁹. In aqueous phases, their retentions are related to molecular connectivity¹⁰, numerical descriptors including molecular connectivity, substructure, etc.,¹¹ and length-to-breadth ratios¹². Nevertheless the elution order cannot be simply related to the π energy.

An example is the elution order of anthracene and phenanthrene. The retention of anthracene is always stronger than that of phenanthrene. This means that the retention of PAHs may be controlled by their size and by their π energy in aqueous phase liquid chromatography¹³. Therefore two factors, Van der Waals volume and π energy, were considered in an investigation of the retention of PAHs, using *n*-alkanes as standard compounds. The experiments were done on in acetonitrile or tetrahydrofuran-water mixtures, with 5- μm octadecyl bonded end-capped monolayer silica gels. The pore size was 100 Å. The nature of the packings was further tested in *n*-hexane. The above approach was applied to examine the chromatographic behavior of alkylbenzenes and chlorobenzenes.

EXPERIMENTAL

The details of the instruments used were previously described⁵. The columns were Develosil ODS-5, kindly given by Mr. M. Nomura (Nomura Chemical, Aichi, Japan), and ERC-ODS-1000, given by ERMA Optical Works (Tokyo, Japan). The former column was 15 cm \times 4.6 mm I.D., packed with 5 μm Develosil ODS, and the latter column was 10 cm \times 6.0 mm I.D., packed with 5 μm Hypersil ODS. Their theoretical plate number is over 74,000/m and their pore size is 100 Å. The column temperature was 30°C. The chemicals are listed in Table I with their physical parameters.

RESULTS AND DISCUSSION

The Van der Waals volume was calculated by Bondi's method¹⁴, the connectivity was estimated according to Kier and Hall's method¹⁵, and the log *P* value was calculated by Rekker's method¹⁶. The delocalization energy was obtained from the literature^{8,9,18}. All the values are collected in Table I, and examples of relations

between Van der Waals volume (VWV) or connectivity (X) or partition coefficient ($\log P$) and $\log k'$ are shown in Figs. 1-3. The eluent was an 80% acetonitrile-water mixture. The $\log k'$ values obtained on Develosil ODS are given in Table I. The void volume used for the calculation is also listed in Table I¹⁹.

For discussion of the elution volume changes inside each series of compounds, any of the above parameters can be used for optimization of the separation, and the addition of isomeric effects can further improve the accuracy. To optimize the separation of a mixture of the different types of compound, the $\log P$ system was the best choice. However, we obtained good accuracy only for mixtures with 30-70% of acetonitrile in water. The selectivity between aliphatic and aromatic compounds is obvious from the results obtained in a acetonitrile-water (80:20) mixture (Fig. 3).

The calculation of molecular connectivity seemed simple, but the values reported by different authors are seldom the same, and therefore the Van der Waals volume was preferred.

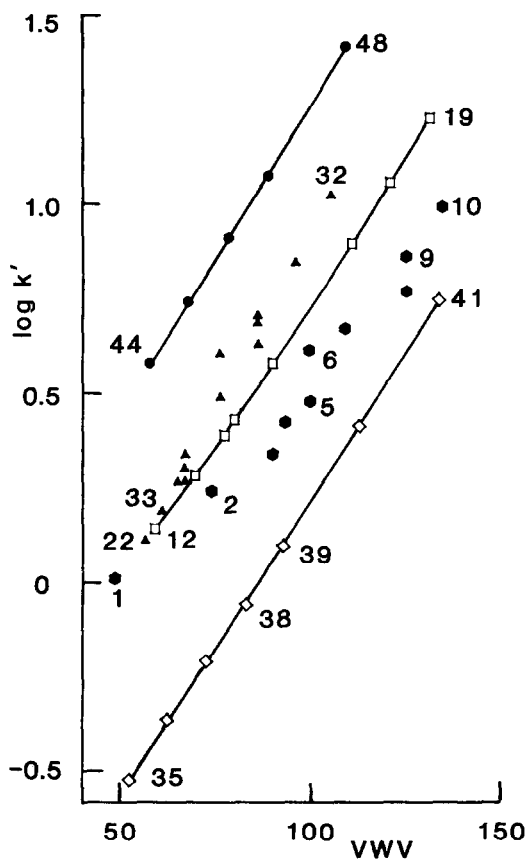


Fig. 1. Relationship between Van der Waals volume (VWV) and $\log k'$ values. Each symbol indicates a group of compounds and the numbers are the same as in Table I. \blacklozenge = PAHs; \square = alkylbenzenes; \blacktriangle = halogenated benzenes; \diamond = alcohols; \bullet = alkanes. Column, Develosil ODS; eluent, acetonitrile-water (80:20); column temperature, 30°C.

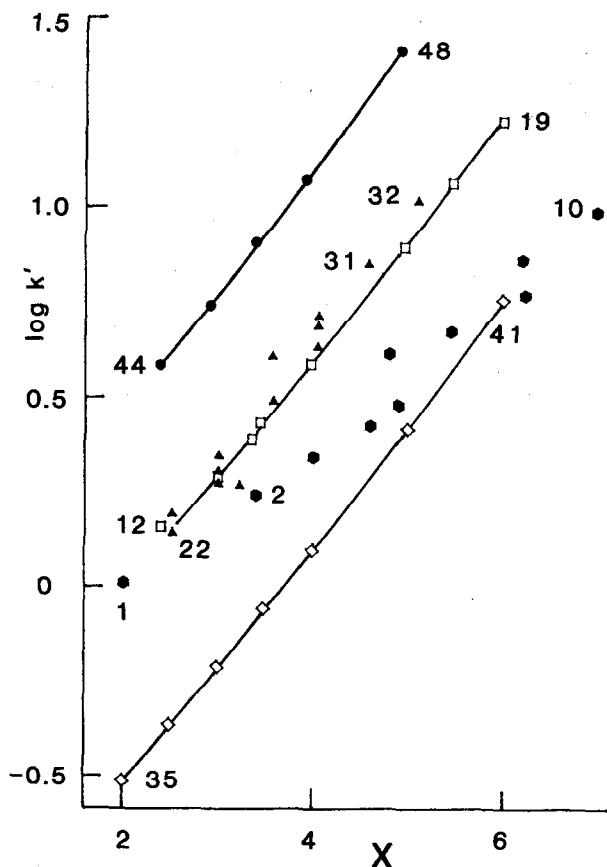


Fig. 2. Relationship between connectivity (X) and $\log k'$ values. For details see Fig. 1.

TABLE I
PHYSICAL PARAMETERS AND LOGARITHM OF CAPACITY RATIOS OF STANDARD COMPOUNDS

		VWV^*	X^{**}	$\log P^{***}$	DLE^{\S}	$\log k'$	
						Percent acetonitrile	
						95	90
1	Benzene	48.36	2.000	2.280	2.000	-0.3648	-0.2112
2	Naphthalene	73.96	3.405	3.208	3.683	-0.1681	-0.0108
3	Biphenyl	90.08	4.017	3.772	4.383	-0.1177	0.0591
4	Fluorene	93.22	4.611	3.906	4.75	-0.0366	0.1376
5	Phenanthrene	99.56	4.815	4.378	5.448	0.0233	0.1960
6	Anthracene	99.56	4.809	4.378	5.314	0.1395	0.3186
7	Pyrene	109.04	5.559	5.030	6.506	0.1998	0.3764
8	Chrysene	125.16	6.226	5.545	7.190	0.2531	0.4445
9	Tetrasene	125.16	6.214	5.790	6.932	0.3307	0.5268
10	Benzopyrene	134.64	6.970	6.200	-	0.4640	0.6587
11	Pentacene	150.76	7.619	6.960	-	-	-

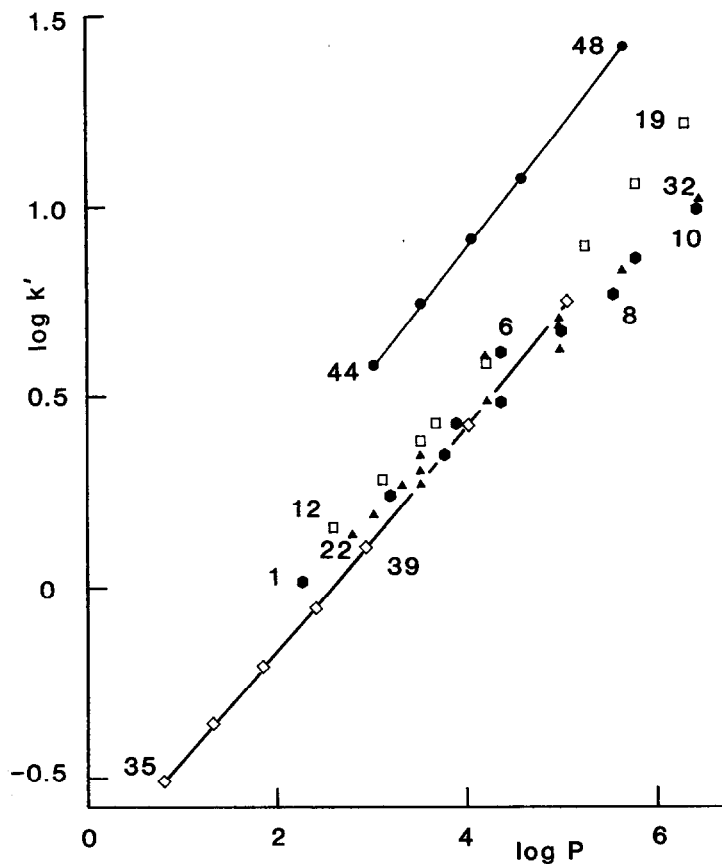


Fig. 3. Relationship between $\log P$ and $\log k'$ values. For details see Fig. 1.

in water				Percent THF in water			π^{88}	
				90	70	50	I	II
85	80	70	60					
-0.0841	0.0109	0.2343	0.4535	-0.4335	0.0706	0.4780	1.948	1.856
0.1181	0.2371	0.4963	0.7648	-0.4687	0.0808	0.5853	3.874	3.893
0.2050	0.3424	0.6311	0.9348	-0.4901	0.1225	0.6979	5.625	5.693
0.2825	0.4216	0.7091	1.013	-0.4635	0.1346	0.7149	5.285	5.375
0.3409	0.4800	0.7706	1.081	-0.5127	0.0891	0.6682	5.708	5.789
0.4692	0.6133	0.8160	1.132	-0.5069	0.1085	0.6977	4.513	5.387
0.5248	0.6678	0.9104	1.227	-0.5244	0.0908	0.6807	5.414	5.351
0.6098	0.7677	0.9644	1.285	-0.5304	0.1101	0.7582	7.413	7.289
0.6980	0.8605	1.092	1.444	-0.5304	0.1949	0.8158	6.326	6.425
0.8283	0.9918	1.322	-	-0.5617	0.1148	0.7779	6.226	6.488
-	-	-	-	-	-	-	-	-

(Continued on p. 202)

TABLE I (continued)

		VWV^*	X^{**}	$\log P^{***}$	DLE^{\S}	$\log k'$	
						Percent acetonitrile	
						95	90
12	Toluene	59.51	2.411	2.588	2.15	-0.2407	-0.0804
13	Ethylbenzene	69.74	2.971	3.118	—	-0.1464	0.0229
14	Isopropylbenzene	77.02	3.354	3.525	—	-0.0672	0.1113
15	Propylbenzene	79.97	3.471	3.648	—	-0.0284	0.1512
16	Butylbenzene	90.20	3.971	4.178	—	0.0871	0.2770
17	Hexylbenzene	110.66	4.971	5.238	—	0.3221	0.5394
18	Heptylbenzene	120.89	5.471	5.768	—	0.4444	0.6758
19	Octylbenzene	131.12	5.971	6.297	—	0.5667	0.8132
20	Nonylbenzene	141.35	6.471	6.828	—	—	—
21	Decylbenzene	151.58	6.971	7.358	—	—	1.091
22	Chlorobenzene	57.84	2.513	2.808	2.05	-0.2514	-0.0921
23	1,2-Dichlorobenzene	67.32	3.031	3.532	—	-0.1360	0.0244
24	1,3-Dichlorobenzene	67.32	3.025	3.532	—	-0.0726	0.0924
25	1,4-Dichlorobenzene	67.32	3.025	3.532	—	-0.1138	0.0464
26	1,2,4-Trichlorobenzene	76.80	3.544	4.197	—	0.0510	0.2215
27	1,3,5-Trichlorobenzene	76.80	3.538	4.197	—	0.1503	0.3247
28	1,2,3,4-Tetrachlorobenzene	86.28	4.068	4.944	—	0.1682	0.3631
29	1,2,3,5-Tetrachlorobenzene	86.28	4.062	4.944	—	0.2355	0.4166
30	1,2,4,5-Tetrachlorobenzene	86.28	4.062	4.944	—	0.2111	0.3935
31	Pentachlorobenzene	95.76	4.587	5.691	—	0.3473	0.5390
32	Hexachlorobenzene	105.24	5.105	6.438	—	0.4823	0.6861
33	Bromobenzene	60.96	2.492	3.017	—	-0.2053	-0.0509
34	Iodobenzene	65.48	3.215	3.334	—	-0.1339	0.0229
35	Butyl alcohol	52.40	2.023	0.801	—	-0.6588	-0.5852
36	Pentyl alcohol	62.63	2.523	1.331	—	-0.5497	-0.4588
37	Hexyl alcohol	72.86	3.023	1.861	—	-0.4248	-0.3413
38	Heptyl alcohol	83.09	3.525	2.391	—	-0.2968	-0.2060
39	Octyl alcohol	93.32	4.023	2.921	—	-0.1704	-0.0729
40	Decyl alcohol	113.78	5.024	3.981	—	0.0796	0.2000
41	Dodecyl alcohol	134.24	6.024	5.041	—	0.3412	0.4852
42	Tetradecyl alcohol	154.70	7.024	6.071	—	0.5987	0.7679
43	Hexadecyl alcohol	175.16	8.024	7.101	—	0.8465	1.049
44	Pentane	58.03	2.414	2.994	—	0.1384	0.3070
45	Hexane	68.26	2.914	3.524	—	0.2647	0.4483
46	Heptane	78.49	3.414	4.054	—	0.3945	0.5876
47	Octane	88.72	3.914	4.584	—	0.5206	0.7302
48	Decane	109.18	4.914	5.644	—	0.7752	1.015
49	Dodecane	129.64	5.914	6.704	—	1.032	1.306
	Void volume (ml) ^{§§§}					1.525	1.455

* Van der Waals volume (cm³/mole) calculated by Bondi's method (ref. 12).

** Molecular connectivity (refs. 10, 15, 17).

*** Partition coefficient between octanol and water calculated by Rekker's method (ref. 16).

§ Delocalization energy (kcal) from refs. 8, 9 and 18.

§§ π energy effect: for details, see text; I and II were obtained on Develosil and Hypersil ODS, respectively.

§§§ The void volume in acetonitrile-water mixtures was obtained from the elution volume of fructose and in tetrahydrofuran-water mixtures from the elution volume of tetrahydrofuran (ref. 19).

							π^{55}	
<i>in water</i>				<i>Percent THF in water</i>			<i>I</i>	<i>II</i>
85	80	70	60	90	70	50		
0.0369	0.1536	0.3942	0.6410	-0.3877	0.0989	0.6033	2.322	2.303
0.1525	0.2808	0.5388	0.8124	-0.3877	0.1916	0.7180	2.755	2.752
0.2501	0.3871	0.6641	0.9602	-0.3834	0.2455	0.8095	2.879	2.878
0.2934	0.4325	0.7134	1.014	-0.3624	0.2512	0.8356	2.900	2.927
0.4331	0.5844	0.8878	1.214	-0.3543	0.3067	0.9480	3.061	3.092
0.7211	0.8971	1.247	-	-0.3270	0.4021	1.161	3.312	3.336
0.8719	0.060	1.432	-	-0.3050	0.4502	1.260	3.365	3.385
1.023	1.223	-	-	-0.2943	0.4974	1.359	3.489	3.478
-	-	-	-	-	-	1.461	-	3.453
1.329	-	-	-	-0.2639	0.5907	1.552	-	3.655
0.0279	0.1409	0.3851	0.6307	-0.4433	0.0875	0.5493	2.153	2.194
0.1490	0.2696	0.5258	0.7890	-0.4532	0.0924	0.5845	2.378	2.343
0.2209	0.3446	0.6072	0.8767	-0.4146	0.1687	0.7121	1.678	1.608
0.1779	0.3023	0.5661	0.8383	-0.4193	0.1770	0.7254	2.043	2.100
0.3611	0.4927	0.7703	1.060	-0.3791	0.2327	0.8342	1.747	1.763
0.4681	0.6050	0.8875	1.182	-0.3086	0.3422	0.9784	0.763	0.834
0.4890	0.6281	0.9168	1.222	-0.3707	0.2467	0.8660	1.897	1.924
0.5681	0.7114	1.006	1.316	-0.3050	0.3549	1.021	1.248	1.217
0.5442	0.6878	0.9829	1.294	-0.3159	0.3486	1.019	1.259	1.451
0.6999	0.8514	1.161	-	-0.2639	0.4119	1.115	1.230	1.212
0.8580	1.020	1.347	-	-0.2146	0.5036	1.262	1.084	1.157
0.1178	0.1885	0.4356	0.6859	-0.4367	0.0924	0.5723	2.161	2.205
0.1406	0.2670	0.5222	0.7840	-0.4433	0.1085	0.6165	2.180	2.241
-0.5254	-0.5200	-0.3508	-0.2461	-	-0.3670	-0.2522	-	-
-0.4073	-0.3640	-0.1903	-0.0637	-	-0.2974	-0.0991	-	-
-0.2641	-0.2210	-0.0304	0.1321	-0.7250	-0.2270	0.0616	-	-
-0.1318	-0.0630	0.1414	0.3320	-0.7250	-0.1847	0.2001	-	-
0.0145	0.0961	0.3150	0.5315	-0.7156	-0.1267	0.3232	-	-
0.3127	0.4179	0.6733	0.9412	-0.6396	-0.0128	0.5429	-	-
0.6235	0.7511	1.048	1.364	-0.5682	0.0875	0.7588	-	-
0.9302	-	1.416	-	-0.2002	0.1890	0.9600	-	-
1.236	-	-	-	-0.1422	0.2788	1.147	-	-
0.4478	0.5784	0.8561	1.130	-0.2264	0.3682	0.9587	0	0
0.5974	0.7424	1.046	1.347	-0.2117	0.4393	1.068	0	0
0.7522	0.9088	1.230	-	-0.2031	0.4874	1.174	0	0
0.9072	1.076	1.417	-	-0.1836	0.5378	1.275	0	0
1.215	1.415	-	-	-0.1398	0.6011	-	0	0
-	-	-	-	-0.1573	0.6978	-	0	0
1.430	1.430	1.360	1.305	1.310	1.160	1.290	-	-

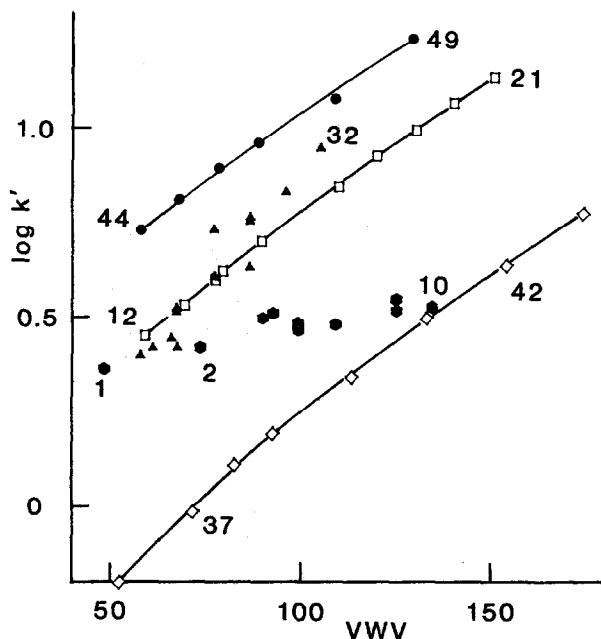


Fig. 4. Relationship between Van der Waals volumes and $\log k'$ values on a Hypersil ODS column in tetrahydrofuran-water (60:40). For details see Fig. 1.

At present, few accurate data related to energy have been reported. The maximum $\log k'$ values were obtained from the relation between the retention of the *n*-alkanes and the Van der Waals volumes (Fig. 1). Values for $\Delta \log k'$ were calculated as the difference between this maximum $\log k'$ and the observed $\log k'$ values of PAHs. The result for the PAHs was applied to other compounds, and the PAHs selected for further calculations were benzene, naphthalene, phenanthrene, chrysene and tetrasene. The π energy effects derived from the $\Delta \log k'$ values are listed in Table I.

When we used these ODS columns in 100% *n*-hexane, the elution volumes of alkanes, alkylbenzenes, chlorobenzenes and PAHs were small and similar on all columns. However, the retention behavior of the alcohols was different: the elution volumes of alcohols could be easily measured on Develosil ODS, but were very difficult to measure on Hypersil ODS owing to strong retention. Addition of 2.5% of ethyl acetate in *n*-hexane resulted in the retention of alcohols on Hypersil ODS being about double that on Develosil ODS; e.g. decyl alcohol, 4.69 and 2.47 ml respectively.

When the separation was carried out in 100% tetrahydrofuran, we could measure the exclusion limit of these columns by size exclusion chromatography. The elution volume of polystyrene was 0.96 and 1.00 ml from Develosil and Hypersil ODS columns, respectively. No selectivity for alcohols was observed on either packing with this eluent.

Some results on Develosil ODS in tetrahydrofuran-water mixtures are listed in Table I, and one example of studies on Hypersil ODS is shown in Fig. 4. In highly concentrated tetrahydrofuran-water mixtures, the retention of these compounds was

very weak and a size exclusion effect was observed. The retention was considerably increased in eluents with low concentrations of tetrahydrofuran. The selectivity between aliphatic and aromatic compounds was very high. Separation of PAHs was very difficult, and a good selectivity was found for the chlorobenzene isomers. The retention of those with chloro groups in 1- and 2-positions was lower than those with chloro groups in 1- and 3- or 1- and 4-positions, and the selectivity between 1,3- and 1,4-dichlorobenzenes was negligible. Although tetrahydrofuran is not a good solvent for discussing the π energy effect in liquid chromatography, it was an effective solvent for improving the selectivity between aliphatic and aromatic compounds.

Develosil ODS had *ca.* 4% less capacity than Hypersil ODS. The correlation coefficient between the capacity ratios of these compounds on the previous packings was 0.9975 ($n = 44$). However, there is some selectivity between them. When the average capacity ratio of alkylbenzenes on both columns was fixed at 1.00, the ratio of the average capacity ratios for PAHs hydrocarbons was 0.97 on Develosil ODS/Hypersil ODS, and those for chlorobenzenes, alkanes and alcohols were respectively 1.06, 1.10 and 0.93. The selectivity for alcohols was more clearly observed in *n*-hexane. However, the π energy effect calculated from $\Delta \log k'$ values was very similar, except for anthracene (Table I).

This means that we can optimize the retention of these compounds from the knowledge of their Van der Waals volume and π energy, except for alcohols which require the introduction of hydrogen bonding effect. The retention is given by $\log k' = \log k'_v$ (related to Van der Waals volume) $- \log k'_\pi$ (related to π energy). The maximum capacity ratio related to Van der Waals volume is obtained from the retention of *n*-alkanes. The linear relationships between the logarithm of capacity ratios and their Van der Waals volumes obtained in different concentration of acetonitrile–water mixtures are represented by lines that all merge at one point, and therefore the same procedure can be used as for the $\log P$ system¹⁻⁵. The π energy effect in given acetonitrile–water mixtures can be also calculated by the same approach used for Van der Waals volumes.

However, the π energy effect was not constant. Among PAHs, biphenyl and pyrene have different tendencies. Decreasing the acetonitrile concentration increases the π energy of pyrene and decreases that of biphenyl; however, the elution order did not change in the above systems. The π energy effect of alkylbenzenes was almost constant, but that of chlorobenzenes changed significantly even through the elution order was the same. This indicates the necessity of the addition of resonance effect in the above system.

CONCLUSION

The retention of aromatics can be controlled in reversed-phase liquid chromatography from a knowledge of their Van der Waals volumes and π energy. The accuracy of the calculation of Van der Waals volume is good enough for this purpose, but the determination of π energy effect is not simple, and the values are influenced by the solvent effect. Therefore, the introduction of the resonance effect is necessary to improve the accuracy of the above optimization system. Furthermore, hydrogen bonding must be considered in the analysis of compounds that can form hydrogen bonds.

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