STUDIA UNIVERSITATIS BABEŞ-BOLYAI, CHEMIA, XLIII, 1-2, 1998

LIPOPHILICITY CHARACTERIZATION OF A LARGE NUMBER OF DIOXANES AND SPIRANS BY REVERSED-PHASE THIN-LAYER CHROMATOGRAPHY

**GABRIELA CÎMPAN*, SIMION GOCAN, NELI OLAH,
ION GROSU, SORIN MAGER**

ABSTRACT. The lipophilicity of over 70 compounds, dioxanes and spirans, was studied by reversed phase thin layer chromatography, on silica-C18 plates, and methanol-water or acetone-water as mobile phase. The R_{Mw} values were obtained by extrapolation to 100% water as mobile phase and these are a measure of the compounds lipophilicity. The partition coefficient between n-octanol and water, CLogP, was obtained from Pomona College database (Claremont, CA, USA). Linear correlations have been obtained between the R_{Mw} values and the calculated LogP values.

INTRODUCTION

The lipophilicity of substances can be expressed by the partition coefficient between n-octanol and water, $P_{o/w}$ [1-3]. The $LogP_{o/w}$ values can be measured experimentally by the shake-flask method or can be calculated by using different calculation procedures. The direct measurement of $LogP_{o/w}$ values by equilibration between n-octanol and water faces some difficulties as the necessary high purity of the substance that must be available in an adequate quantity. In addition, this method is time consuming and can be applied only in a limited range on the lipophilicity scale. The difficulties can be overcame by using Reversed Phase Liquid Chromatography (RPLC), and these methods have been applied for some years [4-7]. The chromatographic methods show distinct advantages as speed of determination, better reproducibility, only small amounts of sample are necessary, and high purity of the sample is not a condition. Among liquid chromatographic methods, Reversed Phase Thin-Layer Chromatography (RP-TLC) is an alternative technique that can correlate the lipophilicity of compounds with the retention parameters [8, 9]. Martin and Synge [10] and Consden *et al.* [11] derived a relationship between the partition coefficient *P* and R_f values in partition chromatography. Bate-Smith and Westall [12] introduced the term $R_M = \log(1/R_f-1)$. Boyce and Milborrow [13] suggested the use of this value in order to avoid the practical difficulties that often arise in the direct determination of the partition coefficient. The R_M value measured by RP-TLC has been used as a reliable alternative to the classical LogP in order to express the lipophilic character of a substance [14-16].

---

[*] *Faculty of Chemistry and Chemical Engineering, "Babeş-Bolyai" University, 11 Arany Janos street, 3400, Cluj-Napoca, Romania.*

The aim of the present study is to find a linear correlation between the R_M values obtained for a large number of dioxanes and spirans by RP-TLC and the calculated LogP values. Similar studies on a few numbers of the same compounds were successful and encouraged to increase the number of compounds on the same structures [17]. Methanol-water and acetone-water was used as a binary mobile phase on silica gel C18 as non-polar stationary phase. The LogP values were obtained from the Pomona College database (Claremont, CA, USA).

EXPERIMENTAL

The structures of the studied compounds are shown in Figure 1. The RPTLC experiments were performed on silica gel C18 plates, which have fluorescence indicator for 254 nm, obtained from Macherey-Nagel (Germany). The plate dimensions were 10x20 cm and the layer width was 0.25 mm. The samples were prepared as 0.1 mg/ml solutions in methanol-chloroform (1:1, v/v). Mixtures of methanol-water and acetone-water were used as polar mobile phase. The concentration of organic modifier was modified in the range 95-70%. The samples were applied onto the plates as spots by using an automated applicator Desaga AS-30, 1.5 cm from the bottom edge. The plates were developed in normal chambers, previously equilibrated for 30 minutes. The migration distance was 8 cm in all cases. After development, the plates were dried in a gentle air stream. The visualisation was performed in UV light, in the cases were this was possible, or in VIS after spraying with a mixture of vanillin (1% in ethanol) and sulphuric acid (20% in ethanol) in equal parts, followed by heating at 110^0C for 5 minutes. The derivatisation reaction leads to coloured spots, from light pink, purple, to dark green. The R_f values were measured with a Shimadzu CS-9000 dual-wavelength flying spot scanner, in reflection mode at a suitable wavelength according to the visualisation method.

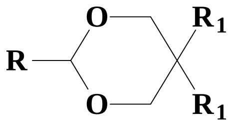
RESULTS AND DISCUSSION

The studied compounds were synthesised at Organic Chemistry Department (Faculty of Chemistry and Chemical Engineering, "Babe¿-Bolyai" University, Cluj-Napoca, Romania) [18-29].

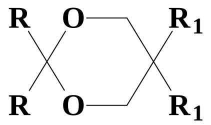
The R_M values, $R_M = \log(1/R_f-1)$, were measured for both elution systems, methanol-water and acetone-water, for the concentrations 70/30, 75/25, 80/20, 85/15 and 90/10 (v/v). The corresponding values are shown in Tables 1 and 2. Between the R_M values and the concentration of organic modifier in the mobile phase, a linear correlation can be established (equation 1):

$$R_M = a_0 + a_1X \qquad (1)$$

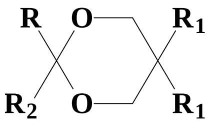
where X is the molar fraction of methanol or acetone in the eluent. The a_0 values are the intercept, R_{Mw} values, for 100% water as mobile phase, taking into account that the linearity of equation 1 is maintained even at low concentration of organic solvent in the eluent. The R_{Mw} values for both eluent systems, methanol-water and acetone-water, are presented in Table 1 and 2. Usually, the correlation coefficient, r, is very good (r>0.99). The few exemptions are due to experimental errors, because the front line was no always straight. We assumed that the non-polar stationary phase, silica-C18 (from Macherey-Nagel) has a high degree of free silanol groups, which induce secondary interactions between the compounds, mobile phase and stationary phase. In order to check this hypothesis, a standard mixture test of lipophilic coloured substances: Sudan red, bromophenol blue and alizarin yellow, from Merck (Darmstadt, Germany) was separated by thin-layer chromatography on plates with silica and silica-C18 layers, both from Macherey-Nagel (Germany). The mobile phase was benzene in both cases. The elution order of the three dyes was the same in both cases, although the partition mechanism should be different. Surprisingly, the R_f values differ by only 3% for the two plates. These observations confirm that the secondary interactions are very strong on the used plates and the linearity of the correlation (1) can not be very good.



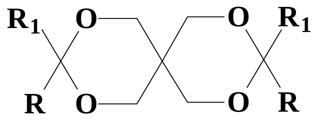
R = *m*-O_2N-C_6H_4-, $R_1 = COOC_2H_5$ **D_1**
R = *o*-O_2N-C_6H_4-, $R_1 = COOC_2H_5$ **D_2**
R = *p*-O_2N-C_6H_4-, $R_1 = COOC_2H_5$ **D_3**
R = *β*-$C_{10}H_7$-, $R_1 = CH_3$ **D_{45}**
R = *i*-C_3H_7, $R_1 = CH_3$ **D_{56}**
R = *p*-$(CH_3)_2N$-C_6H_4, $R_1 = CH_3$ **D_{37}**



R = C_6H_5-CH(Br)-, $R_1 = COOC_2H_5$ **D_9**
R = C_6H_5-CH_2-, $R_1 = COOC_2H_5$ **D_{11}**
R = C_6H_5-, $R_1 = COOC_2H_5$ **D_{13}**
R = C_2H_5-CH(Br)-, $R_1 = CH_3$ **D_{48}**
R = CH_2(Br), $R_1 = CH_3$ **D_{72}**

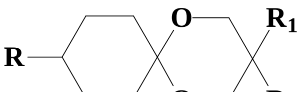


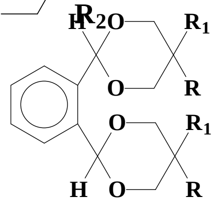
R = CH_3, $R_2 = C_6H_5$-, $R_1 = COOC_2H_5$ **D_5**
R = CH_3, $R_2 = C_6H_5$-, $R_1 = COOCH_3$ **D_6**
R = CH_2-Br, $R_2 = C_6H_5$, $R_1 = COOC_2H_5$ **D_{12}**
R = C_6H_5-CH(OOC-CH_3)-, $R_2 = C_6H_5$,
$R_1 = CH_3$ **D_{38}**
R = C_6H_5-CH(OH)-, $R_2 = C_6H_5$,
$R_1 = CH_3$ **D_{40}**

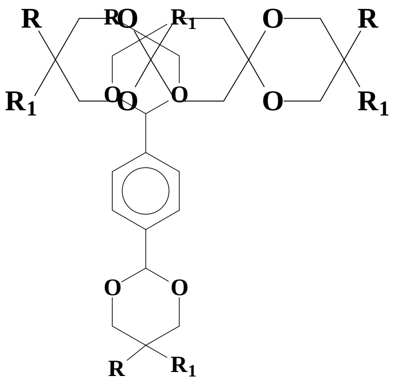


R = C_6H_5, $R_1 = CH_3$ **D_7**
R = *i*-C_3H_7, $R_1 = CH_3$ **D_8**
R =CH_2(Br), R_1= CH(Br)-CH_3 **D_{10}**
R = R_1 = CH_2(Br) **D_{14}**
R = R_2 = C_6H_5, **D_{15}**
R = *p*-O_2N-C_6H_4-, $R_2 = CH_2Br$ **D_{23}**
R = $(CH_3)_2$C (Br)-, R_1 = H **D_{41}**
R = CH_2(Br), R_1 = H **D_{47}**
R = C_6H_5-, $R_2 = CH_2Br$ **D_{44}**

Figure 1. The structures of studied dioxanes and spirans

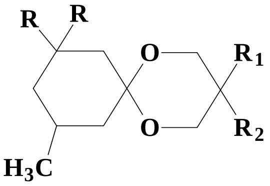


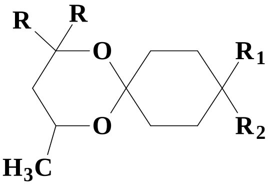




R = R$_1$ = COOC$_2$H$_5$ **D$_{4}$**
R = C$_2$H$_5$, R$_1$ = CH$_3$ **D$_{21}$**
R = H, R$_1$ = CH$_3$ **D$_{27}$**
R = R$_1$ = COOCH$_3$ **D$_{28}$**

R = C$_2$H$_5$, R$_1$ = CH$_3$ **D$_{18}$**
R = R$_1$ = COOC$_2$H$_5$ **D$_{26}$**



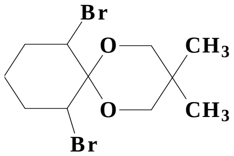


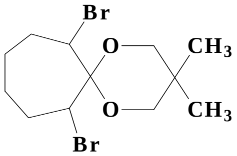
R = R$_1$ = R$_2$ = H **D$_{51}$**
R = CH$_3$, R$_1$ = R$_2$ = COOC$_2$H$_5$ **D$_{52}$**
R = R$_1$ = R$_2$ = CH$_3$ **D$_{55}$**
R = R$_1$ = H, R$_2$ = CH$_3$ **D$_{64}$**

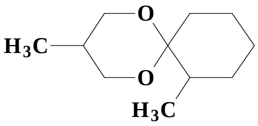
R = R$_1$ = H, R$_2$ = *t*-C$_4$H$_9$- **D$_{57}$**
R = CH$_3$, R$_1$ = R$_2$ = H **D$_{59}$**
R = R$_1$ = H, R$_2$ = CH$_3$ **D$_{61}$**
R = R$_1$ = R$_2$ = H **D$_{67}$**
R = R$_1$ = CH$_3$, R$_2$ = H **D$_{68}$**

D$_{20}$ **D$_{29}$**
R = C$_6$H$_5$-, R$_1$ = R$_2$ = COOC$_2$H$_5$ **D$_{19}$**
R = *t*-C$_4$H$_9$-, R$_1$ = R$_2$ = COOC$_2$H$_5$ **D$_{22}$**

D$_{62}$
R = R$_1$ = COOC$_2$H$_5$ **D$_{17}$**
R = CH$_3$, R$_1$ = C$_2$H$_5$ **D$_{25}$**







R = CH$_3$, R$_1$ = CH$_3$, R$_2$ = C$_2$H$_5$ **D$_{70}$**
R = *t*-C$_4$H$_9$-, R$_1$ = H, R$_2$ = CH$_3$ **D$_{36}$**
R = CH$_3$, R$_1$ = R$_2$ = COOCH$_3$ **D$_{35}$**

R = H, R$_1$ = CH$_3$ **D$_{32}$**
R = R$_1$ = H **D$_{33}$**
R = R$_1$ = C$_6$H$_5$ **D$_{46}$**

Figure 1. The structures of studied dioxanes and spirans (continuation).

R = C$_6$H$_5$-, R$_1$ = R$_2$ = CH$_3$ **D$_{42}$**
R = C$_2$H$_5$-, R$_1$ = R$_2$ = COOC$_2$H$_5$ **D$_{50}$**
R = H-, R$_1$ = R$_2$ = COOC$_2$H$_5$ **D$_{54}$**

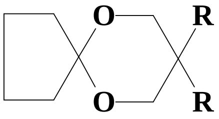
R = CH$_3$, R$_1$ = R$_2$ = H **D$_{58}$**

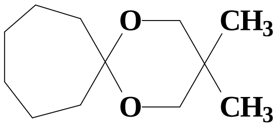
$R = CH_3$, $R_1 = CH_3$, $R_2 = H$ **D_{63}**
$R = t\text{-}C_4H_9\text{-}$, $R_1 = R_2 = H$ **D_{65}**
$R = H$, $R_1 = CH_3$, $R_2 = C_2H_5$ **D_{66}**
$R = H$, $R_1 = CH_3$, $R_2 = H$ **D_{69}**

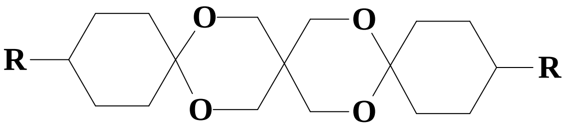
$R = COOC_2H_5$ **D_{53}** **D_{71}**
$R = CH_3$ **D_{60}**

$R = C_2H_5$ **D_{16}**
$R = C_6H_5$ **D_{30}**
$R = t\text{-}C_4H_9$ **D_{31}**
$R = CH_3$ **D_{43}**
$R = H$ **D_{49}**
D_{39}

Figure 1. The structures of the studied dioxanes and spirans (continuation).







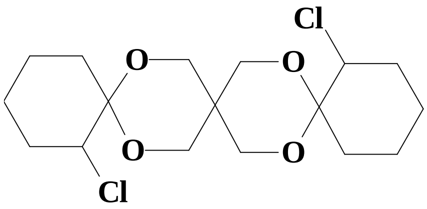


Table 1.

The dependence of R_M values on the acetone molar fraction, X, in the binary mobile phase, acetone-water. The corresponding concentrations are 70/30, 75/25, 80/20, 85/15, 90/10 (v/v). R_{Mw} is the extrapolated value to 100% water as eluent, a_1 is the slope of equation (1), r is the correlation coefficient for 95% confidence limits.

Compound	R_M X/(1-X)					$R_M = R_{Mw} + a_1 X$		
	0.364/0.636	0.424/0.576	0.495/0.505	0.582/0.418	0.688/0.312	R_{Mw}	a_1	r
D1	0.309	0.070	-0.131	-0.257	-0.676	1.319	-2.851	0.989
D2	0.313	0.068	-0.138	-0.265	-0.621	1.258	-2.716	0.990
D3	0.368	0.121	-0.105	-0.246	-0.572	1.324	-2.763	0.991
D4	0.532	0.252	-0.084	-0.261	-0.635	1.744	-3.492	0.991
D5	0.389	0.089	-0.057	-0.203	-0.578	1.331	-2.749	0.985
D6	0.115	0.005	-0.205	-0.445	-0.730	1.109	-2.665	0.998
D7	0.886	0.658	0.345	0.033	-0.304	2.216	-3.705	0.998
D8	0.692	0.508	0.218	-0.068	-0.443	1.984	-3.530	0.999
D9	0.999	0.399	0.333	0.038	-0.317	2.152	-3.648	0.960
D10	0.841	0.515	0.112	-0.126	-0.489	1.160	-2.251	0.790
D11	0.717	0.470	0.160	-0.119	-0.395	1.927	-3.448	0.994
D12	0.387	0.140	-0.075	-0.327	-0.573	1.406	-2.928	0.995
D13	0.607	0.372	0.047	-0.203	-0.503	1.815	-3.429	0.994
D14	0.660	0.403	0.147	-0.165	-0.387	1.715	-3.257	0.992
D15	0.466	0.160	-0.057	-0.229	-0.557	1.481	-2.985	0.989
D16	1.592	1.235	1.061	0.736	0.061	3.214	-4.460	0.988
D17	0.767	0.484	0.192	-0.029	-0.434	2.030	-3.593	0.996
D18	1.032	0.624	0.304	-0.158	-0.480	2.643	-4.658	0.991
D19	0.658	0.372	0.077	-0.080	-0.432	1.766	-3.225	0.989
D20	0.921	0.621	0.391	0.242	-0.389	2.271	-3.748	0.982
D21	0.849	0.550	0.261	0.071	-0.430	2.180	-3.759	0.993
D22	1.005	0.670	0.472	0.296	-0.235	2.252	-3.545	0.987
D23	1.005	0.586	0.276	0.036	-0.360	2.355	-4.007	0.987
D25	0.865	0.575	0.419	0.209	-0.239	2.000	-3.201	0.991
D26	0.463	0.183	-0.098	-0.244	-0.682	1.636	-3.352	0.991
D27	0.261	0.082	-0.115	-0.225	-0.535	1.093	-2.348	0.993
D28	0.042	-0.158	-0.382	-0.441	-0.723	0.802	-2.222	0.981
D29	1.195	0.630	0.209	-0.085	-0.443	2.766	-4.827	0.973
D30	1.317	0.849	0.530	0.254	-0.162	2.773	-4.338	0.986
D31	1.798	1.541	1.369	0.931	0.583	3.173	-3.776	0.996
D32	0.319	0.108	0.016	-0.077	-0.515	1.159	-2.328	0.968
D33	-0.142	-0.202	-0.294	-0.358	-0.673	0.458	-1.551	0.961
D35	0.406	0.169	0.070	-0.064	-0.555	1.388	-2.709	0.973
D36	0.912	0.632	0.484	0.286	-0.163	2.017	-3.107	0.990
D37	-0.115	-0.254	-0.393	-0.427	-0.723	0.500	-1.729	0.977
D38	0.707	0.428	0.163	-0.022	-0.370	1.814	-3.198	0.993
D39	0.720	0.463	0.089	-0.180	-0.499	2.046	-3.775	0.993
D40	0.510	0.257	0.033	-0.117	-0.459	1.498	-2.847	0.992
D42	0.778	0.575	0.288	0.045	-0.271	1.937	-3.240	0.998
D43	1.180	0.785	0.583	0.335	-0.105	2.455	-3.720	0.990
D44	0.979	0.743	0.358	0.056	-0.294	2.398	-3.976	0.995
D45	0.575	0.436	0.149	-0.089	-0.374	1.669	-2.995	0.997
D47	0.016	-0.129	-0.552	-1.005	-1.015	1.282	-3.562	0.953

Compound	R_M X/(1-X)					$R_M = R_{Mw} + a_1 X$		
	0.364/0.636	0.424/0.576	0.495/0.505	0.582/0.418	0.688/0.312	R_{Mw}	a_1	r
D48	1.067	0.727	0.282	-0.064	-0.417	2.665	-4.594	0.991
D49	0.810	0.515	0.383	0.182	-0.252	1.887	-3.055	0.989
D50	0.849	0.523	0.374	0.181	-0.341	2.049	-3.391	0.985
D51	0.432	0.237	0.181	0.036	-0.343	1.221	-2.183	0.975
D52	0.837	0.583	0.412	0.171	-0.313	2.069	-3.388	0.993
D53	0.389	0.140	0.043	-0.091	-0.555	1.341	-2.656	0.995
D54	0.542	0.304	0.192	0.017	-0.461	1.588	-2.877	0.982
D55	1.091	0.796	0.650	0.376	-0.045	2.282	-3.345	0.994
D56	0.242	0.047	0.009	-0.149	-0.661	1.198	-2.547	0.955
D57	0.949	0.727	0.550	0.323	-0.092	2.074	-3.099	0.996
D58	0.423	0.269	0.162	0.014	-0.356	1.266	-2.279	0.985
D59	0.969	0.736	0.552	0.378	-0.017	2.001	-2.894	0.994
D60	0.430	0.271	0.178	-0.017	-0.358	1.296	-2.340	0.990
D61	0.468	0.341	0.174	-0.029	-0.189	1.212	-2.074	0.996
D62	0.397	0.261	0.145	-0.078	-0.207	1.076	-1.905	0.993
D63	0.450	0.252	0.176	-0.052	-0.218	1.153	-2.020	0.991
D64	0.452	0.294	0.180	-0.061	-0.216	1.194	-2.085	0.994
D65	0.679	0.430	0.317	0.040	-0.143	1.539	-2.496	0.990
D66	0.661	0.447	0.319	0.054	-0.153	1.537	-2.490	0.995
D67	0.532	0.137	0.292	0.031	-0.302	1.269	-2.215	0.917
D69	0.327	0.137	0.050	-0.182	-0.302	0.993	-1.932	0.987
D70	0.841	0.583	0.425	0.145	-0.056	1.784	-2.735	0.992
D71	0.621	0.395	0.305	0.010	-0.146	1.441	-2.358	0.986

Table 2.

The dependence of R_M values on the methanol molar fraction, X, in the binary mobile phase, methanol-water. The corresponding concentrations are 70/30, 75/25, 80/20, 85/15, 90/10 (v/v). R_{Mw} is the extrapolated value to 100% water as eluent, a_1 is the slope of equation (1), r is the correlation coefficient for 95% confidence limits.

Compound	R_M X/(1-X)					$R_M = R_{Mw} + a_1 X$		
	0.800/0.200	0.716/0.284	0.640/0.360	0.572/0.428	0.509/0.491	R_{Mw}	a_1	r
D1	-0.386	0.008	0.194	0.442	0.665	2.451	-3.501	0.996
D2	-0.351	0.017	0.159	0.442	0.620	2.291	-3.266	0.994
D3	-0.325	0.028	0.192	0.480	0.717	2.477	-3.489	0.996
D4	-0.146	0.221	0.530	0.870	1.120	3.354	-4.380	0.999
D5	-0.105	0.150	0.281	0.591	0.826	2.389	-3.152	0.990
D6	-0.392	-0.035	0.086	0.299	0.571	2.119	-3.109	0.990
D7	-0.461	-0.219	0.841	1.247	1.753	5.874	-8.097	0.982
D9	0.259	0.945	1.127	1.605	2.102	5.075	-5.973	0.988
D11	0.135	0.709	0.888	1.415	1.720	4.426	-5.333	0.991
D12	-0.186	0.266	0.523	0.787	1.073	3.208	-4.195	0.997
D13	-0.089	0.397	0.593	1.044	1.392	3.876	-4.956	0.993
D15	-0.194	0.122	0.203	0.498	0.651	2.097	-2.843	0.988
D16	0.765	1.303	1.418	1.845	2.115	4.380	-4.466	0.987
D17	-0.506	-0.300	-0.050	0.331	0.641	2.607	-3.991	0.986
D18	-0.176	0.583	0.711	1.313	1.655	4.736	-6.054	0.984

Compound	R_M X/(1-X)					$R_M = R_{Mw} + a_1 X$		
	0.800/0.200	0.716/0.284	0.640/0.360	0.572/0.428	0.509/0.491	R_{Mw}	a_1	r
D19	0.017	0.462	0.633	1.110	1.135	3.446	-4.255	0.987
D20	0.549	1.242	1.626	1.814	2.010	4.606	-4.879	0.972
D21	0.052	0.500	0.659	1.127	1.249	3.416	-4.169	0.987
D22	0.287	0.635	0.940	1.224	1.643	3.875	-4.524	0.995
D25	0.293	0.590	0.738	0.997	1.332	2.991	-3.340	0.988
D26	-0.410	0.014	0.215	0.738	0.894	3.259	-4.587	0.989
D27	-0.347	-0.021	0.145	0.360	0.464	1.917	-2.776	0.992
D28	-0.788	-0.413	-0.296	-0.010	0.136	1.739	-3.110	0.990
D29	0.143	0.655	0.965	1.311	1.580	4.088	-4.876	0.997
D30	0.602	1.058	1.422	1.780	2.110	4.727	-5.149	0.999
D31	1.016	1.556	1.826	2.217	2.551	5.162	-5.142	0.997
D32	-0.045	0.129	0.134	0.394	0.544	1.504	-1.967	0.963
D33	-0.261	-0.124	-0.053	0.103	0.180	0.956	-1.524	0.993
D35	-0.133	0.134	0.241	0.502	0.856	2.391	-3.199	0.976
D36	0.334	0.671	0.961	0.997	1.332	2.935	-3.207	0.982
D37	-0.501	-0.218	-0.137	0.249	0.350	1.878	-2.980	0.980
D38	-0.017	0.408	0.615	1.025	1.263	3.489	-4.372	0.995
D40	-0.176	0.174	0.366	0.826	0.976	3.065	-4.065	0.990
D42	0.179	0.561	0.747	1.140	1.423	3.535	-4.209	0.994
D43	0.443	0.776	1.055	1.326	1.643	3.672	-4.053	0.998
D44	0.242	0.739	0.952	1.710	1.835	4.796	-5.716	0.980
D45	-0.270	0.085	0.155	0.423	0.581	2.017	-2.814	0.986
D47	0.097	0.619	0.799	1.580	1.653	4.579	-5.607	0.974
D48	0.318	0.727	0.895	1.505	1.886	4.527	-5.340	0.982
D49	0.258	0.535	0.710	0.961	1.230	2.843	-3.250	0.995
D50	0.148	0.461	0.705	0.961	1.332	3.265	-3.929	0.994
D51	0.008	0.240	0.297	0.526	0.639	1.720	-2.129	0.987
D52	0.158	0.486	0.705	0.982	1.332	3.256	-3.898	0.994
D53	-0.201	0.046	0.123	0.422	0.608	1.967	-2.730	0.985
D54	-0.052	0.227	0.326	0.645	0.903	2.471	-3.184	0.985
D55	0.394	0.695	0.817	1.224	1.643	3.622	-4.121	0.974
D56	0.456	0.704	0.887	1.247	1.643	3.559	-3.973	0.979
D57	0.389	0.695	0.940	1.272	1.643	3.720	-4.221	0.992
D58	0.072	0.240	0.450	0.998	1.332	3.501	-4.452	0.966
D59	-0.524	0.070	0.316	0.572	1.332	4.086	-5.766	0.973
D60	-0.454	0.112	0.235	0.572	1.332	3.919	-5.499	0.961
D61	0.021	0.375	0.713	0.751	0.851	2.387	-2.850	0.958
D62	0.021	0.375	0.713	0.751	0.851	2.387	-2.850	0.958
D63	0.021	0.375	0.713	0.751	0.851	2.387	-2.850	0.958
D64	0.023	0.268	0.491	0.680	0.877	2.358	-2.919	0.999
D65	0.211	0.607	0.825	1.089	1.182	2.961	-3.365	0.989
D66	-0.096	0.607	0.693	0.974	1.097	3.144	-3.846	0.951
D67	-0.065	0.243	0.385	0.518	0.691	1.955	-2.473	0.991
D68	0.429	0.807	0.947	1.237	1.440	3.160	-3.380	0.993
D69	-0.060	0.398	0.478	0.587	0.851	2.255	-2.788	0.963
D70	0.248	0.653	0.720	1.040	1.415	3.226	-3.724	0.977
D71	0.103	0.510	0.677	1.097	1.415	3.611	-4.403	0.991

Table 3.

The CLogP values for the studied dioxanes and spirans.

Compound	CLogP	Compound	CLogP	Compound	ClogP	Compound	CLogP
D1	2.576	D20	3.256	D39	2.147	D58	2.091
D2	2.496	D21	4.688	D40	3.690	D59	3.129
D3	2.576	D22	4.626	D41	1.099	D60	2.051
D4	3.474	D23	3.313	D42	4.018	D61	2.610
D5	3.352	D24	5.929	D43	2.819	D62	2.610
D6	2.294	D25	2.924	D44	3.827	D63	2.610
D7	3.421	D26	3.524	D45	4.085	D64	2.610
D8	2.529	D27	2.592	D46	2.606	D65	3.418
D9	5.929	D28	1.358	D47	-0.757	D66	3.139
D10	1.745	D29	3.815	D48	4.179	D67	2.091
D11	4.663	D30	4.597	D49	1.781	D68	3.129
D12	3.555	D31	5.473	D50	3.828	D69	2.091
D13	4.391	D32	0.828	D51	2.091	D70	3.658
D14	0.687	D33	-0.210	D52	4.337	D71	3.169
D15	2.383	D34	4.188	D53	2.221		
D16	3.877	D35	2.241	D54	2.780		
D17	2.206	D36	3.937	D55	4.167		
D18	4.738	D37	3.106	D56	2.066		
D19	4.188	D38	4.527	D57	3.937		

The relationship between the R_{Mw} values obtained in acetone-water system and the calculated CLogP values is shown in equation 2:

$$R_{Mw}(X) = 0.801(\pm 0.286) + 0.298(\pm 0.085)\ \mathrm{CLogP} \qquad (2)$$

$$s = 0.441,\ F = 49,\ r = 0.653,\ n = 68$$

where s is the fit standard error, F is the statistic parameter for F test, n is the number of compounds and r is the correlation coefficient for 95% confidence limits.

In order to improve the linearity of equation 2, only the compounds, which have two dioxanic cycles, were included in equation 3.

$$R_{Mw}(X) = 1.044(\pm 0.325) + 0.390(\pm 0.113)\ \mathrm{CLogP} \qquad (3)$$

$$s = 0.352,\ F = 53,\ r = 0.878,\ n = 18$$

The similar correlations with equations 2 and 3 but for methanol-water as eluent are shown in equations 4 and 5. Equation 4 takes into account all the compounds and equation 5 only the compounds with two dioxanic cycles in the structures, except D7 and D47, which were eliminated as outliers.

$$R_{Mw}(X) = 1.605(\pm 0.588) + 0.507(\pm 0.171)\ \mathrm{CLogP} \qquad (4)$$

$$s = 0.846,\ F = 35,\ r = 0.601,\ n = 64$$

$$R_{Mw}(X) = 0.981(\pm 0.626) + 0.818(\pm 0.196)\ \mathrm{CLogP} \qquad (5)$$

$$s = 0.452,\ F = 89,\ r = 0.953,\ n = 11$$

In literature, the R_{Mw} values are arbitrarily correlated with X, the molar fraction of organic modifier in the mobile phase, or φ, the same concentration, but expressed as volumetric percent. No improvement in the linearity of relationships 2 and 3 was found by replacing X with φ. No significant rules were found between the R_{Mw} values obtained for acetone-water and methanol-water as mobile phase. Theoretically, these data should have the same value. This fact was observed in the literature and was attributed to the role of organic modifier in the compound partition between the stationary and the mobile phase and to secondary interactions.

REFERENCES

1. T. Fujita, J. Iwasa, C. Hansch, *J. Am. Chem. Soc*., 1964, **86,** 5175.
2. C. Hansch, S. M. Anderson, *J. Org. Chem*., 1967, **32,** 2583.
3. R. N. Smith, C. Hansch, M. A. Ames, *J. Pharm. Sci*., 1975, **64,** 65.
4. Th. Braumann, *J. Chromatogr*., 1986, **373,** 1981.
5. L. G. Danielson, Yu-Hui Zhang, *Trends Anal. Chem*., 1996, **15,** 188.
6. R. Kaliszan, *Anal. Chem*., 1992, **64,** 619A.
7. R. J. E. Grouls, E. W. Ackerman, H. H. M. Korsten, D. D. Breimer, *J. Chromatogr. B*, 1997, **694,** 421.
8. K. P. Dross, R. Mannhold, R. F. Rekker, *Quant. Struct.-Act. Relat*., 1992, **11,** 36.
9. K. Dross, C. Sonntag, R. Mannhold, *J. Chromatogr. A*, 1994, **673,** 113.
10. A. J. P. Martin, R. L. M. Synge, *Biochem. J*., 1941, **35,** 1358.
11. R. Consden, A. H. Gordon, A. J. P. Martin, *Biochem. J*., 1944, **38**, 224.
12. E. C. Bate-Smith, R. G. Westall, *Biochim. Biophys. Acta*, 1950, **4**, 427.
13. C. B. C. Boyce, B. V. Milborrow, *Nature*, 1965, **208**, 537.
14. G. L. Biagi, A. M. Barbaro, A. Sapone, M. Recanatini, *J. Chromatogr. A*, 1994, **662**, 341.
15. G. L. Biagi, A. M. Barbaro, A. Sapone, M. Recanatini, *J. Chromatogr. A*, 1994, **669**, 246.
16. G. L. Biagi, A. M. Barbaro, M. Recanatini, *J. Chromatogr. A*, 1994, **678**, 127.
17. S. Gocan, Gabriela Cimpan, I. Fromondi, I. Grosu, *Proceedings of the Conference of Chemistry and Chemical Engineering*, Bucharest, 1995, 433.
18. S. Mager, M. Horn, I. Grosu, M. Bogdan, *Monatsh. Chem*., 1989, **120**, 735.
19. I. Grosu, S. Mager, G. Plé, M. Horn, *J. Chem. Soc. Chem. Commun*., 1995, 167.
20. I. Grosu, G. Plé, S. Mager, *Tetrahedron*, 1995, **52**, 2659.
21. I. Grosu, S. Mager, G. Plé, *J. Chem. Soc. Perkin Trans. 2*, 1995, 1351.
22. I. Grosu, S. Mager, G. Plé, R. Martinez, M. Horn, R. R. Gavino, *Monasth. Chem*., 1995, **126**, 1021.
23. I. Grosu, S. Mager, G. Plé, E. Mesaros, *Tetrahedron*, 1996, **52**, 12783.
24. I. Grosu, S. Mager, G. Plé, L. Muntean, I. Schirger, *Heterocyclic Communications*, 1996, **2**, 423.
25. I. Grosu, B. C. Camacho, A. Toscano, G. Plé, S. Mager, R. Martinez, R. R. Gavino, *J. Chem. Soc. Perkin Trans. 1*, 1997, 775.
26. I. Grosu, G. Plé, S. Mager, R. Martinez, C. Mesaros, B. C. Camacho, *Tetrahedron*, 1997, **53**, 6215.
27. S. Mager, I. Grosu, M. Horn, I. Hopârtean, M. Darabantu, C. Puscas, D. Kovacs, G. Plé, *Romanian Quatery Reviews*, 1995, **3**, 221.
28. S. Mager, I. Hopârtean, M. Horn, I. Grosu, *Studia Univ. "Babes-Bolyai", Chemia*, 1979, **24**, 32.
29. S. Mager, I. Grosu, *Studia Univ. "Babes-Bolyai", Chemia*, 1988, **33**, 47.