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MICROCOMPUTER-AIDED CHARACTERIZATION OF MOBILE PHASES FOR NORMAL-PHASE LIQUID–SOLID CHROMATOGRAPHY BASED ON SNYDER'S THEORY AND DATA

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SUMMARY

A microcomputer program of practical importance is described that permits the characterization of any mobile phase for normal-phase separations on silica or alumina by means of Snyder's parameters solvent strength, ε, localization, m, and polarity, P'. The calculations follow the guidelines proposed by Snyder. In addition, an algorithm is developed that permits the choice of mobile phases of equal strength, the so-called equi-eluotropic mobile phases.

The microcomputer program was tested against approximately 250 mobile phases which were characterized by values of the above three parameters. Good agreement was found with the calculated or experimental values of either ε and m reported earlier by Snyder and co-workers for some of the mobile phases. Some of the computer-calculated ε values are presented in an easy-to-use nomograph form.

INTRODUCTION

The application of Snyder's theory[1–3] for the treatment of the thin-layer chromatographic (TLC) behaviour of numerous diastereoisomers[4–6] convinced us that this theory is very useful for the characterization of mobile phases. Solvent strength and selectivity effects of the latter in normal-phase separations can be described in terms of certain parameters introduced by Snyder. These parameters are derived from the displacement model for normal-phase retention. The parameter ε is a direct measure of solvent strength. Overall changes in sample retention as a function of mobile phase composition can be predicted if values of ε for various mobile phases are known. Likewise, a second parameter, localization, m, is useful for characterizing the selectivity effects of various mobile phases.

The polarity P' is a third parameter of interest, derived by Snyder[7,8] on the basis of a given solubility parameter[9]. Solvent strength in normal-phase separations seems to be better understood by both ε and P' as discussed at the end of this paper. The P' value of any mobile phase is obtained in a simple manner[7,8].

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Procedures for obtaining values of ε and m for different mobile phases and either alumina and silica as adsorbent have been described by Snyder and co-workers[1–3,5,10–13]. However, the associated calculations are tedious[14], which accounts for the fact that the useful Snyder theory is rarely used in every-day chromatographic practice. We undertook this study for several reasons. First, because of the relative complexity of the calculations, it seemed worthwhile to verify independently the originally reported values of ε and m in another laboratory. Second, a considerable number of experimental ε values have been reported in the literature[3,5,6,10–13], and it seemed appropriate to compare these data with values calculated by the present program. Finally, many workers would like to see the results of such calculations expressed as an expanded eluotropic series for silica or alumina. One such example has appeared[14], but it is based on older calculation procedures that are less accurate, and does not include many solvents that are now more popular for either high-performance liquid chromatographic (HPLC) or TLC separations.

THEORY

The calculations of solvent strength, ε, localization, m, and polarity, P', follow the guidelines proposed by Snyder and co-workers[1–3,5,10–13], but are described here in sufficient detail to allow other workers to write similar programs.

Calculation of mobile phase strength, ε

Solvent strength values for pure solvents commonly used in liquid–solid chromatography (LSC) and other characteristics are given in Table I in ref. 3. According to the developed displacement model[3,5,10–13], the calculation of ε values for mobile phases containing 2–z solvents includes the steps described below.

(1) Calculation of molar fraction, N_i, for each solvent of the mobile phase on the basis of its volume percentage P_i using the following equation:

$$N_i = (d_iP_i/\mathrm{MW}_i)/\sum_{i=1}^{z}(d_iP_i/\mathrm{MW}_i) \quad (1)$$

where d_i is the density of solvent i and MW_i is its molecular weight. Let us arbitrarily assume that i corresponds to the solvent number when the solvents of the mobile phase are arranged in increasing order of their individual ε values with the first and last solvents having i = 1 and z, respectively.

(2) Calculation of the "mean" area $\bar{n}$ which the solvents of the mobile phase occupy on the adsorbent surface is based on the equation

$$\bar{n} = \sum_{i=2}^{z}(N_in_i)/(1 - N_1) \quad (2)$$

where n_i is the molecular area of the solvent i, denoted by n^b in Table I in ref. 3. The value obtained is further specified in (8) because two equations are proposed for calculation of $\bar{n}$ (see ref. 3, p. 217).

(3) Calculation of R_i, *i.e.*, the ratio of the molar fractions of solvent i and the preceding solvent $i-1$:

$$R_i = N_i/N_{i-1} \quad (3)$$

(4) Values of the parameters ε'_i and ε''_i are necessary for the following calculations. The two parameters correspond to strength ε_i of the solvent i when its molar fraction N_i in the mobile phase approaches 0 or 1, respectively. ε''_i values are included in Table I in ref. 3 together with ε'_i values which are valid if the first solvent has $\varepsilon''_1 = 0$. In contrast, ε'_i values are calculated by means of the following equation:

$$\varepsilon'_i = \varepsilon'_{i(\mathrm{Table})} - [f_i(C)/n_i]\varepsilon''_1 \tag{4}$$

where $\varepsilon'_{i(\mathrm{Table})}$ is the ε' of solvent i given in Table I in ref. 3 and $f_i(C)/n_i$ is a parameter whose values are included in the same table. The calculation of ε' should ensure a value that is not lower than the corresponding ε''_i value of the same solvent.

(5) The strength ε_i of solvent i in the mobile phase is calculated according to the equation

$$\varepsilon_i = \varepsilon''_i + \%_{\mathrm{lc}(i)}(\varepsilon'_i - \varepsilon''_i) \tag{5}$$

The parameter $\%_{\mathrm{lc}}$ is a measure of the localization of solvent i on the adsorbent surface and is arbitrarily assumed to be 50% at the beginning of an iterative procedure.

(6) The equilibrium constant K for adsorption of the solvent i with desorption of the preceding solvent $i-1$ is calculated using the following equation:

$$K_i = 10^{\alpha'/\bar{n}(\varepsilon_i - \varepsilon_{i-1})} \tag{6}$$

where α' is an adsorbent activity function which is usually equal to 0.57 for silica and 0.65 for alumina.

(7) The molar fraction in the adsorbed phase of the first solvent θ_1 and the following solvents up to the last one, θ_z, are obtained on the basis of the following equations:

$$\theta_1 = 1/\{1 + R_2K_2[1 + \ldots R_{z-1}K_{z-1}(1 + R_zK_z)]\} \tag{7}$$

$$\vdots$$

$$\theta_z = \theta_{z-1}R_zK_z \tag{8}$$

(8) Specification of parameter $\bar{n}$ is done on the basis of the following equation:

$$\bar{n} = \sum_{i=2}^{z} (\theta_i n_i)/(1 - \theta_i) \tag{9}$$

(9) The parameter $\%_{\mathrm{lc}(i)}$ is then calculated:

$$\%_{\mathrm{lc}(i)} = (1 - \theta_i)[1/(1 - 0.94\theta_i) - 14.5\theta_i^9] \tag{10}$$

If the value of this parameter is not equal to 50% as assumed at the beginning, then the arithmetic mean of the two values is taken and the calculations return to entry 5. This iteration continues until the input value of $\%_{1c}$ in entry 5 becomes equal to its output value in entry 9. The current value of θ_i is then registered.

The final value of strength ε of the mobile phase, denoted originally by ε^0, is calculated by means of the following equation:

$$\varepsilon = \varepsilon_1 + \log(N_1/\theta_1)/\alpha'\bar{n} \tag{11}$$

Calculation of localization, m

The calculations are performed according to the equation

$$m = \sum_{i=2}^{z} \left\{ m_i \left[\mathrm{f} \sum_{j=1}^{z} (\theta_j) - \mathrm{f} \sum_{k=i+1}^{z} (\theta_k) \right] \right\} \tag{12}$$

where the localization parameters of any solvent i and the last solvent z are denoted by m_i and m_z, respectively. The values of the localization function $\mathrm{f}(\theta)$ are obtained on the basis of the corresponding θ values using the plot in Fig. 5 in ref. 13.

Calculation of polarity, P′

The polarity parameter, P', of a given mobile phase is calculated by means of volume percentage P_i of each solvent and its own polarity P'_i value:

$$P' = \sum_{i=1}^{z} P_i P'_i \tag{13}$$

The values do not depend on the adsorbent used.

EXPERIMENTAL

A Pravetz-16 microcomputer compatible with an IBM-PC and having a memory of 256 kbytes is used. The microcomputer program is written in Turbo Pascal and registered elsewhere[15].

RESULTS AND DISCUSSION

Description of the microcomputer program

The microcomputer program has three main modes:

(1) organization of a file containing the basic literature data necessary for the calculations;

(2) characterization of mobile phases by values of ε, m and P'; and

(3) choice of equi-eluotropic mobile phases of any desired ε value.

Each mode is described below.

The first mode permits the organization of a file containing the characteristics of pure solvents, namely density d, molecular weight MW, polarity P', molecular area n, solvent strength ε' and ε'', the parameter $f_1(C)/n$ and localization m^0. Such a file was made for 28 pure solvents as the data are taken from Table 6-1 in ref. 2 and Table I in ref. 3, replacing some of them by more recent values in ref. 6. The values of the latter four parameters are different for silica and alumina whose α' values are 0.57 and 0.65,

TABLE I

VALUES OF THE SOLVENT LOCALIZATION FUNCTION f(θ_i) *VS.* THE FRACTIONAL COVERAGE θ_i OF THE ADSORBENT SURFACE BY THE LOCALIZING SOLVENT (FROM FIG. 5 IN REF. 13)

θ_i	$f(\theta_i)$	θ_i	$f(\theta_i)$	θ_i	$f(\theta_i)$	θ_i	$f(\theta_i)$	θ_i	$f(\theta_i)$
0.00	0.000								
0.01	0.005	0.21	0.118	0.41	0.338	0.61	0.700	0.81	0.930
0.02	0.008	0.22	0.128	0.42	0.350	0.62	0.710	0.82	0.940
0.03	0.011	0.23	0.132	0.43	0.362	0.63	0.730	0.83	0.945
0.04	0.016	0.24	0.142	0.44	0.380	0.64	0.748	0.84	0.948
0.05	0.020	0.25	0.150	0.45	0.395	0.65	0.760	0.85	0.952
0.06	0.025	0.26	0.162	0.46	0.410	0.66	0.780	0.86	0.960
0.07	0.030	0.27	0.170	0.47	0.420	0.67	0.793	0.87	0.965
0.08	0.035	0.28	0.180	0.48	0.440	0.68	0.805	0.88	0.968
0.09	0.038	0.29	0.190	0.49	0.470	0.69	0.820	0.89	0.970
0.10	0.040	0.30	0.200	0.50	0.478	0.70	0.830	0.90	0.975
0.11	0.048	0.31	0.210	0.51	0.495	0.71	0.840	0.91	0.980
0.12	0.052	0.32	0.220	0.52	0.510	0.72	0.850	0.92	0.982
0.13	0.060	0.33	0.235	0.53	0.530	0.73	0.860	0.93	0.985
0.14	0.068	0.34	0.248	0.54	0.550	0.74	0.870	0.94	0.988
0.15	0.072	0.35	0.260	0.55	0.560	0.75	0.880	0.95	0.990
0.16	0.080	0.36	0.270	0.56	0.580	0.76	0.890	0.96	0.992
0.17	0.088	0.37	0.280	0.57	0.600	0.77	0.900	0.97	0.994
0.18	0.095	0.38	0.295	0.58	0.620	0.78	0.910	0.98	0.996
0.19	0.102	0.39	0.308	0.59	0.650	0.79	0.920	0.99	0.998
0.20	0.110	0.40	0.320	0.60	0.680	0.80	0.925	1.00	1.000

respectively. The file also contains the data necessary for calculating the function $f(\theta_i)$ on the basis of the molar fraction in the adsorbed phase θ_i. The data are read from the plot in Fig. 5 in ref. 13 and are presented in Table I. The file is automatically used by the computer during the two calculation modes.

Choosing the second mode, the user inputs the adsorbent and the mobile phase of interest, specifying its solvents and their volume percentages. The computer calculates and prints out the values of the solvent strength, ε, localization, m, and polarity, P', using the algorithm described under Theory.

When the third mode of the program is activated, the user inputs the adsorbent, the solvents of the mobile phases and the desired ε value. The computer calculates and prints out a set of mobile phases composed of the input solvents and the corresponding percentages in which they should be mixed in order to ensure the input ε value. The algorithm used to this end is described below.

(1) To start the calculations, given values of the volume percentage P_i of each solvent are automatically input by computer. A ratio of 50:50 is arbitrarily used for mobile phases composed of two solvents. For the case of more than two solvents, the input value for the first solvent P_1, the last solvent P_z and any other solvent P_i is calculated on the basis of the following equations:

$$P_1 = P_z = (100 - A)/2 \qquad (14)$$

$$P_i = A/(Z - 2) \qquad (15)$$

where A is a variable parameter equal to 10 at the beginning and Z is the total number of the solvents of the mobile phase. Alternatively, the possibility is given for the user to change the automatically input values of P_i according to his or her own requirements.

(2) Current values of the mobile phase strength, $\varepsilon_{\text{current}}$, and percentages of the solvents, $P_{i(\text{current})}$, are obtained on the basis of the algorithm described under Theory.

(3) The difference between the input value and the current value of the solvent strength ε is found:

$$D = \varepsilon_{\text{input}} - \varepsilon_{\text{current}} \tag{16}$$

(4) If the value of D differs from zero, then the percentages of the first and the last solvents only are changed. As the last solvent is the strongest of all solvents of the mobile phase, it has the greatest effect on mobile phase strength, ε. It is assumed that ε is proportional to the percentage of the last solvent raised to the power of 1/5 because the plot of such a relationship has a steep part at the beginning followed by a part with small changes. To find the new percentage of the last solvent P_z which is necessary to continue the calculations, the following equations are written:

$$\varepsilon_{\text{current}} = kP_{z(\text{current})}{}^{1/5} \tag{17}$$

$$\varepsilon_{\text{input}} = kP_z{}^{1/5} \tag{18}$$

where k is a constant.

The ratio between these two equations leads to the following equation:

$$P_z = P_{z(\text{current})}\left(\varepsilon_{\text{input}}/\varepsilon_{\text{current}}\right)^5 \tag{19}$$

Then the percentage of the first solvent P_1 is found from the equation

$$P_1 = P_{1(\text{current})} + [P_{z(\text{current})} - P_z] \tag{20}$$

(5) Using the values of P_1 and P_z found without any change in the percentages of the remaining solvents, the calculations return to entry 2. The iterative procedure from entry 2 to entry 4 continues until the difference D becomes equal to zero, which means that the input ε value is obtained. Then the current percentage of each solvent in which we are interested is printed out, together with the values of localization, m, and polarity, P', calculated by means of eqns. 12 and 13, respectively.

The calculations in the third mode of the microcomputer program continue further with repeated increases of 10 in the value of the variable parameter A, which leads to a set of mobile phases composed of the solvents initially specified by the user but with different proportions. However, all mobile phases of this set have the input strength $\varepsilon_{\text{input}}$.

Application of the microcomputer program

The microcomputer program was applied to calculate the values of ε, m and P' of approximately 250 mobile phases, 92 of which had already been characterized by Snyder and co-workers[3,11–13] by their calculated and experimental ε or m values. The

TABLE II

COMPUTER ε, m AND P' VALUES OF MOBILE PHASES COMPOSED OF TWO TO THREE SOLVENTS: COMPARISON WITH LITERATURE $\varepsilon_{calc.}$ AND $\varepsilon_{exptl.}$ VALUES

No.	*Mobile phase*	*Proportions (%, v/v)*	*Computer values*			*Literature values*		
			m	P'	ε	$\varepsilon_{calc.}$	$\varepsilon_{exptl.}$	*Ref.*
Silica as adsorbent								
1	Hexane–diethyl ether	95.95:4.05	0.56	0.21	0.207	0.207	0.222	12, Table II
2		91.82:8.18	0.61	0.32	0.243	0.243	0.248	
3		83.3:16.7	0.63	0.55	0.277	0.277	0.279	
4		65.16:34.84	0.65	1.04	0.316	0.316	0.308	
5		34.82:65.18	0.66	1.86	0.378	0.379	0.358	
6	Benzene–diethyl ether	97.65:2.35	0.03	2.70	0.264	0.267	0.216	
7		77.26:22.74	0.37	2.72	0.348	0.358	0.351	
8		26.69:73.31	0.64	2.77	0.406	0.404	0.409	
9	Hexane–ethyl acetate	98.48:1.52	0.53	0.17	0.204	0.204	0.185	
10		84.12:15.88	0.59	0.78	0.302	0.302	0.318	
11		36.21:63.79	0.60	2.84	0.436	0.433	0.444	
12	Benzene–ethyl acetate	97.79:2.21	0.04	2.74	0.267	0.267	0.259	
13		78.31:21.69	0.44	3.07	0.362	0.361	0.356	
14	Hexane–acetone	98.86:1.14	0.79	0.16	0.215	0.242	0.238	
15		87.6:12.4	0.92	0.72	0.337	0.346	0.332	
16		43.08:56.92	0.95	2.95	0.475	0.475	0.477	
17	Benzene–acetone	98.33:1.67	0.08	2.74	0.281	0.292	0.300	
18		82.8:17.2	0.77	3.11	0.416	0.421	0.415	
19		64.35:35.65	0.88	3.56	0.458	0.476	0.463	
20	Hexane–dioxane	85.87:14.13	–	0.76	0.323	0.324	0.340	
21		39.44:60.56	–	2.95	0.471	0.471	0.477	
22	Benzene–dioxane	80.55:19.45	–	3.11	0.429	0.428	0.445	
23		30.74:69.26	–	4.16	0.474	0.473	0.498	
24	Benzene–acetonitrile	87.12:12.88	0.50	3.10	0.367	0.388	0.373	
25		42.01:57.99	1.02	4.50	0.475	0.477	0.488	
26	Hexane–isopropanol	72.3:27.7	–	1.15	0.459	0.477	0.458	
27	Hexane–methylene chloride	59.82:40.18	0.10	1.31	0.223	0.223	0.223	11, Table III
28	Hexane–methyl *tert.*-butyl ether	96.14:3.86	0.72	–	0.249	0.223	0.226	
29	Hexane–methylene chloride–methyl *tert.*-butyl ether	82.9:16.03:1.07	0.41	–	0.260	0.223	0.229	
Alumina as adsorbent								
30	Pentane–dioxane	90:10	–	0.48	0.388	0.383	0.372	3, Table V
31		50.05:49.95	–	2.40	0.549	0.547	0.549	
32	Pentane–pyridine	89.98:10.02	1.22	0.53	0.476	0.465	0.435	
33		75.01:24.99	1.22	1.32	0.572	0.566	0.565	
34	Pentane–benzene–methylene chloride	60:30:10	0.01	1.12	0.266	0.266	0.220	11, Table I
35		30:30:40	0.24	2.05	0.345	0.344	0.320	
36	Pentane–benzene–dioxane	60:38:2	–	1.12	0.366	0.365	0.350	
37		60:35:5	–	1.19	0.402	0.404	0.400	
38		60:30:10	–	1.29	0.429	0.431	0.440	
39	Pentane–methylene chloride–dioxane	60:38:2	–	1.27	0.382	0.382	0.390	
40		60:35:5	–	1.33	0.442	0.439	0.430	
41		60:30:10	–	1.41	0.472	0.472	0.470	
42		60:20:20	–	1.58	0.490	0.493	0.520	

TABLE III

COMPUTER ε, m AND P' VALUES OF MOBILE PHASES COMPOSED OF TWO TO FOUR SOLVENTS: COMPARISON WITH LITERATURE $m_{\text{calc.}}$ AND $m_{\text{exptl.}}$ VALUES

No.	*Mobile phase*	*Proportions (%, v/v)*	*Computer values*			*Literature values*	
			ε	P'	m	$m_{\text{calc.}}$	$m_{\text{exptl.}}$
Silica as adsorbent[a]							
43	Hexane–methylene chloride	59.82:40.18	0.223	1.31	0.10	0.10	0.09
44	Hexane–chloroform	35.05:64.95	0.225	2.70	0.10	0.10	0.05
45	Hexane–methyl *tert.*-butyl ether	95.95:4.05	0.252	–	0.72	0.74	0.81
46	Hexane–methylene chloride–methyl *tert.*-butyl ether	83.19:15.37:1.44	0.278	–	0.49	0.36	0.44
47	Hexane–chloroform–methylene chloride	46.8:34.48:18.72	0.225	2.04	0.10	0.10	0.16
48	Hexane–chloroform–methylene chloride–methyl *tert.*-butyl ether	89.08:4.61:2.53:3.78	0.293	–	0.71	0.71	0.60
49	Hexane–methyl *tert.*-butyl ether	97.98:2.02	0.216	–	0.67	0.68	0.71
50		91.97:8.03	0.284	–	0.76	0.77	0.66
51	Hexane–methylene chloride–acetonitrile	92.48:5.02:2.5	0.302	0.39	0.84	0.93	0.85
52	Hexane–methylene chloride–acetonitrile	90.95:5.02:4.03	0.336	0.48	0.90	1.02	0.83
53	Hexane–methyl *tert.*-butyl ether	96.14:3.86	0.249	–	0.72	0.73	0.68
54	Hexane–methylene chloride–acetonitrile	71.8:28.04:0.16	0.222	0.95	0.17	0.13	0.16
Alumina as adsorbent[b]							
55	Pentane–acetonitrile	99.9:0.1	0.126	0.01	0.50	0.45	0.39
56		99.86:0.14	0.152	0.01	0.65	0.57	0.46
57		99.7:0.3	0.207	0.02	0.93	0.85	0.87
58		99.6:0.4	0.225	0.02	1.00	0.91	0.95
59		99.4:0.6	0.248	0.04	1.07	0.94	0.98
60		99.3:0.7	0.257	0.04	1.09	1.04	1.09
61	Pentane–pyridine	98:2	0.304	0.11	1.20	1.14	1.16
62		95:5	0.399	0.27	1.21	1.17	1.14
63	Pentane–acetone	99.8:0.2	0.133	0.01	0.61	0.58	0.42
64		99.6:0.4	0.171	0.02	0.80	0.74	0.79
65		99.4:0.6	0.192	0.03	0.85	0.80	0.77
66		99.2:0.8	0.205	0.04	0.88	0.83	0.91
67	Pentane–tetrahydrofurane	98:2	0.194	0.08	0.74	0.72	0.73
68		95:5	0.240	0.20	0.78	0.77	0.77
69	Pentane–triethylamine	95:5	0.188	0.10	0.78	0.77	0.77
70	Pentane–ethyl acetate	99:1	0.171	0.04	0.67	0.65	0.65
71		96:4	0.255	0.18	0.74	0.72	0.72
72	Pentane–diethyl ether	98:2	0.070	0.06	0.19	0.26	0.32
73		95:5	0.128	0.14	0.42	0.47	0.55
74		91:9	0.168	0.25	0.52	0.53	0.47
75		77:23	0.231	0.64	0.59	0.58	0.43
76	Pentane–1,2-dichloroethane	85:15	0.244	0.53	0.34	0.33	0.33
77	Pentane–chloroform	85:15	0.179	0.62	0.31	0.30	0.23
78		70:30	0.246	1.23	0.33	0.33	0.41
79	Pentane–methylene chloride	87:13	0.193	0.40	0.26	0.25	0.25
80		77:23	0.253	0.71	0.28	0.27	0.26
81		65:35	0.298	1.09	0.29	0.28	0.33

TABLE III (*continued*)

No.	*Mobile phase*	*Proportions (%, v/v)*	*Computer values*			*Literature values*	
			ε	P'	m	$m_{calc.}$	$m_{exptl.}$
82		40:60	0.354	1.86	0.29	0.29	0.22
83	Pentane–ethyl sulphide	92:8	0.141	–	0.23	0.20	0.18
84		85:15	0.191	–	0.27	0.25	0.27
85	Pentane–chlorobenzene	70:30	0.207	0.81	0.12	0.12	0.12
86	Pentane–bromoethane	60:40	0.253	0.80	0.08	0.08	0.08
87	Pentane–tetrachloromethane	50:50	0.117	0.80	−0.08	−0.08	−0.08
88	Pentane–benzene	85:15	0.158	0.41	−0.14	−0.13	−0.04
89		72:28	0.210	0.76	−0.15	−0.14	−0.02
90		50:50	0.261	1.35	−0.15	−0.15	−0.25
91		20:80	0.302	2.16	−0.15	−0.15	−0.29
92	Pentane–toluene	70:30	0.197	0.72	−0.16	−0.15	−0.15

[a] Literature values from ref. 13 (Table V).
[b] Literature values from ref. 13 (Table II).

TABLE IV

AGREEMENTS WITHIN THE COMPUTER-CALCULATED VALUES OF ε OR m, AND CORRESPONDING CALCULATED AND EXPERIMENTAL VALUES REPORTED BY SNYDER AND CO-WORKERS FOR THE MOBILE PHASES PRESENTED IN TABLES II AND III

Compared values[a]	*S.D.*	*Compared values*[a]	*S.D.*
$\varepsilon_{comp.}$ *vs.* $\varepsilon_{calc.}$	0.010	$m_{comp.}$ *vs.* $m_{calc.}$	0.05
$\varepsilon_{comp.}$ *vs.* $\varepsilon_{exptl.}$	0.018	$m_{comp.}$ *vs.* $m_{exptl.}$	0.08
$\varepsilon_{calc.}$ *vs.* $\varepsilon_{exptl.}$	0.017	$m_{calc.}$ *vs.* $m_{exptl.}$	0.07

[a] Abbreviations of subscripts: comp. = computer-calculated values; calc. = literature calculated values; exptl. = literature experimental values.

TABLE V

COMPUTER ε, m AND P' VALUES OF SOME SETS OF MOBILE PHASES COMPOSED OF 2–5 SOLVENTS

In each column of three values, ε is the upper value, m is the middle value and P' is the lower value.

Set No.	*Volume percentage x of the most polar solvent of the indicated set of mobile phases*										
	1	*5*	*10*	*20*	*30*	*40*	*50*	*60*	*70*	*80*	*90*
Silica as adsorbent											
93	Pentane–ethyl acetate [(100 − x):x]										
	0.183	0.246	0.274	0.310	0.340	0.370	0.398	0.423	0.442	0.458	0.470
	0.51	0.56	0.58	0.59	0.59	0.60	0.60	0.60	0.60	0.60	0.60
	0.04	0.22	0.44	0.88	1.32	1.76	2.20	2.64	3.08	3.52	3.96
94	Pentane–methyl *tert.*-butyl ether [(100 − x):x]										
	0.168	0.256	0.289	0.321	0.340	0.356	0.374	0.397	0.423	0.447	0.467
	0.56	0.73	0.76	0.79	0.80	0.80	0.81	0.81	0.82	0.82	0.82
	–										

(*Continued on p. 244*)

TABLE V (*continued*)

Set No.	*Volume percentage x of the most polar solvent of the indicated set of mobile phases*										
	1	*5*	*10*	*20*	*30*	*40*	*50*	*60*	*70*	*80*	*90*
95	Pentane–methylene chloride–methyl *tert.*-butyl ether $[(90-x):10:x]$										
	0.224	0.322	0.357	0.390	0.409	0.422	0.433	0.442	0.452	0.461	
	0.43	0.70	0.75	0.78	0.78	0.79	0.80	0.80	0.81	0.81	
	—										
96	Chloroform–diethyl ether $[(100-x):x]$										
	0.265	0.282	0.302	0.335	0.362	0.380	0.393	0.401	0.405	0.409	0.417
	0.01	0.05	0.12	0.27	0.43	0.52	0.57	0.61	0.63	0.64	0.65
	4.09	4.04	3.97	3.84	3.71	3.58	3.45	3.32	3.19	3.06	2.93
97	Chloroform–acetone $[(100-x):x]$										
	0.275	0.325	0.369	0.420	0.446	0.462	0.472	0.481	0.490	0.503	0.518
	0.04	0.24	0.47	0.75	0.84	0.88	0.90	0.92	0.93	0.94	0.95
	4.11	4.15	4.20	4.30	4.40	4.50	4.60	4.70	4.80	4.90	5.00
98	Methylene chloride–ethyl acetate $[(100-x):x]$										
	0.302	0.311	0.322	0.343	0.362	0.380	0.398	0.415	0.432	0.448	0.464
	0.01	0.02	0.07	0.16	0.28	0.41	0.49	0.54	0.57	0.59	0.59
	3.11	3.17	3.23	3.36	3.49	3.62	3.75	3.88	4.01	4.14	4.27
99	Methylene chloride–methyl *tert.*-butyl ether–ethyl acetate–isopropanol $[(80-x):10:10:x]$										
	0.384	0.402	0.423	0.459	0.489	0.516	0.540	0.561	0.581		
	—										
	—										
100	Diethyl ether–acetonitrile $[(100-x):x]$										
	0.432	0.440	0.449	0.464	0.476	0.485	0.493	0.500	0.506	0.511	0.516
	0.01	0.06	0.15	0.37	0.59	0.82	0.91	0.98	1.01	1.03	1.04
	2.83	2.95	3.10	3.40	3.70	4.00	4.30	4.60	4.90	5.20	5.50
101	Tetrahydrofuran–acetonitrile $[(100-x):x]$										
	0.481	0.483	0.486	0.492	0.497	0.501	0.505	0.509	0.512	0.515	0.518
	0.01	0.04	0.09	0.22	0.40	0.59	0.80	0.90	0.98	1.02	1.04
	4.02	4.09	4.18	4.36	4.54	4.72	4.90	5.08	5.26	5.44	5.62
Alumina as adsorbent											
102	Pentane–toluene–pyridine $[(90-x):10:x]$										
	0.306	0.408	0.477	0.551	0.592	0.620	0.641	0.658	0.671	0.682	
	1.15	1.20	1.21	1.22	1.22	1.22	1.22	1.22	1.22	1.22	
	0.29	0.51	0.77	1.30	1.83	2.36	2.89	3.42	3.95	4.48	
103	Pentane–diethyl ether–methylene chloride–acetone $[(80-x):10:10:x]$										
	0.388	0.467	0.496	0.523	0.539	0.550	0.559	0.566	0.573		
	0.75	0.94	0.97	0.99	1.00	1.00	1.00	1.01	1.01		
	0.64	0.85	1.10	1.61	2.12	2.63	3.14	3.65	4.16		
104	Pentane–diisopropyl ether $[(100-x):x]$										
	0.010	0.044	0.076	0.122	0.153	0.177	0.197	0.215	0.233	0.250	0.266
	—										
	0.02	0.12	0.24	0.48	0.72	0.96	1.20	1.44	1.68	1.92	2.16
105	Pentane–diisopropyl ether–chloroform $[(90-x):10:x]$										
	0.091	0.135	0.174	0.226	0.261	0.286	0.306	0.323	0.336	0.348	
	—										
	0.28	0.45	0.65	1.06	1.47	1.88	2.29	2.70	3.11	3.52	
106	Pentane–diisopropyl ether–chloroform–tetrahydrofuran $[(80-x):10:10:x]$										
	0.265	0.346	0.378	0.410	0.430	0.446	0.461	0.473	0.485		
	—										
	0.69	0.85	1.05	1.45	1.85	2.25	2.65	3.05	3.45		
107	Pentane–diisopropyl ether–chloroform–tetrahydrofuran–acetonitrile $[(70-x):10:10:10:x]$										
	0.597	0.655	0.675	0.687	0.689	0.688	0.685	0.682			
	—										
	1.11	1.34	1.63	2.21	2.79	3.37	3.95	4.53			

data obtained by means of the second mode of the microcomputer program together with the corresponding literature data are presented in Tables II and III and were used for some comparisons, summarized in Table IV. Table V shows the data obtained for the remaining mobile phases that had not been studied previously and Fig. 1 presents their ε values in nomograph form. We shall discuss the previously made[16,17] choice of mobile phases for given TLC separations by means of the third mode of the microcomputer program at the end of the paper.

It is noteworthy that the calculation of "mean" mobile phase area $\bar{n}$ based on eqns. 2 and 9 leads to the values of ε and m as presented in Tables II, III and V which were very close to those obtained when eqn. 9 was excluded from the calculation procedure. The agreement between these two types of values was ± 0.012 units in ε and ± 0.03 units in m. This shows the accuracy of eqn. 2.

The mobile phases included in Tables II and III were selected from about 400 mobile phases studied so far[1–3,5,6,10–13,16,17] by means of Snyder's theory.

The 42 mobile phases presented in Table II are composed of two or three of the solvents pentane, hexane, benzene, methylene chloride, diethyl ether, methyl *tert.*-butyl ether, ethyl acetate, acetone, dioxane, acetonitrile, isopropanol and pyridine. Mobile phases 1–29 and 30–42 have been used for separations on silica and alumina, respectively, and characterized by calculated and experimental literature values of ε. The former values were obtained by means of the algorithm described under Theory but with some differences in the input values of the solvent molecular area n, solvent strength ε' and ε'' and localization parameter $f_l(C)/n$.

Table III includes 50 mobile phases composed of two to four of the solvents pentane, hexane, chloroform, methylene chloride, 1,2-dichloroethane, ethyl sulphide, bromoethane, tetrachloromethane, chlorobenzene, benzene, toluene, diethyl ether, methyl *tert.*-butyl ether, acetone, ethyl acetate, tetrahydrofuran, acetonitrile, triethylamine and pyridine. Mobile phases 43–54 and 55–92 have been used for separations on silica and alumina, respectively, and characterized by literature calculated and experimental values of m. The former values were obtained using eqn. 12 and m^0 values which differ in some instances from those recently reported and used in this study.

Let us discuss the comparisons within the various values of ε or m presented in the corresponding three columns in Tables II and III. According to Table IV, the agreement between the computer values and literature calculated values is very good, especially for the ε values, where S.D. = ± 0.01. This means that the calculation procedures presented under Theory are properly incorporated in the microcomputer program. In addition, the process of specifying the values of the parameters $n, f_l(C)/n$ and m^0 for pure solvents is successful but still requires further attention.

Table IV also shows the important fact that both the computer and literature calculated values agree equally well with the literature experimental values. The agreement is again better for the ε values, with S.D. $\approx \pm 0.02$ units.

To generalize, the data discussed here and the other data reported so far show agreement between the calculated and experimental values within ± 0.02 units for ε and ± 0.08 units for m. This conclusion is based on hundreds of HPLC and TLC separations performed on different types of silica or alumina using different types of solutes and approximately 400 mobile phases composed of two to six solvents. The experimental data were mainly obtained by Snyder and co-workers, but also by Hara

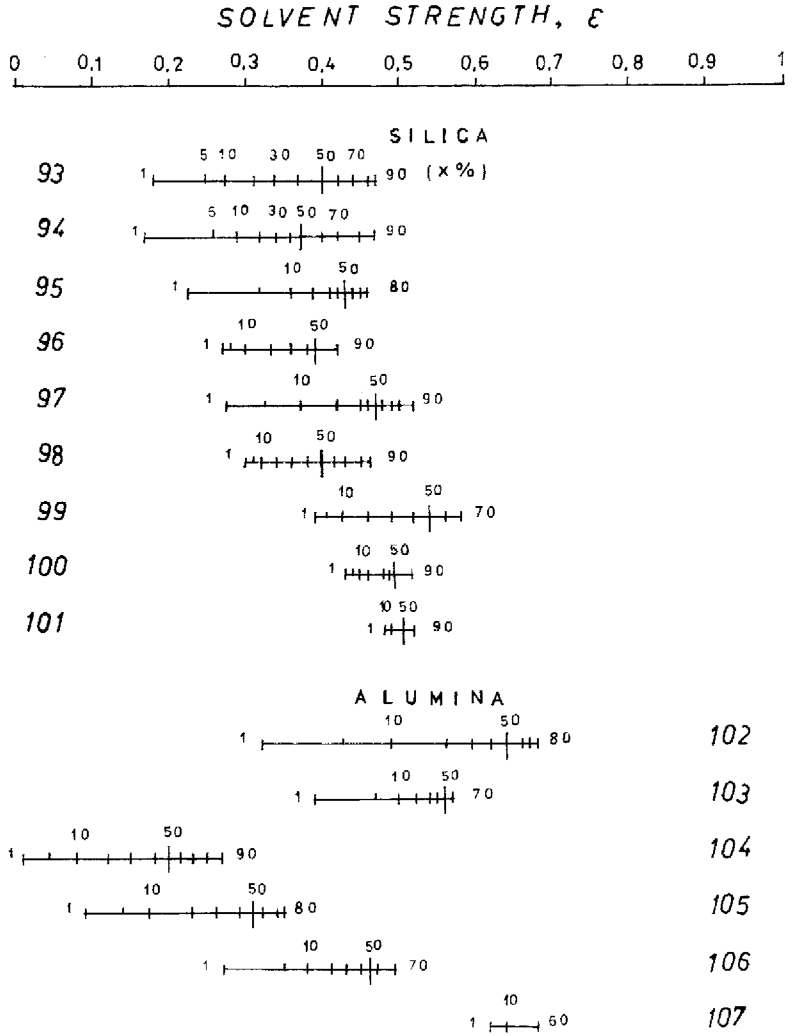

Fig. 1. Nomogram form expressing the solvent strength, ε, of sets of mobile phases 93–107 as a function of the volume percentage x of the most polar solvent. The composition of these sets is as follows: 93 = pentane–ethyl acetate $[(100-x){:}x]$; 94 = pentane–methyl *tert.*-butyl ether $[(100-x){:}x]$; 95 = pentane–methylene chloride–methyl *tert.*-butyl ether $[(90-x){:}10{:}x]$; 96 = chloroform–diethyl ether $[(100-x){:}x]$; 97 = chloroform–acetone $[(100-x){:}x]$; 98 = methylene chloride–ethyl acetate $[(100-x){:}x]$; 99 = methylene chloride–methyl *tert.*-butyl ether–ethyl acetate–isopropanol $[(80-x){:}10{:}10{:}x]$; 100 = diethyl ether–acetonitrile $[(100-x){:}x]$; 101 = tetrahydrofuran–acetonitrile $[(100-x){:}x]$; 102 = pentane–toluene–pyridine $[(90-x){:}10{:}x]$; 103 = pentane–diethyl ether–methylene chloride–acetone $[(80-x){:}10{:}10{:}x]$; 104 = pentane–diisopropyl ether $[(100-x){:}x]$; 105 = pentane–diisopropyl ether–chloroform $[(90-x){:}10{:}x]$; 106 = pentane–diisopropyl ether–chloroform–tetrahydrofuran $[(80-x){:}10{:}10{:}x]$; 107 = pentane–diisopropyl ether–chloroform–tetrahydrofuran–acetonitrile $[(70-x){:}10{:}10{:}10{:}x]$. Characterization of given mobile phases from the sets by values of ε, m and P' is presented in Table V.

and co-workers (see ref. 12) and ourselves[4,6,16,17]. It should be mentioned that m is better expressed by m^0 of the most polar solvent instead of by the corresponding calculated values in a given study[6], but this seems to be a separate case[16]. Consequently, the data available show unequivocally the ability of Snyder's theory to predict the solvent strength and selectivity of mobile phases in normal-phase liquid–solid chromatography (LSC).

As seen under Theory, ε of a given mobile phase is a function of the molar fractions of individual solvents. Hence, a considerable part of the data are reported together with corresponding molar fractions (*e.g.*, see ref. 12) instead of with the convenient to use volume percentages. The 153 mobile phases in Table V characterized for the first time by calculated values of ε, m and P' belong to fifteen sets as the ratio among the solvents is expressed in percentages as in Tables II and III. The data of sets 93–101 refer to silica and those of sets 102–107 are valid for alumina. Each set is composed of two to five solvents and the percentage of the last solvent increases with the corresponding decrease in that of the first solvent. Table V shows that the values of ε and m increase within any set because the last solvent has the greatest individual values of these two parameters. A slight deviation in ε values for the last three mobile phases of set 107 is observed.

All mobile phases studied show a great difference in their TLC properties as the computer-calculated values of ε, m and P' vary within the ranges 0.010–0.682, -0.16 to 1.22 and 0.01–5.50, respectively (see Tables II, III and V). The mobile phases characterized can easily be used because they are composed of practically important solvents and cover a considerable part of the experimentally accessible ranges of the three parameters. The plot in Fig. 1 is a nomograph presentation of the ε values in Table V which enables mobile phases of intermediate ε values which are not included in the table to be found.

Although the microcomputer program is universal for normal-phase LSC, we applied it first[16,17] to choose mobile phases of constant ε value for optimizing TLC separations of different diastereoisomers on silica. (Note: eqn. 9 was not yet incorporated in the program.) Thus, 41 mobile phases having three different ε values and composed of two to six solvents were found by means of the third mode of the microcomputer program. The corresponding experimental R_F values of the three groups of compounds studied vary within the ranges 0.12–0.82, 0.11–0.89 and 0.01–0.75, independently of the number and nature of solvents included in their composition and independently of the presence of complicating factors such as the formation of a second front in some instances. The agreement between the computer and experimental ε values is within ± 0.016 units, which shows for the first time the applicability of Snyder's theory to characterizing mobile phases composed of more than four solvents.

The above-mentioned scatter of the experimental R_F values, when there is no second front formation, is probably due to the fact that the mobile phases used for a given group of compounds have different P' values in spite of their constant ε value. The tendency found[16,17] for an increase in R_F values with an increase in P' values is reasonable, bearing in mind that a higher P' value means a better solution of a solute in the corresponding mobile phase. Concerning HPLC, another example for the importance of P' can be given. Snyder and Glajch have established a surprisingly poorer agreement of ± 0.043 units between calculated and experimental values of ε in the case of some acetonitrile-containing mobile phases (see Table IV and related discussion of ref. 12). The data show a tendency for higher $\varepsilon_{\text{exptl.}}$ values which can be explained by the fact that acetonitrile has the highest P' value (5.8) among all solvents investigated. Thus, solvent strength is mainly determined by ε but influenced by P' too. Consequently, polarity P' appears to be a co-parameter in determining solvent strength in normal-phase LSC (*cf.* ref. 2, p. 258).

CONCLUSION

The parameters solvent strength, ε, localization, m, and polarity, P', proposed by Snyder characterize well the solvent strength and selectivity effects of mobile phases for normal-phase LSC techniques such as HPLC and TLC using silica or alumina as adsorbents. The microcomputer program described calculates in a few seconds the values of the three parameters for mobile phases composed of two to several solvents and finds equi-eluotropic mobile phases of any desired ε value. This permits the easy application of Snyder's useful theory in every-day chromatographic practice.

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