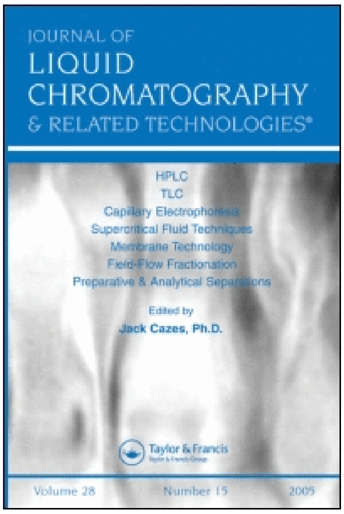

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Automatic Selection of Mobile Phases. VII. Thin-Layer Chromatography on Silica and Alumina of 11,12-Disubstituted *trans/cis*-11,12-Dihydro-6*H*-dibenzo[*c,h*]chromen-6-ones

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Automatic Selection of Mobile Phases. VII. Thin-Layer Chromatography on Silica and Alumina of 11,12-Disubstituted *trans*/*cis*-11,12-Dihydro-6*H*-dibenzo[*c,h*]chromen-6-ones

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Abstract: Fifteen title compounds with four fused rings and two varying substituents were used to further specify the scope and limitation of a theoretical approach (the Snyder theory and LSChrom software) for selection of mobile phases avoiding any trial and error experiments. Based on the structure of the compounds, the theoretical treatment predicted values of strength ε of suitable mobile phases for TLC, namely 0.311 for silica and 0.446 for alumina. Sixteen specific mobile phases with such or close values of ε were arbitrarily selected from lists prepared by complex calculations. They were used to perform TLC. The data obtained showed that the retentions in all 256 measurements done were above the origin and below the solvent front. Thus, a good agreement between the theoretical and experimental data was established, thus proving a successful application of the approach. The retentions of all compounds and separation of one *cis*/*trans* pair depended on the stationary phase, ε, and the tuning parameters m and P' of the mobile phases.

Keywords: Normal-phase liquid chromatography, Thin-layer chromatography, Silica, Alumina, O-containing heterocycles, Dibenzo[*c,h*]chromen, *Cis*/*trans* isomers, Mobile-phase selection, Snyder theory in LSChrom software

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INTRODUCTION

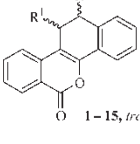
Selection of mobile phases for normal-phase liquid chromatography (NPLC) is of practical importance, since TLC and HPLC on silica or alumina are used daily for the analysis of organic compounds in laboratories where the users may not be chromatographers. For these users, this problem is difficult. Moreover, the trial and error approach is time consuming. Thus, any theoretical approach that easily solves the problem is important.

Until now, precise theoretical prediction of retention in NPLC was not possible on the basis of the structures of the analytes. The well known Snyder theory[1−3] incorporated in the LSChrom[4−6] software predicts retention in NPLC in first approximation by the following equation:

$$R_M = \log\left(\frac{1}{R_F} - 1\right) = \log k = \underbrace{R_{M\,(shift)}}_{\mathrm{I}} + \underbrace{\alpha'}_{\mathrm{I}} \left(\underbrace{\sum Q_i^o}_{\mathrm{IIa}} - \varepsilon \cdot \underbrace{\sum a_i}_{\mathrm{IIb}}\right) \quad (1)$$

where I, IIa, & IIb, and ε depend on the adsorption properties of stationary phase (adsorbent), compound X, and mobile phase, respectively. Parameters $S_X = \mathrm{IIa}$ and $A_X = \mathrm{IIb}$ are retention of X and its area under adsorption, respectively. They are sums of the relevant contribution of any functional group available in the structure, namely Q_i^o (energy of adsorption) and a_i area under adsorption of group i.

The present series of papers[7−12] adopts the following theoretical approach for selection of mobile phase without any preliminary experiments: a) calculation of retention by Eq. (1) as a function of ε, b) selection of a suitable or recommended value of $\varepsilon(\varepsilon_{recommended})$ where all analytes have proper retention and best separation of the poorest separated pair of compounds, c) calculation by a complex procedure of the proportions of the solvents of mobile phases that will ensure $\varepsilon_{recommended}$, and d) experimental verification of the predictions in a-c) using mobile phases having $\varepsilon_{recommended}$ or similar values. The large TLC data base obtained[7−12] for 118 compounds, 4 adsorbents, and 71 theoretically selected mobile phases shows that, with limited exceptions of experimental $R_F = 0$ (7 within 849 measurements), the approach gives very good results. Trying to enlarge the database, the present paper applies this approach to the heterocyclic compounds **1–15** having four fused rings and two varying substituents that are new points for the series.



1 – 15, *trans* or *cis*

EXPERIMENTAL

Tables 1–5 summarize the data obtained in this study. Compounds **1–15** (see Table 3) belong to four groups, since R^1 is phenyl, 3,4-methylenedioxyphenyl (piperonyl), 4-nitrophenyl and 4-methoxyphenyl. The variation of R^2 is greater: methoxycarbonyl and six different amide groups. The compounds were prepared[13–15] from homophthalic anhydride in excess and an aromatic aldehyde and subsequent transformations of the heterocyclic acids obtained. The compounds contain two stereogenic centers that result in *cis* and *trans* isomers. The structures and configuration of all compounds (see Table 3) were elucidated by ^{1}H-NMR spectra. The majority of the compounds have *trans* configuration. Compounds *trans*-**10** and *cis*-**10** only are diastereomers.

The stationary phases for TLC were: silica = pre-coated TLC plastic sheets: polygram sil G/UV$_{254}$ (Macherey-Nagel, Germany) and alumina = pre-coated TLC plates: alumina F$_{254}$, type E (Merck, Germany). TLC was performed with a solvent front of 8 cm and a distance between the adjacent spots of 11 mm for silica and 5 mm for alumina. The solvents were of analytical reagent grade.

The computer program used was LSChrom Version 2.1 for Windows[10] with which calculation procedure 3 was made active.

Table 1 shows the structures of compounds **1–15** expressed by the composing structural elements and their adsorption properties for silica and alumina. The mobile phases selected by LSChrom are shown in Table 2. These mobile phases are composed of two to three solvents. The experimental values of R_F, using the computer selected mobile phases are summarized for silica and alumina in Table 3 and Table 4, respectively. Table 5 gives data for R_F, R_M, and separation α of the *cis/trans* isomers of compound **10**. The last parameter was calculated by the following equation:

$$\log \alpha = R_{M(cis-\mathbf{10})} - R_{M(trans-\mathbf{10})} \qquad (2)$$

RESULTS AND DISCUSSION

Automatic Selection of Mobile Phases

The automatic selection of suitable mobile phases for a given separation performed by LSChrom in seconds requires values for all parameters of Eq. (1), except those of strength (energy of adsorption) ε.

From a list, the user selects an adsorbent with known values of $R_{M(shift)}$ and α', including them in the calculations. These parameters should be established preliminarily for any other adsorbent.[5] Their proper values are of significant importance for the theoretical predictions. The silica used in this

Table 1. Structure description by functional groups and adsorption properties of compounds **1–15**

Group i^a	Q_i°	a_i	Number of relevant functional groups in compounds														
			1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
Silica: $R_{M(shift)} = -1.76$, $a' = 0.57$																	
C=	0.25	1.00	20	20	20	26	20	20	20	26	20	20	20	26	20	20	26
Al-CH_2-Al	−0.05	0.90	2	6	7	6	2	6	7	6	2	6	7	6	2	7	6
Al-CH_3	0.07	1.60	−1	−1	−1	−1	−2	−2	−2	−2	−1	−1	−1	−1	−1	−1	−1
Al-N (tert)	5.80	10.50				1				1				1			1
Al-$CONH_2$	9.60	10.30		1	1	1		1	1	1		1	1	1		1	1
Ar-NO_2	2.77	7.50									1	1	1	1			
Al-CO_2-CH_3	5.27	10.50	1				1				1				1		
Ar-CO_2-CH_3	3.45	8.10	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Ar-O-CH_3	1.83	4.60					2	2	2	2							
Ar-F	−0.15	0.40								3							1
ΣQ_i°			13.55	17.68	17.63	24.98	17.14	21.27	21.22	28.12	16.32	20.45	20.40	29.58	15.38	19.46	26.66
Σa_i			38.80	42.20	43.10	58.70	46.40	49.80	50.70	67.50	46.30	49.70	50.60	70.80	43.40	47.70	63.70
R_F (calc. at $\varepsilon = 0.311$)			0.81	0.12	0.17	0.01	0.57	0.03	0.04	0.01	0.75	0.07	0.11	0.01	0.76	0.11	0.01
Alumina: $R_{M(shift)} = -4.25$, a$' = 0.65$																	
ΣQ_i°			14.67	18.65	18.67	24.91	18.24	22.22	22.24	28.81	17.42	21.40	21.42	29.43	16.44	20.44	26.79
Σa_i			26.40	29.90	30.80	39.10	28.80	32.30	33.20	42.70	28.90	32.40	33.30	43.60	28.40	32.80	41.50
R_F (calc. at $\varepsilon = 0.446$)			0.91	0.79	0.83	0.18	0.77	0.12	0.19	0.01	0.87	0.32	0.45	0.01	0.90	0.68	0.06

[a] Al = Alkyl; Ar = Aryl.

Table 2. Computer selected mobile phases 1–16 belonging to four groups

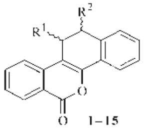
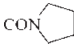
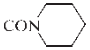
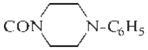
No	Composition	Vol. (%)[a]	ε	m	P'
Silica					
Group a					
1	Dichloromethane-ethyl acetate	95.121:4.879	0.311	0.025	3.164
2	Chloroform-acetone	96.102:3.898	0.311	0.170	4.139
3	Hexane-dichloromethane-methanol	9.989:90:0.011	0.311	—	2.801
Group b					
4	Hexane-ethyl acetate	71.131:28.869	0.344	0.589	1.341
5	Dichloromethane-ethyl acetate	79.315:20.685	0.344	0.168	3.369
6	Chloroform-acetone	92.308:7.692	0.344	0.336	4.177
7	Hexane-dichloromethane-methanol	19.086:80:0.914	0.344	—	2.546
8	Hexane-dichloromethane-ethyl acetate	3.725:95:1.275	0.344	0.174	3.005
Alumina					
Group c					
9	Hexane-ethyl acetate	76.023:23.977	0.446	0.765	1.131
10	Dichloromethane-ethyl acetate	95.212:4.788	0.446	0.175	3.162
11	Hexane-dichloromethane-ethyl acetate	14.284:80:5.716	0.446	0.414	2.746
Group d					
12	Hexane-ethyl acetate	72.422:27.587	0.462	0.766	1.286
13	Dichloromethane-ethyl acetate	92.160:7.840	0.462	0.264	3.202
14	Chloroform-acetone	94.950:5.050	0.462	0.484	4.150
15	Hexane-dichloromethane-ethyl acetate	41.451:50:8.549	0.462	0.580	1.968
16	Cyclohexane-dichloromethane-acetone	27.997:70:2.003	0.462	0.574	2.216

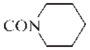
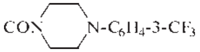
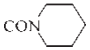
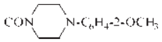
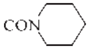
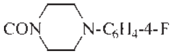
[a] The numbers are given in three digit precision to ensure the same values of ε, m and P' repeting the calulations.

study is equivalent to that applied in Ref. [11] where it was characterized by $R_{M(shift)} = -1.76$ and $\alpha' = 0.57$. These values are applicable for other TLC silicas.[7–10,12] The alumina used was defined by $R_{M\ (shift)} = -4.25$ and $\alpha' = 0.65$ similarly to the case of another TLC alumina.[11]

The user describes the structure of any compound analysed, selecting from a list of corresponding structural fragments, and specifies their number. Thus, the values of IIa and IIb for compounds **1–15** became known, as shown in Table 1. The details given in this table are important, since some structural fragments

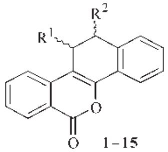
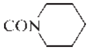
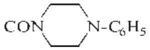
Table 3. Experimental R_F values of compounds **1–15** on silica with computer selected mobile phases 1–8

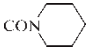
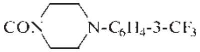
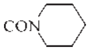
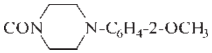
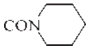
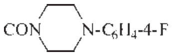
	Compound			R_F on silica for a given mobile phase[a]							
No	R^1	R^2		1	2	3	4	5	6	7	8
	 1–15		ε	0.311	0.311	0.311	0.344	0.344	0.344	0.344	0.344
			m	0.025	0.170	—	0.589	0.168	0.336	—	0.174
			P'	3.16	4.14	2.80	1.341	3.369	4.177	2.546	3.005
trans-1	C_6H_5	$COOCH_3$		0.81	0.84	0.50	0.48	0.94	0.88	0.81	0.75
trans-2	″			0.10	0.31	0.01	0.04	0.61	0.49	0.12	0.06
trans-3	″			0.21	0.48	0.05	0.14	0.79	0.63	0.20	0.14
trans-4	″			0.20	0.44	0.04	0.16	0.84	0.61	0.18	0.12
trans-5	$3+4\text{-}(OCH_2O)\text{-}C_6H_3$	$COOCH_3$		0.80	0.82	0.49	0.41	0.97	0.85	0.81	0.69
trans-6	″			0.19	0.47	0.05	0.11	0.76	0.62	0.21	0.11

trans-7	″		0.18	0.48	0.06	0.11	0.76	0.63	0.24	0.10
trans-8	″		0.32	0.53	0.09	0.19	0.88	0.66	0.31	0.18
trans-9	4-O_2N-C_6H_4	$COOCH_3$	0.83	0.80	0.49	0.36	0.95	0.84	0.85	0.69
trans-10	″		0.12	0.31	0.06	0.02	0.51	0.41	0.19	0.06
cis-10	″		0.04	0.18	0.01	0.01	0.24	0.28	0.10	0.01
trans-11	″		0.26	0.48	0.08	0.06	0.76	0.61	0.33	0.13
trans-12	″		0.11	0.34	0.05	0.04	0.65	0.48	0.23	0.06
trans-13	4-CH_3O-C_6H_4	$COOCH_3$	0.80	0.84	0.44	0.41	0.94	0.85	0.84	0.68
trans-14	″		0.20	0.50	0.05	0.10	0.74	0.66	0.29	0.11
trans-15	″		0.16	0.41	0.04	0.10	0.79	0.56	0.29	0.08

[a] For composition of mobile phases 1–8, see Table 2.

Table 4. Experimental R_F values on alumina of compounds **1**–**15** with computer selected mobile phases 9–16

	Compound			R_F on alumina for a given mobile phase[a]							
No	R^1	R^2		9	10	11	12	13	14	15	16
	 1–15		ε	0.446	0.446	0.446	0.462	0.462	0.462	0.462	0.462
			m	0.765	0.175	0.414	0.766	0.264	0.484	0.580	0.574
			P'	1.131	3.162	2.746	1.286	3.202	4.150	1.968	2.216
trans-1	C_6H_5	$COOCH_3$		0.81	0.93	0.94	0.78	0.91	0.94	0.91	0.89
trans-2	″			0.11	0.30	0.29	0.15	0.49	0.85	0.20	0.23
trans-3	″			0.33	0.54	0.56	0.39	0.66	0.90	0.44	0.39
trans-4	″			0.29	0.63	0.66	0.40	0.74	0.93	0.40	0.41
trans-5	3 + 4-(OCH_2O)-C_6H_3	$COOCH_3$		0.84	0.93	0.95	0.69	0.89	0.95	0.89	0.85
trans-6	″			0.23	0.53	0.53	0.29	0.66	0.91	0.35	0.38

trans-7	″		0.23	0.50	0.54	0.28	0.68	0.90	0.35	0.38
trans-8	″		0.24	0.71	0.73	0.34	0.79	0.92	0.44	0.44
trans-9	4-O_2N-C_6H_4	$COOCH_3$	0.57	0.95	0.94	0.60	0.86	0.93	0.86	0.83
trans-10	″		0.08	0.38	0.40	0.09	0.55	0.85	0.18	0.23
cis-10	″		0.04	0.20	0.18	0.05	0.28	0.81	0.09	0.11
trans-11	″		0.18	0.65	0.68	0.23	0.66	0.90	0.40	0.42
trans-12	″		0.09	0.59	0.55	0.13	0.63	0.90	0.23	0.29
trans-13	4-CH_3O-C_6H_4	$COOCH_3$	0.73	0.95	0.94	0.73	0.86	0.93	0.86	0.85
trans-14	″		0.23	0.52	0.56	0.29	0.58	0.86	0.39	0.35
trans-15	″		0.20	0.60	0.59	0.26	0.64	0.89	0.31	0.33

[a] For composition of mobile phase 9–16, see Table 2.

Table 5. Experimental R_F values and derived values of R_M and log α^a for the diastereoisomeric compounds **10** on silica and alumina

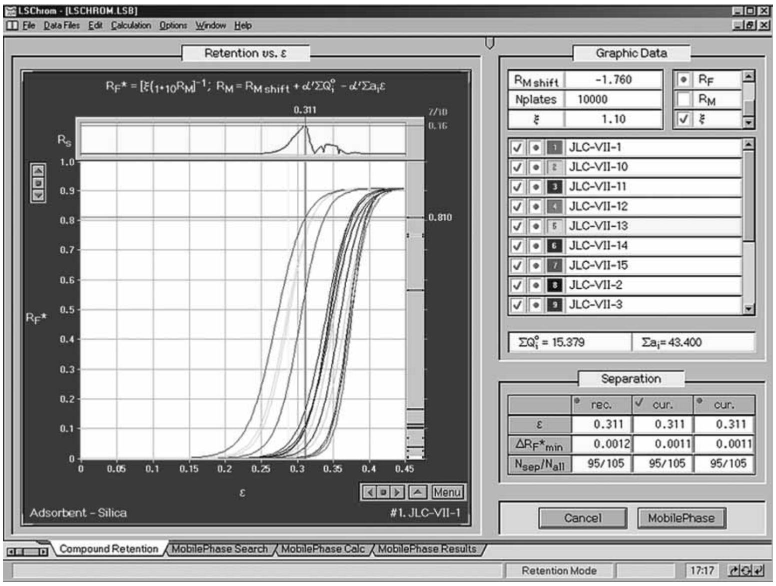
	Mobile phases[b] for Silica								
Parameter	1	2	3	4	5	6	7	8	Average
R_F of *cis*-10	0.04	0.18	0.01	0.01	0.24	0.28	0.10	0.01	0.11
R_F of *trans*-10	0.12	0.31	0.06	0.02	0.51	0.41	0.19	0.06	0.21
R_M of *cis*-10	1.38	0.66	1.99	1.99	0.50	0.41	0.95	1.99	1.23
R_M of *trans*-10	0.87	0.35	1.19	1.69	-0.02	0.16	0.63	1.19	0.76
log α	0.51	0.31	0.80	0.30	0.52	0.25	0.32	0.80	0.48
	Mobile phases[b] for Alumina								
	9	10	11	12	13	14	15	16	
R_F of *cis*-10	0.04	0.20	0.18	0.05	0.28	0.81	0.09	0.11	0.22
R_F of *trans*-10	0.08	0.38	0.40	0.09	0.55	0.85	0.18	0.23	0.35
R_M of *cis*-10	1.38	0.60	0.66	1.28	0.41	-0.63	1.01	0.91	0.70
R_M of *trans*-10	1.06	0.21	0.18	1.01	-0.09	-0.75	0.66	0.52	0.35
log α	0.32	0.39	0.48	0.27	0.50	0.12	0.35	0.39	0.35

[a] The values of R_M and log α were calculated from the experimental R_F by Eqs. 1 and 2.

[b] For composition of mobile phases 1–16, see Table 2.

are not available in the list; they are substituted by other fragments (see details in Refs. [8–12]. Moreover, a specific structural fragment is excluded by taking its number with a negative sign as shown in Table 1. For instance, compounds **1–15** contain a lactone O-CO group; it was represented by one Ar-CO_2CH_3 group minus one Al-CH_3 (notations Ar and Al mean that the relevant group is attached to an aryl and alkyl group, respectively). The structures of the diastereomeric compounds *trans*-**10** and *cis*-**10** were described in the same way, since the standard approach in LSChrom does not differentiate between any kind of isomers. This does not cause a problem, since the diastereomers have similar energy of adsorption and a mobile phase that is suitable for the one isomer is suitable also for the other isomer. In the present study, the CF_3 group in compound **8** was expressed by three Ar-F ($Q_i^o = -0.15$) instead with Al-F ($Q_i^o = 1.54$) since similar compounds are less retained than the unsubstituted compounds. Ar-F only with its negative value of Q_i^o corresponds to this phenomenon.

Including the above mentioned values of I, IIa, and IIb in the calculations, LSChrom simulated retention R_M by Eq. (1) and predicted the value of the recommended mobile phase strength ε ($\varepsilon_{recommended}$), namely 0.311 for silica as illustrated in Figure 1 and 0.446 for alumina. We also took into account other values (0.344 and 0.462, respectively) close to them. The reason for this was



$R_{M\,shift}$	-1.760
Nplates	10000
ξ	1.10

● R_F
☐ R_M
☑ ξ

☑ ● 1 JLC-VII-1
☑ ● 2 JLC-VII-10
☑ ● 3 JLC-VII-11
☑ ● 4 JLC-VII-12
☑ ● 5 JLC-VII-13
☑ ● 6 JLC-VII-14
☑ ● 7 JLC-VII-15
☑ ● 8 JLC-VII-2
☑ ● 9 JLC-VII-3

$\Sigma Q_i^o = 15.379$ $\Sigma a_i = 43.400$

	● rec.	✓ cur.	● cur.
ε	0.311	0.311	0.311
$\Delta R_F{}^*_{min}$	0.0012	0.0011	0.0011
N_{sep}/N_{all}	95/105	95/105	95/105

Figure 1. Illustration of the mode of LSChrom Version 2.1 for calculation and analysis of retention. The value of the recommended mobile phase strength, $\varepsilon_{recommended}$, was 0.311 for compounds **1–15** on silica.

based on the upper graphics of Figure 1 showing the resolution R_s of the poorest separated pair of compounds vs. ε. It is seen that the recommended value 0.311 of ε for silica corresponds to best separation R_s at the highest peak of the graphics. However, in this case, there is a smaller peak showing a relevant value of 0.344 for ε.

To find mobile phases having the above mentioned values of ε for silica or alumina, LSChrom performed complex calculations[1] and proposed different lists. We selected, arbitrarily, some of the mobile phases that are shown in Table 2. Note that any mobile phase is characterized by values of ε and the tuning parameters localization m and polarity P'. Selectivity of mobile phases is related to m and its solvation ability is proportional to P'. Table 2 shows that the mobile phases of any group a-d have a given value of ε and different values of m and P', leading to modification of their properties. This is due to the specific values of m and P' of the individual solvents comprising the mobile phases. For instance, the solvents used are non-localizing (hexane and cyclohexane), weak localizing (dichloromethane and chloroform) and strong localizing (ethyl acetate, acetone and methanol) having low, intermediate, and high values of m, respectively.

TLC with the Automatically Selected Mobile Phases: Retention and Isomer Separation

Verification of the theoretical predictions was done by TLC of compounds **1–15** on the selected stationary phase with the theoretically found mobile phases. The experimental values of R_F obtained on silica (Table 3) or alumina (Table 4) showed that the retention in all cases was in the favorable range, above the origin and below the solvent front, namely $0.01 \leq R_F \leq 0.95$. This is the most important result, showing a successful application of the Snyder theory and LSChrom for an automatic selection of mobile phases on the basis of the structures of the compounds studied. The structures of compounds **1–15** were intentionally made more complex in comparison with the structures of other compounds studied in this series of papers.[7–12] Nevertheless, the Snyder theory deduced, on the basis of model compounds given for the seventh time in this series of papers, good results. The reason for this is probably that a precise prediction of retention is not necessary in the approach used in LSChrom and the major requirement is an adequate prediction of a suitable (recommended) value/s of ε. Keeping this strategy in mind, we will not compare, here, the theoretical retentions shown in Table 1 with the experimental values found. The successful application of the Snyder theory and LSChrom is also due to the properly selected values of both parameters defining the adsorbents. It seems that any TLC silica and alumina can be characterized by the values of $R_{M\ (shift)}$ and α' used in this study.

Let us consider some details of the data obtained. In the present study, contrary to Ref. [11], decomposition of the compounds on alumina was not established.

The expected decrease of retention and higher R_F values with the increase of ε is seen only as a tendency, since the difference in ε of the mobile phases of groups a-b and c-d (see Table 2) is small, namely 0.03 and 0.02 units, respectively. The expected tendency for a decrease of retention with the increase of P' was also established. Thus, within mobile phases 12–16 of group d, retention of the compounds is usually greatest with mobile phase 12 having the smallest value (1.286) of P'. The opposite is true for mobile phase 14, having the greatest value (4.150) of P'.

Table 5 shows that the separation of the diastereomeric compounds *cis*-**10** and *trans*-**10** was better on silica than on alumina on the basis of the average values of $\log\alpha$ (0.48 for silica vs. 0.35 for alumina). Moreover, the best separation and the highest values of $\log\alpha$ were obtained on silica with mobile phases 3 and 8 and on alumina with mobile phases 11 and 13 of intermediate values of m. This is an important result, since the Snyder theory expects the best correlation with the smallest or greatest values of m. These data unequivocally indicate that the use of mobile phases with a given favorable value of ε and different values of m and P' is a strategy for optimization of separation. An important result is that the *cis* isomer was always better retained than the *trans* isomer. This relative retention is seen by the positive values of $\log\alpha$ and is probably due to the specific pattern of adsorption of the two diastereomers effectuating different steric hindrance.[16]

CONCLUSIONS

1. The application of the Snyder theory and LSChrom software was successful in the automatic prediction of mobile phases for TLC on silica or alumina of dibenzo[*c,h*]chromenones **1–15** with four fused rings and two varying substituents. The predictions are based on the structure of the compounds. The calculations give a suitable (recommended) value of mobile phase strength ε (0.311 for silica and 0.446 for alumina) and specific mobile phases having such or close values of ε. The experimental TLC with 16 mobile phases proved, in 256 measurements, the validity of the theoretical predictions.
2. The separation of the *cis*/*trans* isomers of compound **10** depended on the properties of the mobile phases as measured by ε and the tuning parameters localization m and polarity P' and was more successful on silica than on alumina.
3. The LSChrom software incorporates the Snyder theory and enables any user to apply it for automatic selection of mobile phases for TLC and HPLC on silica or alumina of non-ionic compounds, provided the compound structures are known and can be expressed by the structural fragments available in the software.

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REFERENCES

1. Snyder, L.R. *Principles of Adsorption Chromatography*; Marcel Dekker: New York, 1968.
2. Snyder, L.R.; Kirkland, J.J. *Introduction to Modern Liquid Chromatography*, 2nd Ed.; Wiley-Interscience: New York, 1979.
3. Snyder, L.R. *High-Performance Liquid Chromatography*; Horváth, Cs., Ed.; Academic Press: New York, 1983; Vol. 3, 157–223.
4. Palamareva, M.D.; Palamarev, H.E. Microcomputer-aided characterisation of mobile phases for normal-phase liquid-solid chromatography based on Snyder's theory and data. J. Chromatogr. **1989**, *477*, 235–248.
5. Palamarev, Ch.E.; Meyer, V.R.; Palamareva, M.D. New approach to the computer-assisted selection of mobile phases for high-performance liquid chromatography on the basis of the Snyder Theory. J. Chromatogr. A **1999**, *848*, 1–8.
6. Palamarev, Ch.E.; Palamareva, M.D. *LSChrom, Ver 2.1, Demo version*, 1999, http://www.members.tripod.com/LSChrom.
7. Palamareva, M.D.; Koleva, R.I.; Kozekov, I.D. Automatic selection of mobile phases. TLC on silica of 2-benzyl-3-(1-methylpyrol-2-yl)-4-substituted-tetrahydroisoquinolines and corresponding 1-ones. J. Liq. Chromatogr. & Rel. Technol. **2001**, *24*, 1411–1424.
8. Koleva, R.I. Palamareva, M.D. Automatic selection of mobile phases. II. TLC on silica of *trans* and *cis*-2-phenethyl-3-(9-methylcarbazol-3-yl)-4-substituted isoquinolines. J. Liq. Chromatogr. & Rel. Technol. **2002**, *25*, 3129–3138.
9. Palamareva, M.D.; Stoyanova, M.P.; Kozekov, I.D. Automatic selection of mobile phases. III. TLC on silica of 2,3,4-trisubstitued tetrahydroisoquinolinones. J. Liq. Chromatogr. & Rel. Technol. **2003**, *25*, 1255–1266.
10. Palamarev, Ch.E.; Kandinska, M.I.; Palamareva, M.D. Automatic selection of mobile phases. IV. Thin-layer chromatography on silica of simple and complex organic compounds. J. Liq. Chromatogr. & Rel. Technol. **2004**, *27*, 2003–2018.
11. Bogdanov, M.G.; Kandinska, M.I.; Palamarev, Ch.E.; Palamareva, M.D. Automatic selection of mobile phases. V. Thin-layer chromatography on silica vs. alumina of 3,4-disubstituted isochroman-1-ones including spiro analogues. J. Liq. Chrom. & Rel. Technol. **2005**, *28*, 2539–2550.
12. Burdzhiev, N.T.; Palamarev, Ch.E.; Palamareva, M.D. Automatic selection of mobile phases. VI. Thin-layer chromatography on silica of libraries of piperidinones. J. Liq. Chrom. & Rel. Technol. **2006**, *29*, 2045–2057.
13. Bogdanov, M.G.; Palamareva, M.D. *Cis/Trans*-Isochromanones. DMAP induced cycloaddition of homophthalic anhydride and aldehydes. Tetrahedron **2004**, *60*, 2525–2530.
14. Bogdanov, M.G.; Todorov, I.S. Methyl *trans*-6-oxo-11-thiophen-2-yl-11,12-dihydro-6*H*-dibenzo[*c,h*]chromene-12-carboxylate. Acta Crystalogr. Sect. E **2006**, *E62*, 03334–03336.

15. Bogdanov, M.G.; Svinyarov, I.V.; Mitrev, Y.N.; Palamareva, M.D., to be published.
16. Palamareva, M.; Kozekov, I. Chromatographic behaviour of diastereoisomers. XIII. Adsorptivity of esters of Z- and E-2,3-diphenylpropenic acids and similar compounds on silica in terms of the Snyder theory. J. Chromatogr. A **1997**, *758*, 135–144.

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