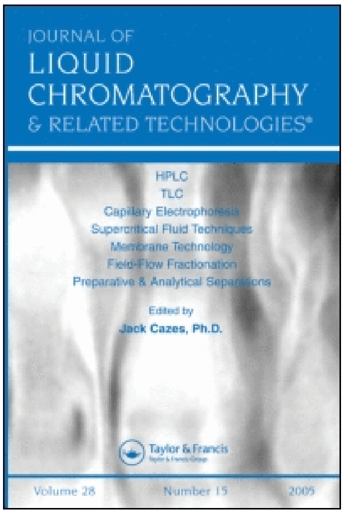

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A First-Level Analysis of The Adsorption Mechanism of Esters of Racemic and Meso-2,3-dibromobutane 1,4-dioic Acids on Silica

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A FIRST-LEVEL ANALYSIS OF THE ADSORPTION MECHANISM OF ESTERS OF RACEMIC AND MESO-2,3-DIBROMOBUTANE-1,4-DIOIC ACIDS ON SILICA

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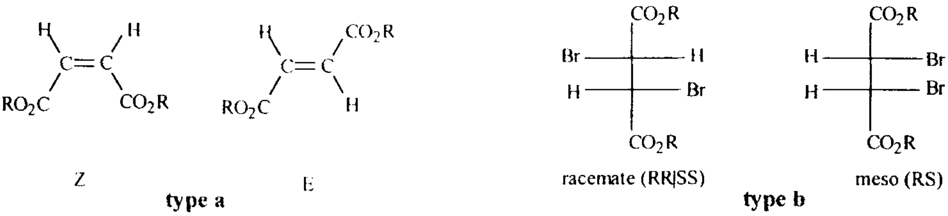
ABSTRACT

The thin-layer chromatographic (TLC) retention of eighteen diastereoisomers of type $RO_2C\text{-}CH(Br)\text{-}CH(Br)\text{-}CO_2R$ on silica was studied with 20 computer-selected on the basis of Snyder theory mobile phases having strength, ε, in the range 0.215-0.305 and significantly greater variation in localization, m, and polarity, P'.

A theoretical analysis, using Soczewiński method, the ε values of the mobile phases used and the stereochemical particularities of the compounds, showed that the two ester groups are the main adsorbing groups, shielded by the bromine atoms, which accounts for the relative retention: racemate > meso found in all cases studied. Two mobile phases of intermediate m values lead to best separation of all diastereoisomeric pairs studied.



$R = \begin{bmatrix} CH_3, C_2H_5, n-C_3H_7, iso-C_3H_7, \\ n-C_4H_9, sec.-C_4H_9, iso-C_4H_9, \\ n-C_5H_{11}, iso-C_5H_{11}, cyclohexyl \end{bmatrix}$

$R = \begin{bmatrix} CH_3, C_2H_5, n-C_3H_7, iso-C_3H_7, \\ n-C_4H_9, sec.-C_4H_9, iso-C_4H_9, \\ n-C_5H_{11}, iso-C_5H_{11} \end{bmatrix}$

Figure 1. Types of the diastereoisomers studied recently[8] and in this paper. One of the enantiomers is represented for the racemate.

INTRODUCTION

In a series of papers,[1] we have reported the TLC adsorptivity of a vast number of conformationally flexible threo-erythro and cis-trans diastereoisomers and rigid Z-E diastereoisomers on, mainly, silica or alumina, with numerous mobile phases. The retention, relative retention and separation of the diastereoisomers have been treated in terms of Snyder theory,[2-4] the Soczewiński method[5] and the Hammett equation.[6,7] Recently, we have studied[8] TLC on silica, of diastereoisomers of type **a** with an increasing size of group R as a simple case of conformationally rigid diastereoisomers possessing only two equal substituents (see Figure 1).

This paper reports the TLC adsorptivity of the related, but conformationally flexible, diastereoisomers of type **b**, containing two bromine atoms instead of the double bond, enabling us to further compare the role of conformational effects. The mobile phases used were selected on the basis of Snyder theory by a computer program[9] whose general validity in this respect has been recently summarised.[10] The discussion of the data obtained includes the application of the Soczewiński method and a first-level analysis of the adsorption mechanism by a newly proposed procedure.[11]

THEORY

The conversion of the experimental R_F to the TLC retention, R_M, and separation, α, was done by the following equations:

$$R_M = \log k' = \log (1/R_F - 1) \qquad (1)$$

$$\log \alpha = R_{M(\text{racemate})} - R_{M(\text{meso})} \qquad (2)$$

where k' is the HPLC retention and the subscripts to R_M in the last equation show the configuration of the compound. According to Eq. 2, positive values of log α correspond to relative retention racemate > meso and vice versa. In addition, a greater absolute log α value indicates a better separation of the corresponding diastereoisomeric pair.

For the case of retention, R_M, of a sample with mobile phases composed of a non-polar or weakly polar solvent A and a polar solvent B, Soczewiñski[5] derived the following equation:

$$R_M = R_{M(B)} - n \log N_B \qquad (3)$$

where N_B is the molar fraction of solvent B, $R_{M(B)}$ is the retention when the solvent is pure B and n is the slope of the linear plot. For a given set of mobile phases, n is proportional to the area of solute molecule under adsorption.[12,13]

According to Snyder theory,[2-4] mobile phases are characterised by strength, ε, proportional to the dimensionless Gibbs energy ($\Delta G^o/RT$ ln 10) of adsorption of the mobile phase, localization, m, measuring the specific interactions adsorbent-composing solvents and polarity, P', measuring the interactions sample (solute)-composing solvents (*cf.*, ref. 10). The greater the ε value, the weaker is the sample retention; m and P' tune the selectivity as measured by log α of solute pairs and strength, respectively.

The dimensionless Gibbs energy of adsorption, Q_i, of a solute group i when $\varepsilon > 0$ is expressed by

$$Q_i = Q_i^o - \varepsilon a_i \qquad (4)$$

where Q_i^o refers to the case when pentane is the mobile phase having $\varepsilon = 0$ and a_i is the relative effective area of group i under adsorption. Adsorption of group i is possible if

$$Q_i > 0 \qquad (5)$$

Q_i^o and, therefore, Q_i refer to the case where group i is substantially free from interactions with other solute groups. The greater Q_i, the stronger is the adsorption of group i.

Table 1

Data for the Mp's or Bp's and Chemical Shift, δ, of the Proton next to Bromine in ^{1}H-NMR Spectra of the Compounds 1-18 Studied of Type b

R	Configuration	No.	mp °C	bp °C	δ_{CHBr}
CH_3	racemate	**1**	42-43		4.75
	meso	**2**	60-61		4.60
CH_2CH_3	racemate	**3**		137-138/12	4.75
	meso	**4**	56-58		4.60
$CH_2CH_2CH_3$	racemate	**5**		155-160/12	4.78
	meso	**6**		165-166/12	4.70
$CH(CH_3)_2$	racemate	**7**		138-140/12	4.68
	meso	**8**	62-63		4.63
$CH_2CH_2CH_2CH_3$	racemate	**9**		178-182/12	4.73
	meso	**10**		186-188/12	4.65
$CH(CH_3)CH_2CH_3$	racemate	**11**		83-85/0.04	4.70
	meso	**12**		170-172/12	4.60
$CH_2CH(CH_3)_2$	racemate	**13**		90-91/0.03	4.73
	meso	**14**		95-96/0.02	4.68
$CH_2CH_2CH_2CH_2CH_3$	racemate	**15**		117-118/0.10	4.73
	meso	**16**		109-110/0.03	4.65
$CH_2CH_2CH(CH_3)_2$	racemate	**17**		102-103/0.03	4.75
	meso	**18**		113-114/0.03	4.70

The mp's are of samples recrystallized from ethanol.
The bp's were measured under vacuum given in mm Hg.
The δ values are in ppm.
The signal for the CHBr proton is a singlet. Its chemical shift is in a higher field for any meso isomer.

The procedure proposed recently by us[11] for a first-level analysis of the adsorption mechanism is based on calculation of Q_i of all groups i participating in the solute structure under conditions used and discussion of the possible electronic and steric interactions between the adsorbing and non-adsorbing groups i.

EXPERIMENTAL

Compounds **1-18** of type **b** were prepared in good to high yields by the following stereospecific reactions: (a) addition of bromine to maleic anhydride and following esterification gave the racemic compounds and (b) addition of bromine to the corresponding ester of fumaric acid resulted in the meso compounds.

The ^{1}H-NMR spectra of compounds **1-18** were measured on a TESLA 80 MHz spectrometer in acetone solutions with TMS as internal standard. Compounds **1-5**, **8**, **9** and **18** are known.[14-19]

TLC was performed on silica 60 DG (Readel de Haen, Germany) using the procedure given in ref. 20. The solvents were of analytical-reagent grade. The R_F values were arithmetic means of four to six measurements, showing a reproducibility of ±0.025. The computer program[9] used was LSChrom Ver. 2 for Windows.

RESULTS AND DISCUSSION

The mp's or bp's and data from ^{1}H-NMR spectra of compounds **1-18** are given in Table 1. Table 2 summarizes the mobile phases 1-20 used with their computer - calculated[9] values of ε, m and P', including N_B for the binary mobile phases. The computer choice of mobile phases 1-18 was similar to that described in ref. 10. The mobile phases are composed of two to four solvents comprising eight non-localizing or weakly-localizing solvents and the localizing diethyl ether, ethyl acetate, methyl *tert*-butyl ether, acetonitrile and tetrahydrofurane.[4] Mobile phases 1-10 and mobile phases 11-15 have equal ε of 0.253 and 0.240, respectively. Mobile phases 5 and 16-20 are composed of hexane (solvent A) and ethyl acetate (solvent B) in different ratios, showing molar fraction, N_B, from 0.026 to 0.201 and ε in the range 0.215-0.303. Thus, all mobile phases used have minimum and maximum ε of 0.215 and 0.303, respectively. They show greater variations in m and P', namely $-0.15 \leq m \leq 0.95$ and $0.19 \leq P' \leq 2.75$.

Table 3 includes the data for the experimental R_F values obtained in TLC on silica of compounds **1-18** with mobile phases 1-20. The values of log α derived by Eqns. 1 and 2 and their average values are also included. The tuning effect of P' on ε is seen. For instance, mobile phases 9 and 10 with the greatest P' when $\varepsilon = 0.253$, lead to reduction in retention and higher R_F. The small difference in ε of mobile phases 1-10 and 11-15 (0.013) results in

Table 2

Mobile Phases used in TLC on Silica and the Corresponding Computer-Calculated[9] Values of Strength, ε, Localization, *m* and Polarity, *P′*, including Binary Mobile Phases

No.	Components	Composition (vol %)	N_B	ε	*m*	*P′*
1	Hexane-diethyl ether	90.00 : 10.00	0.122	0.253	0.61	0.37
2	Hexane-1,2-dichloroethane	60.40 : 39.60	0.516	0.253	0.14	1.45
3	Hexane-dichloromethane	44.11 : 55.89	0.721	0.253	0.10	1.78
4	Hexane-Acetone	97.64 : 2.36	0.041	0.253	0.85	0.22
5	Hexane-ethyl acetate	94.65 : 5.35	0.070	0.253	0.57	0.33
6	Hexane-methyl *tert*-butyl ether	95.85 : 4.15	0.045	0.253	0.73	--
7	Hexane-acetinitrile	97.97 : 2.03	0.049	0.253	0.82	0.22
8	Hexane-tetrahydrofuran	92.61 : 7.39	0.113	0.253	0.95	0.39
9	Chlorobenzene-dichloromethane	87.24 :12.76	0.190	0.253	0.01	2.75
10	Toluene-bromoethane	27.99 : 72.01	0.810	0.253	-0.15	2.11
11	Cyclohexane-tetrachloromethane -diethyl ether	83.72 : 10.00 : 6.28	--	0.240	0.54	0.17
12	Cyclohexane-toluene-benzene -diethyl ether	85.75 : 5.00 : 5.00 : 4.25	--	0.240	0.46	0.20
13	Cyclohexane-toluene-benzene -diethyl ether	77.20 : 10.00 : 10.00 : 2.80	--	0.240	0.34	0.43

(continued)

Table 2 (continued)

Mobile Phases used in TLC on Silica and the Corresponding Computer-Calculated[9] Values of Strength, ε, Localization, *m* and Polarity, *P′*, including Binary Mobile Phases

No.	Components	Composition (vol %)	N_B	ε	*m*	*P′*
14	Cyclohexane-toluene-benzene -diethyl ether	68.00 : 15.00 : 15.00 : 2.00	--	0.240	0.17	0.69
15	Cyclohexane-toluene-benzene -diethyl ether	58.57 : 20.00 : 20.00 : 1.43	--	0.240	0.04	0.94
16	Hexane-ethyl acetate	98.00 : 2.00	0.026	0.215	0.54	0.19
17	Hexane-ethyl acetate	96.14 : 3.86	0.050	0.240	0.56	0.27
18	Hexane-ethyl acetate	92.00 : 8.00	0.103	0.270	0.58	0.44
19	Hexane-ethyl acetate	88.00 : 12.00	0.153	0.288	0.58	0.62
20	Hexane-ethyl acetate	84.00 : 16.00	0.201	0.303	0.59	0.79

Table 3

Experimental R_F Values and Derived Values of log α for the Diastereomeric Compounds 1-18 of Type b

R	Config.	Solute No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	Avg.
A	Racemate	1	0.27	0.26	0.42	0.18	0.24	0.21	0.08	0.34	0.40	0.56	0.26	0.20	0.28	0.26	0.29	0.11	0.19	0.31	0.46	0.55	0.29
	Meso	2	0.41	0.41	0.51	0.27	0.35	0.29	0.13	0.45	0.51	0.62	0.37	0.31	0.39	0.37	0.39	0.18	0.28	0.42	0.58	0.67	0.40
B	Racemate	3	0.36	0.42	0.50	0.26	0.34	0.26	0.11	0.46	0.47	0.61	0.38	0.26	0.36	0.33	0.36	0.16	0.25	0.40	0.58	0.67	0.38
	Meso	4	0.50	0.48	0.55	0.33	0.42	0.33	0.16	0.53	0.54	0.67	0.48	0.38	0.46	0.44	0.47	0.21	0.33	0.49	0.67	0.76	0.46
C	Racemate	5	0.45	0.50	0.55	0.31	0.40	0.31	0.12	0.54	0.55	0.69	0.48	0.32	0.45	0.43	0.45	0.18	0.29	0.47	0.66	0.77	0.45
	Meso	6	0.56	0.56	0.59	0.38	0.48	0.37	0.18	0.59	0.60	0.72	0.54	0.43	0.51	0.49	0.51	0.24	0.37	0.53	0.73	0.84	0.51
D	Racemate	7	0.47	0.50	0.54	0.31	0.42	0.31	0.13	0.55	0.50	0.66	0.44	0.33	0.42	0.39	0.41	0.20	0.31	0.48	0.68	0.78	0.44
	Meso	8	0.56	0.56	0.59	0.38	0.48	0.37	0.18	0.60	0.56	0.71	0.53	0.42	0.50	0.49	0.50	0.25	0.37	0.55	0.74	0.83	0.51
E	Racemate	9	0.50	0.60	0.62	0.37	0.45	0.35	0.18	0.60	0.64	0.75	0.50	0.38	0.49	0.48	0.51	0.21	0.33	0.52	0.73	0.84	0.50
	Meso	10	0.61	0.61	0.62	0.40	0.51	0.38	0.21	0.63	0.65	0.78	0.58	0.47	0.54	0.53	0.55	0.26	0.40	0.58	0.79	0.88	0.55
F	Racemate	11	0.56	0.63	0.58	0.41	0.48	0.42	0.25	0.58	0.58	0.72	0.53	0.47	0.51	0.47	0.51	0.23	0.35	0.56	0.78	0.87	0.52
	Meso	12	0.61	0.64	0.58	0.44	0.52	0.46	0.28	0.61	0.60	0.74	0.60	0.55	0.57	0.52	0.59	0.28	0.40	0.61	0.82	0.89	0.57
G	Racemate	13	0.53	0.63	0.58	0.38	0.48	0.42	0.23	0.56	0.60	0.75	0.53	0.47	0.54	0.49	0.55	0.20	0.32	0.55	0.79	0.87	0.52
	Meso	14	0.63	0.65	0.60	0.45	0.53	0.47	0.28	0.61	0.65	0.77	0.60	0.54	0.58	0.54	0.59	0.26	0.39	0.60	0.84	0.90	0.57
H	Racemate	15	0.53	0.67	0.59	0.39	0.47	0.45	0.24	0.60	0.68	0.80	0.55	0.48	0.57	0.54	0.60	0.22	0.34	0.55	0.78	0.89	0.55
	Meso	16	0.64	0.70	0.61	0.46	0.55	0.51	0.33	0.65	0.69	0.80	0.63	0.57	0.62	0.57	0.64	0.27	0.40	0.61	0.84	0.91	0.60
I	Racemate	17	0.56	0.69	0.60	0.38	0.47	0.44	0.25	0.62	0.64	0.79	0.58	0.53	0.59	0.55	0.60	0.22	0.35	0.56	0.80	0.89	0.56
	Meso	18	0.66	0.69	0.61	0.46	0.55	0.53	0.34	0.68	0.68	0.81	0.64	0.58	0.63	0.57	0.64	0.28	0.41	0.61	0.87	0.91	0.61

(continued)

Table 3 (continued)

Experimental R_F Values and Derived Values of log α for the Diastereomeric Compounds 1-18 of Type b

R	Config.	Solute No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	Avg.
		1-2	0.27	0.30	0.16	0.23	0.23	0.19	0.24	0.20	0.19	0.11	0.22	0.25	0.22	0.22	0.19	0.25	0.22	0.21	0.21	0.22	0.22
		3-4	0.25	0.11	0.09	0.15	0.15	0.15	0.19	0.12	0.12	0.11	0.18	0.24	0.18	0.20	0.20	0.14	0.17	0.16	0.17	0.19	0.16
		5-6	0.19	0.10	0.07	0.13	0.14	0.12	0.21	0.09	0.09	0.06	0.10	0.20	0.10	0.11	0.10	0.16	0.16	0.10	0.14	0.20	0.13
		7-8	0.16	0.10	0.09	0.13	0.11	0.12	0.17	0.09	0.10	0.10	0.16	0.17	0.14	0.18	0.16	0.12	0.12	0.12	0.13	0.14	0.13
		9-10	0.19	0.02	0.00	0.06	0.10	0.06	0.08	0.06	0.02	0.07	0.14	0.16	0.09	0.09	0.07	0.12	0.13	0.11	0.14	0.15	0.09
		11-12	0.09	0.02	0.00	0.05	0.07	0.07	0.07	0.05	0.04	0.04	0.12	0.14	0.11	0.09	0.14	0.11	0.09	0.09	0.11	0.08	0.08
		13-14	0.18	0.04	0.04	0.13	0.09	0.09	0.11	0.09	0.09	0.05	0.12	0.12	0.07	0.09	0.07	0.15	0.13	0.09	0.14	0.03	0.10
		15-16	0.20	0.06	0.04	0.12	0.14	0.10	0.19	0.09	0.02	0.00	0.14	0.16	0.09	0.05	0.07	0.12	0.11	0.11	0.17	0.10	0.10
		17-18	0.18	0.00	0.02	0.14	0.14	0.16	0.19	0.11	0.08	0.05	0.11	0.09	0.07	0.04	0.07	0.14	0.11	0.09	0.22	0.10	0.11
		log α	0.19	0.08	0.05	0.13	0.13	0.12	0.16	0.10	0.08	0.07	0.14	0.17	0.12	0.12	0.12	0.15	0.14	0.12	0.16	0.14	

A: CH_3; B: CH_2CH_3; C: $CH_2CH_2CH_3$; D: $CH(CH_3)_2$; E: $CH_2CH_2CH_2CH_3$; F: $CH(CH_3)CH_2CH_3$; G: $CH_2CH(CH_3)_2$; H: $CH_2CH_2CH_2CH_2CH_3$; I: $CH_2CH_2CH(CH_3)_2$. For composition of mobile phases, see Table 1. The log α values were calculated from R_F by Eq. 1 and 2. The log α values are average values of *log α for all diastereomeric pairs obtained with a given mobile phase.*

practically equal average R_F of 0.49 and 0.48, respectively. Similarly to a previous study,[10] a linear relationship was found between the average R_F values of the individual compounds of a given configuration with mobile phases 1-10 and 11-15 of equal ε and the corresponding standard deviations, S.D., within R_F.. The plots show S.D. in the range 0.003-0.012. The relative retention racemate > meso was established in all cases studied as seen from the positive log α independently of the size of group R and the variation in ε, m, P' and N_B.

Using linear regression analysis, the retention, R_M, of compounds **1-18** with mobile phases 5 and 16-20 and the corresponding N_B showed a good agreement with Eq. 3. The resulting data for the slope, n, intercept, $R_{M(B)}$, correlation coefficient, r, and S.D. are summarised in Table 4.

Table 5 includes literature data[2] for Q_i^o, a_i and calculated by eqn. 4 Q_i values for the groups i participating in the structure of compounds **1-18** under the conditions used specified by the mobile phases 16 and 20 of minimum and maximum ε, respectively.

Application of the Soczewiñski Method

The data of Table 4 show that the Soczewiñski method is applicable to the cases studied showing average r of 0.957 and *S.D.* of 0.11. The very close n values for any diastereoisomeric pair support practically equal, within the experimental error, solute areas under adsorption and, therefore, same adsorbing groups for the individual diastereoisomers. For all compounds studied, the absolute n values increase from 1.11 to 1.63 with the increase in the size of group R supporting that the two ester groups are adsorbing in any case. The increase in the area of the ester groups is expected on the basis of their increasing a_i values given in Table 5. The values of the slope, n, and intercept, $R_{M(B)}$, found determine practically parallel plots for any diastereoisomeric pair showing always a stronger retention for the racemic isomer (see Figure 2), which means that the relative retention racemate > meso cannot change with any variation of N_B.

The Relative Retention of Diastereoisomers 1-18 in Terms of a First-level Analysis of the Adsorption Mechanism

As seen from Table 5, the Q_i values of bromine and the ester groups are positive under conditions used. Considerable changes in Q_i are not expected because both bromine and the ester groups have negative inductive effects and

Table 4

Data for the Slope, *n*, Intercept, $R_{M(B)}$, Correlation Coefficient, *r*, and S.D. of the Linear Relationships R_M vs. log N_B * Found for Compounds of Type b with Mobile Phases 5 and 16-20 Composed of Hexane and Ethyl Acetate

R	Configuration	No.	*n*	$R_{M(B)}$	*r*	*S.D.*
CH_3	Racemate	**1**	-1.11	-0.82	0.986	0.05
	Meso	**2**	-1.08	-1.00	0.980	0.06
CH_2CH_3	Racemate	**3**	-1.15	-1.06	0.978	0.06
	Meso	**4**	-1.19	-1.26	0.975	0.07
$CH_2CH_2CH_3$	Racemate	**5**	-1.31	-1.35	0.973	0.08
	Meso	**6**	-1.32	-1.51	0.951	0.11
$CH(CH_3)_2$	Racemate	**7**	-1.28	-1.35	0.966	0.09
	Meso	**8**	-1.29	-1.49	0.962	0.09
$CH_2CH_2CH_2CH_3$	Racemate	**9**	-1.42	-1.59	0.957	0.11
	Meso	**10**	-1.45	-1.74	0.948	0.12
$CH(CH_3)CH_2CH_3$	Racemate	**11**	-1.51	-1.75	0.953	0.12
	Meso	**12**	-1.49	-1.82	0.946	0.13
$CH_2CH(CH_3)_2$	Racemate	**13**	-1.61	-1.84	0.960	0.12
	Meso	**14**	-1.60	-1.95	0.944	0.14
$CH_2CH_2CH_2CH_2CH_3$	Racemate	**15**	-1.60	-1.85	0.939	0.15
	Meso	**16**	-1.61	-1.98	0.941	0.15
$CH_2CH_2CH(CH_3)_2$	Racemate	**17**	-1.62	-1.89	0.945	0.14
	Meso	**18**	-1.63	-2.04	0.930	0.16
Average					0.957	0.11

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* N_B is the molar fraction of ethyl acetate in mobile phases 5 and 16-20.

resonance between them cannot occur. In addition, the bromine atom is bulkier than CO_2CH_3 on the basis of their conformational energies of 1.3 kcal/mol and 0.9 kcal/mol,[21] respectively. To evaluate the relative role of the adsorptivity and size of bromine, we calculated the average R_F on same silica of the compounds of type **a** and type **b** established with hexane-ethyl acetate 92:8 (ε = 0.270, mobile phase 19 of ref. 8 and mobile phase 18 of this study). The values found were 0.37 and 0.52, respectively. This shows that compounds **1-18** of type **b** have smaller adsorptivity. The same phenomenon is seen with hexane-ethyl acetate 98:2 with ε = 0.215. Thus, the presence of two bromine atoms

Table 5

Data According to Snyder[2] for the Adsorption Properties on Silica of Groups *i* Participating in the Compounds Studied

Group *i*	Q_i^0	a_i	$Q_i = Q_i^0 - \varepsilon a_i$ $\varepsilon=0.215$	 $\varepsilon=0.303$
Br	1.94	1.80	1.55	1.39
CH_3	0.07	1.60	-0.27	-0.41
CH_2	-0.05	0.90	-0.24	-0.32
CO_2CH_3	5.27	10.50	3.01	2.09
$CO_2C_2H_5$	5.22	11.40	2.77	1.77
$CO_2C_3H_7$-n	5.17	12.30	2.53	1.44
$CO_2C_3H_7$-iso	5.29	13.00	2.50	1.35
$CO_2C_4H_9$-n	5.12	13.20	2.28	1.12
$CO_2C_4H_9$-sec	5.24	13.90	2.25	1.03
$CO_2C_4H_9$-iso	5.24	13.90	2.25	1.03
$CO_2C_5H_{11}$-n	5.07	14.10	2.04	0.80
$CO_2C_5H_{11}$-iso	5.19	14.80	2.01	0.71

The data for Q_i^0 and a_i are taken from ref. 2, p. 200 and p. 264 or calculated by summation of the contribution of the composing fragments. The calculated by Eq. 4 Q_i values refer to the mobile phases of minimum and maximum ε value used.

with $Q_i > 0$ does not increase the retention of the compounds of type **b** and, therefore, these atoms are expected to have mainly a shielding role. Consequently, adsorption of any two equal ester groups, hindered by the bromine atoms, is the expected simplified adsorption mechanism. The ester groups and, more precisely, their carbonyls having an increased electron density can form hydrogen bonds with the silanol groups. The two-point adsorption occurs *via* site chelation (see ref. 2, p. 315), *i.e.*, interaction of two adjacent adsorbing groups with a given adsorption site. Conformations suitable for site chelation of the two ester groups are M for the racemates and N for the meso isomers having these two groups in *gauche* position (see Figure 3). For the racemate, another conformation M' with *gauche* esters hindered by each of the bromine atoms is not taken into account because the conformational equilibrium is expected to shift to the conformation which will give best adsorption.

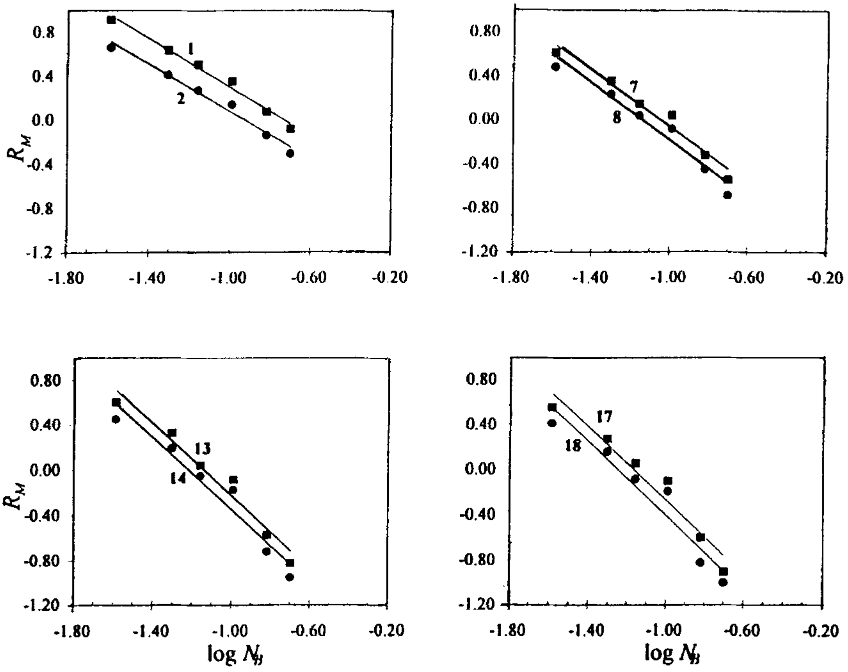

Figure 2. R_M vs. log N_B plots on the basis of the data of Table 2 and Table 3 for diastereoisomers **1**, **2**, **7**, **8**, **13**, **14**, **17** and **18**. N_B is the molar fraction of ethyl acetate in mobile phases 5 and 16-20.

Any racemic compound is expected to show a stronger adsorption because the adsorbing ester groups are not hidered by a bromine atom. On the contrary, such a hindrance is present in the corresponding meso isomer, leading to the relative retention racemate > meso which was found in fact (see Figure 4).

Separation, α, of the Diastereoisomers Studied and Some Comparisons

A fair linear relationship between log α and *m* was not observed in this study (cf., refs. 4, 7, 8, 20 and 22). Best separations of all diastereoisomeric pairs studied were obtained with mobile phase 1 and mobile phase 12, showing average log α values, $\overline{\log \alpha}$, of 0.19 and 0.17, respectively (see Table 3). These two mobile phases are of intermediate *m* values (0.61 and 0.46) and contain the strongly localizing diethyl ether.

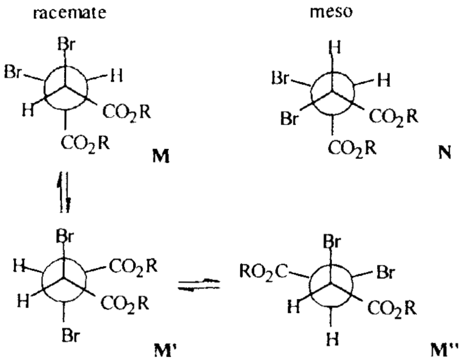

Figure 3. Conformations of the diastereoisomers studied.

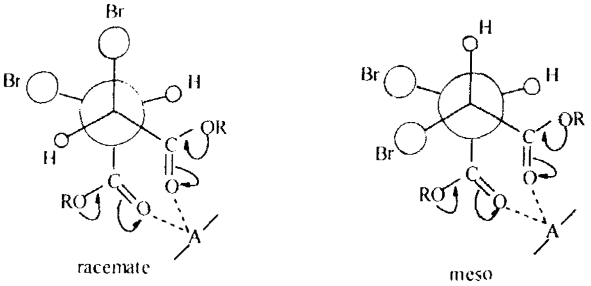

Figure 4. Schematic illustration of the expected adsorption mechanism on silica for the diastereoisomers studied. A is an adsorption site, probably reactive silanols (see ref. 2, p. 157) suitable for site chelation.

The absence of such a solvent, as in mobile phases 2, 3, 9 and 10, reduces the separation and $\log \alpha$ is in the range 0.05-0.08. Mobile phases 12-15 are composed of cyclohexane, toluene, benzene and diethyl ether in different ratios. Best separation was established with mobile phase 12 having the greatest m (0.46) because of the greatest content of diethyl ether.

Let us discuss the average separation of any diastereoisomeric pair obtained with all mobile phases used. According to Table 3, the diastereoisomeric pairs **1-2** and **3-4** with group R equal to methyl and ethyl show best separation and average log α of 0.22 and 0.16, respectively. This probably is due to the stronger adsorptivity of these compounds than that of the remaining compounds with a bulkier group R. The opposite is true for the compounds of type **a.**[1]

Taking into account all log α values found in ref. 8 and this study, we calculated the corresponding average values for the diastereoisomers of type a and type **b** being 0.34 and 0.12, respectively. In our opinion, this reduction in the separation of the diastereoisomers of type **b** is due to changes both in the structure and the conformational stability of the two types of compounds. The presence of the shorter double bond in the compounds of type **a** will lead to an increase in the site chelation of the two ester groups in any Z isomer and a greater difference in the retention of the corresponding E isomer where site chelation is not possible because of the rigid conformation. Such an improvement in the site chelations for the two diastereoisomers of type **b** cannot occur owing to the presence of the longer C(2) - C(3) bond. This assumption is further supported by the fact that the conformationally rigid diastereoisomers of type C_6H_5-CH=C(CO_2R)-C_6H_5, with expected one-point adsorption of the ester group and, therefore, without site chelation, show the same smaller separation[11] as the compounds of type b studied.

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