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# Chromatographic behaviour of diastereoisomers XIII[1]. Adsorptivity of esters of Z- and E-2,3-diphenylpropenoic acids and similar compounds on silica in terms of the Snyder theory

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## Abstract

Thin-layer chromatography (TLC) of eight $Z$ and $E$ esters of the type $C_6H_5CH=C(C_6H_5)CO_2R$ was studied using 20 computer-selected mobile-phases on the basis of the Snyder theory, the mobile phases having strength, $\varepsilon$, equal to 0.165 or 0.250 and different values of localization, $m$ and polarity, $P'$. The available values of $\varepsilon$ enabled the calculation of the energy of adsorption of all groups $i$ participating in the solute structures under selected conditions. The ester group proved to be the only adsorbing group. This, in combination with the configuration of the diastereoisomers, explained their adsorptivity including the relative retention $E>Z$ found in all cases studied. The approach was applied to data found by Cooper for eight similar diastereoisomers. The tuning effect of $P'$ on $\varepsilon$ and adsorptivity is discussed, both being of importance in the selection of mobile phases for liquid–solid chromatography (LSC), including preparative separations. The application of the Snyder theory to the diastereoisomers studied in this series of papers is summarised.

*Keywords:* Diastereoisomer separation; Adsorption; Mobile phase composition; Diphenylpropenoic acid esters; Organic acids

## 1. Introduction

Throughout this series of papers [1,2], we have studied the TLC of a vast number of acyclic and cyclic diastereoisomers including $Z$ and $E$ alkenes in an effort to elucidate their experimental adsorptivity and expected adsorption mechanism on the basis of the Snyder theory [3–5] and Soczewiński's method [6]. Some progress has been made in the development of a computer program [7] which enabled us to

apply the Snyder theory in a quantitative form [2,8,9], in contrast to our first attempts [10,11]. Our main aims have been the relative retention of the diastereoisomers studied, i.e., which isomer is better adsorbed and retained, and the separation of the diastereoisomers. The above mentioned computer program allows a wide range of mobile phases in LSC to be studied in detail [8]. All these aspects are of great importance in practice.

This paper reports the TLC adsorptivity on silica of eight $Z$ and $E$ diastereoisomers of type $a$ (see Fig. 1) which share structural similarities with the diastereoisomers of type $b$ and type $c$. For the last two

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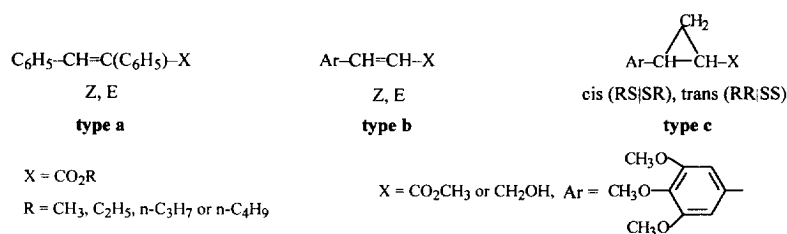[1] For part XII, see Ref. [2].

Fig. 1. Types of the compounds studied.

cases, the relative retentions on silica established by Cooper [12] have not been understood until now, so we include them in the discussion.

The size of group R in the diastereoisomers of type *a* shows a similar increase to that in our previous studies [2,8,13–18] which could, in principle, induce a change in the relative retention of the diastereoisomers of a given type as found for some diastereoisomers and explained by a change of the adsorption mechanism [13,14,18].

## 2. Theory

Because of the generalised character of this paper, we would like to reiterate some of the important points of Snyder's theory [3–5]. Its model, the so-called displacement model, regards retention as a displacement process where a sample (solute) molecule S displaces $n$ molecules of mobile phase M from the adsorbent surface.

$$S_n + nM_a = S_a + nM_n \qquad (1)$$

where the subscripts n and a denote non-adsorbed and adsorbed state, respectively.

The mobile phases are characterised by the following dimensionless parameters:

1. Strength, $\varepsilon$, measuring the dimensionless Gibbs energy ($\Delta G^\circ/RT$ ln 10) of adsorption of the mobile phase per unit area of the adsorbent surface; according to Eq. (1), the greater the value of $\varepsilon$, the weaker the sample retention is.
2. Localization, $m$, measuring the capability of the mobile phase for interaction via the available functional group(s) of the composing solvent(s)

with specific adsorption sites such as silanol hydroxyl group for silica; it determines to a great extent the selectivity of the mobile phase.
3. Polarity, $P'$, measuring the total interaction of the mobile phase with sample; it tunes the mobile phase strength: a greater value of $P'$ within mobile phases of given $\varepsilon$ means a better solubility of the sample in the corresponding mobile phase and therefore leads to a weaker retention (see for instance [8,9]).

The adsorptivity of a group $i$ in the solute molecule is measured by the dimensionless Gibbs energy of adsorption, $Q_i^\circ$, with pentane having $\varepsilon = 0$. If the mobile phase has $\varepsilon$ greater than zero, the net energy of adsorption, $Q_i$, is reduced by the energy loss for desorption of mobile-phase molecule(s) from the adsorbent surface.

$$Q_i = Q_i^\circ - \varepsilon a_i \qquad (2)$$

where $a_i$ is the relative effective area of group $i$ under adsorption. $Q_i$ refers to the case where group $i$ is substantially free from interactions with other solute groups. Only positive values of $Q_i$ denote adsorption of group $i$. The higher $Q_i$, the stronger is the adsorption of group $i$.

In this study, we calculated the TLC retention, $R_M$, and selectivity (separation factor or simply separation), $\alpha$, of diastereoisomeric pairs on the basis of the experimentally measured parameter $R_F$ and the following equations:

$$R_M = \log k' = \log (1/R_F - 1) \qquad (3)$$

$$\log \alpha = R_{M(Z)} - R_{M(E)} \qquad (4)$$

$$\log \alpha = R_{M(cis)} - R_{M(trans)} \qquad (4a)$$

were $k'$ is the HPLC retention and subscripts to $R_M$ in the last two equations show the configuration of the compound. Positive values of log $\alpha$ correspond to relative retention $Z > E$ or $cis > trans$ and vice versa. The absolute values of log $\alpha$ measure the separation within diastereoisomeric pairs. The greater this value of log $\alpha$, the better the separation is.

According to Snyder, the retention, $R_M$, of a given compound is a function of $Q_i$ of the adsorbing group(s) $i$, the electronic and steric interaction between all groups $i$, their localization and secondary effects if any [3,10]. This generalisation will be used for elucidation of the adsorption mechanism and relative retention of the diastereoisomers studied.

## 3. Experimental

Compounds **1–8** of type $a$ were prepared by esterification of the corresponding diastereoisomeric acids [19]. Compounds **1, 3, 5** and **7** were purified from small amounts of $E$ isomer by low-pressure column chromatography on silica HF (Merck, Germany) with hexane–toluene (85:15). Compounds **3–8** are newly synthesised. The boiling points of compounds **4, 6** and **8** are 169–170°C/2 mmHg (1 mmHg = 133.322 Pa), 180–182°C/2 mmHg and 175–177°C/1 mmHg, respectively. In the $^1$H NMR spectra, the proton next to the double bond is a singlet with the following shifts in ppm for the compounds given in parentheses: 7.08 (**1**), 7.88 (**2**), 6.95 (**3**), 7.88 (**4**), 7.08 (**5**), 7.90 (**6**), 7.10 (**7**) and 7.88 (**8**). Thus, any $Z$ isomer has this signal in a higher field than its diastereoisomer.

From compounds **9–16** of type $b$ and type $c$, only compounds **11** and **15** show intramolecular hydrogen bonds of type Ar···HO on the basis of their IR spectra in $10^{-3}$ $M$ chloroform solutions.

TLC of compounds **1–8** was performed on silica 60 GF$_{254}$ (Merck, Germany) using the procedure given in Ref. [16]. The solvents were of analytical-reagent grade. The $R_F$ values were arithmetic means of four to six measurements showing a reproducibility of ±0.02.

The computer program [7] used was LSChrom Ver. 2 for Windows.

## 4. Results and discussion

Table 1 shows the mobile phases 1–20 used by us and mobile phases 21–25 used by Cooper [12] for TLC on silica of compounds **1–8** and compounds **9–16**, respectively. The computer calculated [7] values of $\varepsilon$, $m$ and $P'$ of all mobile phases are also included. The computer choice of mobile phases 1–20 was similar to that described in Ref. [2]. All mobile phases are composed of one to four solvents comprising the non-localizing or weakly localizing hexane, cyclohexane, benzene, chlorobenzene, toluene, chloroform, tetrachloromethane, dichloromethane and 1,2-dichloroethane and the localizing diethyl ether, diisopropyl ether, ethyl acetate, acetone, tetrahydrofurane and isopropanol [5].

The strength, $\varepsilon$, is equal for mobile phases 1–15 (0.165) and for mobile phases 16–20 (0.250) but $m$ and $P'$ vary considerably in the ranges $-0.42 < m < 0.95$ and $-0.14 < P' < 2.70$. For mobile phases 21–25, $\varepsilon$ is in the range from 0.337 to more than 0.401. In the calculations of $\varepsilon$, $m$ and $P'$ of mobile phases 21–25, light petroleum was substituted by hexane and mobile phase 25 (light petroleum–methanol, (6:1)) was characterised by the similar hexane–isopropanol (6:1) because of the absence of input data for methanol.

Table 2 summarises the data for the experimental $R_F$ values on silica of compounds **1–8**, their retention, $R_M$, and separation, $\alpha$, derived by Eq. (3) and Eq. (4) and some average values. These data for compounds **9–16** [12] are shown in Table 3.

Table 4 includes literature data [3] for $Q_i^{\,\circ}$, $a_i$ and $Q_i^{\,\circ}$ values calculated by Eq. (2) for the groups $i$ participating in the structure of compounds **1–16** under the conditions specified by the mobile phases of minimum and maximum $\varepsilon$.

Based on the generalization given under (Section 2), we propose the following procedure for a first level analysis of adsorptivity and adsorption mechanism:

1. Calculation of $Q_i$ for all groups $i$ participating in the structure of the compounds of a given type.
2. Discussion of the possible electronic interactions between groups $i$ that can change the $Q_i$ values and specification of the adsorbing group(s) $i$.

Table 1

Mobile phases used in TLC on silica and the corresponding computer-calculated [7] values of strength, $\varepsilon$, localization, $m$ and polarity, $P'$

| No. | Components | Composition (%, v/v) | $\varepsilon$ | $m$ | $P'$ |
|---|---|---|---|---|---|
| *For compounds 1–8* | | | | | |
| 1 | Hexane–toluene | 50.00:50.00 | 0.165 | −0.42 | 1.25 |
| 2 | Hexane–chloroform | 68.18:31.82 | 0.165 | 0.09 | 1.37 |
| 3 | Hexane–dichloromethane | 78.74:21.26 | 0.165 | 0.09 | 0.74 |
| 4 | Hexane–diisopropyl ether | 85.90:14.10 | 0.165 | 0.08 | 0.42 |
| 5 | Hexane–1,2-dichloroethane | 85.05:14.95 | 0.165 | 0.12 | 0.61 |
| 6 | Hexane–benzene | 65.80:34.20 | 0.165 | −0.40 | 0.99 |
| 7 | Cyclohexane–diethylether | 97.91:2.09 | 0.165 | 0.38 | −0.14 |
| 8 | Cyclohexane–tetrahydrofurane | 98.26:1.74 | 0.165 | 0.68 | −0.13 |
| 9 | Cyclohexane–chlorobenzene | 58.61:41.39 | 0.165 | −0.11 | 1.00 |
| 10 | Hexane–toluene–diisopropyl ether | 81.12:10.00:8.88 | 0.165 | −0.05 | 0.53 |
| 11 | Hexane–tetrachloromethane–toluene | 24.00:30.00:46.00 | 0.165 | −0.42 | 1.61 |
| 12 | Hexane–1,2-dichloroethane–diisopropyl ether | 87.40:5.00:7.60 | 0.165 | 0.10 | 0.45 |
| 13 | Hexane–tetrachloromethane–chloroform–dichloromethane | 68.24:10.00:5.00:16.76 | 0.165 | 0.06 | 0.95 |
| 14 | Hexane–tetrachloromethane–dichloromethane–diisopropyl ether | 73.93:10.00:10.00:6.07 | 0.165 | 0.05 | 0.69 |
| 15 | Hexane–diethyl ether | 98.05:1.95 | 0.165 | 0.48 | 0.15 |
| 16 | Benzene | 100.00 | 0.250 | −0.42 | 2.70 |
| 17 | Hexane–diethyl ether | 90.62:9.38 | 0.250 | 0.61 | 0.35 |
| 18 | Hexane–diisopropyl ether | 55.49:44.51 | 0.250 | 0.10 | 1.12 |
| 19 | Hexane–1,2-dichloroethane | 61.62:38.38 | 0.250 | 0.14 | 1.41 |
| 20 | Hexane–tetrahydrofurane | 92.98:7.02 | 0.250 | 0.95 | 0.37 |
| *For compounds 9–16* | | | | | |
| 21 | Hexane–acetone | 75.00:25.00 | 0.382 | 0.93 | 1.35 |
| 22 | Benzene–ethyl acetate | 80.00:20.00 | 0.357 | 0.42 | 3.04 |
| 23 | Benzene–ethyl acetate | 60.00:40.00 | 0.402 | 0.55 | 3.38 |
| 24 | Hexane–acetone | 87.50:12.50 | 0.337 | 0.92 | 0.73 |
| 25 | Hexane–isopropanol | 85.71:14.29 | 0.401 | | 0.64 |

Mobile phases 21–25 are used by Cooper [12] for TLC on silica of compounds **9–16**.

3. Discussion of the expected steric interactions of the adsorbing group(s) $i$ with the non-adsorbing groups $i$ taking into account the configuration and conformation of the compounds.

4. Discussion of the possible secondary effects, if any.

Considerable differences in the localization of diastereoisomers are not expected because of the equal adsorbing groups supported by the application of Soczewiński's method [13,15].

Section 4.1 and Section 4.2 below show such a type of analysis for compounds **1–8** and compounds **9–16**, respectively. In addition, it also generalises the importance of the computer program [7] used for selection of mobile phases for analytical and preparative normal-phase LSC emphasising the tuning effect of $P'$ on $\varepsilon$ and the solute adsorptivity.

### 4.1. Retention, relative retention and separation of diastereoisomers 1–8 of type a

For compounds **1–8** of type $a$, the adsorption of the double bond and the two phenyl groups is unimportant because the corresponding $Q_i$ values are close or equal to zero under the conditions used (see Table 4). Any ester group shows considerably greater $Q_i$ values in the range 1.82–3.54. Consequently, the only adsorbing group for compounds **1–8** is the ester group (ester carbonyl) which is a better electron-donating group than the etherial part in the formation of hydrogen bonds with the silanol hydroxyl groups. This fact together with the decreasing values of $Q_{CO_2R}$ with the increase of the size of group R from Table 4 accounts for the decreasing adsorptivity of the compounds with a given configuration when the same mobile phase is used. For

Table 2
Experimental $R_F$ values and derived values of $R_M$ and log $\alpha$ for the diastereoisomeric compounds 1–8 of type $a$

**$R_F$ for indicated mobile phase**

| X | Config-uration | No. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | Average |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $CO_2CH_3$ | Z | 1 | 0.24 | 0.33 | 0.14 | 0.49 | 0.15 | 0.20 | 0.28 | 0.23 | 0.15 | 0.41 | 0.32 | 0.44 | 0.18 | 0.54 | 0.12 | 0.67 | 0.42 | 0.84 | 0.60 | 0.47 | 0.36 |
| | E | 2 | 0.17 | 0.27 | 0.10 | 0.46 | 0.10 | 0.13 | 0.21 | 0.19 | 0.09 | 0.36 | 0.22 | 0.39 | 0.13 | 0.49 | 0.08 | 0.55 | 0.38 | 0.84 | 0.45 | 0.47 | 0.30 |
| $CO_2C_2H_5$ | Z | 3 | 0.26 | 0.30 | 0.14 | 0.52 | 0.15 | 0.21 | 0.29 | 0.25 | 0.15 | 0.45 | 0.33 | 0.48 | 0.19 | 0.54 | 0.11 | 0.67 | 0.48 | 0.86 | 0.60 | 0.52 | 0.38 |
| | E | 4 | 0.19 | 0.27 | 0.11 | 0.50 | 0.11 | 0.15 | 0.24 | 0.23 | 0.10 | 0.41 | 0.24 | 0.43 | 0.14 | 0.50 | 0.09 | 0.58 | 0.44 | 0.87 | 0.51 | 0.52 | 0.33 |
| $CO_2C_3H_{7-n}$ | Z | 5 | 0.29 | 0.34 | 0.15 | 0.57 | 0.17 | 0.22 | 0.35 | 0.29 | 0.17 | 0.50 | 0.37 | 0.52 | 0.19 | 0.54 | 0.12 | 0.71 | 0.50 | 0.87 | 0.65 | 0.55 | 0.40 |
| | E | 6 | 0.23 | 0.29 | 0.12 | 0.54 | 0.13 | 0.20 | 0.28 | 0.26 | 0.12 | 0.46 | 0.29 | 0.48 | 0.15 | 0.50 | 0.10 | 0.63 | 0.49 | 0.87 | 0.58 | 0.55 | 0.36 |
| $CO_2C_4H_{9-n}$ | Z | 7 | 0.34 | 0.35 | 0.15 | 0.59 | 0.18 | 0.23 | 0.35 | 0.31 | 0.19 | 0.54 | 0.40 | 0.54 | 0.21 | 0.55 | 0.12 | 0.71 | 0.53 | 0.88 | 0.67 | 0.56 | 0.42 |
| | E | 8 | 0.26 | 0.31 | 0.12 | 0.57 | 0.14 | 0.21 | 0.31 | 0.29 | 0.13 | 0.50 | 0.32 | 0.50 | 0.16 | 0.53 | 0.10 | 0.66 | 0.51 | 0.88 | 0.52 | 0.56 | 0.38 |

**$R_M$ for indicated mobile phase**

| X | Config. | No. | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 | Average |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| $CO_2CH_3$ | Z | 1 | 0.50 | 0.31 | 0.79 | 0.02 | 0.75 | 0.60 | 0.41 | 0.52 | 0.75 | 0.16 | 0.33 | 0.10 | 0.66 | -0.07 | 0.87 | -0.31 | 0.14 | -0.72 | -0.18 | 0.05 | 0.28 |
| | E | 2 | 0.69 | 0.43 | 0.95 | 0.07 | 0.95 | 0.83 | 0.58 | 0.63 | 1.00 | 0.25 | 0.55 | 0.19 | 0.83 | 0.02 | 1.06 | -0.09 | 0.21 | -0.72 | 0.09 | 0.05 | 0.43 |
| $CO_2C_2H_5$ | Z | 3 | 0.45 | 0.37 | 0.79 | -0.03 | 0.75 | 0.58 | 0.39 | 0.48 | 0.75 | 0.09 | 0.31 | 0.03 | 0.63 | -0.07 | 0.91 | -0.31 | 0.03 | -0.79 | -0.18 | -0.03 | 0.26 |
| | E | 4 | 0.63 | 0.43 | 0.91 | 0.00 | 0.91 | 0.75 | 0.50 | 0.52 | 0.95 | 0.16 | 0.50 | 0.12 | 0.79 | 0.00 | 1.00 | -0.14 | 0.10 | -0.79 | -0.02 | -0.03 | 0.37 |
| $CO_2C_3H_{7-n}$ | Z | 5 | 0.39 | 0.29 | 0.75 | -0.12 | 0.69 | 0.55 | 0.27 | 0.39 | 0.69 | 0.00 | 0.23 | -0.03 | 0.63 | -0.07 | 0.87 | -0.39 | 0.00 | -0.83 | -0.27 | -0.09 | 0.20 |
| | E | 6 | 0.52 | 0.39 | 0.87 | -0.07 | 0.83 | 0.60 | 0.41 | 0.45 | 0.87 | 0.07 | 0.39 | 0.03 | 0.75 | 0.00 | 0.95 | -0.23 | 0.02 | -0.83 | -0.14 | -0.09 | 0.29 |
| $CO_2C_4H_{9-n}$ | Z | 7 | 0.29 | 0.27 | 0.75 | -0.16 | 0.66 | 0.52 | 0.27 | 0.35 | 0.63 | -0.07 | 0.18 | -0.07 | 0.58 | -0.09 | 0.87 | -0.39 | -0.05 | -0.87 | -0.31 | 0.10 | 0.16 |
| | E | 8 | 0.45 | 0.35 | 0.87 | -0.12 | 0.79 | 0.58 | 0.35 | 0.39 | 0.83 | 0.00 | 0.33 | 0.00 | 0.72 | -0.05 | 0.95 | -0.29 | -0.02 | -0.87 | -0.03 | -0.10 | 0.26 |

**Log $\alpha$ for indicated mobile phase**

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | 20 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **1-2** | -0.19 | -0.12 | -0.17 | -0.05 | 0.20 | -0.22 | -0.17 | -0.10 | -0.25 | -0.09 | -0.22 | -0.09 | -0.17 | -0.09 | -0.20 | -0.22 | -0.07 | 0.00 | -0.26 | 0.00 |
| **3-4** | -0.18 | -0.06 | -0.12 | -0.03 | -0.15 | -0.18 | -0.11 | -0.05 | -0.20 | -0.07 | -0.19 | -0.09 | -0.16 | -0.07 | -0.10 | -0.17 | -0.07 | 0.00 | -0.16 | 0.00 |
| **5-6** | -0.14 | -0.10 | -0.11 | -0.05 | -0.14 | -0.05 | -0.14 | -0.07 | -0.18 | -0.07 | -0.16 | -0.07 | -0.12 | -0.07 | -0.09 | -0.16 | -0.02 | 0.00 | -0.13 | 0.00 |
| **7-8** | -0.17 | -0.08 | -0.11 | -0.04 | -0.13 | -0.05 | -0.08 | -0.04 | -0.20 | -0.07 | -0.15 | -0.07 | -0.14 | -0.03 | -0.09 | -0.10 | -0.03 | 0.00 | -0.27 | 0.00 |
| $\overline{\log\alpha}$ | -0.17 | -0.09 | -0.13 | -0.04 | -0.16 | -0.13 | -0.12 | -0.06 | -0.21 | -0.08 | -0.18 | -0.08 | -0.15 | -0.07 | -0.12 | -0.16 | -0.05 | 0.00 | -0.21 | 0.00 |

For composition of mobile phases, see Table 1. The values of $R_M$ and log $\alpha$ were calculated from $R_F$ by Eq. (3) and Eq. (4).
The $\overline{\log\alpha}$ values are average values of log $\alpha$ for all diastereoisomeric pairs obtained with a given mobile phase.

Table 3
Experimental $R_F$ values established by Cooper [12] and derived values of $R_M$ and log $\alpha$ for the diastereoisomeric compounds **9–16** of type $b$ and type $c$

| X | Solute | | $R_F$ for indicated mobile phase | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Configuration | No. | 21 | 22 | 23 | 24 | 25 | Average |
| *Type b* | | | | | | | | |
| $CO_2CH_3$ | Z | **9** | 0.69 | 0.70 | 0.86 | 0.49 | 0.47 | 0.64 |
| | E | **10** | 0.66 | 0.68 | 0.86 | 0.40 | 0.35 | 0.59 |
| $CH_2OH$ | Z | **11** | 0.28 | 0.09 | 0.49 | | | 0.29 |
| | E | **12** | 0.23 | 0.09 | 0.46 | | | 0.26 |
| *Type c* | | | | | | | | |
| $CO_2CH_3$ | cis | **13** | 0.63 | 0.57 | 0.80 | 0.35 | 0.26 | 0.52 |
| | trans | **14** | 0.65 | 0.65 | 0.84 | 0.43 | 0.38 | 0.59 |
| $CH_2OH$ | cis | **15** | 0.27 | 0.07 | 0.43 | | | 0.26 |
| | trans | **16** | 0.24 | 0.07 | 0.43 | | | 0.25 |
| | | | $R_M$ for indicated mobile phase | | | | | |
| $CO_2CH_3$ | Z | **9** | −0.35 | −0.37 | −0.79 | 0.02 | 0.05 | −0.29 |
| | E | **10** | −0.29 | −0.33 | −0.79 | 0.18 | 0.27 | −0.19 |
| $CH_2OH$ | Z | **11** | 0.41 | 1.00 | 0.02 | | | 0.48 |
| | E | **12** | 0.52 | 1.00 | 0.07 | | | 0.53 |
| $CO_2CH_3$ | cis | **13** | −0.23 | −0.12 | −0.60 | 0.27 | 0.45 | −0.05 |
| | trans | **14** | −0.27 | −0.27 | −0.72 | 0.12 | 0.21 | −0.18 |
| $CH_2OH$ | cis | **15** | 0.43 | 1.12 | 0.12 | | | 0.56 |
| | trans | **16** | 0.50 | 1.12 | 0.12 | | | 0.58 |
| | | | log $\alpha$ for indicated mobile phase | | | | | |
| | | **9–10** | −0.06 | −0.04 | 0.00 | −0.16 | −0.22 | −0.10 |
| | | **11–12** | −0.11 | 0.00 | −0.05 | | | −0.06 |
| | | **13–14** | 0.04 | 0.15 | 0.12 | 0.15 | 0.24 | 0.14 |
| | | **15–16** | −0.07 | 0.00 | 0.00 | | | −0.02 |

For composition of mobile phases, see Table 1. The values of $R_M$ and log $\alpha$ were calculated from $R_F$ by Eq. (3), Eq. (4) and Eq. (4a).

instance the average $R_M$ values of compounds **2, 4, 6** and **8**, with $E$ configuration for all mobile phases used, decreases from 0.43 to 0.26 (see Table 2).

The fact that the ester carbonyl is adsorbing and the phenyl groups are non-adsorbing also explains the relative retention $E>Z$ expressed by the negative values of log $\alpha$ found in all cases of compounds **1–8** when separation is achieved (see Table 2). The ester carbonyl is not hindered by the bulky ([20], p. 298) phenyl group in position 3 in any $E$ isomer as shown in Fig. 2, on the contrary, the ester carbonyl is hindered by this phenyl group in the corresponding $Z$ isomer. Reduction of adsorption because of steric hindrance is well-known in normal-phase LSC [3]. The relative retention $E>Z$ of the diastereoisomers

found in all cases studied shows that both the increase of the size of group R in compounds **1–8** and the variation of $\varepsilon$, $m$ and $P'$ of the mobile phases do not change the relative retention.

As seen from the absolute values of average log $\alpha$, log $\alpha$, in Table 2, there is a tendency towards improved separation of the diastereoisomeric pairs of type $a$ when the mobile phase has low or minimum $m$ and does not contain a localizing solvent as in the case of mobile phases 1, 9, 11, 16 and 19 showing absolute values of log $\alpha$ in the range 0.16–0.21. On the contrary, the presence of a localizing solvent such as diisopropyl ether or tetrahydrofurane in mobile phases 4, 10, 12, 14, 18 and 20 leads to considerable reduction or lack of separation when the

Table 4

Data according to Snyder [3] for the adsorption properties on silica of groups $i$ participating in the compounds studied

| Group $i$ | $Q_i^a$ | $a_i$ | $Q_i = Q_i^a - \varepsilon a_i$ | |
|---|---|---|---|---|
| | | | $\varepsilon_{min}$ | $\varepsilon_{max}$ |
| For compounds 1–8 | | | $\varepsilon = 0.165$ | $\varepsilon = 0.250$ |
| C=C | 0.50 | 2.0 | 0.17 | 0.00 |
| $C_6H_5$ | 1.50 | 6.0 | 0.51 | 0.00 |
| $CO_2CH_3$ | 5.27 | 10.5 | 3.54 | 2.65 |
| $CO_2C_2H_5$ | 5.22 | 11.4 | 3.34 | 2.37 |
| $CO_2C_3H_{7-n}$ | 5.17 | 12.3 | 3.14 | 2.10 |
| $CO_2C_4H_{9-n}$ | 5.12 | 13.2 | 2.94 | 1.82 |
| For compounds 9–16 | | | $\varepsilon = 0.337$ | $\varepsilon = 0.402$ |
| $CH_2$ | −0.05 | 0.9 | −0.35 | −0.41 |
| C=C | 0.50 | 2.0 | −0.17 | −0.30 |
| $C_6H_5$ | 1.50 | 6.0 | −0.52 | −0.91 |
| $CH_3O$ | 1.83 | 4.6 | 0.28 | −0.02 |
| $(CH_3O)_3C_6H_2$, planar | 6.99 | 19.8 | 0.32 | −0.97 |
| $(CH_3O)_3C_6H_2$, perpendicular | 6.99 | 4.6 | 5.44 | 5.14 |
| $(CH_3O)_3C_6H_2$, semiplanar | 6.99 | 9.2 | 3.89 | 3.29 |
| $CO_2CH_3$ | 5.27 | 10.5 | 1.73 | 1.05 |
| $CH_2OH$ | 5.55 | 9.4 | 2.38 | 1.77 |

The data for $Q_i^a$ and $a_i$ are taken from Ref. [3], p. 200 and p. 264 or calculated by summation of the contribution of the composing fragments. The calculated Eq. (2) $Q_i$ values refer to the mobile phases of minimum and maximum $\varepsilon$ value used. The values of $a_{(CH_3O)_3C_6H_2}$ in perpendicular and semiplanar configuration were assumed to be equal to $a_{CH_3O}$ and $2a_{CH_3O}$, respectively.

absolute values of $\overline{\log \alpha}$ vary from 0 to 0.08. This tendency was expected from theoretical predictions [5], and has been established elsewhere [15,16,21].

The increase in the size of group R from methyl to $n$-butyl decreases the separation of the diastereoisomers 1–8 which is seen from the decrease in the absolute values of average $\log \alpha$ from 0.14 to 0.09 (see Table 2). The opposite and considerably better separation ($\log \alpha$ up to 0.94) has been found in the case of two-point adsorption of $Z$ and $E$ isomers of type $RO_2C$–CH=CH–$CO_2R$ [15].
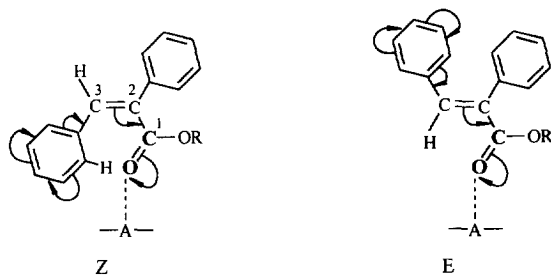


Fig. 2. Schematic illustration of the expected adsorption mechanism for diastereoisomers 1–8 of type $a$ where A is an adsorption site. The adsorbing group is shown in bold. The resonance between the two phenyl groups is not represented.

### 4.2. Retention and relative retentions of diastereoisomers 9–16 of type b and type c

Table 4 shows that the trimethoxyphenyl group under conditions specified has a greatly varying $Q_{(CH_3O)_3C_6H_2}$ value depending on its conformation relative to the adsorbent surface. The tendency for stronger adsorption and conformation factors will lead to some non-planar conformation having $Q_{(CH_3O)_3C_6H_2} > 0$. Moreover, as an aryl group, this group is bulky. The group X (methoxycarbonyl or hydroxymethyl) shows positive values of $Q_i$ being equal to 1.05 or greater.

Any diastereoisomeric pair of type $b$ and type $c$ has its own particularities and will be discussed separately.

As seen from Fig. 3, the presence of a double bond in diastereoisomeric pair 9–10 of type $b$ leads to enhanced resonance ([20], p. 148) from the electron-donating methoxyl groups to the electron-withdrawing ester carbonyl which will significantly decrease $Q_{(CH_3O)_3C_6H_2}$ and increase $Q_{CO_2CH_3}$ (cf., [9]). Hence, we can assume that group X equal to ester carbonyl is the main adsorbing group and the aryl group acts mainly as a shielding group which
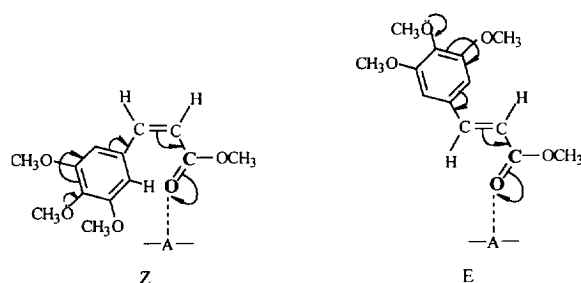
Fig. 3. Schematic illustration of the expected adsorption mechanism for diastereoisomers **9–10** of type *b* where A is an adsorption site. The adsorbing group is shown in bold. The conformation of the aryl group is not specified. The resonance of the methoxyls in the metha position with the aromatic ring is not represented.
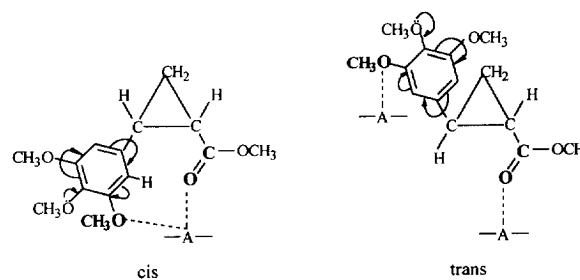


Fig. 4. Schematic illustration of the expected adsorption mechanism for diastereoisomers **13–14** of type *c* where A is an adsorption site. The adsorbing groups are shown in bold. The conformation of the aryl group is not specified. The resonance of the methoxyls in the metha position with the aromatic ring is not represented.

accounts for the relative retention $E > Z$ found by Cooper [12] and seen from the negative values of log $\alpha$ in Table 3 for diastereoisomeric pair **9–10**. The same relative retention is expected and found with mobile phases 21 and 23 for diastereoisomeric pair **11–12** as the group X equal to $CH_2OH$ has a greater adsorptivity than $CO_2CH_3$. Consequently, the presence of intramolecular hydrogen bonds of type Ar··· HO in compound **11** does not alter the relative retention which is consistent with our hypothesis for cleavage of intramolecular hydrogen bonds under the action of the more acidic silanol hydroxyl groups if the distance between them is similar to that of the intramolecularly bonded atoms (cf., [1,10]). Methanol, itself capable of hydrogen bonding, is not present in the mobile phases used and therefore the hypothesis proposed by Drefahl et al. [22] is not applicable for the explanation of the relative retention of diastereoisomeric pair **11–12**.

Cyclopropyl compounds **13–16** of type *c* do not contain a double bond and enhanced resonance from the methoxyl groups to group X is not possible which is consistent with two-point adsorption by one methoxyl group and group X as shown in Fig. 4. In such a case, the site chelation ([3], p. 315) of these two groups, i.e., their simultaneous adsorption on a given adsorption site, possible only in a *cis* isomer, will result in stronger adsorption of this isomer and a relative retention *cis* > *trans* as found for diastereoisomeric pair **13–14** with mobile phases 21–25 (see the positive values of log $\alpha$ in Table 3). Two-point adsorption in the case of cyclopropyl compounds

**13–16** vs. one-point adsorption in the case of alkene compounds **9–12** leads to the unexpected, but improved adsorption of the cyclopropyl compounds which can seen from the comparison of the average $R_M$ values in Table 3 for compounds **9** and **13**, **10** and **14** etc. According to Table 4, the value of $Q_i^{\circ}$ for a double bond is positive in contrast to the negative value for a methylene group available in the cyclopropyl structure, i.e., an alkene is to be adsorbed more strongly than the corresponding cyclopropane (cf., [12]).

The presence of intramolecular hydrogen bonds of type Ar···HO in compound **15** leads probably to the opposing relative retention *trans* > *cis* and log $\alpha < 0$ values found for diastereoisomeric pair **15–16** with mobile phase 21 indicating that cleavage of the intramolecular hydrogen bonds under the action of the adsorbent does not occur in this case (cf., [10]). The different behaviour of compounds **13** and **15**, i.e., cleavage vs. non-cleavage, can be attributed to the different lengths of the double and the single bond in a cyclopropane ring.

## 4.3. Importance of the computer program used for an easier choice of mobile phases for normal-phase LSC

We will shortly discuss the utility of the computer program [7] used paying particular attention to the role of $\varepsilon$ and $P'$ on solute adsorptivity. This study, the recent papers of this series [2,15,23,24] and our other studies on solutes that are not diastereoisomers

[8,9] use for the first time, computer-selected [7] mobile phases of equal $\varepsilon$ and varying $m$ and $P'$ for analytical LSC. In these cases, the adsorbent is usually silica and alumina [2,24].

As predicted by the Snyder theory and established in the above mentioned studies, the increase of $\varepsilon$ results in decrease of retention, $R_M$, in the present study. Thus, the average $R_M$ of compounds **1–8** with mobile phases 1–15 ($\varepsilon = 0.165$) and mobile phases 16–20 ($\varepsilon = 0.250$) were calculated as being 0.42 and $-0.24$, respectively. The tuning effect of $P'$ on $\varepsilon$ and the adsorptivity can also be seen. For instance, mobile phases 17 and 20 have the smallest $P'$ within mobile phases 16–20 and show the expected greatest retention of the individual compounds (see Table 1 and Table 2). The opposite tendency is true for mobile phase 16 of greatest $P'$ (cf., [8,9,23,24]). Compounds **9–16** are studied [12] with mobile phases of different $\varepsilon$.

When selecting mobile phases for preparative separations, there are two requirements: a suitable value of $\varepsilon$ and maximum solubility of the sample in the mobile phase, i.e., maximum $P'$ (cf., [4], p. 635). This requirement will be of the greatest importance for samples of low solubility. The influence of $P'$ on separation, $\alpha$, has to be taken also into account. The above mentioned analytical separations show tendencies to both increase, as in this study, and decrease the $\alpha$ parameter by increasing $P'$.

## 5. Conclusions

The data reported in this series of papers and in Refs. [8,9,14] include about 4000 measurements of TLC retentions on silica or alumina of some 300 conformationally flexible or rigid diastereoisomers with known configurations and other compounds with about 400 mobile phases.

These data were examined in terms of basicity [10], the Snyder theory [3–5] including Soczewiń-ski's method [6] and the Hammett equation [9]. The quantitative application of the Snyder theory became possible following the development of an appropriate computer program [7] which enables the calculation of the parameters strength, $\varepsilon$, localization, $m$ and polarity, $P'$, characterising mobile phases. The com-

puter program proved to be of general importance in easier selection of mobile phases for normal-phase LSC of organic compounds relative to the trial-and-error approach (see Section 4.3 of this paper and Ref. [8]).

Based on the broad data base and the analyses done, various conclusions about the retention, relative retention, separation and adsorption mechanism of the diastereoisomers studied were derived. Here, we will summarise the most important of them which highly support the Snyder theory:

1. Except in isolated cases [10,16], the relative retention (log $\alpha > 0$ or log $\alpha < 0$) of the diastereoisomers of a given group does not change with variation in the solute structure and $\varepsilon$, $m$ and $P'$ of the mobile phases used. The exceptions are understood in terms of $m$ and intramolecular bonding.
2. One-point adsorption mechanism favours a stronger retention of the diastereoisomer where the adsorbing group is less sterically hindered by the other solute groups.
3. Two-point adsorption mechanism favours a stronger retention of the diastereoisomer having the two adsorbing groups in close vicinity enabling their site chelation.
4. The tendency for maximum separation, $\alpha$, of the diastereoisomers of a given group with mobile phases of minimum $m$, being the usual case, or maximum $m$, is noted.
5. TLC can be used as a method for configurational determinations in other cases if as proposed in this paper analysis of adsorption mechanism is possible. This requires data for $\varepsilon$ of the mobile phases used and data for adsorptivity and size of all groups $i$ participating in the structure of the diastereoisomers.

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