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Chromatographic behaviour of diastereoisomers

X.[a] Thin-layer chromatographic retentions on silica of some (*E*)- and (*Z*)-oxazolones and related cinnamates as a function of mobile phase effects or Hammett constants

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ABSTRACT

The thin-layer chromatographic behaviour of twenty diastereoisomeric 1,1-disubstituted 2-arylethenes [(*Z*)- and (*E*)-oxazolones and -cinnamates] on silica was studied using 40 mobile phases. The (*E*)-oxazolone and the (*Z*)-cinnamate were the stronger adsorbing isomers in all instances. The relative retentions and the retentions themselves were correlated with solvent selectivity effects or Hammett constants of the various substituents on the aryl group. Solvent selectivity effects were approximated on the basis of Snyder's theory by the parameter localization, m, for experiments with mobile phases of constant strength, ε, and by the molar fraction of one of the solvents for the experiments with binary mobile phases of increasing ε. According to the data obtained, electronic effects determine the model of adsorption of any Z/E pair and steric effects modify it, controlling the relative retention which is not affected by solvent selectivity effects and the nature of the aryl group.

INTRODUCTION

This series of papers reports studies performed during the last two decades on thin-layer chromatographic (TLC) separations of over 110 diastereoisomeric pairs of tetrasubstituted ethanes and related cyclic compounds (see refs. 1 and 2 and the literature cited therein). The data obtained have been analysed on the basis of the general Snyder theory [3–5], including Soczewiński's method [6]. The relative retention of the diastereoisomers, showing which isomer is better retained, is attributed to steric hindrance control of adsorption in most instances and to mobile phase composition, or so-called solvent selectivity effects, in some particular instances. The latter

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[a] For Part IX, see ref. 1.

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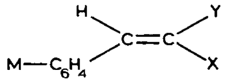
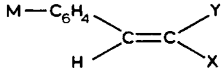
are shown to be predictable nowadays [7] on the basis of variation of the solvent localization, *m*, keeping the strength, ε, constant, as described in refs. 3–5. Such predictions are important in connection with the use of TLC for assigning the relative configurations of diastereoisomers [8,9]. In addition to interest in relative retention, attention has been paid to the separation α (band spacing) of diastereoisomers. Maximum separation [2,7,10] corresponds to mobile phases of minimum localization, *m*, as predicted by the theory [5].

Broading the type of diastereoisomers, we deal here with the TLC behaviour of *Z* and *E* isomers of 1,1-disubstituted 2-arylethenes of type 1, namely (*Z*)- and (*E*)-oxazolones and -cinnamates:



Z

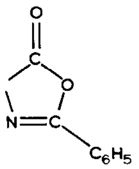
Type 1



E

M = H, 4-Cl, 4-CH_3, 3-CH_3O, 4-CH_3O or 3-NO_2

Cyclic compounds (oxazolones): X + Y =



(X is the imino group and Y is the ester group of this fragment)

Acyclic compounds (cinnamates): X = $NHCOC_6H_5$, Y = CO_2CH_3

This paper reports TLC retentions of twenty diastereoisomeric compounds of type 1 with 40 mobile phases which are either of constant strength, ε, or of increasing ε, being sets of binary mobile phases with various ratios of the components. The considerable database was aimed at a better understanding of the relative retention and separation of these *Z*/*E* pairs, whose TLC behaviour has been preliminarily studied [11–13]. The data obtained with mobile phases of constant ε [13] were updated using a new version of a microcomputer program [14] for the calculation of ε and *m* and included in this study.

THEORY

This study used Snyder's developed displacement model [3–5] and Soczewiński's simplified model [6] concerning the mechanism in normal-phase liquid–solid chromatography (LSC).

According to Snyder's developed displacement model, the properties of mobile phases used in LSC are well understood having in mind the values of the parameter strength, ε, localization, m, and polarity, P', being easily calculated nowadays [14]. The strength, ε, is a measure of the adsorption energy of the mobile phase per unit surface area of the adsorbent and m measures the capability of the mobile phase for a given specific interaction with adsorbent sites. Polarity, P', refers to the solvation ability of the mobile phase and is a co-parameter in determining its strength in normal-phase LSC [14].

Localization, m, is considered to be an approximation of solvent selectivity effects. The following recently derived equation describes the influence of these effects on the separation, α, of a pair of compounds:

$$\log \alpha = A + Bm \tag{1}$$

where A and B are constants for a given solute pair and adsorbent. The equation has been widely verified when ε is kept constant [1] or relatively constant [2,5,7,10].

Concerning diastereoisomers [1,2,7,10], log α is related to their relative retentions. Values of A correspond to the relative retention in the absence of mobile phase localization ($m = 0$) and express the relative steric hindrance in diastereoisomers to adsorption [7]. According to eqn. 1, relative retention is a result of relative steric effects and relative solvent selectivity effects. On increasing the localization, m, from the minimum value up to the maximum experimental value of 1.05, relative retention will be determined by one of the two effects depending on the absolute values of the terms A and Bm in eqn. 1. The parameter $m_{\text{crit.}} = -A/B$ obtained from eqn. 1 when log α is equal to zero indicates the intercept of the log α *vs.* m plot with the abscissa with a subsequent change in log α values from positive to negative and *vice versa.* Hence this value of m can predict an inversion of relative retention as a result of the dominant role of solvent selectivity effects [7].

In a simplified chromatographic system including mobile phases of two given solvents A and B in various ratios, solvent selectivity effects are approximated by the molar fraction N_B of the more polar solvent B. The basic equation proposed by Soczewiński [6] for such systems of increasing N_B, and thus increasing ε [5,14], has the following two equivalent forms:

$$R_M = A - n\log X_S \tag{2}$$

$$R_M = A - n\log N_B \tag{2a}$$

where A is a constant for a given solute and set of mobile phases, X_S denotes the concentration of solvent B in the mobile phase and the slope of the plot, n, is the number of solvent molecules displaced by a solute molecule from the adsorbent surface. Eqn. 2 has been shown to be valid [9,10] for some diastereoisomers giving some information about the molecular mechanism of adsorption.

The Hammett equation [15,16], which is a tool for obtaining information on transition states in chemical reactions, seems to be applicable to the LSC of some *meta-* and *para-*substituted arenes (see ref. 3, p. 303). A convenient form of this equation for LSC systems is

$$R_{M(\text{subst.})} = R_{M(\text{unsubst.})} + \rho\sigma \tag{3}$$

where $R_{M(\text{subst.})}$ and $R_{M(\text{unsubst.})}$ are R_M values of *meta*- or *para*-substituted M–Ar–X and the unsubstituted arene H–Ar–X, respectively. Being the intercept of the plot, $R_{M(\text{unsubst.})}$ presents the calculated value of R_M for the unsubstituted arene. σ is Hammett's constant of the substituent M, which depends mainly on its electronic effects in a corresponding position; ρ is the susceptibility of the adsorption centre X to the influence of substituent M. Positive and negative values of ρ refer to an anionic and a cationic adsorption centre X, respectively. Enhanced resonance or direct conjugation of this centre with a substituent M requires the use of the modified constants σ^- or σ^+.

EXPERIMENTAL

The synthesis and configuration of the diastereoisomeric oxazolones **1–12** and cinnamates **13–20** in Tables II and III, respectively, have been described [12,13,17].

TLC was performed as in ref. 2 on the same type of silica. The solvents used were of analytical-reagent grade. The R_F values are arithmetic means of three to six measurements. The reproducibility of R_F was ± 0.025. TLC with mobile phases 23–28 showed the presence of second fronts (see Table III). The diastereoisomeric pairs **7–8**, **9–10** and **11–12** were at the start with mobile phase 8 and separation was not observed, as shown in Table II. These particular data were not included in the quantitative treatments described below.

RESULTS AND DISCUSSION

Table I lists the mobile phases used. The values of strength, ε, localization, m, polarity, P', and molar fraction, N_B, in the case of binary mobile phases were calculated by means of a microcomputer program [14] based on Snyder's theory [3–5]. The mobile phases differ significantly in their properties, based on the values of the three parameters, namely $0.1 \leqslant \varepsilon \leqslant 0.42$, $-0.42 \leqslant m \leqslant 0.98$ and $0.19 \leqslant P' \leqslant 3.79$.

Mobile phases with strength ε in the range 0.10–0.25 and 0.29–0.42 were used for TLC of oxazolones **1–12** and cinnamates **13–20**, respectively. The lower strengths ε in the former instance show that cyclic compounds of type 1 have significantly weaker adsorption than that of acyclic compounds, and this was the reason for studying each group of compounds separately.

Tables II and III summarize the TLC data for the diastereoisomeric oxazolones and cinnamates, respectively. Except for the R_F values, they include the derived values of the separation α of Z/E pairs calculated by the following equations:

$$\log \alpha = R_{M(Z)} - R_{M(E)} = A + Bm \qquad (1a)$$

$$R_M = \log k' = \log (1/R_F - 1) \qquad (4)$$

where k' is the capacity factor. The subscripts written in parentheses in eqn. 1a specify the isomer.

We used the definition of α in eqn. 1a to express the relative retentions of the diastereoisomers in a shorter manner, namely positive and negative values of log α correspond to a stronger adsorption of Z and E isomers, respectively.

TABLE I

MOBILE PHASES STUDIED AND THE CORRESPONDING COMPUTER-CALCULATED [13,14] VALUES OF STRENGTH, ε, LOCALIZATION, m, AND POLARITY, P'

N_B is molar fraction of the second solvent for binary mobile phases 8–16 and 29–40. Using a previous version [13] of the microcomputer program [14], the values of ε were 0.233 and 0.378 for mobile phases 1–7 and 17–28, respectively.

No.	Composition (vol.%), N_B	ε	m	P'
For oxazolones ***1–12***				
1	Hexane–benzene (20:80)	0.233	−0.42	2.18
2	Tetrachloromethane–diethyl ether (95:5)	0.233	0.36	1.66
3	Tetrachloromethane–ethyl acetate (98:2)	0.234	0.37	1.66
4	Hexane–chloroform–diethyl ether (68.9:30:1.1)	0.226	0.24	1.33
5	Hexane–1,2-dichloroethane (68:32)	0.233	0.14	1.19
6	Cyclohexane–toluene–tetrahydrofuran (64:35:1)	0.211	0.18	0.75
7	Toluene–methylene chloride (91.5:8.5)	0.233	0.01	2.46
8	Cyclohexane–benzene (86.6:13.4), 0.158	0.100	−0.21	0.19
9	(70.6:29.4), 0.336	0.150	−0.37	0.65
10	(44:56), 0.607	0.200	−0.41	1.42
11	(29.6:70.4), 0.743	0.220	−0.42	1.84
12	(2:98), 0.983	0.248	−0.42	2.64
13	Tetrachloromethane–chloroform (84.7:15.3), 0.180	0.150	0.03	1.98
14	(56.7:43.3), 0.481	0.200	0.08	2.68
15	(41.2:58.8), 0.634	0.220	0.09	3.07
16	(12.5:87.5), 0.895	0.250	0.10	3.79
For cinnamates ***13–20***				
17	Hexane–diethyl ether (35:65)	0.378	0.66	1.86
18	Hexane–methyl *tert.*-butyl ether (51.9:48.1)	0.377	0.81	–
19	Toluene–diethyl ether (66:34)	0.378	0.57	2.54
20	Benzene–acetone (89.8:10.2)	0.378	0.57	2.95
21	Hexane–chloroform–diethyl ether (51.2:32:16.8)	0.379	0.60	1.83
22	Hexane–chloroform–diisopropyl ether–ethyl acetate–acetone (75.8:20:2:2:0.2)	0.376	0.59	1.04
23	Cyclohexane–tetrachloromethane–benzene–tetrahydrofuran (55.3:2.5:2.5:39.7)	0.378	0.98	1.59
24	(26.6:25:25:23.4)	0.379	0.92	1.96
25	(8.2:37.5:37.5:16.8)	0.378	0.86	2.27
26	(10.1:30:45:14.9)	0.378	0.83	2.27
27	Hexane–chloroform–diisopropyl ether–ethyl acetate–acetonitrile (77.85:18:2:2:0.15)	0.364	0.59	0.96
28	Hexane–chloroform–diisopropyl ether–acetonitrile (69.6:19:10:1.4)	0.348	0.69	1.17
29	Hexane–diethyl ether (78.4:21.6), 0.256	0.290	0.64	0.68
30	(57.6:42.4), 0.479	0.330	0.65	1.25
31	(34:66), 0.708	0.380	0.66	1.88
32	(10:90), 0.918	0.420	0.66	2.53
33	Benzene–diethyl ether (92.5:7.5), 0.064	0.290	0.11	2.71
34	(82.8:17.2), 0.150	0.330	0.28	2.72
35	(62.6:37.4), 0.337	0.380	0.54	2.74
36	(8:92), 0.907	0.420	0.66	2.79
37	Benzene–acetone (97.8:2.2); 0.026	0.290	0.12	2.75
38	(94.9:5.1), 0.061	0.330	0.29	2.82
39	(89.5:10.5), 0.124	0.380	0.57	2.95
40	(81.6:18.4), 0.213	0.420	0.78	3.14

TABLE II

EXPERIMENTAL R_F VALUES AND DERIVED VALUES OF LOG α FOR THE DIASTEREOISOMERIC OXAZOLONES **1–12** OF TYPE 1

For compositions of mobile phases, see Table I. The values of log α were calculated from R_F values of the corresponding *Z–E* pair using eqns. 1a and 4.

M	Solute		R_F for indicated mobile phase															
	Configuration	No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
4-Cl	*Z*	**1**	0.77	0.69	0.39	0.46	0.43	0.30	0.70	0.06	0.18	0.43	0.62	0.74	0.25	0.46	0.57	0.73
	E	**2**	0.53	0.51	0.31	0.37	0.33	0.20	0.51	0.02	0.07	0.20	0.33	0.49	0.11	0.25	0.38	0.56
H	*Z*	**3**	0.70	0.67	0.39	0.43	0.40	0.27	0.65	0.05	0.16	0.37	0.55	0.69	0.20	0.41	0.51	0.69
	E	**4**	0.48	0.50	0.30	0.34	0.30	0.19	0.45	0.02	0.06	0.16	0.29	0.43	0.09	0.22	0.33	0.51
4-CH_3	*Z*	**5**	0.68	0.65	0.38	0.41	0.40	0.23	0.63	0.04	0.13	0.33	0.50	0.67	0.19	0.40	0.50	0.68
	E	**6**	0.47	0.49	0.30	0.33	0.29	0.17	0.43	0.01	0.05	0.15	0.27	0.41	0.09	0.22	0.33	0.52
3-CH_3O	*Z*	**7**	0.53	0.50	0.30	0.31	0.25	0.18	0.48	0.01	0.05	0.17	0.33	0.52	0.08	0.22	0.32	0.51
	E	**8**	0.32	0.38	0.24	0.23	0.16	0.14	0.30	0.01	0.02	0.07	0.15	0.26	0.03	0.11	0.18	0.32
4-CH_3O	*Z*	**9**	0.45	0.41	0.26	0.26	0.20	0.17	0.41	0	0.04	0.13	0.27	0.46	0.06	0.19	0.28	0.48
	E	**10**	0.26	0.30	0.19	0.20	0.12	0.10	0.26	0	0.01	0.05	0.12	0.23	0.03	0.09	0.15	0.30
3-NO_2	*Z*	**11**	0.51	0.50	0.33	0.30	0.25	0.21	0.49	0.01	0.05	0.17	0.33	0.51	0.09	0.22	0.33	0.52
	E	**12**	0.31	0.39	0.25	0.23	0.16	0.15	0.30	0.01	0.02	0.08	0.15	0.26	0.05	0.12	0.20	0.34
			Log α for indicated mobile phase															
		1–2	−0.47	−0.33	−0.16	−0.16	−0.19	−0.23	−0.35	−0.50	−0.46	−0.48	−0.52	−0.47	−0.43	−0.41	−0.33	−0.33
		3–4	−0.40	−0.31	−0.18	−0.17	−0.19	−0.20	−0.36	−0.41	−0.47	−0.49	−0.48	−0.47	−0.40	−0.39	−0.33	−0.33
		5–6	−0.38	−0.29	−0.16	−0.15	−0.21	−0.17	−0.35	−0.62	−0.45	−0.44	−0.43	−0.47	−0.37	−0.37	−0.31	−0.30
		7–8	−0.38	−0.21	−0.13	−0.17	−0.24	−0.13	−0.34	0	−0.41	−0.43	−0.44	−0.48	−0.45	−0.36	−0.33	−0.35
		9–10	−0.36	−0.21	−0.18	−0.15	−0.27	−0.26	−0.29	0	−0.62	−0.45	−0.44	−0.45	−0.32	−0.37	−0.34	−0.34
		11–12	−0.37	−0.19	−0.17	−0.15	−0.24	−0.17	−0.35	0	−0.41	−0.37	−0.44	−0.47	−0.28	−0.32	−0.29	−0.32

Concerning log α, Tables II and III show negative values for oxazolones **1–12** and positive values for cinnamates **13–20**. These different relative retentions were independent of the type of substituent M, the nature of the mobile phase and the presence of second fronts in some instances (see Experimental).

The R_F values obtained with mobile phases 1–7 and 17–28 having constant strengths ε of 0.23 and 0.38 (mean values), respectively, showed that Snyder's theory and the microcomputer program used [13,14] permit suitable mobile phases to be selected with minimum experimental effort (see details in refs. 1 and 13). The mobile phases mentioned were used to study the influence of solvent selectivity effects with the cyclic and acyclic diastereoisomers by means of eqn. 1a. The fit of the corresponding data to this equation is shown in Table IV and illustrated in Fig. 1.

The data obtained with sets of mobile phases 8–12, 13–16, 29–32, 33–36 and 37–40 of increasing ε agree well with eqn. 2a as the standard deviation (S.D.) and correlation coefficient, R, show mean values of ± 0.07 and -0.990, respectively, as presented in Table V and illustrated in Fig. 2.

Examples of the data necessary to verify the Hammett eqn. 3 are shown in Table VI. Application of this equation to the corresponding data is illustrated in Fig. 3.

Role of solvent selectivity effects on retention of diastereoisomers

Sets of mobile phases of constant strength, ε (verification of eqn. 1a). The data obtained when the mobile phase strength, ε, was kept constant and the localization, m, was varied in the ranges $-0.42 \leqslant m \leqslant 0.37$ and $0.57 \leqslant m \leqslant 0.81$ for the oxazolones and cinnamates, respectively, correlated with eqn. 1a, as can be seen from Table IV and Fig. 1. The overall S.D. is ± 0.07, similar to that reported earlier [2]. In addition, maximum absolute values of log α and maximum separation of diastereoisomers correspond to minimum values of m, as established also [2,7,10] for conformationally flexible diastereoisomeric compounds.

According to Table IV, the values of A are negative for the oxazolones and positive for the cinnamates. Taking into account what was said under Theory, these data show that the relative steric effects favour the stronger adsorption of (E)-oxazolone and (Z)-cinnamate then that of the corresponding isomers when solvent selectivity effects are absent. The relative steric effects are equal ($A = -0.3$) for any oxazolone pair. However, A varies in the range 0.32–0.70 for the cinnamates.

The values of $m_{\text{crit.}} = -A/B$ from Table IV exceed the maximum experimentally accessible value of m (1.05 [2]) in all instances except those concerning the pairs **1–2**, **11–12** and **7–8**, where this parameter is 0.93 or 0.87. Consequently, the relative retentions of the diastereoisomers found for oxazolones **1–12** with mobile phases 1–7 and for cinnamates **13–20** with mobile phases 17–22 are determined by relative steric effects. A change in the relative retention induced by solvent selectivity effects could occur only for oxazolones **1–2**, **11–12** and **7–8** with mobile phases whose values of m exceed 0.93 for the first two pairs and 0.87 for the third. However, it does not seem possible because of the weak adsorption of oxazolones mentioned above, which will make it difficult to find mobile phases of low ε and m greater than 0.87.

Sets of mobile phases of increasing strength, ε (verification of eqn. 2a). The construction of R_M *vs.* log N_B plots was based on the sets of binary mobile phases 8–12 and 13–16 for the oxazolones and 29–32, 33–36 and 37–40 for the cinnamates,

TABLE III

EXPERIMENTAL R_F VALUES AND DERIVED VALUES OF LOG α FOR THE DIASTEREOISOMERIC CINNAMATES **13–20** OF TYPE 1

For compositions of mobile phases, see Table I. Values of log α were calculated from R_F values of the corresponding *Z–E* pair using eqns. 1a and 4.

M	Solute		R_F for indicated mobile phase[a]									
	Configuration	No.	17	18	19	20	21	22	23	24	25	26
4-Cl	*Z*	**13**	0.41	0.57	0.52	0.56	0.25	0.03	0.62	0.66	0.55	0.54
	E	**14**	0.53	0.65	0.68	0.68	0.39	0.08	0.66	0.75	0.66	0.68
H	*Z*	**15**	0.40	0.56	0.48	0.53	0.24	0.03	0.61	0.63	0.52	0.52
	E	**16**	0.50	0.64	0.62	0.62	0.35	0.07	0.64	0.71	0.64	0.65
4-CH_3O	*Z*	**17**	0.28	0.49	0.39	0.47	0.16	0.02	0.52	0.47	0.43	0.44
	E	**18**	0.37	0.56	0.52	0.55	0.22	0.03	0.55	0.57	0.53	0.57
3-NO_2	*Z*	**19**	0.27	0.49	0.43	0.50	0.14	0.01	0.52	0.44	0.44	0.45
	E	**20**	0.42	0.61	0.56	0.58	0.24	0.03	0.58	0.59	0.58	0.61
			Log α for indicated mobile phase									
		13–14	0.21	0.16	0.30	0.23	0.29	0.45	0.08	0.19	0.20	0.26
		15–16	0.18	0.15	0.24	0.16	0.23	0.39	0.06	0.16	0.22	0.24
		17–18	0.18	0.12	0.22	0.14	0.17	0.18	0.06	0.17	0.17	0.22
		19–20	0.29	0.22	0.22	0.14	0.29	0.49	0.11	0.26	0.24	0.28

[a] Second fronts were established for the following mobile phases as their R_F values are 0.52 (mobile phase 23), 0.39 (mobile phase 24), 0.24 (mobile phase 25), 0.21 (mobile phase 26), 0.12 (mobile phase 27) and 0.04, 0.23 and 0.30 (mobile phase 28).

TABLE IV

FIT OF LOG α FOR INDIVIDUAL DIASTEREOISOMERIC PAIRS WITH MOBILE PHASES 1–7 AND 17–22 OF CONSTANT ε TO THE EQUATION LOG $\alpha = A + Bm$ (EQN. 1a) WHERE m IS LOCALIZATION OF MOBILE PHASE

The structures of the solute pairs and their values of log α are shown in Tables II and III. The values of m were taken from Table I. The values of A, B and the S.D. were calculated by linear regression analysis of log α *vs.* m data using the method of least squares. The critical values $m_{\text{crit.}} = -A/B$ were calculated on the basis of the data for A and B from preceding columns. Mean values of ε are shown.

Solute pair	A	B	S.D.	$m_{\text{crit.}}$
Oxazolones, mobile phases 1–7, ε = 0.23, log α < 0				
1–2	−0.31	0.33	±0.08	0.93
3–4	−0.29	0.25	0.07	1.16
5–6	−0.28	0.25	0.07	1.12
7–8	−0.27	0.31	0.06	0.87
9–10	−0.28	0.23	0.04	1.21
11–12	−0.27	0.29	0.05	0.93
Cinnamates, mobile phases 17–22, ε = 0.38, log α > 0				
13–14	0.70	−0.67	0.09	1.04
15–16	0.50	−0.43	0.09	1.16
17–18	0.32	−0.24	0.03	1.33
19–20	0.37	−0.17	0.13	2.17
			overall ±0.07	

27	28	29	30	31	32	33	34	35	36	37	38	39	40
0.03	0.09	0.02	0.15	0.43	0.70	0.28	0.46	0.66	0.82	0.14	0.31	0.53	0.70
0.08	0.20	0.09	0.28	0.55	0.78	0.48	0.66	0.78	0.87	0.26	0.48	0.63	0.77
0.03	0.10	0.03	0.16	0.44	0.70	0.24	0.43	0.64	0.81	0.12	0.29	0.50	0.66
0.06	0.17	0.09	0.27	0.53	0.77	0.39	0.59	0.74	0.86	0.20	0.40	0.58	0.73
0.01	0.06	0.01	0.07	0.29	0.59	0.16	0.33	0.55	0.72	0.08	0.22	0.44	0.61
0.03	0.09	0.03	0.15	0.40	0.67	0.27	0.48	0.67	0.79	0.14	0.32	0.52	0.68
0.01	0.05	0.01	0.07	0.29	0.58	0.20	0.38	0.56	0.73	0.10	0.26	0.47	0.63
0.03	0.10	0.03	0.15	0.42	0.69	0.29	0.50	0.68	0.81	0.15	0.34	0.54	0.69
0.45	0.40	0.69	0.34	0.21	0.18	0.38	0.36	0.26	0.17	0.34	0.32	0.18	0.15
0.32	0.26	0.51	0.29	0.15	0.15	0.31	0.28	0.20	0.16	0.27	0.21	0.14	0.14
0.49	0.19	0.49	0.37	0.21	0.15	0.29	0.28	0.22	0.17	0.27	0.22	0.13	0.14
0.49	0.33	0.49	0.37	0.25	0.21	0.21	0.21	0.23	0.20	0.20	0.16	0.12	0.12

composed of cyclohexane–benzene, tetrachloromethane–chloroform, hexane–diethyl ether, benzene–diethyl ether and benzene–acetone, respectively. The molar fraction, N_B, of the second solvent was $0.026 \leqslant N_B \leqslant 0.983$.

The values of the slope n vary from *ca.* 1 to 4. However, the diastereoisomeric compounds show close values, which indicate that they adsorb via the same groups. As can be seen from Table V and Fig. 2, almost equal values of n and parallel plots are established for the diastereoisomers with mobile phases 8–16, which do not contain a strongly adsorbing second solvent. The remaining mobile phases, 29–40, contain a solvent such as diethyl ether or acetone and the slopes are usually not parallel. Hence the solvent selectivity effects vary with the change in molar fraction, N_B, in this instance as the maximum separation of diastereoisomers corresponds to minimum values of N_B.

When N_B approaches unity, A in eqn. 2a is equal to R_M and the relative parameter $\Delta A = A_Z - A_E$ is equal to log α. The values of ΔA are negative for the oxazolones and positive for the cinnamates, similarly to log α, indicating that the relative retentions found will not alter as a result of solvent selectivity effects if the mobile phase is composed mainly of the second solvent. The diastereoisomeric pair **13–14** shows a particularity with mobile phases 37–40 as ΔA is equal to zero, *i.e.*, separation will not occur in this instance. The R_M *vs.* log N_B plots for diastereoisomers do not cross and consequently a change in relative retentions is not expected for the whole range of N_B from 0 to 1.

TABLE V

FIT OF R_M OF INDIVIDUAL COMPOUNDS OBTAINED WITH BINARY MOBILE PHASES 8–16 AND 29–40 OF INCREASING ε TO THE EQUATION $R_M = A + n \log N_B$ (EQN. 2a), WHERE N_B IS MOLAR FRACTION OF THE SECOND SOLVENT

The structures and R_F values of oxazolones **1–12** and cinnamates **13–20** are presented in Tables II and III, respectively. The values of R_M were calculated on the basis of eqn. 4. The values of N_B were taken from Table I. The values of A, n and the S.D. were calculated by linear regression analysis of R_M *vs.* log N_B data using the method of least squares. The values of $\Delta A = A_Z - A_E$ were calculated on the basis of A for the indicated isomer.

Solute	Configuration	Binary mobile phases 8–12, ε = 0.100–0.248				Binary mobile phases 13–16, ε = 0.150–0.250			
		A	n	S.D.	ΔA	A	n	S.D.	ΔA
1	Z	−0.42	2.09	±0.09	−0.49	−0.41	1.25	±0.09	−0.33
2	E	0.07	2.09	0.08		−0.08	1.40	0.11	
3	Z	−0.31	2.05	0.08	−0.49	−0.33	1.30	0.09	−0.33
4	E	0.18	1.97	0.10		0.00	1.40	0.10	
5	Z	−0.25	2.11	0.09	−0.42	−0.31	1.31	0.09	−0.30
6	E	0.17	2.31	0.06		−0.01	1.41	0.11	
7	Z	−0.02	2.82	0.08	−0.47	−0.01	1.49	0.09	−0.32
8	E	0.45	2.68	0.08		0.31	1.65	0.07	
9	Z	0.10	2.81	0.10	−0.41	0.04	1.60	0.10	−0.40
10	E	0.51	3.20	0.07		0.44	1.51	0.15	
11	Z	−0.01	2.80	0.08	−0.44	−0.01	1.42	0.11	−0.32
12	E	0.43	2.68	0.04		0.31	1.37	0.11	

Solute	Configuration	Binary mobile phases 29–32, ε = 0.290–0.420				Binary mobile phases 33–36, ε = 0.290–0.420			
		A	n	S.D.	ΔA	A	n	S.D.	ΔA
13	Z	−0.46	3.68	±0.05	0.10	−0.71	0.94	±0.02	0.17
14	E	−0.56	2.73	0.11		−0.88	0.74	0.03	
15	Z	−0.43	3.36	0.08	0.09	−0.69	0.99	0.02	0.15
16	E	−0.52	2.67	0.12		−0.84	0.85	0.02	
17	Z	−0.22	3.86	0.11	0.13	−0.50	0.99	0.06	0.17
18	E	−0.35	3.23	0.09		−0.67	0.88	0.07	
19	Z	−0.21	3.83	0.10	0.19	−0.49	0.89	0.04	0.21
20	E	−0.40	3.31	0.09		−0.70	0.89	0.05	

Solute	Configuration	Binary mobile phases 37–40, ε = 0.290–0.420			
		A	n	S.D.	ΔA
13	Z	−1.21	1.27	±0.02	0.00
14	E	−1.21	1.04	0.03	
15	Z	−1.15	1.27	0.01	0.02
16	E	−1.17	1.12	0.02	
17	Z	−1.13	1.38	0.02	0.02
18	E	−1.15	1.22	0.01	
19	Z	−1.11	1.30	0.02	0.05
20	Z	−1.16	1.20	0.01	

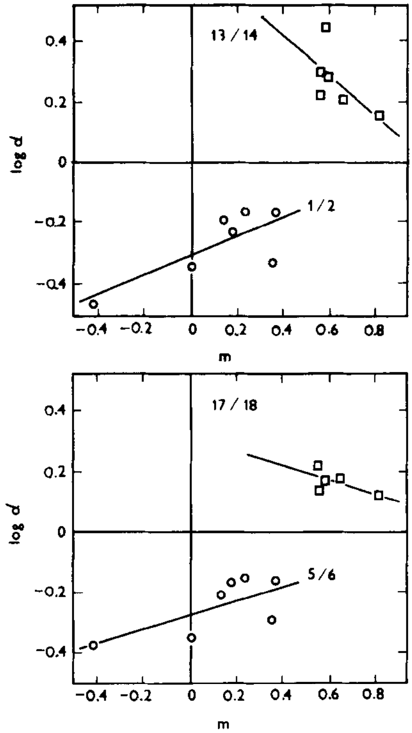


Fig. 1. Log α *vs.* localization (m) plots from Table IV for diastereoisomeric pairs **1–2**, **5–6**, **13–14** and **17–18**.

TABLE VI

FOUR EXAMPLES OF DATA NECESSARY TO VERIFY THE HAMMETT EQN. 3

R_F values referring to mobile phases 1 and 20 were taken from Tables II and III. R_M values were obtained by eqn. 4. The compounds are arranged in order of increasing retention. The values of σ^+ were taken from ref. 15. See text for the deviations from eqn. 3 of *meta*-substituted derivatives **7**, **11** and **19**.

Z isomers	R_F	R_M	*E* isomers	R_F	R_M	Substituent M	σ^+ values
Oxazolones, mobile phase 1							
1	0.77	−0.52	**2**	0.53	−0.05	4-Cl	0.11
3	0.70	−0.37	**4**	0.48	0.03	H	0
5	0.68	−0.33	**6**	0.47	0.05	4-CH_3	−0.31
7	0.53	−0.05	**8**	0.32	0.33	3-CH_3O	0.05
11	0.51	−0.02	**12**	0.31	0.35	3-NO_2	0.67
9	0.45	0.09	**10**	0.26	0.45	4-CH_3O	−0.78
Cinnamates, mobile phase 20							
13	0.56	−0.10	**14**	0.68	−0.33	4-Cl	0.11
15	0.53	−0.05	**16**	0.62	−0.21	H	0
19	0.50	0	**20**	0.58	−0.14	3-NO_2	0.67
17	0.47	0.05	**18**	0.55	−0.09	4-CH_3O	−0.78

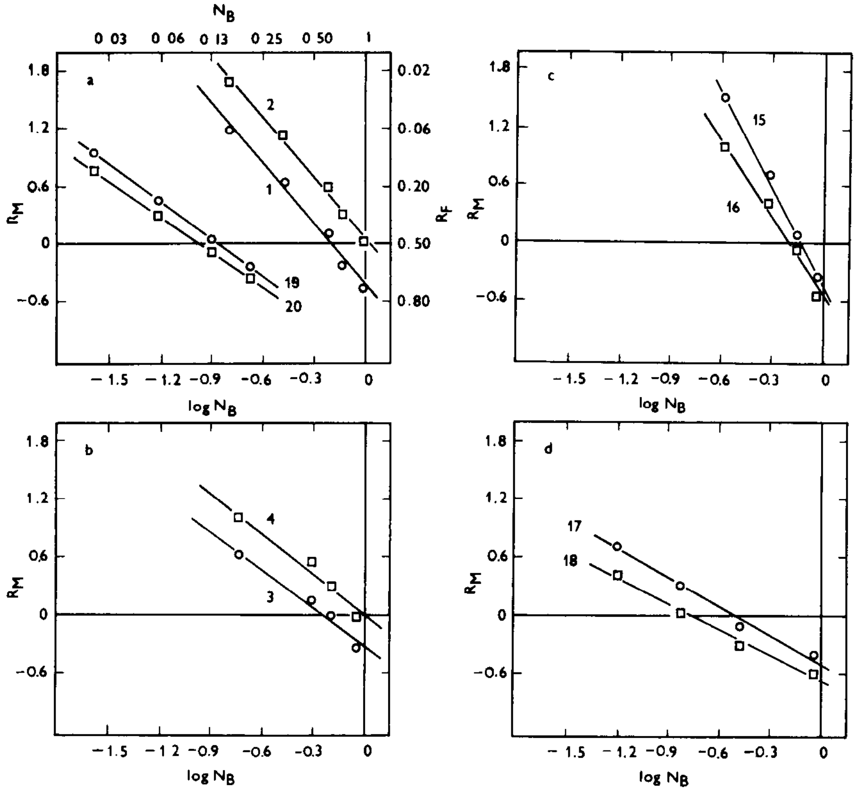


Fig. 2. R_M *vs.* log [molar fraction (N_B)] plots from Table V for indicated sets of binary mobile phases and diastereoisomers shown in parentheses: (a) set 8–12 (**1–2**) and set 37–40 (**19–20**); (b) set 13–16 (**3–4**); (c) set 29–32 (**15–16**); (d) set 33–36 (**17–18**).

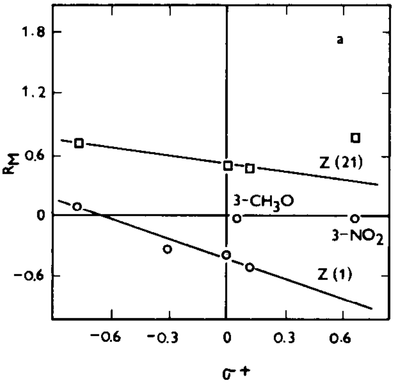


Fig. 3. R_M *vs.* Hammett σ^+ plots for compounds of indicated configuration and mobile phases shown in parentheses.

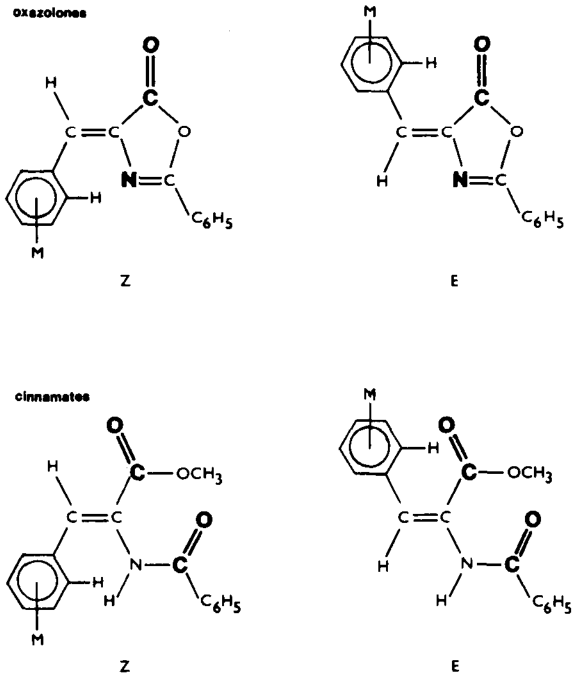


Fig. 4. Schematic illustration of the steric hindrance of the adsorbing groups shown in bold for the diastereoisomeric oxazolones and cinnamates. The hydrogen atom in the *ortho* position in the aryl group induces this hindrance (see text).

Role of the substituent of the aromatic ring on retention of the diastereoisomers (verification of eqn. 3)

Oxazolones **1–12** and cinnamates **13–20** are suitable for studying the applicability of Hammett eqn. 3 because the compounds of any group differ only in the substituent M in the aryl group.

The R_M *vs.* σ^+ plots for the compouds of a given configuration and mobile phase showed a good correlation with eqn. 3 in all instances except the 3-CH_3O and 3-NO_2 derivatives, as illustrated in Fig. 3 for *Z* isomers when mobile phases 1 and 21 were used. Owing to the absence of a general validity of the Hammett equation, we do not consider the values of ρ obtained. Additional data for other *meta* substituents are required in order to explain the deviations.

According to Tables II, III and VI, the substituent M has an influence on the retention of the compounds studied but it does not affect the relative retentions of the diastereoisomers.

Deduced models of adsorption for the oxazolones and cinnamates

The application of eqns. 1a and 2a as discussed above showed that the model of adsorption for a given *E–Z* pair of type 1 is equal as steric hindrance controls the relative retention of the diastereoisomers. The phenomenon has been widely established [1,2,7,9] for conformationally flexible diastereoisomers on the basis of eqns. 1 and 2 taking into account also the pK_a values.

As done previously [7,9], we shall look for different models of adsorption to explain the different relative retentions found for the oxazolones and cinnamates. Taking into account the above conclusion about the role of steric effects, the greater adsorption energy [3] of groups X and Y than that of M and the fact that only the oxazolones are bases, we considered that the adsorption of cyclic and acyclic compounds of type 1 occurs via the nitrogen atom and ester carbonyl and via amide carbonyl and ester carbonyl, respectively. Inspection of models showed that substituents M in *meta* and *para* positions are far from the adsorbing groups and the hydrogen atom in an *ortho* position in the aryl group hinders them.

The presence of an olefinic carbon atom as a member of a five-membered ring distorts the geometry of oxazolones relative to that of the usual olefins. Fig. 4 shows that the aryl group hinders more the nitrogen atom in (*Z*)-oxazolones than the ester carbonyl in the *E* isomers, which is the reason for the stronger adsorption of the latter isomers and the negative values of log α established. The amide carbonyl in the cinnamates is far from the aryl group. Hence, the ester carbonyl is not hindered in the *Z* isomers, which determines their stronger adsorption and the positive values of log α found.

CONCLUSIONS

The TLC behaviour of (*Z*)- and (*E*)-oxazolones (**1–12**) and related cinnamates (**13–20**) on silica was studied using 40 mobile phases, and showed a better retention of (*E*)-oxazolones and (*Z*)-cinnamates in all cases studied.

The theoretical relationship between the separation α of diastereoisomers and solvent selectivity effects as measured by the localization, m, was studied when the strength, ε, was kept constant. The results showed that a mobile phase-induced change in the relative retentions established cannot be obtained. In addition, the best separations were obtained with mobile phases showing minimum values of m as predicted by the theory.

Using sets of mobile phases composed of two solvents with increasing molar fraction N_B of the more polar solvent and thus increasing ε, the plots of R_M *vs.* log N_B were similar for the diastereoisomers, indicating that their adsorption occurs via similar groups.

Electronic effects related to the substituent M do not control the relative retentions of the diastereoisomers studied. The Hammett equation is of limited validity because of the considerable deviation of *m*-CH_3O and *m*-NO_2 derivatives.

The relative retentions established were attributed to adsorption models including two adsorbing groups, namely the nitrogen atom and ester carbonyl for the oxazolones and the amide carbonyl and ester carbonyl for the cinnamates. Each adsorption model ensures less steric hindrance of the adsorbing groups for the better retained isomer.

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