Separation Science and Technology
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713708471

Thin-Layer Chromatography of the N-Substituted Maleimides and Chlorosuccinanils on Silica Gel. Stereochemical Factors

John V. Dichiaro[ab]; Roger A. Bate[ac]; Wendell Johnson[a]; Roy A. Keller[a]
[a] Department of Chemistry, University of Arizona, Tucson, Arizona [b] Monsanto Research Corporation, Mount Laboratory, Miamisburg, Ohio [c] Northrup Corporation, Asheville, North Carolina

To cite this Article Dichiaro, John V. , Bate, Roger A. , Johnson, Wendell and Keller, Roy A.(1968) 'Thin-Layer Chromatography of the N-Substituted Maleimides and Chlorosuccinanils on Silica Gel. Stereochemical Factors', Separation Science and Technology, 3: 1, 67 — 76

To link to this Article: DOI: 10.1080/01496396808052207

URL: http://dx.doi.org/10.1080/01496396808052207

SEPARATION SCIENCE, 3(1), pp. 67–76, Feb., 1968

Thin-Layer Chromatography of the N-Substituted Maleimides and Chlorosuccinanils on Silica Gel. Stereochemical Factors*

JOHN V. DICHIARO,† ROGER A. BATE,‡
WENDELL JOHNSON, and ROY A. KELLER
DEPARTMENT OF CHEMISTRY
UNIVERSITY OF ARIZONA
TUCSON, ARIZONA

Summary

The NO_2-, MeO-, Cl-, and Me-phenyl- N-substituted maleimides, N-phenyl- and N-benzylmaleimides, and the chlorosuccinanils were chromatographed on two grades of Silica Gel-G in thin-layer systems using developers of benzene and of mixtures of cyclohexane/ethyl acetate, 2:1 and 3:2. Isomers within any family were not separated, which, contradicts previous results with alumina, while families were resolved. The nonconjugated chlorosuccinanils behaved identically with the hindered and unhindered N-(chlorophenyl)maleimides. There is no evidence of charge-transfer interaction of delocalized π electrons of planar conjugated maleimides with the silica surface.

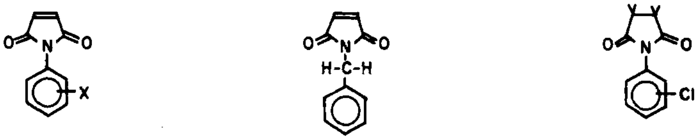
Dichiaro et al. (*1*) and Dichiaro and Keller (*2*) chromatographed the *N*-phenyl-; *N*-benzyl-; *o*-, *m*-, and *p*- *N*-(methylphenyl)-; *o*-, *m*-, and *p*- N-(chlorophenyl)-; *o*- and *p*- N-(methoxyphenyl)-; and *o*-, *m*-, and *p*- N-(nitrophenyl)maleimides and the *o*-, *m*-, and *p*-chlorosuccinanils on Alumina-G using benzene/cyclohexane, 2:1 (v/v) and 1:1 (v/v); cyclohexane/ethyl acetate, 4:1 (v/v); benzene/hexane, 1:1

---

[*] Presented at the Southwest Regional Meeting, American Chemical Society, Albuquerque, N.M., November 30, 1966.

[†] Present address: Monsanto Research Corporation, Mount Laboratory, Miamisburg, Ohio.

[‡] Present address: Northrup Corporation, Asheville, North Carolina.



Substituted N-Phenylmaleimides

N-Benzylmaleimide

Chlorosuccinanils

FIG. 1.

(v/v); and benzene. The structural relations of these compounds are shown in Fig. 1. These earlier papers give the details of the synthesis and the UV spectra. A comparison of the spectra shows a pronounced shift of an absorption peak for N-phenylmaleimide from 322 to 295 mμ for N-benzylmaleimide and the appearance of "fine structure" in the benzenoid absorbance at 260 mμ for the N-benzyl derivative. These observations are characteristic of π-electron delocalization across the two rings of the conjugated N-phenyl derivative and its absence in the N-benzyl derivative because of interference by the bridging methylene group. Ring systems exhibiting such delocalization are thought to be coplanar or nearly so. Adrian (3) assumed that for compounds such as biphenyl there would be steric repulsion between hydrogens at the ortho positions of the two rings which would resist assumption of a coplanar configuration, while π-electron delocalization would favor it. The true situation must be a compromise. His theoretical calculations of the effective resonance energy, the sum of the resonance energy and the steric energy, show a minimum at an angle between 20° to 30° between the rings and that a completely coplanar configuration is as energetically unlikely as an angle of 50° or greater. The increase in resonance energy of biphenyl over that of two isolated benzene rings is about 5% at an angle of 60°. Almost identical shifts were observed for this same absorbance peak on going from *p*-Me to *o*-Me and from *p*-Cl and *m*-Cl to *o*-Cl derivatives. Steric hindrance by groups in the ortho position would twist the rings out of a common plane and interfere with π-electron delocalization to give rise to this same shift. The shifts observed for the *p*-MeO to *o*-Meo and *p*-NO_2 to *o*-NO_2 were complicated by the strong delocalization and inductive effects of these groups. When these were considered as superimposed on the conjugative effects, there was sufficient reason to also propose the same geometrical change for these isomers.

Snyder (*4*), in a detailed discussion of the earlier work of Beaven et al. (*5*), points out that if loss of conjugation is already complete with *o*-methyl substitution of both rings of biphenyl, then further methyl substitution cannot increase nonplanarity. The change of retention volume in gas-liquid chromatography with further substitution, as observed by Beaven et al., can be due only to shielding of the individual aromatic rings from solvent interaction, and the observed further shifts (*6*) in the UV spectra with substitution cannot be due to increased orthogonality of the rings. Thus UV-spectral shifts which occur after initial ortho substitution are not always reliable measures of steric hindrance of conjugation.

The hypothesis which initiated the study of this group of isomers was that the planar *m*- and *p*-isomers would be retained on alumina more strongly than the *o*-isomer because of charge-transfer interaction of the delocalized π electrons, present in the planar isomers, with the positive alumina surface. Contrary to expectation chromatography in four solvent systems consistently showed the *o*-Me and *o*-Cl compounds to be more firmly retained than the *m*- and *p*-isomers, while the *o*-MeO- and *o*-NO_2- isomers preceded the *m* and *p* isomers. The chromatographic sequence for the chlorosuccinanils, where π-electron delocalization across the rings is absent because the five-membered ring lacks a double bond, was identical with that of the N-(chlorophenyl)maleimides. Charge-transfer interaction plays only a minor role if any. The authors proposed that retention was primarily due to interaction of the carbonyl group with the positive alumina surface and that in the hindered *o*-Me and *o*-Cl systems this group projects out of the plane of the rings and is made available for bonding. Snyder (*3*), however, prefers to base the argument on the nitrogen atom. Experiments could not decide if the five-membered ring was perpendicular to the surface with one carbonyl group attached or planar to the surface with both carbonyl groups interacting with the surface. The authors suggested that for the MeO and NO_2 derivatives, concerted action of the carbonyl groups and these substitutents with the surface coupled with intramolecular electronic effects favored retention of the planar *m*- and *p*-isomers. Certainly a stronger argument for specific group interaction with the surface gave clearer explanations than π-electron interaction.

Snyder (*7,8*) has argued that the principal adsorption sites on alumina correspond to strong, positive electric force fields at specific points on the alumina surface. Unlike silica, the hydroxyl

TABLE 1

Variation of the R_f Value with the Weight of Solute per Solute Spot for N-(*p*-Methylphenyl)maleimide on Silica Gel-G (RS) with a Developer of 2:1 Cyclohexane/Ethyl Acetate

Weight, μg	R_f Value
1.0	n.d.[a]
2.0	n.d.
5.0	0.52
10	0.52
20	0.52
50	0.53
100	0.55
150	0.57
200	0.57
400	0.59
600	0.60

[a] n.d., not detectable.

groups on the alumina surface are believed to be unimportant as adsorption sites. This work supports this contention by demonstrating the dramatically different behavior of this series of compounds on silica gel, relative to alumina.

EXPERIMENTAL

Synthesis

The synthesis, properties, and spectra of the solutes are reported elsewhere (*1*,*2*).

Thin-Layer Plates

The gel was applied as an aqueous slurry (50 g/100 ml) to 20 × 20 cm plates to give a layer thickness of 0.30 mm. The adsorbent was activated after preparation of the plates.

Adsorbent

There were two sources of Silica Gel-G: RS (Research Specialties Co., Richmond, Cal.) activated at 110°C for 1 hr and at 150°C for 12 hr; ES (Prepared according to Stahl, Brinkman Instruments, Westbury, L.I., N.Y.) activated at 110°C for 1 hr and 150°C for 2 hr.

Sample Load

Solute samples in chloroform were applied with a 2-μl micropet. Sample spots were 1.5 cm apart and 2.0 cm from the base of the plate. Because R_f values depend on sample load, a representative of the solutes was tested over a wide range of sample weight to determine the sample load sufficiently large to be detected but small enough that the R_f value was independent of this load. Table 1 shows the result of this study. A sample weight of 10 μg was used throughout.

Developer Solvents

All solvents were redistilled before use. Developer designations and compositions were: Bnz., benzene; CyHx/EtAc, 2:1, cyclohexane/ethyl acetate 2:1 (v/v); CyHx/EtAc, 3:2, cyclohexane/ethyl acetate, 3:2 (v/v).

Ascending Chromatography

The chamber used is described elsewhere (*1*). Freshly activated plates were suspended in the solvent atmosphere 1 hr prior to chromatography. On lowering the plates, the solvent covered the first 1 cm of the plate placing the solvent line 1 cm from the sample line. The plates were withdrawn from the solvent when it had risen 10 cm above the sample line. This required 20–40 min, depending on the solvent. The plates were quickly withdrawn and dried in the atmosphere of the laboratory.

Temperature variations were from 24.5–27°C during the course of the study.

Visualization of solute spots with sulfuric acid is described in the earlier papers.

RESULTS AND DISCUSSION

The results in terms of absolute and relative R_f values are shown in Tables 2, 3, and 4. The number of determinations is indicated parenthetically under the operator's initials. Where replicate independent determinations were made, the R_f value reported is the mean. The distinction between horizontal rows is that each represents the solutes chromatographed simultaneously on a single plate. Snyder (9) suggested that at best the reproducibility of R_f values is

TABLE 2

R_f Values and Relative R_f Values[a] of the N-Substituted Maleimides and Chlorosuccinanils on Silica Gel Developed with Benzene

Silica grade[b]	Opr.[c]	N-Substituted maleimides															
		N-(Me-phenyl)			N-(Cl-phenyl)			N-(NO_2-phenyl)			N-(MeO-phenyl)				Chlorosuccinanils		
		o	*m*	*p*	*o*	*m*	*p*	*o*	*m*	*p*	*o*	*p*	N-(phenyl)	N-(Bnz)	*o*	*m*	*p*
RS 110	JD (1)	0.22 (0.85)	0.21 (0.81)	0.21 (0.81)	0.16 (0.62)	0.17 (0.65)	0.16 (0.62)	0.08 (0.31)	0.08 (0.31)	0.07 (0.27)	0.13 (0.50)	0.13 (0.50)	0.21 (0.81)	0.26* (1.00)			
RS 110	WJ (3)	0.10 (0.67)	0.13 (0.86)	0.13 (0.86)	0.15 (1.00)	0.17 (1.13)	0.18 (1.20)						0.12 (0.80)	0.15* (1.00)			
RS 110	WJ (4)							0.10 (0.62)	0.10 (0.62)	0.10 (0.62)	0.06 (0.38)	0.06 (0.38)	0.13 (0.81)	0.16* (1.00)			
RS 110	JD (1)				0.18 (1.06)	0.17 (1.00)	0.17* (1.00)								0.18 (1.06)	0.18 (1.06)	0.18 (1.06)
RS 110	WJ (4)				0.14 (0.70	0.20 (1.00	0.20* (1.00)								0.03 (0.15)	0.04 (0.20)	0.04 (0.20)
ES 110	WJ (4)	0.11 (0.73)	0.14 (0.93)	0.13 (0.86)	0.14 (0.93)	0.18 (1.20)	0.16 (1.06)						0.12 (0.80)	0.15* (1.00)			
ES 110	WJ (3)							0.11 (0.78)	0.09 (0.64)	0.09 (0.64)	0.06 (0.43)	0.05 (0.36)	0.12 (0.86)	0.14* (1.00)			
ES 110	WJ (2)				0.10 (1.00)	0.12 (1.2)	0.10* (1.00)								0.01 (0.10)	0.01 (0.10)	0.01 (0.10)
ES 150	WJ (3)							0.11 (0.78)	0.08 (0.57)	0.09 (0.64)	0.06 (0.43)	0.06 (0.43)	0.11 (0.78)	0.14* (1.00)			

[a] These were calculated relative to the compound marked with the asterisk in the horizontal row and appear in parentheses below the absolute R_f value.
[b] RS, Research Specialties; ES, prepared according to Stahl. Plate activation temperatures are given below the source.
[c] Operators are distinguished by their initials.

TABLE 3

R_f Values and Relative R_f Values[a] of the N-Substituted Maleimides and Chlorosuccinanils on Silica Gel Developed with Cyclohexane/Ethyl Acetate, 2:1 (v/v)

		N-Substituted maleimides															
		N-(Me-phenyl)			N-(Cl-phenyl)			N-(NO_2-phenyl)			N-(MeO-phenyl)				Chlorosuccinanils		
Silica grade[b]	Opr.[c]	*o*	*m*	*p*	*o*	*m*	*p*	*o*	*m*	*p*	*o*	*p*	N-(phenyl)	N-(Bnz)	*o*	*m*	*p*
RS 110	JD (1)	0.52 (0.87)	0.53 (0.88)	0.52 (0.87)	0.47 (0.78)	0.48 (0.80)	0.48 (0.80)	0.34 (0.57)	0.35 (0.58)	0.34 (0.57)	0.43 (0.72)	0.43 (0.72)	0.51 (0.85)	0.60* (1.00)			
RS 110	WJ (3)	0.40 (0.93)	0.42 (0.98)	0.40 (0.93)	0.36 (0.84)	0.36 (0.84)	0.35 (0.81)						0.37 (0.86)	0.43* (1.00)			
RS 110	WJ (3)							0.22 (0.61)	0.21 (0.58)	0.19 (0.53)	0.26 (0.72)	0.25 (0.69)	0.30 (0.83)	0.36* (1.00)			
RS 110	JD (1)				0.48 (0.98)	0.48 (0.98)	0.49* (1.00)								0.50 (1.02)	0.49 (1.00)	0.50 (1.02)
ES 110	WJ (3)	0.37 (0.95)	0.38 (0.97)	0.38 (0.97)	0.35 (0.90)	0.36 (0.92)	0.34 (0.87)						0.33 (0.85)	0.39* (1.00)			
ES 110	WJ (3)							0.23 (0.59)	0.24 (0.61)	0.24 (0.61)	0.30 (0.77)	0.29 (0.74)	0.35 (0.87)	0.39* (1.00)			
RS 150	JD (1)	0.54 (0.87)	0.54 (0.87)	0.53 (0.85)	0.50 (0.81)	0.51 (0.82)	0.50 (0.81)	0.31 (0.50)	0.31 (0.50)	0.30 (0.48)	0.44 (0.71)	0.44 (0.71)	0.53 (0.85)	0.62* (1.00)			

[a] These were calculated relative to the compound marked with the asterisk in the horizontal row and appear in parentheses below the absolute R_f value.

[b] RS, Research Specialties; ES, prepared according to Stahl. Plate activation temperatures are given below the source.

[c] Operators are distinguished by their initials.

TABLE 4

R_f Values and Relative R_f Values[a] of the N-Substituted Maleimides and Chlorosuccinanils on Silica Gel Developed with Cyclohexane/Ethyl Acetate, 3:2 (v/v)

Silica grade[b]	Opr.[c]	N-Substituted maleimides												
		N-(Me-phenyl)			N-(Cl-phenyl)			N-(NO_2-phenyl)			N-(MeO-phenyl)			
		o	*m*	*p*	*o*	*m*	*p*	*o*	*m*	*p*	*o*	*p*	N-(Phenyl)	N-(Bnz)
RS	JD	0.62	0.63	0.62	0.56	0.56	0.56	0.44	0.45	0.43	0.51	0.51	0.61	0.68*
110	(1)	(0.91)	(0.93)	(0.91)	(0.82)	(0.82)	(0.82)	(0.65)	(0.66)	(0.63)	(0.75)	(0.75)	(0.90)	(1.00)
RS	WJ	0.43	0.43	0.42	0.38	0.38	0.36						0.38	0.43*
110	(3)	(1.00)	(1.00)	(0.97)	(0.88)	(0.88)	(0.84)						(0.88)	(1.00)
RS	WJ							0.29	0.30	0.28	0.36	0.36	0.41	0.46*
110	(3)							(0.63)	(0.65)	(0.61)	(0.78)	(0.78)	(0.89)	(1.00)
ES	WJ	0.46	0.48	0.47	0.45	0.45	0.43						0.44	0.46*
110	(3)	(1.00)	(1.04)	(1.02)	(0.98)	(0.98)	(0.93)						(0.95)	(1.00)
ES	WJ							0.28	0.29	0.28	0.33	0.35	0.39	0.45*
110	(3)							(0.62)	(0.64)	(0.62)	(0.73)	(0.78)	(0.86)	(1.00)

[a] These were calculated relative to the compound marked with the asterisk in the horizontal row and appear in parentheses below the absolute R_f value.

[b] RS, Research Specialties; ES, prepared according to Stahl. Plate activation temperatures are given below the source.

[c] Operators are distinguished by their initials.

about 0.02 R_f units. The data of Lisboa (*10*) shows a standard deviation of ±0.03 units. The wealth of data presented here allows a similar calculation. The mean value of the R_f's of a particular compound on different plates run at different times was determined and used to calculate the small sample standard deviation. This gave a standard deviation for 21 groups of quadruplicates, 82 groups of triplicates, and 6 groups of duplicates. The variances were pooled and an overall small sample standard deviation of 0.025 R_f units calculated for the 342 data points. Our statistical hypothesis is that if the average R_f value for a particular isomer, e.g., N-(*o*-methylphenyl)maleimide (0.10), exceeds the mean value of the average R_f of the isomeric group, e.g., the mean of the average R_f's of *o*-, *m*-, and *p*-N-(methylphenyl)maleimides $[(0.10 + 0.13 = 0.13)/3]$, by more than one standard deviation (68% confidence limit), then the behavior of that isomer is significantly different. This is true only for N-(*o*-chlorophenyl)maleimide on RS silica gel activated at 110°C developed with benzene and run by WJ. We conclude that silica gel cannot distinguish between isomers of the present families of compounds, which is contrary to the behavior of alumina. In general the separation of isomers, where intramolecular electronic effects are the principal distinguishing characteristic, is less pronounced on silica than on alumina.

There are vagaries and inconsistencies when different families are compared. A few examples will suffice: (1) N-(Methylphenyl)-maleimides by JD and WJ on RS silica gel activated at 110°C and developed with benzene show similar relative R_f values but significantly different values of the absolute R_f. The N-(chlorophenyl)-maleimides on the same plates do not compare at all well for the relative R_f values but are statistically identical with regard to absolute R_f values. Agreement is quite good for CyHx/EtAc, 2:1, and CyHx/EtAc, 3:2. (2) JD found almost identical behavior for the N-(chlorophenyl)maleimides and the chlorosuccinanils on RS silica gel activated at 110°C when developed with benzene. WJ's data in this same system shows a dramatic difference. Note, however, that both JD and WJ indicate small R_f values in a region where they are unreliable ($R_f < 0.02$). WJ supports his observation with a different grade of silica gel (ES) with the same developer, while JD supports his with the same adsorbent but a different developer, i.e., CyHx/EtAc, 2:1. We have no explanation for these differences between families.

These vagaries vanish in Tables 3 and 4 where the absolute R_f values lie between the acceptable limits of 0.2 and 0.8. (1) The behavior of the isomers of any one family in any one run is statistically identical. (2) The relative R_f values of any family on different grades of silica gel by different operators show moderately close agreement. The order of retention is fairly consistent as NO_2-Ph > MeO-Ph > Cl-Ph ~ Ph > MePh > Bnz. On alumina (*1*) the order was NO_2-Ph > MeO-Ph > Me-Ph > Ph > Cl-Ph > Bnz. (3) The chlorosuccinanils behaved identically to that of the N-(chlorophenyl)maleimides.

Strictly within the limits of the particular solutes of this study, we are confident that silica gel does not distinguish between the members of any one family containing coplanar and noncoplanar conjugated systems and there is strong evidence for the identical behavior of planar conjugated N-(chlorophenyl)maleimides and the nonconjugated chlorosuccinanils. Silica gel is insensitive to charge-transfer interaction and spatial orientation. This is quite contrary to the behavior on alumina.

Acknowledgment

We are indebted to the National Science Foundation, NSF-G14216, in support of this project.

REFERENCES

1. J. V. Dichiaro, R. A. Bate, and R. A. Keller, *Separation Sci.*, **2**, 357 (1967).

2. J. V. Dichiaro and R. A. Keller, *Separation Sci.*, **2**, 501 (1967).

3. J. Adrian, *J. Chem. Phys.*, **28**, 608 (1958).

4. L. R. Snyder, *J. Phys. Chem.*, **65**, 246 (1961).

5. G. A. Beaven, A. T. James, and E. A. Johnson, *Nature*, **179**, 490 (1957).

6. R. A. Friedel and M. Orchin, *Ultraviolet Spectra of Organic Compounds*, Wiley, New York, 1951.

7. L. Snyder, *Principles of Adsorption Chromatography*, Dekker, New York, 1968.

8. L. Snyder, *153rd National Meeting, American Chemical Society, Miami Beach, April 1967.*

9. L. R. Snyder, *Advan. Chromatog. 4*, 3 (1967).

10. B. P. Lisboa, *J. Chromatog.*, **19**, 81 (1965).

Received by editor November 29, 1967
Submitted for publication December 26, 1967