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Thin layer chromatographic R_f data on silica gel are reported for 64 compounds containing either a thiole sulfur atom, one or more azine nitrogen atoms, or both. Thiole adsorbates are compared with 28 aromatic hydrocarbons and non-heterocyclic sulfur compounds. In general the orders of R_f values found are thioles > sulfides > sulfones > sulfoxides > azine N -oxides, and azines > azine- N -oxides. Results are interpreted in terms of hydrogen bonding from the silica gel to the adsorbate. The different orders of adsorbability found amongst four series of condensed thiophenes and their arene analogs for chromatography on silica gel and on alumina are rationalized in terms of planarity and acid-base interactions. Correlations of the tlc data with separations on columns are presented.

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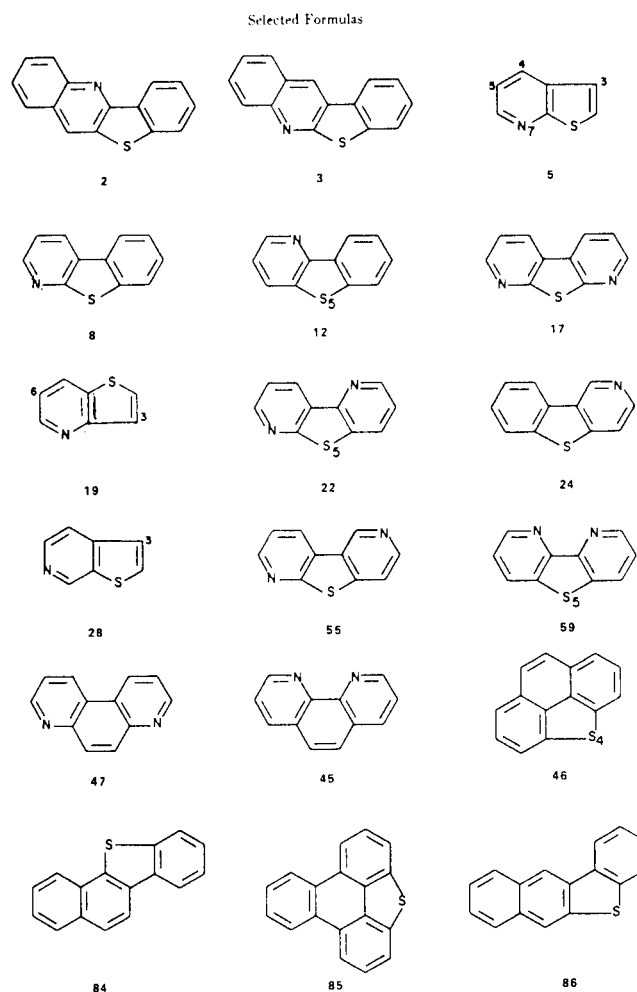
Thin-layer chromatographic (tlc) R_f values are quantitative measures (inverse functions) of relative adsorbabilities of compounds in the presence of a particular solvent-adsorbent combination. The difference in R_f values (ΔR_f) for two compounds is an approximate measure (direct function) of the ease of separation of a mixture of these components on a preparative scale by means of a column or a thick-layer plate. In this paper are presented R_f values on silica gel for a variety of parent azine and thiole heterocycles containing 1-5 rings, as well as for some of their C -substituted derivatives and their N - and S -oxides. An attempt is made to correlate these data with structural and hydrogen-bonding features of the adsorbate molecules and with preparative separations.

Table I shows R_f values obtained with ethyl acetate-silica gel for 57 azines, including pyridine (41), quinoline (23), isoquinoline (27), 3,3'-bipyridine (48), quinoxaline (18), phenazine (13), two diazaphenanthrenes (47 and 55), and the twelve thienopyridine parent systems shown in the list of Selected Formulas. These R_f values were obtained under conditions of constant temperature ($24 \pm 1.5^\circ$) and constant relative humidity (*ca.* 47%) and are reproducible (after correction for variation in activity of the adsorbent from plate to plate) to ± 0.02 .

Examination of Table I shows that, in the presence of ethyl acetate, N -oxides are adsorbed far more strongly to silica gel than are their corresponding parent azine molecules; *cf.*, the pairs 5 and 52, 13 and 40, 18 and 42, 33 and 51, 34 and 56, 36 and 54, 39 and 53, 41 and 57. This relationship has also been observed by Polish workers (4) for use of other polar eluents (acetone, diethylamine, ethanol) plus parent systems of 23, 27, 35, 36, 41, various other 4-substituted pyridines, 2,2'-biquinoline and acridine. While we did not find a report on the separation of azines and their N -oxides on a preparative scale, it is apparent that the process should be facile.

Adsorption sites on silica gel consist of hydroxyl

groups which interact with the adsorbate by hydrogen bonding (8a). From a simplified point of view one might expect, then, that R_f values of azines should decrease monotonously with increasing pK_a value. It is clear from Table I that in our studies such a relationship



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Table I

Thin-Layer Chromatographic R_f Values for Some Azines and Thienopyridines on Silica Gel (a)

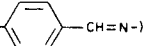
Compound No.	Parent Molecule (c)	Substituent(s) (d)	pK_a (e)	R_f Values (f)	
				For Ethyl Acetate	For Chloroform
1	quinoline	2-Ph		0.70	[58-64]
2				0.69	0.58
3	5	5-(PhCH ₂ NH-)		0.68	[66]
4				0.66	0.55
5				0.64	
6	pyridine	2-Ph	4.48	0.63	
7	5	3-NO ₂		0.63	0.36
8				0.61	
9	quinoline	3-Ph		0.60	
10	pyridine	2-Ac		0.58	[67-69]
11	5	5-Ac		0.58	
12			3.09	0.58	0.29
13	phenazine	none	1.23	[71]	[70-71]
14	12	5,5-dioxide		0.57	
15	19	3-NO ₂		0.56	
16	19	6-Ac		0.51	
17				0.46	
18	quinoxaline	none	2.35 (g)	0.46	
19			0.56	0.46	
20	5	5-(Me ₂ N-  -CH=N-)		0.45	
21	5	5-(PhCH=N-)		0.44	
22			2.46	0.43	
23(b)	quinoline	none	4.87	0.43	
24				[72]	[72]
25	22	5-oxide		0.42	
26	22	5,5-dioxide		0.42	
27(b)	isoquinoline	none		[74]	
28			5.40	0.41	
29	5	4-Cl-7-oxide	5.58	0.39	0.11
30	28	3-NO ₂		0.36	
31	pyridine	4-Ph	5.55	0.36	
32	5	4-NO ₂ -7-oxide		0.36	[73-74]
33	pyridine	2,6-diMe		0.35	
34	pyridine	3-Me	6.75	0.35	
35(b)	pyridine	4-Ac	5.68	0.35	
36(b)	pyridine	4-Me		0.33	
37	pyridine	3-Ac	6.02	0.32	
38	46	5,5-dioxide	3.18	0.32	
39	pyridine	2-Me		0.31	
40	phenazine	5,10-dioxide	5.97	0.30	
41(b)	pyridine	none	5.16	0.30	
42	quinoxaline	1,4-dioxide		0.29	
43	pyridine	3-Ph	4.80	0.27	
44	12	5-oxide		0.25	
45				[75]	[75]
46			2.96	0.20	
47			4.0	0.17	
				0.16	
				[76]	[76]

Table I (Continued)

Compound No.	Parent Molecule (c)	Substituent(s) (d)	pK_a (e)	R_f Value (f)	
				For Ethyl Acetate	For Ethanol
48	3,3'-bipyridine	none	4.60	0.12	0.47
49	46	5-oxide		0.07	
50(b)	quinoline	1-oxide	0.70	0.06	0.47
51	pyridine	2,6-diMe-1-oxide	1.44	0.06	0.47
52	5	7-oxide		0.06	
53	pyridine	2-Me-1-oxide	1.02	0.03	0.38
54(b)	pyridine	4-Me-1-oxide	1.29	0.03	0.35
55			4.86	0.03	0.35
56	pyridine	3-Me-1-oxide	1.08	0.03	0.34
57(b)	pyridine	1-oxide	0.79	0.02	0.31

(a) Run at constant temperature ($24 \pm 1.5^\circ$) and constant relative humidity (*ca.* 47%). See Experimental for details. (b) These compounds were also studied by Bieganska and Wawrzynowicz (4). (c) Where no parent molecule is indicated, see the structural formula in the accompanying text. (d) On the parent molecule. (e) See tables in references 5, 6, and 7. (f) The ethanol solvent was 100%. Numbers shown in brackets refer to compounds (sulfides, sulfoxides, and sulfones) from Table II. They permit direct correlation of R_f values from Tables I and II. (g) Estimated, see reference 6.

does not hold in general, or even for special series of azines of similar structure. Polish workers claimed a linear relationship between R_M and pK_a for nitrogen-bearing adsorbates in various solvents (9), but they obtained different correlation lines for the various series of amines (*e.g.*, anilines and quinolines) studied and noted that structural factors, such as steric hindrance to bonding at the nitrogen atom and polarizability of the adsorbate molecule, must also be important. French scientists (10) reported that mobility of substituted pyridines, thiazoles, and benzothiazoles on silica gel is influenced equally by electronic and steric effects. For a group of 8 azines they found an approximately linear relationship between pK_a and R_f in tlc with methylene chloride on silica gel and a better linearity when the eluent contained 4% of added acetic acid. Wagner and Lehmann (11) reported that orders of adsorbability of substituted pyridines, quinolines, and isoquinoline change on altering the eluent from benzene-methanol to ethyl acetate-methanol-acetic acid or ethyl acetate-methanol-formic acid. Steric hindrance by substituents located α to the anchoring site (*i.e.*, the azine nitrogen) in our amines is apparent in Table I; *cf.*, 1 with 9 and 23; 6 with 31, 41, and 43; 10 with 35 and 37; 33 with 39 and 41; 51 with 53 and 57. The monomethylpyridines, 34, 36, and 39, however, do not fall in a logical sequence based primarily on steric effects.

It is also apparent from Table I that opposing dipoles in the adsorbate decrease adsorbability. Thus, quinoxaline (18) has a slightly larger R_f value than does quinoline (23) despite the fact that the former molecule has two anchoring sites (12). Larger differences of this type are

apparent in other instances; *cf.*, 29 and 32 with 52; 42 with 50. As with alumina (12) one notes exceptionally strong adsorbability of diazines which contain two nitrogen atoms that can be anchored to the surface at the same time (or in rapid alternation); see 45-48 and 55.

Table II contains reference tlc R_f data for a group of 20 alkyl and aryl sulfides, disulfides, sulfoxides, and sulfones with chloroform and silica gel, measured under the same conditions of constant temperature and relative humidity as used for the adsorbates in Table I. In analogy to the *N*-oxides of Table I, the sulfoxides of Table II are generally the most strongly retained compounds. In fact, the general order of R_f values is sulfide > sulfone > sulfoxide; *cf.*, the dibenzothiophene series 58, 66, 72; the diphenyl sulfide series 63, 65, 71; and the pairs 62 plus 67, 64 plus 70, 68 plus 75, 69 plus 76, and 73 plus 77. The same order of adsorbability amongst the triads of parent sulfur compound, its sulfone, and its sulfoxide on silica gel was reported in the following series (listed with respective R_f values and eluent in selected cases): phenanthro[4,5-*bcd*]thiophene (59), 0.86, 0.22, < 0.1, with benzene (13); tetrahydrothiophene, 0.74, 0.49, 0.25 (14); bis-(4-chlorophenyl) sulfide, 0.91, 0.73, 0.56 (14); bis-(4-nitrophenyl)sulfide, 0.56, 0.43, 0.38, with 60:30:10:1 hexane-acetone-benzene-methanol (15); di-*n*-propyl, di-*n*-butyl, di-isobutyl, and di-*n*-pentyl sulfides (14); phenyl benzyl sulfide, 0.95, 0.27, 0.08, with chloroform (16); and triphenyl[4,5-*bcd*]thiophene (85), 0.77, *ca.* 0, *ca.* 0, with carbon tetrachloride (17). Fishbein and Fawkes (14) also studied a number of adsorbate pairs, as follows: sulfide > sulfone in R_f for diisopropyl, di-*sec*-butyl, diisopentyl, and bis-(4-aminophenyl) cases; sulfide

Table II
Thin-Layer Chromatographic R_f Values for Some Sulfides, Sulfoxides, and Sulfones on Silica Gel (a)

Compound No.	Formula or Name	R_f Value (c)	
		For Chloroform	For Ethyl Acetate
58	Dibenzothiophene	0.88	
59(d)	Phenanthro[4,5- <i>bcd</i>]thiophene	0.88	
60	PhS ₂ Me	0.78	
61	(PhCH ₂) ₂ S ₂	0.78	
62	PhSMe	0.77	
63(b)	Ph ₂ S	0.77	
64	PhCH ₂ SMe	0.75	
65(b)	Ph ₂ SO ₂	0.60	
66	Dibenzothiophene 5,5-dioxide	0.56	
67	PhSO ₂ Me	0.34	
68(b)	(<i>n</i> -Bu) ₂ SO ₂	0.29	
69(b)	(<i>n</i> -Pr) ₂ SO ₂	0.29	
70	PhCH ₂ SO ₂ Me	0.23	
71(b)	Ph ₂ SO	0.22	0.58
72	Dibenzothiophene 5-oxide	0.12	0.43
73(b)	Me ₂ SO ₂	0.10	
74(b)	(PhCH ₂) ₂ SO	0.09	0.42
75(b)	(<i>n</i> -Bu) ₂ SO	0.06	0.23
76(b)	(<i>n</i> -Pr) ₂ SO	0.04	0.14
77(b)	Me ₂ SO	0.01	

(a) See footnote (a), Table I. (b) Compounds for which R_f values (under different conditions) were reported by Fishbein and Fawkes (*cf.*, reference 14). (c) R_f values in this table may be directly correlated with those in Table I. (d) The structural formula is shown in the text.

> sulfoxide for di-*n*-hexyl and dibenzyl cases; and sulfone > sulfoxide for the bis-(4-tolyl) case.

On a preparative scale, sulfides, including condensed thiophenes as special cases, have been separated from mixtures with hydrocarbons and elemental sulfur by means of successive steps of oxidizing the sulfides to sulfoxides (in order to improve separability), column chromatography on silica gel, and, if desired, reduction of the isolated sulfoxides back to the sulfides. This scheme was employed by Karaulova and associates (18) and by Drushel and Sommers (19) to isolate sulfur-containing components from petroleum. Analogously, Bateman and Shipley (20) separated methyl 2-cyclohexenyl sulfide from its oxidation products, including the sulfoxide. More recently, in the syntheses of condensed polycyclic aromatic thiophenes by insertion of a sulfur bridging atom into a *phene*-type arene, Klemm and coworkers (13,17) used the procedure to purify products **59** and **85**.

Combining (a) the interpretation of Fishbein and Fawkes (14) that the R_f values of the aforementioned sulfides, sulfoxides, and sulfones correlate inversely with their hydrogen bonding propensities and (b) the infrared spectral data of Lygin and coworkers (21) for strengths of hydrogen bonding of various sulfur-containing adsorbates to silica gel, one obtains the expected general order of R_f values: thiophenes > disulfides > thiols > sulfides > sulfones > sulfoxides. Except for the fact that

we did not study any thiols, the data of Table II are consistent with this order. In contrast, however, Pape, *et al.* (22), found that diphenyl sulfide (**63**) was less strongly retained (R_f 0.54) than dibenzothiophene (**58**) (R_f 0.50) with petroleum ether on silica gel. Also slightly changed adsorbability orders were reported in column chromatography on silica gel by Prinzier and Oehler (23) (alkyl disulfides < thiophene < thiols < alkyl sulfides < thiacycloalkanes) with isopropanol as eluent, by Hesp and Barabás (24) (alkyl disulfides < thiophene derivatives < aryl disulfides < thiols < alkyl sulfides < thiacycloalkanes) with ethanol as eluent, and by Haresnape, *et al.* (25), (thiophenes < alkyl thiols < alkyl disulfides < arene-thiols < alkyl sulfides < thiacycloalkanes) also with ethanol as eluent.

The data on R_f values with ethyl acetate in Table II and with chloroform in Table I serve as points of cross reference for compounds run in both of the main series in these tables. Since no inversions in orders of adsorbability for the two different eluents are noted, we have also interpolated into Table I bracketed numbers to designate the approximate, expected locations which the corresponding compounds should have in the R_f arrays. It is readily seen that azine *N*-oxides are generally more strongly retained than are sulfoxides. Adsorption chromatography on silica gel thus offers a means of separating and, perhaps, distinguishing *N*-oxides, *S*-oxides, and *S,S*-

dioxides from one another, though the applicability to thienopyridine systems is uncertain at this point (26).

Similarities in basic properties of *N*-oxides and *S*-oxides are remarkable. Both can be titrated with perchloric acid in acetic anhydride (28,29), form isolable salts with mineral acids (7,29-31), and are hygroscopic or crystallize with water of hydration (7,30,32,33). Hadži and co-workers (34) noted that these oxobases are very strong proton acceptors in hydrogen bonding, but weak in extent of ionization. They found that the order of basicity depends on the nature of the proton acid (HX) used and the method of measurement. When they measured basicity by the magnitude of the ionization constant for the hydroperchlorate salt in glacial acetic acid solution, they obtained the order 2,6-dimethylpyridine 1-oxide (51) > pyridine 1-oxide (57) >> thiacyclohexane 1-oxide > diisopropyl sulfoxide \approx diethyl sulfoxide > dimethyl sulfoxide (77) \approx 2,6-dibromopyridine 1-oxide > dibenzyl sulfoxide > diphenyl sulfoxide (71). But when they measured basicity by the change in the infrared stretching frequency of the H-X bond upon hydrogen bonding to the oxo base, the order varied with the HX used and was ascribed at least partially to steric hindrance effects. Toward methanol or phenol (perhaps reasonable analogs to silica gel in hydrogen bonding properties) the *N*-oxides 51 and 57 were still considerably more basic than the

various sulfoxides. Bonding to an *N*-oxide is generally believed to occur through the oxygen atom (7).

Drago, *et al.* (35), found that in complexation with phenol the order in $-\Delta H$ of adduct formation is thiacyclopentane-1-oxide \approx dimethyl sulfoxide > thiacyclopentane-1,1-dioxide \approx diethyl sulfide. They proposed that hydrogen bonding occurs through sulfoxide (30) and sulfone oxygen atoms, in a linear S-O-H geometric arrangement for the sulfoxides, but through a four-membered chelate ring (with hydrogen coordinated equally to both oxygen atoms) in the sulfone. The difference in strength of hydrogen bonding in sulfoxides and sulfones was attributed to an appreciably larger electron density on an oxygen atom of the former. For sulfides and disulfides hydrogen bonding should occur by coordination to sulfur, while in azines (including thienopyridines) it should involve coordination to nitrogen. Both nitrogen and sulfur are less electronegative atoms than oxygen.

We propose that, in general, the order of adsorbability shown in Tables I and II can be rationalized in terms of the preceding concepts for hydrogen bonding that occurs in solution. To a first approximation, the measured R_f value varies in an inverse manner with the electron density on the Lewis basic atomic site(s) of the adsorbate. This electron density may be markedly decreased by electron-withdrawing groups on the adsorbate molecule (as in

Table III

Comparative Thin-Layer Chromatographic R_f Values for Condensed Thiophenes and Analogous Hydrocarbons (a)

Compound No.	Name	R_f (for 30-60° petroleum ether)	
		On Silica Gel (b)	On Alumina (c)
78	Biphenyl	0.42	0.82
58	Dibenzothiophene	0.40	0.66
59(d)	Phenanthro[4,5- <i>bcd</i>]thiophene	0.40	0.54
79	Phenanthrene	0.34	0.59
80	4,5-Methylenephenanthrene	0.34	0.59
81	Fluorene	0.34	0.71
82	Pyrene	0.32	0.45
83	2-Phenylnaphthalene	0.27	0.58
84(d)	Benzo[<i>b</i>]naphtho[2,1- <i>d</i>]thiophene	0.27	0.22
85(d)	Triphenylo[4,5- <i>bcd</i>]thiophene	0.27	
86(d)	Benzo[<i>b</i>]naphtho[2,3- <i>d</i>]thiophene	0.24	
87	Benzo[<i>a</i>]fluorene	0.20	
88	Triphenylene	0.20	
89	Benz[<i>a</i>]anthracene	0.19	
90	Benzo[<i>b</i>]fluorene	0.19	
91	Chrysene	0.19	
92	Benzo[<i>e</i>]pyrene	0.18	

(a) Run at room temperature without control of humidity (see Experimental). (b) R_f values were closely reproducible. (c) Only the order of R_f values was reproducible on various plates of alumina. Compounds 85-92 gave such diffuse spots that an R_f value could not be assigned. (d) The structural formula is shown in the text.

compounds **29** and **32**) or by the presence of an opposing internal dipole (e.g., in **42**). Secondly, but possibly overwhelmingly, R_f may be increased by steric hindrance to hydrogen bonding at the basic site (e.g., in **1** and **6**) or markedly decreased by cooperativity of two basic sites in close proximity (e.g., in **55**). The increase in R_f value with increasing size of the alkyl group in di-*n*-alkyl sulfides, sulfoxides, and sulfones (14 and Table II) is consistent with the Drago model.

The inversion in order of relative R_f values for the isoelectronic systems of dibenzothiophene and diphenyl sulfide is noteworthy. Thus, the sulfones (**65** and **66**) have closely similar adsorbabilities, while the sulfide is somewhat more strongly retained in the latter system (cf., **58** and **63**) and the sulfoxide is considerably more strongly retained in the former system (cf., **71** and **72**). The higher R_f of dibenzothiophene (**58**) is easily rationalized in terms of greater delocalization of electronic charge from the sulfur atom into the planar π -system of **58** and smaller delocalization into the non-coplanar benzene rings of **63**. Contrariwise, in the sulfoxides the planar skeleton of **72** may offer less steric hindrance to hydrogen bonding to the oxygen atom than is the case in **71**.

Table III gives a comparison of the relative adsorbabilities on silica gel and alumina of five aromatic condensed thiophenes (**58**, **59**, **84**, **85**, and **86**) which were prepared in our laboratory by insertion of a sulfur-bridging atom (13,17,36-38), with their hydrocarbon precursors (**78**, **79**, **83**, and **88**) and with analogous arenes (39). The analogs selected either have a methylene bridge in place of a sulfur bridge (as in the pairs **58** and **81**, **59** and **80**, **84** and **87**, and **86** and **90**) for geometric similarity alone, or a vinylene bridge in place of a sulfur bridge (as in the pairs **58** and **79**, **59** and **82**, **84** and **91**, **85** and **92**, and **86** and **89**) for both π -electronic and geometric similarities. For simplicity in discussion, in each series we designate these compounds by the symbols U (unbridged precursor), S (sulfur-bridged product), M (methylene-bridged analog), and V (vinylene-bridged analog). On alumina one finds the R_f order of biphenyl > fluorene > dibenzothiophene > phenanthrene, i.e., $U > M > S > V$ (40). This order is readily interpreted (8b,41) in terms of two effects, viz., (a) a geometric effect, whereby planar molecules M, S, and V are more readily adsorbed flatwise than for the twisted (in solution) U, plus (b) an electronic effect, whereby the bridge in V or, to a smaller extent, that in S contribute positive increments to the π -electronic system in M and, thus, enhance Lewis-type acid-base, i.e., adsorbent-adsorbate, interaction. In the 2-phenylnaphthalene system on alumina one also has the incomplete series $U > S$ and $U > M$ (40,44). On silica gel as adsorbent there are the R_f orders of biphenyl \approx dibenzothiophene > fluorene = phenanthrene, and 2-phenylnaphthalene = **84** \approx **86** > benzofluorenes **87** and **90** = chrysene = benz[*a*]anthracene,

i.e., $U \geq S > M = V$. Here again geometric effect (a) is apparent in M, but the vinylene bridge contributes no net additional electronic effect, while the sulfur bridge introduces a decremental electronic effect which counteracts to a large or complete extent the geometric effect. Presumably, S is weaker than V in basicity toward hydrogen bonding from silica gel.

Confirmation of effects (a) and (b) on alumina is found in the R_f series phenanthrene (**79**) = 4,5-methylene-phenanthrene (**80**) > phenanthrothiophene (**59**) > pyrene (**82**), i.e., $U = M > S > V$. In this case all molecules are planar so that the geometric effect is zero. On silica gel these compounds fall in the predicted order $S > U = M \approx V$, as based on the aforementioned electronic effects. The partial series for silica gel of triphenylthiophene (**85**) > triphenylene (**88**) \approx benzo[*e*]pyrene (**92**), i.e., $S > U \approx V$, is likewise consistent with expectations.

EXPERIMENTAL

N-Oxides **40**, **42**, and **50** were synthesized from the corresponding amines (45,46). All other adsorbates used in this study were commercial samples or were available from previous research in this laboratory (13,17,32,33,36-38,47). Data in Tables I and II were obtained with soft glass plates (20 x 20 cm.) coated with E. Merck (Darmstadt, G.F.R.) silica gel H (according to Stahl, without binder), dried in air for 4 hours, activated at 110-120° for 1 hour, and then transferred to a chamber maintained at ca. 47% relative humidity by means of a saturated aqueous solution of potassium thiocyanate (48). The plates were equilibrated, and chromatograms were run in this chamber at $24 \pm 1.5^\circ$ over a period of 30-40 minutes in the manner previously described (49). A reference compound (**12** for Table I, **70** for Table II) was run on every plate and R_f values, usually from four separate runs for each substrate, were standardized as before (49,50). Several specific compounds were run in both the Table I and Table II series so that R_f values in both tables are directly comparable. For the former series, spots were detected by means of iodine vapor followed by spraying with fortified Dragendorff's reagent (50). With the latter series, only iodine was used. Data in Table III were obtained with pre-coated commercial thin-layer plates (EM Reagents silica gel F-254 and Kodak 6063-13252 alumina) run at room temperature without activation or control of humidity. Spots were detected by means of ultraviolet light at 254 nm.

REFERENCES AND NOTES

- (1) This investigation was supported by research grants MPS 75-04116 from the National Science Foundation and CA-5969 from the National Cancer Institute, U. S. Public Health Service.
- (2) National Science Foundation, Undergraduate Research Participant, 1968-1969.
- (3) Research Assistant, 1977-1978.
- (4) M. Bieganska and T. Wawrzynowicz, *Chem. Anal. (Warsaw)*, **21**, 211 (1976).
- (5) A. Albert, "Physical Methods in Heterocyclic Chemistry", Vol. I, A. R. Katritzky, Ed., Academic Press, New York, N. Y., 1963, Chap. 1.
- (6) L. H. Klemm and R. D. Jacquot, *Electroanal. Chem. Interfac. Electrochem.*, **45**, 181 (1973).

- (7) A. R. Katritzky and J. M. Lagowski, "Chemistry of the Heterocyclic N-Oxides", Academic Press, New York, N. Y., 1971, pp. 144-152.
- (8a) L. R. Snyder, "Principles of Adsorption Chromatography", Marcel Dekker, New York, N. Y., 1968, pp. 156-162; (b) L. R. Snyder, *ibid.*, pp. 321-330.
- (9) E. Soczewinski and W. Golkiewicz, *Chem. Anal. (Warsaw)*, **14**, 465 (1969); *Chem. Abstr.*, **71**, 74438m (1969).
- (10) G. Vernin, R. Cottet, R. Gallo, J. M. Surzur and J. Metzger, *Bull. Soc. Chim. Fr.*, 4492 (1967).
- (11) H. Wagner and H. Lehmann, *Z. Anal. Chem.*, **283**, 115 (1977).
- (12) A discussion of this effect was presented by L. H. Klemm, C. E. Klopfenstein and H. P. Kelly, *J. Chromatogr.*, **23**, 428 (1966).
- (13) L. H. Klemm and W. Hsin, *J. Heterocyclic Chem.*, **13**, 1245 (1976).
- (14) L. Fishbein and J. Fawkes, *J. Chromatogr.*, **22**, 323 (1966). R_f data quoted from this paper were obtained for an eluent of toluene-ethyl acetate (1:1). Analogous data were also reported for an eluent of 2.5% acetone in benzene.
- (15) A. G. Popova, A. V. Ivanov and Z. A. Lerman, *Zh. Anal. Khim.*, **21**, 408 (1976); *Anal. Abstr.*, **31**, 4C57 (1976).
- (16) H. Ertel and L. Horner, *J. Chromatogr.*, **7**, 268 (1962).
- (17) L. H. Klemm and R. F. Lawrence, unpublished observation from this laboratory.
- (18) E. N. Karaulova, G. D. Galpern and B. A. Smirnov, *Tetrahedron*, **18**, 1115 (1962); E. N. Karaulova and G. D. Galpern, *Khim. Seraorg. Sovdin. Soderzh. Neftnyakh Nefteprod.*, **3**, 227 (1960); *Chem. Abstr.*, **57**, 2489 (1962).
- (19) H. V. Drushel and A. L. Sommers, *Anal. Chem.*, **39**, 1819 (1967), and references cited therein. As noted in this article, an earlier separation was effected by oxidation of sulfur components to sulfones prior to column chromatography.
- (20) L. Bateman and F. W. Shipley, *J. Chem. Soc.*, 1996 (1955).
- (21) V. I. Lygin, N. K. Lyapina and A. D. Ulendeeva, *Zh. Fiz. Khim.*, **50**, 2032 (1976); *Chem. Abstr.*, **85**, 182738g (1976).
- (22) D. Pape, M. Teppke and H. W. Prinzler, *Conf. Chem. Chem. Process Petrol. Natur. Gas, Plenary Lect., Budapest*, 579 (1965); *Chem. Abstr.*, **70**, 53766f (1969).
- (23) H. Prinzler and R. Oehler, *Chem. Technol.*, **15**, 31 (1963); *Chem. Zentr.*, **134**, 21399 (1963).
- (24) V. Hesp and J. Barabás, *Magyar Kém. Lapja*, **10**, 269 (1955); *Chem. Abstr.*, **52**, 8523 (1958).
- (25) D. Haresnape, F. A. Fidler and R. A. Lowry, *Ind. Eng. Chem.*, **41**, 2691 (1949).
- (26) Only one parent thienopyridine N-oxide (**52**) was investigated in our tlc studies. In the systems **12**, **22** and **46** there is no consistency in the order of adsorbability for the parent molecule plus its S-oxide and S,S-dioxide. For chemical and spectral methods of distinguishing amongst thienopyridine N- and S-oxides see references 27 and 33.
- (27) L. H. Klemm, S. Rottschaefer and R. E. Merrill, *J. Heterocyclic Chem.*, **12**, 1265 (1975).
- (28) D. C. Wimer, *Anal. Chem.*, **30**, 2060 (1958); **34**, 873 (1962).
- (29) C. W. Muth, R. S. Darlak, W. H. English and A. T. Hamner, *ibid.*, **34**, 1163 (1962).
- (30) H. H. Szmant, "Organic Sulfur Compounds", Vol. I. N. Kharasch, Ed., Pergamon Press, New York, N. Y., 1961, pp. 156-159.
- (31) W. J. Hickinbottom, "Reactions of Organic Compounds", 3rd Ed., John Wiley, New York, N. Y., 1957, p. 578.
- (32) L. H. Klemm, I. T. Barnish and R. Zell, *J. Heterocyclic Chem.*, **7**, 81 (1970).
- (33) L. H. Klemm, S. B. Mathur, R. Zell and R. E. Merrill, *ibid.*, **8**, 931 (1971).
- (34) D. Hadži, C. Klofutar and S. Oblak, *J. Chem. Soc. A*, 995 (1968).
- (35) R. S. Drago, B. Wayland and R. L. Carlson, *J. Am. Chem. Soc.*, **85**, 3125 (1963).
- (36) L. H. Klemm, D. R. McCoy and D. R. Olson, *J. Heterocyclic Chem.*, **7**, 1347 (1970).
- (37) L. H. Klemm and J. J. Karchesy, *ibid.*, **15**, 561 (1978).
- (38) L. H. Klemm, J. J. Karchesy and R. F. Lawrence, *ibid.*, **15**, 773 (1978).
- (39) It should be noted that data in Table III are not directly correlatable with R_f values in Tables I and II.
- (40) For separations of **78** and **81**: of **58** and **79**; and of **83** **87** and **90** on columns of alumina see references 41-43, respectively.
- (41) L. H. Klemm, D. Reed, L. A. Miller and B. T. Ho, *J. Org. Chem.*, **24**, 1468 (1959).
- (42) L. H. Klemm, E. P. Antoniadis, G. Capp, E. Chiang and E. Y. K. Mak, *J. Chromatogr.*, **6**, 420 (1961).
- (43) M. Orchin and L. Reggel, *J. Am. Chem. Soc.*, **70**, 1245 (1948).
- (44) In column chromatography on alumina, **86** is more strongly adsorbed than its isomer **84** (38).
- (45) E. Ochiai, "Aromatic Amine Oxides", Elsevier Publishing Co., New York, N. Y., 1967, pp. 24-25.
- (46) H. McIlwain, *J. Chem. Soc.*, 322 (1943); G. R. Clemo and H. McIlwain, *ibid.*, 479 (1938).
- (47) L. H. Klemm and R. Zell, *J. Heterocyclic Chem.*, **5**, 773 (1968); L. H. Klemm, D. R. McCoy, J. Shabtaf and W. K. T. Kiang, *ibid.*, **6**, 813 (1969); L. H. Klemm, R. Zell, I. T. Barnish, R. A. Klemm, C. E. Klopfenstein and D. R. McCoy, *ibid.*, **7**, 373 (1970); L. H. Klemm, D. R. McCoy and C. E. Klopfenstein, *ibid.*, **8**, 383 (1971); L. H. Klemm, I. T. Barnish and D. R. McCoy, *ibid.*, **14**, 299 (1977); L. H. Klemm, C. E. Klopfenstein, R. Zell, D. R. McCoy and R. A. Klemm, *J. Org. Chem.*, **34**, 347 (1969).
- (48) L. H. Klemm, D. S. W. Chia and H. P. Kelly, *J. Chromatogr.*, **150**, 129 (1978).
- (49) L. H. Klemm, D. S. W. Chia, C. E. Klopfenstein and K. B. Desai, *ibid.*, **30**, 476 (1967).
- (50) See reference in footnote 12.