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THIN-LAYER CHROMATOGRAPHY OF ARYLSULFONAMIDES AND ISOMERIC AMINOSULFONES

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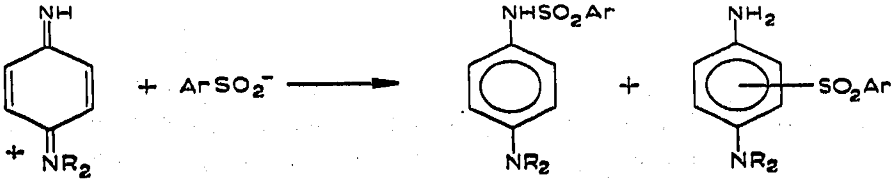
SUMMARY

The separation of ten arylsulfonamides and isomeric aminosulfones by thin-layer chromatography has been achieved on both silica gel and alumina. 2-Phenylsulfonyl- and 3-phenylsulfonyl-4-amino-N,N-dimethylaniline can also be separated on alumina. In selected cases, the N',N'-disulfonamide of N,N-dialkyl-*p*-phenylenediamines were also chromatographed. The observed relative R_F values are discussed in terms of the structure of the compounds. There appears to be no need to activate silica gel plates for these separations.

INTRODUCTION

We have been studying the addition of arylsulfinate anions to N,N-dialkyl quinonediimines as shown in the following equation[1]. Other sulfonamides and sulfones have been the subject of thin-layer chromatographic studies[2-5], but this appears to be the first report of the separation of sulfonamides from isomeric aminosulfones. The N,N-dialkyl quinonediimines are known to undergo a variety of reactions[6,7]; thus, we required a sensitive method for the detection of several products. In addition, we were concerned with the identity of the two possible isomeric sulfones and the conditions under which they are formed.



EXPERIMENTAL

Materials

All of the compounds investigated were prepared and/or isolated by methods to be described[1]. Solvents used for spotting and developing were Eastman Spectro grade. Both alumina and silica gel were used in the form of Brinkmann precoated analytical plates containing a fluorescent indicator (254 nm). The plates were activated for 1 h at 100° before use.

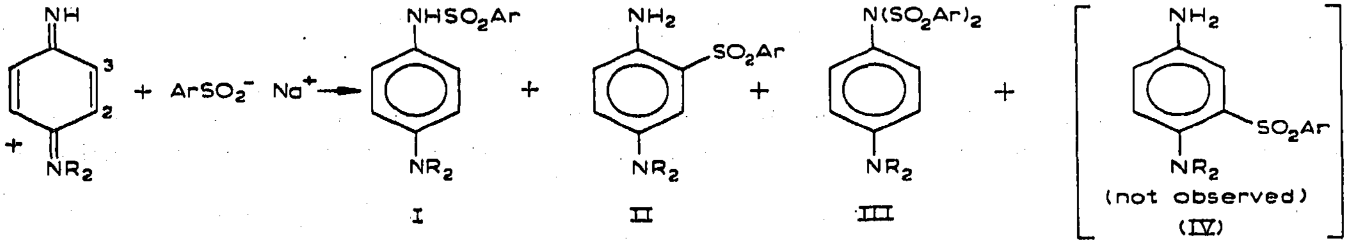
Procedure

Samples of the reaction mixtures[1] were diluted with chloroform to a concentration of 4 mmolar in total products. More concentrated solutions were used for spotting in experiments designed to detect competition from side reactions. Spots of about $10\ \lambda$ were applied 10 mm from the bottom of the plate, flushed with dry air, and developed for 110 to 150 mm. The most satisfactory development solvent was 20 % (v/v) ethyl acetate in benzene and was used for all R_F values reported. A Desaga tank with a ground glass cover was used for all runs.

The separated spots could be detected either by their quenching of the ultraviolet indicator or by allowing the plates to stand in the air. Over a period of a day or less the products became colored, presumably by aerial oxidation.

RESULTS

We found three products in the reaction shown below, where R = Me and Ar = Ph, only two of which were expected (I and II). The third product proved to be the N′, N′-disulfonamide (III)[1]; there was no evidence for the isomeric sulfone in which the linkage is adjacent to the NMe_2 group (IV), *i.e.*, in the 2-position.



Since it was possible that the two sulfones were not being separated, we prepared authentic samples of both for study of their chromatographic properties. Table I shows the R_F values for I, II and IV; obviously if IV had formed, it would be separated by alumina.

TABLE I

R_F VALUES FOR THE REACTION PRODUCTS OF N,N-DIMETHYLQUINONEDIIMINE WITH SODIUM BENZENESULFINATE

R = Me, Ar = Ph.

Compound	*Silica gel*	*Alumina*
I	0.64	0.19
II	0.43	0.51
IV	0.43	0.24

Tables II and III contain the R_F values for the products observed in a number of reactions of substituted sulfinic acids (X varies) with two different quinonediimines (R = Me or Et).

TABLE II

R_F VALUES OF SUBSTITUTED SULFONAMIDES (I) AND AMINOSULFONES (II)

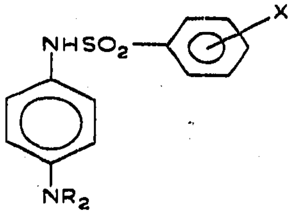
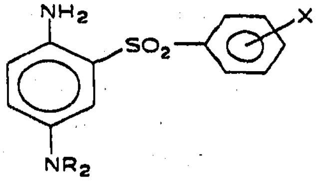
	 I		 II	
X	*R = Me*	*R = Et*	*R = Me*	*R = Et*
	Silica gel			
H	0.64	0.73	0.43	0.56
4-Me	0.66	0.74	0.46	0.56
4-Cl	0.71	0.78	0.55	0.72
4-CN	0.58	0.72	0.42	0.54
3,4-Me_2	0.66	0.75	0.47	0.57
	Alumina			
H	0.19	0.33	0.51	0.75
4-Me	0.25	0.38	0.52	0.67
4-Cl	0.21	0.38	0.60	0.76
4-CN	0.11	0.27	0.52	0.64
3,4-Me_2	0.32	0.47	0.58	0.73

TABLE III

R_F VALUES FOR N′,N′-DISULFONAMIDES (III)

X	*Silica gel*		*Alumina*	
	R = Me	*R = Et*	*R = Me*	*R = Et*
H	0.89	0.91	1.0	1.0
4-Me	0.91	0.93	1.0	1.0
3,4-Me_2	0.92	0.94	1.0	1.0

Some preliminary experiments were made with a few other sulfonamides (I), but they were not used in our studies[1]. The observed R_F values are presented in Table IV.

The compounds studied were also chromatographed on unactivated silica gel plates, and the observed R_F values are reported in Table V.

A concentration series of mixtures of I, II, and III (R = Me; Ar = Ph) was chromatographed to determine the limit of detection for these compounds. A solution which was 10^{-3} *M* in each component was spotted in amounts ranging from 1–10 λ.

TABLE IV

R_F VALUES FOR SOME ADDITIONAL SULFONAMIDES (I)

X	*Silica gel*		*Alumina*	
	R = *Me*	*R* = *Et*	*R* = *Me*	*R* = *Et*
4-OMe	0.52	0.64	0.13	0.36
4-NHCOMe	—	0.05	—	0.02
4-NO_2	0.67	0.77	0.17	0.22

TABLE V

R_F VALUES FOR PRODUCTS I, II, AND III ON UNACTIVATED SILICA GEL PLATES

X	*R* = *Me*			*R* = *Et*		
	I	*II*	*III*	*I*	*II*	*III*
H	0.64	0.47	0.87	0.74	0.57	0.90
4-Me	0.63	0.50	0.82	0.71	0.58	0.85
4-Cl	0.75	0.63	—	0.82	0.72	—
4-CN	0.54	0.42	—	0.65	0.55	—
3,4-Me_2	0.62	0.48	0.84	0.73	0.57	0.87

All of the spots were clearly visible under U.V. light of 254 nm, although the 1 λ (0.3 μg) spot probably represents the lower limit of reliable visual detection.

DISCUSSION

Since only the compounds in Tables I, II, and III proved useful in our studies[1], they are the only ones for which complete data were obtained and our discussion will center on them. The first, and from our point of view most important, general observation is that all N-alkyl isomeric pairs (*i.e.*, R = Me and R = Et) are cleanly separated on either adsorbent. It should be expected that a sulfonamide and its isomeric aminosulfone would be quite different in basicity. This is clearly illustrated by the inversion of relative R_F values on changing from silica gel ("acidic") to alumina ("basic"). The strongest base (sulfone) has the lower R_F value on silica gel, and the weaker base (sulfonamide) has a lower R_F value on alumina. These observations are in accord with the usually accepted generalizations[8] and the recent literature[4,9].

The question of the structure of the sulfones was of some interest to us and, as can be seen in Table I, only alumina separated the 3- and 2-phenylsulfonyl isomers (II and IV, R = Me, Ar = Ph). This is in accord with the general preference for alumina in the separation of bases[8]. The much higher R_F value for the 3-isomer could be due to intramolecular hydrogen bonding. An example of this effect has been observed by us in an earlier study[10].

The effect of substituents in the phenylsulfonyl group is very weak. In fact, on silica gel only the 4-Cl group caused differences from the average for that structural group of more than the usually accepted experimental error (± 0.05). Even on alumina the sulfones show remarkably similar R_F values. When this fact is taken with the low

R_F value for the 2-phenylsulfonyl isomer (IV) on alumina, it strongly suggests that all five compounds have the structural arrangement represented by II. This assignment is supported by the similarity of their mass spectra[1]. The very low R_F value observed for the 4-acetamidosulfonamide is reasonable in view of the high adsorption affinity of this group[11].

The final points to be mentioned are: the difference in R_F value for a given N,N-dimethyl compound and the N,N-diethyl homolog, and the high R_F value for N',N'-disulfonamides. There are no exceptions to the trend of higher R_F value for diethylamino compounds as compared with analogous dimethylamino compounds. This same effect has been observed by us in another series of aromatic compounds and was attributed to the greater hydrocarbon character of the diethyl compound[10]. The high R_F value observed for the disulfonamides is consistent with the fact that the nitrogens are completely substituted and therefore less available for adsorption.

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