thiobromodifluoride, b.p. 35°, for the thiochloro compound but room temperature and atmospheric pressure would be used in the reactions.

IV. *Preparation of N-arylphosphoramidothioic difluorides from phosphorus thiofluoride.* Phosphorus thiofluoride 13.6 g. (0.1 mole), b.p. −53° was dissolved at −70° in 100 ml. of toluene. A cold solution of 0.2 mole of the aromatic amine in toluene (50 ml.) was added and the stirred mixture kept at this temperature for 3 hr. After allowing to warm up slowly to room temperature, the partly separated amine hydrofluoride was removed by filtration and the filtrate fractionated. On removing a part of the solvent, a substantial amount of amine hydrofluoride separated again and was removed by filtration.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CENTRAL STATE COLLEGE]

p-Phenylazobenzenesulfonyl Chloride—a New Reagent for Identification and Separation of Amines

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p-Phenylazobenzenesulfonyl chloride has been found to form solid derivatives with a large number of amines. The derivatives are easily prepared and purified and are therefore suitable for use in identification. Anhydrous and aqueous amines were both used to give good yields of the amides. The amide derivatives can be hydrolyzed to the amine hydrochloride. The Tswett adsorption method has been applied to the separation of mixtures of these colored amides. A new method for the separation of mixtures of the three classes of amines is proposed.

Benzoyl chloride has wide applicability for the identification of active hydrogen compounds such as alcohols, amines and phenols. In previous papers it has been shown that the substituted benzoyl chloride, *p*-Phenylazobenzoyl chloride, is an excellent reagent for the identification of alcohols,[2] amines[3] and phenols.[4] In addition, the *p*-phenylazobenzoyl derivatives of these classes of compounds were highly colored (orange to red) and were found to be suitable derivatives for separation of mixtures of them by chromatographic adsorption.

The general use of benzenesulfonyl chloride for the identification and separation of amines has suggested the use of *p*-phenylazobenzenesulfonyl chloride as a derivatizing reagent for amines. It was hoped that the *p*-phenylazobenzenesulfonyl derivatives would be useful for identification of amines and also for the separation, by chromatography, of mixtures of amines. We wish to report the preparation of a large number of derivatives of aliphatic and aromatic amines with this reagent and consider its advantages over presently used reagents.

We have found *p*-phenylazobenzenesulfonyl chloride to have general usefulness in the identification of amines. The reagent has been used to characterize nineteen aliphatic, eighteen aromatic, six mixed aliphatic aromatic, and two heterocyclic amines. It is superior, in general, to the common reagents for amines—even the most widely used reagent, benzenesulfonyl chloride. The derivatives are easily prepared in good yields upon refluxing a mixture of the amine and the sulfonyl chloride in pyridine. This reagent is particularly useful in identifying aliphatic amines which give either oils or low melting solids with other reagents. The sulfonamides are highly crystalline, orange to red solids and may be easily purified by crystallizing from Skellysolve B or ethanol, or by chromatographing on a silicic acid–celite mixture. All of the derivatives prepared melt without decomposition and in a convenient melting point range. A distinct advantage of this reagent over the commonly used reagents is its high molecular weight, which allows for easy identification of small amounts of amines. It has the added advantage of being a stable solid (m.p. 124–125°) which does not deteriorate on standing for long periods of time and is not easily hydrolyzed by water. Therefore, the reagent can be used successfully in preparing derivatives of amines from their dilute aqueous solutions. The derivatives of methyl amine and dimethyl amine were prepared from their 0.25 aqueous solutions in 89 and 75% yields respectively.

The *N*-substituted *p*-phenylazobenzenesulfonamides that have been characterized are recorded in Table I. Six of the sulfonamides have been previously reported.[5] Their recorded melting points are listed in Table I. There is a large discrepancy between the melting point values obtained in this study

(1) This paper is based on work presented by W. E. Reynolds and J. L. Mason in partial fulfillment of requirements for undergraduate Honors Course offered in the Department of Chemistry of Central State College.

(2) E. O. Woolfolk, F. E. Beach, and S. P. McPherson, *J. Org. Chem.*, 20, 391 (1955).

(3) E. O. Woolfolk and E. H. Roberts, *J. Org. Chem.*, 21, 436 (1956).

(4) E. O. Woolfolk and J. M. Taylor, *J. Org. Chem.*, 22, 827 (1957).

(5) W. H. Gray, G. A. H. Buttle and D. Stephenson, *Biochem. J.*, 31, 724 (1937); I. A. Pearl, *J. Org. Chem.*, 10, 205 (1945); I. A. Pearl and A. R. Ronzio, *J. Org. Chem.*, 12, 785 (1947); R. D. Desai and C. V. Mehta, *Indian J. Pharm.*, 13, 211 (1951). These studies dealt with the synthesis of several sulphanilamides of azobenzene, their reduction and their chemotherapeutic action against various bacterial infections.

TABLE I

AMIDES OF *para*-PHENYLAZOBENZENESULFONIC ACID

Amine used	M. P., °C.[a] Corrected	Yield,[b] %	Yield (%)[c] of amine on Hydrolysis
Primary Aliphatic			
n-Amylamine	97.4– 98.2	47	
Isoamylamine	104.4–105.0	89	38
n-Butylamine	91.4– 92.0	88	94
Isobutylamine	120.6–121.0	71	
sec-Butylamine	123.2–124.4	89	58
tert-Butylamine	159.8–160.3	77	85
Ethylamine	137.2–138.0	62	
Methylamine	156.0–157.3	89	64
n-Propylamine	101.6–102.2	60	
Isopropylamine	119.0–120.6	69	
Secondary Aliphatic			
Di-*n*-amylamine	97.4– 98.4	80	
Di-isoamylamine	118.5–119.3	78	33
Di-*n*-butylamine	99.4–100.0	84	66
Di-isobutylamine	138.7–140.6	78	
Di-*sec*-butylamine	93.6– 95.0	21	
Di-ethylamine	104.6–105.3	76	
Di-methylamine	166.6–168.0	75	80
Di-*n*-propylamine	98.6– 99.2	66	
Di-isopropylamine	138.4–139.4	21	
Primary Aromatic			
o-Aminophenol	178.0–178.9	81	
m-Aminophenol	190.0–191.0	48	
p-Aminophenol	213.0–213.9	32	
Aniline	156.0–156.8 (Lit. 152)	89	
m-Bromoaniline	168.0–169.8	38	
p-Bromoaniline	188.0–188.9	40	
o-Chloroaniline	139.0–140.2	35	
p-Chloroaniline	167.0–168.0	60	45
o-Ethoxyaniline	143.0–144.5	58	
m-Ethoxyaniline	132.0–132.9	73	
p-Ethoxyaniline	158.0–159.5	45	
o-Methoxyaniline	122.0–123.0	35	
p-Methoxyaniline	140.0–141.8	44	
1-Naphthylamine	189.0–191.0 (Lit. 156)	61	37
2-Naphthylamine	158.0–159.5 (Lit. 170)	88	37
o-Toluidine	171.2–172.2 (Lit. 138–139)	57	
m-Toluidine	140.0–141.2 (Lit. 168)	53	
p-Toluidine	166.0–166.8 (Lit. 163–164)	79	71
Mixed Secondary			
n-Butylaniline	153.0–154.9	46	
Ethylaniline	144.0–145.2	46	
Isoamylaniline	156.0–157.2	22	
Methylaniline	168.8–168.9	66	
Methyl-*o*-toluidine	141.0–142.0	24	
Methyl-*p*-toluidine	134.0–135.2	52	
Heterocyclic			
Morpholine	217.0–218.0	46	
Piperidine	191.0–191.9	95	

[a] Melting points were taken on a modified Hershberg type apparatus. [b] Yields are on products purified by chromatography. The found analyses agreed with the calculated to within ±0.2% Nitrogen except in 8 cases, and the difference was not greater than ±0.3% except in 4 cases. Microanalyses were performed by the Du Good Chemical Laboratories, St. Louis, Mo. [c] The recovered aliphatic amines were identified as their hydrochlorides. The recovered aromatic amines were identified by mixture melting point.

and those previously reported for the derivatives of *ortho*- and *meta*-toluidine and 1- and 2-naphthylamine. Comparison of these two sets of melting point values indicates that the previous workers may have recorded inversely the melting points of these isomeric sulfonamides. Another possibility is that these derivatives might have been prepared from the amines, contaminated with their isomers, which might have led to the isolation of a mixture of isomeric sulfonamides. These same derivatives have been reported by the previous workers as having a brown color. In this study the crude derivatives were observed to have a brown-yellow color, but this was due to traces of *p*-phenylazobenzenesulfonic acid and some foreign material (See Experimental) which were occluded by the derivatives. These impurities were removed chromatographically to give pure orange-red products.

To some extent the usefulness of a reagent for the identification of an organic compound is dependent upon the ease with which the original compound may be obtained from its derivative. Many alkyl- and arylsulfonyl chlorides have been used for the identification of primary and secondary amines. However, one disadvantage with all of these reagents in actual practice is that once the sulfonamide is obtained, it hydrolyzes with great difficulty to give the original amine.[6]

The *p*-phenylazobenzenesulfonamides are hydrolyzed on refluxing with concentrated hydrochloric acid. In this study no attempt was made to determine the optimum conditions for quantitative hydrolysis of the sulfonamides. The results of the hydrolysis of certain sulfonamides are recorded in Table I.

Chromatographic Adsorption Studies. The Tswett Adsorption method has been applied to the separation of very small quantities (10–20 mg. of each component) of mixtures of these brilliantly colored *N*-substituted *p*-phenylazobenzenesulfonamides. Therefore *p*-phenylazobenzenesulfonyl chloride affords an advantage over the reagents which are commonly used for identification of amines in that it forms colored derivatives which can be separated on the Tswett column in the usual manner. The individual compounds may then be recovered and identified or reconverted into the original colorless amines.

Table II shows the results obtained upon chromatographing nineteen pairs of *N*-alkyl and seventeen pairs of *N*-aryl *p*-phenylazobenzenesulfonamides on mixtures of two parts of silicic acid to one part of celite 535 by weight. The solvents used for developing the chromatograms were Skellysolve B, benzene, mixtures of these two solvents and mixtures of Skellysolve B-ethyl acetate. Sixteen pairs of the alkyl derivatives, ten pairs of the aryl derivatives,

(6) For a study of hydrolysis of sulfonamides see W. Seaman, A. R. Norton, J. T. Woods and H. N. Bank, *J. Am. Chem. Soc.*, 67, 1571 (1945).

and one pair of heterocyclic derivatives were separated sufficiently to make two zones visible with a colorless zone between. The sulfonamides were recovered from the colored zones in 90 to 95% yield. Six pairs of the aryl derivatives formed a continuous band. Sectioning of this continuous band with sebsequent elution yielded homogeneous top and bottom sections with an intervening section of varying composition. Listed in Table II under the heading "Incompletely Separated" are three pairs of alkyl and one pair of aryl derivatives. These mixtures formed a continuous band, which upon sectioning gave impure materials from the top and bottom sections, which were of different melting points, indicating that a mixture was initially present. The first member of each pair listed in Table II where separation was obtained was the most strongly adsorbed derivative.

The results of the chromatographic studies indicated that resolution of a binary mixture of *N*-alkyl and/or *N,N'*-dialkyl sulfonamides into its components could be obtained only if the carbon content of the alkyl portion of the two sulfonamides differed by at least two carbon atoms. With a difference of one carbon atom in the alkyl radicals of the sulfonamides, a continuous band was obtained, except in the case of the binary mixture of *N*-methyl and *N,N'*-dimethyl sulfonamides which gave complete resolution. Materials from the upper and lower parts of the continuous bands showed different melting points, indicating that a mixture was present. Also, the sulfonamides of isomeric aliphatic amines formed a continuous band. However, these mixtures gave no degree of resolution. When the chromatograms of the six possible binary mixtures between *n*-butyl, *iso*-butyl, *sec*-butyl and *tert*-butyl sulfonamides were sectioned, the materials isolated from the different sections did not show any variation in melting point.

The chromatography of binary mixtures of the *N*-(ortho-substituted phenyl) sulfonamide mixed with the sulfonamide of the meta or para isomer showed that the sulfonamide of the ortho isomer had a markedly less adsorption affinity than its meta or para isomers. An exception was found in the case of the possible binary mixtures of the sulfonamides of *ortho, meta,* and *para*-toluidines. This ortho effect has been observed in previous chromatographic studies[3,4] involving *ortho*-substituted benzenes.

Of the three ternary mixtures studied (See Table II) resolution was obtained for only two. In the two ternary mixtures wherein separation was obtained the derivative of the ortho isomer was least strongly adsorbed and separated from a continuous band of the derivatives of the meta and para isomers. Sectioning of this continuous band yielded the derivative of the para isomer and the derivative of the meta isomer from the top and bottom sections respectively.

It was of further interest to observe the chromatographic separation of a model mixture composed of the *p*-phenylazobenzenesulfonyl derivatives of primary and secondary amines and the corresponding tertiary amine. Table III shows the results obtained by the adsorption of five such mix-

TABLE II

CHROMATOGRAPHIC SEPARATION OF MODEL MIXTURES OF *N*-SUBSTITUTED *p*-PHENYLAZOBENZENESULFONAMIDES

A. Binary mixtures of *N*-alkyl sulfonamides

Separated into zones	
Methyl	*n*-Propyl
Ethyl	*n*-Butyl
Isopropyl	Isoamyl
Dimethyl	Diethyl
Dimethyl	Di-*n*-propyl
Diethyl	Di-*n*-propyl
Diethyl	Di-*n*-butyl
Diisobutyl	Diisoamyl
Methyl	Dimethyl
Ethyl	Diethyl
n-Propyl	Di-*n*-propyl
Isopropyl	Diisopropyl
Isobutyl	Diisobutyl
n-Butyl	Di-*n*-butyl
n-Amyl	Di-*n*-amyl
Isoamyl	Diisoamyl
Incompletely separated	
Methyl	Ethyl
n-Propyl	*n*-Butyl
Ethyl	Propyl

B. Binary mixture of *N*-aryl sulfonamides

Separated into zones	
p-Hydroxyphenyl	*o*-Hydroxyphenyl
p-Ethoxyphenyl	*o*-Ethoxyphenyl
m-Ethoxyphenyl	*o*-Ethoxyphenyl
m-Hydroxyphenyl	*o*-Hydroxyphenyl
p-Chlorophenyl	*o*-Chlorophenyl
Ethyl, phenyl	*n*-Butyl, phenyl
Methyl, phenyl	Ethyl, phenyl
o-Tolyl	Methyl, *o*-Tolyl
Phenyl	Methyl, phenyl
p-Tolyl	Methyl, *p*-Tolyl
Forming continuous band	
p-Bromophenyl	*m*-Bromophenyl
p-Ethoxyphenyl	*m*-Ethoxyphenyl
1-Naphthyl	2-Naphthyl
o-Tolyl	*p*-Tolyl
o-Tolyl	*m*-Tolyl
m-Tolyl	*p*-Tolyl
Incompletely separated	
Methyl, *o*-Tolyl	Methyl, *p*-Tolyl

C. Binary mixture of sulfonyl heterocyclic derivatives

Separated into zones	
Morpholine	Piperidine

D. Ternary mixtures of ortho, meta and para isomers

Topmost zone (continuous)		Bottom zone
Most strongly absorbed	Least strongly absorbed	
p-Ethoxyphenyl	*m*-Ethoxyphenyl	*o*-Ethoxyphenyl
p-Hydroxyphenyl	*m*-Hydroxyphenyl	*o*-Hydroxyphenyl

No separation obtained for a mixture of ortho-, Meta- and Para-tolyl sulfonamides.

tures of the sulfonamides. The *N*-Mono- and, *N,N'*-disubstituted sulfonamides separated on the column into zones with a colorless zone between. The tertiary amine appeared in the effluent. The sulfonamides were obtained in 77 to 95% recovery and identified by mixture melting points. The tertiary amines were isolated from the effluent in 49 to 72% recovery.

TABLE III

CHROMATOGRAPHIC SEPARATION OF MODEL MIXTURES OF *N*-MONO- AND *N,N*-DISUBSTITUTED *p*-PHENYLAZOBENZENESULFONAMIDES AND TERTIARY AMINES

Original Mixture	Column after Development
	15 mm. colorless
20 mg. *n*-butyl	37 mm. orange [16 mg. *n*-butyl (80%)]
	121 mm. colorless
15 mg. Di-*n*-butyl	30 mm. orange [12 mg. di-*n*-butyl (80%)]
	77 mm. colorless
778 mg. tri-*n*-butylamine	Effluent [384 mg. tri-*n*-butylamine (49%)]
	10 mm. colorless
22 mg. isoamyl	23 mm. orange [21 mg. isoamyl (95%)]
	40 mm. colorless
26 mg. diisoamyl	30 mm. orange [20 mg. diisoamyl (77%)]
	197 mm. colorless
197 mg. tri-isoamylamine	Effluent [101 mg. tri-isoamylamine (51%)]
	10 mm. colorless
22 mg. *n*-amyl	24 mm. orange [21 mg. *n*-amyl (95%)]
	43 mm. colorless
20 mg. di-*n*-amyl	29 mm. orange [19 mg. di-*n*-amyl (95%)]
	184 mm. colorless
422 mg. tri-*n*-amylamine	Effluent [tri-*n*-amylamine (wt. not taken)]
	10 mm. colorless
21 mg. phenyl-	43 mm. orange [20 mg. phenyl (95%)]
	45 mm. colorless
21 mg. methyl, phenyl	100 mm. yellow orange [19 mg. methyl, phenyl (90%)]
	130 mm. colorless
1337 mg. dimethylaniline	Effluent [865 mg. dimethylaniline (65%)]
	20 mm. colorless
22 mg. *o*-tolyl	60 mm. orange [21 mg. *o*-tolyl (95%)]
	75 mm. colorless
21 mg. methyl, *o*-tolyl	112 mm. orange [20 mg. methyl, *o*-tolyl (95%)]
	57 mm. colorless
1617 mg. dimethyl-*a*-toluidine	Effluent [1157 mg. Dimethyl-*o*-toluidine (72%)]

Separation and Determination of Primary, Secondary and Tertiary Amines. In this work, we have found that model mixtures composed of the sulfonamides of corresponding primary and secondary amines and the corresponding tertiary amine can be separated into their individual components by chromatographic adsorption. This observation provided the basis for a study of the following method for separating the three classes of amines.

The procedure involves treating a mixture of the three classes of amines with *p*-phenylazobenzenesulfonyl chloride. Only the primary and secondary amines react. When the reaction mixture is distributed between benzene and dilute hydrochloric acid the unreacted tertiary amine forms a water-soluble hydrochloride salt. The aqueous phase is separated and made alkaline to liberate the tertiary amine as the free base which is extracted with benzene, and the amine is recovered upon evaporating the solvent; or the aqueous phase is evaporated to dryness and the tertiary amine is recovered as its hydrochloride. The benzene solution of *p*-phenylazobenzenesulfonic acid, unreacted sulfonyl chloride and the sulfonamides of the primary and secondary amines is chromatographed. The unreacted sulfonyl chloride and/or the free sulfonic acid are strongly adsorbed on the adsorbent, while the monosubstituted sulfonamide and di-substituted sulfonamide are separated into two distinct zones. The sulfonamides are then recovered in the usual manner.

The analyses of six mixtures of the three classes of amines by this method are:

(1) A mixture of 13 mg. methylamine, 19 mg. dimethylamine, 1446 mg. trimethylamine (25% aqueous solutions of the methylamines were used. The weight of each amine is therefore a calculated value) and 251 mg. sulfonyl chloride was treated as described above. Trimethylamine hydrochloride [462 mg. (20%)] was recovered from the acid extract. The top 4 mm. of the chromatogram was an orange zone from which was isolated *p*-phenylazobenzenesulfonic acid. Below a 7 mm. colorless zone was found a 32 mm. orange zone which yielded 65 mg. (55%) methyl sulfonamide. Following the latter a 25 mm. colorless zone was found. Below this, a 108 mm. orange zone was found from which 113 mg. (90%) dimethyl sulfonamide was recovered. The bottom portion (137 mm.) of the column was colorless.

(2) A mixture of 23 mg. ethylamine, 24 mg. diethylamine, 5030 mg. triethylamine and 252 mg. sulfonyl chloride was treated as described above. Triethylamine hydrochloride [4342 mg.(64%)] was recovered from the acid extract. The chromatogram was similar to the one described in part one: 3 mm. orange zone which yielded the sulfonic acid, 10 mm. colorless zone, 42 mm. orange zone which yielded 138 mg. (95%) ethyl sulfonamide, 15 mm. colorless zone, 60 mm. orange zone which yielded 57 mg. (55%) diethyl sulfonamide, and a 203 mm. colorless zone.

(3) A mixture of 25 mg. *n*-butylamine, 45 mg. di-*n*-butylamine, 5813 mg. tri-*n*-butylamine and 233

mg. sulfonyl chloride was treated as described above. Tri-*n*-butylamine hydrochloride [6336 mg. (91%)] was recovered from the acid extract. The chromatogram was similar to the one described in part one: 9 mm. orange zone which yielded the sulfonic acid, 11 mm. colorless zone, 75 mm. orange zone which yielded 98 mg. (85%) *n*-butyl sulfonamide, 145 mm. colorless zone, 85 mm. orange zone combined with some colored material which was washed into the effluent yielded 115 mg. (88%) di-*n*-butyl sulfonamide.

(4) A mixture of 66 mg. isoamylamine, 104 mg. diisoamylamine, 5140 mg. triisoamylamine and 428 mg. sulfonyl chloride was treated as described above. Triisoamylamine hydrochloride [5117 mg. (89%)] was recovered from the acid extract. The chromatogram was similar to the one described in part one: 14 mm. orange zone which yielded the sulfonic acid, 32 mm. colorless zone, 52 mm. orange zone which yielded 201 mg. (79%) isoamyl sulfonamide, 41 mm. colorless zone, 69 mm. orange zone which yielded 212 mg. (79%) diisoamyl sulfonamide and 183 mm. colorless zone.

(5) A mixture of 25 mg. aniline, 23 mg. methylaniline, 1711 mg. dimethylaniline, and 147 mg. sulfonyl chloride was treated as described above. Dimethylaniline [1479 mg. (87%)] was recovered from the acid extract. The chromatogram was similar to the one described in part one: 30 mm. orange zone which yielded the sulfonic acid, 10 mm. colorless zone, 60 mm. orange zone which yielded 87 mg. (96%) phenyl sulfonamide, 120 mm. colorless zone, 105 mm. orange zone which yielded 51 mg. (69%) methyl, phenyl sulfonamide, and 10 mm. colorless zone.

(6) A mixture of 21 mg. *o*-toluidine, 22 mg. methyl-*o*-toluidine, 2888 mg. dimethyl-*o*-toluidine and 109 mg. sulfonyl chloride was treated as described above. Dimethyl-*o*-toluidine [1850 mg. (64%)] was recovered from the acid extract. The chromatogram was similar to the one described in part one: 20 mm. colorless zone, 75 mm. orange zone which yielded 58 mg. (85%) *o*-tolyl sulfonamide, 85 mm. colorless zone, 120 mm. yellowish orange zone which yielded 44 mg. (66%) methyl, *o*-tolyl sulfonamide, and 18 mm. colorless zone.

The yields of the monosubstituted sulfonamides ranged from 55 to 96% with an average value of 83%. The yields of the disubstituted sulfonamides ranged from 55 to 90% with an average value of 75%. The tertiary amines were recovered in yields ranging from 20 to 91% with an average value of 69%. The quantitative separation of the three classes of amines was not of paramount interest in this study. However, the recoveries of the different classes of amines from the mixtures are satisfactory for identification purposes.

The method proposed herein for the separation of the three classes of amines appears to offer promise for the quantitative separation of mixtures of both aliphatic and aromatic amines. A quantitative study of the separation of mixtures of the three classes of amines is now under investigation. This method, also, appears to have advantages over the commonly used Hinsberg Method.[7]

EXPERIMENTAL

Reagents. Amines of commercially available grades were used without further purification.

p-Phenylazobenzenesulfonyl chloride was prepared as described by Desai and Mehta.[5]

The adsorbent used in preparing the chromatographic columns was a mixture of silicic acid (Mallinckrodt, prepared by the method of Ramsey and Patterson) and Celite-535 (Johns-Manville).

The solvents Skellysolve B and A.C.S. grade benzene were redistilled and absolute ethyl alcohol and A.C.S. grade ethyl acetate were used as purchased.

Preparation of N-substituted p-phenylazobenzenesulfonamides. A mixture of *p*-phenylazobenzenesulfonyl chloride (approximately 100 mg.), amine (10% by weight excess), and 3 to 6 ml. of pyridine was refluxed for 1 hr. The clear red solution was poured with stirring into ice and 50 ml. of 10% sodium bicarbonate solution. The derivatives of the aliphatic amines, aniline and methylaniline crystallized immediately, and the derivatives of the other aromatic amines crystallized on further cooling. The crystalline product was filtered, washed with water, 1% hydrochloric acid, water, and then air dried. The crude product was dissolved in either Skellysolve B, benzene or a mixture of the two and chromatographed on a mixture of silicic acid–celite (2 to 1 by weight) on which any free acid and/or unreacted acid chloride was strongly adsorbed. The sulfonamide was desorbed with absolute ethyl alcohol and the solvent removed. The colored solid (orange to red) was then recrystallized. The derivatives of the aliphatic amines were recrystallized from Skellysolve B. The derivatives of the aromatic amines were recrystallized from ethyl alcohol–water mixtures, using as little water as possible. The derivatives crystallized as fluffy solids, plates or fine needles.

Chromatography of the crude aromatic amine derivatives usually gave three colored zones a strongly adsorbed acid zone and two zones separated by a colorless zone. Of the latter two colored zones the lower one gave sharp melting points and good analysis, whereas the higher one gave less than 10 mg. of tacky or solid material of indefinite melting point. This material was considered to be derived from an impurity of the original amine.

Acid Hydrolysis of the Sulfonamides. A typical acid hydrolysis was conducted as described below. A mixture of each sulfonamide (methyl, 112 mg.; dimethyl, 184 mg.; *n*-butyl, 188 mg.; di-*n*-butyl, 91 mg.; *tert*-butyl, 102 mg.; *sec*-butyl, 120 mg.; isoamyl, 179 mg.; di-isoamyl, 132 mg.; p-chlorophenyl, 102 mg.; 2-naphthyl, 96 mg.; 1-naphthyl, 105 mg.; *p*-tolyl, 114 mg.) with 50 ml. of concentrated hydrochloric acid in the case of an aliphatic amine and with 10 ml. of concentrated hydrochloric acid and 10 ml. of dioxane in the case of an aromatic amine was refluxed for approximately 6 hr. The dioxane was used with the aromatic amines to effect a homogeneous reaction mixture. The reaction mixture was poured into 100 ml. of distilled water and filtered to remove a negligible amount (1 to 3 mg.) of dark material suspended in the clear red solution. This material did not melt under 300°.

The filtered reaction mixture from the hydrolysis of the sulfonamides of the aliphatic amines was evaporated to dryness *in vacuo* to give a white residue with reddish tinge. The solid or oily residue was dissolved in 95% ethanol and the ethanol solution treated with norit to give a clear, color-

(7) O. Hinsberg, *Ber.*, **23**, 2961 (1890).

less solution. The solvent was removed *in vacuo* under a stream of nitrogen to give the amine hydrochloride (see Table I for % recovery).

The filtered reaction mixture from the hydrolysis of the sulfonamides of the aromatic amines was made basic with 10% sodium hydroxide and then extracted with several portions of benzene. The benzene extracts were combined and dried over anhydrous sodium sulfate, and then treated with norit. The solvent removed *in vacuo* under a stream of nitrogen and the aromatic amine so obtained was identified by mixture melting point (See Table I for % recovery).

Chromatographic Separations of Model Mixtures. A typical chromatographic separation was conducted as described below. A tube 20 mm. × 400 mm. was connected to a suction flask. A 2 to 1 mixture by weight of silicic acid and celite was prepared for use as the adsorbent. The tube was packed to a height of approximately 300 mm. with the adsorbent by adding it batchwise while tapping simultaneously the opposite sides of the column with two cork rings. Then full suction of the water aspirator was applied to the suction flask for about 2 minutes. The adsorbent was then washed with 100 ml. Skellysolve B, 100 ml. of a 50–50 mixture of Skellysolve B and ethyl acetate, and finally 100 ml. of Skellysolve B.

A binary mixture of sulfonamides (10 to 20 mg. of each component) was dissolved in the minimum volume of benzene and then adsorbed on the column. The chromatogram was developed with Skellysolve B, then solutions of 5% up to 10% of benzene in Skellysolve B, and finally solutions of 1% up to 4% of ethyl acetate in Skellysolve B. The zones were dug out of the column by a long narrow spatula and desorbed by shaking with absolute ethanol. When a continuous band was obtained, the band was arbitrarily dug out in several sections. The pure components were obtained from the top and bottom sections and the intervening section was a mixture. The eluents were concentrated, filtered into a tared flask, and the last traces of solvent removed *in vacuo* under a stream of nitrogen. The weights and melting points of the residues were determined.

The ternary mixtures of the *N*-substituted sulfonamides of ortho, meta and para isomers of the aromatic amines were chromatographed by the same general procedure as described above. The chromatogram showed two colored zones separated by a colorless zone. The sulfonamide of the ortho isomer was isolated from the bottom zone. The top zone contained the sulfonamides of the meta and para isomers which upon sectioning as described above gave pure components from the top and bottom sections.

The mixtures of *N*-mono- and *N,N'*-disubstituted sulfonamides and tertiary amines were chromatographed by the same general procedure as described above. The chromatograms are described in Table III. It was assumed that on developing the chromatogram by washing with 50 ml. of Skellysolve B, 100 ml. of 2% ethyl acetate in Skellysolve B and 200 ml. of 4% ethyl acetate in Skellysolve B that the tertiary amine had been completely washed into the effluent. The tertiary amine was then recovered from the effluent by removal of the solvent. The mono- and di-substituted sulfonamides separated into two distinct colored zones with a colorless zone between. The mono- and di-substituted sulfonamides were isolated from the top and bottom zones respectively. They were identified by mixture melting point.

Analysis of Mixtures of Amines. A mixture of primary, secondary, and tertiary amine and the molar quantity of *p*-phenylazobenzenesulfonyl chloride required for reaction with the primary and secondary amines was refluxed for one hour. Homogeneous reaction mixtures were obtained in all cases except with the mixture of aqueous solutions of methyl amines.

The red-colored reaction mixture was cooled and dissolved in benzene. The benzene layer was extracted with several portions of 6*N* hydrochloric acid and the aqueous layers were collected. The benzene layer was washed with water which was added to the aqueous layers. The benzene layer was than washed with saturated sodium chloride solution, dried over anhydrous sodium sulfate, and the benzene solution was concentrated. The benzene concentrate of the sulfonamides was saved for subsequent chromatography.

In the analysis of aliphatic amines the aqueous layer was evaporated to dryness *in vacuo*. The residue was dissolved in 95% ethyl alcohol, treated with norit, filtered into a tared flask, concentrated and the last traces of solvent removed *in vocuo* under a stream of nitrogen. The residue was the hydrochloride of the aliphatic tertiary amine.

In the analysis of mixtures of aromatic amines the aqueous layer was made basic with 10% sodium hydroxide. The aqueous solution was extracted with several portions of benzene. The benzene extracts were washed with saturated sodium chloride, dried over anhydrous sodium sulfate, treated with norit, filtered, and the solvent removed *in vacuo* under a stream of nitrogen. The residue was confirmed as the aromatic amine through picrate formation.

The benzene concentrate of the sulfonamides of the primary and secondary amines was chromatographed in the manner previously described for the chromatographic separation of binary mixtures. The mono- and di-substituted sulfonamides separated into two distinct colored zones with a colorless zone between. The mono- and di-substituted sulfonamides were isolated from the top and bottom zones respectively. They were identified by mixture melting point

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