

[CONTRIBUTION NO. 10 FROM THE EXPLORATORY RESEARCH LABORATORY OF DOW CHEMICAL OF CANADA, LIMITED]

## Organophosphorus Compounds. VI. *N*-Arylphosphoramidic and *N*-Arylphosphoramidothioic Difluorides

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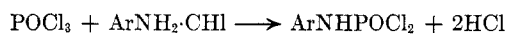
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*N*-Arylphosphoramidic and *N*-arylphosphoramidothioic difluorides were prepared from phosphorus oxy- and thio-halides and aromatic amines.

The preparation of the *N*-arylphosphoramidic dichlorides has been investigated by many authors,<sup>2-6</sup> most systematically by Michaelis.<sup>7,8</sup> The syntheses were based on the reaction of one mole phosphorus oxychloride with two moles of an aromatic amine in the cold.



or with one mole of an amine hydrochloride on warming.



This paper describes the synthesis of the previously unknown *N*-arylphosphoramidic difluorides from phosphorus oxyfluoride and aromatic amines:

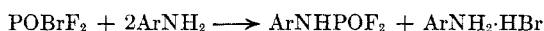
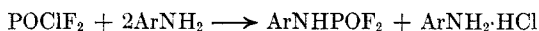


The syntheses of *N*-phenyl, *N*-*m*- and *N*-*p*-tolyl-phosphoramidic difluorides were performed at temperatures between  $-80$ – $+30^\circ$ . *o*-Toluidine and *o*-anisidine required more drastic conditions to effect reaction. Due to the high volatility of phosphorus oxyfluoride, the reactions were carried out in sealed glass tubes.

The *N*-phenyl-, *N*-*o*- and *N*-*p*-tolyl-, and *N*-anisyl-phosphoramidic difluorides were colorless crystalline substances. All of these substances were distillable *in vacuo* without decomposition. But on overheating they easily lose hydrogen fluoride. Table I shows some of the characteristics of the compounds prepared and reaction yields.

*N,N*-Ethylphenylphosphoramidic difluoride was prepared by a similar method from phosphorus oxyfluoride and *N*-ethylaniline in a sealed glass tube at room temperature.

Phosphorus oxychlorodifluoride and phosphorus oxybromodifluoride were used similarly as starting materials.



(1) Present address: Research Department, Imperial Oil Limited, Sarnia, Ontario, Canada.

(2) P. Otto, *Ber.*, **28**, 613 (1895).

(3) E. Uhlfelder, *Ber.*, **36**, 1826 (1903).

(4) R. M. Caven, *J. Chem. Soc.*, **83**, 1045 (1903).

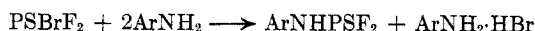
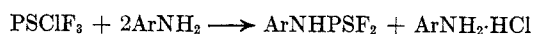
(5) W. Autenrieth and E. Bolli, *Ber.*, **58**, 2144 (1925).

(6) F. Zetsche and W. Buttiker, *Ber.*, **73**, 47 (1940).

(7) A. Michaelis and G. Schulze, *Ber.*, **26**, 2937 (1893); **27**, 2572 (1894).

(8) A. Michaelis, *Ann.*, **326**, 129 (1903).

The present authors have previously described the preparation of *N*-arylphosphoramidic dichlorides and *N*-arylphosphoramidothioic chlorofluorides from phosphorus thiochlorodifluoride.<sup>9</sup> Now we have prepared the previously unknown *N*-arylphosphoramidothioic difluorides, as shown below.



Of the compounds obtained, the *N*-phenyl-, *N*-*o*-, *N*-*m*- and *N*-*p*-tolylphosphoramidothioic difluorides were colorless, musky-smelling liquids. The *N*-anisylphosphoramidothioic difluoride was colorless, crystalline substance. The liquids were not miscible with water, but on standing under water they hydrolyzed at room temperature. *N*-Arylphosphoramidothioic difluorides were more stable in respect to loss of hydrogen halide than the corresponding dichlorides. No decomposition was observed nor was there any substantial imido-phosphorothioate residue left in the distillation flask. Table II shows some of the characteristics of the compounds prepared and reaction yields. The *N*-arylphosphoramidothioic difluorides were also prepared from phosphorus thiofluoride.



If an excess of the aromatic amine was used *N,N*-diarylphosphoramidothioic difluorides were formed.

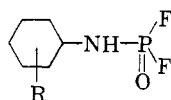


### EXPERIMENTAL

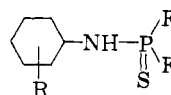
Strictly anhydrous conditions were maintained throughout all operations to avoid hydrolysis of reagents and products.

I. Preparation of *N*-arylphosphoramidic difluorides from phosphorus oxyfluoride. A. *N*-Phenyl-, *N*-*m*- and *N*-*p*-tolylphosphoramidic difluorides. An aromatic amine (0.2 mole) dissolved in 80 ml. anhydrous toluene was added to a suspension of 0.11 mole, 11.5 g. of phosphorus oxyfluoride in 100 ml. of anhydrous toluene with stirring at a temperature between  $-40$  and  $-50^\circ$ . The reaction mixture was stirred for 0.5 hr. and then allowed to stand for 3 hr. at  $-20^\circ$  and finally allowed to reach room temperature. The amine hydrofluoride was removed by filtration and then washed

(9) G. A. Olah and A. A. Oswald, Organophosphorus Compounds IV, *Ann.*, **1625**, 92 (1959).

TABLE I  
 N-ARYLPHOSPHORAMIDIC DIFLUORIDES


R	Yield, %	B.P. (°C./mm.)	M.P. (°C.)	N	Calcd.		Found	
					F	N	F	F
H	62	103-104/5	48-49	7.90	21.45	8.03	21.4	
<i>o</i> -CH <sub>3</sub>	59	98-100/6	40	7.32	19.87	7.54	19.7	
<i>m</i> -CH <sub>3</sub>	60	124-125/6	—	7.32	19.87	7.60	19.6	
<i>p</i> -CH <sub>3</sub>	58	118/6	79-80	7.32	19.87	7.25	20.1	
<i>o</i> -OCH <sub>3</sub>	65	105-106/6	61	6.76	18.34	6.54	18.1	

 TABLE II  
 N-ARYLPHOSPHORAMIDOTHIOIC DIFLUORIDES


R	Yield, %		B.P. (°C./mm.)	<i>n</i> <sub>D</sub> <sup>20</sup>	Calcd.		Found	
	Method A	Method B			N	F	N	F
H	91	93	86/1	1.5414	7.25	19.66	7.52	19.9
<i>o</i> -CH <sub>3</sub>	95	—	76/0.9	1.5223	6.76	18.33	6.80	18.6
<i>m</i> -CH <sub>3</sub>	90	93	85.5/0.9	1.5361	6.76	18.33	6.86	18.3
<i>p</i> -CH <sub>3</sub>	88	86	98/1	1.5358	6.76	18.33	6.89	18.5
<i>o</i> -OCH <sub>3</sub>	90	—	93/1	M.P. 46-47°	6.27	17.02	6.31	17.1

with toluene. The filtrate and washings were distilled and after removal of toluene the remaining liquid was fractionated *in vacuo*. The *N*-phenyl-, *N*-*m*- and *N*-*p*-tolyl-phosphoramidic difluorides were obtained which solidified to colorless crystalline states. Some physical and analytical data and yields are shown in Table I.

B. *N*-*o*-Tolyl- and *N*-anisyl-phosphoramidic difluorides. Phosphorus oxyfluoride, 10.4 g. (0.1 mole) was bubbled into 200 ml. of toluene cooled in a dry ice acetone bath and 0.2 mole of an aromatic amine was added to the mixture. The mixture was transferred to a glass tube and the tube was then sealed. The tube was refrigerated at  $-20^{\circ}$  for 12 hr. It was agitated occasionally at  $-20^{\circ}$  and then allowed to reach room temperature and to stand for an additional 12 hr. The phosphorus oxyfluoride was consumed as noted by lack of excess pressure when the tube was opened. The amine hydrofluorides were removed by filtration. Colorless crystalline *N*-tolyl- and *N*-anisyl-phosphoramidic difluorides were obtained by distillation *in vacuo* as described above. Table I shows the pertinent data.

*N,N*-Ethylphenylphosphoramidic difluoride. 10.7 g. (52%) of *N,N*-ethylphenylphosphoramidic difluoride was obtained by reacting 10.4 g. (0.1 mole) of phosphorus oxyfluoride and 24.2 g. (0.2 mole) of *N*-ethyl-aniline as described above. The compound was colorless liquid with an acrid odor boil at  $119-120^{\circ}\text{C}/9$  mm. with decomposition.

Anal. Calcd. for C<sub>8</sub>H<sub>8</sub>F<sub>2</sub>OP: F, 18.51; N, 5.82. Found: F, 18.1; N, 7.18.

II. Preparation of *N*-arylphosphoramidic difluorides from phosphorus oxychlorodifluoride and phosphorus oxybromodifluoride. Phosphorus oxychlorodifluoride 12 g. (0.1 mole) or 16.5 g. (0.1 mole) of phosphorus oxybromodifluoride was dissolved in 15 ml. of ice cold toluene. A solution of 0.2 mole of an aromatic amine in 50 ml. of toluene was added to the mixture with cooling. The reaction mixture was allowed to stand 24 hr. at  $-20^{\circ}$ , then at room temperature for an addi-

tional 12 hr. The precipitated amine hydrohalide was removed by filtration and washed with toluene. The filtrate and washings were fractionated as above.

III. Preparation of *N*-arylphosphoramidothioic difluorides from phosphorus thiochlorodifluoride and phosphorus thio-bromodifluoride. *N*-Phenyl-, *N*-*m*- and *N*-*p*-tolyl-phosphoramidothioic difluoride. Phosphorus thiochlorodifluoride 14.3 g. (0.105 mole) or 19 g., (0.105 mole) of phosphorus thio-bromodifluoride was dissolved in 150 ml. of cold toluene. A solution of 0.2 mole of an aromatic amine in 50 ml. of toluene was added to the mixture with cooling. The mixture was placed in a refrigerator at  $0^{\circ}$  for 24 hr. after which time it was allowed to reach room temperature and left unopened for an additional 12 hr. The amine hydrofluoride was removed by filtration and washed with toluene. The filtrate and washing were fractionated, as above, yielding the *N*-phenyl-, *N*-*m*- and *N*-*p*-tolyl-phosphoramidothioic difluorides as colorless, musky-smelling liquids, more dense than and not miscible with water. Physical and analytical data and yield of the products are given in Table II. Decomposition during distillation did not occur. The compounds did not hydrolyze at room temperature on standing under water and only minute quantities of residue remained.

*N*-*o*-Tolyl- and *N*-*o*-anisyl-phosphoramidothioic difluorides. In a 600 ml. thick-walled glass tube was placed a solution of 13.6 g. (0.1 mole) of phosphorus thiochlorodifluoride in anhydrous benzene. *o*-Toluidine, 2.14 g. (0.2 mole) or 24.6 g. (0.2 mole) of *o*-anisidine was added to the solution. The tube was then sealed, the reaction mixture allowed to stand for 4 days at room temperature. As above vacuum distillation yielded musky-smelling, colorless *N*-*o*-tolyl- and *N*-*o*-anisyl-phosphoramidothioic difluorides. The *N*-*o*-anisyl-phosphoramidothioic difluoride solidified to a white crystalline substance. Physical and analytical data of the compounds and their yields are shown in Table II.

Similar products are obtained by substituting phosphorus

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,<sup>2</sup> amines<sup>3</sup> and phenols.<sup>4</sup> 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.<sup>5</sup> 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.