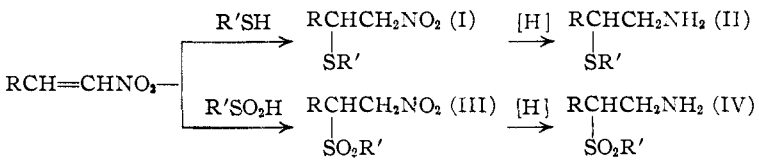
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF TUSKEGEE INSTITUTE]

The Preparation of Some Aryl Aminoalkyl Sulfides and Sulfones[1,2]

BY LOUIS F. CASON AND CALVIN C. WANSER

As a part of a study on the synthesis of sulfur-containing compounds of pharmacological interest, β-(arylmercapto)-phenethylamines (II) and β-(arylsulfonyl)-phenethylamines (IV) were prepared through the addition of aromatic thiols and sulfinic acids to β-nitrostyrenes and the subsequent reduction of the nitro sulfide (I) or sulfone (III).



(R and R' are aromatic groups)

Although the addition of organic sulfur compounds to β-nitrostyrene and its derivatives has not been extensively investigated, addition products have been obtained from β-nitroölefins and aromatic amines, hydrazines, and other organic bases.[3,4,5] Similarly, alcohols add to β-nitrostyrene forming the corresponding β-nitro ethers,[6,7] and Kohler and Stone[8] apparently obtained 1,4-addition products exclusively from the reaction of Grignard reagents with certain conjugated nitroölefins. While this investigation was in progress, Heath and Lambert[9] reported the preparation of several β-nitro sulfides and thiols from the addition of thiols or hydrogen sulfide to nitroölefins. The corresponding sulfones were secured from the oxidation of the sulfides with hydrogen peroxide, or, more directly, from the addition of the appropriate sulfinic acid to the unsaturated nitro compound.

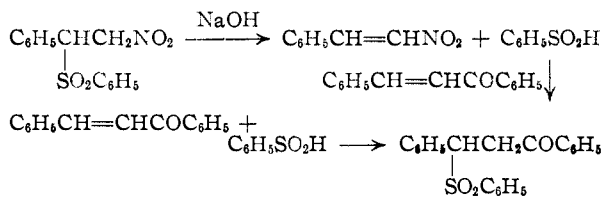
The aromatic thiols employed in this investigation generally reacted with β-nitrostyrene and some of its derivatives to give the corresponding nitro sulfide in 51–100% yields (Table I). All of the sulfides were sharp-melting crystalline compounds except those resulting from α-toluenethiol and β-nitrostyrene or *p*-methoxy-β-nitrostyrene. These products were oils, one of which (Tables I and II) was oxidized to the crystalline sulfone by 30% hydrogen peroxide.

In the somewhat related addition of amines to β-nitrostyrene, Worrall and associates[4a,10a] observed that *p*-chloro- and *p*-nitroaniline failed to undergo the reaction, whereas a halogen in the para position of the aromatic ring of β-nitrostyrene has a favorable influence on the ease of addition of the amines. When we attempted to add *p*-chlorobenzenethiol to β-nitrostyrene, the only product isolated was bis-(*p*-chlorophenyl) disulfide. On the other hand, α-(nitromethyl)-*p*-chlorobenzyl phenyl sulfide was formed in 84% yield from the addition of benzene-thiol to *p*-chloro-β-nitrostyrene.

Although no attempt was made to correlate the position of a substituent on the aromatic nucleus of the thiols with their ease of addition to the unsaturated nitro compounds, we found that the yield of the nitro sulfide from *o*-toluenethiol and β-nitrostyrene was approximately 40% less than that obtained from the para isomer.

The nitro sulfones listed in Table II were conveniently prepared by the direct addition of aromatic sulfinic acids to the nitroölefins in ethanol or other suitable solvents. In contrast to the analogous addition of the thiols, no catalyst was required for the reaction, and the nitro sulfones were sparingly soluble in refluxing ethanol.

The pure β-nitro sulfides and sulfones were stable under normal conditions and in boiling hydrochloric acid, but were decomposed into the original components by cold or refluxing 10% alcoholic sodium hydroxide. The regenerated thiol or sulfinic acid was readily characterized by the formation of an adduct with benzalacetophenone.[10b,c]



Since the mechanism of 1,4-addition of unsymmetrical reagents to conjugated nitroölefins and of thiols and sulfinic acids to analogous α,β-unsaturated compounds is rather well established, it seems reasonable to assume that the β-nitro sulfides and sulfones prepared in this study are 1,4-addition products with structures like (I) and (III). Evidence for the structure of the β-nitro sulfides was secured through the alternate synthesis represented below.

The reduction of the aliphatic nitro group of the sulfides and sulfones was accomplished with stannous chloride and hydrochloric acid or with zinc and glacial acetic acid. The conversion of the nitro compounds to the corresponding amine hydrochlorides by the first method varied from 19 to 78%, but the isolation of the free amines was complicated by the formation of considerable amounts of insoluble inorganic residues. When

(1) A part of this paper is taken from a thesis presented to the graduate faculty of Tuskegee Institute by Calvin C. Wanser in partial fulfillment of the requirement for the degree of Master of Science.

(2) This work was aided by a grant from the Upjohn Company to the George Washington Carver Foundation of Tuskegee Institute, Alabama.

(3) Posner, *Ann.*, **389**, 114 (1912).

(4) (a) Worrall, THIS JOURNAL, **49**, 1598 (1927); (b) **62**, 2449 (1940).

(5) Musante, *Gazz. chim. ital.*, **67**, 579 (1937).

(6) Weiland, *Ber.*, **36**, 2567 (1903).

(7) Meisenheimer and Heim, *ibid.*, **38**, 469 (1905).

(8) Kohler and Stone, THIS JOURNAL, **52**, 761 (1930).

(9) Heath and Lambert, *J. Chem. Soc.*, 1477 (1947).

(10) (a) Worrall and Benington, THIS JOURNAL, **60**, 2844 (1938). (b) Gilman and King, *ibid.*, **47**, 1136 (1925). (c) Kohler and Reimer, *Am. Chem. J.*, **31**, 163 (1904); Gilman and Cason, THIS JOURNAL, **72**, 3469 (1950).

TABLE I

NITRO SULFIDES $RCH(SR')CHNO_2$ (R'')

No.	R	R'	R''	Yield, %	M. p.,[a] °C.	Formula	S, Analyses, %[b] Calcd.	Found
1	C_6H_5	C_6H_5	H	75	72–73	$C_{14}H_{13}O_2NS$	12.36	12.35
2	C_6H_5	p-$CH_3C_6H_4$	H	89[c]	76–77	$C_{15}H_{15}O_2NS$	11.72	11.79
3	C_6H_5	p-iso-$C_3H_7C_6H_4$	H	84	74–75	$C_{17}H_{19}O_2NS$	10.63	10.53
4	C_6H_5	p-$CH_3CONHC_6H_4$	H	58[d]	122–123	$C_{16}H_{16}O_3N_2S$	10.12	10.06
5	C_6H_5	o-$CH_3C_6H_4$	H	51	62.5[e]	$C_{15}H_{15}O_2NS$	11.72	11.61
6	C_6H_5	$C_6H_5CH_2$	H	..[f]	.....	.....	...	...
7	C_6H_5	p-ClC_6H_4	H	..[g]	.....	.....	...	...
8	C_6H_5	C_6H_5	CH_3	79	65.6[e]	$C_{15}H_{15}O_2NS$	11.72	11.59
9	p-$CH_3OC_6H_4$	C_6H_5	H	100	100–101	$C_{15}H_{15}O_3NS$	11.07	10.97, 10.91
10	p-$CH_3OC_6H_4$	p-$CH_3C_6H_4$	H	100	73–74	$C_{16}H_{17}O_3NS$	10.56	10.22, 10.44
11	p-$CH_3OC_6H_4$	$C_6H_5CH_2$	H	..[h]	.....	.....	...	...
12	p-ClC_6H_4	C_6H_5	H	84	63–64	$C_{14}H_{12}O_2NSCl$	10.90	10.82[i]
13	3,4-$CH_2O_2C_6H_3$	C_6H_5	H	83[j]	70–71	$C_{15}H_{13}O_4NS$	10.56	10.28
14	p-iso-$C_3H_7C_6H_4$	C_6H_5	H	90	76.5–77	$C_{17}H_{19}O_2NS$	10.63	10.58

[a] All melting points are uncorrected. Unless otherwise mentioned, the nitro sulfides were recrystallized from 95% ethanol. [b] The sulfur analyses were performed by the macro Parr bomb method. [c] This reaction was also carried out in 84% yield with benzene as the solvent. [d] The reaction proceeded at room temperature under nitrogen and with 95% ethanol as the solvent. [e] The product was recrystallized from absolute ethanol. [f] An oil was obtained which could not be crystallized. This oil was oxidized to the corresponding sulfone. See Table II. [g] A grayish crystalline product was obtained; m. p. 63–64°. *Anal.* Calcd. for $C_{14}H_{12}O_2NSCl$: S, 10.90; Cl, 12.10. Found: S, 21.85; Cl, 24.21. [h] An oil was obtained which could not be crystallized. Oxidation to the sulfone was not possible. [i] Calcd. for $C_{14}H_{12}O_2NSCl$: Cl, 12.10. Found: Cl, 12.22. [j] The reaction proceeded in absolute ethanol under reflux on the water-bath.

TABLE II

NITRO SULFONES, $RCH(SO_2R')CH_2NO_2$

No.	R	R'	Yield, %	M. p.,[a] °C.	Formula	S Analyses, %[b] Calcd.	Found
1	C_6H_5	C_6H_5	71	186–187	$C_{14}H_{13}O_4NS$	10.99	10.86
2	C_6H_5	p-$CH_3C_6H_4$	75[c]	147.5–148	$C_{15}H_{15}O_4NS$	10.49	10.50
3	C_6H_5	$C_6H_5CH_2$	18[d]	143–145	$C_{15}H_{15}O_4NS$	10.49	10.38
4	C_6H_5	p-$CH_3CONHC_6H_4$	91[e]	176–177.5	$C_{16}H_{16}O_5N_2S$	9.19	8.81
5	p-$CH_3OC_6H_4$	p-$CH_3CONHC_6H_4$	95	185–187 dec.	$C_{17}H_{18}O_6N_2S$	8.49	8.26

[a] All melting points are uncorrected. The nitro sulfones were difficultly soluble in absolute ethanol and, in many cases, were purified by extraction with ethanol. Glacial acetic acid and ethyl acetate gave low recoveries of the nitro sulfones and were not desirable as solvents for recrystallizations. [b] See note *b*, Table I. [c] This compound was prepared by Method B, using 6 *N* sulfuric acid. (See Experimental.) The other nitro sulfones, except No. 3, were prepared by Method A using glacial acetic acid. [d] This compound was obtained by the oxidation of No., 6 Table I, with 30% hydrogen peroxide according to the procedure of Gilman and Beaber, THIS JOURNAL, **47**, 1450 (1925). [e] The intermediate p-acetamidobenzenesulfinic acid was prepared in 58% yield according to the procedure of Smiles and Bere, "Organic Syntheses," Coll. Vol. I, 7, John Wiley and Sons, Inc., New York, N. Y., 1941, and was converted to the corresponding sodium salt by the method of Ferry and co-workers.[19]

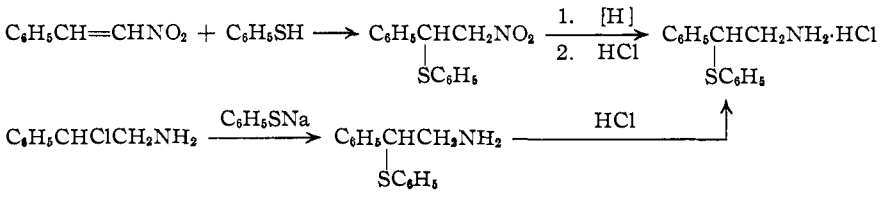
TABLE III

β-(ARYLMERCAPTO)-PHENETHYLAMINE HYDROCHLORIDES, $RCH(SR')CH_2NH_2 \cdot HCl$

No.	R	R'	Yield, % Method A	Method B	M. p.,[a,b] °C.	Formula	Analyses,[c] % Sulfur Calcd.	Sulfur Found	Chlorine Calcd.	Chlorine Found
1	C_6H_5	C_6H_5		48	192	$C_{14}H_{16}NSCl$	12.05	12.08	13.37	13.63
2	C_6H_5	p-$CH_3C_6H_4$	78	85	184–185	$C_{15}H_{18}NSCl$	11.46	11.24	12.70	12.66
3	C_6H_5	p-iso-$C_3H_7C_6H_4$		48.6	162.5–163.5	$C_{17}H_{22}NCSl$	10.41	10.20	11.54	11.70
4	p-$CH_3OC_6H_4$	C_6H_5		50	177–178	$C_{15}H_{18}ONSCl$	10.83	10.32	12.01	11.77
5	p-$CH_3OC_6H_4$	p-$CH_3C_6H_4$		18.9	196.5–197	$C_{16}H_{20}ONSCl$	10.34	10.22	11.47	11.11
6	3,4-$CH_2O_2C_6H_3$	C_6H_5	56.6		185–187	$C_{15}H_{16}O_2NSCl$	10.34	10.24	11.47	11.58

[a] The β-(arylmercapto)-phenethylamine hydrochlorides were recrystallized from a mixture of absolute ethanol and anhydrous ethyl ether. [b] See note *a*, Table I. [c] The sulfur and chlorine analyses were made by the macro Parr bomb method.

zinc and acetic acid were used, the reactions were much smoother, and purer products resulted. The yields ranged from 18 to 85%. The attempted catalytic hydrogenation of α-(nitromethyl)-benzyl *p*-tolyl sulfide in ethanol or methanol over Raney nickel at room temperature and under an initial pressure of approximately three atmospheres failed to yield the expected amines. However, a small amount of β-(phenyl-



sulfonyl)-phenethylamine resulted from the corresponding nitro sulfone when glacial acetic acid was used as the solvent. In this connection, Mozingo and others[11] have pointed out that Raney nickel is generally not a suitable catalyst for the hydrogenation of sulfur-containing compounds since it promotes the hydrogenolysis of the molecule. On the other hand, Heath and Lambert[9] apparently experienced no difficulty in reducing β-nitro sulfides and sulfones to the corresponding amines over Raney nickel under moderate or elevated temperature and pressure.

N,N-Dimethyl-β-(*p*-tolylmercapto)-phenethylamine was obtained in low yield (35%) from the alkylation of β-(*p*-tolylmercapto)-phenethylamine with formaldehyde and formic acid.

Some of the nitro sulfides and sulfones prepared in this study were tested as antibacterial agents against *Escherichia coli* and *Staphylococcus aureus*. The aminosulfides were ineffective in antihistaminic and antispasmodic tests. A more detailed report of the pharmacological tests will be published elsewhere. The authors are grateful to the Upjohn Company, Kalamazoo, Michigan, for the testing of the compounds and to Mr. John A. Jones for his assistance.

Experimental

Preparation of the Nitroölefins.—The procedure of Worrall[12] was generally employed in preparing the nitroölefins used in this investigation. 3,4-Methylenedioxy-β-nitrostyrene was made according to a procedure described by Lange and Hambourger[13]; the method followed in preparing β-methyl-β-nitrostyrene was similar to the one described by Alles[14] except that benzylamine was used as the catalyst.

***p*-Isopropyl-β-nitrostyrene.**—This compound was prepared from 75 g. (0.5 mole) of *p*-isopropylbenzaldehyde and 30 g. (0.5 mole) of nitromethane. The yield of the pure product was 15.2 g. (16%); m. p. 37°.

Anal. Calcd. for $C_{11}H_{13}O_2N$: N, 7.33. Found: N, 7.20.

Preparation of the Thiols.—*p*-Isopropylbenzenethiol,[15] b. p. 95–6° at 15 mm., *p*-chlorobenzenethiol,[16] m. p. 50–51°, and *p*-acetamidobenzenethiol,[17] m. p. 146–148°, were prepared by the reduction of the requisite sulfonyl chloride with zinc dust and sulfuric acid or alcoholic hydrochloric acid. The general procedure of Urquhart[18] and co-workers was followed in the preparation of α-toluenethiol (b. p. 104–108° at 44–46 mm.) from benzyl chloride and thiourea.

General Procedure for the Addition of Thiols to the Nitroölefins.—Two methods were used in the preparation of the nitro sulfides listed in Table I. (A) Equimolar quantities of the unsaturated nitro compound and the thiol were placed in an erlenmeyer flask and warmed on the water-bath until all of the solid had melted. Five drops of piperidine were then added to the mixture, and after the slight exothermic reaction had subsided, the flask was allowed to stand at room temperature until all of the material resolidified. Seeding was necessary in some cases. The product was recrystallized to constant melting point from ethanol.

(B) Equivalent amounts of the nitrostyrene and the thiol were dissolved in benzene at room temperature. Five drops of piperidine were added, and the mixture was allowed to stand overnight. The solvent was removed by distillation and the residue recrystallized from ethanol. When ethanol was used as the solvent, the reaction proceeded at room temperature or under refluxing, and the pure product usually crystallized directly from this solution.

General Procedure for the Addition of Sulfinic Acids to Nitroölefins.—The procedures which follow are typical of those used in the preparation of the nitro sulfones listed in Table II. (A) The pulverized sodium arylsulfinate was suspended in an appropriate volume of ethanol and then acidified with an equivalent amount of glacial acetic acid. After shaking and warming the mixture until all of the solid had dissolved, one molar equivalent of the nitrostyrene in ethanol was added to the clear solution. The resulting solution was mixed well and set aside for crystallization. The product was purified by recrystallization from ethanol.

(B) The free sulfinic acid was secured by acidifying an aqueous solution of the sodium sulfinate with 6 *N* sulfuric acid. The product was rapidly collected on a Büchner funnel, washed with cold water and immediately dissolved in a suitable volume of ethanol. Then, to this solution there was added a molar equivalent of the nitroölefin in ethanol. The product was isolated as described in (A).

Reduction of the Nitro Sulfides.—Two procedures were employed in reducing the nitro sulfides to the corresponding amines (Table III): (A) an adaptation of the method of Ferry and associates[19] for the reduction of *p*-acetamido-*p'*-nitrodiphenyl sulfone with stannous chloride and concentrated hydrochloric acid and (B) the procedure of Zenitz and co-workers[20] for the reduction of aliphatic nitro compounds with zinc dust and glacial acetic acid.

β-Phenylmercaptophenethylamine Hydrochloride.—To a suspension of sodium thiophenoxide, prepared from 3 g. (0.025 mole) of benzenethiol and 0.6 g. (0.025 g. atom) of sodium in refluxing toluene, there was added 2.4 g. (0.0125 mole) of β-phenyl-β-chloroethylamine hydrochloride.[21] After refluxing the mixture for two hours, the undissolved solids were removed by filtration, and the product isolated as the amine hydrochloride after saturating the cooled solution with anhydrous hydrogen chloride. One and six-tenths grams (48%) of the pure product resulted after recrystallization from a mixture of ethanol and ether; m. p. 191–192°. This product was identical with the one obtained from the reduction of α-(nitromethyl)-benzyl phenyl sulfide (m.p. and mixed m.p.).

β-(Phenylsulfonyl)-phenethylamine Hydrochloride.—α-(Nitromethyl)-benzyl phenyl sulfone was reduced to the corresponding amine according to procedure (A) for the reduction of the nitro sulfides. There was obtained from 8.5 g. (0.02 mole) of the nitro sulfone, 18 g. (0.8 mole) of stannous chloride dihydrate, 18 ml. of hydrochloric acid and 35 ml. of ethanol 4 g. (68%) of the crude product; m.p. 192–194°. Pure β-(phenylsulfonyl)-phenethylamine hydrochloride melted at 207–208° after recrystallization from a mixture of ethanol and ether. When the reduction was carried out in an aqueous medium, the yield of the amine hydrochloride was 19% of the theoretical amount.

Anal. Calcd. for $C_{14}H_{16}O_2NClS$: S, 10.77; Cl, 11.78. Found: S, 10.55; Cl, 12.01.

N,N-Dimethyl-β-(*p*-tolylmercapto)-phenethylamine Hydrochloride.—Four and eight-tenths grams (0.017 mole) of β-(*p*-tolylmercapto)-phenethylamine hydrochloride suspended in 40 ml. of water was neutralized with 20% sodium hydroxide. The free amine was extracted with ether and dried over anhydrous sodium sulfate. After filtering and removing the excess solvent, 5.2 ml. of 90% formic acid, followed by 3.5 ml. of formalin was added to the residue. The mixture was refluxed for 12 hours on an oil-bath maintained at 80–90°, then cooled, acidified with 5 ml. of concentrated hydrochloric acid, and finally evaporated to dryness *in vacuo*. The amine hydrochloride was then purified by conversion to the free base, drying, and reprecipitating the hydrochloride from a mixture of ethanol and ether. The yield of the compound was 1.8 g. (35%); m. p. 165.5°.

Anal. Calcd. for $C_{17}H_{22}NClS$: S, 10.42; Cl, 11.54. Found: S, 10.40; Cl, 11.17.

Summary

α-(Nitromethyl)-benzyl aryl sulfides and sulfones

(11) Mozingo, Wolf, Harris and Folkers, THIS JOURNAL, **65**, 1013 (1943); Mozingo, Harris, Wolf, Hoffhine, Easton and Folkers, *ibid.*, **67**, 2092 (1945).

(12) Worrall, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, N. Y., 413 (1941).

(13) Lange and Hambourger, THIS JOURNAL, **53**, 3865 (1931).

(14) Alles, *ibid.*, **54**, 271 (1932).

(15) Gilman and Broadbent, *ibid.*, **69**, 2053 (1947).

(16) Senear, Rapport and Koepfli, *J. Biol. Chem.*, **167**, 229 (1947).

(17) Zincke and Jorg, *Ber.*, **42**, 3367 (1909).

(18) Urquhart, Gates and Connor, *Org. Syntheses*, **21**, 36 (1941).

(19) Ferry, Buck and Baltzly, *ibid.*, **22**, 31 (1942).

(20) Zenitz, Mack and Moore, THIS JOURNAL, **70**, 955 (1948).

(21) Kindly supplied by Dr. R. V. Heinzelmann, The Upjohn Company, Kalamazoo, Michigan.

have been prepared by the addition of aromatic thiols or sulfinic acids to β-nitrostyrene and some of its derivatives. Some of the sulfides and sulfones have been reduced to the corresponding β-(arylmercapto)- or β-(arylsulfonyl)-phenethylamines by zinc and acetic acid or stannous chloride and alcoholic hydrochloric acid.

The preparation of N,N-dimethyl-β-(*p*-tolylmercapto)-phenethylamine is described.

TUSKEGEE INSTITUTE, ALABAMA RECEIVED JUNE 5, 1950

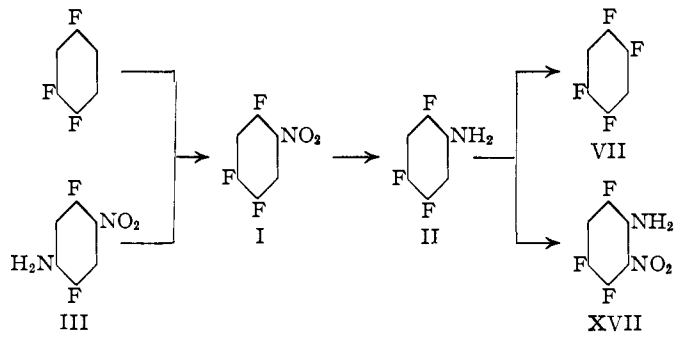
[CONTRIBUTION FROM THE GEOCHEMICAL SECTION OF THE ILLINOIS STATE GEOLOGICAL SURVEY]

Aromatic Fluorine Compounds. II. 1,2,4,5-Tetrafluorobenzene and Related Compounds[1,2]

BY G. C. FINGER, F. H. REED, D. M. BURNESS, D. M. FORT AND R. R. BLOUGH

The synthesis of a complete series of fluorinated benzenes would reveal the effect of progressive fluorine substitution upon the physical and chemical properties of benzene and benzenoid structures. A tetra- and pentafluorobenzene are needed to complete such a series. In addition, a study of the effect on properties of other substituents in the polyfluorobenzenes would lead to generalizations of theoretical and practical value.

1,2,4,5-Tetrafluorobenzene has been synthesized and the properties of its intermediates were studied in detail. For comparative purposes, a number of chlorofluorobenzenes possessing the 1,2,4,5-structure are reported. Flash points and other physical data accumulated thus far on the fluoro- and chlorofluorobenzenes are summarized. It was discovered that 1,2,4,5-tetrafluorobenzene gave a quinone rather than a nitro derivative under nitration conditions. The anomalous behavior of 2-nitro-3,4,6-trifluoroaniline under diazotization conditions was studied.



The nitration of 1,2,4-trifluorobenzene gave 2,4,5-trifluoronitrobenzene (I) as expected by analogy to the trichloro compound. A Schiemann reaction on 4-nitro-2,5-difluoroaniline (III) produced the same compound, and the position of the nitro group was established by the identity of the acetyl derivatives at II. Reduction gave 2,4,5-trifluoroaniline (II) and a Schiemann conversion formed 1,2,4,5-tetrafluorobenzene (VII), and a small amount of 2-chloro-1,4,5-trifluorobenzene (VIII) as a by-product.[3]

1,2,4,5-Tetrafluorobenzene resisted photochemical chlorination to a remarkable degree and the only reaction product isolated was a trace of a cyclohexane derivative, $C_6H_2Cl_6F_4$ (X). In other words, any chlorination that took place did not involve hydrogen substitution, but chlorine addition across the double bonds to form a saturated ring system. This is hardly comparable to the tetrachlorobenzene analog. In contrast, 1,4-difluoro- and 1,2,4-trifluorobenzene halogenated normally, thus making available bromo and chloro derivatives with a 1,2,4,5 structure. The 2-bromo (XI) and 2,5-dibromo (XII) derivatives of 1,4-difluorobenzene were obtained by bromination; likewise, the 2-bromo (IX) derivative of 1,4,5-trifluorobenzene. Sulfuryl chloride[4] chlorination of 1,4-difluorobenzene gave such derivatives as 2-chloro- (XIII), 2,5-dichloro- (XIV) and a small amount of 2,6-dichloro- (XV) and 2,3,5-trichloro-1,4-difluorobenzene (XVI). A trace of hexachlorobenzene was isolated. Apparently the aluminum chloride catalyst caused substitution of fluorine with chlorine in the formation of the hexachloro compound.

The behavior of 1,2,4,5-tetrafluorobenzene with such acids as nitric, sulfuric and their mixtures is unique and in sharp contrast to the chlorine analog. Attempts to form a nitro derivative were unsuccessful. The tetrafluoro compound appeared to be inert to concentrated or fuming nitric and sulfuric acids; with fuming nitric acid in a glass-sealed tube at 125° for four hours, a slight etching of the tube was the only evidence of reaction. There was no reaction with nitric–sulfuric acid mixtures if (1) both components were concentrated, or (2) if one component was fuming and the other concentrated. A nitric–sulfuric acid mixture of fuming reagents reacted with avidity, at times almost uncontrollable even at 5°; 2,5-difluoro-1,4-benzoquinone was identified in the decomposition products. This implies a fluorine displacement–oxidation mechanism involving a pair of fluorine atoms para to each other.

Since it was not feasible to obtain a nitro derivative of 1,2,4,5-tetrafluorobenzene by direct nitra-

(1) Presented in part before the Organic and Industrial and Engineering Divisions at the 109th (April, 1946) and 116th (September, 1949) Meetings of the American Chemical Society, Atlantic City, N. J. The material in this paper is based on reports submitted to the Office of Scientific Research and Development under Contract OEMsr-469 (1942–43), and the Office of Naval Research under Contract N6ori-71; Task XIV (1946–50). The financial assistance of these agencies is gratefully acknowledged.

(2) Published with the permission of the Chief of the Illinois State Geological Survey.

(3) The formation of chloro by-products in Schiemann reactions is quite common if diazotization is effected in strong hydrochloric acid solutions.

(4) Cutter and Brown, *J. Chem. Ed.*, **21**, 443 (1944).