

anhydride containing a trace of sulfuric acid produced 76 mg. of crystalline material identical with the original *p*-(tetraacetyl- $\beta$ -D-glucopyranosyl)-nitrobenzene.

1-(Tetraacetyl- $\beta$ -D-glucopyranosyl)-3,4-dibromobenzene (III).—Tetraacetyl- $\beta$ -D-glucopyranosylbenzene (5.0 g.) was dissolved in bromine (25 ml.) and powdered, freshly fused ferric chloride (0.5 g.) was added. The flask was protected with a calcium chloride tube and the reaction mixture allowed to stand for four hours at room temperature. The bulk of the excess bromine was removed in three hours with a stream of dry air, leaving a dark red viscous gum which was dissolved in chloroform (100 ml.). The chloroform solution was washed with saturated aqueous solutions of sodium bisulfite and sodium bicarbonate, and finally with water. After drying over calcium chloride the chloroform was distilled to leave 5.1 g. of light yellow glass. This was treated with acetic anhydride (40 ml.) and a drop of sulfuric acid. The yellow glass recovered by processing the acetylation mixture in the usual manner did not crystallize and was acetylated again. The product obtained was a thick sirup which partially crystallized. This was recrystallized from 2-propanol to yield 1.29 g. of white needles, m. p. 124.5–132.5°. Six additional recrystallizations from the same solvent gave 0.32 g. of pure 1-(tetraacetyl- $\beta$ -D-glucopyranosyl)-3,4-dibromobenzene, m. p. 164.5–165°,  $[\alpha]^{20}_D -29.0^\circ$  (*c*, 2.893, chloroform).

*Anal.* Calcd. for  $C_{20}H_{22}O_6Br_2$ : C, 42.42; H, 3.92; Br, 28.23. Found: C, 42.68; H, 4.03; Br, 28.40, 28.28.

An alkaline potassium permanganate oxidation of 87 mg. of the pure product gave 59 mg. of white solid, m. p. 228–234°. This was sublimed at reduced pressure to give pure 3,4-dibromobenzoic acid, m. p. 235–237°, mixed m. p. with an authentic sample<sup>3</sup> 235–237°.

On concentration of the original mother liquors there was obtained additional crystalline material, m. p. 105–108°,  $[\alpha]^{20}_D -28.8^\circ$  (*c*, 0.555, chloroform). This could not be purified by further recrystallization, and was apparently identical with the mixture described below.

The procedure described above was repeated using 4.0 g. of starting material and reducing the reaction time to 3.25 hours. The colorless sirup obtained was recrystallized from 2-propanol to yield 1.65 g. of product, m. p. 104–110°. Several more recrystallizations resulted in an apparently pure product, m. p. 111.5–112.5°. Oxidation of 0.20 g. of this material with alkaline permanganate solution produced 0.11 g. of crystals, m. p. 237–247° after two recrystallizations from a mixture of ethanol and water. Sublimation of this product gave two fractions, m. p. 246–249° and m. p. 234–245°. The first fraction gave a mixed m. p. of 249.5–251.5° with pure *p*-bromobenzoic acid, m. p. 251–253°. The second fraction was impure 3,4-dibromobenzoic acid as seen from the oxidation described below.

The crystalline product, m. p. 111.5–112.5°, was treated with acetic anhydride and a trace of sulfuric acid, but was recovered unchanged, m. p. 111.5–112.5,  $[\alpha]^{20}_D -29.6^\circ$  (*c*, 2.67, chloroform). It analyzed for an approximately equimolar mixture of III and *p*-(tetraacetyl- $\beta$ -D-glucopyranosyl)-bromobenzene (IV).

*Anal.* Calcd. for  $C_{20}H_{23}O_6Br$ : C, 49.29; H, 4.75; Br, 16.40. Calcd. for  $C_{20}H_{22}O_6Br_2$ : C, 42.42; H, 3.92; Br, 28.23. Calcd. for  $C_{16}H_{15}O_6Br_3$ : C, 45.6; H, 4.32; Br, 22.8. Found: C, 46.88; H, 4.49; Br, 21.43.

Oxidation of this product with permanganate was repeated as before to yield a crystalline solid, m. p. 232–233°, which did not depress the m. p. of 3,4-dibromobenzoic acid, m. p. 235–236°.

The original mother liquors were concentrated to dryness leaving 1.28 g. of yellow sirup which produced no further crystalline material.

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(3) Neville and Winther, *Ber.*, **18**, 962 (1880).

## Synthesis of Aromatic Fluorides through Diazotization in Anhydrous Hydrogen Fluoride

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Although fluorobenzene was obtained from aniline by the preparation and decomposition of benzenediazonium fluoride in anhydrous hydrogen fluoride as early as 1934,<sup>2</sup> the general applicability of this method for the synthesis of aromatic fluorides has not been investigated. Our studies have shown that this procedure is successful in many cases, and that, because of its simplicity, it is often preferable to the methods commonly used<sup>3</sup> for the synthesis of aromatic fluorides.

The following compounds were prepared successfully by this method in the percentage yields indicated: fluorobenzene (87), *o*-fluorotoluene (73), *m*-fluorotoluene (82), *p*-fluorotoluene (78), 4-fluoro-1,3-dimethylbenzene (57), 2-fluoro-1,4-dimethylbenzene<sup>4</sup> (43), *m*-fluorochlorobenzene (81), *p*-fluorochlorobenzene (74), *m*-nitrofluorobenzene (39), *p*-nitrofluorobenzene (62), *m*-fluorophenol (46) *o*-fluorobenzoic acid (57), *m*-fluorobenzoic acid (78), *p*-fluorobenzoic acid (98) and *o*-fluorodiphenyl (82).

In many cases, the yields of fluorides are approximately as good or better than those reported<sup>5</sup> for the same compounds by the familiar Schiemann method, in which the diazonium fluoborates are isolated and thermally decomposed. It is noteworthy that the three fluorobenzoic acids and *m*-fluorophenol can be prepared directly from the corresponding amines, in contrast to results obtained by use of the Schiemann reaction. Similarly, the yield of *o*-fluorotoluene is considerably better than that obtained by the latter method.<sup>6</sup>

The following amines, all of which are substituted in the ortho position with groups which contain one or more atoms with unshared electron pairs, failed to give satisfactory yields of fluorides: *o*-chloroaniline, *o*-nitroaniline, *o*-aminophenol and *o*-anisidine. In each of these cases little nitrogen was evolved during the attempted decomposition of the corresponding diazonium fluoride, and failure of the synthesis apparently resulted from the fact that the diazonium salt was not decomposed at the highest temperature obtainable in anhydrous hydrogen fluoride under reflux at atmospheric pressure. Attempted decomposition of the diazonium fluorides at higher temperatures

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(2) Osswald and Scherer, German Patent 600,706, July 30, 1934 [*C. A.*, **28**, 7260 (1934)].

(3) See Bockemüller, "Organische Fluorverbindungen," Ferd. Enke, Stuttgart, 1936, pp. 54–66.

(4) M. p.  $-6^\circ$ . *Anal.* Calcd. for  $C_8H_8F$ : C, 77.4; H, 7.3. Found: C, 77.4; H, 7.4.

(5) For a summary, see Bockemüller in "Newer Methods of Preparative Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1948, p. 246.

(6) Workers in this Laboratory have consistently obtained very low yields of *o*-fluorotoluene following Schiemann's directions.

under pressure led to the formation of a complex mixture of high melting solids. The fact that the types of *o*-substituted diazonium salts mentioned are relatively stable has been observed previously in the cases of some of the corresponding diazonium chlorides<sup>7</sup> and may possibly result from a type of electronic interaction involving an unshared electron pair of the ortho-substituted atom or group and the outer nitrogen atom in the diazonium group.

The following compounds were obtained from the corresponding amines only in very poor yields: 1-fluoro-2,4-dinitrobenzene, *p*-fluorophenol, *p*-fluoroanisole,  $\alpha$ -fluoronaphthalene,  $\beta$ -fluoronaphthalene, *p*-fluoroaniline (from *p*-aminoacetanilide) and 2-fluoro-3-methylpyridine.<sup>8</sup>

Treatment of sulfanilamide in the usual manner gave a small amount of *p*-fluorobenzenesulfonyl fluoride, which was obtained in 38% yield when a two-molar ratio of sodium nitrite was used. The general applicability of this hitherto unreported reaction was shown by its extension to the synthesis of *p*-toluenesulfonyl fluoride from *p*-toluenesulfonamide in 70% yield.

#### Experimental

**General Procedure.**—Approximately 20 moles of anhydrous hydrogen fluoride was added slowly to 1 mole of the purified amine contained in a 1-liter, 2-necked monel metal flask<sup>9</sup> cooled in ice. The solution was stirred at 0° by means of a stainless steel paddle stirrer while 82.8 g. (1.2 moles) of dried, reagent grade sodium nitrite was added in small portions over a period of one hour. The flask was then connected to an ice-cooled copper reflux coil and the reaction mixture was warmed slowly by means of an electrically heated water-bath until moderately rapid evolution of nitrogen ceased. In most cases, the reaction mixtures were then cooled, diluted with ice, and steam distilled. In the synthesis of 2-fluoro-3-methylpyridine and *p*-fluoroaniline, excess hydrogen fluoride was evaporated, the residue neutralized with aqueous potassium hydroxide, and the products steam distilled. In the cases of the fluorobenzoic acids and of *o*-fluorodiphenyl, the reaction mixtures were cooled, diluted with ice, and the precipitated products removed by filtration.

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(7) See, for example, Euler, *Ann.*, **325**, 292 (1902); Cain and Nicoll, *J. Chem. Soc.*, **81**, 1412 (1902); Gubelmann, Weiland and Stallmann, U. S. Patent 1,623,949, April 5, 1927; Snow, *Ind. Eng. Chem.*, **24**, 1420 (1932); Yamamoto, *J. Soc. Chem. Ind., Japan*, **35**, Suppl. binding 298 (1932); *ibid.*, **35**, Suppl. binding, No. 12, 564 (1932); *ibid.*, **36**, Suppl. binding 59 (1933).

(8) B. p. 144–146° at 737 mm. *Anal.* Calcd. for C<sub>6</sub>H<sub>5</sub>NF: C, 64.9; H, 5.4; N, 12.6. Found: C, 64.8; H, 5.6; N, 12.5.

(9) Monel metal proved superior to copper or stainless steel.

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## Vapor Phase Alkylation of Phenols and Thio-phenols<sup>1</sup>

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For the synthesis of thianaphthenes and benzo-

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furans<sup>2</sup> by dehydrocyclization it was necessary to synthesize a number of *o*-alkylphenols and thio-phenols. Among the methods investigated for the preparation of these compounds was the vapor phase alkylation mentioned by Aleksandrova.<sup>3</sup> Aleksandrova processed phenol and ethanol in a 1/7 ratio over a thoria on alumina catalyst at 440–460° at a very slow space velocity. He obtained an alkylated product consisting of about half mono and half higher alkylated phenols.

A study of this reaction for the preparation of *o*-ethylphenol reveals that the optimum temperature is 350° with a space velocity of 600–900 (Table Ib) with a mol ratio of 1 to 1 of 95% ethanol and phenol.

Under these conditions about 53% of the phenol is converted to alkylphenols and 18% is converted to *o*-ethylphenol. Using a mol ratio of 2 alcohol to 1 phenol gave 80% conversion to alkylphenols with about the same per cent. *o*-ethylphenol. At a temperature of 450°, 70% alkylation was obtained of which only 4% was *o*-ethylphenol. In each case only the *o*-ethylphenol was isolated by fractionation through a 20 plate spinning band column, b. p. 201–203° (730 mm.).

Absolute ethanol gave the same conversion as 95% ethanol. Also it was discovered that pure alumina<sup>4</sup> was just as effective as the thoria on alumina reported by Aleksandrova. Neither catalyst caused noticeable charring and both seemed resistant to poisoning. The catalyst activity did not decrease during the longest runs made in this research, 10 hr.

Two other phenols were also alkylated with ethanol with the results indicated in Table I.

TABLE I<sup>a</sup>

	Moles phenol	Moles eth-anol	Temp., °C.	S. V. <sup>b</sup>	% Conversion to <sup>c</sup> alkyl-phenols	% Conversion to <sup>c</sup> <i>o</i> -alkyl-phenol
<i>p</i> -Methylphenol	0.5	0.5	350	1245	75	15.0 <sup>d</sup>
<i>p</i> -Chlorophenol	.5	.5	350	647	48	7.5 <sup>e</sup>
<i>p</i> -Chlorophenol	.5	1.0	350	365	72	15.0

<sup>a</sup> The results reported here are with thorium on alumina catalysts, although later work indicated alumina alone to be just as effective. <sup>b</sup> Calculated as ml. of phenol vapor s. t. p./ml. cat./hr. <sup>c</sup> The results are calculated as mono-ethylphenol and hence are high since some higher alkylphenols were also formed. <sup>d</sup> The 2-ethyl-4-methylphenol had a b. p. 216–219° (730 mm.). Hill and Graf, *THIS JOURNAL*, **37**, 1843 (1915) report 216–218°. Further identification was obtained by preparation of the phenoxyacetic acid m. p. 130–131°. Niederl and co-workers report 133° (*THIS JOURNAL*, **59**, 1114 (1939)). <sup>e</sup> The 2-ethyl-4-chlorophenol boiled at 238–241° (730 mm.). Other investigators (Auwers and Wittig, *Ber.*, **57**, 1270 (1924)) have reported the boiling point at reduced pressure. The phenol was identified by its phenoxyacetic (Newman, Fones and Renoll report m. p. 109–112°, *THIS JOURNAL*, **69**, 720 (1947)) acid m. p. 111–112°.

(2) Hansch, Saltonstall and Settle, *THIS JOURNAL*, **71**, 943 (1949).

(3) Z. P. Aleksandrova, *J. Gen. Chem.* (U. S. S. R.), **12**, 522 (1942); *C. A.*, **37**, 2723 (1943).

(4) The alumina used in this work was ALRCO type H-40, Grade R 2300, 8–14 mesh. In all of the runs reported in this paper 10 cc. of catalyst was used.