

## Preparation of Aromatic Fluorine Compounds Using Diazonium Fluosilicates

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The Schiemann reaction<sup>1</sup> is a convenient method of preparing many aromatic and heterocyclic<sup>2</sup> fluorine compounds. In some cases, however, the yields are low; this is true of many nitrofluoro and hydroxyfluoro compounds. The preparation of *p*-fluorobenzoic acid from ethyl *p*-aminobenzoate using the diazonium fluosilicate instead of the diazonium fluoborate has been reported recently.<sup>3</sup> It was of interest to see how this method of preparing fluorine compounds would compare with the Schiemann method, and if it would give better results with those types of compounds for which the Schiemann reaction is not too satisfactory.

The results are shown in the accompanying table. In every case but one—*p*-fluorophenol—the Schiemann reaction gave a better yield than the diazonium fluosilicate method. In another instance, the preparation of methyl 5-fluoronicotinate,<sup>4</sup> the diazonium fluosilicate method has been successful where all other methods failed.

TABLE I

Fluorine compound	% Yield diazonium fluosilicate	% Yield F compd. from amine	% Yield F compd. Schiemann reaccn.
Fluorobenzene	87	30.4	51-97 <sup>1,5,6,7</sup>
<i>m</i> -Nitrofluorobenzene	86	22.3	43-54 <sup>8,9,10,11</sup>
<i>p</i> -Nitrofluorobenzene	85	33.8	40-60 <sup>9,11,12,13</sup>
<i>p</i> -Fluorophenol	79.2	6.5	0 <sup>9</sup>
Ethyl <i>p</i> -fluorobenzoate	82.5	38.8	71 <sup>14</sup>
2-Fluoropyridine	0	..	34 <sup>2</sup>

### Experimental

**Preparation of the Amine Fluosilicates.**—This was usually accomplished by dissolving the amine in the minimum quantity of 95% ethanol, warming if necessary to keep the volume of ethanol down, and adding slightly more than the theoretical amount of 27% fluosilicic acid. The solution was then cooled in an ice-bath and the precipitated salt washed with ether and dried in a desiccator or by warming to 30-40° in an oven for a short time. Methanol

was tried as a solvent in the case of *p*-nitroaniline; the yield was lower (72%) than with ethanol (89.5%). With *p*-aminophenol, methanol and ethanol gave similar results.

**Preparation of the Diazonium Fluosilicates.**—A typical procedure was as follows: 134 g. of *p*-nitroaniline fluosilicate was suspended in 500 ml. of glacial acetic acid, and ethyl nitrite was passed into the mixture with stirring until all the solid had dissolved. The temperature was allowed to rise to about 40°, and kept there by an ice-bath. The solution was then cooled to room temperature, 600 ml. of absolute ether added, and the solution then cooled to 0° and allowed to stand tightly covered in the ice-box overnight. The oil which appeared upon addition of the ether slowly changed to a solid. The product was filtered, washed twice with 150 ml. of absolute ethanol, twice with 150 ml. of absolute ether, and dried at 40°. The yield was 114-120 g.

All of the compounds tried gave lower yields at temperatures much above 40°; with aniline fluosilicate, at 50° for instance, the yield dropped to 67% although with the *p*-hydroxyaniline fluosilicate the yield was 89% at 40° and 88% at 60°.

**Decomposition of the Diazonium Fluosilicates.**—In most cases the diazonium salt was diluted with an inert material, such as sodium fluoride, to make the decomposition less vigorous. A typical example: 108 g. of *p*-nitrobenzenediazonium fluosilicate (dried overnight over phosphorus pentoxide) was mixed with an equal weight of sodium fluoride (dried overnight at 107° in an oven). The decomposition was carried out in a 2-liter flask connected to a series of traps; this consisted of five eight-inch test-tubes each fitted with a two-holed rubber stopper carrying an inlet and outlet tube, and filled about two-thirds full of broken glass tubing; all were immersed in an ice-salt-bath. The diluted diazonium salt was decomposed in eight separate lots of approximately 27 g. each. The initial lot was set off by heating gently with a bunsen burner; the others started to decompose shortly after being added to the flask warm from the previous decomposition. Decomposition was smooth, but rapid.

Steam was blown through the traps to remove any product in them; the material so collected was added to the decomposition flask, more water was added, and the mixture steam distilled. The oil was extracted from the distillate with ether, the ether dried, and the *p*-fluoro-nitrobenzene recovered by distillation; yield, 27.5 g., b. p. 203°.

All the fluorine compounds reported in this investigation had been prepared previously, as indicated in the table. The boiling points and refractive indices of our compounds checked the literature values.

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## Sodium Hydride and Alkyl Halides<sup>1</sup>

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The recent report of the lack of reaction of sodium hydride with diethyldichlorosilane<sup>2</sup> prompts us to report at this time our results on the attempted reaction of sodium hydride with certain alkyl halides. In the course of this investigation it was found that sodium hydride did not react with any of the eight halides studied. The com-

(1) This work was conducted as part of a program of research under a contract between the Office of Naval Research and the University of Colorado.

(2) Finholt, Bond, Wilzbach and Schlesinger, *THIS JOURNAL*, **69**, 2692 (1947).

pounds and the conditions employed are listed in Table I.

TABLE I  
TREATMENT OF VARIOUS ORGANIC HALIDES WITH SODIUM HYDRIDE

Halide	Temp., °C.	Time of stirring, hours
Benzyl chloride <sup>a,b</sup>	170	3
Benzyl chloride <sup>a,c</sup>	100	1
Benzyl bromide <sup>a,b</sup>	180	2
Triphenylmethyl chloride <sup>b</sup>	<sup>d</sup>	<sup>d</sup>
<i>n</i> -Butyl bromide <sup>b,e</sup>	75	4
<i>s</i> -Butyl bromide <sup>b,e</sup>	70	4
<i>s</i> -Butyl iodide <sup>a,b</sup>	95	2
<i>t</i> -Butyl chloride <sup>b,e</sup>	85	4
Bromobenzene <sup>a,b</sup>	135	3

<sup>a</sup> No solvent. <sup>b</sup> Low speed laboratory stirrer used. <sup>c</sup> High speed (4100 r.p.m.) stirrer used. <sup>d</sup> See experimental section. <sup>e</sup> Purified ligroin (b.p. 90–120°) used to suspend or dissolve reactants.

The halides used included those which are active in nucleophilic substitution reactions of either the S<sub>N</sub>1- or the S<sub>N</sub>2-type<sup>3</sup> as well as one aromatic halide. This lack of reaction is especially interesting in view of the high reactivity of sodium alkides with alkyl halides.<sup>4</sup> The apparent inertness of sodium hydride may possibly be due to a surface film, but reaction could not be forced by activation with a small amount of ethanol, a special high-speed stirrer, or by grinding the reactants together in a nitrogen atmosphere for one hour. Two different samples of du Pont sodium hydride were used.

As sodium hydride has been used successfully in effecting Claisen-type condensations of carbonyl compounds,<sup>5</sup> and as no reaction occurred between alkyl halides and sodium hydride, we decided to see whether reaction with alkyl halides could be induced by the action of ethyl acetate in providing a fresh surface for the sodium hydride. When equimolar quantities of benzyl chloride and ethyl acetate were treated with sodium hydride, no toluene was formed, but instead a fair yield of ethyl dibenzylacetate was isolated. Apparently the sodio derivative of the ester was alkylated by the benzyl chloride.<sup>6</sup>

When similar experiments were run with *n*-butyl chloride and ethyl acetate, the sodium hydride caused the ethyl acetate to self-condense, forming ethyl acetoacetate. There was no indi-

(3) Hughes, *Trans. Faraday Soc.*, **37**, 603 (1941).

(4) See, for example, Bergmann, *Helv. Chim. Acta*, **20**, 590 (1907); Whitmore and Zook, *THIS JOURNAL*, **64**, 1783 (1942); Morton, Davidson and Hakan, *ibid.*, **64**, 2242 (1942).

(5) See, for example, Swamer and Hauser, *ibid.*, **68**, 2647 (1946); Hansley and Carlisle, *Chem. Eng. News*, **23**, 1332 (1945); Green and La Forge, *THIS JOURNAL*, **70**, 2287 (1948).

(6) It is of interest to note that no monoalkylation product was isolated. This is in agreement with the observation of Nef<sup>7</sup> and of Dunn, Redemann and Lauritsen<sup>8</sup> regarding the large amounts of dialkylation product in treatment of benzyl chloride with sodio-acetoacetic ester and sodio-malonic ester.

(7) Nef, *Ann.*, **266**, 52 (1891).

(8) Dunn, Redemann and Lauritsen, *THIS JOURNAL*, **54**, 4335 (1932).

cation of the alkylation product, ethyl caproate, being formed, and only a negligible quantity of chloride ion was produced.

### Experimental

(a) **Halides.**—In a typical experiment 53 g. (0.42 mole) of freshly distilled benzyl chloride and 15 g. (0.63 mole) of sodium hydride<sup>9</sup> were stirred and heated at about 170° for three hours in a round-bottom flask. The mixture was cooled, and the liquid was decanted and distilled. The liquid comprised only benzyl chloride. Similar experiments with benzyl bromide, *s*-butyl iodide and bromobenzene resulted in recovery of starting materials. The addition of a few drops of ethanol did not initiate reaction (except for the expected hydrogen evolution). See Table I for conditions.

In the experiment with triphenylmethyl chloride, purified ligroin (b.p. 90–120°) was used to suspend the reactants (0.25 mole excess of sodium hydride), and the mixture was heated at 85° for six hours. As no reaction was noted, the ligroin was removed by distillation and the mixture heated above the m. p. of triphenylmethyl chloride for one hour. The mixture was decomposed carefully with water, and the organic reactant was recovered quantitatively as triphenylcarbinol.

With the butyl chloride and bromides a gas-trap was set up to collect any butanes or butenes developed. Ligroin was used as solvent and the solutions were heated at reflux with a 25% excess of sodium hydride. No gas condensable at –78° was obtained.

(b) **Ethyl Acetate and Benzyl Chloride.**—Ethyl acetate (52.8 g., 0.6 mole) and benzyl chloride (76.0 g., 0.6 mole) were placed in a three-neck flask fitted with a thermometer, Hershberg stirrer and reflux condenser. The system was purged with nitrogen and the sodium hydride (7.2 g., 0.3 mole) added. The reaction started immediately; the mixture was heated at 80° for five hours. The contents of the flask were poured into ice-water and extracted with ether. The chloride content of the aqueous layer was determined by the Volhard procedure, indicating that 46% of the benzyl chloride had reacted. The ethereal layer was dried over anhydrous sodium sulfate and distilled. Besides the unreacted products, there was obtained 24 g. (0.089 mole, 59%) of ethyl dibenzylacetate, b. p. 201–203° (18 mm.).<sup>10</sup>

Calcd. for C<sub>15</sub>H<sub>20</sub>O<sub>2</sub>: sap. equiv., 268; mol. wt., 268. Found: sap. equiv., 255; mol. wt., 254 (cryoscopic in benzene). *Mol. ref.* Calcd. for ethyl dibenzylacetate: 79.79. Found: 79.94.

Saponification of the ester gave dibenzylacetic acid, m. p. 87–88°.<sup>11</sup> The amide m. p. of 127°<sup>12</sup> was prepared as a further derivative.

No toluene or ethyl benzylacetate fractions were obtained in the distillation.

(c) **Ethyl Acetate and *n*-Butyl Chloride.**—A reaction was carried out using the above procedure with ethyl acetate (88.1 g., 1.0 mole), *n*-butyl chloride (92.6 g., 1.0 mole) and sodium hydride (24 g., 1.0 mole). Less than 4% of the chloride present had been converted to chloride ion in the course of the reaction. Besides unreacted products there was 3.27 g. (0.014 mole) of acetoacetic ester, b. p. 157–158° (621 mm.).<sup>13</sup> This formed a semicarbazone, m. p. 129°.<sup>14</sup> There was no evidence of ethyl caproate in the reaction product.

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(9) We are indebted to the Electrochemicals Department of E. I. du Pont de Nemours & Co. for a generous supply of sodium hydride.

(10) Dieckmann and Kron, *Ber.*, **41**, 1260 (1908).

(11) Fichter and Schiess, *ibid.*, **34**, 1991 (1901); Michael and Palmer, *Am. Chem. J.*, **7**, 65 (1885).

(12) Schneidewind, *Ber.*, **21**, 1323 (1888).

(13) R. Schiff, *ibid.*, **19**, 560 (1886).

(14) Thiele and Stange, *Ann.*, **283**, 1 (1894).

(15) Original manuscript received January 15, 1948.