158. *Heterocyclic Fluorides from Diazonium Fluorosilicates.*

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The decomposition of diazonium fluorosilicates is compared with that of the diazonium fluoroborates as a means of preparing fluorides of pyridine, quinoline, and 5-methylthiazole. In two cases the results have been compared with those obtained by diazotisation of the amine in anhydrous hydrogen fluoride, followed by decomposition *in situ*, and it has been shown that in these cases Ferm and Van der Werf's conclusions (*J. Amer. Chem. Soc.*, 1950, **72**, 4809) for aromatic fluorides do not apply.

Although a considerable amount of work has been carried out on the preparation of organic fluorides by decomposition of diazonium fluoroborates (Roe, " Organic Reactions," Vol. 5, p. 193), yet in very few cases have the diazonium salts of other complex acids been used. Lange and Muller (*Ber.*, 1930, **63**, 1058) have prepared 4 : 4′-difluorodiphenyl in low yield from the corresponding diazonium fluorophosphate, and Wiley (U.S.P. 2,423,359) has described the preparation of several diazonium fluorosilicates together with that of *p*-fluorobenzoic acid (12% crude yield from the diazonium salt), and the decomposition of benzenediazonium fluorosilicate by heat, but, in the last case, did not isolate any product and made no further attempt to use the diazonium fluorosilicate for purposes other than the preparation of dyes. Hawkins and Roe (*J. Org. Chem.*, 1949, **13**, 328) decomposed the diazonium fluorosilicate of methyl 5-aminonicotinate by heating it in dry toluene and obtained a crude fluoro-compound in a yield of about 15%, and Cheek, Wiley, and Roe (*J. Amer. Chem. Soc.*, 1949, **71**, 1863) applied the method to the preparation of several aromatic fluorides. In all cases except one their yields were lower than those from the fluoroborates, and attempts to prepare 2-fluoropyridine failed completely, it being impossible even to prepare the diazonium salt. The experiments now described are concerned only with heterocyclic compounds and differ from those of Roe *et al.* in that the diazonium fluorosilicates were decomposed either in suspension in organic liquids or in solution in inorganic acids. The best results for 2- and 3-fluoropyridine were obtained by diazotising the bases in aqueous fluorosilicic acid and decomposing the diazonium salts *in situ*. The amount of 2-fluoropyridine obtained was appreciably greater than that from the Schiemann method (Roe and Hawkins, *J. Amer. Chem. Soc.*, 1947, **69**, 2443) but when the same procedure was applied to 3-aminopyridine the reverse was the case. Trial experiments with both 2- and 3-aminopyridine, in which the process was carried out in three separate stages, indicated that the reduction in yield occurred in the conversion of the diazonium fluorosilicate into fluoro-compound. We presume that the failure of Roe *et al.* to prepare pyridine-2-diazonium fluorosilicate was due to inadequate control of the temperature of reaction or to small amounts of water in the glacial acetic acid. Its conversion, and that of pyridine-3-diazonium fluorosilicate, into fluoro-compound was best carried out in anhydrous hydrogen fluoride. Preparation of 2-fluoroquinoline and 2-fluoro-4-methylthiazole by the same method gave smaller yields than by the Schiemann reaction.

It seems probable that, except in special cases, the decomposition of the diazonium fluorosilicates is not such a good method for preparing heterocyclic fluorides as is the Schiemann method. This may be due to the fact that in the diazonium fluorosilicate there are two diazonium groups in the molecule whereas in the diazonium fluoroborates there is only one, and, if we postulate either a free-radical mechanism or an intramolecular rearrangement for the decomposition of $(RN_2)_2SiF_6$, then the two groups R may be in closer proximity than during the decomposition of RN_2BF_4. We might therefore expect more side reactions, such a polymerisation, to occur. In only one case during this series of reactions was any polymeric material (dipyridyl) identified, but the residues were not examined in detail : there may have been more highly polymerised material present.

In view of the experiments of Ferm and Van der Werf (*loc. cit.*), who state that results as good as, and in some cases better than, those obtained in the Schiemann reaction can be obtained by diazotisation of an amine in anhydrous hydrogen fluoride followed by decomposition *in situ*, the preparations of 2-fluoropyridine and 2-fluoroquinoline were carried out as they describe. In these two cases, as in that of the one heterocyclic amine which they mention, it was shown that their conclusions do not apply. For 2-aminoquinoline the amount of fluoro-compound obtained was the same as by the decomposition of the diazonium fluorosilicate in anhydrous acid but less than that obtained by the Schiemann reaction (Roe and Hawkins, *J. Amer. Chem. Soc.*, 1949, **71**, 1785), but from 2-aminopyridine the yield was considerably less than by the Schiemann reaction (*idem, ibid.*, 1947, **69**, 2443) or from the diazonium fluorosilicate.

EXPERIMENTAL

Preparation and Decomposition of Pyridine-2-diazonium Fluorosilicate Aqueous Fluorosilicic Acid.—2-Aminopyridine (10 g.) was dissolved in 30% aqueous fluorosilicic acid (35 c.c.) and cooled to 5° in ice and salt. The mixture was carefully diazotised by addition of sodium nitrite (7·4 g.) during 1½ hours, the temperature being kept below 5°, and then kept in the cold bath for 1 hour. To complete the decomposition of the diazonium fluorosilicate the reaction mixture was heated at 40—50° for 1 hour (until evolution of nitrogen ceased.) Finally, the solution was called to 0°, exactly neutralised with sodium carbonate, and extracted with ether (4 times). The ethereal solution was dried ($MgSO_4$), and the ether removed at atmospheric pressure through a short fractionating column. The residue was found on distillation to be 2-fluoropyridine (4·2 g., 42%), b. p. 124·5° (Found : F, 19·5. Calc. for C_5H_4NF; F, 19·6%). Experiments in which (*a*) more fluorosilicic acid was used, (*b*) the product was isolated by steam-distillation (Roe and Hawkins, *loc. cit.*), (*c*) diazotisation was effected by means of ethyl nitrite all gave yields of 40%. The use of nitrosylsulphuric acid as diazotising agent gave a much smaller yield (10%).

Preparation and Decomposition of Pyridine-3-diazonium Fluorosilicate in Aqueous Fluorosilicic Acid.—3-Aminopyridine (3·0 g.) was dissolved in 30% fluorosilicic acid (30 c.c.) and the solution cooled to about 0°. It was diazotised by passage of a slow stream of ethyl nitrite for 1½ hours, and, after 1 hour at 0°, it was warmed slowly to 25° until all ethyl nitrite was removed. Exact neutralisation was effected by adding ice-cold aqueous sodium hydroxide, the solution was steam-distilled, and the distillate treated with solid sodium hydroxide until a brown oil separated. This was extracted with ether and dried ($MgSO_4$). The ethereal solution was then saturated with dry hydrogen chloride, and the ether distilled while a slow stream of hydrogen chloride was passed into the solution in the distilling flask. This prevented the 3-fluoropyridine from distilling in the ether as an azeotrope (Roe and Hawkins, *loc. cit.*, 1947). After complete removal of the ether the residue in the flask weighed 1·9 g. To this was added the calculated quantity (1·05 c.c.) of diethylamine, and the 3-fluoropyridine liberated was distilled first under reduced pressure and then under atmospheric pressure (1·1 g., 36%), b. p. 105—106° (Found : F, 19·4. Calc. for C_5H_4NF : F, 19·6%).

Fluorosilicates of 2- and 3-aminopyridine, 2-aminoquinoline, and 2-amino-4-methylthiazole were prepared by Wiley's procedure, silicon tetrafluoride being used. Titration of aqueous solutions with 0·1N-sodium hydroxide showed that they had the general formula $(RNH_2)_2,H_2SiF_6$.

Diazonium Fluorosilicates.—2-Aminopyridine fluorosilicate (10 g.) was suspended in glacial acetic acid (100 c.c.) which had been made truly anhydrous by addition of the calculated quantity of acetic anhydride. (This precaution was particularly important, otherwise hydrolysis occurred.) A slow stream of ethyl nitrite was passed in for 4 hours and the mixture was stirred at < 20° (cold running water). Ether (100 c.c.) was then added and the solid was filtered off, washed with cold absolute alcohol and then ether (sodium-dried), and dried under a vacuum (9 g.). The purity was determined by the method of Schiemann and Pillarsky (*Ber.*, 1929, **62**, 3035). It was necessary to pass in ethyl nitrite for about 8 hours to obtain pure (at least 93%) pyridine-2-diazonium fluorosilicate. The other diazonium salts were obtained, at least 90% pure, by passage of ethyl nitrite for 1½—2 hours.

2-*Fluoropyridine.*—(*a*) Anhydrous hydrogen fluoride (40—50 g.) was distilled into a copper vessel containing the diazonium fluorosilicate (10 g.) and the resulting solution was poured into an autoclave. The temperature was raised to 80—85° during an hour and kept at this value for a further hour, and then the vessel was cooled to 0°. The product was transferred to a copper distillation apparatus, the excess of hydrogen fluoride removed, and the residue treated with an excess (20 c.c.) of diethylamine. After transference to glass apparatus, the excess of diethylamine and volatile products were distilled under reduced pressure. Fractionation gave 2-fluoropyridine (2·1 g., 38%), b. p. 124—126°. Extraction with ether, after treatment with diethylamine, followed by distillation led to lower yields (30%). The use of larger amounts of anhydrous hydrogen fluoride did not affect the amount of product.

(*b*) The diazonium fluorosilicate (2·5 g.) in dry trichloroethylene (25 c.c.) was refluxed until nitrogen evolution ceased and then for a further 20 minutes (about 2 hours in all). The solvent was then distilled at atmospheric pressure and shown, by sodium fusion, not to contain fluorine. Distillation of the semi-solid residue gave 2-fluoropyridine (0·1 g., 7%) and left a solid (0·2 g.) which gave a red colour with an acid solution of ferrous sulphate, and a picrate, m. p. 155—156°, and must have consisted mainly of 2 : 2′-dipyridyl. Repetition of the process in light petroleum (b. p. 60—80°) gave no 2-fluoropyridine and left a solid residue which was not examined.

After the reaction had been carried out in dioxan, the solution was saturated with hydrogen chloride while the dioxan was distilled. The residue was treated with diethylamine to decompose the hydrochloride and then fractionated first under reduced pressure and then under atmospheric pressure, to give 2-fluoropyridine in 12% yield.

(*c*) When the solutions of the diazonium fluorosilicate in either 30% aqueous fluorosilicic acid or 40% aqueous hydrofluoric acid were warmed, good yields (75%) of 2-pyridone, m. p. 105°, were obtained. It gave a 3 : 5-dibromide, m. p. 205°.

(*d*) The preparation and decomposition of the diazonium fluoride were effected, by means of anhydrous hydrogen fluoride (50 g.) and 2-aminopyridine (5 g.), as described by Ferm and Van der Werf (*loc. cit.*). After the reaction mixture had been cooled in ice, the excess of acid was neutralised with sodium carbonate, and the neutral solution extracted with ether (4 × 30 c.c.). Fractionation of the dried ($MgSO_4$) extract gave 2-fluoropyridine (1 g., 20%), b. p. 125°.

3-*Fluoropyridine.*—Decomposition in anhydrous hydrogen fluoride, the reaction being carried out as for 2-fluoropyridine except that the product was isolated by steam-distillation (Roe and Hawkins, *loc. cit.*), gave 3-fluoropyridine (13%), b. p. 107—108°. Decomposition in dioxan gave 3-fluoropyridine (7%), b. p. 107°.

Decomposition of pyridine-3-diazonium fluorosilicate in aqueous fluorosilicic acid gave 3-pyridone in good yield (60%). It gave an acetate, b. p. 210°.

2-*Fluoroquinoline*.—(*a*) A solution of quinoline-2-diazonium fluorosilicate (10 g.) in anhydrous hydrogen fluoride (*ca.* 150 g.) was heated in the autoclave for 1½ hours at 80° and, after cooling, the excess of hydrogen fluoride was distilled as previously described. The residue was cooled to 0° and treated with an excess of diethylamine (20 c.c.), and the resultant suspension extracted with ether (3 × 20 c.c.). The ethereal extract was filtered, dried ($MgSO_4$), and fractionated; 2-fluoroquinoline (1·5 g., 21%), b. p. 130°/30 mm., was obtained (Found: F, 12·7. Calc. for C_9H_6NF: F, 12·9%).

(*b*) Quinoline-2-diazonium fluoride was prepared according to the method of Ferm and Van der Werf, from anhydrous hydrogen fluoride (20 g.), 2-aminoquinoline (4 g.), and sodium nitrite (1·8 g.). The solution was heated to 60° to decompose the diazonium salt and, after neutralisation with sodium carbonate, the product was steam-distilled. The distillate was treated with sodium hydroxide, and the oil which separated was isolated and dried ($MgSO_4$). Distillation gave 2-fluoroquinoline (0·66 g., 17%), b. p. 132°/30 mm.

Preparation of 2-*Fluoro*-4-*methylthiazole*.—(i) *By the Schiemann method.* 2-Amino-4-methylthiazole (10 g.) was dissolved in 40% aqueous fluoroboric acid (40 c.c.), and the clear solution cooled to 0° in an ice-salt bath. Diazotisation was effected by slow addition of sodium nitrite (7·0 g.) and the mixture was then kept at 0° for 1 hour. After being heated to 70° for a further hour it was filtered, cooled, and extracted with ether (4 × 30 c.c.). The ethereal extract was dried ($MgSO_4$), and the ether distilled, leaving 2-*fluoro*-4-*methylthiazole* (0·98 g.) as an orange-red crystalline solid which was soluble in benzene, light petroleum, chloroform, acetone, and alcohol. It recrystallised from water as pale yellow crystals (0·5 g., 5%), m. p. 70° (Found: F, 16·0. C_4H_4NSF requires F, 16·2%). If the reaction mixture was neutralised before being extracted with ether, the yield of product was reduced to one-third.

(ii) *From the diazonium fluorosilicate.* The diazonium salt (10 g.) was dissolved in anhydrous hydrogen fluoride (50 c.c.) and decomposed by heating it in an autoclave at 80° for 1 hour. The excess of hydrogen fluoride was then distilled off and the residue treated with an excess of diethylamine (30 c.c.) in ether (50 c.c.). The mixture was transferred to a beaker, and the ether was decanted from the crystals of diethylamine hydrofluoride. These were washed with ether (20 c.c.) three more times by decantation, and the extracts were combined and filtered. After drying ($MgSO_4$), the ether was distilled, and the residue extracted with hot water (50 c.c.). Concentration of the extract gave, on cooling, orange-red crystals of 2-fluoro-4-methylthiazole (150 mg.), m. p. 69°. Recrystallisation from water gave a pale yellow product, m. p. 70° (Found: F, 16·2%).

We are grateful to the Imperial Smelting Corporation Ltd. for supplies of anhydrous hydrogen fluoride, and one of us (R. D. B.) thanks the Department of Scientific and Industrial Research for a maintenance grant.

THE UNIVERSITY, SOUTH ROAD, DURHAM. [*Received, September* 25*th*, 1951.]