

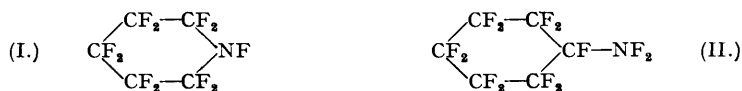
402. The Fluorination of Organic Compounds Containing Nitrogen.

By R. N. HASZELDINE.

The fluorination of pyridine and aniline by the cobalt fluoride and catalytic methods yields the non-basic perfluoropiperidine and perfluorocyclohexylamine, respectively. The fluorination of dimethylaniline gives perfluorocyclohexane, perfluorodimethylamine, and possibly perfluorodimethylcyclohexylamine. Methylaniline similarly yields perfluorocyclohexane and perfluoromethylamine; the latter compound, which is non-basic, is also obtained by the passage of methylamine over cobalt trifluoride.

THE fluorination of hydrocarbons has been achieved by several methods, notably those involving fluorine itself in the presence of a "catalyst" (Bigelow, *Chem. Reviews*, 1947, **40**, 51; Haszeldine and Smith, *J.*, in press; Grosse and Cady, *Ind. Eng. Chem.*, 1947, **39**, 290), the use of cobalt trifluoride (Fowler *et al.*, *Ind. Eng. Chem.*, 1947, **39**, 292; Haszeldine and Smith, forthcoming communication), and more recently the electrolysis of compounds dissolved in anhydrous hydrogen fluoride (Simons, *J. Electrochem. Soc.*, 1949, **95**, 47; and Abstracts, 116th Meeting, American Chemical Society, Sept. 1949). The unusual properties associated with the products are well-established (Smith, *Ann. Reports*, 1947, **44**, 86). Apart from a recent note (Haszeldine, *J.*, 1950, 1638), the successful direct fluorination of heterocyclic nitrogen compounds or of aromatic amines has not been described. Simons (*loc. cit.*), for example, has reported that the electrolysis of pyridine in anhydrous hydrogen fluoride yields perfluoropentane and nitrogen trifluoride.

The fluorination of pyridine, aniline, and dimethylaniline, and preliminary results with methylaniline and methylamine, are described in the present communication. Both the cobalt fluoride and the catalytic methods of fluorination were used successfully, although the yields of the corresponding perfluoro-compounds were extremely low. Pyridine was converted into perfluoropiperidine (I), and aniline yielded perfluorocyclohexylamine (II).



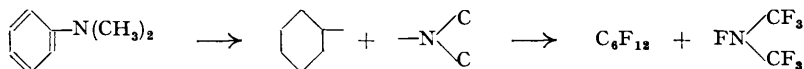
The vapour-phase fluorination of basic compounds is difficult, probably because of the formation of a non-volatile hydrofluoride when the entering gas stream encounters hydrogen fluoride produced during the fluorination. This can be overcome to some extent by carrying the organic compound to be fluorinated in a stream of nitrogen, which also sweeps out the hydrogen fluoride formed. The basicity and tendency for hydrofluoride formation to occur is steadily reduced, whilst the volatility is increased as fluorine is introduced into the molecule,

and it is the initial reaction which is important in determining the yield. The fluorination of heterocyclic compounds or of aromatic amines which already contain fluorine should give yields much superior to those recorded here. The bisfluoromethylpyridines (McBee, Hass, and Hodnett, *Ind. Eng. Chem.*, 1947, **39**, 389), tristrifluoromethyltriazine (McBee, Pierce, and Bolt, *Ind. Eng. Chem.*, 1947, **39**, 391) and 2-fluoropyridine (Hawkins and Roe, *J. Org. Chem.*, 1949, **14**, 328) are examples of such non-basic compounds.

The elimination of the nitrogen atom in pyridine during fluorination was shown by the isolation of the straight-chain fluorocarbon, C_5F_{12} . Other compounds, in which carbon-carbon bond fission instead of carbon-nitrogen bond fission had occurred, were also present in the reaction products but were not separated. Perfluoropiperidine is non-basic, and preliminary examination suggests that it has a stability similar to that of the fluorocarbons. Whether there is any specific reactivity associated with the N-F bond has yet to be determined; Ruff and Giese (*Ber.*, 1936, *B*, **69**, 598), for example, postulated that mercury attacks the N-F link in compounds such as $CF_2 \cdot NF \cdot NF \cdot CF_2$. Relative to pyridine or piperidine, perfluoropiperidine has a low boiling point and refractive index, and a high density. These values—b. p. 49–50°, n_D^{25} 1.279, d_4^{25} 1.738—are similar to those of comparable fluorocarbons (C_6F_{12} , a solid, sublimates at 52°; C_7F_{14} , b. p. 76.2°, n_D^{25} 1.276, d_4^{25} 1.784).

The fluorination of aniline yielded perfluorocyclohexane as well as the non-basic perfluorocyclohexylamine, and showed that appreciable carbon-nitrogen bond fission with subsequent complete fluorination of the ring had occurred. Perfluorocyclohexylamine has a boiling point close to that of perfluoromethylcyclohexane, and the density and refractive index are only slightly higher. Thus, the replacement of carbon by nitrogen to produce a compound with one less fluorine atom scarcely alters these physical properties.

The fission of the carbon-nitrogen bond during the fluorination of aniline produced perfluorocyclohexane and presumably nitrogen trifluoride, although the latter compound was not identified. When dimethylaniline was fluorinated, however, both products from the carbon-nitrogen bond fission (perfluorocyclohexane and perfluorodimethylamine) were identified:



Perfluorodimethylamine has been prepared recently in these laboratories (Emeléus and Thompson, *J.*, 1949, 3080) by the fluorination of trimethylamine. Perfluorodimethylcyclohexylamine was not definitely identified. The fluorination of methylaniline followed a similar course, and perfluorocyclohexane and perfluoromethylamine were isolated. The latter compound, which is also obtained by the direct fluorination of methylamine, was claimed by Ruff and Giese (*loc. cit.*) as one of the products from the fluorination of silver cyanide, but these authors were unable to effect its separation from hexafluoroethane. Perfluoromethylamine and perfluorodimethylamine are both non-basic compounds which are stable to dilute aqueous alkali. These and the compounds described earlier contain electronegative fluorine atoms and trifluoromethyl groups attached to a nitrogen atom, and should not strictly be termed amines; they are more related to the inert nitrogen trifluoride. It should eventually be possible to synthesise complete series of compounds [*e.g.*, $\text{NH}(\text{CH}_3)_2$, $\text{NH}(\text{CF}_3)(\text{CH}_3)$, $\text{NH}(\text{CF}_3)_2$, $\text{NF}(\text{CF}_3)_2$] of steadily decreasing basicity and reactivity.

EXPERIMENTAL.

The Cobalt Fluoride Apparatus.—The compound to be fluorinated was added as a liquid or passed as a gas into a steel preheater, 12" long and of 2" internal diameter, heated electrically to 200° or 250° depending upon the boiling point of the compound. A stream of dry nitrogen was admitted through a second inlet tube, and the organic vapour was thereby carried into a second furnace, 48" long and of 2" internal diameter, containing cobalt trifluoride. The cobalt trifluoride was prepared *in situ* by the passage of fluorine over trays of cobalt difluoride (2500 g.) heated to 350° until a strong positive test for fluorine was obtained at the exit. At the end of an experiment, the cobalt trifluoride was regenerated. Since profound decomposition occurred during most of the experiments described here, and since complete fluorination was desired, considerably less of the organic compound was added than that which could theoretically be caused to react with the available fluorine (500 g.). At the end of the experiment, and half way through those experiments in which comparatively large amounts of material were fluorinated, addition of the organic compound was stopped, the temperature of the vessel was raised to 450°, and the apparatus was shaken vigorously by two vibro-shakers whilst nitrogen was swept through the apparatus for two hours to remove and fluorinate any hydrofluorides formed during the reaction. Appreciable quantities of product were thereby obtained. The temperature was then re-adjusted, and the experiment continued. The reaction temperatures and conditions quoted below are not necessarily the best, and variation in the conditions would probably lead to improved yields.

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The Catalytic Fluorination Apparatus.—A vertical steel tube, 24" long and of 2" internal diameter, was filled with gold-plated copper turnings, and heated electrically. The vapour of the organic compound, diluted by nitrogen, and fluorine, also diluted by nitrogen, were passed into the vessel through diametrically-opposed tubes situated 2" from its top. The exit gases from the reactor base were collected in a series of cooled traps. The apparatus was similar in design to that described by Hazeldine and Smith (*loc. cit.*); see also Cady and Grosse (*loc. cit.*).

Fluorination of Pyridine by Means of Cobalt Trifluoride.—Pyridine (50 g.) was passed at a rate of 10 ml./hour over cobalt trifluoride heated to 350°; the nitrogen dilution was 10 l./hour. The product collected in the traps was allowed to warm slowly to room temperature and, by being heated on a boiling-water bath in a stream of nitrogen, the material of b. p. <100° was passed through a copper tube, 24" long, packed with sodium fluoride pellets and heated electrically at 100°. The products from six such experiments (47.3 g.), now free from hydrogen fluoride, were distilled from sodium fluoride and phosphoric oxide through an efficient fractionating column. Apart from an unidentified, nitrogen-containing fraction, b. p. 75–77° (0.8 g.), the only plateau on the distillation curve of the material boiling below 100° was that due to *perfluoropiperidine* (2.1 g., 0.2%) (Found: C, 20.6; N, 4.1; F, 73.2%; *M*, 283. C_5NF_{11} requires C, 21.2; N, 5.0; F, 73.8%; *M*, 283). Perfluoropiperidine, b. p. 49–50°, n_D^{25} 1.279, d_4^{25} 1.738, has a characteristic musty smell.

Fluorination of Pyridine by the Catalytic Method.—Pyridine (4 g./hour), diluted with nitrogen (8 l./hour), was passed into the reaction vessel, heated to 280°. Fluorine (10 g./hour), diluted with nitrogen (8 l./hour), was admitted simultaneously. After a total operating time of 24 hours, 101 g. of pyridine had been added. The product boiling below 100° was passed over sodium fluoride as described above, and taken into a vacuum system for examination. Repeated fractionation afforded perfluoropiperidine (0.9 g., 0.3%), n_D^{25} 1.278 (Found: *M*, 282), and a fraction (1.3 g.) corresponding to perfluoropentane, b. p. 29° (Found: *M*, 290. Calc. for C_5F_{12} : *M*, 288). Simons (*loc. cit.*) reports b. p. 27–28°.

Fluorination of Aniline by Means of Cobalt Trifluoride.—Aniline (40 g.) was added to the reaction vessel, heated to 300°, at a rate of 6 ml./hour and nitrogen (10 l./hour) was passed in simultaneously. The products (53.4 g.) from five such experiments were combined and passed, in a slow stream of nitrogen, through a tube of sodium fluoride pellets heated to 120°. The condensed liquid was distilled through an efficient column, and two fractions were identified. (a) A compound solidified in the condenser (thermometer temperature 50–52°). It was taken into the vacuum system, fractionated further, and found to be perfluorocyclohexane (2.2 g., 0.3%), subliming at 50–52° (Found: *M*, 298. Calc. for C_6F_{12} : *M*, 300). In view of the well-known difficulty of purifying this compound the yield was undoubtedly much higher than indicated here. (b) *Perfluorocyclohexylamine* (1.7 g., 0.2%), b. p. 75–76°, n_D^{25} 1.286, d_4^{25} 1.787 (Found: C, 21.7; N, 3.9; F, 73.5%; *M*, 332. C_6NF_{13} requires C, 21.6; N, 4.2; F, 74.2%; *M*, 333).

Fluorination of Aniline by the Catalytic Method.—Aniline (2 g./hour), diluted with nitrogen (6 l./hour), was allowed to react with fluorine (10 g./hour), diluted with nitrogen (6 l./hour), on the surface of the catalyst heated to 290°. When 100 g. of aniline had been passed, the total product was treated with sodium fluoride, as described earlier, and distilled. Perfluorocyclohexane (1.7 g.; *M*, 297) and perfluorocyclohexylamine (0.7 g.; *M*, 330) were again isolated. No attempt was made to investigate the material which boiled below room temperature.

Fluorination of Dimethylaniline by Means of Cobalt Trifluoride.—Dimethylaniline (50 g.) was added to the reaction vessel heated to 300° over a period of 12 hours. A nitrogen flow of 10 l./hour was used. The products from two such experiments, freed from hydrogen fluoride as described above, were separated into two portions: (a) The material boiling below 80°, which constituted the bulk of the product, and was taken into the vacuum system for examination. Exhaustive fractionation yielded perfluorocyclohexane (1.1 g.), identified as described earlier, and perfluorodimethylamine, b. p. –38° (Found: F, 77.0%; *M*, 170. Calc. for C_2NF_7 : F, 77.8%; *M*, 171). Emelús and Thompson (*loc. cit.*) report b. p. –37.0°. The yield of pure compound was 1.3 g., but an appreciable quantity was lost by the fractionation procedure. Perfluorodimethylamine, which has a musty odour, was not absorbed by 5*N*-hydrochloric acid or hydrolysed by 5*N*-alkali at room temperature. (b) The material, b. p. >80°, was distilled. A fraction (1.05 g.), b. p. 116–120°, n_D^{25} 1.305, was possibly perfluorodimethylcyclohexylamine (Found: N, 3.0%; *M*, 428. C_6NF_{17} requires N, 3.2%; *M*, 433). Insufficient material was available for full identification.

Fluorination of Methylaniline.—The fluorination of methylaniline (50 g.), as described for dimethylaniline, gave *perfluoromethylamine*, b. p. –75°, amongst the volatile products (Found: N, 11.4; F, 77.6%; *M*, 120. CNF_5 requires N, 11.6; F, 78.4%; *M*, 121). Ruff and Giese (*loc. cit.*) report b. p. –80° for a fraction believed to contain CF_3NF_2 and C_2F_6 . A fraction which might correspond to perfluoromethylcyclohexylamine could not be isolated from the small amount of material, b. p. >80°, available for examination. Perfluorocyclohexane was again detected.

The Fluorination of Methylamine.—Methylamine (20 g.) passed over cobalt trifluoride at 190° gave a product which contained perfluoromethylamine, b. p. –75°; *M*, 120. This compound is not decomposed by 5% sodium hydroxide or absorbed by 5*N*-hydrochloric acid; it has a characteristic musty odour.

The author is indebted to Professor M. Stacey and Dr. F. Smith in whose laboratory he first attempted the fluorination of pyridine.