FLUOROCARBON CHEMISTRY. PART I.
THE FLUORINATION OF ORGANIC COMPOUNDS

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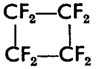
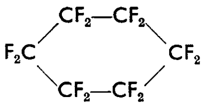
IT is now obvious that the carbon–fluorine system forms the basis of a new branch of organic chemistry, paralleling the vast and better known field arising from carbon and hydrogen.

The carbon–fluorine bond is a very stable one; fluorine is univalent, and it has a fairly small atomic size which enables it to take the place of hydrogen in organic chemistry. The bond of carbon with chlorine is rather less stable, and the atomic size of chlorine is appreciably greater than that of fluorine, so that chlorocarbon chemistry is not as comprehensive as fluorocarbon chemistry and in the latter, but not the former, almost complete duplication of the major sections of hydrocarbon chemistry is possible. Nearly all the most important organic functional groups can be linked to fluorocarbon chains or rings, giving rise to stable series of fluorocarbon derivatives. The range of compounds capable of existence is thus enormous, particularly since mixed fluorohydrocarbon species, and their derivatives, are usually stable, and can give rise to vast numbers of isomers.

The size of the fluorine atom (van der Waals radius 1·35 Å; cf. hydrogen 1·2 Å, chlorine 1·8 Å) is such that saturated fluorocarbon chains or rings, *e.g.*,

$CF_3{\cdot}[CF_2]_n{\cdot}CF_3$





can exist with little steric strain. This would not be so if the atomic size were much greater (there would then be insufficient room for all the necessary fluorine atoms on the carbon skeleton without some interactions occurring between them). The greater atomic size means, however, that a fluorocarbon chain is stiffer than a hydrocarbon chain, and further, that the fluorine atoms shield the backbone of carbon atoms against chemical attack much more effectively than hydrogen atoms are able to do. Great chemical stability is one of the chief characteristics of saturated fluorocarbons and many of their derivatives and it is due, not only to the intrinsic stability of the carbon–fluorine bond, but also to the difficulty of approach of chemical reagents to the carbon atoms.

This Review and a later one will summarise the main features of fluorocarbon chemistry, treating the fluorocarbons and their simple derivatives in the same manner as that in which orthodox organic chemistry is dealt with in general text-books. At present, organic fluorine compounds are nearly always made from related hydrocarbon-type materials, and in the present article the methods available for the introduction of fluorine into organic structures are described systematically.

Methods for the Introduction of Fluorine into Organic Structures

Only two organic fluoro-compounds have so far been found[1,2] occurring naturally (potassium monofluoroacetate in the South African plant gifblaar, and fluoro-oleic acid in ratsbane from West Africa). Perfluoropropane and higher members of the series of saturated fluorocarbons were first recognised[3] after synthesis from carbon and elementary fluorine. Similar reactions of carbon with halogen fluorides or with mixtures of fluorine and another halogen gave[4,5] perfluorohalogenocarbons or, under certain drastic conditions,[6] tetrafluoroethylene (in this Review halogen means chlorine, bromine, or iodine). However, these reactions have not so far been used widely; and most organic fluorides are made by the introduction of fluorine into hydrocarbon or halogeno-hydrocarbon precursors of similar carbon skeletons. One of the reasons for the comparatively late development of fluorocarbon chemistry has been undoubtedly the relative difficulty of fluorination. Even now this is often troublesome to carry out, and routes to desired compounds are usually sought *via* conversions of commercially available precursors containing fluorine. Though more stages may be involved, such an overall process is often preferable to one involving introduction of fluorine.

The methods available for forming a carbon–fluorine bond may be divided into two broad types. In Section A, fluorine is introduced only at functional groups in the organic molecule, by exchange or addition, hydrogen normally being unattacked. The fluorinating agent used is hydrogen fluoride, or an inorganic fluoride in which in general the other constituent, if multivalent, exerts a lower valency and can be made without the use of elementary fluorine. Section B consists of processes for exhaustive fluorination of organic compounds, in which all substituents on a carbon chain, functional groups and hydrogen, can be replaced by fluorine and unsaturation can be removed. Though a saturated fluorocarbon is the ultimate end-product of such a reaction, it is usually possible to arrange either for a functional group or for some hydrogen to be retained. The fluorinating agents are either elementary fluorine or some related species, for example a halogen fluoride or a high-valency fluoride of a transition metal, which can be made conveniently only with elementary fluorine.

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[1] Marais, *Onderstepoort J. Vet. Sci. An.*, 1943, **18**, 203; 1944, **20**, 67.

[2] Peters, *Biochem. J.*, 1960, **76**, 32 P.

[3] Simons and Block, *J. Amer. Chem. Soc.*, 1937, **59**, 1407; 1939, **61**, 2962.

[4] Collins, Wadsworth, and Leech, B.P. 653,879/1951.

[5] Mantell, Passino, and Teeters, U.S.P. 2,670,389/1954, 2,684,987/1954, 2,774,797/1956.

[6] Farlow and Muetterties, U.S.P. 2,732,410/1956.

Another, closely related, method is electrochemical fluorination, *i.e.*, electrolysis of anhydrous hydrogen fluoride containing the organic starting material; it resembles the process used for the generation of fluorine.

This classification, though useful, is not completely rigid, partly because reactions are not always carried out under comparable conditions. Thus, for example, under mild conditions a high-valency fluoride might give an exchange reaction typical of Section A. In fact, one or two high-valency fluorides are useful exchange reagents of type A.

SECTION A

This section can be further sub-divided into five main types of process: (i) exchange of fluorine for another halogen atom; (ii) exchange of fluorine for some other univalent functional group, usually hydroxyl or a sulphonated hydroxyl group; (iii) exchange of fluorine for oxygen in carbonyl or carboxyl groups; (iv) additions to unsaturated linkages; (v) exchange of fluorine for diazonium groups in aromatic and heterocyclic compounds.

A(i) Exchange of Fluorine for Other Halogen Atoms.—This was one of the earliest fluorination methods, alkyl fluorides being made[7] from silver monofluoride and alkyl iodides in the 1880's. It was exploited extensively by Swarts, who used antimony trifluoride to make a variety of aliphatic fluorides in his pioneer researches in the field.[8] It was developed further by Henne[9] and put into commercial operation[10] for the production of refrigerants, with hydrogen fluoride as the source of fluorine. Quite large quantities of organic fluorides are now made,[11] mostly still by this general method. Many fluorinating agents have been used but the most important are hydrogen fluoride, antimony trifluoride and related systems, potassium fluoride, silver monofluoride, mercurous and mercuric fluoride, and antimony pentafluoride. Silver, mercurous, and potassium fluoride exchange isolated halogen atoms for fluorine, hydrogen fluoride and antimony trifluoride systems both exchange halogen in polyhalogenated groups but not usually in monohalogenated groups, whilst mercuric fluoride and antimony pentafluoride are the most reactive exchange agents and often effect both reactions. Brief accounts have appeared[12,13] of the fluorinating activities of various inorganic fluorides.

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[7] Moissan, *Compt. rend.*, 1888, **107**, 260; Moissan and Meslans, *Compt. rend.*, 1888, **107**, 1155; Meslans, *Compt. rend.*, 1889, **108**, 352.

[8] Swarts, *Bull. Soc. chim. belges*, 1930, **39**, 444.

[9] Henne, "Organic Reactions," 1944, Vol. II, John Wiley, New York, p. 49.

[10] Midgley, Henne, and McNary, U.S.P. 1,930,129/1933; Daudt and Youker, U.S.P. 2,005,705—11/1935; Holt and Mattison, U.S.P. 2,005,712, 2,005,713/1935.

[11] *Chem. Eng. News*, July 18th 1960, p. 92.

[12] Lovelace, Rausch, and Postelnek, "Aliphatic Fluorine Compounds," Reinhold Publ. Corp., New York, 1958, p. 1.

[13] Park, in "Fluorine Chemistry," ed. Simons, Academic Press, New York, Vol. I, 1950, p. 523.

Silver monofluoride. This converts alkyl monohalogeno-compounds into fluorides, having been employed by Moissan and Meslans[7] to make the lower alkyl fluorides from the iodides: $C_nH_{2n+1}\cdot X + 2AgF \rightarrow C_nH_{2n+1}\cdot F + AgF, AgX$. Since an organic fluoride boils lower than analogous halides, the technique is straight-forward, the product being distilled from a mixture of the organic halide and an excess of silver fluoride. The reaction, modified where necessary, has been used in the synthesis of ω-fluorocarboxylic acid derivatives[14] (*e.g.*, $Br\cdot[CH_2]_{11}\cdot CO_2Et \rightarrow F\cdot[CH_2]_{11}\cdot CO_2Et$) and of fluoro-steroids.[15] Though this salt has been applied mostly to monohalogeno-compounds there are a few reports of its effecting conversions involving polyhalogeno-groups, *e.g.*,[16] $CF_3\cdot CO\cdot CBr_3 \rightarrow CF_3\cdot CO\cdot CBr_2F \rightarrow CF_3\cdot CO\cdot CBrF_2$. Silver fluoride is rather difficult to prepare, and it forms troublesome complexes with the silver halide produced during the exchange;[9,13] these also reduce the amount of fluorine available for reaction. For many purposes potassium fluoride is superior, but silver fluoride still finds uses, as in the recent synthesis[17] of 2,4,6-trifluoropyrimidine by refluxing the chloro-analogue with the reagent.

Mercurous fluoride. This is similar in reactivity to silver fluoride but is claimed to be better.[18] It gives alkyl fluorides fairly readily.

Potassium fluoride. This easily available and convenient reagent has found extensive use. Reactive halogen atoms in aliphatic compounds are exchanged readily, as, for example, in the preparation of acyl fluorides[19] and of derivatives of α-fluoro-carboxylic acids[20,21] from analogous chlorides. A mixture of the reactants is heated to about 200° and agitated, often in an autoclave. Alkyl fluorides and esters of fluoro-alcohols can be made[21] with potassium fluoride, best in a solvent, either ethylene glycol[22] or acetamide,[23] at 150—200°. Use of a solvent avoids trouble due to coating of the potassium fluoride with potassium chloride and allows otherwise difficult exchanges in the groups $-CH_2X$ and $>CHX$ to be effected in ordinary glass equipment. Further, a small amount of moisture in one of the re-

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[14] Buckle, Pattison, and Saunders, *J.*, 1949, 1471; Pattison and Saunders, *J.*, 1949, 2745.

[15] Tannhauser, Pratt, and Jensen, *J. Amer. Chem. Soc.*, 1956, **78**, 2658.

[16] Shepard and Loiselle, *J. Org. Chem.*, 1958, **23**, 2012.

[17] Schroeder, *J. Amer. Chem. Soc.*, 1960, **82**, 4115.

[18] Swarts, *Bull. Soc. chim. belges*, 1924, **35**, 1533; Henne and Renoll, *J. Amer. Chem. Soc.*, 1938, **60**, 1060.

[19] Nesmeyanov and Kahn, *Ber.*, 1934, **67**, 370.

[20] Saunders and Stacey, *J.*, 1948, 1773.

[21] Gryszkiewicz-Trochimowski, Sporzynski, and Wnuk, *Rec. Trav. chim.*, 1947, **66**, 413; Gryszkiewicz-Trochimowski, *ibid.*, p. 427.

[22] Hoffmann, *J. Amer. Chem. Soc.*, 1948, **70**, 2596; *J. Org. Chem.*, 1949, **14**, 105; 1950, **15**, 425.

[23] Bergmann and Blank, *J.*, 1953, 3786.

actants can apparently lead to dangerous pressure increases in a closed system. If the reaction mixture is irradiated with ultraviolet light, mild conditions suffice for the exchange;[24] irradiation under more drastic conditions effects exchange with chloroform and carbon tetrachloride.[25]

Toluenesulphonyloxy and similar groups can be exchanged with potassium fluoride (see p. 52). Fluoroformates (*e.g.*, $F{\cdot}CO_2Et$) can be made[26] from chloroformates (*e.g.*, $Cl{\cdot}CO_2Et$) and, on treatment with pyridine or boron trifluoride, give alkyl fluorides (*e.g.*, EtF).

In some cases aryl fluorides can be made from aryl chlorides and potassium fluoride. This conversion was originally thought to be confined to compounds with a very reactive halogen, *e.g.*, 1-chloro-2,4-dinitrobenzene, but other examples are now known.[27,28] One interesting case[29] is the conversion of tetrachloro- into tetrafluoro-*p*-benzoquinone.

The successful exchange of the halogen in less activated halides with potassium fluoride has been achieved by the use of non-aqueous solvents such as dimethylformamide and dimethyl sulphoxide. An explanation of this effect has been based[30] on the lower degree of solvation of the fluoride ion in dipolar aprotic solvents.

A study[28] of the relative efficiencies of the alkali-metal fluorides in this type of fluorination has revealed a much greater ease of exchange with cæsium fluoride ($CsF>RbF>KF>NaF>LiF$). Thus, whereas 1-chloro-2,4-dinitrobenzene did not react with lithium fluoride at 200°, cæsium fluoride gave a quantitative yield of 1-fluoro-2,4-dinitrobenzene.

Systems based on antimony trifluoride and hydrogen fluoride. Antimony trifluoride alone is not a very vigorous exchange reagent but if bromine,[31] antimony pentachloride,[10] or chlorine[32] is added a much more reactive quinquevalent species (*e.g.*, SbF_3Cl_2) is formed. The reactions are carried out[9,13] simply by heating the organic halide with the fluorinating agent, usually without a solvent. Glass apparatus can be used sometimes but metal (steel, nickel, or copper) is best.

Anhydrous hydrogen fluoride is an exchange reagent, though not a particularly vigorous one, but if a small amount of an antimony salt is added[10] the reactivity is enhanced considerably. Many different systems have been suggested, hydrogen fluoride–antimony pentachloride being used most widely; presumably a species such as antimony dichlorode trifluoride is continuously generated. The reactions can be conducted in the liquid phase in a pressure vessel, with due precautions for handling

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[24] Oláh and Pavláth, *Acta Chim. Acad. Sci. Hung.*, 1953, **3**, 191, 199.

[25] Oláh and Pavláth, *Acta Chim. Acad. Sci. Hung.*, 1954, **4**, 119.

[26] Oláh and Kuhn, *J. Org. Chem.*, 1956, **21**, 1319.

[27] Finger and Kruse, *J. Amer. Chem. Soc.*, 1956, **78**, 6034.

[28] Vorozhtsov and Yakobson, *Khim. Nauk i Prom.*, 1958, **3**, 403.

[29] Wallenfels and Draber, *Chem. Ber.*, 1957, **90**, 2819.

[30] Miller and Parker, *J. Amer. Chem. Soc.*, 1961, **83**, 117, Tulloch and Coffman, *J. Org. Chem.*, 1960, **25**, 2016.

[31] Swarts, *Bull. Acad. roy. Belg.*, 1892, **24**, 309, 474.

[32] Henne, U.S.P. 1,978,840/1934, 1,990,692/1935.

hydrogen fluoride. Alternatively, a vapour-phase process can be used, hydrogen fluoride and the organic halide being passed through a tube at fairly high temperatures, usually over a catalyst.[10,33,34] This catalyst is generally activated carbon (alone or impregnated with a metal halide) or a metal halide; many different systems have been claimed in the patent literature. A catalyst is, however, not always essential.[34] Antimony trifluoride systems and hydrogen fluoride systems have roughly equivalent reactivities: hydrogen fluoride is used commercially and is best for large-scale work; antimony trifluoride has advantages for isolated small-scale conversions. Hydrogen fluoride can, of course, add to olefins (see p. 53).

In general, the reactivities of organic halides are as follows: (i) Aryl (*e.g.*, C_6H_5Cl) and alkyl halides (*e.g.*, $R{\cdot}CH_2Cl$) are unattacked; vinyl halides are not attacked directly, but if hydrogen fluoride is used addition followed by exchange may occur ($CH_2{=}CHCl \rightarrow CH_3{\cdot}CHClF \rightarrow CH_3{\cdot}CHF_2$). (ii) CCl_3 groups are most reactive; if attached to an aryl or heterocyclic ring or to an ethylenic group they are readily converted into CF_3 groups ($Ph{\cdot}CCl_3 \rightarrow Ph{\cdot}CF_3$; $CCl_2{=}CCl{\cdot}CCl_3 \rightarrow CCl_2{=}CCl{\cdot}CF_3$); if they are attached to a saturated aliphatic chain the reaction is slower, giving CCl_2F and thence $CClF_2$ but only rarely CF_3 groups. (iii) $>CCl_2$ and $-CHCl_2$ groups behave similarly but are in general less reactive. (iv) The presence of fluorine decreases the ease of replacement of halogen on an adjacent carbon atom. (v) If they are in equivalent positions, the order of reactivity is iodine>bromine>chlorine, but chlorine in a more reactive position may be replaced before bromine in a less reactive one. Since polyhalogeno-compounds are fluorinated most easily, the usual starting materials are chloro-derivatives. The commercially important conversions are the following.

$$CCl_4 \rightarrow CCl_3F \rightarrow CCl_2F_2 \rightarrow CClF_3 \qquad \text{(refs. 9, 10, 13, 34)}$$

$$CHCl_3 \rightarrow CHCl_2F \rightarrow CHClF_2 \qquad \text{(refs. 9, 10, 13)}$$

$$CCl_3{\cdot}CCl_3 \rightarrow CCl_3{\cdot}CCl_2F \rightarrow CCl_2F{\cdot}CCl_2F \rightarrow CCl_2F{\cdot}CClF_2 \rightarrow CClF_2{\cdot}CClF_2 \qquad \text{(refs. 9, 13)}$$

They are usually carried out with hydrogen fluoride and a catalyst. Amongst the many other reactions reported are:

$$CHBr_2{\cdot}CH_2Br \xrightarrow{1} CHBrF{\cdot}CH_2Br \rightarrow CHF_2{\cdot}CH_2Br \qquad \text{(ref. 35)}$$

$$CHCl_2{\cdot}CCl_2{\cdot}CCl_3 \xrightarrow{2} CHCl_2{\cdot}CCl_2{\cdot}CCl_2F \rightarrow CHCl_2{\cdot}CCl_2{\cdot}CClF_2$$
$$\rightarrow CHCl_2{\cdot}CClF{\cdot}CClF_2 \rightarrow CHClF{\cdot}CClF{\cdot}CClF_2 \qquad \text{(ref. 36)}$$

$$CBrCl_2{\cdot}CH_2Br \xrightarrow{3} CF_3{\cdot}CH_2Br \qquad \text{(ref. 37)}$$

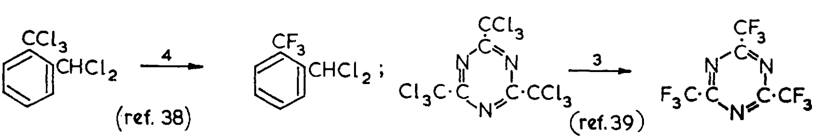
[33] Leicester, B.P. 468447/1937; Woolff and Miller, U.S.P. 2,673,139/1954.

[34] McBee, Hass, Frost, and Welch, *Ind. Eng. Chem.*, 1947, **39**, 404.

[35] Swarts, *Bull. Acad. roy. Belg.*, 1909, 728.

[36] Henne and Haeckl, *J. Amer. Chem. Soc.*, 1941, **63**, 3476.

[37] Dickey, Towne, Bloom, Taylor, Hill, Corbitt, McCall, and Moore, *Ind. Eng. Chem.*, 1954, **46**, 2213.



Reagents: 1, $SbF_3 + Br_2$. 2, SbF_3. 3, HF–$SbCl_5$. 4, HF.

Mercuric fluoride. This reagent is similar in behaviour to those described in the previous sub-section, though rather more reactive.[9,13] It seems to fluorinate a polyhalogeno-compound to a higher degree more readily and will replace a lone halogen atom on carbon by fluorine if it is not adjacent to fluorine or to other halogens:[40]

$$CHBr_2{\cdot}CHBr_2 \rightarrow CHBr_2{\cdot}CHBrF + CHBr_2{\cdot}CHF_2$$
$$(C_6H_5)_2CCl_2 \rightarrow (C_6H_5)_2CF_2$$
$$CHCl_2{\cdot}CClF_2 \rightarrow CHF_2{\cdot}CClF_2$$

The reagent may be prepared from mercuric chloride and elementary fluorine, or made *in situ* by passing hydrogen fluoride into a mixture of mercuric oxide and the organic halide.[40] Though the latter method is more convenient experimentally, water is liberated and may be harmful, *e.g.*, in the synthesis of benzyl fluorides where the preformed difluoride was used.[41]

Very rapid exchanges such as occur with ethyl iodide or iodoform must be performed in a solvent, *e.g.*, chloroform or methylene chloride, to moderate the reaction. An alcohol, ester, or ether must not be used as solvent since the exchange is then inhibited. Such easy exchanges may be carried out in glass vessels. With polyhalides requiring temperatures in the range 80—160° a copper reaction vessel is suitable, and from 160° to 240° nickel is unaffected. The fluorinated product is usually distilled from the reaction mixture.

Antimony pentafluoride. This is a very reactive compound which has some of the character of other high-valency fluorides (p. 61), but is a liquid (b.p. 150°) and so cannot be employed analogously. It is included here since its main use has been as a drastic halogen-exchange agent, as, for example, in routes [42] to C_7 and C_8 fluorocarbons and chlorofluorocarbons requiring a minimum of elemental fluorine and involving exhaustive chlorination followed by halogen exchange. Complete replacement of chlorine in a chlorofluoroalkane is seldom possible, however. Addition as well as exchange can occur readily, as, for example,[43] in the conversion of hexachlorobenzene into 1,2-dichloro-octafluorocyclohexene

[38] Fernandez-Bolaños, Overend, Sykes, Tatlow, and Wiseman, *J.*, 1960, 4003.

[39] McBee, Pierce, and Bolt, *Ind. Eng. Chem.*, 1947, **39**, 391.

[40] Henne and Midgley, *J. Amer. Chem. Soc.*, 1936, **58**, 884; Henne, *ibid.*, 1938, **60**, 1569; Henne and Flanagan, *ibid.*, 1943, **65**, 2362.

[41] Bernstein, Roth, and Miller, *J. Amer. Chem. Soc.*, 1948, **70**, 2310.

[42] Couper, Downing, Lulek, Perkins, Stilmar, and Struve, *Ind. Eng. Chem.*, 1947, **39**, 346.

[43] McBee, Wiseman, and Bachman, *Ind. Eng. Chem.*, 1947, **39**, 415; Leffler, *J. Org. Chem.*, 1959, **24**, 1132.

and of hexachlorocyclopentadiene into 1,2-dichlorohexafluorocyclopentene. This reagent was also used in the first reported synthesis of hexafluorobenzene (p. 66). Most reactions have involved compounds with little hydrogen; if much were present it would be attacked. Antimony pentafluoride can be made from hydrogen fluoride and antimony pentachloride, and this system, though probably rather less reactive, is often used under drastic conditions in preference to the pentafluoride alone.

Sulphur tetrafluoride. It has been reported very recently[44] that this reagent will exchange fluorine for chlorine or bromine in halogeno-alkanes, -alkenes, and -pyrimidines and for chlorine in cyanuric chloride. The replacement was usually incomplete, even though elevated temperatures and pressures were employed, *e.g.*, carbon tetrachloride gave chlorofluoromethanes.

The halogenoalkanes higher than those of methane underwent exchange less readily, even under extreme conditions. Thus, hexachloroethane gave tetrachloro-1,2-difluoroethane, and 2,2,3,3-tetrachlorohexafluorobutane gave 2,2,3-trichloroheptafluorobutane.

Hexachlorobenzene reacted both by addition and exchange, affording dichloro-octafluorocyclohexene and trichlorononafluorocyclohexane, a reaction analogous to that with antimony pentafluoride.[43]

Other fluorides. Various other metallic and non-metallic fluorides have been mentioned as possible exchange agents but it does not appear that any has outstanding advantages. Thallous fluoride has been used[45] to make fluoroformates, and cæsium fluoride[28] to make fluoro-aromatic compounds, instead of potassium fluoride. They appeared to be more reactive (see p. 48).

The use of aprotic solvents in exchange methods of fluorination has recently been extended.[30] Sodium fluoride in solution in tetrahydrothiophen 1,1-dioxide, acetonitrile, or dimethylformamide has been found to exchange halogen rapidly with carboxylic acid chlorides, α-chloro-ethers, trichloromethanesulphenyl chloride, thiocarbonyl chloride, selenium oxychloride, thiophosphoryl chlorides, and phosphonitrilic chlorides. The conversion was usually accomplished by heating the reactants at temperatures up to 250° at atmospheric pressure. In general, sodium fluoride seems less reactive than potassium fluoride, as was demonstrated in the aromatic field.[28]

If the readily available calcium fluoride could be used to fluorinate organic compounds directly, some economies might result, but no really competitive processes appear to have been found.

A(ii) Exchange of Fluorine for Univalent Functional Groups other than halogen.—It was early found[46] that reactions of an alcohol with hydrogen

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[44] Tullock, Carboni, Harder, Smith, and Coffman, *J. Amer. Chem. Soc.*, 1960, **82**, 5107.

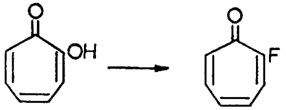
[45] Nakanishi, Myers, and Jensen, *J. Amer. Chem. Soc.*, 1955, 77, 3099, 5033.

[46] Moissan and Meslans, *Compt. rend.*, 1888, **107**, 1155; Meslans, *Compt. rend.*, 1892, **115**, 1080.

fluoride or phosphorus fluorides gave very little alkyl fluoride, too many side reactions interfering. Sulphur tetrafluoride can apparently effect this conversion; other alternatives are treatment of a sulphonate ester with potassium fluoride, or the sequence:[45] ROH → RO·COCl → RO·COF → RF + CO_2. The halogen exchange can be effected with thallous fluoride[45] or potassium fluoride.[26] The hydrogen in activated methylene groups can be replaced by use of perchloryl fluoride.

Sulphur tetrafluoride. This new reagent[47] apparently converts hydroxyl groups into fluoride. Though few examples have been reported as yet, it appears that acidic hydroxyl groups are exchanged best: *e.g.*:

$$HO\cdot CH_2\cdot CO_2H \rightarrow F\cdot CH_2\cdot CF_3$$



With simple aliphatic alcohols there is some ether formation.

Potassium fluoride with sulphonate esters. This typical nucleophilic substitution is one of the oldest routes[48] to alkyl fluorides. The usual technique[49,50] is to reflux a toluenesulphonic ester with potassium fluoride in 2,2′-dihydroxydiethyl ether. Fairly vigorous conditions are required since fluoride ion is a weak nucleophile. Even more drastic conditions than usual are needed to replace[49] the tightly held oxygen of the toluenesulphonate of a fluoro-alcohol such as trifluoroethanol.

Perchloryl fluoride. Though this reacts with aromatic compounds under Friedel–Crafts conditions to give aryl perchlorates, it will replace the hydrogen of activated methylene groups by fluorine. Thus, from diethyl sodiomalonate, diethyl difluoromalonate was prepared;[51] and fluorine was introduced into certain keto-steroids in a related fashion.[52]

A(iii) Exchange of Fluorine for Oxygen in Carbonyl and Carboxyl Groups.—*Sulphur tetrafluoride.* This remarkable reagent is a gas (b.p. —38°) which can be made by reaction of (*a*) sulphur with fluorine or iodine pentafluoride, (*b*) sulphur dichloride with sodium fluoride, or (*c*) sulphur and chlorine with sodium fluoride. It can effect the following conversions directly:[47] $>C{=}O \rightarrow >CF_2$; $-CO_2H \rightarrow -COF \rightarrow -CF_3$. Reactions are carried out in pressure vessels at up to 300°, and in the more difficult conversions a catalyst (HF, BF_3, AsF_3, or TiF_4) is added. Both alkyl and

[47] Hasek, Smith, and Englehardt, *J. Amer. Chem. Soc.*, 1960, **82**, 543.
[48] Dumas and Peligot, *Annalen*, 1835, **15**, 59.
[49] Edgell and Parts, *J. Amer. Chem. Soc.*, 1955, **77**, 4899.
[50] Bergmann and Shahak, *Chem. and Ind.*, 1958, 157.
[51] Inman, Oesterling, and Tyczkowski, *J. Amer. Chem. Soc.*, 1958, **80**, 6533.
[52] Kissman, Small, and Weiss, *J. Amer. Chem. Soc.*, 1960, **82**, 2312.

aryl compounds react, and ethylenic, acetylenic, and ether groupings are unattacked. Some representative conversions out of a considerable number described[47] are as follows:

$CH_3{\cdot}CH_2{\cdot}CO_2H \rightarrow CH_3{\cdot}CH_2{\cdot}CF_3$ $CH_2{=}CH{\cdot}CO_2H \rightarrow CH_2{=}CH{\cdot}CF_3$
$HC{\equiv}C{\cdot}CO_2H \rightarrow HC{\equiv}C{\cdot}CF_3$ $o\text{-}C_6H_4(CO_2H)_2 \rightarrow o\text{-}C_6H_4(CF_3)_2$
$C_6H_5{\cdot}CHO \rightarrow C_6H_5{\cdot}CHF_2$ $CH_3{\cdot}CO{\cdot}CH_3 \rightarrow CH_3{\cdot}CF_2{\cdot}CH_3$

This process undoubtedly is one of the most important recent advances in synthetic fluorine chemistry.

Phenylsulphur trifluoride. This is made from diphenyl disulphide and silver difluoride, and appears[53] to have similar reactivity to that of sulphur tetrafluoride, though only the synthesis of benzylidene fluoride has been reported so far; being a liquid it should be easier to use.

A(iv) Additions to Unsaturated Compounds.—*Hydrogen fluoride.* This can react analogously to the other hydrogen halides towards unsaturated compounds, as was shown long ago[54] in the synthesis of pentyl fluoride from pentene. Under fairly drastic conditions, additions to simple olefins[55] and acetylenes[56] proceed normally and with the expected orientation of the products. There is an extensive patent literature on the process (*e.g.*, for vinyl fluoride and fluoroprene). Boron trifluoride has been suggested as a catalyst;[57] in the patent literature[58] a specially prepared aluminium fluoride has been recommended.

Chloro-olefins have been used widely as starting materials in a combination[59,37] of addition and exchange processes (see p. 48). A typical conversion was: $CH_3{\cdot}CO{\cdot}C_2H_5$ ($+PCl_5$) $\rightarrow$ $CH_3{\cdot}CCl{=}CH{\cdot}CH_3$ ($+HF$) $\rightarrow$ $CH_3{\cdot}CF_2{\cdot}C_2H_5$; there are various other examples of syntheses of compounds containing $>CF_2$ groups.

Additions of hydrogen fluoride to fluoro-olefins have been carried out with potassium fluoride in formamide.[60] This is a difficult reaction with hydrogen fluoride itself, but in the solvent used, owing presumably to the absence of solvation,[30] the fluoride ion exhibits a considerable degree of nucleophilic activity. Hexafluoropropene gave 2*H*-heptafluoropropane—the expected orientation. Other reactions can occur, notably rearrangement by elimination of fluoride ion from the intermediate carbanion ($F^- + CF_2{=}CF{\cdot}CF_2R \rightarrow CF_3{\cdot}{}^{-}CF{\cdot}CF_2R \rightarrow CF_3{\cdot}CF{=}CFR + F^-$).

Additions of hydrogen fluoride are not limited to carbon–carbon bonds, being possible with $>C{=}N{-}$ groups. Isocyanates gave *N*-fluoroformyl-

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[53] Sheppard, *J. Amer. Chem. Soc.*, 1960, **82**, 4751.

[54] Young, *J.*, 1881, **39**, 489.

[55] Grosse and Linn, *J. Org. Chem.*, 1939, **3**, 26.

[56] Grosse and Linn, *J. Amer. Chem. Soc.*, 1942, **64**, 2289; Henne and Plueddeman, *ibid.*, 1943, **65**, 587.

[57] Henne and Arnold, *J. Amer. Chem. Soc.*, 1948, **70**, 758.

[58] Miller and Smith, U.S.P. 2,669,590/1954.

[59] Henne and Haeckl, *J. Amer. Chem. Soc.*, 1941, **63**, 2692; Renoll, *ibid.*, 1942, **64**, 1115; Henne and Plueddeman, *ibid.*, 1943, **65**, 1271.

[60] Fried and Miller, *J. Amer. Chem. Soc.*, 1959, **81**, 2078; Miller, Fried, and Goldwhite, *ibid.*, 1960, **82**, 3091.

ated amines,[61] whilst perfluoro-azomethines afforded perfluoro-secondary amines[62] (*e.g.*, $C_2F_5{\cdot}N{=}CF_2 \rightarrow C_2F_5{\cdot}NH{\cdot}CF_3$). The group $>CF{\cdot}NH—$ is stable only in the absence of water.

Ethylene oxide rings are broken by hydrogen fluoride,[63] to give β-fluoro-hydroxy-groupings. An extension of this process has been used[64] to make fluoro-steroids.

Other fluorides. Certain high-valency metallic fluorides or metal oxide–hydrogen fluoride systems have been used to add two atoms of fluorine across the double bonds of halogeno-olefins (see p. 65). As has been mentioned (pp. 50, 51), antimony pentafluoride and sulphur tetrafluoride can add to, as well as exchange with, unsaturated chloro-compounds.

A(v) Exchange of Fluorine for Diazonium Groups in Aromatic or Heterocyclic Compounds.—This cannot be done by a Sandmeyer-type reaction but is possible by diazotisation in hydrogen fluoride itself. Alternatively, the diazonium tetrafluoroborate or hexafluorosilicate may be made and decomposed to give the aryl fluoride.

Hydrogen fluoride. This reagent was originally used to decompose diazoamino-compounds or diazopiperidides. The exchange is now effected by diazotising the amine in anhydrous hydrogen fluoride, with sodium nitrite[65] or nitrosyl chloride,[66] and warming the system to decompose the diazonium fluoride formed. Benzenes,[65,66] naphthalenes,[65] and pyridines[67,68] have been made, but only with one fluorine atom.

Tetrafluoroboric acid. This, or its sodium salt, is the usual fluorinating agent of the Balz–Schiemann reaction,[69] being added to the solution obtained after normal diazotisation of an aromatic amine, with consequent precipitation of the diazonium fluoroborate. Such a salt is usually almost insoluble in water and relatively stable. It may be dried and, if heated, decomposes at a definite temperature: $ArN_2^+BF_4^- \rightarrow ArF + BF_3 + N_2$. A review of the process has been published.[70] The reaction has been used to prepare fluoro-benzenes, -biphenyls, -naphthalenes, -fluorenes, -phenanthrenes, -pyridines, -quinolines, -isoquinolines, -benzothiazoles, and -carbazoles. It is possible to introduce fluorine stepwise by repetition of the sequence: nitration, reduction, diazotisation, introduction of fluorine. From benzene itself, 1,2,4,5-[71] and 1,2,3,5-tetrafluorobenzene[72] were made

[61] Buckley, Piggott, and Welch, *J.*, 1945, 864.

[62] Pearlson and Hals, U.S.P. 2,643,267/1954; Barr and Haszeldine, *J.*, 1955, 2532.

[63] Knunyants, *Compt. rend. Acad. Sci. U.S.S.R.*, 1947, **55**, 223; Knunyants, Kil'disheva, and Petrov, *Z. obshchei Khim.*, 1949, **19**, 95; Knunyants, Kil'disheva and Bykhovskaya, *ibid.*, p. 101.

[64] Fried and Sabo, *J. Amer. Chem. Soc.*, 1954, **76**, 1455; Fried, Herz, Sabo, Borman, Singer, and Numeroff, *ibid.*, 1955, **77**, 1068; Herr, Hogg, and Levin, *ibid.*, 1956, **78**, 500.

[65] Ferm and Van der Werf, *J. Amer. Chem. Soc.*, 1950, **72**, 4809.

[66] Shenk and Pellon, U.S.P. 2,563,796/1952.

[67] Beaty and Musgrave, *J.*, 1952, 875.

[68] Gruber, *Canad. J. Chem.*, 1953, **31**, 1020.

[69] Balz and Schiemann, *Ber.*, 1927, **60**, 1186.

[70] Roe, "Organic Reactions," 1949, Vol. V, John Wiley, New York, p. 193.

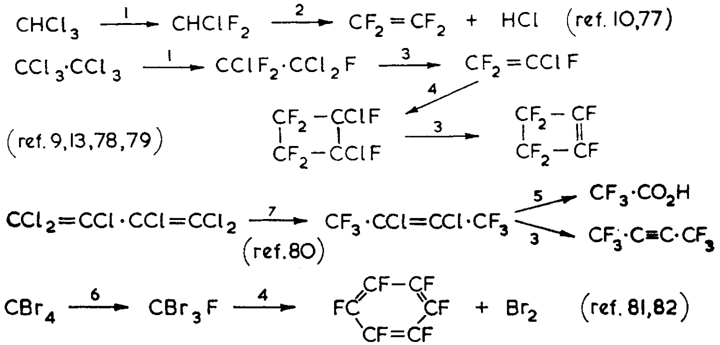
[71] Finger, Reed, Burness, Fort, and Blough, *J. Amer. Chem. Soc.*, 1951, **73**, 145.

[72] Finger, Reed, and Oesterling, *J. Amer. Chem. Soc.*, 1951, **73**, 152.

thus, but further nitration was not possible. A complication is that fluorine in a fluorobenzenediazonium fluoroborate is activated to nucleophilic displacement and may be replaced[73] by chlorine from co-precipitated sodium chloride. Alternative conditions have been proposed[74] for the decomposition of diazonium fluoroborates.

Diazonium hexafluorophosphates[75] and hexafluorosilicates[76,67] have been used in a similar manner but with no real advantage.

Only in a very few cases do the methods of Section A give full fluorination in one operation. Usually reactions stop when some hydrogen and/or halogen remains and sometimes very little fluorine is introduced. However, the products can usually be subjected to preferential dehydrohalogenation or dehalogenation. These processes can be carried out either by pyrolysis or with chemical reagents. Dehydrohalogenation can be done with alcoholic alkali, and dehalogenation with zinc dust in a medium such as ethanol or acetamide. Halogens other than fluorine are almost always eliminated preferentially and only rarely is fluorine itself removed as well. Such treatment can be followed if necessary by other fluorination stages. In this way fluorocarbon-type materials can often be synthesised without undue difficulty. Some examples are:



Reagents: 1, HF. 2, Pyrolysis. 3, Zn–EtOH. 4, Heat, 5, KMnO$_4$. 6, SbF$_3$.

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[73] Finger and Oesterling, *J. Amer. Chem. Soc.*, 1956, **78**, 2593.

[74] Bergmann and Bentov, *J. Org. Chem.*, 1954, **19**, 1594; Bergmann, Berkovic, and Ikan, *J. Amer. Chem. Soc.*, 1956, **78**, 6037; Brunton and Suschitzky, *J.*, 1955, 1035; Barben and Suschitzky, *Chem. and Ind.*, 1957, 1039.

[75] Lang and Müller, *Ber.*, 1930, **63**, 1058.

[76] Cheek, Wiley, and Roe, *J. Amer. Chem. Soc.*, 1949, **71**, 1863.

[77] Park, Benning, Downing, Laucius, and McHarness, *Ind. Eng. Chem.*, 1947, **39**, 354.

[78] Booth, Burchfield, Bixby, and McElvey, *J. Amer. Chem. Soc.*, 1933, **55**, 2231; Locke, Brode, and Henne, *ibid.*, 1934, **56**, 1726.

[79] Henne and Ruh, *J. Amer. Chem. Soc.*, 1947, **69**, 279; Harmon, U.S.P. 2,404,374/1946, 2,436,142/1948; Buxton, Ingram, Smith, Stacey, and Tatlow, *J.*, 1952, 3830.

[80] Henne and Trott, *J. Amer. Chem. Soc.*, 1947, **69**, 1820; Henne and Finnegan, *ibid.*, 1949, **71**, 298.

[81] Désirant, *Bull. Classe Sci., Acad. roy. Belg.*, 1955, **41**, 759; *Bull. Soc. chim. belges*, 1958, **67**, 676; Hellmann, Peters, Pummer, and Wall, *J. Amer. Chem. Soc.*, 1957, **79**, 5654.

[82] Birchall and Haszeldine, *J.*, 1959, 13.

The products of these sequences are important synthetic intermediates in fluorocarbon chemistry. Their general reactivities have been described in earlier reviews[83] and will be dealt with again in the second part of this one.

SECTION B

This section deals with methods for exhaustive fluorination, of which there are four, all capable of producing fluorocarbon-type material directly. Reagents are: (i) elementary fluorine; (ii) transition-metal fluorides in which the metal has a high valency; or (iii) a halogen fluoride. In method (iv) (electrochemical fluorination) a current is passed through a solution of a carbon compound in anhydrous hydrogen fluoride. With all of these methods, unsaturation and hydrogen in organic compounds are attacked, and when the reactions are allowed to go to completion saturated perfluoro-compounds are formed. Functional groups are often attacked but are sometimes preserved.

B(i) Direct Fluorination with Elementary Fluorine.—There is a very recent review[84] on this subject. In all early attempts at direct fluorination of organic compounds, the violence of the reaction could not be controlled and little progress was made until the mid-1930's. Then, two techniques were evolved, vapour-phase fluorination in a packed vessel, and a simple liquid-phase reaction in which fluorine, usually diluted with nitrogen, was bubbled through an organic compound normally in a solution. Subsequently, it was found practicable to carry out vapour-phase fluorinations in unpacked vessels.

All reactions between elementary fluorine and hydrocarbon-type compounds are highly exothermic, since heats of formation of $\geqslant$C–F and H–F bonds are high (*ca.* 105 and 134 kcal./mole, respectively) and the dissociation energy of the F–F bond is low (37 kcal./mole). Unless this heat is rapidly dissipated, combustion and fragmentation of the carbon skeleton ensue. The techniques evolved have all achieved, to some extent at least, rapid removal of heat from the reaction site.

Direct vapour-phase fluorination over a metal packing. This process, usually called the "catalytic method," followed from the observation that fluorine and an organic vapour reacted smoothly within the meshes of a finely divided metal packing, particularly at elevated temperatures; compounds with a high degree of fluorination were produced. It was developed by Bigelow[85,86] and was subsequently adapted as part of the original Atomic Energy Projects for the production of fluorocarbons from hydro-

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[83] Musgrave, *Quart. Rev.*, 1954, **8**, 331; Haszeldine, *Ann. Reports*, 1954, **51**, 279.

[84] Tedder in "Advances in Fluorine Chemistry," ed. Stacey, Tatlow, and Sharpe, Butterworths Scientific Publs., London, 1961, Vol. II, p. 104.

[85] Bigelow, *Chem. Rev.*, 1947, **40**, 51.

[86] Bigelow in "Fluorine Chemistry," ed. Simons, Academic Press, New York, Vol. I, 1950, p. 373.

carbons, a typical form of apparatus being illustrated in Fig. 1. Usually, streams of the organic vapour and of fluorine, both diluted with nitrogen, were mixed in a metal tube, filled with some form of finely divided metal such as gauze, turnings, or shot, and heated to about 200—250°.

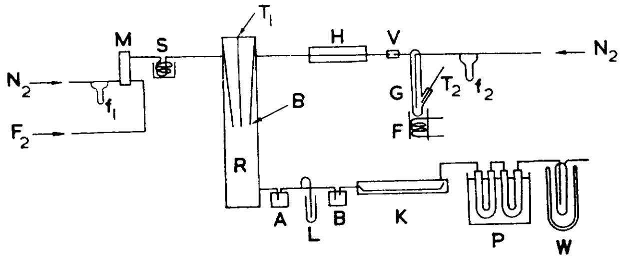

FIG. 1. *Apparatus for vapour-phase fluorination.*

f_1 and f_2,	Pyrex flow-meters.
M,	Mixing chamber for fluorine and nitrogen.
S,	Copper spiral for preheating the fluorine–nitrogen mixture.
R,	Steel reaction vessel (34″ × 3″) filled with gold-plated copper turnings.
T_1,	Thermometer pocket.
B,	Nickel baffle plate, extending $\frac{1}{3}$ length of R; lower half drilled with $\frac{1}{32}$″ holes $\frac{1}{2}$″ apart.
H,	Furnace for preheating hydrocarbon–nitrogen mixture.
V,	Copper–glass ground joint.
G,	Graduated 50-c.c. Pyrex vessel carrying a thermometer, T_2
F,	Silica tube furnace for heating the hydrocarbon reservoir.
A and B,	Traps for the condensation of polymeric material.
L,	Copper tube dipping into "Cerechlor" or a fluorinated oil to act as a safety valve.
K,	Potassium fluoride scrubber (removed during preparation of high-boiling fluorocarbons).
P,	Two copper U tubes joined in series and cooled by a mixture of solid carbon dioxide and alcohol.
W,	Liquid-air trap to condense any volatile decomposition products.

(*Reprinted, by permission, from Haszeldine and Smith,* J., 1950, 2689.)

The direct fluorination of organic compounds is undoubtedly a free-radical process with the usual type of chain mechanism. Products can be partially or completely fluorinated derivatives, *viz.*, of the original carbon skeleton, of shorter carbon chains resulting from C–C bond rupture, or of longer carbon chains due to polymerisation. Some isomerisation or cyclisation can also occur. Many hydrocarbons have been fluorinated by this technique. Ethane and methane were investigated early,[85,86] and a range of fluorocarbons was later made[87,88] from higher homologues. In this process an aromatic ring is saturated at the outset,[89] and benzenoid hydrocarbons give alicyclic fluoro-derivatives. Yields of fluorocarbons are reasonable, reaching about 60% in the best cases;[87] *e.g.*, perfluoro-n-heptane from n-heptane, 62%; perfluorocyclohexane from benzene, 58%.

[87] Cady, Grosse, Barber, Burger, and Sheldon, *Ind. Eng. Chem.*, 1947, **39**, 290.

[88] Musgrave and Smith, *J.*, 1949, 3021; Haszeldine and Smith, *J.*, 1950, 2689, 2787.

[89] Fukuhara and Bigelow, *J. Amer. Chem. Soc.*, 1941, **63**, 2792; Gilbert and Bigelow, *ibid.*, 1950, **72**, 2411.

However, yields are normally less than these, with much by-product formation. Though different metal packings have given somewhat different yields,[90] the effect is not great and it appears that the primary function of a packing is to disperse the heat of reaction, and that it is not a true catalyst.

Successful fluorinations of some organic derivatives have been reported. Methyl alcohol or carbon monoxide gave trifluoromethyl hypofluorite,[91] and methanethiol gave trifluoromethylsulphur pentafluoride.[92] From acetone, there were obtained hexafluoroacetone and trifluoroacetyl fluoride, besides other breakdown products.[93] Perfluoro-ketones were obtained also from ethyl methyl ketone and from cyclopentanone.[94]

Certain nitrogenous compounds have been fluorinated. Mono-, di- and tri-ethylamine gave a range of nitrogen-containing fluorocarbon derivatives such as $CF_3{\cdot}NF_2$, $CF_3{\cdot}CF_2{\cdot}NF_2$, $(CF_3)_2NF$, etc.[95] Acetonitrile under mild conditions afforded fluorohydrocarbons and a nitrogenous polymer, but no volatile fluorocarbon nitride or free nitrogen;[96] use of more drastic conditions led to $CF_3{\cdot}CF_2{\cdot}NF_2$ and $CF_2{=}NF$. Malononitrile afforded $\overline{\mathrm{CF_2{\cdot}CF_2{\cdot}CF_2{\cdot}NF{\cdot}N}}\mathrm{F}$, $CF_3{\cdot}CF_2{\cdot}CF_2{\cdot}NF_2$, $NF_2{\cdot}CF_2{\cdot}CF_2{\cdot}CF_2{\cdot}NF_2$, and other breakdown products.[97] Acid amides[98] are much more unstable, for example acetamide was cleaved even before replacement of hydrogen, to give acetyl fluoride in 52% yield. Cyanides[98] gave perfluoroazo-compounds and, under vigorous conditions, pentafluoroethyl cyanide gave heptafluoropropylnitrogen difluoride. Methyl thiocyanate gave pentafluorosulphur cyanide ($F_5S{\cdot}CN$) under mild conditions, but the derived nitride ($F_5S{\cdot}CF_2{\cdot}NF_2$) together with sulphur hexafluoride under vigorous conditions.[98]

Direct vapour-phase fluorination without a catalyst. In the first apparatus[99] for this type of reaction concentric tubes were used for introducing the different gas streams, carbon disulphide giving, *inter alia*, $CF_3{\cdot}SF_5$, $CF_3{\cdot}SF_3$, $SF_3{\cdot}CF_2{\cdot}SF_5$, and $SF_5{\cdot}CF_2{\cdot}SF_5$.

Subsequently, a jet fluorination reactor was devised[100] in which reactor gases helped to dilute the incoming fluorine stream (see Fig. 2). Hexafluoroethane was formed from ethane in 85% yield. This seems to be the best method of direct fluorination found so far. More recently, the process has been refined and very mild fluorinations achieved with a triple jet reactor.[101]

[90] Musgrave and Smith, *J.*, 1949, 3026.
[91] Kellogg and Cady, *J. Amer. Chem. Soc.*, 1948, **70**, 3986.
[92] Silvey and Cady, *J. Amer. Chem. Soc.*, 1950, **72**, 3624.
[93] Fukuhara and Bigelow, *J. Amer. Chem. Soc.*, 1941, **63**, 788.
[94] Holub and Bigelow, *J. Amer. Chem. Soc.*, 1950, **72**, 4879.
[95] Gervasi, Brown, and Bigelow, *J. Amer. Chem. Soc.*, 1956, **78**, 1680.
[96] Cuculo and Bigelow, *J. Amer. Chem. Soc.*, 1952, **74**, 710.
[97] Avonda, Gervasi, and Bigelow, *J. Amer. Chem. Soc.*, 1956, **78**, 2798.
[98] Attaway, Groth, and Bigelow, *J. Amer. Chem. Soc.*, 1959, **81**, 3599.
[99] Tyczkowski and Bigelow, *J. Amer. Chem. Soc.*, 1953, **75**, 3523.
[100] Tyczkowski and Bigelow, *J. Amer. Chem. Soc.*, 1955, **77**, 3007.
[101] Maxwell, Detono, and Bigelow, *J. Amer. Chem. Soc.*, 1960, **82**, 5827.

Kinetic studies have been carried out[102] on the gas-phase reactions of fluorine with hydrocarbons, by diluting the system with an inert gas (nitrogen) to give very low concentrations of reactants and to avoid increases of temperature. Useful information about the process was obtained,[84] but the method has not been used preparatively.

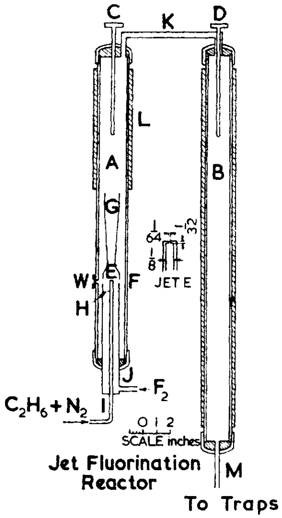

FIG. 2.

A,	Primary reactor.	H,	Centring device.
B,	Secondary reactor.	I,	Inlet tube (Ethane + N_2).
C and D,	Weston thermometers.	J,	Inlet tube (F_2).
E,	Jet.	K,	Inlet and exit tube.
F,	Gas inlets.	L,	Heater.
G,	Mouth of inlet tube J.	W,	Circular observation window.

(*Reproduced, by permission, from Tyczkowski and Bigelow*, J. Amer. Chem. Soc., 1955, 77, 3007.)

Liquid-phase fluorination. This technique, though apparently simple, poses many problems in practice. It is desirable to use a solvent, but there are few with sufficient stability towards fluorine. Of those that have, fluorocarbons are very poor solvents, whilst hydrogen fluoride has a low boiling point. Much work has been done with chloro- or chlorofluorocarbons, but these often react slowly with fluorine. Further, owing to the free-radical nature of the fluorination process, the carbon skeletons of the starting materials are very often linked together to give polymeric products. Though fluorine is not very soluble in most organic liquids, it is probable that few reactions have been true gas–liquid ones at an interface, gas–vapour reactions in bubbles predominating.

The first successful liquid-phase fluorinations were done in carbon

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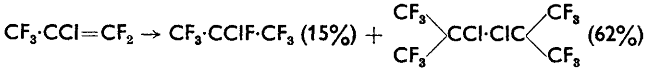
[102] Anson, Fredricks, and Tedder, *J.*, 1959, 918; Fredricks and Tedder, *J.*, 1960, 144; Fettis, Knox, and Trotman-Dickenson, *J.*, 1960, 1064.

tetrachloride. By using fluorine diluted with carbon dioxide and nickel apparatus, n-hexadecane, cyclohexane, and n- and iso-butyric acid were monofluorinated.[103] Fluorination of the acids did not occur at the α-position. Crotonic acid gave difluorobutyric acid and a dimer.[103] It was found[104] that fluorine liberated chlorine from carbon tetrachloride at 0° in a sufficiently active state to bring about the chlorination of toluene. From aromatic compounds no fluoro-substitution products were formed;[104] as with vapour-phase fluorination, saturation of the ring occurred in the early stages.

The fluorination of halogeno-olefins in the liquid phase has been studied by Miller.[105] Addition of fluorine was accompanied by much dimerisation, together with some replacement of chlorine by fluorine and also reaction of the displaced chlorine with organic material. Examples are:

$$\mathrm{CClF{=}CClF \rightarrow CClF_2{\cdot}CClF_2\ (17\%) + CClF_2{\cdot}CClF{\cdot}CClF{\cdot}CClF_2\ (30\%)}$$

$$\mathrm{(together\ with\ CClF_2{\cdot}CF_3,\ CCl_2F{\cdot}CClF_2,\ CCl_2F{\cdot}CCl_2F,\ C_4Cl_5F_5,\ and\ C_4Cl_6F_4)}$$



$$\mathrm{CF_3{\cdot}CCl{=}CF_2 \rightarrow CF_3{\cdot}CClF{\cdot}CF_3\ (15\%) + (CF_3)_2CCl{\cdot}CCl(CF_3)_2\ (62\%)}$$

These reactions, carried out at <−50°, proceed by a free-radical chain mechanism, which explains the dimerisations, and it has been suggested,[106] though not proved, that molecular fluorine can act as the initiator. An interesting consequence of this work is the promotion,[106] by small amounts of fluorine, of free-radical oxidations and chlorinations of halogeno-olefins by the respective elements.

An application[107] of polymerisation initiated by fluorine and accompanied by fluorination was the production of fluoro-oils and resins from benzotrifluoride in solution in fluorocarbons, even the C_6 ring system undergoing dimerisation. A consequence of all this, however, is that no preparations of fluorocarbons by liquid-phase processes have been reported. Fluorinations of undiluted hydrocarbons at very low temperatures in glass apparatus have been described,[108] in which fluorine highly diluted with nitrogen (at least $N_2 : F_2 = 4:1$) and very efficient stirring are used. Whilst fluorination was fairly rapid in the dark, it was accelerated by light and it was concluded that reaction occurred mainly in the gas phase of the bubbles. Another case of catalysis by ultraviolet light has been

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[103] Bockemüller, *Annalen*, 1933, **506**, 20.

[104] Bigelow, Pearson, Cook, and Miller, *J. Amer. Chem. Soc.*, 1933, **55**, 4614.

[105] Miller, *J. Amer. Chem. Soc.*, 1940, **62**, 341; Miller, Ehrenfeld, Phelan, Prober, and Reed, *Ind. Eng. Chem.*, 1947, **39**, 401; Miller in "Preparation, Properties and Technology of Fluorine and Organic Fluoro-compounds" (eds. Slesser and Schram), McGraw-Hill, New York, 1951, p. 567.

[106] Miller and Dittman, *J. Amer. Chem. Soc.*, 1956, **78**, 2793; Miller, Koch, and McLafferty, *ibid.*, p. 4992; Miller and Koch, *ibid.*, 1957, **79**, 3084.

[107] Smith, Stacey, Tatlow, Dawson, and Thomas, *J. Appl. Chem.*, 1952, **2**, 97.

[108] Tedder, *Chem. and Ind.*, 1955, 508; Anson and Tedder, *J.*, 1957, 4390.

observed in the liquid-phase fluorination of certain chlorocyclohexanes in carbon tetrachloride; γ-rays and peroxides were also effective.[109]

Fluorinations of solids. It has been mentioned above that aliphatic fluorocarbons are produced when fluorine reacts[3] with various forms of carbon, a mercury salt often being employed as catalyst. This reaction has been carried out[110] by a fluidised-bed technique. Reaction of carbon from an arc with fluorine at >1400°C has been claimed[111] to give tetrafluoroethylene. There are a few examples of the fluorinations of organic salts, but no advantageous synthesis of organic fluorides seems to have emerged. An interesting reaction[112] was the direct fluorination of polyethylene: a controlled substitution was achieved to give a polymer resembling polytetrafluoroethylene, but the process was apparently not competitive with polymerisation.

B(ii) Fluorination with High-valency Transition-metal Fluorides.—This method of exhaustive fluorination has recently been reviewed in detail.[113] The sources of fluorine are compounds such as cobalt trifluoride, silver difluoride, manganese trifluoride, cerium tetrafluoride, or lead tetrafluoride, made from a lower-valency fluoride or a chloride and fluorine. They react with organic matter, usually at 100—400°, and revert to a fluoride of lower valency:

$$\geqslant\text{CH} + 2\text{MF}_n \rightarrow \geqslant\text{CF} + \text{HF} + 2\text{MF}_{n-1}$$
$$>\text{C}{=}\text{C}< + 2\text{MF}_n \rightarrow >\text{CF}{\cdot}\text{FC}< + 2\text{MF}_{n-1}$$

The "active" fluorine is not evolved as the element by a prior decomposition of the high-valency fluorides; these react directly with organic compounds. The latter can be in either vapour or liquid phase, though the vapour-phase process has been by far the more useful. As with fluorine itself, aromatic compounds give alicyclic fluorides when treated with these reagents.

Vapour-phase reactions with cobalt trifluoride. These were originally conducted[114,115] by passing the organic compound over a thinly spread bed of cobaltic fluoride in a metal tube heated to 300—350°. When the high-valency fluoride is exhausted it is regenerated by passing fluorine through the tube. The latter stage can be carried out overnight, giving a convenient two-stage sequence. It is advantageous to agitate the bed of fluorinating agent and this is usually achieved[114,116] in a horizontal

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[109] Germano, U.S.P. 2,905,609/1959.

[110] Passino, Teeters, and Mantell, U.S.P. 2,770,660/1956.

[111] Farlow and Muetterties, U.S.P. 2,732,411/1956.

[112] Rudge, B.P. 710,523/1954.

[113] Stacey and Tatlow in "Advances in Fluorine Chemistry," eds. Stacey, Tatlow, and Sharpe, Butterworths Scientific Publs., London, Vol. I, 1960, p. 166.

[114] Fowler, Burford, Hamilton, Sweet, Weber, Kasper, and Litant, *Ind. Eng. Chem.*, 1947, **39**, 292.

[115] Haszeldine and Smith, *J.*, 1950, 3617.

[116] Barbour, Barlow, and Tatlow, *J. Appl. Chem.*, 1952, **2**, 127.

tubular reactor carrying a coaxial stirrer shaft. A typical design is illustrated in Fig. 3.

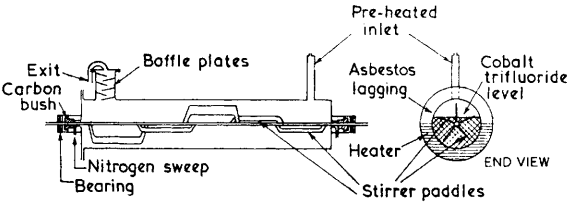

FIG. 3. *Fluorination apparatus for vapour-phase fluorination with cobalt trifluoride. The tube is of nickel,* 3 *ft.* 6 *in. long and of* 3⅜ *in. internal diameter and wall thickness* $\frac{3}{32}$ *in., holding about* 3½ *kg. of cobaltic fluoride.*
(*Reproduced, by permission, from Barbour, Barlow, and Tatlow,* J. Appl. Chem., 1952, **2**, 127.)

It has been shown[117] that when cobaltic fluoride is used as a fluorinating agent the heat of an overall reaction between elementary fluorine and an organic compound is divided approximately equally between the two stages: (*a*) formation of cobalt trifluoride from the difluoride and fluorine; and (*b*) reaction of the trifluoride with organic material. With comparatively little of the fragmentation or polymerisation that fluorine itself gives, open-chain and cyclic fluorocarbons[114–116,118] have been produced readily from cobaltic fluoride and the appropriate aliphatic or aromatic hydrocarbon. The reactions are easy to carry out and yields are usually in the range 50—75%. The appropriate aliphatic hydrocarbon gave perfluorobutane,[114] -pentane,[114] -heptane,[114,115] -cyclopentane,[114] and -dimethylcyclohexane;[115] toluene afforded perfluoro(methylcyclohexane);[115,118] naphthalene and tetralin gave perfluorodecalin;[115,116] and biphenyl gave perfluorobicyclohexyl.[116] This is probably the best general synthesis of saturated fluorocarbons. Cyclic members of this series are now of synthetic value as precursors of perfluoro-aromatic compounds *via* defluorination[119] with heated metals.

It is possible to produce fluorohydrocarbons by fluorination of hydrocarbons at temperatures too low to give full fluorination, *e.g.*, at 150—200°. Most work has been done with benzene, and the products[120,121] were chiefly a range of fluorocyclohexanes of formula $C_6H_nF_{12-n}$ (n = 1—4), including undecafluorocyclohexane,[120] the six possible decafluorides ($C_6H_2F_{10}$),[121,122] the four possible 1*H*,2*H*,4*H*-nonafluorides ($C_6H_3F_9$),[123,124] and four of the five possible 1*H*,2*H*,4*H*,5*H*-octafluorides ($C_6H_4F_8$).[125]

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[117] Jessup, Brickwedde, and Wechsler, *J. Res. Nat. Bur. Stand.*, 1950, **44**, 457.
[118] Barlow and Tatlow, *J.*, 1952, 4695.
[119] Gething, Patrick, Stacey, and Tatlow, *Nature*, 1959, **183**, 588.
[120] Barbour, Mackenzie, Stacey, and Tatlow, *J. Appl. Chem.*, 1954, **4**, 341, 347.
[121] Smith and Tatlow, *J.*, 1957, 2505.
[122] Evans, Godsell, Stephens, Tatlow, and Wiseman, *Tetrahedron*, 1958, **2**, 183.
[123] Godsell, Stacey, and Tatlow, *Tetrahedron*, 1958, **2**, 193.
[124] Stephens, Tatlow, and Wiseman, *J.*, 1959, 148.
[125] Nield, Stephens, and Tatlow, *J.*, 1959, 159.

Preparative-scale gas chromatography[126,127] was used in order to isolate pure samples of some of these products, the structures of which were established[121–126] by conversion with concentrated aqueous alkali into fluoro-cyclohexenes and -cyclohexadienes followed by oxidations to fluoro-dicarboxylic acids. These structures were confirmed by stepwise fluorinations, with cobaltic fluoride, of each octafluoride to the expected nonafluorides,[125] and of each nonafluoride to the expected decafluorides.[122–124]

When the fluorocyclohexenes obtained by dehydrofluorination were passed over cobaltic fluoride, the double bonds were saturated before the hydrogen was replaced.[124,125]

Very small amounts of two fluorocyclohexenes and of fluoro- and *p*-difluoro-benzene were found[113] in the mixed fluorocyclohexanes from the original benzene–cobalt trifluoride reaction. The mechanism is not yet certain; a possible path[113] is addition of fluorine to benzene followed by elimination of hydrogen fluoride to give fluorobenzene, which by an analogous 1,4-addition–elimination goes to *p*-difluorobenzene. 1,4-Addition of fluorine to this would give 3,3,6,6-tetrafluorocyclohexa-1,4-diene, from which elimination of hydrogen fluoride is difficult, but which can add further to give the octafluorocyclohexanes.

Comparatively little has been achieved by the reaction with cobaltic fluoride of organic compounds containing functional groups. Chlorine from a chloro-compound was largely retained overall, but considerable displacement and re-entry of it occurred, giving rise to much isomerisation.[128] Bromine and iodine are removed more easily. Ketones are cleaved completely,[94] and methanol gave[91] no trifluoromethyl hypofluorite (cf. the reactions with fluorine). Amines (aliphatic and aromatic) and pyridine gave[129] perfluoronitrides (*e.g.*, $C_6F_{11}{\cdot}NF_2$ from aniline) but in very low yields, and, though trifluoromethylsulphur pentafluoride was obtained[92] from carbon disulphide or methanethiol, other sulphur compounds suffered rupture of C–S links (cf. electrochemical fluorinations with nitrogen and sulphur-containing compounds).

Vapour-phase reactions with silver difluoride. Fluorocarbons may be made just as with cobaltic fluoride; a series of saturated fused-ring perfluoro-derivatives[130] and perfluoroalkylcyclohexanes[131] has been made in static reactors. Though about as reactive as cobaltic fluoride, silver difluoride appears to be more difficult to handle.[113]

Though chlorine is removed more easily from organic structures by silver difluoride than by cobalt trifluoride, there are suggestions that some

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[126] Evans and Tatlow, *J.*, 1955, 3779.

[127] Evans, Massingham, Stacey, and Tatlow, *Nature*, 1958, **182**, 591.

[128] Tatlow and Worthington, *J.*, 1952, 1251; Roylance, Tatlow, and Worthington, *J.*, 1954, 4426.

[129] Haszeldine, *J.*, 1950, 1638, 1966; 1951, 102.

[130] McBee and Bechtol, *Ind. Eng. Chem.*, 1947, **39**, 380.

[131] McBee and Ligett, U.S.P. 2,606,212/1952.

functional groups are retained better from fluorinations involving the former. Cyanogen chloride gave hexafluoroazomethane and trifluoronitrosomethane,[132] and perfluoro-2-azapropene gave[133] a dimeric form, $(CF_3)_2N{\cdot}CF{=}N{\cdot}CF_3$, and the substituted hydrazine, $(CF_3)_2N{\cdot}N(CF_3)_2$, at 15°, but $(CF_3)_2NF$ and $(CF_3)_2N{\cdot}N(CF_3)_2$ at 100°. Information[133] has been obtained about the relative ease of reaction of silver difluoride with an unsaturated carbon, a carbonyl carbon, and a substituted nitrogen centre by studying the fluorination of $CF_3{\cdot}CN$, $C_3F_7{\cdot}CN$, $(CF_3)_2NH$, $(CF_3)_2N{\cdot}COF$, $C_2F_5{\cdot}NCO$, $CF_3{\cdot}CO{\cdot}NH_2$, and $(CF_3{\cdot}CO)_2NH$. It was found that N–F bond formation was accompanied by rearrangement and coupling of the free-radical intermediates. Volatile fluorocarbon isocyanates were prepared from the corresponding amides, and fluorocarbon azoalkanes, $R_f{\cdot}CF_2N{=}NCF_2{\cdot}R_f$ from nitriles (R_f = perfluoroalkyl). One report[134] suggested that carbonyl groups could be retained in fluorinations with silver difluoride.

Vapour-phase fluorinations with other high-valency fluorides. Manganese trifluoride has been proposed as an alternative[135] to cobaltic fluoride but is a much milder reagent. Synthesis of fluorocarbons with it would be difficult, and fluorination of benzene has given little, if any, perfluorocyclohexane and much unsaturated material[136,124]—a useful feature.

Cerium tetrafluoride[135] is another mild fluorinating agent which might have advantages for synthesis of partially fluorinated compounds.

Lead tetrafluoride, despite handling difficulties,[135] can be used for exhaustive fluorination of hydrocarbons;[137,138] fluorocarbons can be made by its use, though apparently less readily than with cobaltic and silver fluorides. It was again claimed[138] that a perfluoro-ketone could be made from a ketone. The use of lead tetrafluoride for additions to olefins is mentioned below.

Liquid-phase fluorinations with high-valency fluorides. These have been limited in the main to fluorinations of oils, etc.,[139,140] with fluorocarbons as diluents, and to completions of fluorinations[105,107] of high-boiling fluorocarbon material still containing residual hydrogen. Cobalt trifluoride and silver difluoride have both been used, the latter being probably better but more difficult to handle. One use of silver difluoride was the conversion[17] of 2,4,6-trifluoropyrimidine in solution in perfluorotributylamine into tetrafluoropyrimidine, a direct replacement of hydrogen without addition to the unsaturated system.

[132] Glemser, Schröder, and Haeseler, *Z. anorg. Chem.*, 1955, **282**, 80.

[133] Young, Durrell, and Dresdner, *J. Amer. Chem. Soc.*, 1959, **81**, 1587; 1960, **82**, 4553.

[134] McBee and Ligett, U.S.P. 2,614,129/1952.

[135] Fowler, Anderson, Hamilton, Burford, Spadetti, Bitterlich, and Litant, *Ind. Eng. Chem.*, 1947, **39**, 343.

[136] Fear and Thrower, *J. Appl. Chem.*, 1955, **5**, 353.

[137] McBee and Robb, U.S.P. 2,533,132/1950, 2,533,133/1950, 2,487,820/1949.

[138] McBee and Robb, U.S.P. 2,567,569/1951.

[139] Struve, Benning, Downing, Lulek, and Wirth, *Ind. Eng. Chem.*, 1947, **39**, 352.

[140] Stilmar, Struve, and Wirth, *Ind. Eng. Chem.*, 1947, **39**, 348.

Saturation of olefinic double bonds. A mixture of lead dioxide and anhydrous hydrogen fluoride will react with halogeno-olefins to give[141] the difluoro-addition product (*e.g.*, $CF_3{\cdot}CCl{=}CCl_2 \rightarrow CF_3{\cdot}CClF{\cdot}CCl_2F$; and $CCl_2{=}CCl_2 \rightarrow CCl_2F{\cdot}CCl_2F$). In view of the behaviour of fluorine itself (p. 60) this is a useful process. The active species is probably lead tetrafluoride and it appears that if the olefin contains much hydrogen it will be attacked. Replacement of lead dioxide by cobaltic oxide or by manganic oxide has been suggested.[142]

B(iii) Fluorination by Halogen Fluorides. This method of fluorination has also been comprehensively reviewed quite recently.[143] The halogen fluorides are all made from fluorine and the second halogen, and their application as fluorinating agents for organic compounds is limited since this second halogen is usually introduced as well as fluorine.

The uses of chlorine fluorides. Controlled reactions have been described[144] in which perchloro-compounds, hydrocarbons, and chlorohydrocarbons, dissolved in an inert solvent, were fluorinated with chlorine monofluoride diluted with nitrogen; the vigour of the reaction decreased with increase of halogen content. Mixtures of chlorofluoro-compounds were obtained. Chlorine trifluoride reacts similarly, but apparently more vigorously. The catalysed reaction with benzene in carbon tetrachloride was mainly one of substitution to give chlorobenzene and fluorobenzene.[145] A small quantity of addition products was formed also. Mercuric or cobaltous chloride, or silver or cobaltous fluoride, was used as catalyst. The last appeared the most effective and a mechanism was advanced involving the production of positive fluoride ions. An alternative suggestion involved a transition complex between cobalt trifluoride, chlorine trifluoride, and benzene. Benzene derivatives reacted analogously to benzene, and since the entering chlorine or fluorine took up the position expected from the directive effects, an electrophilic mechanism was indicated.[146] In most of the cases studied in the liquid phase, the degree of chlorination was greater than that of fluorination. Since steric compression is considerable with higher degrees of chlorination, the production of hydrogen-free compounds is difficult without thermal degradation occurring. Perhalogenation was achieved[147] with 1,2,3,4-tetrachlorobutadiene, however (to give chlorofluorobutanes) and obviously with unsaturated perchloro-compounds; for example, hexachlorobutadiene and octachloronaphthalene gave[148] stable chlorofluoro-compounds. A range of

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[141] Henne and Waalkes, *J. Amer. Chem. Soc.*, 1945, **67**, 1639; 1946, **68**, 496.

[142] Benning and Park, U.S.P. 2,437,993/1948.

[143] Musgrave, "Advances in Fluorine Chemistry," Butterworths Scientific Publs., London, Vol. I, 1960, p. 1.

[144] Murawski and Burnett, B.P. 738,289/1955; Muray and Wadsworth, B.P. 760,489/1956.

[145] Ellis and Musgrave, *J.*, 1950, 3608.

[146] Ellis and Musgrave, *J.*, 1953, 1063.

[147] Muray, *J.*, 1959, 1884.

[148] Burnett, B.P. 695,811/1953.

commercially important chlorofluoro-oils and -greases has been made[149] by variations of this liquid-phase process. Few compounds with functional groups have been fluorinated thus; trichloroacetic acid and its acid chloride suffered loss of the carbonyl group, apparently by a free-radical mechanism.[150]

Vapour-phase fluorination with chlorine trifluoride has been limited to benzene. Treated as in the catalytic method of direct fluorination (p. 56), this gave[143] mainly chlorofluoro-addition products, with very little substitution. The mechanism obviously differed from that operating in the liquid phase, and appeared to be of a free-radical type.

Solids fluorinated have been carbon (see p. 45), from which chlorofluorocarbons were produced,[4,5] and coal to give a range of chlorofluoro-oils and -greases.[151]

Bromine fluorides. Bromine trifluoride is very reactive towards organic material. With carbon tetrahalides,[152] the expected products were obtained ($CCl_4 \rightarrow CCl_3F + CCl_2F_2 + CClF_3$; $CBr_4 \rightarrow CBr_3F + CBr_2F_2 + CBrF_3$; $CI_4 \rightarrow CBr_2F_2$). Hexachlorobenzene gave a complex mixture of addition compounds with composition approximating to $C_6Br_2Cl_4F_6$.[153] After further fluorination with antimony pentafluoride to an average composition $C_6BrCl_4F_7$, dechlorination with zinc and alcohol gave a little hexafluorobenzene, together with various chlorofluoro-cyclohexenes and -cyclohexadienes. Analogous reactions were carried out on pentachlorobenzotrifluoride.[153]

An interesting reaction[154] is that of a mixture of bromine trifluoride and bromine with halogeno-olefins; bromine and fluorine are added and the active species may well be bromine monofluoride ($CF_2{=}CH_2 \rightarrow CF_3{\cdot}CH_2Br$; $CF_3{\cdot}CF{=}CF_2 \rightarrow CF_3{\cdot}CFBr{\cdot}CF_3$).

Reactions of carbon with bromine and fluorine have been reported.[4-6]

Iodine fluorides. Iodine pentafluoride is the least reactive of the halogen fluorides, though some hydrogen-containing compounds are attacked vigorously. The most important reaction[152] has been that with carbon tetraiodide to give trifluoromethyl iodide. This is a source of trifluoromethyl radicals and from it the extensive work[83] on additions to unsaturated systems and syntheses of perfluoroalkyl derivatives has originated.

Tetraiodoethylene and iodine pentafluoride afforded pentafluoroethyl iodide.[152] A number of perfluoro-alkyl and -cycloalkyl iodides were made from perfluoro-olefins and iodine pentafluoride.[155] This addition of iodine and fluorine is best done[154] with a mixture of iodine and its pentafluoride:

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[149] Leech and Burnett, B.P. 633,678/1949; Burnett, B.P. 676,374/1952.
[150] Cuthbertson, Holmes, Musgrave, and Tanner, *J. Appl. Chem.*, 1958, **8**, 390.
[151] Farenden, ref. 143, p. 25.
[152] Banks, Emeléus, Haszeldine, and Kerrigan, *J.*, 1948, 2188.
[153] McBee, Lindgren, and Ligett, *Ind. Eng. Chem.*, 1947, **39**, 378.
[154] Chambers, Musgrave, and Savory, *Proc. Chem. Soc.*, 1961, 113.
[155] Simons and Brice, U.S.P. 2,614,131/1952.

hexafluoropropene gave heptafluoro-2-iodopropane, a source of the heptafluoroisopropyl radical and Grignard reagent. Carbon disulphide and iodine pentafluoride gave bistrifluoromethyl di- and tri-sulphide.[156] Iodine pentafluoride was apparently the best of the halogen fluorides for the fluorination[6] of carbon to give tetrafluoroethylene.

In general, the introduction of both fluorine and the other halogen complicates the reactions of halogen fluorides, complex mixtures being formed. Simple fluorination occurs only when a perhalogeno-compound is used with the corresponding halogen fluoride.

B(iv) Electrochemical Fluorination.—This process was devised by Simons,[157,158] and little new work on it has been reported since the last comprehensive review.[159] Many organic compounds, especially those containing polar groups, form conducting solutions in anhydrous hydrogen fluoride. When such a solution is electrolysed, hydrogen is evolved at the cathode and the organic compound is fluorinated, presumably at the anode. A cell such as that represented in Fig. 4 is used, the electrodes being a pack of alternate anodes and cathodes insulated by spacers. Anodes have been of nickel almost without exception, cathodes of nickel or iron. Cells have varied in size so that the current they can pass has ranged from 10 to 10,000 amp.;[158] voltages are usually between 5 and 7. Operating temperatures are generally close to 0° with an efficient condenser to return hydrogen fluoride (b.p. 19°) to the cell. The fluorinated product is

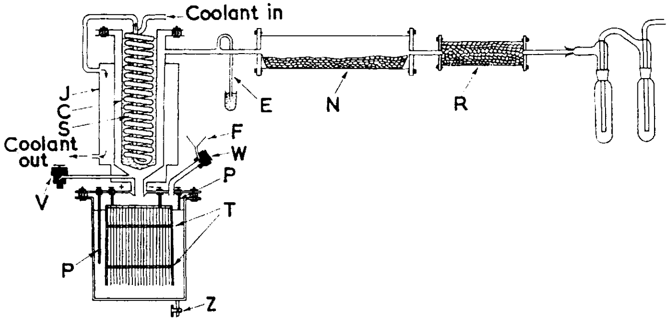

FIG. 4. *Cell for electrochemical fluorination.*

C, *Condenser;* E, *mercury safety valve;* F, *funnel for liquid additions;* J, *condenser jacket;* N, *sodium fluoride pellets;* P, *liquid-level probes;* R, *rubber pellets;* S. *cooling spiral;* T, *polytetrafluoroethylene spacers between anodes and cathodes;* V, *valve for addition of hydrogen fluoride;* W, *valve for liquid addition;* Z, *valve for draining cell.*
(*Reproduced, by permission, from Gramstad and Haszeldine,* J., 1956, 173.)

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[156] Haszeldine and Kidd, *J.*, 1953, 3219.

[157] Simons, *J. Electrochem. Soc.*, 1949, **95**, 47; Simons and his co-workers, *ibid.*, pp. 53, 55, 59, 64.

[158] Simons in "Fluorine Chemistry," Academic Press, New York, Vol. I, 1950, p. 414; Simons and Brice, *op. cit.*, Vol. II, 1954, p. 340.

[159] Burdon and Tatlow, "Advances in Fluorine Chemistry," Butterworths, London, 1960, Vol. I, p. 129.

usually insoluble and either distils over or may be run off from the bottom of the cell.

Hydrocarbons are difficult to fluorinate electrochemically since they are not very soluble in anhydrous hydrogen fluoride and the solutions are non-conducting. Suspensions or emulsions can be used, in the presence of conductivity additives. These may be of two types, fluoride salts, or compounds (water, alcohols, pyridine, carboxylic acids, etc.) which are themselves fluorinated as electrolysis proceeds. Though claims have been made for the fluorination of hydrocarbons,[157,158,160] details are few and it seems that this particular fluorination is not very efficient. However, though the great advantage of the electrochemical process is that many functional groups are retained during fluorination, fluorocarbons are in fact formed, sometimes in good yield, from almost all organic compounds. Alcohols, for example, form conducting solutions but lose their oxygen to give fluorocarbons.

With chlorohydrocarbons the same difficulties apply as with hydrocarbons, but it appears[161] that hydrogen is replaced before chlorine; thus, dichloromethane gave dichloro-fluoro- and -difluoro-methane. Bromine and iodine are lost very readily in electrochemical fluorination.

Ethers are fluorinated easily,[162] often in reasonable yields, to give the corresponding perfluoro-ether {*e.g.*, $(C_4H_9)_2O \rightarrow (C_4F_9)_2O$; $\overline{CH_2\cdot[CH_2]_n\cdot O} \rightarrow \overline{CF_2\cdot[CF_2]_n\cdot O}$ (n = 1—4)}. Cyclic perfluoro-ethers are also formed in the electrochemical fluorination of carboxylic acids. Though perfluoro-ethers are very inert chemically, their α-fluorine atoms can be replaced by chlorine and then hydrolytic removal of the chlorine gives carbonyl groups.[163]

All types of amine have been fluorinated electrochemically,[164,165] all of the hydrogen atoms, including those linked to nitrogen, being replaced. The products, perfluoronitrides, have no basic properties {$C_6H_5\cdot NH_2 \rightarrow [CF_2]_5{>}CF\cdot NF_2$; $[CH_2]_5{>}NH \rightarrow [CF_2]_5{>}NF$; $(C_4H_9)_3N \rightarrow (C_4F_9)_3N$}. A detailed study[166] of the electrochemical fluorination of pyridine and morpholine and their derivatives has been made, with nuclear magnetic resonance spectroscopy for the establishment of structures. 4-Isopropylpyridine gave heptadecafluoro-4-isopropylpiperidine containing some of the 4-n-propyl isomer, together with nitrogen trifluoride and a fluorocarbon (C_8F_{18}). The last product was largely perfluoro-(3-ethylhexane) and contained only a little of the product expected from loss of nitrogen—

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[160] Simons, U.S.P. 2,519,983/1950.

[161] Wolfe, U.S.P. 2,601,014/1952; B.P. 668,609/1952; B.P. 758,492/1956.

[162] Simons, B.P. 659,251/1951; U.S.P. 2,500,388/1950; Kauck and Simons, B.P. 672,720/1952; U.S.P. 2,594,272/1952.

[163] Tiers, *J. Amer. Chem. Soc.*, 1955, **77**, 4837, 6703, 6704.

[164] Simons, U.S.P. 2,490,098, 2,490,099/1949.

[165] Kauck and Simons, U.S.P. 2,616,927/1952, 2,631,151/1953.

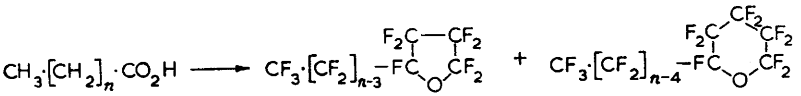
[166] Simmons, Hoffmann, Beck, Holler, Katz, Koshar, Larsen, Mulvaney, Paulson, Rogers, Singleton, and Sparks, *J. Amer. Chem. Soc.*, 1957, **79**, 3429.

perfluoro-(3-ethyl-2-methylpentane). Thus appreciable isomerisation of an isopropyl to an n-propyl group occurred, perhaps because the fluorination is a free-radical process.[159] Perfluoro-nitrides are very inert chemically, but reactions of them are now known. Pyrolysis of perfluoro-tertiary amines gives[167] azomethines:

$$(C_2F_5)_3N \xrightarrow{\text{Heat}} C_2F_5{\cdot}N = CF_2 + C_2F_5{\cdot}N = CF{\cdot}CF_3$$

Defluorination of perfluoropiperidines affords perfluoropyridines:[168]

Carboxylic acids and their anhydrides or acid fluorides give perfluorocarboxylic acid fluorides on electrochemical fluorination.[158,160,169,170] Best yields are given by acid fluorides. By-products are perfluoro-acid fluorides with fewer carbon atoms, and fluorocarbons, particularly those with the same number of carbon atoms as the starting acid and one less. From acids with sufficient carbon atoms, perfluorocyclic ethers are formed[171] often in good yield:



Though yields of perfluoro-acid fluorides have often been quite low, this fluorination has been of the utmost importance in making available the homologous series of fluorocarbon carboxylic acids and thence a wide variety of fluorocarbon derivatives.

Organic sulphides[172,173] and disulphides[173,174] have given, besides sulphur hexafluoride and fluorocarbons, corresponding to C–S bond rupture, bisperfluoroalkylsulphur tetrafluorides and perfluoroalkylsulphur pentafluorides, *e.g.*:

$$(CH_3)_2S \rightarrow (CF_3)_2SF_4 + CF_3{\cdot}SF_5$$

Carbon disulphide gave trifluoromethylsulphur pentafluoride.[175] The oxidation of sulphur to the sexivalent stage occurs early in the fluorina-

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[167] Pearlson and Hals, U.S.P. 2,643,267/1953.

[168] Burdon, Gilman, Patrick, Stacey, and Tatlow, *Nature*, 1960, **186**, 231; Banks, Ginsberg, and Haszeldine, *J.*, 1961, 1740.

[169] Kauck and Diesslin, *Ind. Eng. Chem.*, 1951, **43**, 2332.

[170] Diesslin, Kauck, and Simons, U.S.P. 2,567,011/1951; U.S.P. 2,593,737/1952; Scholberg and Bryce, U.S.P. 2,717,871/1955.

[171] Kauck and Simons, U.S.P. 2,644,823/1953; B.P. 718,318/1954.

[172] Clifford, El-Shamy, Emeléus, and Haszeldine, *J.*, 1953, 2372.

[173] Hoffmann and Simmons, with Beck, Holler, Katz, Koshar, Larsen, Mulvaney, Rogers, Singleton, and Sparks, *J. Amer. Chem. Soc.*, 1957, **79**, 3424; Dresdner, Reed, Taylor, and Young, *J. Org. Chem.*, 1960, **25**, 1464.

[174] Dresdner and Young, *J. Amer. Chem. Soc.*, 1959, **81**, 574.

[175] Silvey and Cady, *J. Amer. Chem. Soc.*, 1952, **74**, 5792.

tion.[174] Mercaptoacetic acid gave[176] very little of the expected product, $SF_5{\cdot}CF_2{\cdot}COF$, and rather more of the quadrivalent sulphur compound, $SF_3{\cdot}CF_2{\cdot}COF$. Sulphonyl chlorides and fluorides afforded[177] the corresponding perfluoroalkanesulphonyl fluorides (*e.g.*, $C_8F_{17}{\cdot}SO_2F$) in quite good yield, again the fluorocarbon being the main by-product.

In all of these fluorinations, aryl derivatives were saturated, giving perfluorocycloalkyl derivatives, yields were usually inferior to those obtained from aliphatic precursors, and some tarry products were formed.

The mechanism of electrochemical fluorination is obscure; some possibilities have been discussed,[159] but insufficient evidence is available at present to go beyond speculation. It seems likely that the reaction is of a free-radical type.

Electrochemical fluorination is undoubtedly a valuable process since so many compounds with functional groups can be made. However, yields are often poor and experimentally the method is not an easy one to apply.

Summarising the fluorination methods of group B: halogen fluorides are useful only if fluorohalogeno-compounds are required; reactions with elementary fluorine are often troublesome, though much valuable synthetic work has been done. Cobaltic fluoride is easy to use but limited in scope; and electrochemical fluorination is relatively difficult but gives a wide range of fluorocarbon derivatives. All of these methods require specialist apparatus and techniques, but so, to some degree, do many of the methods of group A. Methods of group B provide the only practicable synthetic routes to many perfluoro- and polyfluoro-compounds.

[176] Haszeldine and Nyman, *J.*, 1956, 2684.

[177] Brice and Trott, U.S.P. 2,732,398/1956; Gramstad and Haszeldine, *J.*, 1956, 173; 1957, 2640; Burdon, Farazmand, Stacey, and Tatlow, *J.*, 1957, 2574.