QUARTERLY REVIEWS

THE REACTIONS OF ORGANIC FLUORINE COMPOUNDS

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The chemistry of organic fluorine-containing compounds can be divided, historically, into three periods. The first extends up to 1939 and includes the most important pioneering work of Moissan, Ruff, Swarts, Henne, and Bigelow, dealing mainly with replacement of other halogens by fluorine,[1] and the early, comparatively ineffectual, direct fluorinations with elementary fluorine.[2] The second period came as a result of the impetus provided by the last war and resulted, with the discovery of efficient electrolytic methods for producing fluorine,[3] in the preparation of the perfluorocarbons and chloro-fluoro-compounds [4] for use mainly as buffer gases and lubricating oils in the separation of uranium isotopes by the diffusion method. The main object at that time was to produce particularly inert materials which would not be affected by uranium hexafluoride but, with the relaxation of this restriction, the third period started with highly successful attempts to prepare and examine the reactions of fluorocarbons and fluorohydrocarbons containing reactive groups. These are generally prepared by the Simons electrochemical fluorination method [5] or from fluorinated olefins and acids. At one time it seemed, because of the stability of some of the products, that this would result in a special, isolated, branch of organic chemistry but it is now known that other fluoro-compounds are highly reactive and apart from their intrinsic interest, their value as reagents in other branches of organic chemistry is now being realised. The uses of trifluoroacetic anhydride will be described later, others are 1-fluoro-2 : 4-dinitrobenzene which can be used for the characterisation of alcohols [6] or amines,[7] and 3-hydroxy-2 : 4 : 6-trinitrobenzotrifluoride which is a good reagent for the characterisation of primary, secondary, and tertiary amines and also forms pyrylium trifluoromethopicrates with pyranol bases.[8]

Fluorine-containing compounds have not yet found any outstanding

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[1] Henne, "Organic Reactions", John Wiley and Sons, New York, 1946, Vol. II, p. 49.

[2] Bigelow, *Chem. Reviews*, 1947, **40**, 51.

[3] Leech, *Quart. Reviews*, 1949, **3**, 22.

[4] Various authors, *Ind. Eng. Chem.*, 1947, **39**, 236–434 ; Slesser and Schram, "Preparation, Properties, and Technology of Fluorine and Organic Fluoro-compounds", McGraw-Hill, New York, 1951.

[5] Stacey, "Progress in Organic Chemistry", Butterworths, London, 1953, Vol. II, p. 29.

[6] Whalley, *J.*, 1950, 2241.

[7] Sanger, *Biochem. J.*, 1945, **39**, 507.

[8] Whalley, *J.*, 1950, 2792.

application as chemotherapeutic agents [9] but great success has been achieved in the field of toxicology with the monofluoroacetate convulsant poisons.[10] It seems that any compound, *e.g.*, esters, amides, acid halides, which can give rise to monofluoroacetic acid on hydrolysis or oxidation can act in this way. Acids and their derivatives of the series $F\cdot[CH_2]_n\cdot CO_2H$, when n is odd but not when n is even, are also effective. This confirms the theory that oxidation in the animal body occurs by loss of two carbon atoms at a time, *i.e.*, oxidation at the β-position with respect to the carboxyl group. Thus when n is odd such acids would eventually give monofluoroacetic acid while acids with even numbers of methylene groups would give rise to β-fluoropropionic acid. The monofluoroacetic acid is converted in the body into monofluorocitric acid, the real poison, which inhibits the citric acid metabolism.

The properties of almost all fluorine-containing compounds are dominated by the powerful electronic effects, inductive, mesomeric, and hyperconjugative, which can come into play and, now that a reasonable body of evidence has been built up, it is often possible, by using them, to explain known reactions and predict the properties of unknown compounds. This is not always so, however ; it is not easy to find an adequate explanation for the hydrolysis of α-trifluoromethylpropionic acid to methylmalonic acid while the corresponding alcohol, 2-trifluoromethylpropanol, is unaffected.[11]

Another point which is becoming apparent is that in some reactions such as Grignard formation, and Hofmann and Curtius degradations, the trifluoromethyl and pentafluoroethyl derivatives react differently from the higher members of the perfluoro-series.[12] There is insufficient evidence available to say more about this since it does not apply in every perfluoroalkyl series but some explanation will, no doubt, be offered soon.

In the discussions which follow, on the properties of some of these compounds, no mention has been made of absorption spectra but in many of the references quoted, and in others which have been devoted more or less entirely to this subject,[13] a body of evidence is being built up which will help considerably in future structural and analytical work.

Fluorocarbons.—The physical properties of the fluorocarbons are quite remarkable, surface tensions, boiling points, viscosities, and refractive indexes being very low and densities being high. They have low solubilities in the usual organic solvents, their insolubility in alcohol being used in separations from fluorohydrocarbons. These properties are probably due to the operation of low intermolecular and high intramolecular forces.[14, 15]

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[9] VanderWerf *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 654 ; 1950, **72**, 1886 ; Kraft, *Chem. Ber.*, 1951, **84**, 150 ; 1952, **85**, 577 ; *Angew. Chem.*, 1948, **60**, *A*, 248 ; Chapman and James, *J.*, 1953, 1865.

[10] Saunders, " The Chemistry and Toxicology of Organic Fluorine and Phosphorus Compounds ", R.I.C. Lectures, Monographs, and Reports, 1953, No. 1 ; Peters, *Endeavour*, 1954, **51**, 147.

[11] Buxton, Stacey, and Tatlow, *J.*, 1954, 366.

[12] Husted and Ahlbrecht, *J. Amer. Chem. Soc.*, 1953, **75**, 1605.

[13] Haszeldine, *Nature*, 1951, **168**, 1028 ; *J.*, 1953, 1757, 1764, 2525, 2622 ; 1954, 691.

[14] Grosse and Cady, *Ind. Eng. Chem.*, 1947, **39**, 367.

[15] McBee and Bechtol, *ibid.*, p. 380 ; Fowler *et al.*, *ibid.*, p. 375.

(a) *Aromatic.* The aromatic fluorocarbons perfluorobenzene and perfluorotoluene have been prepared in small amounts but chemical properties have not been recorded.[16]

(b) *Alkanes.* The main characteristic of fluorocarbons is the great stability of the C–F bond, by virtue of which they show remarkable thermal and chemical inertness, being quite stable to boiling concentrated acids, alkalis, and oxidising agents. The only reactions possible are those involving breakage of C–F or C–C bonds ; it is found that, in most reactions which involve the former, there is complete breakdown of the molecule as when they are heated with sodium or potassium at 400—500° to give carbon and alkali fluoride, or in treatment with sodium in liquid ammonia, processes which are used in their analysis.[17] Decomposition also occurs on heating above 400° with silica to give carbon dioxide and silicon tetrafluoride.[18]

Thermal fission of the C–C bonds can be effected at 600—650° if tertiary carbon atoms are involved. Perfluorodi*cyclo*hexyl when heated to this temperature with chlorine or bromine gives the corresponding halogenoundecafluoro*cyclo*hexane.[19] Since at this temperature there can be only slight dissociation of the chlorine or bromine into atoms it is assumed that first the bond between the two tertiary carbon atoms splits homolytically and then reaction with the halogen occurs. Support for this is gained by heating the compound with excess of toluene at the same temperature, when the free radicals formed abstract hydrogen from the toluene giving undecafluoro*cyclo*hexane and dibenzyl. The bond between the tertiary carbon atoms in perfluoro(*iso*propyl*cyclo*hexane) appears to react similarly but higher temperatures are needed to break bonds between primary, or primary and secondary, carbon atoms : when *n*-perfluorocarbons are heated with chlorine or bromine temperatures between 800° and 900° are required, mixtures of perfluoroalkyl halides being formed.[20] As would be expected, fission by fluorine occurs at lower temperatures during fluorination reactions, giving other fluorocarbons with smaller numbers of carbon atoms.[14]

Polymeric polyfluoro-compounds break down at lower temperatures, thermal degradation of polytetrafluoroethylene or polymonochlorotrifluoroethylene beginning at 450—600° and giving good yields of monomer together with some cyclic compounds.[21]

Hydrogenolysis of C–C bonds in fluorocarbons also needs temperatures of the order of 800°, mixtures of mono- and di-hydro-polyfluoro-compounds being formed. Octafluoropropane splits when heated with hydrogen at 800° in a carbon tube to give fluoroform, difluoromethane, pentafluoroethane,

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[16] McBee, Lindgren, and Ligett, *Ind. Eng. Chem.*, 1947, **39,** 378.

[17] Musgrave and Smith, *J.*, 1949, 3021 ; Miller, Hunt, and McBee, *Ind. Eng. Chem. Anal.*, 1947, **19,** 148.

[18] McKenna and Teston, *ibid.*, p. 193 ; Rice and White, *J. Amer. Chem. Soc.*, 1947, **69,** 267.

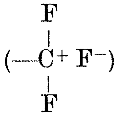
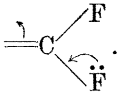
[19] Barlow and Tatlow, *J.*, 1952, 4695.

[20] Brice, Pearlson, and Simons, *J. Amer. Chem. Soc.*, 1949, **71,** 2499.

[21] Lewis and Naylor, *ibid.*, 1947, **69,** 1968 ; Benning and Park, U.S.P. 2,420,222.

and a little carbon. Even under these conditions 52% of the octafluoropropane remains unchanged.[22]

(c) *Alkenes.* The reactions of the fluorinated olefins follow the same general trend as those of the hydrocarbon olefins. They can be divided into (i) electrophilic addition, (ii) nucleophilic addition, (iii) radical addition, and (iv) polymerisation. In the hydrocarbons the electrophilic addition reactions predominate while in the fluorinated derivatives the nucleophilic reactions often proceed more easily. There are also differences in the polymerisation processes, the fluorinated olefins showing a tendency, which does not exist in the hydrocarbon and chlorinated analogues, to form cyclic dimers and short-chain polymers.

(i) Electrophilic addition of halogens,[1, 23] HBr,[24, 25] HCl,[26] HF,[27] ICl,[28] IBr,[29] halogenated paraffins,[28, 30] N_2O_4, NO_2Cl, NOCl, and NOBr[31] occurs with or without a catalyst such as $AlCl_3$, BF_3, or $ZnCl_2$ depending on the inertness of the olefin. In these reactions the polarisation of the double bond depends on the various electronic effects which are possible in the molecule. In many cases it is possible to predict the structure of an addition product bearing in mind such points as the strong positive inductive effect, the hyperconjugative effect  $(-\overset{\text{F}}{\underset{\text{F}}{\text{C}}}{}^{+}\ \text{F}^{-})$ of the trifluoromethyl group if it is present, and the mesomeric effect when a halogen is connected directly to a carbon atom which is unsaturated  $=\text{C}\langle^{\text{F}}_{\ddot{\text{F}}}$. Thus the reaction $CF_3{\cdot}CF{:}CF_2 + HBr \longrightarrow CF_3{\cdot}CHF{\cdot}CF_2Br$ occurs, as would be expected from a consideration of these points. In certain cases there are opposed electronic effects and the direction of addition has had to be settled by experiment :

$$CH_3{\cdot}CH{:}CF_2 + HF \rightarrow CH_3{\cdot}CH_2{\cdot}CF_3 \ ^{1}$$
$$CF_3{\cdot}CH{:}CH{\cdot}CO_2Et + HBr \rightarrow CF_3{\cdot}CHBr{\cdot}CH_2{\cdot}CO_2Et \ ^{32}$$
$$CF_2{:}CFCl + ICl \rightarrow CF_2Cl{\cdot}CFClI \ ^{28,\,29}$$

As would be expected from the electronegative nature of fluorine, in electrophilic additions the rate of addition decreases with increase in the number of fluorine atoms in the compound and, in the following compounds relative reactivities are : $CH_3{\cdot}CH{:}CH_2 > CF_3{\cdot}CH{:}CH_2 > CF_3{\cdot}CF{:}CF_2$.[33]

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[22] James, Pearlson, and Simons, *J. Amer. Chem. Soc.*, 1950, **72,** 1761.
[23] Coffmann, Reasch, Rigby, Barrick, and Hanford, *J. Org. Chem.*, 1949, **14,** 747.
[24] Henne, *J. Amer. Chem. Soc.*, 1951, **73,** 5527.
[25] Park *et al.*, *ibid.*, 1949, **71,** 2339. [26] Henne and Kaye, *ibid.*, 1950, **72,** 3369.
[27] Henne and Arnold, *ibid.*, 1948, **70,** 758.
[28] Barr, Gibson, and Lafferty, *ibid.*, 1951, **73,** 1352.
[29] Haszeldine, *J.*, 1952, 4423.
[30] Henne and Kraus, *J. Amer. Chem. Soc.*, 1951, **73,** 5303.
[31] Haszeldine, *J.*, 1953, 2075 ; Haszeldine and Jander, *J.*, 1954, 912.
[32] Walborsky and Schwartz, *J. Amer. Chem. Soc.*, 1953, **75,** 3241.
[33] Haszeldine, *J.*, 1953, 3559.

(ii) Nucleophilic addition occurs in presence of alkaline catalysts and, certainly in the case of highly fluorinated olefins, more readily than electrophilic addition. Amines,[23, 34] alcohols,[23, 24, 35–39] thiols,[40] phenols,[41, 42] bisulphites,[23, 43] and Grignard reagents [44] are added in the presence of basic catalysts such as sodium alkoxides, caustic alkali, potassium cyanide, benzyltrimethylammonium hydroxide, and borax. Again the direction of addition is predictable from the same considerations as in electrophilic attack. These reactions were first reported by Hanford and Rigby and were carried out at elevated temperatures under autogenous pressure but such drastic conditions are unnecessary and they usually proceed smoothly and with good results at room temperatures and atmospheric pressure:

$$\mathrm{CF_2{:}CClF + CH_3{\cdot}OH \xrightarrow{KOH} CH_3O{\cdot}CF_2{\cdot}CHFCl}$$

$$\mathrm{CF_2{:}CF_2 + R{\cdot}SH \xrightarrow{CH_2Ph{\cdot}NMe_3\}OH} RS{\cdot}CF_2{\cdot}CHF_2}$$

It has been shown that the formation of ethers from saturated fluorohalogenohydrocarbons occurs by the same mechanism, dehydrohalogenation occurring first, followed by addition of alcohol, since 2-chloro-1 : 1-difluoroethane gives the same product as 1-chloro-1 : 1-difluoroethane.[45]

$$\mathrm{CH_3{\cdot}CF_2Cl + EtO^- \rightarrow CH_2{:}CF_2 \xrightarrow{Et{\cdot}OH} CH_3{\cdot}CF_2{\cdot}OEt}$$

In all of these compounds, especially those formed by the addition of amines, the fluorine atoms on the α-carbon atom with respect to the nucleophilic group are quite labile and hydrolyse quite easily : [34, 37, 39]

$$\mathrm{CF_2{:}CFCl + R_2NH \rightarrow R_2N{\cdot}CF_2{\cdot}CHFCl \xrightarrow{H_2O}}$$
$$\mathrm{R_2N{\cdot}C(OH)_2{\cdot}CHFCl + 2HF \rightarrow R_2N{\cdot}CO{\cdot}CHFCl + H_2O}$$

$$\mathrm{R_2N{\cdot}CF_2{\cdot}CHFCl \xrightarrow{R'OH}}$$
$$\mathrm{R_2N{\cdot}C(OR')_2{\cdot}CHFCl + 2HF \rightarrow R_2N{\cdot}CO{\cdot}CHFCl + R'_2O}$$

In fact, if the addition is carried out at a high temperature the product is very often saturated owing to removal of hydrogen fluoride. This property is very pronounced in the case of perfluoro*cyclo*butene which adds these nucleophilic groups and then loses hydrogen fluoride spontaneously even at

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[34] Rapp, Pruett, Barr, Bahner, Gibson, and Lafferty, *J. Amer. Chem. Soc.*, 1950, **72,** 3646.

[35] Hanford and Rigby, U.S.P. 2,409,274.

[36] Pruett *et al.*, *J. Amer. Chem. Soc.*, 1950, **72,** 4480.

[37] Miller, Fager, and Griswold, *ibid.*, 1948, **70,** 431.

[38] Park, Vail, Lea, and Lacher, *ibid.*, p. 1550 ; Park, Sharrah, and Lacher, *ibid.*, 1949, **71,** 2337.

[39] Tarrant and Brown, *ibid.*, 1951, **73,** 1781.

[40] Pruett *et al.*, *ibid.*, 1950, **72,** 3642.

[41] *Idem*, *ibid.*, p. 4480.

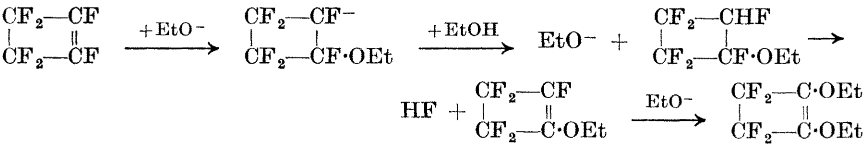
[42] Tarrant and Brown, *ibid.*, 1951, **73,** 5831.

[43] Kosher, Trott, and La Zerte, *ibid.*, 1953, **75,** 4594.

[44] Tarrant and Warner, *ibid.*, 1954, **76,** 1624.

[45] Tarrant and Young, *ibid.*, 1953, **75,** 932.

room temperature:[36, 46]



Only one molecule of a phenol adds to perfluoro*cyclo*butene. Tertiary amines do not react with straight-chain olefins and are used as catalysts in the addition of alcohols, etc., even to cyclic olefins such as C_4F_6,[36] but they can react with this, replacing fluorine and giving first a quaternary ammonium salt which hydrolyses easily, possibly to a betaine structure.[47, 48] *iso*Quinoline and 3-methyl*iso*quinoline have a similar effect [49] but pyridine simply produces dimers and trimers of the C_4F_6.[50]

(iii) Whereas electrophilic addition to fluorinated olefins, especially those containing the trifluoromethyl group, is often difficult owing to the drain of electrons from the double bond, and base-catalysed nucleophilic addition often leads to hydrolysis unless the reaction is carried out under very mild conditions, addition of free radicals generally proceeds quite smoothly and easily. Most of the results have been obtained by the addition of halogens, hydrogen bromide, and perfluoroalkyl iodides,[24, 29, 33, 51–59] where initiation of the addition is by halogen atoms or perfluoroalkyl radicals. The reactions have been started in some cases by heat and in others by the action of peroxides or light with or without the addition of mercury. It has been claimed that the presence of mercury does not affect the rate of addition [24] but there seems no doubt that it does. Addition of hydrogen bromide is quite straightforward and if, as is thought, the bromine atom initiates the reaction, we have

$$\mathrm{HBr} \xrightarrow[\text{heat}]{h\nu\ \text{or}} \mathrm{H}\cdot + \mathrm{Br}\cdot$$

$$\mathrm{Br}\cdot + \mathrm{CF_3{\cdot}CH{:}CH} \longrightarrow \mathrm{CF_3{\cdot}\dot{C}H{\cdot}CH_2Br}$$

$$\mathrm{CF_3{\cdot}\dot{C}H{\cdot}CH_2Br} + \mathrm{HBr} \longrightarrow \mathrm{CF_3{\cdot}CH_2{\cdot}CH_2Br} + \mathrm{Br}\cdot \text{ etc.}$$

There is apparently no tendency for the $\mathrm{CF_3{\cdot}\dot{C}H{\cdot}CH_2Br}$ radical to react with

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[46] Park, Snow, and Lacher, *J. Amer. Chem. Soc.*, 1951, **73**, 2342.

[47] Rapp, *ibid.*, p. 5901.

[48] Pruett, Bahner, and Smith, *ibid.*, 1952, **74**, 1633.

[49] *Idem*, *ibid.*, p. 1642.

[50] *Idem*, *ibid.*, p. 1638.

[51] Prober, *ibid.*, 1951, **73**, 4495.

[52] McBee, Pierce, and Chen, *ibid.*, 1953, **75**, 2324.

[53] Haszeldine, *J.*, 1949, 2856; Haszeldine, Leedham, and Steele, *J.*, 1954, 2040; Tarrant and Lovelace, *J. Amer. Chem. Soc.*, 1954, **76**, 3466.

[54] Haszeldine, *J.*, 1952, 2504.

[55] *Idem*, *J.*, 1953, 922.

[56] Haszeldine and Steele, *ibid.*, p. 1199.

[57] *Idem*, *ibid.*, p. 1592.

[58] Haszeldine, *ibid.*, p. 3565.

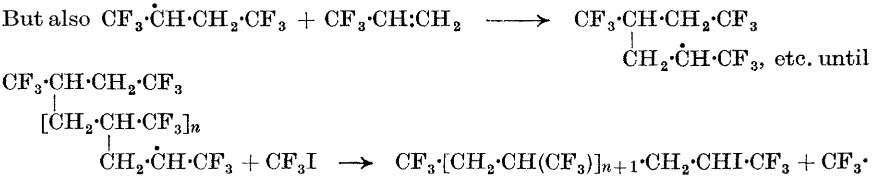
[59] *Idem*, *ibid.*, p. 3761.

another molecule of trifluoropropene but when trifluoroiodomethane is used instead of HBr this can happen and does do so in all known cases :

$$CF_3I \xrightarrow[\text{heat}]{h\nu\text{ or}} CF_3\cdot + I\cdot$$

$$CF_3\cdot + CF_3\cdot CH{:}CH_2 \longrightarrow CF_3\cdot\dot{C}H\cdot CH_2\cdot CF_3$$

$$CF_3\cdot\dot{C}H\cdot CH_2\cdot CF_3 + CF_3I \longrightarrow CF_3\cdot CHI\cdot CH_2\cdot CF_3 + CF_3\cdot,\ \text{etc.}$$



$$\text{But also } CF_3\cdot\dot{C}H\cdot CH_2\cdot CF_3 + CF_3\cdot CH{:}CH_2 \longrightarrow \begin{array}{l} CF_3\cdot CH\cdot CH_2\cdot CF_3 \\ \quad | \\ \quad CH_2\cdot\dot{C}H\cdot CF_3 \end{array}\text{, etc. until}$$

$$\begin{array}{l} CF_3\cdot CH\cdot CH_2\cdot CF_3 \\ \quad | \\ \quad [CH_2\cdot CH\cdot CF_3]_n \\ \qquad | \\ \qquad CH_2\cdot\dot{C}H\cdot CF_3 \end{array} + CF_3I \longrightarrow CF_3\cdot[CH_2\cdot CH(CF_3)]_{n+1}\cdot CH_2\cdot CHI\cdot CF_3 + CF_3\cdot$$

Similarly $CF_3I + CF_2{:}CF_2 \longrightarrow CF_3\cdot[CF_2\cdot CF_2]_n\cdot I$

and $CF_3I + CF_2{:}CFCl \longrightarrow CF_3\cdot[CF_2Cl]_n\cdot I$

The value of n can be controlled by varying the proportion of trifluoroiodomethane in the reaction mixture. Thus a molar ratio of trifluoroiodomethane to tetrafluoroethylene of 10 : 1 results in 94% of heptafluoroiodopropane. Equimolecular amounts give products with $n = 1, 2, 3$, and > 3 in 16, 10, 5, and 63% yields respectively. This method, using trifluoromethyl and pentafluoroethyl iodides with tetrafluoroethylene, can be used to give a complete series of perfluoroalkyl iodides but yields are good only if the series is ascended one step at a time, using a high proportion of perfluoroalkyl iodide to tetrafluoroethylene in order to ensure that a complex mixture is not obtained.[59]

The results indicate that the atom or radical initiating the process does not act as an electrophilic agent and add to the carbon atom of higher electron density,[60] but that the direction of addition is independent of the polarisation of the double bond :

$$CF_3\cdot CH{:}CH_2 + CCl_3I \xrightarrow[\text{heat}]{h\nu\text{ or}} CF_3\cdot CHI\cdot CH_2\cdot CCl_3\ ^{55}$$

$$CF_3\cdot CF{:}CF_2 + HBr \xrightarrow{h\nu} CF_3\cdot CHF\cdot CF_2Br\ ^{33}$$

$$R\cdot CH{:}CH_2 + CF_3I \longrightarrow CF_3\cdot CH_2\cdot CHIR$$

$$(R = Me,\ Cl,\ F,\ CO_2Me,\ CF_3,\ CN\ ^{56})$$

It seems probable that the product depends on the stability of the radical produced in the initial reaction, *e.g.*, $CF_3\cdot\dot{C}F\cdot CF_2Br$, must be more stable than $CF_3\cdot CFBr\cdot CF_2\cdot$ since radical addition of hydrogen bromide to hexafluoropropene gives $CF_3\cdot CHF\cdot CF_2Br$ and therefore, from experiment, that tertiary are more stable than secondary which are more stable than primary radicals.[58] (The terms primary, secondary, and tertiary refer to the number of atoms or groups other than hydrogen attached to the carbon atom carrying the odd electron.) However, results so far have not ruled out altogether the possible influence of the steric factor.

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[60] Hey and Waters, " Chemistry of Carbon Compounds ", Elsevier, Amsterdam, 1951, Vol. I*A*, p. 204.

(iv) Numerous long-chain polymers of the fluoro-olefins, such as polytetrafluoroethylene (Teflon), polymonochlorotrifluoroethylene (Kel-F), and mixed polymers containing vinyl fluoride, butadiene, styrene, etc., are known. These are prepared in the usual ways. Some of the possible polyfluorostyrenes have also been prepared.[61] Those polymers containing high proportions of fluorine are particularly stable and, because of their high cost, are generally used only where this stability is of the utmost importance.

Shorter-chain polymers can also be prepared by a process somewhat similar to the free-radical addition of perfluoroalkyl iodides to the fluorinated olefins. The process, which has been termed telomerisation, involves the polymerisation of the olefin, generally in presence of a peroxide catalyst, but sometimes of alkali or catalysts of the Friedel–Crafts type, together with some other molecule which causes chain termination.[62] Temperatures between 50° and 350° are used.

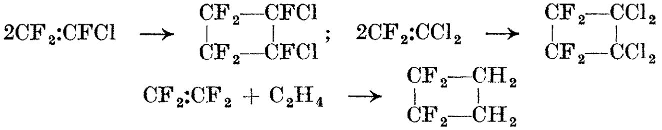
$$CF_2{:}CF_2 + C_2H_5{\cdot}SH \xrightarrow{\text{Peroxides}} H{\cdot}[CF_2{\cdot}CF_2]_n{\cdot}C_2H_4{\cdot}SH$$

$$C_2F_4 + CH_3{\cdot}OH \longrightarrow H{\cdot}[CF_2{\cdot}CF_2]_n{\cdot}CH_2{\cdot}OH \qquad (n = 1\text{—}8, \text{ and } 12)$$

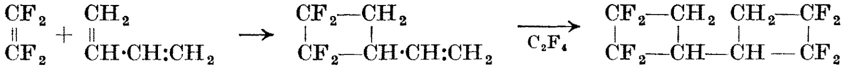
$$C_2F_4 + (EtO)_2P{\cdot}OH \longrightarrow H{\cdot}[CF_2CF_2]_n{\cdot}PO(OH)_2 \qquad \text{(after hydrolysis)}$$

The compounds used to terminate the chain have included alcohols, ethers, hydrocarbons, saturated halogen compounds, and saturated carbonyl compounds. In many cases where alkaline or Friedel–Crafts catalysts have been used the product has $n = 1$ almost entirely and it is probable that polar addition and not free-radical addition has occurred, but since so few details are given it is impossible to be definite about this. If conditions can be controlled so that values of n are limited, these reactions will be useful as sources of series of almost fully fluorinated compounds each with its characteristic group. They have been used commercially as lubricants, dielectrics, solvents, etc.

One reaction which appears to be characteristic of the fluorinated olefins is the ability to form cyclic dimers by head-to-head and tail-to-tail combination, not only among themselves, but also with non-fluorinated olefins:[63, 64]



With butadiene, formation of *cyclo*butanes occurs in preference to a Diels–Alder reaction:[63]



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[61] Prober, *J. Amer. Chem. Soc.*, 1953, **75**, 968.

[62] Hanford, U.S.P. 2,443,003; du Pont, B.P. 583, 874; Joyce, U.S.P. 2,559,628; Hanford and Joyce, U.S.P. 2,562,547; Bittles and Joyce, U.S.P. 2,559,754.

[63] Coffman, Barrick, Cramer, and Reasch, *J. Amer. Chem. Soc.*, 1949, **71**, 490.

[64] Henne and Ruh, *ibid.*, 1947, **69**, 279; Lacher, Tompkin, and Park, *ibid.*, 1952, **74**, 1693; Buxton, Ingram, Smith, Stacey, and Tatlow, *J.*, 1952, 3830.

Cyclic dimers do not appear to be formed by hydrocarbon or chlorinated olefins.

Other reactions of the fluorinated olefins are as follows. Compounds of the type $CF_3{\cdot}CH{:}CHX$ (X = Cl, Br, or I) lose HX on treatment with solid or alcoholic alkali, but reactions must be carried out at low temperatures or solvolysis of the allylic fluorine atoms occurs. Such compounds, with hydrogen atoms on the carbon atom adjacent to the trifluoromethyl group, lose the elements of halogen acid fairly readily because the inductive effect of the trifluoromethyl group makes ionisation of the hydrogen easier. A halogen atom in the adjacent position is more firmly bound and compounds such as $CF_3{\cdot}CHX{\cdot}CH_3$ or $CF_3{\cdot}CX{:}CH_2$ can be dehydrohalogenated only with difficulty.[65] In order to prepare acetylenes it is better to treat compounds of the type $CF_3{\cdot}CX{:}CHX$ with zinc and ethyl alcohol or glacial acetic acid.

Ketones can be prepared by oxidation of olefins of the type $CH_2{:}C(CF_3)_2$ but better yields result when one of the hydrogen atoms of the methylene group has been replaced by halogen.[58] Acids can be prepared by oxidation of olefins of the type $C_nF_{2n+1}{\cdot}CH{:}CHX$.[66] Hydrogenolysis of vinylic ethers gives mainly aldehydes :[67]

$$CF_3{\cdot}CH{:}CH{\cdot}OMe \xrightarrow{H_2} CF_3{\cdot}CH_2{\cdot}CHO$$

(d) *Alkynes.* After allowing for the deactivating influences of the trifluoromethyl group (inductive effect and hyperconjugation) on the triple bond, and the direction in which it guides the polarisation, the properties of those alkynes which have been investigated in any detail are very similar to those of the corresponding hydrocarbons. A hydrogen atom attached to carbon involved in the acetylenic link is acidic and gives rise to silver, cuprous, and mercury acetylides in the usual way,[68, 69] and from them the alkynes can be regenerated on treatment with acid. Similarly Grignard reagents (*e.g.*, $CF_3{\cdot}C{\vdots}C{\cdot}MgCl$) can be prepared.[69] Electrophilic addition [67] to trifluoromethylacetylene is slower than to propyne, and hexafluorobut-2-yne is even less reactive. The first of these can add halogen acids (except hydrogen iodide) smoothly without catalysts, to give $CF_3{\cdot}CH{:}CHX$, but the last needs such catalysts as boron trifluoride or aluminium trichloride and, even so, the reaction is slow. Addition of hydrogen cyanide to trifluoromethylacetylene is also slow and is carried out in the presence of potassium and cuprous chlorides. In no case is more than one molecule added.

Decreased activity towards electrophilic attack is accompanied by increased susceptibility to nucleophilic reagents.[67] Both alkynes add one molecule of methyl or ethyl alcohol below 0°, in the presence of the sodium alkoxide, and at higher temperatures (about 80°) add two molecules of alcohol although the process is accompanied by a certain amount of hydrolysis of the trifluoromethyl groups :

$$CF_3{\cdot}C{\vdots}CH \xrightarrow[20^\circ]{EtO^-} CF_3{\cdot}\overset{-}{C}{:}CH{\cdot}OEt \xrightarrow[80^\circ]{2EtOH} CF_3{\cdot}CH_2{\cdot}CH(OEt)_2 + EtO^-$$

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[65] Haszeldine, *J.*, 1951, 2495. [66] Haszeldine and Leedham, *J.*, 1953, 1548.

[67] Haszeldine, *J.*, 1952, 3490 ; Leedham and Haszeldine, *J.*, 1954, 1634.

[68] Haszeldine, *J.*, 1951, 588.

[69] Henne and Nager, *J. Amer. Chem. Soc.*, 1952, **74**, 650.

Diethylamine and *cyclo*hexylamine [70] can also be added easily in the presence of cuprous chloride, to give $CF_3{\cdot}CH{:}CH{\cdot}NEt_2$ and $CF_3{\cdot}CH{:}C(NEt_2){\cdot}CF_3$, etc.

Free-radical addition of hydrogen bromide and perfluoroalkyl halides gives the same products as does electrophilic addition. Addition of the former reagent seems unaffected by the deactivation of the molecules, as in the case of its reaction with hexafluorobut-2-yne, but addition of the latter proceeds more readily to alkylacetylenes than to perfluoroalkylacetylenes.[67] Trichloromethyl iodide has also been added to trifluoromethylacetylene under the influence of ultra-violet light, the product being an intermediate in the preparation of $\gamma\gamma\gamma$-trifluorocrotonic acid: [55]

$$CF_3{\cdot}C{\vdots}CH + CCl_3I \xrightarrow{h\nu} CF_3{\cdot}CI{:}CH{\cdot}CCl_3 \xrightarrow[\text{HCl}]{\text{Zn–}}$$
$$CF_3{\cdot}CH{:}CH{\cdot}CCl_3 \xrightarrow[\text{H}_2\text{SO}_4]{\text{Conc.}} CF_3{\cdot}CH{:}CH{\cdot}CO_2H$$

In view of the polarisation of the triple bond it was expected that hydration, by sulphuric acid in the presence of mercuric sulphate, of trifluoromethyl- and pentafluoroethyl-acetylene would give $\beta\beta\beta$-trifluoropropaldehyde and $\beta\beta\gamma\gamma\gamma$-pentafluorobutyraldehyde respectively: [71]

$$CF_3{\cdot}C{\vdots}CH + H_2O \longrightarrow CF_3{\cdot}CH{:}CH{\cdot}OH \longrightarrow CF_3{\cdot}CH_2{\cdot}CHO$$

but it was found that both the aldehyde and the corresponding ketone were produced, the latter being in greater yield:

$$CF_3{\cdot}C{\vdots}CH \xrightarrow[\text{temp.}]{\text{Room}} CF_3{\cdot}CH_2{\cdot}CHO\ (1\text{ part}) + CF_3{\cdot}CO{\cdot}CH_3\ (2\text{ parts})$$

there being two competing reactions:

$$(a)\ CF_3{\cdot}\overset{\delta-}{C}{\equiv}\overset{\delta+}{CH} + HgY_2 \longrightarrow CF_3{\cdot}C(HgY){:}CHY \xrightarrow[-HgY]{+H_2O}$$
$$CF_3{\cdot}CH{:}CH{\cdot}OH \longrightarrow CF_3{\cdot}CH_2{\cdot}CHO$$
$$(b)\ CF_3{\cdot}C{\equiv}CH + HgY_2 \longrightarrow CF_3{\cdot}C{\vdots}C{\cdot}HgY + HY$$

In the product from (*b*), the mercury exerts a greater influence on the triple bond than does the trifluoromethyl group, and addition of another molecule of mercuric sulphate occurs in the opposite direction from (*a*):

$$CF_3{\cdot}C{\vdots}C{\cdot}HgY + HgY_2 \longrightarrow CF_3{\cdot}CY{:}C(HgY)_2 \xrightarrow[-HY]{H_2O}$$
$$CF_3{\cdot}C(OH){:}CH_2 \longrightarrow CF_3{\cdot}CO{\cdot}CH_3$$

This scheme is supported by the formation of only 4 : 4 : 4-trifluorobutan-2-one from 1 : 1 : 1-trifluorobut-2-yne.[72] At higher temperatures (110—130°) any aldehyde formed as a result of reaction (*a*) is oxidised to the acid.

Fluorohalogenocarbons.—The most important of the fluorohalogenocarbons (" halogen " here excluding fluorine) are the perfluoroalkyl halides and of these the iodides are the most useful since the chlorides and bromides are quite unreactive, the chlorides in particular approaching the perfluorocarbons in inertness. This is illustrated by the activation energies (1·7, 2·3,

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[70] Pearson, *Chem. Abs.*, 1952, **46**, 1580.

[71] Haszeldine and Leedham, *J.*, 1952, 3483.

[72] *Idem*, *J.*, 1954, 1261.

and 7·4 kcal./mole respectively) required to convert trifluoromethyl iodide, bromide, and chloride into free radicals [73] and by attempts to prepare silicon derivatives from perfluoromethyl and perfluoroethyl chlorides and silicon or copper–silicon alloy [74] (there is little reaction at up to 500° and, at higher temperatures, complete decomposition with the formation of silicon halides).

The absence of the simple nucleophilic reactions of the alkyl halides results from the powerful electron attraction of the perfluoroalkyl groups. Thus, monochloroundecafluoro*cyclo*hexane does not react with aqueous alkali, metallic salts such as acetates, cyanides, or nitrates, or metals such as sodium and mercury, but reduction with lithium aluminium hydride occurs readily giving undecafluoro*cyclo*hexane.[75] Trifluoromethyl iodide does not react with moist silver oxide, potassium phthalimide, or metallic cyanides or nitrites at up to about 150° and at higher temperatures decomposition occurs. Its treatment with alcoholic potassium hydroxide gives fluoroform, showing that heterolytic fission gives the negative trifluoromethyl ion and positive iodide ion. The pure liquid trifluoromethyl and pentafluoroethyl iodides are not appreciably ionised but the existence of ions in alcoholic solution is deduced from exchange with sodium iodide containing radioactive iodine : [76]

$$\begin{aligned} CF_3I &\rightleftharpoons CF_3^- + I^+ \\ I^+ + {}^*I^- &\rightleftharpoons I_2 \rightleftharpoons {}^*I^+ + I^- \\ CF_3^- + {}^*I^+ &\rightleftharpoons CF_3{}^*I \end{aligned}$$

(*I represents the radioactive atom)

The way in which fission occurs can however be influenced by solvents and, in the presence of electron donors (straight-chain or cyclic ethers), Grignard reagents [77] and organozinc [78] compounds can be prepared at low temperatures, a complex being postulated in which electrons from the solvent cause the carbon–iodine bond to behave as in an alkyl iodide. Probably the same mechanism holds in the formation of perfluoropropyl-lithium [79] by exchange between methyl-lithium and perfluoropropyl iodide in ether at about – 40°, and also in the Wurtz-type reaction where two molecules of halogeno-compounds such as perfluoropropyl iodide or bromotetrachlorotrifluoropropane are combined in dioxan, ethyl alcohol, or acetic anhydride.[57, 80] The removal of halogen by zinc with the formation of a double bond is carried out in the same solvents at higher temperatures.[57]

Other reactions of the fluorohalogenocarbons are radical reactions. The perfluoroalkyl iodides are particularly suitable as a source for the study of perfluoroalkyl radicals since only light or heat is required for their dissociation, peroxide or other initiators can be avoided, and initiation of reactions

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[73] Hodgins and Haines, *Canad. J. Chem.*, 1952, **30**, 473.

[74] Izard and Kwalek, *J. Amer. Chem. Soc.*, 1951, **73**, 1156.

[75] Tatlow and Worthington, *J.*, 1952, 1251.

[76] Banus, Emeléus, and Haszeldine, *J.*, 1951, 60.

[77] Haszeldine, *J.*, 1952, 3423 ; Henne and Francis, *J. Amer. Chem. Soc.*, 1953, **75**, 992 ; Pierce and Levine, *ibid.*, p. 1254 ; Pierce, Meiners, and McBee, *ibid.*, p. 2516 ; Haszeldine, *J.*, 1954, 1273.

[78] Haszeldine and Walaschewski, *J.*, 1953, 3607.

[79] Pierce, McBee, and Judd, *J. Amer. Chem. Soc.*, 1954, **76**, 474.

[80] Henne, *ibid.*, 1953, **75**, 5750.

by iodine atoms is unlikely.[81] Some of the addition reactions to fluoroalkenes and -alkynes have already been mentioned but similar additions to simple alkenes [53] and alkynes [82] take place and this technique has been particularly fertile as a source of intermediates in the production of fluorinated olefins, acetylenes, acids, and ketones. Although reactions are slow, yields are good and it is claimed that the presence of mercury in the reaction mixture to prevent recombination of the radicals results in a lowering of the minimum temperature for complete reaction by 20—30° in the case of the thermal reactions, and increases the yields in the case of photosensitised reactions.[83] Di-iodides, such as perfluoroethylene di-iodide, and secondary iodides react similarly to the mono-iodides with olefins and acetylenes.[84]

Other organometallic and organometalloid compounds can be prepared by using free radicals. Arsenic and trifluoromethyl iodide at about 200° give mixtures of tristrifluoromethylarsenic, bistrifluoromethylarsenic iodide, and trifluoromethylarsenic di-iodide.[85] Phosphorus [86] reacts similarly, and mercury gives trifluoromethylmercuric iodide if mercury is used alone but bistrifluoromethylmercury if silver, copper, or cadmium amalgam is used.[87] Sulphur gives a mixture of bistrifluoromethyl di-, tri-, and tetra-sulphide, the disulphide being the main product.[88]

Other radical reactions include reduction to the monohydrofluorocarbon,[57] photochemical halogenation which may be initiated by halogen atoms or by perfluoroalkyl radicals, reaction with fluorinating agents to give perfluorocarbons,[89] and abstraction of hydrogen or halogen atoms from solvents.[83] The trifluoromethyl radical removes hydrogen from ethyl alcohol with the formation of fluoroform and acetaldehyde :

$$CF_3\cdot + CH_3\cdot CH_2\cdot OH \longrightarrow CHF_3 + CH_3\cdot\dot{C}H\cdot OH$$
$$2CH_3\cdot\dot{C}H\cdot OH \longrightarrow CH_3\cdot CH_2\cdot OH + CH_3\cdot CHO$$

and chlorine from carbon tetrachloride to give monochlorotrifluoromethane and hexachloroethane in good yield. Of other radicals, the less reactive such as $Ph_3C\cdot$, $Ph\cdot CH_2\cdot$ and $Me_3C\cdot$ do not, but the more reactive, *e.g.*, $CH_3\cdot$ and $Ph\cdot$, do react similarly.

The free-radical reaction with cyanogen gives cyanogen iodide and perfluoropropane or perfluorobutane, depending on whether trifluoromethyl or pentafluoroethyl iodide is used.[83] No perfluoroalkyl cyanide is formed. Nitric oxide gives perfluoroalkylnitroso-compounds in the form of blue gases which unlike their hydrocarbon analogues do not isomerise or dimerise and are easily oxidised to the perfluoronitro-compounds.[31, 90]

[81] Haszeldine, *J.*, 1951, 2504. [82] *Idem*, *J.*, 1950, 2789, 3037 ; 1952, 3483.

[83] Banus, Emeléus, and Haszeldine, *J.*, 1950, 3041.

[84] Haszeldine, *Nature*, 1951, **167**, 139.

[85] Brandt, Emeléus, and Haszeldine, *J.*, 1952, 2552.

[86] Bennett, Emeléus, and Haszeldine, *J.*, 1953, 1565.

[87] Emeléus and Haszeldine, *J.*, 1949, 2953.

[88] Brandt, Emeléus, and Haszeldine, *J.*, 1952, 2198.

[89] Haszeldine, *J.*, 1953, 3761. [90] Banus, *J.*, 1953, 3755.

Organometallic and Organometalloid Compounds.—*Magnesium.* The value of fluorohydro- and perfluoro-Grignard reagents for synthesis has always been appreciated, but earlier attempts at their preparation were always unsuccessful unless at least two carbon atoms with no fluorine attached intervened between any perfluoroalkyl group present and the reactive chlorine, bromine, or iodine atom.[91] Thus, compounds such as $C_3F_7{\cdot}CH_2{\cdot}CH_2Cl$ and $CF_3{\cdot}C_6H_4Br$ formed Grignard reagents under normal conditions at room temperature, but if the above condition was not fulfilled there was either no reaction or a vigorous reaction with the formation of an olefin. All of the perfluoroalkyl iodides except trifluoromethyl iodide, and compounds such as 2 : 2 : 2-trifluoroethyl iodide, react vigorously at room temperature in ether, to give olefins.[77, 91] For isolation of the Grignard reagent reaction must be carried out at temperatures of about − 60°. Above this, the compound rapidly breaks down with the formation of negative ions which lose fluorine and form the olefin :

$$C_3F_7{\cdot}MgI \longrightarrow C_3F_7^- + MgI^+ \longrightarrow C_3F_6 + MgIF$$
$$CF_3{\cdot}CH_2{\cdot}MgI \longrightarrow CF_3{\cdot}CH_2^- \longrightarrow CF_2{:}CH_2 + F^-$$

Other factors which appear to influence the yield are the use of pure magnesium and a large excess of a solvent which is an electron donor and, if these conditions are fulfilled, up to 65% yields of the Grignard reagent are obtained. The preparation of trifluoromethylmagnesium iodide is the most difficult to reproduce. In view of the instability of these compounds the common practice is to prepare them in the presence of the compound with which they are to react, and it is found that under these conditions most of the reactions are normal and, although reaction may be slow because of the low temperatures, overall yields are generally of the order of 45—50%. Most of the work to date has been with perfluoro-*n*-propylmagnesium iodide which reacts normally with active hydrogen, formaldehyde, acetone, carbon dioxide, and hydrocarbon esters, to give heptafluoropropane, heptafluorobutanol, 2-heptafluoropropylpropan-2-ol, heptafluorobutyric acid, and tertiary alcohols respectively.[77, 84, 92] In regard to reactions with fluorocarbon aldehydes, ketones, esters, and acid chlorides, opinions differ and in certain cases it is said that no reaction occurs or, at any rate, that reaction does not proceed beyond the ketone stage.[77] There are two reasons for this : first, the reaction with the carbonyl group depends on the polarisation $>C\overset{\frown}{=}O$ and this is opposed by the inductive effect of the perfluoroalkyl groups. Consequently reactions with aldehydes and ketones are very slow at the low temperatures employed and, if the temperature is raised side reactions occur to lower the yield. Secondly, reduction of the aldehyde or ketone by the Grignard reagent also occurs and gives the respective primary or secondary alcohols. As a result it is not unlikely that failure to prepare secondary or tertiary alcohols from fluorocarbon aldehydes or ketones respectively has been due to one or both of these factors. Reduction of

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[91] Henne, *J. Amer. Chem. Soc.*, 1938, **60**, 2275 ; Gilman and Jones, *ibid.*, 1943, **65**, 2047 ; McBee and Truchan, *ibid.*, 1948, **70**, 2910.

[92] Haszeldine, *J.*, 1953, 1748.

aldehydes and ketones by the hydrocarbon Grignard reagent occurs by formation of a complex between the Grignard reagent and the carbonyl compound, followed by intramolecular rearrangement with migration of H^-,[93] but no adequate explanation has yet been given of the reducing action of perfluoro-Grignard.[92]

Fluorohydro-Grignard reagents, but not, so far, perfluoro-Grignard reagents, have been used to yield organosilicon derivatives : [94]

$$C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}MgBr + SiCl_4 \longrightarrow (C_3F_7{\cdot}CH_2{\cdot}CH_2)_3SiCl$$

$$C_3F_7{\cdot}CH_2{\cdot}CH_2{\cdot}MgBr + Si(OEt)_4 \longrightarrow (C_3F_7{\cdot}CH_2{\cdot}CH_2)Si(OEt)_3 + (C_3F_7{\cdot}CH_2{\cdot}CH_2)_2Si(OEt)_2$$

Hydrolysis of chlorine or ethoxyl groups in these products gives the hydroxy-compounds.

Zinc. Heptafluoropropylzinc iodide [78] is prepared more or less in the same way as the Grignard compound, but it is much more stable than the Grignard reagent and, although better yields are obtained at lower temperatures, the preparation has been carried out quite satisfactorily at 70°. Evaporation of the dioxan solution leaves a molecular complex, $C_3F_7ZnI,C_4H_8O_2$, from which the pure organometallic compound can be isolated by sublimation. Isolation incurs considerable wastage, decomposition occurring by the same mechanism as for fluoro-Grignard reagents. Like the hydrocarbon analogues these organozinc halides should be useful for the preparation of fluoro-ketones because reaction with acid chlorides etc., stops there, whereas the Grignard reagents react further to give the tertiary alcohols. It is interesting that the perfluoro-Grignard reagents are more reactive than their hydrocarbon counterparts while the zinc and mercury derivatives are less reactive towards functional groups.

Lithium. Lithium perfluoroalkyls [95] are prepared by exchange between methyl-lithium and the perfluoroalkyl iodide at low temperatures in ether. Although trifluoromethyl iodide reacts under these conditions there is no evidence that trifluoromethyl-lithium is produced, and workers have concentrated on heptafluoro-*n*-propyl-lithium which decomposes even at low temperatures, as do the Grignard reagents, into hexafluoropropene and lithium fluoride ; it reacts normally with propaldehyde, acetone, benzaldehyde, acetyl chloride, ethyl heptafluorobutyrate, and diethylsilicon dichloride but does not react with benzophenone or perfluorobutyraldehyde. With organolithium compounds, as with Grignard reagents, there is always the possibility of the catalysis, with consequent reduction in the yield of useful product, of aldol condensations when compounds of suitable structure are present.

Mercury. Diperfluoroalkyl mercurials are less stable to heat than are the dialkyl compounds [87] and serve as an excellent source of free perfluoroalkyl radicals on heating or photolysis.[83] They, or the perfluoroalkylmercuric halides, react with halogens to form the corresponding perfluoro-

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[93] Swain and Boyles, *J. Amer. Chem. Soc.*, 1951, **73**, 870.
[94] Pierce, McBee, and Cline, *ibid.*, 1953, **75**, 5618.
[95] Pierce, McBee, and Judd, *ibid.*, 1954, **76**, 474.

alkyl halide and mercuric halide. A solution of bistrifluoromethylmercury in water is reduced by zinc or magnesium amalgam and water to fluoroform. Neither bistrifluoromethylmercury nor trifluoromethylmercuric iodide reacts with magnesium or zinc to give organometallic compounds.[87]

Arsenic. Arsenicals such as 3 : 4-difluorophenylarsonic acid have been prepared in the usual way from the diazonium compounds,[96] and their chemotherapeutic properties have been tested ; but so far nothing of outstanding importance has arisen and, chemically, the perfluoroalkyl arsenicals are more interesting. These are prepared by slow thermal free-radical reactions between the perfluoroalkyl iodides and arsenic, the main product being tristrifluoromethylarsenic, when trifluoromethyl iodide is used, together with small amounts of the bis- and mono-trifluoromethylarsenic iodides.[85] These iodides undergo disproportionation on heating, and tristrifluoromethylarsenic gives the iodides when heated with iodine. All of these trifluoromethylarsenic compounds, unlike their hydrocarbon analogues, are hydrolysed easily on treatment with aqueous alkali, with the liberation of fluoroform, the strong inductive effect of the trifluoromethyl group making the central atom susceptible to nucleophilic attack. This is characteristic of compounds of the type $M(CF_3)_n$ and $M(CF_3)_{n-m}X_m$, where M is As, P, or Hg and X is halogen or pseudohalogen. This susceptibility is decreased on the replacement of the trifluoromethyl groups by methyl groups as in methylbistrifluoromethylarsenic which is prepared from tristrifluoromethylarsenic and methylmagnesium iodide.[97] Treatment of bistrifluoromethylarsenic iodide with mercury at room temperature gives perfluorocacodyl $(CF_3)_2As{\cdot}As(CF_3)_2$, which is also hydrolysed by sodium hydroxide :[85]

$$\begin{aligned}(CF_3)_2As{\cdot}As(CF_3)_2 &\xrightarrow{\text{Hydrol.}} (CF_3)_2AsH + (CF_3)_2As{\cdot}OH\\ (CF_3)_2AsH &\xrightarrow{\text{Hydrol.}} CHF_3 + F^- + CO_3^{--}\\ (CF_3)_2As{\cdot}OH &\xrightarrow{\text{Hydrol.}} 2CHF_3\end{aligned}$$

This reaction is general for compounds of the formula $(CF_3)_2M{\cdot}M(CF_3)_2$ where M is As, P, or S.

The perfluoroalkylarsenic iodides can also be reduced to the hydrides by lithium aluminium hydride or zinc and hydrochloric acid, and the monoiodide undergoes oxidative hydrolysis by hydrogen peroxide to bistrifluoromethylarsenic acid.

Tristrifluoromethylarsenic does not form quarternary compounds.

Phosphorus. Perfluoroalkyl derivatives of phosphorus[86] are very similar to those of arsenic.

Sulphur. The perfluoroalkyl derivatives of sulphur are rather different from those of arsenic and phosphorus. Bistrifluoromethyl disulphide[88] is rapidly and completely hydrolysed by aqueous alkali, but gives no fluoroform. Its photolysis results in bistrifluoromethyl sulphide which is quite stable to alkali, and treatment with ultra-violet light in the presence of

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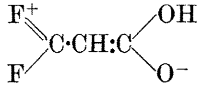
[96] Helin and VanderWerf, *J. Amer. Chem. Soc.*, 1951, **73,** 5884.

[97] Emeléus, Haszeldine, and Walaschewski, *J.*, 1953, 1552.

mercury gives bis(trifluoromethylthio)mercury. The latter gives trifluoromethanethiol[98] with hydrochloric acid, and this also is rapidly hydrolysed by aqueous alkali or more slowly by water, all the fluorine becoming fluoride ion. Both bis(trifluoromethylthio)mercury and bistrifluoromethyl disulphide with chlorine give trifluoromethanesulphenyl chloride, a compound which is relatively stable, unlike the alkanesulphenyl chlorides few of which are known. Trifluoromethanesulphenyl chloride reacts with trifluoromethanethiol to give bistrifluoromethyl disulphide and with hydrogen sulphide to give bistrifluoromethyl trisulphide.

Trifluoromethylsulphur pentafluoride[99] has been prepared and is very stable, 6N-sodium hydroxide having no action on it, but the monohydrogen compound $CSHF_7$ is hydrolysed immediately and completely under the same conditions. Mixed derivatives such as methyl trifluoromethyl sulphide, chlorodifluoromethyl methyl sulphide, and chloromethyl trifluoromethyl sulphide have been made by fluorination of chloro-compounds.[100] They can be oxidised by chromic acid to the sulphones.

Carboxylic Acids and their Derivatives.—The saturated perfluoro-acids approach the mineral acids in strength because of the strong electron attraction of the perfluoroalkyl group, but the presence of a double bond in the α-position reduces the acid strength considerably owing to mesomerism of the type  ${}^{F^{+}}_{F}\!>\!C\cdot CH{:}C\!<^{OH}_{O^{-}}$. The presence of fluorine instead of hydrogen on the α-carbon atom counterbalances this by its inductive effect but the mesomerism still predominates, $CF_2{:}CF\cdot CO_2H$ being a much weaker acid than $CCl_2{:}CCl\cdot CO_2H$.[101]

The strength of the saturated acids is also shown by the formation of addition compounds with ethers and amines[102] of the types : $3CF_3\cdot CO_2H,2Et_2O$; $2C_3F_7\cdot CO_2H,Et_2O$; $3CF_3\cdot CO_2H,NPhMe_2$; $5C_3F_7\cdot CO_2H,NPhMe_2$. They are formed simply by mixing the components at room temperature and fractionating. Some are hydrolysed rapidly in water but others are not hydrolysed even by hot water in a sealed tube. There is probably oxonium or nitronium salt formation with the proton of the acid and also hydrogen bonding between the fluorine atoms and the hydrogen of the ether or amine. It may be that the complexes $RN_2{}^+\{CF_3\cdot CO_2{}^-,CF_3\cdot CO_2H$ formed when amines are diazotised in trifluoroacetic acid[103] are similar in structure.

The fluorocarbon acids furnish the usual derivatives which, on the whole, behave in a normal manner. Salts are prepared quite normally and can be decomposed under a variety of conditions to give useful fluorocarbon intermediates. Many (Na, K, Hg^{II}, Pb, Ba, and Ag) decompose when heated with an excess of halogen, to give the perfluoroalkyl halide, but the silver salts are the best since they decompose at moderate temperatures (*ca.* 100°)

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

[99] Silvey and Cady, *J. Amer. Chem. Soc.*, 1950, **72**, 3624.

[100] Truce, Bircum, and McBee, *ibid.*, 1952, **74**, 3594.

[101] Henne and Fox, *ibid.*, 1951, **73**, 2323 ; 1953, **75**, 5750 ; 1954, **76**, 479.

[102] Hauptschein and Grosse, *ibid.*, 1951, **73**, 5139.

[103] Pettit, Stacey, and Tatlow, *J.*, 1953, 3081.

and are easily obtained dry.[104–106] The reaction, which is general for silver salts of organic acids,[107, 108] proceeds *via* the perfluoroacyl hypohalite and, if carried out under suitable conditions (nitrobenzene solution or in the compound to be halogenated), can be stopped at this stage and the hypohalite can be used as a source of positive halogen ion for reactions such as the halogenation of benzene and its derivatives.[104, 109] These substitutions occur in positions which would be predicted by the electronic theory. Heating the hypohalite gives the perfluoroalkyl halide :

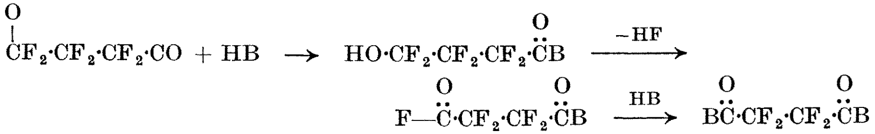
$$CF_3\cdot CO_2Ag + X_2 \longrightarrow CF_3\cdot CO_2X + AgX \longrightarrow CF_3X + CO_2$$
$$(X = Cl,\ Br,\ \text{or}\ I)$$

A similar reaction with nitrosyl chloride gives an alternative, although poor, method for the preparation of nitroso- and nitro-compounds.[110] The virtue of the method lies only in that it avoids the isolation of the perfluoroalkyl iodide and its irradiation in the presence of the nitroysl chloride as previously described :

$$C_nF_{2n+1}\cdot CO_2Ag + NOCl \longrightarrow C_nF_{2n+1}\cdot CO_2\cdot NO + AgCl \longrightarrow C_nF_{2n+1}\cdot NO + C_nF_{2n+1}\cdot NO_2$$

Trifluoroacetyl, pentafluoropropionyl, and possibly heptafluorobutyryl hypofluorites [111] have also been prepared by the action of fluorine on the corresponding perfluoro-acid in the presence of water but they are explosive and no reactions are yet known apart from the liberation of iodine from potassium iodide solution.

The silver salts of dibasic acids also decompose in the presence of excess of halogen to give dihalides, but in certain cases side reactions may occur. Thus silver perfluoroglutarate also gives perfluoro-γ-butyrolactone by cyclisation of the intermediate silver perfluoro-γ-iodoglutarate,[112, 113] and some workers claim a similar reaction with silver perfluoroadipate. As is to be expected from the reactions of the highly fluorinated esters, these lactone rings are broken very easily by water, alkali, alcohols, ammonia, halogen acids, or thiols to give the corresponding derivative of the lower dibasic acid : [105, 113]



$$\overset{\overset{\text{O}}{|}}{\text{C}}F_2\cdot CF_2\cdot CF_2\cdot CO + HB \longrightarrow HO\cdot CF_2\cdot CF_2\cdot CF_2\cdot\overset{O}{\ddot{C}}B \xrightarrow{-HF} F\text{—}\overset{O}{\ddot{C}}\cdot CF_2\cdot CF_2\cdot\overset{O}{\ddot{C}}B \xrightarrow{HB} B\overset{O}{\ddot{C}}\cdot CF_2\cdot CF_2\cdot\overset{O}{\ddot{C}}B$$

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[104] Henne and Finnegan, *J. Amer. Chem. Soc.*, 1950, **72**, 3806.

[105] Hauptschein and Grosse, *ibid.*, 1951, **73**, 2461.

[106] Henne and Zimmer, *ibid.*, p. 1362 ; Brice and Simons, *ibid.*, p. 4016 ; Crawford and Simons, *ibid.*, 1953, **75**, 5337 ; Haszeldine, *J.*, 1951, 584.

[107] Klewberg, *Chem. Reviews*, 1947, **40**, 381.

[108] Haszeldine, *J.*, 1952, 4259.

[109] Haszeldine and Sharpe, *J.*, 1952, 993.

[110] Haszeldine and Jander, *J.*, 1953, 4172.

[111] Cady and Kellog, *J. Amer. Chem. Soc.*, 1953, **75**, 2501 ; Menefee and Cady, *ibid.*, 1954, **76**, 2020.

[112] Haszeldine, *Nature*, 1951, **168**, 1028.

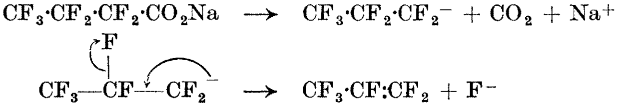
[113] Hauptschein, Stokes, and Grosse, *J. Amer. Chem. Soc.*, 1952, **74**, 1974.

Thermal decomposition of the silver salts alone occurs in two steps *via* the anhydride, and it has been suggested, by a free-radical mechanism, to give the fluorocarbon with twice as many carbon atoms as were present in the perfluoroalkyl radical of the silver salt : [114]

$$2C_nF_{2n+1}\cdot CO_2Ag \longrightarrow (C_nF_{2n+1}\cdot CO)_2O + Ag_2O \longrightarrow C_{2n}F_{4n+2} + 2Ag + 2CO_2$$
$$(n = 1\text{—}3)$$

The presence of silver oxide is essential in the second stage.

In the case of the sodium salts, thermal decomposition of those with three or more carbon atoms gives the perfluoro-olefin with the double bond in terminal position.[108, 115] Potassium and alkaline-earth-metal salts behave in much the same way but the potassium salts are liable to give mixtures of olefins, *e.g.*, potassium perfluorovalerate gives a mixture of perfluorobut-1- and -2-ene in the ratio 1 : 4.[116] These salts, unlike the silver salts, appear to undergo heterolytic fission, sodium being more electropositive than silver : [114]



$$CF_3\cdot CF_2\cdot CF_2\cdot CO_2Na \longrightarrow CF_3\cdot CF_2\cdot CF_2^- + CO_2 + Na^+$$
$$CF_3\text{—}\overset{F}{\overset{|}{C}}F\text{—}CF_2^- \longrightarrow CF_3\cdot CF{:}CF_2 + F^-$$

When heated alone, sodium trifluoroacetate gives a mixture of trifluoroacetyl fluoride and trifluoroacetic anhydride, but in water or glycol it, and the sodium salts of the higher perfluoro-acids, are decarboxylated to the perfluoromonohydrocarbons.[116, 117]

Acid halides are prepared from the perfluoro-acids by using phosphorus halides [118] or, if the boiling point of the chloride is lower than that of benzoyl chloride, it can be prepared with this reagent.[119] Their treatment with ammonia gives the amide [120] which can be reduced to a mixture of the corresponding amine $R\cdot CH_2\cdot NH_2$ and perfluoro-aldehyde $R\cdot CHO$ with lithium aluminium hydride.[121] Reduction of the acid chloride with hydrogen and poisoned palladised charcoal gives a mixture of alcohol and aldehydrol ; [121] another method of preparing aldehydes is by the vapour-phase Rosenmund reduction of the acid chloride.[122] Ketones can be prepared from the acid chlorides by the Friedel–Crafts method [123] and by reaction with Grignard reagents,[77] alkylzinc halides,[78] or alkyl- or aryl-cadmium.[124] They also react with diazomethane to give diazo-ketones and thence higher acids by the Arndt–Eistert technique.[125]

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[114] Kirshenbaum, Strong, and Hauptschein, *J. Amer. Chem. Soc.*, 1953, **75**, 3141.
[115] Hals, Reid, and Smith, *ibid.*, 1951, **73**, 4054.
[116] La Zerte, Hals, Reid, and Smith, *ibid.*, 1953, **75**, 4525.
[117] Auerbach, Verlock, and Henne, *ibid.*, 1950, **72**, 299.
[118] Simons and Ramler, *ibid.*, 1943, **65**, 389.
[119] Henne, Alm, and Smook, *ibid.*, 1948, **70**, 1968.
[120] Husted and Ahlbrecht, *ibid.*, 1953, **75**, 1605.
[121] *Idem, ibid.*, 1952, **74**, 5422.
[122] Brown and Musgrave, *J.*, 1952, 5049.
[123] Simons, Black, and Clark, *J. Amer. Chem. Soc.*, 1953, **75**, 5621.
[124] Campbell, Knoblock, and Campbell, *ibid.*, 1950, **72**, 4380.
[125] Brown and Musgrave, *J.*, 1953, 2087.

Trifluoroacetic anhydride promises to be an extremely useful reagent in organic chemistry: when mixed in equimolecular proportions with an acid XOH, the mixture forms a particularly efficient acylating agent[126] owing to the formation of mixed anhydrides[127, 128] which, because of the electron-attracting power of the trifluoromethyl group, ionise slightly to produce X^+ ions (X = acyl, etc.):

$$(CF_3{\cdot}CO)_2O + XOH \rightarrow CF_3{\cdot}CO{\cdot}O{\cdot}X + CF_3{\cdot}CO_2H \rightarrow CF_3{\cdot}CO_2^- + X^+ + CF_3{\cdot}CO_2H$$

Acylation of alcohols and phenols often proceeds spontaneously at room temperature and is complete within a few minutes, so the method is particularly suitable for use with acid-labile hydroxy-compounds. It can also be used to produce polyesters from hydroxy-acids. With activated aromatic compounds (polyalkylbenzenes, phenyl ethers, furan, and thiophen), but not with benzene or toluene, ketones can be prepared,[129] and if sulphonic acids are used the products are sulphonate esters and sulphones. Fuming nitric acid[130] can be used under quite mild conditions to give nitrates from hydroxy-compounds, and nitro-derivatives of aromatic compounds, while ethyl or amyl nitrite functions as a nitrosating agent. The reaction does not stop with the introduction of the nitroso-group into the aromatic compound: the less reactive compounds such as naphthalene form nitro-derivatives, while the more reactive such as mesitylene and anisole give diazonium nitrates, probably by reaction with nitric oxide formed by dehydration of the nitrite. Pertrifluoroacetic acid, made by mixing trifluoroacetic acid and hydrogen peroxide, which oxidises amines directly to nitro-compounds, and nitrosamines to nitramines, and hydroxylates double bonds, is another example of this type of reagent.[131]

Acylation and sulphonation are also achieved by using a mixture of an acid anhydride and trifluoroacetic acid because the same equilibrium is set up, but such a procedure is inferior to that using trifluoroacetic anhydride and the acid because the former involves the preparation of each individual acid anhydride.[127] However, it has the advantage that only small amounts of trifluoroacetic acid are needed since this is regenerated as the unsymmetrical anhydride reacts:

$$\begin{array}{lll} X_2O + CF_3{\cdot}CO_2H \rightarrow & CF_3{\cdot}CO{\cdot}O{\cdot}X + XOH & \text{(X = acyl, etc.;} \\ & \quad\downarrow & \text{R}' = \text{alkyl, etc.)} \\ & X^+ + CF_3{\cdot}CO_2^- + R'OH \rightarrow & XOR' + CF_3{\cdot}CO_2H \end{array}$$

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[126] Bourne, Stacey, Tatlow, and Tedder, *J.*, 1949, 2976.

[127] Bourne, Randles, Tatlow, and Tedder, *Nature*, 1951, **168**, 942; Bourne, Randles, Stacey, Tatlow, and Tedder, *J. Amer. Chem. Soc.*, 1954, **76**, 3206; Bourne, Stacey, Tatlow, and Worrall, *J.*, 1954, 2006.

[128] Ferris and Emmons, *J. Amer. Chem. Soc.*, 1953, **75**, 232; Emmons, McCallum, and Ferris, *ibid.*, p. 6047.

[129] Bourne, Stacey, Tatlow, and Tedder, *J.*, 1951, 718.

[130] *Idem*, *J.*, 1952, 1695.

[131] Emmons and Ferris, *J. Amer. Chem. Soc.*, 1953, **75**, 4623; Emmons *et al.*, *ibid.*, 1954, **76**, 3468, 3470, 3472.

When an acetic acid–trifluoroacetic anhydride mixture is used to acylate amines it is found that a mixture of *N*-acetyl and *N*-trifluoroacetyl derivatives results.[132] The same effect is produced in the case of alcohols by adding sodium acetate to the acetylating agent or by using the pure acyl trifluoroacetate in the absence of trifluoroacetic acid.[127] At the same time the acylating power of the mixture is considerably reduced. This is explained adequately by the theory already advanced because both the amine and the sodium acetate increase the concentration of trifluoroacetate anion and consequently reduce the concentration of the reactive cation. Thus in all three cases acylation will depend more on the undissociated anhydrides ($CH_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3$ and $CF_3{\cdot}CO{\cdot}O{\cdot}CO{\cdot}CF_3$) which are principally trifluoroacetylating agents. The pure *N*-trifluoroacetyl derivatives of the amines are prepared under very mild conditions by treatment of the amine at 0°, or with slight warming, with trifluoroacetic anhydride with or without an inert solvent.[132, 133] The products are less easily hydrolysed than the trifluoroacetyl esters but, even so, are decomposed by N-alkali at room temperature. In the case of the primary aromatic amines the amino-hydrogen atom of the *N*-trifluoroacetyl derivatives is acidic and can be titrated with aqueous alkali to give sodio-derivatives. Other substituted amides react with metallic sodium in an inert solvent but this is the only case where aqueous alkali can be used.

Esters of fluorocarbon acids and hydrocarbon alcohols[134] can be made by the Fischer–Speier method or by treating the silver salts with alkyl iodides but, often in this, and in all other cases (fluorocarbon acids with fluorohydrocarbon alcohols,[135] and fluorohydrocarbon alcohols with hydrocarbon acids[136]), it is better to use the acid anhydride or acid chloride with the alcohol. Thiol esters[137] and aryl esters[138] are prepared similarly. In general, the greater the percentage of fluorine in the ester the more easily is it hydrolysed, but the presence of fluorine in the acid portion has a more pronounced effect than in the alcohol portion. This may be due simply to the fact that in all known esters there is at least one methylene group adjacent to the ester link and this will cut down the influence of the fluorine in the alcohol portion. Perfluoroglutarolactone, which does not have this methylene group, is much more easily hydrolysed.[113]

The esters of trifluoroacetic acid appear to be more labile than any of the others. They are best prepared by gently refluxing a mixture of the alcohol, trifluoroacetic anhydride, and sodium trifluoroacetate, but sometimes the reaction occurs at room temperature. They can be distilled under reduced pressure and are hydrolysed by water or by 0·05N-alkali at room temperature in a few hours. Methanolysis occurs when a methanol solution is kept at

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[132] Bourne, Henry, Tatlow, and Tatlow, *J.*, 1952, 4014.
[133] Sawicki and Ray, *J. Amer. Chem. Soc.*, 1953, **75**, 2266.
[134] Filler, O'Brien, Fenner, and Hauptschein, *ibid.*, p. 966.
[135] Hauptschein, O'Brien, Stokes, and Filler, *ibid.*, p. 87.
[136] Filler, Fenner, Stokes, O'Brien, and Hauptschein, *ibid.*, p. 2693.
[137] Hauptschein, Stokes, and Nodeff, *ibid.*, 1952, **74**, 4005.
[138] Clark and Simons, *ibid.*, 1953, **75**, 6305.

room temperature for $\frac{1}{2}$—2 days or refluxed for an hour.[139] These esters have already proved useful in carbohydrate chemistry [140] and show great promise in work on nucleotides where acylated derivatives are required in which the acyl groups are sufficiently labile to permit their removal without rupture of pyrophosphate links.[141]

The reaction of fluorinated esters with Grignard reagents has already been dealt with. They also react with ketones in the presence of sodium methoxide [142] to give β-diketones and with other esters in the presence of sodium alkoxides,[143, 144] or sodium hydride,[145] to give β-keto-esters. Attempts to prepare acetoin from trifluoroacetic ester and sodium failed and resulted in the formation of $\gamma\gamma\gamma$-trifluoroacetoacetic and pentafluoroacetoacetic ester,[146] the latter being formed first and being converted into the former under the conditions of the experiment.

Ethers.—The presence of a perfluoro-group in an ether lowers the basic properties of the oxygen bridge, the effect being greater when the fluorine atoms are on the α-carbon atom than when they are further removed. Presence of fluorine-containing groups on both sides of the oxygen greatly enhances this effect, the solubility in acid and the formation of peroxides being greatly decreased in the first case and reduced to zero in the second.[147]

Fluorine atoms in the α-position are sensitive to hydrolysis except when protected by a perfluoro-group in the β-position. A difluoromethyl group in the β-position, although it stabilises the α-position considerably, still allows hydrolysis to occur, and other halogens in the β-position give no protection. Hydrolysis may occur during the preparation of the ether by addition of an alcohol to a fluorinated olefin in the presence of sodium alkoxide, owing to further action of the alkoxide, and results in the formation of an orthoester: [39]

$$CF_2{:}CFCl + EtOH \xrightarrow{NaOEt} EtO{\cdot}CF_2{\cdot}CHFCl \xrightarrow{NaOEt} CHFCl{\cdot}C(OEt)_3$$

Hydrolyses can also be carried out with sulphuric acid, and even with water in certain cases ; [45] they take place without release of the alkoxy-group.[148] The stability also depends on the structure of the alkyl group of the alcohol—the greater the number of methyl groups on the α-carbon atom the lower the thermal stability.[39] Thus the ether from *iso*propyl alcohol and 1 : 1-dichloro-2 : 2-difluoroethylene decomposes when heated into *iso*propyl fluoride, dichloroacetic acid, and possibly propylene, while those prepared from *tert.*-butyl alcohol are difficult to isolate since they cannot be distilled. In many

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[139] Bourne, Tatlow, and Tatlow, *J.*, 1950, 3067.

[140] Bourne, Stacey, Tatlow, and Tatlow, *J.*, 1951, 826 ; Bourne, Huggard, and Tatlow, *J.*, 1953, 735.

[141] Forrest, Mason, and Todd, *J.*, 1952, 2530.

[142] Barkley and Levine, *J. Amer. Chem. Soc.*, 1951, **73**, 4625 ; 1953, **75**, 2059 ; Park, Brown, and Lacher, *ibid.*, p. 4753.

[143] Swarts, *Bull. Soc. chim. Belg.*, 1926, **35**, 412.

[144] Henne, *J. Amer. Chem. Soc.*, 1947, **69**, 1819.

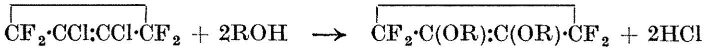
[145] McBee, Pierce, Kilbourne, and Wilson, *ibid.*, 1953, **75**, 3152.

[146] McBee, Pierce, Kilbourne, and Barone, *ibid.*, p. 4090.

[147] Henne and Smook, *ibid.*, 1950, **72**, 4378 ; Henne and Richter, *ibid.*, 1952, **74**, 5420.

[148] Tarrant and Young, *ibid.*, 1949, **71**, 2432.

cases, no matter what the alkoxy-group, there is a tendency to release hydrogen fluoride even on standing to give unsaturated ethers and this is most pronounced, as already seen, in those derived from hexafluoro*cyclo*butene which give the unsaturated compound spontaneously.[41] 1 : 2-Dichloro-3 : 3 : 4 : 4-tetrafluoro*cyclo*butene eliminates hydrogen chloride to give the same product : [46]



$$\overline{CF_2{\cdot}CCl{:}CCl{\cdot}CF_2} + 2ROH \longrightarrow \overline{CF_2{\cdot}C(OR){:}C(OR){\cdot}CF_2} + 2HCl$$

This elimination of hydrogen chloride seems to be possible only in the cyclic compounds.

Aldehydes and Ketones.—Comparatively little detailed work has been published on these compounds. They appear to undergo the normal condensation reactions but it must be borne in mind that perfluoroalkyl groups attached directly to the carbonyl group hinder the polarisation $\rangle C\overset{\curvearrowright}{=}O$ which occurs during an addition reaction. Consequently, as in reactions with Grignard reagents, these processes occur slowly and yields are often low. The perfluoro-aldehydes polymerise very easily but the polymers can be converted back into monomers on warming alone or with concentrated sulphuric acid.[149]

Both types of compound show a pronounced tendency, which increases with increase in fluorine content, to form hydrates [121, 150] which in certain cases mask their normal reactions. The aldehydrols give the free aldehyde when heated with phosphoric oxide, and the ketone hydrates can be dehydrated by keeping the ethereal solutions over anhydrous copper sulphate. Trifluoroacetaldehyde forms hydrazones only in concentrated acid because, otherwise, formation of the hydrate inhibits the reaction ; and hexafluoroacetylacetone gives chelates with copper and uranous compounds only under anhydrous conditions. Trifluoroacetylacetone forms chelates in aqueous solution, but use of anhydrous conditions results in better yields. The hydrates of trifluoroacetaldehyde and heptafluorobutyraldehyde condense with nitroparaffins [121] in the presence of anhydrous potassium carbonate to give nitro-alcohols which are easily dehydrated to the nitro-olefins. This addition reaction proceeds with only moderate success in the case of heptafluoropropyl methyl ketone.

The aldehydes are oxidised to acids by dichromate, and the free aldehyde, but not the aldehydrol, gives Schiff's test. Both aldehydes and ketones can be reduced by lithium aluminium hydride [151] or by hydrogen and a catalyst [152] to the alcohols, and both undergo the haloform reaction with alkali.[149, 153] *β*-Diketones are hydrolysed by aqueous alkali [154] to a ketone and the fluorinated acid :

$$CF_3{\cdot}CO{\cdot}CH_2{\cdot}COPh \longrightarrow CF_3{\cdot}CO_2H + CH_3{\cdot}COPh$$

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[149] Schechter and Conrad, *J. Amer. Chem. Soc.*, 1950, **72**, 3371.

[150] Haszeldine, Musgrave, Smith, and Turton, *J.*, 1951, 609.

[151] Haszeldine, *J.*, 1953, 1748.

[152] Jones, *J. Amer. Chem. Soc.*, 1948, **70**, 143.

[153] Simons, Black, and Clark, *ibid.*, 1953, **75**, 5621.

[154] Whalley, *J.*, 1951, 3235.

and by sodium methoxide [155] to ketone and ester. In this case both possible hydrolyses occur :

$$\mathrm{Ph{\cdot}CO{\cdot}CHMe{\cdot}CO{\cdot}CF_3} \rightarrow \mathrm{CF_3{\cdot}COEt + Ph{\cdot}CO_2Me} \qquad (a)$$

$$\mathrm{Ph{\cdot}CO{\cdot}CHMe{\cdot}CO{\cdot}CF_3} \rightleftharpoons \mathrm{Ph{\cdot}COEt + CF_3{\cdot}CO_2Me}$$

Reaction (*a*) is irreversible and attempts to cause a similar reverse reaction by using the acid chloride instead of the ester led to *O*-acylation:

$$\mathrm{CF_3{\cdot}CO{\cdot}CH_2Et + Ph{\cdot}COCl} \xrightarrow{\mathrm{NaOMe}} \mathrm{CF_3{\cdot}C(O{\cdot}COPh){:}CHEt}$$

The keto–enol equilibrium in β-diketones containing perfluoroalkyl groups seems to be well over on the enol side.[150, 142]

Alcohols.—There has been only one claim to the preparation of a hydroxyfluorocarbon and this compound ($\mathrm{C_8F_{13}{\cdot}OH}$) has not been fully identified.[156] In general it is found that fluorine atoms adjacent to a hydroxyl group are very easily hydrolysed with the production of an acid. This is particularly evident in the hydrolysis of the fluorinated lactones.[113]

Glycols and primary, secondary, and tertiary alcohols have been prepared by the reduction of fluorinated acids and acid derivatives with lithium aluminium hydride and by Grignard reactions. Those with one perfluoroalkyl group attached to the alcohol function are about 10^4 times as acidic as hydrocarbon alcohols and so are not as strongly acid as earlier workers led us to believe ; [157] those with two perfluoroalkyl groups attached are about 10^6 times as acid ; and it is expected that tertiary perfluoro-alcohols will be about as acidic as phenols.[151, 158] As already seen, primary alcohols and glycols form esters with acid chlorides and anhydrides ; primary alcohols can be oxidised to aldehydes, and secondary alcohols to ketones.[159] The presence of a perfluoroalkyl group makes the secondary alcohols particularly difficult to dehydrate.[124] In certain cases heating with potassium hydrogen sulphate, concentrated sulphuric acid, syrupy phosphoric acid, or phosphoric oxide at 235° failed, and activated alumina at 350° caused decomposition, although the last two reagents have produced the olefin on occasion. Pyrolysis of the acetate at 500° seems to be effective in some cases.[160] The tertiary alcohols with only one perfluoroalkyl group are dehydrated more easily, by concentrated sulphuric acid in ether.[52] Phosphorus pentabromide has also been used.[161]

Monofluorides.—The earlier misconception that the alkyl fluorides and, in fact, any aliphatic compounds with only one fluorine atom and no other halogen attached to a particular carbon atom, were most unstable, were easily hydrolysed, and would split off hydrogen fluoride very easily to give an

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[155] Barkley and Levine, *J. Amer. Chem. Soc.*, 1953, **75,** 2059.

[156] Grosse, Abs. Meeting Amer. Chem. Soc., Sept. 1949, 21K.

[157] Swarts, *Bull. Soc. chim. Belg.*, 1929, **38,** 99.

[158] Henne and Francis, *J. Amer. Chem. Soc.*, 1953, **75,** 991.

[159] Henne, Pelley, and Alm, *ibid.*, 1950, **72,** 3370 ; McBee, Pierce, and Marzluff, *ibid.*, 1953, **75,** 1609.

[160] Buxton, Stacey, and Tatlow, *J.*, 1954, 366.

[161] Swarts, *Bull. Soc. chim. Belg.*, 1927, **36,** 191.

olefin,[162] has now been corrected [163] and it has been shown that they are less reactive than the corresponding chloro-compounds; the $\omega\omega'$-difluoroalkanes are not attacked by sodium amalgam or phosphoric oxide, and only slightly by aqueous-alcoholic alkali. They do not form Grignard reagents or react with sodium iodide in acetone. The substituted benzyl fluorides appear to be rather more reactive than the $\omega\omega'$-difluoroalkanes but are considerably less reactive than the corresponding benzyl chlorides. More detailed quantitative work on solvolysis has been carried out by a number of workers.[164] Apart from the points already mentioned they show that *p*-fluoronitrobenzene and 1-fluoro-2 : 4-dinitrobenzene are more reactive than the corresponding chloro-compounds in nucleophilic reactions. This cannot be explained in terms of mesomeric release of electrons from the halogens but may be due to the high degree of solvation of the incipient fluoride ion.

The alkyl fluorides in the presence of boron trifluoride will promote isomerisation, disproportionation, and self-alkylation of saturated *iso*alkanes, the conditions being such that boron trifluoride alone has no effect.[165] Thus *iso*propyl fluoride and boron trifluoride with 3-methylpentane give 2-methylpentane, 2-methylhexane, 3-methylhexane, unchanged material, and decomposition products. With *iso*butane, octane is among the products. An ionic mechanism with preliminary formation of the *iso*propyl cation and BF_4^- is postulated.

Aromatic fluorides are quite stable and unreactive except when there are activating groups present in the ring system; and, although few reactions have been quoted, fluorine atoms in heterocyclic systems [166] are generally quite stable except when in position 4 of the pyridine or quinoline rings.

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[162] Henne and Midgley, *J. Amer. Chem. Soc.*, 1936, **58**, 882.

[163] Birnstein, Roth, and Miller, *ibid.*, 1948, **70**, 2310; Hoffmann, *J. Org. Chem.*, 1949, **14**, 105.

[164] Chapman and Parker, *J.*, 1951, 3300; Chapman and Levy, *J.*, 1952, 1673, 1676; Bevan, *J.*, 1951, 2340; 1953, 654; Bevan and Hudson, *J.*, 1953, 2187; Swain and Scott, *J. Amer. Chem. Soc.*, 1953, **75**, 246.

[165] Schneider and Kennedy, *ibid.*, 1951, **73**, 5013, 5017, 5024; Donnell and Kennedy, *ibid.*, 1952, **74**, 4162.

[166] Roe and Hawkins, *ibid.*, 1947, **69**, 2443; 1949, **71**, 1785; Beaty and Musgrave, *J.*, 1952, 875.