361. *Perfluoroalkyl Grignard Reagents. Part II.* Reaction of Heptafluoropropylmagnesium Iodide with Carbonyl Compounds, and the Mechanism of Reduction during Grignard Reactions.*†

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The interaction of heptafluoropropylmagnesium iodide and acet-, prop-, and butyr-aldehyde, yields the expected secondary alcohols; with the corresponding perfluoro-aldehydes the secondary perfluoro-alcohol is obtained, but reduction to primary alcohol and formation of a polymer of fluoro-aldehyde also occurs. Acid chlorides yield fluoro-ketones and tertiary alcohols; esters give tertiary alcohols, fluoro-ketones and, by reduction, the secondary 1-(perfluoropropyl)alkanols. Reaction of heptafluoropropylmagnesium iodide with esters of perfluoro-acids forms a convenient preparation of perfluoro-ketones, reduction of which with lithium aluminium hydride also affords the secondary perfluoro-alcohols.

The current theory of Grignard reactions is supported by the addition and reduction products obtained by interaction of methyl-, ethyl-, and propylmagnesium iodide and fluoro-aldehydes, -ketones, and -esters, but must be modified to explain the reduction occurring in reactions of perfluoroalkyl Grignard reagents. The influence of solvent, temperature, mode of addition, and magnesium bromide on the yields of addition and reduction products in reactions of certain Grignard reagents has been investigated.

The reaction of heptafluoropropylmagnesium iodide with a variety of carbonyl compounds has thrown light on the mechanism of reduction of the latter by Grignard reagents.

Acetaldehyde, propaldehyde, and butyraldehyde react smoothly but slowly with heptafluoropropylmagnesium iodide in butyl ether at −50° to give severally 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoropentan-2-ol (I; R = Me), 4 : 4 : 5 : 5 : 6 : 6 : 6-heptafluorohexan-3-ol (I; R = Et), and 5 : 5 : 6 : 6 : 7 : 7 : 7-heptafluoroheptan-4-ol (I; R = Pr), in 40—45% yields.

$C_3F_7{\cdot}CHR{\cdot}OH$	$RCH_2{\cdot}OH$	$C_3F_7{\cdot}COR$	$(C_3F_7)_2CR{\cdot}OH$
(I)	(II)	(III)	(IV)

If the formation of Grignard compounds is initiated with a small portion of the fluoro-iodide, and a mixture of heptafluoroiodopropane and the aldehyde is added at low temperature, the yields of the alcohol (as I) are appreciably reduced (25—30%). Alternate addition of heptafluoroiodopropane and only 40% of the quantity of aldehyde theoretically required to react with the Grignard reagent thereby formed (*i.e.* at least 1 equiv. of Grignard reagent in excess throughout) gives yields (40—45%) comparable with those obtained in the first experiments. The products of the Grignard reaction therefore do not interfere with the formation of the heptafluoropropylmagnesium iodide, and the low yields in the second series of experiments are caused by the absence of an excess of Grignard reagent throughout the reaction (see later).

Substantially more heptafluoropropane and fluorine-free material of higher boiling point were produced under the conditions of the second series of experiments, and a possible explanation is that aldol-type condensations are brought about by the Grignard solution. This is also indicated in the reaction of heptafluoropropylmagnesium iodide and acetone (Part I *), since further examination of the residue has revealed the presence of mesityl oxide and phorone (*ca.* 8%).

Perfluoro-acetaldehyde, -propaldehyde, and -butyraldehyde give somewhat lower yields (30%) of the secondary alcohols (I) than their unsubstituted analogues, and the reaction is much slower. Best yields were achieved at −10° to −20° (see Table 5), although the thermal decomposition of the heptafluoropropylmagnesium iodide was thereby increased. The fluoro-aldehydes cannot undergo the aldol condensation, since they

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* Part I, *J.*, 1952, 3423.

† Taken from papers presented at A.C.S. Meetings, New York, 1951; Atlantic City, 1952.

contain no α-hydrogen atoms, and most of the fluoro-aldehyde not giving the secondary alcohol was recovered as aldehyde polymer or as free aldehyde (15—40%), or was reduced to the corresponding primary alcohol (II; R = CF_3, C_2F_5, or C_3F_7) (5—10%). The mechanism of reduction is discussed in more detail below. The polymerisation of the fluoro-aldehydes to a white solid, from which the monomer can be regenerated by heat, can be observed at low temperature in the reaction mixture; similar polymerisation does not take place in reactions with alkyl Grignard reagents (see below).

The fluoro-alcohols (I; R = CF_3, C_2F_5, and C_3F_7) are the first secondary-perfluoro-alcohols prepared, and their ionisation constants, with those of other fluoro-alcohols, are discussed in the following paper.

Acid chlorides do not usually give good yields of ketone when treated with an alkyl-magnesium halide, since addition of a second molecule of Grignard reagent to the intermediate ketone is often fast. When acetyl, propionyl, or butyryl chloride reacts with heptafluoropropylmagnesium iodide, however, the fluoro-ketone formed as intermediate reacts with excess of Grignard reagent more slowly than does an unsubstituted ketone, so that the ketones (III; Me, Et, and Pr) are isolated in 15—20% yield and the *tert.*-alcohols (IV; R = Me, Et, and Pr) are obtained in *ca.* 25% yield. The formation of the *sec.*-alcohol (I; R = Me, Et, or Pr) was not detected (cf. fluoro-esters, below). The corresponding fluoro-acid chlorides give moderately good yields (30—40%) of the perfluoro-ketones (III; R = CF_3, C_2F_5, and C_3F_7), with lower yields of the *tert.*-alcohols (*ca.* 15%), again illustrating the decreased reactivity of the carbonyl groups in the perfluoro-ketones relative to the alkylfluoroalkyl and dialkyl ketones.

It is noteworthy that ethyl heptafluorobutyrate was a by-product (3%) when ether was used as solvent, presumably formed by cleavage of the ether catalysed by magnesium halides:

$$C_3F_7{\cdot}COCl + Et_2O \xrightarrow{MgX_2} C_3H_7{\cdot}CO_2Et + EtCl$$

(cf. Underwood and Wakeman, *J. Amer. Chem. Soc.*, 1930, **52**, 387; Kyrides, *ibid.*, 1933, **55**, 1209; Descudé, *Compt. rend.*, 1901, **132**, 1129).

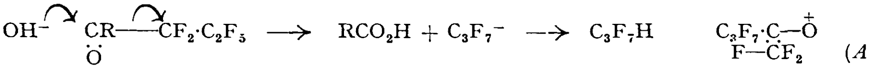
The reaction of an ester with a Grignard reagent is commonly used for the preparation of *tert.*-alcohols, but with heptafluoropropylmagnesium iodide appreciable yields of ketones (particularly perfluoro-ketones) can also be obtained. Ethyl acetate, propionate, and butyrate react smoothly with the Grignard reagent at −50° to give three main products, the fluoro-ketones (III; R = Me, Et, and Pr), the *sec.*-alcohols (I; R = Me, Et, and Pr) arising by reduction of the ketone (see later), and the *tert.*-alcohols (IV; R = Me, Et, and Pr). When the ester is added to the Grignard reagent the yields are *ca.* 10%, 10%, and 20—30%, respectively, *i.e.*, the overall yield is low. Use of equimolar amounts of ester and Grignard reagent gives higher yields of ketone and lower yields of the *tert.*-alcohol than when a ratio *ca.* 1 : 2 is employed; the function of the excess of Grignard reagent is discussed below. Ethyl trifluoroacetate and ethyl pentafluoropropionate give considerably higher yields (40%) of the perfluoro-ketones (III; R = CF_3 or C_2F_5) and about equal yields of (I and IV; R = CF_3 and C_2F_5).

Addition of the Grignard reagent to the unsubstituted ester gives greatly increased yields (40%) of the ketone, no change in the amount of secondary alcohol formed, and a slight reduction in the amount of *tert.*-alcohol obtained. Similar addition to the fluoro-esters gives tertiary (5%) and secondary (5%) alcohols and an increased yield of ketone (50%). The absence of excess of Grignard reagent clearly facilitates ketone formation. The interaction of fluoro-esters and the fluoroalkyl Grignard reagent provides a simple route for the preparation of fluoro-ketones.

The addition of ethereal magnesium bromide solution to the ester before addition of the latter to heptafluoropropylmagnesium iodide does not affect the amount of ketone formed, but there is a marked decrease in the reduction to the secondary alcohol (discussed below) and a slight increase in yield of *tert.*-alcohol.

The fraction of higher boiling point from the above reactions in ether is believed to contain the hemiketal $C_3F_7{\cdot}CR(OEt){\cdot}OH$, since, on decomposition during distillation, small amounts of the perfluoro-ketone and ethyl alcohol were liberated, but precise characterisation could not be effected. Fluoro-ketones and -aldehydes are known to form stable dihydrates, and chloral forms a dihydrate and a hemiacetal.

The various fluoro-ketones obtained show the marked decrease in boiling point on replacement of hydrogen by fluorine, attributed to decreased hydrogen bonding, *viz.*, C_3H_7·COMe, 102°; C_3H_7·COEt, 124°; C_3H_7·COPr, 144°; C_3F_7·COMe, 58°; C_3F_7·COEt, 78°; C_3F_7·COPr, 100°; C_3F_7·$COCF_3$, 29·5° (22°); $C_3F_7COC_2F_5$, 52° (56°); C_3F_7·COC_3F_7, 75° (82°). A similar effect is observed with the *sec.*-fluoro-alcohols (following paper). The boiling points of fluorocarbons containing the same number of carbon atoms, given above in parentheses, show that replacement of two fluorine atoms by an oxygen atom causes only slight change. The decreased basicity of the carbonyl oxygen atom on a fluoro-ketone relative to its hydrocarbon analogue is shown by the insolubility of (III; R = C_2F_5, and C_3F_7) in sulphuric acid and the low solubility in water, although hydrate formation as found with hexafluoroacetone is still apparent. The ketones (III; R = Me, Et, Pr, and C_3F_7) are readily cleaved by dilute sodium hydroxide to give heptafluoropropane, and the reaction of the heptafluoropropyl compound is notably more rapid, despite the decreased water solubility. It is suggested that the haloform reaction involves displacement at the keto-group rather than addition to it :

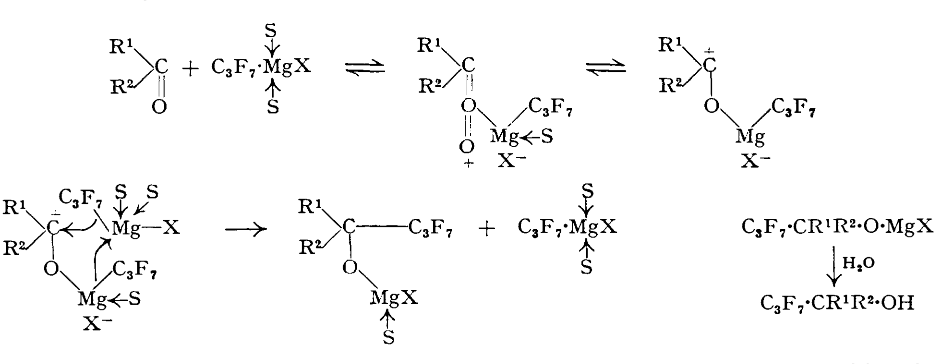

(A)

Addition to the keto-group would involve the electron shift >C=O and this would be opposed by the inductive effect of the fluoroalkyl group and, probably at least as important in the case of fluorine, by hyperconjugation effects (see *J.*, 1952, 3490), *e.g.* (*A*). It is noteworthy that the reaction of heptafluoropropylmagnesium iodide with the fluoro-ketones is markedly slower than with the unsubstituted ketones.

Lithium aluminium hydride reduction of the ketones prepared above gives an alternative and convenient method for the preparation of the *sec.*-alcohols (I; R = Me, Et, Pr, CF_3, C_2F_5, and C_3F_7). Conversely, oxidation of (I; R = Me, Et, and Pr) by Conant and Quayle's general technique (*Org. Synth.*, Coll. Vol. I, p. 211) gives the ketones in good yield. The *tert.*-alcohols mentioned above will be described in detail in a later paper.

The reactions of heptafluoropropylmagnesium iodide will now be examined in the light of current theories of Grignard reaction.

Complex Formation and Effect of Solvent and Concentration of Reactants.—It is assumed (see Swain and Boyles, *J. Amer. Chem. Soc.*, 1951, **73**, 870; Mosher and Combe, *ibid.*, 1950, **72**, 3994, for references) that the reaction of the solvated Grignard reagent (S = ether of solvation) with, say, a ketone or aldehyde, involves formation by co-ordination of a 1 : 1-complex which, in the second step of the reaction, is attacked by a *second* molecule of the Grignard reagent, with transfer of a $C_3F_7^-$ ion in a six-membered ring complex. Hydrolysis then yields the alcohol :



The reactions of heptafluoropropylmagnesium iodide adequately support this scheme. For example, if an excess of the Grignard reagent is not present during most of the reaction, formation of the 1 : 1-complex can occur, but the subsequent step involving a second molecule of the Grignard reagent can proceed only slowly; this is illustrated by the decreased yields of the *sec.*-alcohols when acetaldehyde, propaldehyde, and butyraldehyde react with heptafluoropropylmagnesium iodide in a molar ratio $>1:2$. A $3:1$ molar ratio of the Grignard reagent to ester is similarly advantageous in the preparation of *tert.*-alcohols.

The effect of changing R^1 and/or R^2 from alkyl to perfluoroalkyl cannot be predicted with certainty by the above scheme, since opposing factors are involved. Thus, if R^1 and R^2 are perfluoroalkyl, the reduced basicity of the carbonyl oxygen atom will not favour co-ordination of magnesium to oxygen, which is an electrophilic attack; on the other hand, the nucleophilic attack of the perfluoropropyl ion on the carbonyl carbon atom will be favoured. Again, the ionic nature of the carbon–magnesium bond in heptafluoropropylmagnesium iodide (see Part I) will make the magnesium compound a stronger acid (in the Lewis sense) than, say, propylmagnesium iodide, so that the electrophilic attack and subsequent polarisation of the carbonyl double bond should be facilitated; opposing this will be the fact that displacement of ether of solvation (S) from the strongly solvated Grignard reagent will be difficult. The net effect of the factors is that the ease of reaction of heptafluoropropylmagnesium iodide with a ketone COR^1R^2 decreases in the order R^1, R^2 = alkyl > R^1 = alkyl, R^2 = perfluoroalkyl > R^1, R^2 = perfluoroalkyl.

Reduction during the Reactions of Alkyl Grignard Reagents.—Swarts (*Bull. Soc. chim. Belg.*, 1927, **36**, 191), Campbell, Knobloch, and Campbell (*J. Amer. Chem. Soc.*, 1950, **72**, 4380), and recently McBee, Higgins, and Pierce (*ibid.*, 1952, **74**, 1387, 1736) have shown that fluorine-containing carbonyl compounds react with methylmagnesium iodide only by addition, but that with other alkyl Grignard reagents both reduction and addition occur. The experiments between methyl-, ethyl-, and propyl-magnesium iodides and ethyl heptafluorobutyrate, trifluoroacetaldehyde, heptafluorobutyraldehyde, and heptafluorobutyl methyl ketone, summarised in Table 1, confirm and extend these results.

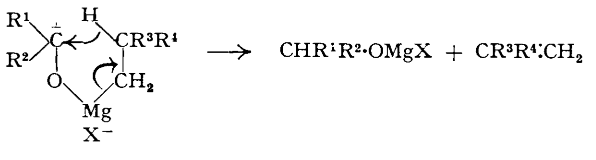
TABLE 1.

Compound	Grignard reagent	Redn. product, %	Addn. product, %	Ketone, %
$C_3F_7{\cdot}CO_2Et$	MeMgI [1]	0	70	—
	EtMgI [1, 2]	62	15	—
	MeMgI [3]	0	51	5
	EtMgI [3]	45	8	10
$CF_3{\cdot}CHO$ ...	MeMgI [1]	trace	65	—
	PrMgI [1, 4]	77	5	—
$C_3F_7{\cdot}CHO$	PrMgI [1, 5]	72	8	
	PrMgI [6]	46	26	
	PrMgI [7]	39	33	
$C_3F_7{\cdot}COMe$	MeMgI [1]	0	71	
	EtMgI [1]	59	14	
	MeMgI [8]	0	66	
	EtMgI [8]	22	37	

[1] Compound added to Grignard reagent. [2] Ethylene liberated. [3] Grignard reagent added to compound. [4] Propylene liberated (58%). [5] Propylene liberated (42%). [6] Aldehyde plus magnesium bromide added to Grignard reagent. [7] Grignard reagent added to aldehyde plus magnesium bromide. [8] Ketone plus magnesium bromide added to Grignard reagent.

It should be noted that the percentage reduction during the reactions of fluorine-containing carbonyl compounds is higher than with the corresponding unsubstituted compounds.

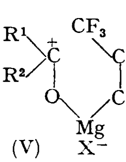
Whitmore's explanation (Whitmore, Atlantic City Meeting, Amer. Chem. Soc., April 1943; see also Swain and Boyles, *loc. cit.*) of the reduction observed during reactions of Grignard reagents is given considerable support by the results in Table 1. Reduction can occur if the formation of a complex from the alkyl Grignard reagent $CHR^3R^4{\cdot}CH_2{\cdot}MgX$ and the carbonyl compound is followed by internal rearrangement with hydride ion shift.

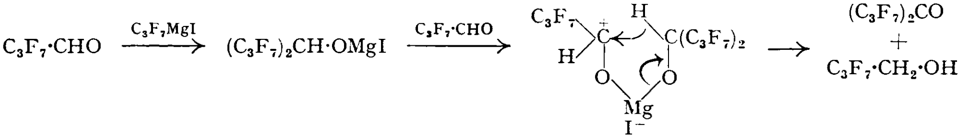


Methylmagnesium iodide gives high yields of only the addition product, since there are no β-hydrogen atoms available for transfer as hydride ion, whereas ethyl- and propylmagnesium iodides react mainly by reduction. The second molecule of the alkyl Grignard reagent acts only as a source of hydride ion, and its efficiency as a reducing agent will depend not only on the number of β-hydrogen atoms available, but also on the ease of transfer of hydride ion from the alkyl groups. This transfer will be facilitated if R^3 or R^4 is an electron-releasing group, and particularly if it can undergo hyperconjugation with the incipient double bond of the olefin $CR^3R^4{:}CH_2$ in the transition state. There is thus a marked similarity between the influence of the alkyl groups in the alkylmagnesium halide and the alkyl groups in alkyl halides undergoing nucleophilic or elimination reactions.

The fluoro-aldehydes (Table 1) and chloral (Gilman and Abbot, *J. Org. Chem.*, 1943, **8**, 234) are reduced to the primary alcohol only during reactions involving Grignard reagents which contain β-hydrogen atoms. Further support for Whitmore's mechanism is given by the marked increase in the ratio of addition to reduction product when magnesium bromide is added to the fluoro-aldehyde or -ketone before its reaction with the alkyl Grignard reagent (Table 1); this is ascribed to the greater efficiency of magnesium bromide relative to the alkylmagnesium halide in co-ordinating to the carbonyl oxygen, thus preventing formation of the complex and, by polarising the carbonyl double bond, facilitating the addition reaction.

Reduction during Reactions involving Perfluoroalkyl Grignard Reagents.—On treatment with heptafluoropropylmagnesium iodide, the fluoro-aldehydes yield 5—10% of the primary alcohol, and ethyl alkane- or perfluoroalkane-carboxylates yield *ca.* 10% of the *sec.*-alcohol. Hydride-ion shift in a complex such as (V) cannot be invoked to explain these reductions, since no β-hydrogen atoms are available. Although the Whitmore mechanism is thus inadequate for perfluoroalkyl Grignard reagents, no satisfactory alternative explanation can yet be given. Reduction by nascent hydrogen during the acid hydrolysis stage can be excluded, since the excess of magnesium is first removed. Reduction of the Meerwein–Ponndorf type by an iodomagnesium alkoxide (Meerwein and Schmidt, *Annalen*, 1925, **444**, 221; Mosher and Combe, *loc. cit.*), *e.g.*,


(V)



is plausible, but must also be excluded, since such a compound can be formed only during ester reactions; furthermore, the aldehyde or ketone, which should also be formed, was not detected. There is no evidence for or against a free-radical mechanism for the reduction, *e.g.*,

$$COR^1R^2 + \cdot MgI \longrightarrow \dot{C}R^1R^2{\cdot}OMgI \xrightarrow[H_2O]{RH} CHR^1R^2{\cdot}OH + R\cdot$$

apart from the low temperatures used, which would not favour radical formation.

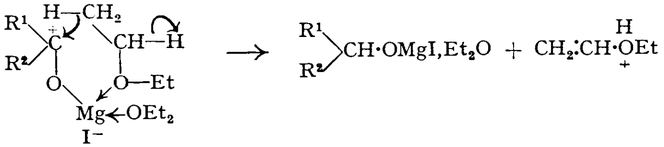
In the reactions of ethyl heptafluorobutyrate with methyl-, ethyl- or propyl-magnesium iodide, and of heptafluoropropylmagnesium iodide with ethyl acetate, propionate, or butyrate, the same intermediate, $C_3F_7{\cdot}CR(OMgI){\cdot}OEt$ (R = Me, Et, or Pr) is formed, but although the same reduction product, $C_3F_7{\cdot}CHR{\cdot}OH$, is produced, the yields are vastly different, as shown in Table 2.

TABLE 2. *Yield of secondary alcohol, %.*

MeMgI + $C_3F_7{\cdot}CO_2Et$	0	$C_3F_7{\cdot}MgI$ + $MeCO_2Et$	8
EtMgI + ,,	62	,, + $EtCO_2Et$	9
PrMgI + ,, (predicted)	>50	,, + $PrCO_2Et$	14

Reduction must occur after the formation of $C_3F_7{\cdot}COR$, therefore, and must involve a second molecule of the Grignard reagent. This is supported by the fact that magnesium bromide, added to an ester before its reaction with heptafluoropropylmagnesium iodide, is preferentially co-ordinated to the $C_3F_7{\cdot}COR$ intermediate and thereby prevents its reduction by the heptafluoropropylmagnesium iodide.

Since the reduction involves the solvated molecule of the Grignard compound, a possible mechanism involves hydride-ion shift from the ether of solvation :



Such a mechanism could be tested by preparation of heptafluoropropylmagnesium iodide in a solvent containing no, or only unreactive, hydrogen atoms, so that hydride-ion transfer from the solvent of solvation would be impossible, but the successful preparation of the Grignard reagent in perfluorotriethylamine, diperfluorobutyl ether, or benzene has so far proved unsuccessful.

EXPERIMENTAL

General Technique.—Sealed Pyrex-glass tubes (50—500 ml.) were used for small-scale experiments, and conventional Grignard apparatus for larger-scale experiments. Extreme precautions were taken to exclude oxygen, carbon dioxide, and moisture. Heptafluoroiodopropane (*J.*, 1949, 2856; 1952, 4259) was dried, purified, and stored *in vacuo*. Spectroscopically pure magnesium was treated as described in Part I (*loc. cit.*). Ethyl and *n*-butyl ethers were used as solvents, the former where possible, the latter where it facilitated isolation of the product. Part I showed that more basic solvents (*e.g.*, tetrahydropyran, tertiary amines) give better yields of the Grignard reagent, but for general convenience the ethers are preferred. Grignard formation was initiated by addition at 0° to $-20°$ of *ca.* 5% of the total fluoro-iodide, and the temperature was then lowered as rapidly as possible without stopping formation of the Grignard reagent. The remaining fluoro-iodide was then added, and the yield of Grignard reagent taken from the data of Part I, periodic checks being made by parallel experiments involving carboxylation or hydrolysis. Yields of reaction products are based on the quantity of heptafluoropropylmagnesium iodide available for reaction, and if low yields were obtained the products of two or three experiments were combined.

The volatile by-products, hexafluoropropene and heptafluoropropane (see Part I), were usually removed before the excess of magnesium was filtered off.

Traces of water were removed from the fluoroalkyl alcohols by heating them at 50° with phosphoric anhydride before final distillation. The perfluoroalkyl alcohols were distilled from phosphoric anhydride without decomposition. The fluoro-ketones form hydrates, boiling in the 90—100° region, which were decomposed at 50—60° by phosphoric anhydride before final distillation.

The fluoroalkyl Grignard reagents invariably yield by-products, often unidentified and of high boiling point. In view of the difficulties of separation of the products, the yields reported are only minimum.

Reaction of Heptafluoropropylmagnesium Iodide with Acetaldehyde, Propaldehyde, and Butyraldehyde.—The aldehydes were carefully purified, dried, and stored in a vacuum system. Heptafluoropropylmagnesium iodide (65% yield) was prepared from heptafluoroiodopropane (10·0 g.) and magnesium (3·2 g.) at $-50°$ in *n*-butyl ether (150 ml.) during 12 hr., and into it was passed an excess of the appropriate aldehyde (3·0 g., 3·2 g., 4·0 g., severally) during 5 hr. The mixture was stirred for 36 hr., and then allowed to warm to room temperature during 24 hr., before being heated at 60° for 1 hr. and filtered. Hydrolysis with ammonium chloride solution, separation, and drying (P_2O_5) and distillation of the ethereal layer gave 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoropentan-2-ol (41%), b. p. 101° (see Part I), 4 : 4 : 5 : 5 : 6 : 6 : 6-*heptafluorohexan*-3-*ol* (45%), b. p. 114—115° (Found : C, 31·8; H, 3·2%. $C_6H_7OF_7$ requires C, 31·6; H, 3·1%), and 5 : 5 : 6 : 6 : 7 : 7 : 7-*heptafluoroheptan*-4-*ol* (40%), b. p. 128—130°, 71°/60 mm. (Found : C, 34·6; H, 3·5%. $C_7H_9OF_7$ requires C, 34·7; H, 3·7%). The use of ethyl ether as solvent for the reaction with propaldehyde and butyraldehyde, with otherwise identical conditions, gave the corresponding alcohols in 49 and 46% yields. Unchanged aldehyde was isolated in every experiment.

In a separate series of experiments, heptafluoroiodopropane (3·0 g.) was slowly added to magnesium (3·2 g.) in *n*-butyl ether (120 ml.) at $-25°$, and the mixture cooled to $-50°$. Immediate addition of a cooled solution of heptafluoroiodopropane (7·0 g.) and the aldehyde

(3·0 g., 3·2 g., 3·9 g., severally) in *n*-butyl ether (30 ml.) was begun and completed during 3 hr. The respective alcohols were obtained in yields of 31, 26, and 24%.

The yields, %, of heptafluoropropane, hexafluoropropene, and recovered heptafluoroiodopropane (based on heptafluoropropylmagnesium iodide), and of the unidentified fluorine-free material (yield based on the aldehyde) which distilled at 155—210° and was distinct from the fluoropolymer described in Part I, are given in Table 3 for the separate (S) and concurrent (C) addition of the aldehyde to the reaction mixture.

TABLE 3.

	C_3F_7H		C_3F_6		C_3F_7I		Higher-boiling material	
	(S)	(C)	(S)	(C)	(S)	(C)	(S)	(C)
MeCHO	15	23	3	2	11	17	12	26
EtCHO	10	22	1	1	9	15	12	31
PrCHO	7	19	—	—	8	13	10	27

The hexafluoropropene and heptafluoropropane were separated as described in Part I.

When addition of 0·5 ml. portions of heptafluoroiodopropane in *n*-butyl ether during Grignard formation was alternated with addition of 40% of the aldehyde theoretically required to react with the Grignard reagent thereby formed, the yields of the fluoro-alcohols were 42, 43, and 42%, respectively.

Reaction of Heptafluoropropylmagnesium Iodide with Trifluoroacetaldehyde, Pentafluoropropaldehyde, and Heptafluorobutyraldehyde.—The aldehydes, prepared by reduction of the corresponding fluoro-acids with lithium aluminium hydride, were stored in a vacuum system at −183° to prevent polymerisation, and were added to the Grignard solution as gases. An attempt to use the solid polymer of trifluoroacetaldehyde was unsuccessful. Heptafluoropropylmagnesium iodide was prepared in 60—65% yield at −50° in *n*-butyl ether from magnesium (3·2 g.) and heptafluoroiodopropane (10·0 g.) during 12—18 hr. The fluoro-aldehyde (3·0 g., 3·8 g., 5·1 g., severally) was then added during 8 hr., the mixture allowed to warm (4 hr.) to room temperature, and stirring continued for 24 hr. 1 : 1 : 1 : 3 : 3 : 4 : 4 : 5 : 5 : 5-*Decafluoropentan-2-ol* (29%), b. p. 51—52°/209 mm. (Found : C, 22·3; H, 0·7; F, 70·7. $C_5H_2OF_{10}$ requires C, 22·4; H, 0·7; F, 70·9%), 1 : 1 : 1 : 2 : 2 : 4 : 4 : 5 : 5 : 6 : 6 : 6-*dodecafluorohexan-3-ol* (30%), b. p. 61°/150 mm. (Found : C, 22·6; H, 0·6. $C_6H_2OF_{12}$ requires C, 22·6; H, 0·6%), and 1 : 1 : 1 : 2 : 2 : 3 : 3 : 5 : 5 : 6 : 6 : 7 : 7 : 7-*tetradecafluoroheptan-4-ol* (27%), b. p. 70°/103 mm. (Found : C, 22·6; H, 0·6. $C_7H_2OF_{14}$ requires C, 22·8; H, 0·5%), were obtained.

The variation in yield, %, of the secondary alcohols with temperature is shown in Table 4. In these experiments the Grignard reagent was prepared at −50° and warmed rapidly to the temperature shown before addition of the aldehyde. The other reaction products were heptafluoropropane, hexafluoropropene, the fluoro-aldehyde (isolated as the polymer and as the hydrate in approximately equal amounts), and the primary alcohols corresponding to the aldehydes, *i.e.*, trifluoroethanol, pentafluoropropanol, and heptafluorobutanol (Haszeldine and Leedham, *loc. cit.*; Haszeldine, *J.*, 1950, 2789) and freed from traces of aldehyde hydrate by distillation from phosphoric anhydride.

TABLE 4.

	$C_3F_7\cdot CHX\cdot OH$			$XCH_2\cdot OH$			XCHO, recovered		
X =	CF_3	C_2F_5	C_3F_7	CF_3	C_2F_5	C_3F_7	CF_3	C_2F_5	C_3F_7
−50°	29(32)	30(29)	27(30)	4(5)	3(−)	4(2)	31(18)	—	40
−30	33	31	38	—	—	—	34	—	—
−20	38	42(46)	43(46)	5	6(3)	8(5)	24	15	18
−10	40	39	41	4	—	—	—	—	—

The results of parallel experiments with ethyl ether as solvent are recorded in parentheses in Table 4.

The formation of the fluoro-aldehyde polymer, observed at −50°, tended to slow the reaction by coating effects, but with prolonged stirring the normal amount of magnesium dissolved, as estimated by weighing the magnesium obtained by filtration before hydrolysis.

Reaction of Acid Chlorides with Heptafluoropropylmagnesium Iodide.—The acid chlorides were prepared from the corresponding acids and phosphorus pentachloride and were purified *in vacuo*. Preliminary experiments showed that reaction with the Grignard reagent was slow below −40°, and that although the yields were approximately the same, the addition of pentafluoropropionyl or heptafluorobutyryl chloride to the Grignard reagent caused a faster reaction than when the acyl halides were added during Grignard formation. In the following experiments heptafluoropropylmagnesium iodide was prepared at −50° and then warmed to −20°, and the acyl halide added during 3 hr. After being stirred for 24 hr., allowed to attain room temperature (12—15 hr.), and then heated to 50° for 30 min., the products were isolated in the usual way.

Acetyl chloride (2·0 g.) gave 3 : 3 : 4 : 4 : 5 : 5 : 5 :-*heptafluoropentan*-2-*one* (15%), b. p. 58—59° (Found : C, 28·3%; *M*, 212. $C_5H_3OF_7$ requires C, 28·3%; *M*, 212), and the *tert.*-alcohol (22%) whose properties, with those of the *tert.*-alcohols mentioned below, will be discussed in a later paper. Propionyl chloride (2·1 g.) similarly gave 4 : 4 : 5 : 5 : 6 : 6 : 6-*heptafluorohexan*-3-*one* (18%), b. p. 78° (Found : C, 31·8%; *M*, 225. $C_6H_5OF_7$ requires C, 31·9%; *M*, 226) and the *tert.*-alcohol (27%). Butyryl chloride (2·7 g.) yielded 5 : 5 : 6 : 6 : 7 : 7 : 7-*heptafluoroheptan*-4-*one* (21%), b. p. 100° (Found : C, 35·3%; *M*, 240. $C_7H_7OF_7$ requires C, 35·0%; *M*, 240), and the *tert.*-alcohol (23%).

Trifluoroacetyl chloride (3·0 g.) was sealed with the Grignard reagent, and yielded the *tert.*-alcohol (11%) and *perfluoropentan*-2-*one* (36%), b. p. 29·5° (Found : C, 22·6%; *M*, 265. C_5OF_{10} requires C, 22·6%; *M*, 266). Pentafluoropropionyl chloride (3·6 g.) similarly gave the *tert.*-alcohol (13%) and *perfluorohexan*-3-*one* (41%), b. p. 52° (Found : C, 22·6%; *M*, 316. C_6OF_{12} requires C, 22·8%; *M*, 316). Heptafluorobutyryl chloride (4·8 g.), added in the conventional Grignard apparatus, gave the *tert.*-alcohol (16%) and *perfluoroheptan*-4-*one* (31%), b. p. 75° (Found : C, 23·1%; *M*, 364. C_7OF_{14} requires C, 23·0%; *M*, 366).

With ethyl ether as solvent, the following yields of ketones were obtained : $C_3F_7{\cdot}COEt$ 25%, $C_3F_7{\cdot}COPr$ 27%, $C_3F_7{\cdot}CO{\cdot}C_2F_5$ (not separated completely from solvent by distillation) 12%.

When the amount of acid chloride used was reduced by 50%, but with otherwise identical conditions and *n*-butyl ether as solvent, the following yields were obtained : $C_3F_7{\cdot}COMe$ 10%, $C_3F_7{\cdot}COEt$ 12%, $C_3F_7{\cdot}COPr$ 13%, $C_3F_7{\cdot}CO{\cdot}CF_3$ 32%, $C_3F_7{\cdot}CO{\cdot}C_2F_5$ 34%, $C_3F_7{\cdot}CO{\cdot}C_3F_7$ 29%.

Reaction of Esters with Heptafluoropropylmagnesium Iodide.—(a) *Addition of ester to Grignard reagent.* The Grignard reagent was prepared at −50° as described above and, after addition of the ester (1 hr.), the reaction mixture was stirred at −40° for 24 hr., for a further 24 hr. during which it warmed to room temperature and finally for a further 24 hr. The volatile products were then removed and the filtered solution was hydrolysed with sulphuric acid. Table 5(*a*) gives the % yields of secondary alcohol, ketone, and tertiary alcohol obtained by reaction of the ester and Grignard reagent (amount present : 60—65% of theory from fluoroiodide used) in molar ratios of (i) 1 : 1 and (ii) 1 : 2·5.

TABLE 5(*a*).

Ester	Quantity, g.	$C_3F_7{\cdot}CHR{\cdot}OH$		$RCO{\cdot}C_3F_7$		$(C_3F_7)_2CR{\cdot}OH$	
		(i)	(ii)	(i)	(ii)	(i)	(i)
$MeCO_2Et$	1·8	2	8	19	11	21	32
$EtCO_2Et$	2·1	8	9	16	10	19	28
$PrCO_2Et$	2·5	15	14	13	5	12	18
$CF_3{\cdot}CO_2Et$	2·9	—	8	—	41	—	8
$C_2F_5{\cdot}CO_2Et$	4·0	—	6	—	39	—	10

TABLE 5(*b*).

$MeCO_2Et$	0·9	—	12	—	43	—	8
$EtCO_2Et$	1·1	—	7	—	37	—	7
$PrCO_2Et$	1·3	—	10	—	39	—	5
$CF_3{\cdot}CO_2Et$	1·4	—	2	—	53	—	5
$C_2F_5{\cdot}CO_2Et$	2·0	—	4	—	51	—	3

TABLE 5(*c*)

$EtCO_2Et$		—	0	—	8	—	26
$PrCO_2Et$		—	6	—	—	—	28
$C_2F_5{\cdot}CO_2Et$		—	0	—	42	—	18

(b) *Addition of Grignard reagent to the ester.* Heptafluoropropylmagnesium iodide was added in five 20% aliquots to a solution of the ester in *n*-butyl ether at −50°, and the mixture then treated as in (*a*) above. The results are given in Table 5(*b*).

(c) *Addition of magnesium bromide to the ester.* Certain of the experiments [Table 5(*a*)] were repeated, an equivalent of magnesium bromide being mixed with the ester solution before its addition to the Grignard reagent. The results are shown in Table 5(*c*).

(d) *Other products.* In the above experiments careful fractionation was required to separate the various products, the boiling points of which often differed by small amounts only (*e.g.*, excess of ester, ketone, and the secondary alcohol). The yields given are thus only the minimum yields, since handling losses in such distillations are necessarily high. Chemical means were used to separate ethyl heptafluorobutyl ketone from traces of ethyl alcohol (distillation; P_2O_5) and heptafluoroheptan-4-ol from ethyl butyrate (hydrolysis, then distillation). In experiments with the fluoro-esters the material of boiling point higher than that of the *tert.*-alcohols decomposed on attempted distillation, with the formation of ethyl alcohol and small amounts of the perfluoro-ketones. Precise identification of these possible hemiacetals was not achieved.

*The Reaction of Methyl-, Ethyl-, and Propyl-magnesium Iodides with Ethyl Heptafluorobutyrate, Trifluoroacetaldehyde, Heptafluorobutyraldehyde and Heptafluoropentan-*2-*one.*—(a) *Compounds added to the Grignard reagent.* To methylmagnesium iodide (from 8·0 g. of methyl iodide) in ethyl ether (120 ml.) was added ethyl heptafluorobutyrate (4·8 g.) in ethyl ether (30 ml.) during 5 hr., and the mixture stirred for 1 hr. 3 : 3 : 4 : 4 : 5 : 5 : 5-Heptafluoro-2-methylpentan-2-ol (70%), b. p. 105—107° (see Part I), was obtained, but no 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoropentan-2-ol.

Ethylmagnesium iodide (from 8·8 g. of ethyl iodide) under similar conditions gave 4 : 4 : 5 : 5 : 6 : 6 : 6-*heptafluoro-2-ethylhexan*-3-*ol* (15%), b. p. 144—146° (Found: C, 37·2; H, 4·7%. $C_8H_{11}OF_7$ requires C, 37·5; H, 4·3%), and 4 : 4 : 5 : 5 : 6 : 6 : 6-heptafluorohexan-3-ol (62%) (see above). Infra-red spectroscopic examination showed ethylene to be a product.

Trifluoroacetaldehyde (3·0 g.), passed into methylmagnesium iodide (from 8·0 g. of methyl iodide) during 5 hr. with conditions as above, gave 3 : 3 : 3-trifluoropropan-2-ol (65%), and only a trace of trifluoroethanol could be detected.

n-Propyl iodide (8·0 g.) was converted into propylmagnesium iodide and similarly treated with trifluoroacetaldehyde, giving trifluoroethanol (77%) and 5 : 5 : 5-trifluoropentan-4-ol (5%; from three similar experiments), b. p. 110—112°. Campbell, Knobloch, and Campbell (*loc. cit.*) report b. p. 109—111°/745 mm. Propylene (identified by its infra-red spectrum) was formed in 58% yield.

Heptafluorobutyraldehyde (4·0 g.) similarly added to propylmagnesium iodide solution gave heptafluorobutanol (72%), 5 : 5 : 6 : 6 : 7 : 7 : 7-heptafluoroheptan-4-ol (8%), and propylene (42%).

Methylmagnesium iodide was prepared from methyl iodide (6·0 g.), and to the filtered solution was added heptafluoropentan-2-one (4·2 g.) in ethyl ether (20 ml.) during 3 hr.; 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoro-2-methylpentan-2-ol (71%) (see Part I, *loc. cit.*) was obtained but no 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoropentan-2-ol.

Ethyl iodide (6·5 g.) was converted into the Grignard reagent, which was similarly treated with the heptafluoropentanone and gave 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoropentan-2-ol (59%) and 4 : 4 : 5 : 5 : 6 : 6 : 6-heptafluoro-3-methylhexan-3-ol (14%), b. p. 124—126° (Found: C, 34·4; H, 4·0%. Calc. for $C_7H_9OF_7$: C, 34·7; H, 3·7%). McBee *et al.* (*loc. cit.*) report b. p. 125° for the tertiary alcohol.

(b) *Addition of Grignard reagent to an excess of the compound.* The experiments with ethyl heptafluorobutyrate, were repeated, but only 80% of the alkylmagnesium iodide theoretically required to give the *tert.*-alcohol was used. The filtered ethereal solution of the Grignard reagent was added to the ester in ethyl ether (10 ml.) during 3 hr. Methylmagnesium iodide gave the tertiary alcohol (51%) and 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoropentan-2-one (5%), but no secondary alcohol. With ethylmagnesium iodide the tertiary alcohol (8%), secondary alcohol (45%), and 4 : 4 : 5 : 5 : 6 : 6 : 6-heptafluorohexan-3-one (10%) were isolated.

(c) *Addition of magnesium bromide.* Magnesium bromide (4·0 g.) was added to heptafluorobutyraldehyde (4·0 g.) dissolved in ether (75 ml.) and, after 10 min., propylmagnesium iodide (from 8·0 g. of propyl iodide) was added during 3 hr., the total volume of solvent being the same as in (a). Heptafluorobutanol (39%) and 5 : 5 : 6 : 6 : 7 : 7 : 7-heptafluoroheptan-4-ol (33%) were obtained.

In another experiment, the fluoro-aldehyde and magnesium bromide solution was added to the propylmagnesium iodide solution. The products were heptafluorobutanol (46%) and 5 : 5 : 6 : 6 : 7 : 7 : 7-heptafluoroheptan-4-ol (26%).

Heptafluoropentan-2-one was mixed with magnesium bromide (4·0 g.) in ethereal solution and, with conditions otherwise the same as in (a) above, was added to methylmagnesium iodide solution. The product was 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoro-2-methylpentan-2-ol (66%), and 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoropentan-2-ol was not detected.

Similar reaction with ethylmagnesium iodide gave 4 : 4 : 5 : 5 : 6 : 6 : 6-heptafluoro-3-methylhexan-3-ol (37%) and 3 : 3 : 4 : 4 : 5 : 5 : 5-heptafluoropentan-2-ol (22%).

Addition of Grignard solution to the ketone–magnesium bromide solution gave tertiary (35%) and secondary alcohol (26%).

Preparation of Secondary Alcohols by Reduction of Ketones.—A solution of the ketone (0·01 mole) in diethyl ether (10 ml.) was slowly added to one of lithium aluminium hydride (0·02 mole) in diethyl ether (10 ml.), stirred vigorously and cooled in ice. After the temperature had slowly risen to boiling point, water and then sulphuric acid were added, and the dried ethereal extracts were distilled. The yields of secondary alcohols obtained were :

Ketone ...	C_3F_7·COMe *	C_3F_7·COEt	C_3F_7·COPr	C_3F_7·CO·CF_3 *	C_3F_7·CO·C_2F_5 *	C_3F_7·CO·C_3F_7
Alcohol, %	67	71	62	61	69	83

* *n*-Butyl ether as solvent.

Oxidation of Certain Secondary Alcohols.—The following general procedure was used for the oxidation of 1-(perfluoropropyl)alkanols to the corresponding ketones. To the alcohol (0·02 mole) and 80% sulphuric acid (3 ml.) was added a solution of potassium dichromate (5 g.) in water (10 ml.) and concentrated sulphuric acid (4 ml.) as fast as was consistent with the temperature remaining below 80°. The ketone was then removed to a vacuum system and purified by fractionation. The yields of heptafluoropentan-2-one, heptafluorohexan-3-one, and heptafluoroheptan-4-one were 71, 75, and 68%, respectively.

Action of Alkali on Alkylheptafluoropropylketones.—The ketone C_3F_7·COR (R = Me, Et, Pr, or C_3F_7) (0·2 g.) was sealed with 5% aqueous sodium hydroxide (5 ml.) at room temperature for 36 hr. The yields of heptafluoropropane, identified spectroscopically (Part I, *loc. cit.*), were 81, 86, 83, and 88%, respectively.

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