Fluorinations with Potassium Tetrafluorocobaltate(III). Part II.[1] Fluorination of Ketones

By R. D. Bagnall, P. L. Coe,* and J. C. Tatlow, Chemistry Department, The University of Birmingham, P.O. Box 363, Birmingham B15 2TT

Diethyl ketone, hexafluoroacetone, and hexachloroacetone have been fluorinated over potassium tetrafluorocobaltate(III) to give polyfluoroacyl fluorides as the major products. Diethyl ketone was completely cleaved by cobalt(III) fluoride, though heptafluoro-n-propyl methyl ketone gave heptafluorobutyryl fluoride.

As part of an investigation of fluorination, by transition metal fluorides, of compounds containing functional groups we report the fluorination of ketones with cobalt(III) fluoride and potassium tetrafluorocobaltate-(III).[1]

Acetone, ethyl methyl ketone, and diethyl ketone have been fluorinated previously with cobalt(III) fluoride.[2] The characterisation of the products from these reactions was limited by the techniques available at the time the work was done. Acetone was reported to give a mixture of acetyl and monofluoroacetyl fluorides, as about 30% of the product, ethyl methyl ketone gave about 20% of fluoroacetyl fluoride, and diethyl ketone gave no acyl fluorides. The remaining products were thought to be polyfluoroethanes or methanes.

We have reinvestigated the fluorination of diethyl ketone at 100, 170, and 250 °C. The major products were polyfluoroethanes and carbonyl difluoride (Table 2) with increasing amounts of tetrafluoromethane and hexafluoroethane as the temperature of fluorination was increased. The proportion of fluorocarbon could be greatly reduced by fluorination over partly spent cobalt(III) fluoride. At all temperatures little or no acyl fluoride was detected, in accord with previous results. Surprisingly (but see later), fluorination over cobalt(III) fluoride of heptafluoro-n-propyl methyl ketone gave high yields of heptafluorobutyryl fluoride.

Since it seems that fluorination of simple ketones with cobalt(III) fluoride gives mainly cleavage products, we investigated fluorination with the milder reagent, potassium tetrafluorocobaltate(III).[1] Passage of diethyl ketone over this compound at 150, 240, or 350 °C gave moderate yields of products which could readily be divided into two fractions by treatment with water. The volatile water-insoluble fraction was shown by g.l.c. analysis to be a mixture of two components in the ratio of 1 : 3. Separation by preparative g.l.c. yielded 1,1,1-trifluoro- and 1,1,1,2-tetrafluoro-ethane, no other gaseous products being detected.

The aqueous layer was extracted with ether; the i.r. spectra of the isolated products suggested the presence of a mixture of acids. Esterification with ethanol or methanol gave mixtures of two esters which in each case were separated easily by g.l.c. These esters were shown by i.r., n.m.r., and mass spectrometry and analysis to be

the ethyl and methyl esters of 2-fluoro- and 2,2-difluoro-propionic acid. The yields of esters and ethanes were similar, suggesting that each was a product of a cleavage process of the ketone. As the fluorination temperature was increased more ester of the difluoro-acid was obtained. No carbonyl fluoride was detected, suggesting that the decomposition of acid fluorides over potassium tetrafluorocobaltate(III) is relatively slow.

Fluorination of hexachloroacetone (which could represent a simple route to trifluoroacetic acid) was carried out over potassium tetrafluorocobaltate(III) at 240° and 350° and yielded a mixture of three products, readily shown to be trichlorofluoromethane, dichlorofluoroacetyl fluoride, and trichloroacetyl fluoride. At lower temperatures mainly trichloroacetyl fluoride and trichloro-fluoromethane were obtained. At the higher temperature none of the dichlorofluoro-compound was isolated. Fluorination of hexafluoroacetone yielded only carbon tetrafluoride, carbonyl fluoride, and a trace of trifluoroacetyl fluoride. It was hoped that this experiment would confirm the stability of polyfluoroacyl fluorides; in fact it now seems likely that trifluoroacetyl fluoride is unstable at the reaction temperatures used.

Our results show that the major reaction in the fluorination of ketones is the cleavage of the C–CO bond, since no ketones were obtained. Fluorination over cobalt(III) fluoride also cleaves acid fluorides[3] if they are indeed intermediates in the fluorination. However, use of potassium tetrafluorocobaltate(III) yields acyl fluorides as major products, and we have subsequently shown[3] that acid fluorides can be smoothly fluorinated by it without cleavage. The intermediacy of acyl fluoride is further indicated by the fluorination of aldehydes;[4] complete loss of the carbonyl group is observed in this case and it is suggested that RĊO or RCO⁺ is an intermediate.

The manner in which the cleavage occurs is open to question. Two of the possible alternatives (Schemes 1 and 2) are illustrated, the second of which, i.e. co-ordination to the fluorinating agent leading to complete cleavage by a radical process, has more supporting evidence.[5] Potassium tetrafluorocobaltate(III), being a weaker Lewis acid, may not be able to co-ordinate to acid fluorides as well as cobalt(III) fluoride and hence they may be released as products. Alternatively cobalt(III)

[1] P. L. Coe, R. G. Plevey, and J. C. Tatlow, *J. Chem. Soc. (C)*, 1969, 1060.
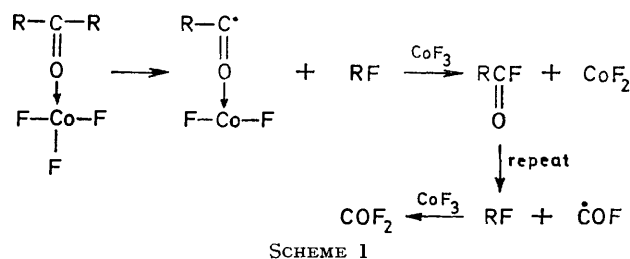[2] F. F. Holub and L. A. Bigelow, *J. Amer. Chem. Soc.*, 1950, 72, 4879.
[3] R. D. Bagnall and P. L. Coe, unpublished work.
[4] J. Burdon and B. L. Kane, unpublished work.
[5] J. Burdon, I. W. Parsons, and J. C. Tatlow, *Tetrahedron*, in the press.

fluoride or the tetrafluorocobaltate(III) salt, which are oxidising agents ($Co^{3+} \longrightarrow Co^{2+}$), can oxidise the ketone by electron abstraction from the carbonyl oxygen atom

SCHEME 1

as shown in Scheme 2 (this idea has been proposed for the oxidation of ketones by Co^{3+} in water [6]). However, potassium tetrafluorocobaltate(III) may not be able to carry out this second sequence, since it is less strongly oxidising than cobalt(III) fluoride, and acid fluorides can thus be isolated. In support of the carbonium ion mechanism it should be noted that in the oxidation of isopropyl methyl ketone by Co^{3+} in water only acetic acid [6] is formed [$(CH_3)_2CH^+$ is more stable than CH_3^+] and that with cobalt(III) fluoride heptafluoroisopropyl methyl ketone is cleaved to give heptafluoroisobutyryl

SCHEME 2
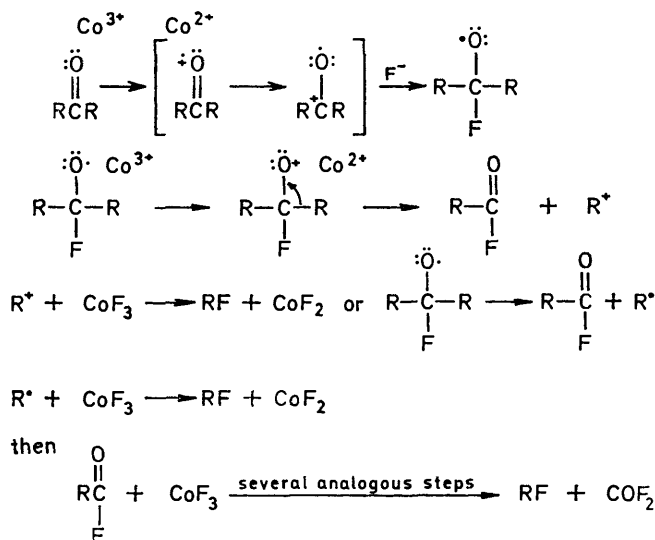
fluoride and fluoromethanes CH_nF_{4-n} (CH_3^+ should be more stable than $C_3F_7^+$). The only ethanes isolated in the fluorination of diethyl ketone by tetrafluorocobaltate(III) are the 1,1,1-trifluoro- and 1,1,1,2-tetrafluoro-derivatives, suggesting that the ketone becomes quite higly fluorinated before cleavage occurs, otherwise a more random mixture of fluoroethanes might have been expected.

Of interest also are the facts that no acid fluoride is isolated in which the β-position is fluorinated and the α- is not, and that the difluoropropionyl fluoride isolated from diethyl ketone is the αα- and not the αβ-derivative.

Possible interpretations of these observations are (i)

that the carbonyl group is co-ordinated to the metal fluoride, making replacement of the adjacent α-hydrogen atoms by fluorine easier, or (ii) that the metal fluoride increases the degree of enolisation of the ketone, which is then fluorinated via the enol form. There seems to be no simple way of distinguishing between these possibilities for diethyl ketone.

Thus, we conclude that whereas cobalt(III) fluoride completely cleaves simple ketones, the milder potassium tetrafluorocobaltate(III) will only cleave them as far as acid fluorides. This work suggested that fluorination of acid fluorides and esters would be more useful for synthetic work, and the results of such experiments will be reported shortly.

EXPERIMENTAL

Fluorination.—Fluorinations were carried out in reactors of conventional design which were packed with either cobalt(III) fluoride or potassium tetrafluorocobaltate(III). Reactors from 100 g to 10 kg capacity were used but the essential features of the results were independent of reactor size.

General Procedure.—The ketone was introduced dropwise in a stream of nitrogen (2—15 l h^{-1}, depending on the reactor size) at 100—350 °C. The effluent gases were passed over sodium fluoride pellets on a copper trap and then into glass traps cooled in liquid air. The product was worked up either by extracting with water or alcohol or by distillation.

Fluorination of Diethyl Ketone.—(a) *Over cobalt*(III) *fluoride.* Diethyl ketone was fluorinated at 100, 170, and 250 °C. The products were crudely separated by trap-to-trap distillation (see Table 1). The highly volatile material

TABLE 1

Fluorination of diethyl ketone over cobalt(III) fluoride

			Wt. (g) of fractions of b.p. (°C)		
T/°C	Input (g)	Yield (g)	< -35	-35 to 15	>15
100	81·5	115	50	37	26
100 *	87·5	125	35	35	53
170	78·5	195	141	46	8
170 *	81	192	65	80	45
250	83·5	210	144	56	9

* Carried out without refluorination of the cobalt fluoride.

was shown in a pilot experiment to be mainly tetrafluoromethane, carbonyl difluoride, hexafluoroethane, and pentafluoroethane (identified by i.r. spectroscopic comparison with standard spectra) and was discarded. Those compounds of b.p. $> -35°$ were separated and identified by i.r. comparison, mass spectrometry, and (where possible) ^1H and ^{19}F n.m.r. spectroscopy.[7] The results of these fluorinations are shown in Tables 1 and 2.

(b) *Over potassium tetrafluorocobaltate*(III). The ketone was fluorinated at 150, 240, and 350 °C. The products were treated with water at 20° and the unhydrolysed volatile materials collected in liquid air. The results are shown in Table 3.

Identification of the Products from the Fluorination of Diethyl Ketone with Potassium Tetrafluorocobaltate(III).— (a) A portion (3·0 g) of the volatile products from the run

[6] K. B. Wiberg, 'Oxidation in Organic Chemistry,' Part A, Academic Press, New York and London, p. 223.

[7] L. F. Thomas and J. C. Lindon, unpublished results.

at 150 °C was separated by g.l.c. [Carbowax 20M on Celite (1 : 5), 48 m × 35 mm, 50°, carrier gas nitrogen at 20 l h⁻¹] to yield 1,1,1-trifluoroethane (0·6 g) and 1,1,1,2-tetrafluoroethane (1·8 g), identified by their i.r. spectra.

TABLE 2

Compounds isolated from fluorination of diethyl ketone; amounts expressed as % total products isolated

Component	100	100 *	170	170 *	250
CHF$_2$·CH$_3$		1·3			
CH$_2$F·CH$_2$F	0·9	5·5	0·3	0·9	0·1
CF$_3$·CH$_3$	Trace	Trace	Trace		
CF$_2$H·CFH$_2$	26·8	51·3	8·8	28·1	8
CF$_3$·CH$_2$F	17·6	10·1	13·1	24·4	15·7
CF$_2$H·CF$_2$H	9·4	2·2	5·5	11·6	7·1

Temp. of fluorination (°C)

* Carried out without refluorination of the reactor.

TABLE 3

Fluorination of diethyl ketone over potassium tetrafluorocobaltate(III)

T/°C	Input (g)	Yield (g)	Wt. (g) of non-hydrolysed product
150	79	75	28
240	78·5	60	14
350	81·5	85	28

(b) The aqueous solution from the hydrolysis of the products of fluorination at 150 °C was neutralised with 10N-sodium hydroxide and extracted with ether (100 cm³ and 2 × 50 cm³). The combined extracts were dried (MgSO$_4$) (extract A). The aqueous layer was diluted with water (2 l) and acidified with 10N-hydrochloric acid. Continuous extraction of the acidified layer with ether gave extract B.

(i) *Extract A*. Careful distillation yielded only diethyl ketone (8·6 g); no fluorinated products were detected.

(ii) *Extract B*. Extract B was dried (MgSO$_4$) and concentrated to a straw-coloured liquid (31·2 g), the i.r. spectrum of which suggested that carboxylic acids were present. To a portion of this liquid (5 g) methanol (25 cm³) and concentrated sulphuric acid (0·5 cm³) were added, and the mixture was stirred at 20° for 24 h. After removal of excess of methanol, water (50 cm³) was added and the organic layer was separated and dried (CaCl$_2$). G.l.c. [dinonyl phthalate on Celite (1 : 4), 4·8 m × 35 mm, 100°, carrier gas nitrogen at 20 l h⁻¹] gave (i) *methyl 2,2-difluoropropionate* (2·4 g), b.p. 94—95° [Found: C, 38·5; H, 5·6; F, 30·1%; M (mass spec.), 124. C$_4$H$_6$F$_2$O$_2$ requires C, 38·7; H, 4·9; F, 30·6%; M, 124], ¹H n.m.r. τ 6·15 (3H, s, OMe) and 8·22 (3H, t, CF$_2$·CH$_3$, J_{HF} 18·9 Hz), ¹⁹F n.m.r. 98·9 p.p.m. (from CFCl$_3$) (q, CF$_2$·CH$_3$, J_{HF} 18·9 Hz); and (ii) methyl 2-fluoropropionate (1·0 g), b.p. 107·5° (lit.,[8] 106·5—108·5°) [Found: C, 45·7; H, 6·8; F, 18·0%; M (mass spec.), 106. Calc. for C$_4$H$_7$FO$_2$: C, 45·3; H, 6·6; F, 17·9%; M, 106], ¹H n.m.r. τ 8·43 (3H, dd, CFH·CH$_3$, J_{HF} 23, J_{HH} 6·8 Hz), 6·21 (3H, s, OMe), and 5·08 (1H, dq, J_{HF} 48·5, J_{HH} 6·7 Hz), ¹⁹F n.m.r. 183·7 p.p.m. (from CCl$_3$F) (dq, J_{HF} 49·2, J_{HH} 23·0 Hz).

A similar experiment in which ethanol was used yielded *ethyl 2,2-difluoropropionate* (2·5 g), b.p. 103—104° [Found: C, 43·6; H, 5·7; F, 27·8%; M (mass spec.), 139. C$_5$H$_8$F$_2$O$_2$ requires C, 43·4; H, 5·8; F, 27·6%; M, 139], and ethyl 2-fluoropropionate (1·0 g), b.p. 123° (lit.,[8] 122·5—123°)

(Found: C, 49·9; H, 7·5%; M, 120. Calc. for C$_5$H$_9$FO$_2$: C, 50; H, 7·5%; M, 120); ¹H and ¹⁹F n.m.r. spectra were consistent with the structures. In the experiments at 240 and 350 °C with a similar work up the products in the proportions indicated as shown in Table 4 were obtained.

TABLE 4

Fluorination of diethyl ketone over potassium tetrafluorocobaltate(III); figures are % total product isolated

	150°	240°	350 °C
1,1,1-Trifluoroethane	9·3	5·8	8·2
1,1,1,2-Tetrafluoroethane	28	17·5	24·7
2-Fluoropropionyl fluoride *	12·1	18	3·6
2,2-Difluoropropionyl fluoride *	30	44·9	44·4
Diethyl ketone	15	13·8	10·6

* Isolated as esters.

Fluorination of Heptafluoro-n-propyl Methyl Ketone over Cobalt(III) *Trifluoride.*—The ketone (8 g) was fluorinated at 80°. The effluent gases were passed over sodium fluoride pellets and were then collected in a liquid-air-cooled trap. The products (7·5 g) were crudely separated by trap-to-trap distillation in three fractions: (i) b.p. <0°, (ii) b.p. 0—20°, (iii) b.p. >20°. Fraction (i) (1·7 g) was examined by gradual evaporation *in vacuo* into an i.r. gas cell; a mercury manometer was used to monitor the evaporation. After the measurement of each spectrum the cell was evacuated before evaporation was continued. The procedure was carried on until all the material had been examined. In this way five components: perfluoropropane, carbonyl difluoride, difluoromethane, trifluoromethane, and carbon tetrafluoride were identified, by comparison of their i.r. spectra with those of authentic samples. Fraction (ii) (2·0 g) was shown by i.r. spectroscopy to be heptafluorobutyryl fluoride; on hydrolysis heptafluorobutyric acid (1·5 g) was obtained. Fraction (iii) (3·4 g) was heptafluorobutyric acid and probably arose from hydrolysis of the acid fluoride by atmospheric moisture.

Fluorination of Hexachloroacetone over Potassium Tetrafluorocobaltate(III).—The ketone (63·5 g) was fluorinated at 230 °C in a stream of nitrogen (15 l h⁻¹). The product was collected in methanol (250 cm³) at −78°. The solution was warmed to 20 °C and poured into water (750 cm³), and the organic layer (24·5 g) was collected. The aqueous layer was extracted with ether but no organic material was thus isolated. The organic layer was separated by g.l.c. to yield (i) trichlorofluoromethane (2·0 g), identified by its i.r. spectrum; (ii) methyl dichlorofluoroacetate (0·3 g) (Found: C, 22·3; H, 1·9. Calc. for C$_3$H$_3$Cl$_2$FO$_2$: C, 22·3; H, 1·9%), identical (i.r. spectrum) with an authentic sample; (iii) methyl trichloroacetate (12 g), identical with an authentic sample; and (iv) hexachloroacetone 0·5 g). In a similar experiment at 350 °C trichlorofluoromethane (6·0 g), methyl dichlorofluoroacetate (5·0 g), and methyl trichloroacetate (6·0 g) were obtained.

Fluorination of Hexafluoroacetone over Potassium Tetrafluorocobaltate(III).—The ketone [from its hydrate (8·5 g)], fluorinated at 250 °C gave a product (0·9 g) shown to be mainly carbon tetrafluoride, with a trace of both carbonyl fluoride and trifluoroacetyl fluoride, by the technique described for heptafluoropropyl methyl ketone.

[8] A. M. Lovelace, D. A. Rausch, I. W. Postelnek, 'Aliphatic Fluoro-compounds,' Reinhold, New York, p. 180.