FLUORINATIONS WITH POTASSIUM TETRAFLUOROCOBALTATE(III) PART III*. FLUORINATION OF ESTERS AND ACYL FLUORIDES AND SOME REACTIONS OF THE DERIVED POLYFLUOROACIDS

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SUMMARY

Esters of propionic, acrylic, succinic, maleic and acetylene dicarboxylic acid have been fluorinated over $KCoF_4$ to give mixtures containing polyfluoroacid fluorides which have been isolated as esters, separated and characterised. Propionyl and isobutyryl fluorides also gave polyfluoroacid fluorides and thence esters on fluorination, but with increasing difficulty as the chain is branched so that pivaloyl fluoride was not fluorinated. Propionyl chloride gave, in addition to the expected acid fluorides, some polyfluorochloro compounds. Some reactions of the new acids and esters are described including the synthesis of benzimidazoles.

INTRODUCTION

In a previous paper[1] we described the fluorination of ketones with $KCoF_4$ to yield polyfluoroacid fluorides. We now report further examples of the fluorination of carbonyl compounds, *i.e.*, those of esters and acid fluorides, these being the first successful fluorinations of such compounds by a transition metal fluoride.

RESULTS AND DISCUSSION

Methyl propionate was fluorinated at 350° over $KCoF_4$ to yield a mixture of products obviously containing acid fluorides (IR spectroscopy) which was collected in cold ethanol, and the derived esters then crudely separated by trap-to-trap distillation. The small amount of highly volatile material obtained was indicated by IR spectroscopy to be mainly polyfluoro-methanes and -ethanes. The less volatile fraction was shown by GLC to be an approximate 5:2:2 mixture of

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* For Part II. see ref. 1.

three products. Separation of the mixture by preparative GLC gave ethyl-2,2-difluoropropionate, ethyl-2,2,3-trifluoropropionate and ethyl-2-fluoropropionate, compounds previously obtained from the fluorination of diethyl ketone[1]. It appeared that at this temperature the ester group had been completely cleaved.

To increase the proportion of the trifluoropropionate, methyl acrylate was fluorinated and the products were collected in ethanol. At 300°, apart from a small amount of very volatile material which was discarded, a mixture of two products in the ratio of 2:3 was obtained. Separation of the mixture afforded methyl- and ethyl-2,2,3-trifluoropropionate showing that part (60%) of the ester was cleaved and part (40%) passed through the reactor with its ester function intact. This contrasts with diethyl ketone which was completely cleaved at this temperature. The fact that only trifluoroesters were isolated suggests that fluorination of the double bond in the starting ester occurs initially, followed by subsequent fluorination at the α-carbon atom. A repeat of the fluorination at 400° gave a mixture of ethyl-2,2,3-trifluoropropionate and ethyl-2,2,3,3-tetrafluoropropionate in a 3:1 ratio, indicating complete cleavage of the acyl oxygen bond. It seems that the carbonyl group itself however will survive quite drastic fluorination conditions with this reagent.

Success with monobasic acid esters prompted us to extend the fluorination to dibasic acid derivatives.

Fluorination of dimethyl succinate at 270°, the products being collected in ethanol, gave a moderate yield of a mixture of esters. The major products (in about equal amounts) were ethyl pentafluoropropionate and ethyl-2,2,3,3-tetrafluoropropionate. Small quantities of methyl pentafluoropropionate and a mixture of other esters were isolated, the latter being too complicated to separate on the scale of the reaction. No polyfluorosuccinic esters were detected. This result suggests that diacid fluorides are unstable under the reaction conditions, readily decomposing to the monoacid derivatives.
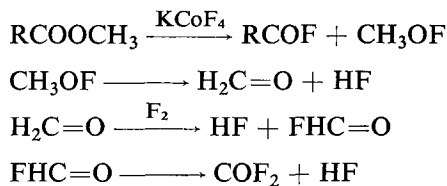
Fluorination of dimethyl maleate at 260° gave a similar pattern of products to dimethyl succinate except that rather more ethyl-2,2,3,3-tetrafluoropropionate was obtained.

In view of the reasonable stability of the carbonyl group in these reactions, we repeated the fluorinations of methyl propionate and dimethyl succinate over cobalt(III) fluoride. The products contained no esters; only polyfluoro-methanes and -ethanes were detected with traces of dimethyl carbonate derived from carbonyl fluoride.

Fluorination of benzoic acid derivatives by the electrochemical method yielded perfluorocyclohexane carboxylic acid which readily decomposed to give perfluorocyclohexene[3]. We attempted the fluorination of methyl benzoate over KCoF$_4$ but obtained no esters, only decafluorocyclohexene and dodecafluoro-cyclohexane. We suggest the acid fluoride was probably formed but decomposed to the cyclohexene and carbonyl fluoride at the reactor temperatures used.

The fate of the alcoholic alkyl groups in these fluorinations has not been determined precisely. n-Propyl trifluoroacetate was fluorinated in the hope that products corresponding to the fluorination of the alkyl group might be isolated. In fact only starting material and methyl trifluoroacetate (from methanol into which the products were passed) were isolated.
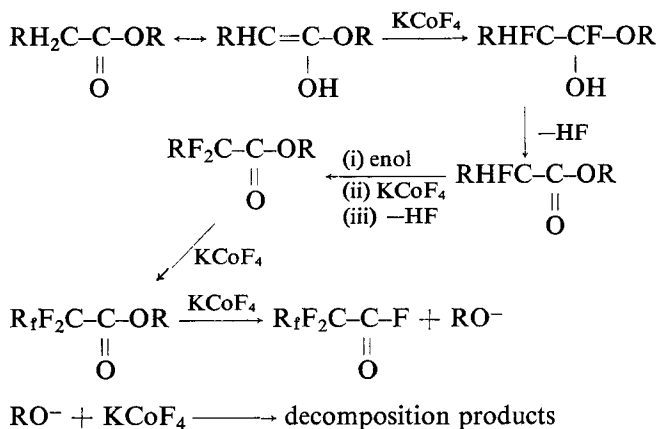
We suggest that the alkyl group probably leaves as an alkoxy species which is further degraded as follows, although a number of other intermediate steps may well be involved.

$$RCOOCH_3 \xrightarrow{\text{KCoF}_4} RCOF + CH_3OF$$

$$CH_3OF \longrightarrow H_2C{=}O + HF$$

$$H_2C{=}O \xrightarrow{\text{F}_2} HF + FHC{=}O$$
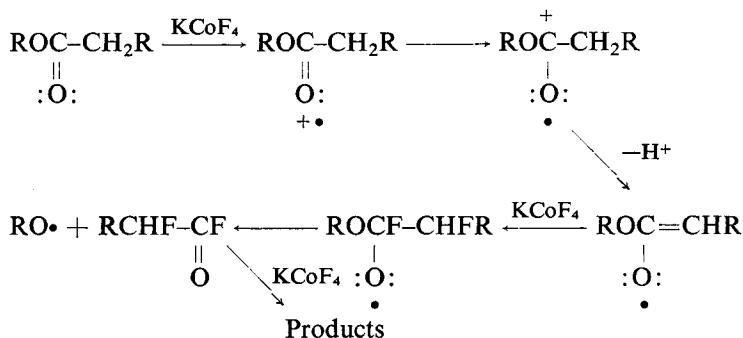
$$FHC{=}O \longrightarrow COF_2 + HF$$

In the above scheme we indicate that acid fluorides are intermediates; fluorination of acid fluorides should therefore give similar products to those from the corresponding esters.

Fluorination of propionyl fluoride at 300° gave, on esterification of the products with methanol, a mixture of methyl-2,2-difluoropropionate and methyl-2-fluoropropionate in the ratio of 2:3; no ester derived from 2,2,3-trifluoropropionic acid was isolated, unlike the corresponding fluorination of methyl propionate. This observation suggests that esters are easier to fluorinate than acid fluorides, and this may be due to the greater ease of enolisation of esters. Thus, we can envisage fluorination of the ester, possibly *via* the enol form, first to give α-fluorination with any fluorination at the β position occurring subsequently. It appears[2] that methyl groups are not readily fluorinated [note that CF₃CH₃ is the predominant ethane obtained in the fluorination of methyl ethyl ketone[1]] and hence we might expect a lower degree of fluorination at the β position. We can then suggest that if the initial steps (*i.e.* enolisation/fluorination) are slow, the product emerges from the reactor only lightly fluorinated, *e.g.* as acid fluorides, whereas ready enolisation or the presence of multiple bonds leads to a higher degree of fluorination, *cf.* methyl acrylate. If this argument is valid, three points emerge: first, the cleavage of esters should occur relatively late in the fluorination; secondly, there should be a predominance of α-fluorination; and thirdly, branched-chain esters or acid fluorides should be more difficult to fluorinate than straight-chain compounds. The first point is partly borne out by the presence of highly fluorinated but uncleaved esters in some fluorinations; thus some methyl pentafluoropropionate, for example, was isolated during the fluorination of dimethyl maleate using an ethanol work-up. The second point is substantiated for although some products are exclusively α-fluorinated no esters were found which were fluorinated to a greater extent on the β-carbon atom than on the α-carbon atom,

i.e., α-fluorination occurs first. The third point was tested by fluorination of isobutyryl and pivaloyl fluorides which yielded 2-fluoro-2-methyl propionic acid and unchanged pivalic acid, respectively, *i.e.*, if there is no α-hydrogen atom for enolisation, fluorination does not readily occur. We can thus suggest the following pathway as being plausible for these fluorinations.

$$
RH_2C\text{-}C\text{-}OR \longrightarrow RHC{=}C\text{-}OR \xrightarrow{\ KCoF_4\ } RHFC\text{-}CF\text{-}OR
$$

with $\underset{O}{\|}$ on first carbonyl, $\underset{OH}{|}$ on enol, $\underset{OH}{|}$ on product

$$
RF_2C\text{-}C\text{-}OR \xleftarrow[\substack{\text{(ii) KCoF}_4\\ \text{(iii) }-HF}]{\text{(i) enol}} RHFC\text{-}C\text{-}OR \qquad \downarrow\ -HF
$$

$\underset{O}{\|}$

$$
\swarrow KCoF_4
$$

$$
R_fF_2C\text{-}C\text{-}OR \xrightarrow{\ KCoF_4\ } R_fF_2C\text{-}C\text{-}F + RO^-
$$

with $\underset{O}{\|}$

$$
RO^- + KCoF_4 \longrightarrow \text{decomposition products}
$$

An alternative explanation is that $KCoF_4$ acts as an oxidising agent as previously postulated[4] and oxidises the carbonyl group with the subsequent steps shown below:

$$
ROC\text{-}CH_2R \xrightarrow{\ KCoF_4\ } ROC\text{-}CH_2R \longrightarrow \overset{+}{R}OC\text{-}CH_2R
$$

with $:\overset{..}{O}:$, then $\underset{+\bullet}{O:}$, then $\overset{\bullet}{:\overset{..}{O}:}$

$$
\searrow -H^+
$$

$$
RO\bullet + RCHF\text{-}CF \longleftarrow ROCF\text{-}CHFR \xleftarrow{\ KCoF_4\ } ROC{=}CHR
$$

with $\underset{O}{\|}$ $\searrow$ $\underset{KCoF_4\ :\overset{\bullet}{\overset{..}{O}}:}{|}$ and $\underset{:\overset{\bullet}{\overset{..}{O}}:}{|}$

Products

The net result of these alternatives is the same except that the former leads to easier fluorination at the α-carbon atom. We cannot as yet choose between the alternatives but we feel that both are plausible.

An interesting result was obtained when propionyl chloride was fluorinated. In addition to the expected product, *i.e.* methyl-2,2-difluoropropionate, esters which contained chlorine on both the α and β positions were isolated although those substituted in the β position, *viz.*, methyl-2-chloro-2-fluoropropionate, 3-chloro-2,2-difluoropropionate and 3-chloro-2,2,3-trifluoropropionate, were favoured.

These fluorinations indicate that under mild conditions with suitable transition metal fluorides it is possible to retain functional groups such as carbonyl. To our knowledge these constitute the first examples of such reactions and represent a practical method of preparation of some fluoroacids of novel structure.

Some of the simple reactions of the fluorination products described above have been studied. Thus, treatment of the esters of 2,2-difluoro- and 2,2,3-trifluoropropionic acids with anilino magnesium iodide yielded the corresponding anilides. Alkaline hydrolysis of the above esters followed by treatment with s-benzyl isothiouronium chloride gave the expected salts.

An attempt to carry out the Hunsdieker reaction, a well tried and useful reaction in the fluorocarbon field, on silver 2,2-difluoropropionate did not give the desired result. Under conditions when silver perfluoropropionate gave a good yield of perfluoroethyl iodide, silver 2,2-difluoropropionate gave 1,1-difluoroethylene as the only isolable product. This suggests that the expected iodide was first formed and then was thermally dehydroiodinated to give the ethylene.

To test the reactivity of partly fluorinated esters in the Claisen condensation, we carried out the reaction between ethyl-2,2-difluoroacetate and ethyl acetate under the conditions used for the reaction between ethyl trifluoroacetate and ethyl acetate[5] using sodium ethoxide as the condensing agent. The condensate was isolated as its copper chelate which readily formed, and from which, by reaction with hydrogen sulphide, ethyl-4,4-difluoro-3-oxopentanoate was isolated in reasonable yield.

As part of a further study[6] on the preparation of benzimidazoles, some of the polyfluoro- and chloropolyfluoro-acids yielded benzimidazoles on reaction with 4,5-dichloro-1,2-phenylenediamine. These benzimidazoles showed some biological activity which is being further investigated.

EXPERIMENTAL

Fluorinations were carried out as previously described[1] in reactors of conventional design. The effluent gases were passed over sodium fluoride pellets to remove hydrogen fluoride and the products collected in glass traps cooled in liquid air.

Fluorination of methyl propionate with potassium tetrafluorocobaltate(III) (KCoF₄)

Methyl propionate (84.0 g) was fluorinated over potassium tetrafluorocobaltate(III) at 350° in a stream of nitrogen (10 l h⁻¹) during 2 h, the nitrogen flow being maintained for a further 2 h. The products were collected in ethanol (100 ml) at −78°. The ethanolic solution was warmed to 20° and the highly volatile material, shown to be a mixture of fluoro-ethanes and -methanes, was allowed to escape. The solution was poured into water (750 ml) and the lower organic layer (40.0 g) was collected, ether extraction of the aqueous layer affording only traces

of organic material which were not investigated. Gas chromatography of the organic layer indicated three product peaks. Separation by preparative GLC (1:2 mixture of dinonyl phthalate/Celite in a 4.8 m × 35 mm column maintained at 100°, N_2 flow rate 20 l h^{-1}) of a portion (9.0 g) gave (i) ethyl-2,2-difluoro-propionate (2.5 g), (ii) ethyl-2,2,3-trifluoropropionate (1.0 g) and (iii) ethyl-2-fluoropropionate (0.8 g) all identical with authentic samples[1].

Fluorination of methyl acrylate with KCoF₄

(a) At 300°

Methyl acrylate (59.0 g) was fluorinated and the products worked up as above to yield mixed esters (40.0 g), the aqueous layer yielding no organic compounds.

A portion (25 g) of the product was separated as above to yield (i) methyl-2,2,3-trifluoropropionate (nc) (7.0 g), b.p. 108° and (ii) ethyl-2,2,3-trifluoro-propionate (nc) (11 g), b.p. 117°[1].

For methyl-2,2,3-trifluoropropionate: Analysis: Found: C, 34.0; H, 3.7; F, 40.4%. $C_4H_5F_3O_2$ requires C, 33.8; H, 3.5; F, 40.1%. ¹H NMR: 6.8 τ (s-OMe) and 5.35 τ (doublet, $J(HF_{gem}) = 45.9$ Hz, of triplet, $J(HF_{vic}) = 11.7$ Hz, CH_2F) in the intensity ratio 3:2. ¹⁹F NMR: 117.4 ppm (doublet, $J(FF) = 16.9$ Hz, of triplet, $J(HF) = 11.7$ Hz, CF_2) and 239.8 ppm (triplet, $J(FF) = 16.9$ Hz, of triplet, $J(HF) = 45.2$ Hz, CFH_2) in the intensity ratio 2:1.

For ethyl-2,2,3-trifluoropropionate: Analysis: Found: C, 38.5; H, 4.7; F, 36.7%; m/e, 156. $C_4H_7F_3O_2$ requires C, 38.4; H, 4.5; F, 36.5%; m/e, 156. ¹H NMR: 8.6 τ (triplet, $J(HA) = 7.2$ Hz), 5.62 τ (quartet, $J(HH) = 7.2$ Hz, OEt) and 5.32 τ (doublet, $J(HF_{gem}) = 46.2$ Hz, of triplet, $J(HF_{vic}) = 11.8$ Hz, CH_2F) in the intensity ratio 3:2:3. ¹⁹F NMR: 117.6 ppm (doublet, $J(FF) = 17.2$ Hz, of triplet, $J(HF) = 11.5$ Hz, H_2CF_2) and 239.8 ppm (triplet, $J(HF) = 45.7$ Hz, of triplet, $J(FF) = 16.9$ Hz, CH_2F) in the intensity ratio 2:1.

(b) At 400°

In a similar fluorination but at 400°, methyl acrylate (60 g) gave ethyl-2,2,3-trifluoropropionate (9.0 g) and ethyl-2,2,3,3-tetrafluoropropionate (3.5 g) identical with authentic samples.

Fluorination of dimethyl succinate with KCoF₄

Dimethyl succinate (74 g) was fluorinated as above at 270° and the products collected in ethanol (150 ml) to yield mixed esters (18.0 g). A portion (10 g) of this mixture was separated as before to yield (i) methyl pentafluoropropionate (0.1 g) identical to a sample prepared from methanol and pentafluoropropionic acid, (ii) ethyl pentafluoropropionate (2.4 g) identical with an authentic sample, (iii) a complex mixture of at least six unidentified minor components (0.5 g) and (iv) ethyl-2,2,3,3-tetrafluoropropionate (2.2 g) identical with an authentic sample[7].

Fluorination of dimethyl maleate with KCoF$_4$

    (a) At 260°

Dimethyl maleate (100 g) was fluorinated as above and the products collected in ethanol (150 ml) yielding mixed esters (28.0 g). A portion (25 g) of the mixture was separated as above to yield (i) methyl pentafluoropropionate (0.1 g), (ii) ethyl pentafluoropropionate (3.8 g), (iii) a complex mixture (3.0 g) and (iv) ethyl-2,2,3,3-tetrafluoropropionate (4.8 g). All the named compounds were identical to authentic samples.

    (b) At 350°

As before, dimethylmaleate (84.0 g) on fluorination at 350° gave esters (22.0 g) which separated as above to give methyl pentafluoropropionate (0.7 g), ethyl pentafluoropropionate (2.8 g), a mixture (1.1 g) and ethyl-2,2,3,3-tetrafluoropropionate (6.0 g).

Fluorination of the dimethyl ester of diethylene dicarboxylic acid

    The ester (50 g) was fluorinated at 300° to yield mixed esters (15 g). Separation (8.0 g) as above gave (i) ethyl pentafluoropropionate (3.0 g) and ethyl-2,2,3,3-tetrafluoropropionate (0.5 g).

Fluorination of esters with cobalt(III) trifluoride

    Methyl propionate (2.8 g) was fluorinated over CoF$_3$ at 200° as previously described. The product (4.0 g) was collected in a glass trap cooled in liquid air, from which it was allowed to evaporate into methanol (4 ml). All products (3.0 g) which passed through the methanol were recondensed and examined by "warm-up" infrared spectroscopy, *i.e.* the temperature of the trap was slowly raised and a spectrum of the compounds in the vapour measured. By this means carbonyl fluoride and a mixture of polyfluoro-methanes and -ethanes were detected; the latter could not be positively identified. Examination of the methanol layer showed methanol and dimethyl carbonate, presumably from the reaction of methanol and carbonyl fluoride, to be present.

    Fluorination of dimethyl succinate (2.5 g) in the manner just described gave a product (4.4 g) of very similar composition.

Fluorination of methyl benzoate with KCoF$_4$

    Methyl benzoate (62 g) was fluorinated at 300° as described above and the product trapped in ethanol (100 ml) yielding on working up an organic layer (70 g). The organic layer showed no absorption in the 1700–1900 cm^{-1} region of the IR spectrum indicating the absence of a carbonyl group. Analytical gas chromatography showed the presence of two major components and ethanol. Separation of a portion (9.0 g) of the mixture gave (i) dodecafluorocyclohexane (2.2 g) and (ii) decafluorocyclohexene (2.0 g), both identical with authentic samples, and (iii) ethanol (2.3 g).

Fluorination of n-propyl trifluoroacetate with KCoF₄

The ester (50 g) was fluorinated at 280° in a nitrogen stream (10 l h⁻¹). The products were collected in methanol (150 ml) which on pouring into water gave an organic layer (11.0 g). Separation as above by gas chromatography gave (i) methyl trifluoroacetate (3.5 g) and (ii) n-propyl trifluoroacetate (3.5 g).

Fluorination of propionyl fluoride with KCoF₄

Propionyl fluoride (46 g) was fluorinated as above at 300°. The effluent gases were passed over heated sodium fluoride and collected in liquid air cooled traps to yield an organic layer (55 g). The product mixture was warmed to 20° and the very volatile components (mainly ethanes) were allowed to escape, only trace quantities being observed. The residue was washed with water (2 l) and 10 mol l⁻¹ hydrochloric acid to give a homogeneous solution. Continuous ether extraction of the latter followed by distillation of the ether afforded a mixture of fluoroacids (53.0 g). Esterification of a portion (4 g) of this mixture with methanol (5 ml) and concentrated sulphuric acid (0.5 ml) gave a mixture of the corresponding methyl esters. Separation of this mixture by gas chromatography as above gave methanol, methyl-2,2-difluoropropionate (1.0 g) and methyl-2-fluoropropionate (1.5 g) identical with authentic samples.

Fluorination of isobutyryl fluoride with KCoF₄

Isobutyryl fluoride (38 g) was fluorinated at 250° and the product collected in methanol (100 ml) cooled to −78°. The methanol layer was poured into water (750 ml) to yield an organic layer (13.0 g). Separation of a portion (10 g) of this layer gave apart from four trace components, methyl isobutyrate (1.3 g) and methyl-2-fluoro-2-methyl propionate (4.3 g) b.p. 109° (cited[8] 108–109°). For the latter compound: Analysis: Found: C, 49.8; H, 7.7%. $C_5H_9FO_2$ requires C, 50.0; H, 7.5%. IR: $v(C=O)$, 1730–1760 cm⁻¹. ¹H NMR: 7.47 τ (6H, doublet, J(HF) = 21.3 Hz, CH₃CF) and 6.23 τ (3H, s-OMe). ¹⁹F NMR: 146.7 ppm (relative to CCl₃F) (1F, septet J(HF) = 21.1 Hz).

Fluorination of pivaloyl fluoride with KCoF₄

Pivaloyl fluoride (43 g) was fluorinated as above to yield a product (3.8 g) identified as methyl pivaloate by IR spectroscopy.

Fluorination of propionyl chloride with KCoF₄

Propionyl chloride (50.0 g) was fluorinated at 280° and worked up as above with methanol to yield mixed esters (45 g). Separation of a portion (35 g) of the mixture as above gave (i) methyl-2,2-difluoropropionate (7.5 g) identical to an authentic sample, (ii) methyl-2-chloro-2-fluoropropionate (nc) (3.0 g), b.p. 122.5°, (iii) a mixture (3.0 g) which was further separated on a Pye 104 instrument using a 2 m × 5 mm column containing dinonyl phthalate/Celite in a 1:2 ratio to give

component (ii) (0.8 g) and methyl-3-chloro-2,2,3-trifluoropropionate (nc) (1.2 g), (iv) a complex mixture (1.0 g) and (v) methyl-3-chloro-2,2-difluoropropionate (nc) (4.3 g) b.p. 129°.

For methyl-2-chloro-2-fluoropropionate: Analysis: Found: C, 34.2; H, 4.0; Cl, 25.3%. $C_4H_6ClFO_2$ requires C, 34.2; H, 4.3; Cl, 25.3%. IR: v(C=O), 1760 (s) cm^{-1}. ^{1}H NMR: 7.93 τ (3H, doublet, J(HF) = 19.8 Hz, CH_3CF) and 6.15 τ (3H, s-OMe). ^{19}F NMR: 108.7 ppm (relative to CCl_5F) (quartet, J(HF) = 20 Hz).

For methyl-3-chloro-2,2,3-trifluoropropionate: Analysis: Found: C, 27.3; H, 2.5; F, 32.3%. $C_4H_4ClF_3O_2$ requires C, 27.2; H, 2.3; F, 32.3%. ^{1}H NMR: 3.64 τ (1H, doublet, J(HF$_{gem}$) = 48 Hz, of triplet, J(HF$_{vic}$) = 7.0 Hz, $CHFCF_2$) and 6.0 τ (3H, s-OMe). ^{19}F NMR: 119.3 ppm (relative to CCl_3F) (1F, complex multiplet) and 156.9 ppm (doublet, J(HF) = 48.8 Hz, of triplet, J(FF) = 15.9 Hz).

For methyl-3-chloro-2,2-difluoropropionate: Analysis: Found: C, 30.5; H, 3.2; Cl, 22.2%. $C_4H_5ClF_2O_2$ requires C, 30.3; H, 3.2; Cl, 22.4%. ^{1}H NMR: 6 τ (3H, s-OMe) and 7.0 τ (1H, triplet, J(HF) = 12.7 Hz, $\underline{CH_2}$Cl). ^{19}F NMR: 109 ppm (relative to CCl_3F) (triplet, J(HF) = 12.74 Hz).

Reactions of esters and acids

(a) Preparation of 2,2-difluoropropionanilide

Anilino magnesium iodide [from aniline (1.0 g) and methyl magnesium iodide] in ether (10 ml) and ethyl-2,2-difluoropropionate (1.0 g) in ether (5 ml) were stirred at 20° for 1 h when 5 mol l^{-1} hydrochloric acid (5 ml) was added. The ether layer was separated, combined with the ether extracts (2 × 10 ml) of the aqueous layer and dried ($MgSO_4$). Evaporation of the ether afforded 2,2-difluoro-propionanilide (nc) (1.0 g) m.p. 68° (after recrystallisation from aqueous ethanol). Analysis: Found: C, 58.2; H, 4.6; F, 20.7; N, 7.5%. $C_9H_9F_2NO$ requires C, 58.4; H, 4.9; F, 20.5; N, 7.6%.

(b) Preparation of 2,2,3-trifluoropropionanilide

In a similar manner to that described above, ethyl-2,2,3-trifluoropropionate (0.9 g) yielded 2,2,3-trifluoropropionanilide (nc) (0.6 g) m.p. 55°. Analysis: Found: C, 52.9; H, 3.9; N, 6.4%. $C_9H_8F_3$ requires C, 53.2; H, 3.9; N, 6.9%.

(c) Hydrolysis of methyl-2,2-difluoropropionate

The ester (19.0 g) and water (100 ml) containing sodium hydroxide (6.12 g) were shaken together for 1 h at 20°. Rotary evaporation of excess water yielded sodium 2,2-difluoropropionate (20.3 g). To a portion of the salt (17.0 g) was added concentrated sulphuric acid (50 ml). Distillation of the mixture yielded 2,2-difluoropropionic acid (8.5 g) b.p. 141° (cited[9] 140–141°). Formation of the s-benzyl isothiouronium salt in the usual way from sodium 2,2-difluoropropionate (1.0 g) gave s-benzyl isothiouronium-2,2-difluoropropionate (nc) (0.8 g) m.p. 191°. Analysis: Found: C, 47.9; H, 5.2; F, 13.3; N, 10.1%. $C_{11}H_{14}F_2N_2O_2S$ requires C, 47.8; H, 5.1; F, 13.8; N, 10.1%.

(d) Hydrolysis of ethyl-2,2,3-trifluoropropionate

In the same manner as described above, ethyl trifluoropropionate (0.8 g) gave s-benzyl isothiouronium-2,2,3-trifluoropropionate (nc) (0.8 g) m.p. 175°. Analysis: Found: C, 45.1; H, 4.6; F, 19.1; N, 9.5%. $C_{11}H_{13}F_3N_2O_2S$ requires C, 44.9; H, 4.4; F, 19.4; N, 9.5%.

Reactions of silver 2,2-difluoropropionate with iodine

Iodine (20.0 g) was sublimed in a stream of nitrogen (10 l h^{-1}) over P_2O_5 and the dried vapour passed through a glass tube containing silver 2,2-difluoro-propionate (15.5 g) [made from the aqueous acid and silver oxide followed by evaporation] at 110°. The product (2.3 g) was collected in a liquid air cooled trap and was shown by GLC to be a single component. The IR spectrum was identical to that of 1,1-difluoroethylene.

Condensation of ethyl-2,2-difluoropropionate with ethyl acetate

To dry ethanol (2.35 g) in ether (25 ml) was added sodium hydride (1.2 g) to give a suspension of sodium ethoxide. To the suspension was added a mixture of ethyl acetate (4.5 g) and ethyl-2,2-difluoropropionate (7.5 g). The mixture was refluxed for 72 h, cooled and 1 mol l^{-1} sulphuric acid (50 ml) added. The ether layer was separated and combined with the ether extracts (2 × 25 ml) of the aqueous layer. Distillation of the dried (MgSO$_4$) extracts yielded (after a pre-run of ethyl acetate and a trace of ethyl-2,2-difluoropropionate) a fraction (5.5 g) b.p. 150–177°. A portion of this latter (4.0 g) on treatment with cupric acetate gave a green solid (3.3 g) which on four recrystallisations from aqueous ethanol gave the copper chelate of ethyl-4,4-difluoro-3-oxopentanoate (nc) (2.1 g) m.p. 150°. Analysis: Found: C, 39.4; H, 4.1; F, 17.5%. $C_{14}H_{18}F_4O_6Cu$ requires C, 39.8; H, 4.3; F, 18.0%.

Hydrogen sulphide was bubbled through a solution of the copper chelate (0.7 g) in ether (20 ml) to yield on filtration and evaporation of the ether, ethyl-4,4-difluoro-3-oxopentanoate (nc) (0.5 g) b.p. 168°. Analysis: Found: C, 46.3; H, 5.3; F, 21.6%. $C_7H_{10}F_2O_3$ requires C, 46.6; H, 5.6; F, 21.1%.

Benzimidazole formation

(a) 5,6-Dichloro-2-(1,1-difluoroethyl)benzimidazole

Sodium 2,2-difluoropropionate (4.8 g), 10 mol l^{-1} hydrochloric acid (50 ml) and 4,5-dichloro-1,2-phenylenediamine (5.0 g) were heated at 105° for 48 h. The reaction mixture was cooled to 20° and poured into water (100 ml) to give a red precipitate (4.7 g). The clear red solution was neutralised with 4 mol l^{-1} ammonium hydroxide to give a brown precipitate (1.0 g). The precipitates were combined and sublimed (200°/15 mmHg) to give a white solid (2.3 g) which on recrystallisation from aqueous ethanol gave 5,6-dichloro-2-(1,1-difluoroethyl)benzimidazole (nc) (1.8 g) m.p. 223°. Analysis: Found: C, 42.8; H, 2.5; F, 14.7; N, 11.0%; *m/e*, 250.

$C_9H_6Cl_2F_2N_2$ requires C, 43.0; H, 2.4; F, 15.3; N, 11.3%; m/e, 250. ^{1}H NMR: 7.82 τ (3H, J(HF) = 19 Hz, CF_2CH_3) and 2.16 τ (2H, sym. aromatic H). ^{19}F NMR: 87.5 ppm (relative to CCl_3F) (quartet, J(HF) = 19.3 Hz).

(b) 5,6-Dichloro-2-(1,1,2-trifluoroethyl)benzimidazole

In a similar manner to that just described, the sodium salt of ethyl-2,2,3-trifluoropropionate (4.0 g) afforded 5,6-dichloro-2-(1,1,2-trifluoroethyl)benzimidazole (nc) (2.2 g) m.p. 210–211°. Analysis: Found: C, 40.2; H, 2.0; Cl, 26.6; N, 10.4%; m/e, 268. $C_9H_5Cl_2F_2N_2$ requires C, 40.0; H, 1.9; Cl, 26.4; N, 10.4%; m/e, 268. ^{1}H NMR: 4.87 τ (2H, doublet, J(HF) = 45.9 Hz, of triplet, J(HF) = 12.9 Hz) and 2.13 (2H, sym. aromatic H). ^{19}F NMR: 107.1 ppm (relative to CCl_3F) (2F, doublet, J(FF) = 17.0 Hz, of triplet, J(HF) = 12.5 Hz) and 237.3 ppm (relative to CCl_3F) (1F, triplet, J(HF) = 45.5 Hz, of triplet, J(FF) = 16.9 Hz).

(c) 5,6-Dichloro-2-(1,1,2,2-tetrafluoroethyl)benzimidazole

Ethyl-2,2,3,3-tetrafluoropropionate (4.0 g) afforded as above 5,6-dichloro-2-(1,1,2,2-tetrafluoroethyl)benzimidazole (nc) (1.9 g) m.p. 205°. Analysis: Found: C, 57.6; H, 1.7; F, 26.7; Cl, 25.0; N, 9.7%. $C_9H_4Cl_2F_4H_2$ requires C, 37.6; H, 1.4; F, 26.5; Cl, 24.7; N, 9.8%. ^{1}H NMR: 3.23 τ (1H, triplet, J(HF$_{gem}$) = 52.8 Hz, of triplet, J(HF$_{vic}$) = 5.1 Hz) and 2.09 τ (2H, sym. aromatic H). ^{19}F NMR: 116.2 ppm (relative to CCl_3F) (2F, triplet, J(FF) = 8.5 Hz, of triplet, J(HF) = 5.0 Hz) and 137.8 ppm (2F, doublet, J(HF) = 52.5 Hz, of triplet, J(HF) = 8.51 Hz).

(d) 5,6-Dichloro-2-(2-chloro-1,1-difluoroethyl)benzimidazole

Methyl-3-chloro-2,2-difluoropropionate (1.4 g) as before yielded 5,6-dichloro-2-(2-chloro-1,1-difluoroethyl)benzimidazole (nc) (0.8 g) m.p. 177°. Analysis: Found: C, 37.6; H, 1.9; F, 14.0; Cl, 37.6; N, 9.7%; m/e, 284. $C_9H_5Cl_3F_2H_2$ requires C, 37.8; H, 1.8; F, 13.3; Cl, 37.3; N, 9.8%; m/e, 284. ^{1}H NMR: 5.49 τ (2H, triplet, J(HF) = 13.9 Hz) and 2.13 τ (2H, sym. aromatic H). ^{19}F NMR: 99.6 ppm (relative to CCl_3F) (triplet, J(HF) = 14.4 Hz, CF_2CH_2Cl).

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