Studies upon α-Trifluoromethylacrylic Acid, α-Trifluoromethylpropionic Acid, and Some Derived Compounds.

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Pyrolyses of the *O*-acetates of trifluoroacetone cyanohydrin and methyl α-hydroxy-α-trifluoromethylpropionate gave α-trifluoromethylacrylonitrile and methyl α-trifluoromethylacrylate, respectively. From these, (*a*) α-trifluoromethylacrylic acid and its amide, and (*b*) α-trifluoromethylpropionic acid, various derived compounds, and derivatives of some substituted acids based on it, were synthesised. These materials show remarkable properties. In particular the unsaturated and some of the saturated compounds possess trifluoromethyl groups which are unusually susceptible to alkaline hydrolysis, possibly owing to hyperconjugation.

The synthesis, in these laboratories, of α-hydroxy-α-trifluoromethylpropionic acid and certain of its derivatives was described recently (Darrall, Smith, Stacey, and Tatlow, *J.*, 1951, 2329). We now report an extension of this study involving conversions of these compounds into α-trifluoromethylacrylic acid derivatives, and additions at the double bonds of these unsaturated products. It was found in the earlier work that the hydroxyl

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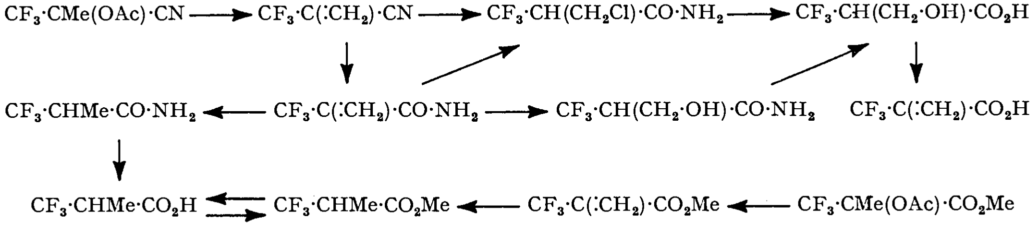
* *Added in Proof.*—This specimen was not optically pure. We are indebted to Dr. W. Gerrard for drawing our attention to his preparation of (—)-1-phenylethyl chloride (*J.*, 1946, 741), having $[\alpha]_D^{16}$ —99·6°, by the action of phosphorus oxychloride and pyridine on the optically active alcohol.

groups of compounds in the α-hydroxy-α-trifluoromethylpropionic acid series are more resistant to elimination than are most tertiary hydroxyl groups, and the only practicable method that we have found so far for their removal and the consequent formation of unsaturated products is pyrolysis of the ester acetates. Hydroxy-groups adjacent to trifluoromethyl residues in other compounds have exhibited similar resistance (Swarts, *Bull. Soc. chim. Belg.*, 1927, **36**, 191; 1929, **38**, 99) and, from secondary alcohols of the type $CF_3{\cdot}CHR{\cdot}OH$, olefins were formed only by pyrolysis of the ester acetates (Campbell, Knobloch, and Campbell, *J. Amer. Chem. Soc.*, 1950, **72**, 4380). Pentafluoroethyl groups have a similar influence (McBee, Higgins, and Pierce, *ibid.*, 1952, **74**, 1387).

Preparations of various fluoromethylacrylic compounds have been reported recently by Dickey, who treated trifluoroacetone cyanohydrin or related compounds with sulphuric acid or alkyl hydrogen sulphates (U.S.P. 2,472,812, 2,541,465; *Chem. Abs.*, 1949, **43**, 8398; 1951, **45**, 5715), or with thionyl chloride (U.S.P. 2,541,466; *Chem. Abs.*, 1951, **45**, 5715). In the last patent there are mentioned also pyrolyses of *O*-acetates. Dickey's main interest apparently was in the production of polymers and copolymers, and he records no properties for the acrylic monomers. We have been unable to make α-trifluoromethylacrylamide by reaction of trifluoroacetone cyanohydrin with sulphuric acid; even when we used the exact conditions described by Dickey we obtained, as before, α-hydroxy-α-trifluoromethylpropionamide, identical with our earlier specimens (*loc. cit.*).



Trifluoroacetone cyanohydrin *O*-acetate and methyl α-acetoxy-α-trifluoromethylpropionate, when passed through a glass tube at about 500°, gave α-trifluoromethylacrylonitrile and methyl α-trifluoromethylacrylate, respectively. Pyrolysis of the corresponding ethyl ester failed to give the unsaturated ethyl ester or the free acid. When α-trifluoromethylacrylonitrile was treated with concentrated sulphuric acid and the mixture poured into water, α-trifluoromethylacrylamide was obtained. With dilute sulphuric acid, this amide afforded, by addition of water across the olefinic double bond, β-hydroxy-α-trifluoromethylpropionamide, which was converted, by acidic hydrolysis under more drastic conditions, into the free acid; this could also be obtained directly from the unsaturated nitrile. β-Hydroxy-α-trifluoromethylpropionic acid was very soluble in water, very hygroscopic, and difficult to purify; attempts at distillation gave traces only of volatile material, and the bulk of the product rapidly became viscous, apparently with evolution of water, and was then only partly soluble in water. It appeared likely that a polyester had been formed by self-esterification; presumably the acid was sufficiently strong, because of the presence of the trifluoromethyl group, itself to catalyse such a reaction. Treatment of the viscous material with dilute mineral acid regenerated the water-soluble hydroxy-acid. β-Hydroxy-α-trifluoromethylpropionic acid was characterised by the formation of a number of derivatives; these had properties different from those of corresponding derivatives of the α-hydroxy-acid. The methyl ester of the β-hydroxy-acid failed to give the amide when treated with ammonia.

Reaction of the β-hydroxy-acid with phosphoric oxide, under conditions which left the α-hydroxy-acid unchanged, effected dehydration with the formation of the crystalline α-trifluoromethylacrylic acid. Though a primary alcoholic group, the hydroxyl function of the first acid is removed more readily than the tertiary group of the second.

Various addition reactions at the ethylenic double bond of the trifluoromethylacrylic derivatives were examined. Hydrogen chloride and the unsaturated nitrile in ether gave β-chloro-α-trifluoromethylpropiononitrile; treatment with methyl-alcoholic hydrogen chloride followed by heating afforded the corresponding chloro-amide, identical with that obtained by direct addition of hydrogen chloride to the unsaturated amide. Acidic hydrolysis of the chloro-amide caused simultaneous loss of the chlorine with the formation of β-hydroxy-α-trifluoromethylpropionic acid, identified as the *p*-phenylphenacyl ester. Hydrogen chloride was added to the unsaturated acid and ester, and bromine to the nitrile and the ester, to give the expected products. With the unsymmetrical reagents used so far the direction of addition is that expected from analogy with acrylonitrile (Bayer, *Angew. Chem.*, 1949, **61**, 229) and with 3 : 3 : 3-trifluoropropene (Henne and Kaye, *J. Amer. Chem. Soc.*, 1950, **72**. 3369; Henne and Nager, *ibid.*, 1951, **73**, 5527; Haszeldine, *J.*, 1952, 2504). Hydrogenation of the unsaturated derivatives, with Raney nickel as the catalyst, proceeded readily at normal temperatures and pressures. α-Trifluoromethylpropionic acid and its amide and methyl ester were obtained by reduction of the corresponding acrylic compounds. Since this saturated ester gave no amide when treated with ammonia, and a more complex reaction occurred with the unsaturated ester, the products of the two pyrolysis series were related by acidic hydrolysis, to the free acid, of methyl α-trifluoromethylpropionate which had been made from methyl α-trifluoromethylacrylate. This sample of the acid was then converted into the amide and anilide and these were shown to be identical with similar specimens prepared from α-trifluoromethylpropionic acid which was derived ultimately from the unsaturated nitrile. Reduction of methyl α-trifluoromethylpropionate and of α-trifluoromethylpropionamide with lithium aluminium hydride afforded 2-trifluoromethylpropan-1-ol and 2-trifluoromethylpropylamine respectively.

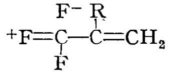
It had been observed during this investigation that many of the new compounds obtained appeared to be attacked by alkali with removal of fluorine; for example, it was usually not possible to obtain the free acids by hydrolysis of their esters. Accordingly, a study was made of the effect of aqueous sodium hydroxide, of varying concentrations, on many of the compounds which had been prepared. The amounts of fluorine which were removed from the compounds by hydrolysis appeared in the aqueous solutions in the ionic form which was determined by the method of Belcher, Caldas, Clark, and Macdonald (*Mikrochem. Mikrochim. Acta*, 1953, 283). It was found that the trifluoromethyl groups of α-trifluoromethylacrylic acid, and its nitrile, methyl ester, and amide, were hydrolysed completely by 2N-sodium hydroxide in 24—30 hr. at room temperature. Much weaker alkali undoubtedly would induce considerable hydrolysis, particularly if hot, and even water, after 3—4 hr.' refluxing with the first three compounds caused the splitting-off of 5—15% of the fluorine. By normal methods of isolation, no organic derivatives were obtained from these hydrolyses. Methylenemalonic acid is known to be very unstable (Bottomley and Perkin, *J.*, 1900, **77**, 294) and (hydroxymethyl)malonic acid is also decomposed fairly readily (Coops, *Rec. Trav. chim.*, 1901, **20**, 430; 1904, **23**, 353). Because the addition of water across double bonds can be catalysed, presumably, by bases as well as by acids, the hydroxy-acid appeared to be the more likely end-product. Accordingly, methyl α-trifluoromethylacrylate was treated with aqueous alkali, and the solution was worked up by the method described by Coops (*loc. cit.*) for the isolation of the calcium salt of (hydroxymethyl)malonic acid. An organic calcium salt was obtained but it could not be purified.

The stabilities to aqueous alkali of certain of the saturated compounds were examined also, and, even more surprisingly, the trifluoromethyl groups of some of them were hydrolysed readily. Though α-hydroxy-α-trifluoromethylpropionic acid was stable to 5N-sodium hydroxide at 100° for 6 hr. and was isolated unchanged, the β-hydroxy-acid had lost all of its fluorine after 3 hr. in 2N-alkali at 100°. Again, solvent extraction gave no organic product, but by Coops's process there was isolated a calcium salt which may have been impure calcium (hydroxymethyl)malonate. Further, α-trifluoromethylpropionic acid had lost 85% of its fluorine after 3 hr. in 2N-alkali at 100°, and in this case the organic product was the well-characterised methylmalonic acid. Hydrolysis under milder conditions (2N- or 5N-sodium hydroxide at room temperature) removed 20—70% of the fluorine but the product consisted of a mixture of the starting material and methylmalonic acid, and no fluorine-containing intermediate could be isolated. When two derivatives of α-trifluoromethylpropionic acid, namely, 2-trifluoromethylpropan-1-ol and 2-trifluoromethylpropylamine, were treated with alkali, no hydrolysis occurred, and they were recovered, in the case of the alcohol even after 4 hr. at 100° with 13N-potassium hydroxide.

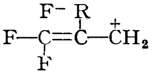
As is now well known, the trifluoromethyl group is normally very stable, though in certain compounds it has been found to be susceptible to hydrolysis. Thus, in many derivatives in which trifluoromethyl groups are carried on aromatic or heterocyclic rings, the fluorine is hydrolysed by hot strong acids (Swarts, *Bull. Acad. roy. Belg.*, 1920, **6**, 389; Rouche, *ibid.*, 1927, **13**, 346; Le Fave, *J. Amer. Chem. Soc.*, 1949, **71**, 4148; 1950, **72**, 2464) though it is often stable to alkali under normal reaction conditions. However, if activating groups are present in a nucleus in positions *ortho* or *para* to a trifluoromethyl group, the latter may be attacked by alkali (Jones, *ibid.*, 1947, **69**, 2346; Whalley, *J.*, 1949, 3016). In the aliphatic series there are fewer reports of labile trifluoromethyl groups. Swarts (*Bull. Acad. roy. Belg.*, 1922, **8**, 331) stated, for example, that (trifluoromethyl)*cyclo*hexane was more resistant to hydrolysis than was benzotrifluoride. Ruff and Willenberg (*Ber.*, 1940, **73**, 724) reported hydrolysis by alkali of the fluorine in bistrifluoromethylamine, and Brandt, Emeléus, and Haszeldine (*J.*, 1952, 2198) noted a similar effect with bistrifluoromethyl disulphide. Henne, Smook, and Pelley (*J. Amer. Chem. Soc.*, 1950, **72**, 4756) described an interesting case of relative instability of a trifluoromethyl group which was linked directly to carbon. When studying the base-catalysed addition of alcohols to 3 : 3 : 3-trifluoropropene they found that, though some addition did occur, an extensive attack on the fluorinated cluster took place also, giving products such as 3-ethoxy-3 : 3-difluoropropene. Henne and Zimmerschied (*ibid.*, 1947, **69**, 281) found that hydrolysis caused loss of fluorine from ethyl ββ-difluorobutyrate.

In the cases reported in this paper the trifluoromethyl group is remarkably labile towards aqueous alkali. The evidence so far available suggests that the group is activated when it is linked to one of the carbon atoms of an ethylenic double bond. The effect is probably enhanced when this carbon atom carries also a carboxyl group or some derived unsaturated function. If a generalisation can be made from the few examples that we have investigated, the even more surprising instability of the trifluoromethyl groups of saturated compounds arises when such groups are substituted, in a carboxylic acid, on an α-carbon atom which carries a hydrogen atom. In the case of 2-trifluoromethylpropanol, even the drastic conditions which cause dehydrofluorination of cyclic fluorohydrocarbons (Tatlow and Worthington, *J.*, 1952, 1251) leave the alcohol unchanged, a remarkable difference of reactivity between the acid and alcohol. It is, of course, possible that base-catalysed addition of water to the olefinic compounds precedes hydrolysis of the CF_3 groups, and that the unstable species are all derivatives of β-hydroxy-α-trifluoromethylpropionic acid. The hydrolysis of the CF_3 groups of the latter and also that of α-trifluoromethylpropionic acid could then be due to the loss, in alkali, of the α-hydrogen atom as a proton, the resultant carbonium anion forming an olefin (*e.g.*, ββ-difluoro-α-hydroxymethylacrylic acid) by elimination of fluoride ion. By further addition and hydrolysis, degradation of the olefin could then proceed.

An alternative explanation of the activation effect may be postulated. Contributors to the ground state of the unsaturated compounds may include resonance forms, such as (I), or hyperconjugated structures, of the type of (II), in which of course the polarity is opposite to that of hydrocarbon-type hyperconjugation forms. This, incidentally, may make hyperconjugation with carbonyl and similar functions less likely with perfluoroalkyl than with alkyl groups The carboxyl group or its anion may well be involved in such

(I) 

$${}^{+}F{=}\underset{F}{\overset{F^{-}\;}{C}}-\overset{R}{C}{=}CH_2$$

 (II)

$$F-\underset{F}{\overset{F^{-}\;}{C}}{=}\overset{R}{C}-\overset{+}{C}H_2$$

effects also; it should assist in the stabilisation of forms such as (II; $R = CO_2^-$). Contributors of this type may explain the lability of the trifluoromethyl groups of the saturated derivatives also, if the "enolic" form of the carboxyl group, or its anion, is assumed to be involved. If hyperconjugation effects are involved, then reactivity towards alkali might be expected; the heterolytic α-methylenic reactions of hydrocarbon olefins may be explained thus (Baker, "Hyperconjugation," Oxford Univ. Press, 1952, p. 115).

It is now apparent that these activating effects, whatever their true nature, can exert very profound influences on some organic fluorine compounds, and can give rise to remarkable differences in reactivity. Haszeldine (*J.*, 1952, 3490) has invoked resonance and hyperconjugation to explain some of the effects associated with addition reactions of trifluoromethyl olefins and acetylenes.

EXPERIMENTAL

1 : 1 : 1-*Trifluoroacetone Cyanohydrin and its Acetate.*—These compounds were prepared as described by Darrall, Smith, Stacey, and Tatlow (*loc. cit.*), the acetate (Found: C, 40·1; H, 3·6; F, 31·5. Calc. for $C_6H_6O_2NF_3$: C, 39·8; H, 3·3; F, 31·5%) being obtained in yields of 60—70%.

The only product obtained by treatment of the cyanohydrin with 98 or 100% sulphuric acid, alone or containing flowers of sulphur, was α-hydroxy-α-trifluoromethylpropionamide (yields, *ca.* 50%), m. p. and mixed m. p. 144° (cf. Dickey, *loc. cit.*).

α-Hydroxy-α-trifluoromethylpropionic Acid and its Derivatives.—The acid, its methyl ester, and the acetate of the methyl ester (yield 91%) (Found: C, 39·1; H, 4·0; F, 26·8. Calc. for $C_7H_9O_4F_3$: C, 39·3; H, 4·2; F, 26·6%) were prepared as described previously. In an analogous way, ethyl α-hydroxy-α-trifluoromethylpropionate (conversion, 91%), b. p. 140—142°, n_D^{20} 1·3577, was made from the acid, ethyl alcohol, and sulphuric acid. Acetylation of this ester gave the *acetate* (90%), b. p. 65—69°/26 mm., n_D^{20} 1·3669 (Found: C, 42·4; H, 5·1; F, 24·7. $C_8H_{11}O_4F_3$ requires C, 42·1; H, 4·9; F, 25·0%).

An aqueous solution of the α-hydroxy-acid was neutralised with aqueous sodium hydroxide, *p*-phenylphenacyl bromide in an equal volume of ethyl alcohol was added, and the mixture was heated at 100° for 1½ hr. The solution was filtered whilst hot, then allowed to cool, and the precipitate was filtered off and recrystallised from benzene–light petroleum (b. p. 80—100°), to give the p-*phenylphenacyl* ester (58%), m. p. 122° (Found: C, 61·1; H, 4·1; F, 16·0. $C_{18}H_{15}O_4F_3$ requires C, 61·4; H, 4·3; F, 16·2%).

α-Trifluoromethylacrylonitrile.—The pyrolysis apparatus comprised a Pyrex glass tube (60 cm. long, 3 cm. int. diam.), mounted vertically in an electrical furnace (heated section 42 cm.), and carrying a dropping funnel and gas inlet at the top, and was connected to a series of cooled traps at the bottom. The tube was packed with pieces of Pyrex tubing (0·5—0·75 cm. long, 0·3 cm. ext. diam.) and was swept with a slow stream of nitrogen. 1 : 1 : 1-Trifluoroacetone cyanohydrin acetate (102 g.) was passed at a steady rate during 2 hr. through the tube which was heated to 500° ± 10°. The product (97 g.) was fractionated through a column (1′) packed with Dixon gauze spirals. The main fraction was the colourless lachrymatory *α-trifluoromethylacrylonitrile* (42 g.), b. p. 75·9—76·2°/759 mm., n_D^{20} 1·3239 (Found: C, 39·7; H, 1·4; F, 46·3%; *M*, 118·5. $C_4H_2NF_3$ requires C, 39·7; H, 1·7; F, 47·1%; *M*, 121). Similar experiments gave yields of about 65%; neutralisation of the still-residues followed by extraction afforded a little of the unchanged acetate.

Addition of Bromine to α-Trifluoromethylacrylonitrile.—The nitrile (1·00 g.) was added to bromine (1·3 g.) in carbon tetrachloride (5 c.c.) and after 24 hr. at 10—15° the solution, then almost colourless, was evaporated. Further distillation of the residue afforded 1 : 2-*dibromo*-2-*cyano*-3 : 3 : 3-*trifluoropropane* (1·70 g.), b. p. 57—58°/20 mm., n_D^{20} 1·4372 (Found: C, 17·1; H, 0·6; F, 20·2. $C_4H_2NBr_2F_3$ requires C, 17·1; H, 0·7; F, 20·3%).

Addition of Hydrogen Chloride to α-Trifluoromethylacrylonitrile.—(*a*) A solution of the nitrile (1·00 g.) in dry ether (25 c.c.) was saturated with dry hydrogen chloride at 0°. After 20 hr. at 10—15° the solvent was distilled, a stream of dry air was passed through the residue for 10 min., and it was then distilled, to give 1-*chloro*-2-*cyano*-3 : 3 : 3-*trifluoropropane* (0·75 g.), b. p. 134—135°, n_D^{13} 1·3649 (Found: C, 30·4; H, 2·1; F, 36·3. $C_4H_3NClF_3$ requires C, 30·5; H, 1·9; F, 36·2%).

(*b*) Dry ether (25 c.c.), containing the nitrile (2·00 g.) and methyl alcohol (1·0 c.c.), was saturated at 0° with hydrogen chloride, and after 44 hr. the volatile constituents were evaporated at 80°/15 mm. The residue was recrystallised from chloroform, to give β-*chloro-α-trifluoromethylpropionamide* (1·16 g.), m. p. 118° (Found: C, 27·4; H, 3·0; F, 32·5. $C_4H_5ONClF_3$ requires C, 27·4; H, 2·9; F, 32·5%).

α-Trifluoromethylacrylamide.—α-Trifluoromethylacrylonitrile (5·00 g.) was added to concentrated sulphuric acid (7·0 c.c.) which was stirred mechanically, a spontaneous reaction occurring. After being heated at 120—130° for 30 min. the mixture was cooled in ice, ice-water

(60 c.c.) was added, and the resulting precipitate was filtered off, washed, and dried. The filtrate was extracted exhaustively with ether, the extracts were washed, dried ($MgSO_4$), and evaporated, and the residue and the original precipitate were combined and recrystallised from benzene, to give *α-trifluoromethylacrylamide* (3·82 g.), m. p. 104° (Found: C, 34·6; H, 2·6; F, 41·2%; *M*, 142. $C_4H_4ONF_3$ requires C, 34·5; H, 2·9; F, 41·0%; *M*, 139).

The amide reacted in the cold with neutral aqueous permanganate. Addition of hydrogen chloride as described for the nitrile [expt. (*a*)] gave β-chloro-α-trifluoromethylpropionamide (52%), m. p. 117°, undepressed in admixture with the specimen mentioned earlier (Found: C, 27·6; H, 2·7%).

Hydrogenation of α-Trifluoromethylacrylamide.—The amide (5·00 g.), ethyl alcohol (50 c.c.), and Raney nickel (*ca.* 1 g.) were shaken together mechanically in an atmosphere of hydrogen. After 3 hr., when the absorption was complete, the solution was filtered and evaporated. The residue (4·8 g., m. p. 138°) was recrystallised from benzene, to give *α-trifluoromethylpropionamide* (2·60 g.), m. p. 139·5° (Found: C, 34·2; H, 4·0; F, 40·4. $C_4H_6ONF_3$ requires C, 34·05; H, 4·3; F, 40·4%).

Addition of Water to α-Trifluoromethylacrylamide.—The amide (16·3 g.) was heated at 100° for ½ hr. with concentrated sulphuric acid (2·7 c.c.) and water (95 c.c.). The solution was extracted exhaustively with ether, the extracts were dried ($MgSO_4$), filtered, and evaporated, and the residue was washed with cold benzene. Two recrystallisations from benzene afforded *β-hydroxy-α-trifluoromethylpropionamide* (7·20 g.), m. p. 134° [depressed in admixture with the α-hydroxy-isomer (m. p. 144°)] (Found: C, 30·8; H, 3·7; F, 36·1%; *M*, 152. $C_4H_6O_2NF_3$ requires C, 30·6; H, 3·8; F, 36·3%; *M*, 157).

β-Hydroxy-α-trifluoromethylpropionic Acid.—(*a*) The hydroxy-amide (2·50 g.) was heated at 120° for 5 hr. with a mixture of concentrated sulphuric acid (27·2 c.c.) and water (50 c.c.), and the solution was then extracted exhaustively with ether, the extracts were dried ($MgSO_4$), filtered, and evaporated, and the residue was heated to *ca.* 60°/30 mm. to leave the crude hydroxy-acid (2·40 g.) as a colourless syrup. This was acidic and water-soluble but could not be crystallised from solvents. When the syrup was heated quickly to 120° and the pressure was reduced to 30 mm. a very small quantity of distillate was obtained, which solidified in the condenser to give hygroscopic crystals of the *acid* (Found: C, 30·5; H, 3·1. $C_4H_5O_3F_3$ requires C, 30·4; H, 3·2%). Distillation ceased almost immediately however, and the still residue darkened, becoming more viscous and only partly soluble in water.

The crude syrup (5·00 g.) in water was treated with freshly prepared silver carbonate (4·3 g.) in the usual way, to give, after recrystallisation from water, the *silver* salt (3·10 g.) (Found: Ag, 40·8. $C_4H_4O_3F_3Ag$ requires Ag, 40·7%).

This salt (0·80 g.) and *p*-phenylphenacyl bromide (0·83 g.) were refluxed in aqueous alcohol for 1 hr., the solution was filtered and evaporated, and the residue was recrystallised from benzene–light petroleum (b. p. 60—80°), to give the *p-phenylphenacyl* ester (0·61 g.), m. p. 91—92° (depressed in admixture with the ester from the α-hydroxy-acid) (Found: C, 61·3; H, 4·2; F, 15·8. $C_{18}H_{15}O_4F_3$ requires C, 61·4; H, 4·3; F, 16·2%).

(*b*) α-Trifluoromethylacrylonitrile (11·1 g.) was added dropwise to concentrated sulphuric acid (17 c.c.) which was stirred mechanically, and, after 30 min. at 120—130°, water (30 c.c.) was added. After 5 hr. at 120° the solution was worked up as before, to give crude syrupy β-hydroxy-α-trifluoromethylpropionic acid (11·9 g.); a portion, after neutralisation with aqueous sodium hydroxide and treatment with *p*-phenylphenacyl bromide as usual, gave the *p*-phenylphenacyl ester, m. p. and mixed m. p. 90—91°.

(*c*) β-Chloro-α-trifluoromethylpropionamide (2·00 g.), water (50 c.c.), and concentrated sulphuric acid (27·2 c.c.) were refluxed together for 5 hr. Isolation as before gave a crude syrupy acid (1·80 g.) which contained no chlorine or nitrogen. Treatment as described previously afforded the silver salt (overall yield, 51%) (Found: Ag, 40·9%) and thence the *p*-phenylphenacyl ester, m. p. and mixed m. p. 92°, depressed in admixture with the ester from the α-hydroxy-acid

Methyl β-Hydroxy-α-trifluoromethylpropionate.—Fluorosulphonic acid (1·0 c.c.), the syrupy hydroxy-acid (4·00 g.), and methyl alcohol (5·0 c.c.) were refluxed together for 15 min., the mixture was poured into ice-water (100 c.c.), and the organic layer was separated, dried ($MgSO_4$), filtered, and distilled to give the *methyl* ester (1·47 g.), b. p. 170—173° (Found: C, 34·6; H, 4·1; F, 33·4. $C_5H_7O_3F_3$ requires C, 34·9; H, 4·1; F, 33·1%).

Treatment at 15° of an ethereal solution of the ester with ammonia gas failed to give the amide, the ester (63%) being recovered.

Methyl β-Methoxy-α-trifluoromethylpropionate.—To a solution of the crude syrupy hydroxy-acid (5·00 g.), in methyl iodide (50 c.c.) and acetone (5·0 c.c.), dry silver oxide (30 g.) was added gradually, a spontaneous reaction occurring. After being refluxed for 36 hr., the solution was filtered, the precipitate was washed with ether, and the solvents were distilled from the combined liquids. The residue was distilled further to give *methyl β-methoxy-α-trifluoromethylpropionate* (1·80 g.), b. p. 137—140° (Found : C, 39·0; H, 4·8. $C_6H_9O_3F_3$ requires C, 38·7; H, 4·9%).

α-Trifluoromethylacrylic Acid.—Syrupy β-hydroxy-α-trifluoromethylpropionic acid (5·06 g.) was mixed with phosphoric oxide (1·5 g.) (heat was generated), and the mixture was heated rapidly to 200—220°. The colourless distillate (4·1 g.; b. p. 140—166°) partly crystallised, and the liquid was decanted off, neutralised with dilute aqueous alkali, and extracted with ether. The aqueous phase was acidified and re-extracted, the second extracts being dried ($MgSO_4$) and evaporated to leave more crystalline acid (*ca.* 0·2 g.). The combined crystalline fractions were *α-trifluoromethylacrylic acid* (2·63 g.), m. p. 50—52°, b. p. 146—148° (Found : C, 34·6; H, 2·0; F, 40·5%; equiv., 140. $C_4H_3O_2F_3$ requires C, 34·3; H, 2·2; F, 40·7%; equiv., 140). The equivalent was determined by titration with 0·05N-alkali, no fluoride ion being detected in the titration liquors.

Addition of Hydrogen Chloride to the Unsaturated Acid.—Ether (25 c.c.) containing α-trifluoromethylacrylic acid (0·99 g.) was saturated at 0° with hydrogen chloride gas. After 16 hr. at 10—15° the solution was evaporated and the residue was distilled twice, to give *β-chloro-α-trifluoromethylpropionic acid* (1·12 g.), b. p. 169—170°, n_D^{20} 1·3768 (Found : C, 37·6; H, 2·5; F, 32·5%; equiv., 174. $C_4H_4O_2ClF_3$ requires C, 27·2; H, 2·3; F, 32·3%; equiv., 176·5).

Hydrogenation of α-Trifluoromethylacrylic Acid.—The acid (0·275 g.), ether (20 c.c.), and Raney nickel (*ca.* 1 g.) were shaken in an atmosphere of hydrogen until absorption was complete. After filtration, and evaporation of the solvent, the residue was heated at 100° with phosphorus pentachloride (0·45 g.) for 1 hr. α-Trifluoromethylpropionyl chloride, b. p. 88—90°, was then distilled from the mixture, and was dissolved in ether (25 c.c.), ammonia gas being passed through the solution, which, after 1 hr., was washed with water, dried ($MgSO_4$), filtered, and evaporated. The residue (0·145 g.; m. p. 138°) was recrystallised from benzene, to give α-trifluoromethylpropionamide (0·112 g.), m. p. 139·5°, alone and in admixture with the specimen described previously.

α-Trifluoromethylpropionic Acid.—The amide (3·58 g.) was heated at 120° for 5 hr. with concentrated sulphuric acid (27 c.c.) and water (50 c.c.), the solution was extracted exhaustively with ether, the extracts were dried ($MgSO_4$), filtered, and evaporated, and the residue was distilled *in vacuo*, to give *α-trifluoromethylpropionic acid* (2·93 g.), b. p. 67°/25 mm., n_D^{15} 1·3441 (Found : C, 33·6; H, 3·8; F, 39·6%; equiv., 143. $C_4H_5O_2F_3$ requires C, 33·8; H, 3·5; F, 40·1%; equiv., 142). Fluoride ion could not be detected in the titration liquors.

By treatment with silver carbonate the acid gave a *silver* salt (yield, 30% after recrystallisation from water) (Found : C, 19·6; H, 1·7; F, 23·1; Ag, 43·2. $C_4H_4O_2F_3Ag$ requires C, 19·3; H, 1·6; F, 22·9; Ag, 43·3%).

The acid (1·80 g.) was heated at 80—100° for 1 hr. with phosphorus pentachloride (2·8 g.). Distillation gave the acid chloride, b. p. 90—93°, to which was added ether (20 c.c.) followed by aniline (3·0 g.) in ether (10 c.c.). After 45 min. the ethereal suspension was washed with dilute hydrochloric acid, then water, and was dried ($MgSO_4$), filtered, and evaporated. The residue, after two recrystallisations from benzene–light petroleum (b. p. 60—80°), afforded the *anilide* (1·07 g.), m. p. 108·5—109° (Found : C, 55·0; H, 4·5; F, 25·8. $C_{10}H_{10}ONF_3$ requires C, 55·3; H, 4·6; F, 26·2%).

Methyl α-Trifluoromethylpropionate.—The acid (3·92 g.), methyl alcohol (10 c.c.), and fluorosulphonic acid (1 c.c.) were refluxed together for 15 min. and then poured into ice-water. The lower layer was taken up in ether, and the solution was washed with sodium hydrogen carbonate, then water, dried ($MgSO_4$), and distilled. After removal of the ether there was obtained the *ester* (2·32 g.), b. p. 101—102°, n_D^{20} 1·3370 (Found : C, 38·1; H, 4·5; F, 35·9. $C_5H_7O_2F_3$ requires C, 38·5; H, 4·5; F, 36·5%).

Treatment at 10—15° of the ester, in ether, with ammonia gas failed to give the amide, the ester being recovered.

The ester (1·00 g.) was heated at 100° for 5 hr. with sulphuric acid (5·5 c.c.) and water (40 c.c.), mechanical stirring being applied. Exhaustive ether-extraction, followed by evaporation of the extract and distillation of the residue, gave the acid (0·474 g.), b. p. 65°/25 mm.

Methyl α-Trifluoromethylacrylate.—Methyl α-acetoxy-α-trifluoromethylpropionate (102·5 g.) was pyrolysed at 500° ± 10° during 2 hr. as described for the nitrile. The product was poured into water, and the organic layer was separated, and the aqueous layer was neutralised with sodium hydrogen carbonate and extracted several times with ether. The combined organic layers were washed with sodium hydrogen carbonate solution, then with water, dried ($MgSO_4$), filtered, and distilled through a 1′ column. The main fraction was a colourless lachrymatory liquid, *methyl α-trifluoromethylacrylate* (32·1 g.), b. p. 103·8—105°, n_D^{20} 1·3528 (Found : C, 39·5; H, 3·5; F, 37·1%; *M*, 149. $C_5H_5O_2F_3$ requires C, 39·0; H, 3·3; F, 37·0%; *M*, 154). Material having b. p. 105—158° (21·3 g.), which was a mixture of product and starting material, was combined with similar residues and recycled.

After being stored the ester left a residue upon distillation; this dissolved in dioxan and was precipitated by ethyl alcohol as a white solid, m. p. 100—200°.

Pyrolysis of ethyl α-acetoxy-α-trifluoromethylpropionate gave no definite products.

Addition of Bromine to the Unsaturated Ester.—Treatment with bromine in chloroform followed by distillation afforded *methyl αβ-dibromo-α-trifluoromethylpropionate* (71%), b. p. 89—90°/32 mm., n_D^{20} 1·4461 (Found : C, 19·2; H, 1·7; F, 18·6. $C_5H_5O_2Br_2F_3$ requires C, 19·1; H, 1·6; F, 18·2%), a colourless lachrymatory liquid.

Addition of Hydrogen Chloride.—Methyl α-trifluoromethylacrylate (2·00 g.), after 14 hr. in ether saturated with dry hydrogen chloride, afforded, on distillation, *methyl β-chloro-α-trifluoromethylpropionate* (1·83 g.), b. p. 126—130°, n_D^{13} 1·3690 (Found : C, 31·4; H, 3·3; F, 29·6. $C_5H_6O_2ClF_3$ requires C, 31·5; H, 3·2; F, 29·9%).

Hydrogenation of Methyl α-Trifluoromethylacrylate.—The ester (5·00 g.), ether (40 c.c.), and Raney nickel (*ca.* 1 g.) were shaken together in an atmosphere of hydrogen until absorption was complete (*ca.* 90 min.), the solution was filtered, the ether was evaporated off, and the residue was distilled, to give methyl α-trifluoromethylpropionate (4·00 g.), b. p. 100—102°, n_D^{20} 1·3370 (Found : C, 38·7; H, 4·6; F, 35·6%; *M*, 147). The ester was recovered after being kept for 5 days at 10—15° in ether saturated with dry ammonia.

Treatment with mineral acid, as described for the sample mentioned previously, gave α-trifluoromethylpropionic acid (60%), b. p. 70°/30 mm., n_D^{20} 1·3444 (Found : C, 34·4; H, 3·5%; equiv., 140), which was converted into the amide (45%), m. p. and mixed m. p. 139·5°, and the anilide (44%), m. p. and mixed m. p. 107° (Found : C, 55·0; H, 4·4; F, 25·9%).

2-*Trifluoromethylpropan*-1-*ol*.—Methyl α-trifluoromethylpropionate (7·85 g.) in ether (10 c.c.) was added gradually to a mechanically stirred suspension of lithium aluminium hydride (2·3 g.) in ether (75 c.c.), heat being generated. After 2 hr.' refluxing following the addition, the mixture was cooled to 0°, and water was added carefully and then concentrated sulphuric acid (5 c.c.). The ethereal layer was separated, further extractions of the aqueous phase were carried out, the combined ethereal layers were dried ($MgSO_4$) and filtered, and the ether was distilled. The residue was distilled, to give 2-*trifluoromethylpropan*-1-*ol* (6·14 g.), b. p. 108·5—109·5°, n_D^{20} 1·3399 (Found : C, 37·4; H, 5·2; F, 44·0. $C_4H_7OF_3$ requires C, 37·5; H, 5·5; F, 44·5%). Treatment of the alcohol with 3 : 5-dinitrobenzoyl chloride in the usual way gave the 3 : 5-*dinitrobenzoate*, m. p. 82·5—83·5° [from light petroleum (b. p. 40—60°)] (Found : C, 40·9; H, 2·5; F, 17·7. $C_{11}H_9O_6N_2F_3$ requires C, 41·0; H, 2·8; F, 17·7%).

2-*Trifluoromethylpropylamine*.—A mechanically stirred suspension of lithium aluminium hydride (5·0 g.) in ether (200 c.c.) was warmed so that the refluxing ether returned *via* a Soxhlet thimble which contained α-trifluoromethylpropionamide (4·77 g.). After 7 hr. the amide had all been carried into the flask, and, after 16 hr. at 10—15°, the mixture was cooled to 0° and water was added cautiously, followed by 2N-sodium hydroxide (20 c.c.). The ethereal layer was separated, the aqueous phase and the precipitate were ether-extracted, the combined layers were dried ($MgSO_4$) and filtered, and the ether was distilled. Distillation of the residue gave the crude amine (0·92 g.), b. p. 50—110°. From one portion, by treatment with benzoyl chloride–sodium hydroxide, the N-*benzoyl* derivative was obtained, m. p. 80·5—81·5° [yield 50% after recrystallisation from aqueous alcohol and then from light petroleum (b. p. 60—80°)] (Found : C, 57·5; H, 5·4. $C_{11}H_{12}ONF_3$ requires C, 57·1; H, 5·2%). Dry hydrogen chloride was passed through a second portion of the crude amine in ether, the precipitate, after recrystallisation from ethyl alcohol–benzene, giving the *amine hydrochloride* (30%), m. p. 266° (subliming above 200°) (Found : C, 29·6; H, 5·7; F, 34·9. $C_4H_9NClF_3$ requires C, 29·4; H, 5·55; F, 34·85%).

Action of Aqueous Alkali on Various Compounds.—Each compound was treated with aqueous sodium hydroxide (or water) under the conditions described, an aliquot portion of the aqueous phase being analysed for fluoride ion by the method of Belcher, Caldas, Clark, and Macdonald (*loc. cit.*). In the cases of the unsaturated nitrile and ester a blank determination was carried out on water which had been shaken with the compound for a few minutes at 15°. The hydrolysis products were isolated by acidification and extraction of the total aqueous phases

Treatment of α-trifluoromethyl-acrylic and -propionic derivatives with aqueous alkali.

Test compound		Reaction conditions					Product	
Formula	(g.)	Vol. of aq. soln. (c.c.)	Concn. of NaOH (N)	Time (hr.)	Temp.	Fluorine removed (%)	Formula	Foot-notes
$CH_2{:}C(CF_3){\cdot}CN$	0·532	10·0	2	28	15°	97	—	I
,,	0·804	10·0	—	3	90	5·5	—	—
$CH_2{:}C(CF_3){\cdot}CO{\cdot}NH_2$	0·394	10·0	2	24	15	92	—	I
,,	0·563	10·0	—	4	100	0	$CH_2{:}C(CF_3){\cdot}CO{\cdot}NH_2$	II
$CH_2{:}C(CF_3){\cdot}CO_2Me$	0·407	10·0	2	24	15	95	—	I
,,	0·804	10·0	—	4	100	4	$CH_2{:}C(CF_3){\cdot}CO_2Me$	III
$CH_2{:}C(CF_3){\cdot}CO_2H$	0·155	10·0	2	24	15	100	—	I
,,	0·151	10·0	—	4	100	15	—	—
$Me{\cdot}CH(CF_3){\cdot}CO_2H$	0·484	10·0	2	3	100	85	$HO_2C{\cdot}CHMe{\cdot}CO_2H$	IV
,,	0·474	10·0	2	49	15	27	Mixture	V
,,	0·484	10·0	5	12	15	66	,,	VI
,,	0·494	3·0	5	5	15	23	,,	VII
$Me{\cdot}C(OH)(CF_3){\cdot}CO_2H$	0·465	10·0	2	3	100	0	$Me{\cdot}C(OH)(CF_3){\cdot}CO_2H$	VIII (*a*)
,,	0·473	10·0	5	6	100	0	,,	VIII (*b*)
$Me{\cdot}CH(CF_3){\cdot}CH_2{\cdot}OH$	0·516	10·0	2	24	15	0	$Me{\cdot}CH(CF_3){\cdot}CH_2{\cdot}OH$	IX (*a*)
,,	0·508	10·0	2	3	100	0	,,	IX (*b*)
,,	0·953	10·0	5	6	100	0	,,	IX (*c*)
,,	0·503	8·0	13	4	100	0	,,	IX (*d*)
$Me{\cdot}CH(CF_3){\cdot}CH_2{\cdot}NH_3^+Cl^-$	0·291	10·0	5	6	100	0	$Me{\cdot}CH(CF_3){\cdot}CH_2{\cdot}NH_2$	X
$HO{\cdot}CH_2{\cdot}CH(CF_3){\cdot}CO_2H$	0·610	10·0	2	3	100	100	—	I

I. No organic product was isolated.

II. Two recrystallisations of the crude product (0·470 g., m. p. 98—100°) from benzene gave the unchanged amide (0·250 g.), m. p. and mixed m. p. 103°.

III. The recovered ester (0·200 g.) had b. p. 103—105°, n_D^{20} 1·3545.

IV. The crude product (0·334 g.; m. p. 127—129°), after recrystallisation from ethyl acetate–light petroleum (b. p. 60—80°), afforded methylmalonic acid (0·250 g.), m. p. 132° (Found : C, 40·3; H, 4·9%; equiv., 58. Calc. for $C_4H_6O_4$: C, 40·7; H, 5·1%; equiv., 59). In admixture with a specimen (m. p. 133°) prepared by treatment of sodiomalonic ester with methyl iodide the m. p. was 132—133°.

V. The semi-solid product was washed with light petroleum (b. p. 40—60°). The solid, treated as above, gave methylmalonic acid (0·047 g.), m. p. and mixed m. p. 133°. The liquid and washings, treated with silver carbonate as before, afforded silver α-trifluoromethylpropionate (0·392 g.).

VI. The semi-solid residue gave methylmalonic acid (0·090 g.), m. p. and mixed m. p. 133°.

VII. The product was distilled, to give α-trifluoromethylpropionic acid (0·255 g.), b. p. 60°/30 mm. (Found : equiv., 147). The residue afforded methylmalonic acid (0·006 g.), m. p. and mixed m. p. 133°.

VIII. Sublimation gave the starting material, from (*a*), 0·221 g., m. p. and mixed m. p. 86—87°; and from (*b*), 0·363 g., m. p. and mixed m. p. 88°.

IX. Distillation afforded the unchanged alcohol, from (*a*), 0·428 g., b. p. 108—109°, n_D^{20} 1·3416; from (*b*), 0·241 g., b. p. 108—109·5°, n_D^{20} 1·3399; from (*c*) 0·616 g., b. p. 108—109·5°, n_D^{20} 1·3399; and from (*d*), 0·210 g., b. p. 108—109°, n_D^{15} 1·3422. Material recovered in expt. (*c*) gave the 3 : 5-dinitrobenzoate, m. p. and mixed m. p. 82·5—83·5°. Potassium hydroxide was used in expt. (*d*).

X. The amine, after isolation as the hydrochloride (0·210 g.), gave the *N*-benzoyl derivative (0·115 g.), m. p. and mixed m. p. 82—83°.

with ether, and washing, drying ($MgSO_4$), and evaporation of the extracts. The complete results are given in the Table, the amount of fluoride ion in the aqueous phase (fluorine removed) being expressed as a percentage of the weight of fluorine contained in the compound under test.

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