# UNSATURATED ACIDS CONTAINING A TRIFLUOROMETHYL GROUP

## COMMUNICATION 3. POLARIZATION OF THE DOUBLE BOND IN β-TRIFLUOROMETHYLCROTONIC ACID

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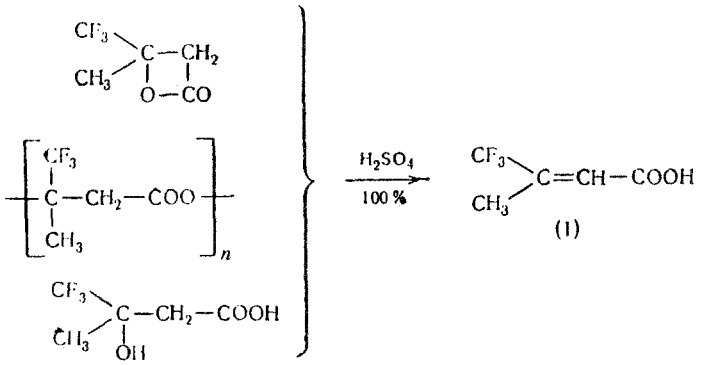
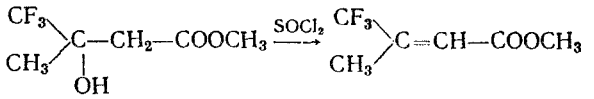
β-Trifluoromethylcrotonic acid (I) was first obtained in 1955 by dehydration of β-trifluoromethyl-β-hydroxybutyric acid with phosphorus pentoxide. Investigations showed that this acid was easily prepared by dissolving β-trifluoromethyl-β-methyl-β-propiolactone, its polymer, or β-trifluoromethyl-β-hydroxybutyric acid in anhydrous (but not 96%) sulphuric acid:



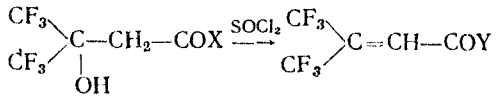
(I)

The peculiar specificity of 100% sulfuric acid relative to β-hydroxy acids containing trifluoromethyl groups in the β-position was discussed earlier [2]. Methyl β-trifluoromethylcrotonate (II) can be obtained by dehydration of the corresponding ester of the β-hydroxy acid with thionyl chloride:



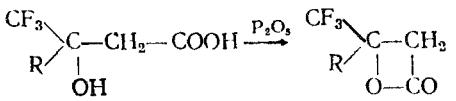
(II)

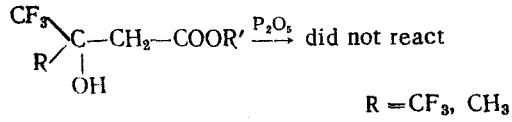
As was found earlier thionyl chloride also easily dehydrates β,β-bistrifluoromethyl-β-hydroxypropionic acid and its ester to give the acid chloride and ester respectively of the unsaturated acid [3].



X = $OC_2H_5$, OH  Y = $OC_2H_5$, Cl

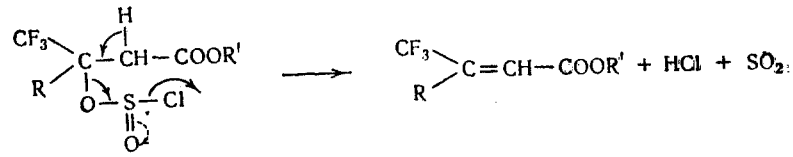
At the same time dehydration with phosphorus pentoxide of a β-hydroxy acid containing fluorine gives the corresponding β-lactone [2, 4], whereas the esters of these acids are not dehydrated at all by phosphorus pentoxide [5]



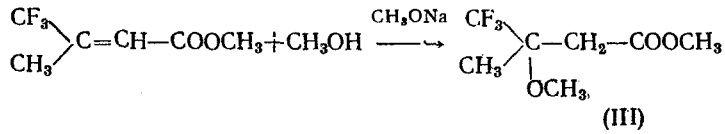


R = $CF_3$, $CH_3$

Such differences in dehydrating power of phosphorus pentoxide and thionyl chloride may be explained by weakening of the link between the tertiary carbon and the hydroxy group in the intermediate reaction product formed by reaction with thionyl chloride consequent upon the possibility of elimination of a chloride atom with a pair of electrons:

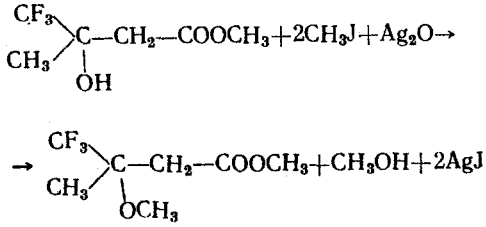


The effect of nucleophiles on β-trifluoromethylcrotonic acid and its ester was studied for the addition of methanol, ammonia, ethanolamine and water. Methanol in the presence of sodium methoxide added to methyl β-trifluoromethylcrotonate to give methyl β-methoxy-β-trifluoromethylbutyrate (III).

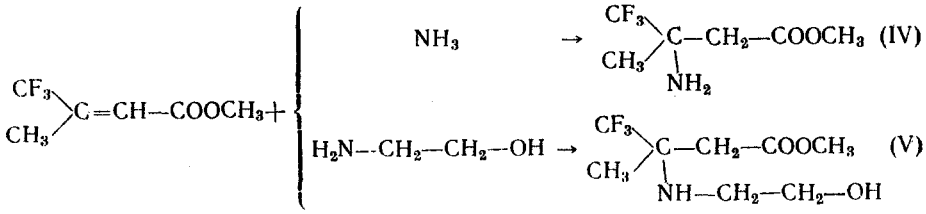


(III)

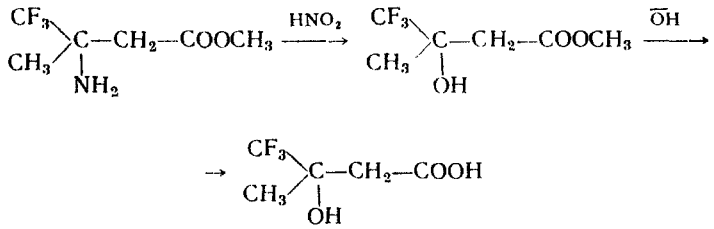
The structure of the product obtained was demonstrated by synthesizing it by methylation of β-trifluoromethyl-β-hydroxybutyric acid using Purdie and Irvin's method [6].



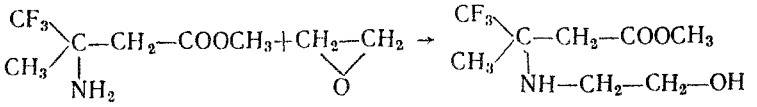
Ammonia and ethanolamine reacted with the unsaturated ester II to give esters of the corresponding amino-acids (IV) and (V).



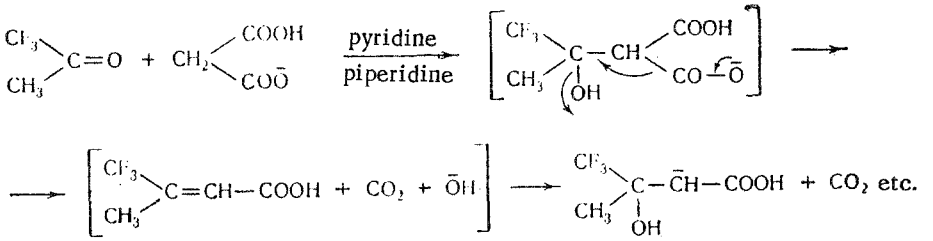
Methyl β-trifluoromethyl-β-amino butyrate (IV), on treatment with nitrous acid and subsequent alkaline hydrolysis gave the known β-trifluoromethyl-β-hydroxybutyric acid.



The structure of methyl β-trifluoromethyl-β-(N-β-hydroxethyl)-aminobutyrate was demonstrated by an opposing synthesis from the amino ester (IV) and ethylene oxide.



Water does not add to β-trifluoromethylcrotonic acid on heating to 150° in the presence of strong bases or mineral acids, nor in pyridine solution in the presence of piperidine. However hydration of β-trifluoromethylcrotonic acid was postulated as one stage in the mechanism of the reaction of trifluoroacetone with malonic acid [1].



Evidently this mechanism needs reexamination.

## EXPERIMENTAL

β-Trifluoromethylcrotonic acid. A mixture of 1.06 g β-trifluoromethyl-β-methyl-β-propiolactone and 1 ml 100% sulphuric acid was left standing for 1 hr, then diluted with water. The acid (I) was steam distilled - it crystallized in the receiver. After drying 0.97 g (91%) of crystals were obtained with m.p. 29.5-31°, b.p. ~182°. Literature data [1] b.p. 80-84°*. Found: C 38.67; H 3.25; F 37.18%. $C_5F_3H_5O_2$. Calculated: C 38.98; H 3.25; F 37.00%.

A mixture of 1.25 g β-trifluoromethyl-β-hydroxybutyric acid and 5 ml (1%) oleum was kept for 12 hr, and then worked up as in the previous experiment. 0.98 g (87%) of acid (I) was obtained.

By similar treatment of 4.2 g of the polymer obtained from β-trifluoromethyl-β-methyl-propiolactone the acid I was obtained in 70% yield.

Methyl β-trifluoromethylcrotonate. The ester (II) was obtained in 75% yield on esterifying the acid (I) with methanol in the presence of sulphuric acid; b. p. 112.5-113.5° (753 mm); $n^{20}D$ 1.3718; $d^{20}_4$ 1.2074; found MR 31.61; calculated MR 31.52. Found: C 42.72; H 4.17; F 33.68%. $C_6F_3H_7O_2$. Calculated: C 42.84; H 4.16; F 33.92%.

A mixture of 9.43 g (0.051 M) methyl β-trifluoromethyl-β-hydroxybutyrate, 6.50 g (0.055 M) thionyl chloride, and 1 ml dry pyridine were refluxed for 8 hr, and then fractionally distilled through a 400 mm column; in this way 6.0 g (71%) of the ester (II) was obtained b. p. 112.5-113° (751 mm); $n^{20}D$ 1.3720.

Methyl β-trifluoromethyl-β-methoxybutyrate. 16.8 g (0.1 M) of (II) and sodium methoxide (obtained from 1 g sodium and 50 ml methanol) were heated in a sealed ampoule for 16 hr at 100°. When the heating was completed the solution was diluted with water, acidified, the oil separated, taken up into ether and dried over calcium chloride. After removal of the solvent the residue was fractionated through a 400 mm column. Fractions were collected: I – b. p. 110-114°, initial ester, 1.57 g; II – b. p. 59.5-60.5° (22 mm), 7.85 g; III – residue ~ 2.5 g.

Fraction II was the pure product (III); b. p. 159° (744 mm); yield 45%, based on ester (II) consumed in the reaction; $n^{20}D$ 1.3766; $d^{20}_4$ 1.230; found MR 37.36; calculated MR 38.25. Found: C 42.36; H 5.43; F 28.45%. $C_7F_3H_{11}O_3$. Calculated: C 42.00; H 5.54; F 28.50%.

A mixture of 12.66 g (0.068 M) methyl β-trifluoromethyl-β-hydroxybutyric acid, 23.2 g (0.1 M) dry silver oxide, and 40 ml methyl iodide was boiled in a flask under reflux for 10 hr. At the end of the reaction the precipitate was sucked out and washed with ether. The ether washings and the solution were combined, dried and distilled after removal of the solvent. 11.54 g of a colorless liquid with b. p. 158-164° (749 mm) was obtained which appeared to be a mixture of the initial hydroxyester and the methoxyester (III). Further separation of the products was carried out by treating the mixture in the cold with 30% alkali. The oil which did not dissolve in the alkali was separated,

* It is possible that a misprint occurred in the constant cited.

taken up in ether and distilled after drying and removing the solvent. 1.8 g (III) (57% based on hydroxyester consumed in the reaction) was obtained with b. p. 158.5-160.5° (749 mm); $n^{20}D$ 1.3769. The product obtained was identical in its properties with that obtained in the first experiment. Thus it did not dissolve in 30% alkali in the cold and it did not react with sodium in ether with the evolution of hydrogen, which distinguished it from methyl β-trifluoromethyl-β-hydroxybutyrate which has similar constants [7].

Methyl β-trifluoromethyl-β-aminobutyrate. A mixture of 7.5 g of the ester (II) and a fivefold excess of dry ammonia were kept in a sealed ampoule for 48 hr at room temperature. The excess ammonia was evaporated and the residue distilled in vacuum to give 7.3 g (89%) of the aminoester (IV), b. p. 93.5 (73 mm); $n^{20}D$ 1.3842; $d^{20}_4$ 1.2501; found MR 34.61; calculated MR 35.40. Found: C 38.99; H 5.45; F 30.26; N 8.02%. $C_6F_3H_{10}O_2N$. Calculated: C 38.92; H 5.42; F 30.82; N 7.56%. The hydrochloride was soluble in water, m. p. 128-129.5° (from ethyl acetate).

The aminoester (IV) (1.35 g) was treated in the cold with a solution of sodium nitrite in the presence of sulphuric acid until an excess of free nitrous acid remained. The precipitated oil was washed with water and heated with 20% alkali on a water bath for 1 hr until it dissolved completely. The solution was acidified and extracted with ether. The ether extracts were combined, dried, and after removal of the solvent, the residue was recrystallized from n-heptane to give 0.56 g (45%) β-trifluoroethyl-β-hydroxybutyric acid. The melting points of the samples and of a mixed melt were 39.5-41°.

Methyl β-trifluoromethyl-β-(N-β-hydroxyethyl) aminobutyrate. 7.23 g (0.043 M) of the ester (II) and 2.64 g (0.043 M) ethanolamine were heated at 80° for 5 hr in a sealed ampoule. On another day the reaction mixture was distilled in vacuum.

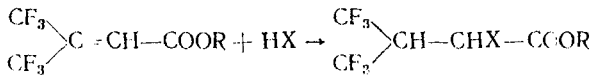
The ester (V) was obtained in 40% yield (3.91 g); b. p. 138.5-141° (18 mm); $n^{20}D$ 1.4165; $d^{20}_4$ 1.2649; found MR 45.47; calculated MR 46.35; the hydrochloride has m. p. 101-103° (reprecipitated with absolute ether from absolute ethanol). Found: C 36.06; H 5.62; F 20.47; N 5.33%. $C_8F_3H_{15}O_3NCl$. Calculated: C 36.15; H 5.65; F 21.46; N 5.27%.

A fraction (3.15g) with b. p. 160-163° (7 mm), $n^{20}D$ 1.4400 was also obtained. It did not dissolve in dilute hydrochloric acid. This fraction was not studied further.

A mixture of 4.6 g (0.025 M) of the ester (IV), 1.25 g (0.028 M) ethylene oxide, and 25 ml 50% acetic acid was kept at room temperature for 12 hr; the solution was then neutralized with dry soda, the oil separated, taken up in ether and dried over magnesium sulfate. After evaporation of the ether and distillation in vacuum, 2.27 g of the initial aminoester (IV) was obtained [b. p. 65-66° (72 mm); $n^{20}D$ 1.3873 (hydrochloride gave no depression of the melting point with an authentic sample)] together with 1.47 g of the ester V; $n^{20}D$ 1.4152 (hydrochloride gave no depression of the melting point with a sample from the first experiment). The yield was 51%, calculated on the aminoester (IV) consumed in the reaction.

## Discussion of Experimental Results

In previous papers of this series it was shown that water, hydrogen bromide, ammonia, and other substances added to β,β-bistrifluoromethylacrylic acid and its esters in the α-position to the carboxyl group [3, 8, 9]:

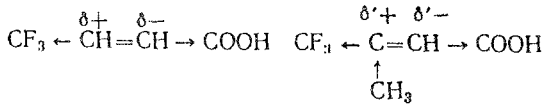


X = OH, $NH_2$, Br etc.

Such a direction of addition has not been observed previously in other α, β-saturated acids. This may be explained either by the electronic effect of the trifluoromethyl group or by steric hindrance to addition of the groups in the β-position.

To estimate the relative importance of these two factors it was of interest to study additions to β-trifluoromethylcrotonic acid in which steric hindrance at the β-carbon atom ought to be about the same as in β,β-bistrifluoromethylacrylic acid because of the small difference in volume of the trifluoromethyl and methyl groups.

At the same time the polarization of the double bond in this acid ought to be the same as in γ,γ,γ-trifluorocrotonic acid in which the effect of the trifluoromethyl group is not weakened by the neighboring methyl which nevertheless appears insufficient to draw away the π-electrons from the α-carbon atom [10]:



$\delta + > \delta' +$

With this polarization the presence of steric hindrance should lead to considerable hindrance or complete impossibility of addition to β-trifluoromethylcrontonic acid.

As our investigations have shown, additions of nucleophilic reagents to β-trifluoromethylcrotonic acid proceed in mild conditions and in accordance with the anticipated polarization of the double bond. Hence it can be concluded that in the case of β,β-trifluoromethylacrylic steric hindrance plays a subordinate part in determining the direction of addition.

## SUMMARY

1. β-Trifluoromethylcrotonic acid was obtained by the action of anhydrous sulfuric acid on β-trifluoromethyl-β-methylpropiolactone or β-trifluoromethyl-β-hydroxybutyric acid.

2. Thionyl chloride in distinction from phosphorus pentoxide easily dehydrates methyl β-trifluoromethyl-β-hydroxybutyrate.

3. After studying the direction of addition of methanol, ammonia, and ethanolamine to esters of β-trifluoromethylcrotonic acid it was concluded that the deciding role in the addition of nucleophilic reagents was played by polarization of the double bond, not steric hindrance.

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All abbreviations of periodicals in the above bibliography are letter-by-letter transliterations of the abbreviations as given in the original Russian journal. *Some or all of this periodical literature may well be available in English translation.* A complete list of the cover-to-cover English translations appears at the back of this issue.

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