SOME REACTIONS OF TRIFLUOROPYRUVIC ESTER WITH NUCLEOPHILIC REAGENTS

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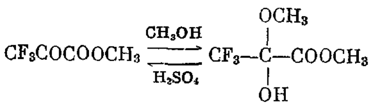
Previously we had shown that the esters of trifluoropyruvic acid are easily obtained from perfluoropropylene oxide [1]. It could be expected that the ketonic carbonyl group in these compounds will be especially electrophilic due to the electron-withdrawing effect of the trifluoromethyl and carbalkoxyl groups; consequently, the chemical properties of the esters of trifluoropyruvic acid should be close to the properties of hexafluoroacetone and other fluoro ketones [2].

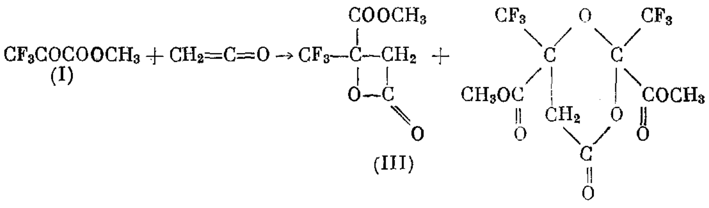
In the present paper was studied the reaction of the methyl ester of trifluoropyruvic acid (I) with some nucleophilic reagents: methanol, ketone, cyclohexyl isocyanide and triethyl phosphite. The completely stable polyketal (II) is formed as the result of vigorous reaction with methanol, which can be distilled at atmospheric pressure without decomposition (in contrast to the polyketals of hexafluoroacetone [3]), but easily cleaves methanol when treated with sulfuric acid.



$$CF_3COCOOCH_3 \underset{H_2SO_4}{\overset{CH_3OH}{\rightleftarrows}} CF_3-\overset{OCH_3}{\underset{OH}{C}}-COOCH_3$$

(I) (II)

As is shown [4], hexafluoroacetone reacts with ketone in the absence of catalysts, forming β,β-bis(trifluoromethyl)propiolactone. It proved that the ester of trifluoropyruvic acid also reacts very easily with ketene without a catalyst. However, besides the 1 : 1 adduct – the β-lactone (III), the 2 : 1 adduct is also formed as a reaction result, to which should be assigned the structure of 1,3-dioxan-4-one (IV).*



Both adducts are converted to the corresponding amides of β-hydroxy-β-carbomethoxy-γ,γ,γ-trifluorobutyric acid (Va) and (Vb) when treated with amines.(scheme at top of next page).

The preparation of anilide (Vb) from adduct (IV) confirms the fact that in this adduct the two moieties of the trifluoropropyruvic esters are connected via the formation of the C – O bond, and not the C – C bond. The two moieties of the trifluoropyruvic ester are connected in the same manner when (I) is reacted with cyclohexyl isocyanide. Iminodioxolane (VI)† is formed as a result, i.e., the reaction is completely analo-

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* The analogous adduct of the ketone with two molecules of formaldehyde is known [5].

† Only (VI) is formed even when equimolar amounts of (I) and the isocyanide are taken, and the hypothetical intermediate product (the 1 : 1 adduct) cannot be isolated.

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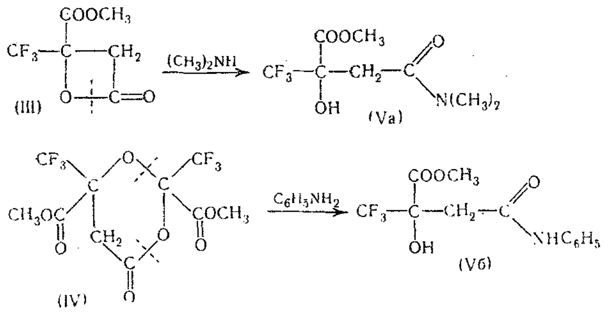
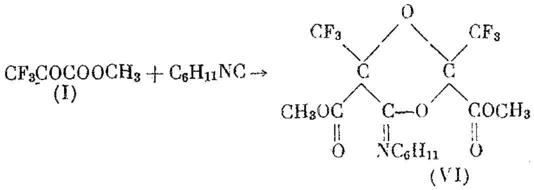


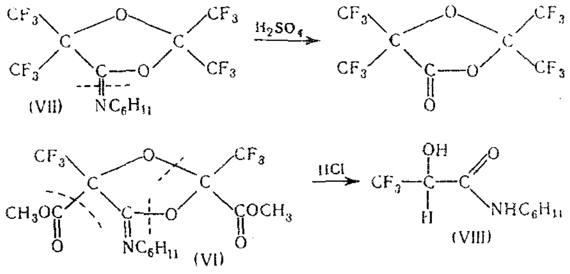
(III) (Va) (IV) (Vб)

gous to the reaction of hexafluoroacetone with cyclohexyl isocyanide [6].



(I) (VI)

The chemical properties of adduct (VI) are sharply different from the properties of the adduct of hexafluoroacetone with cyclohexyl isocyanide (VII). Iminodioxolane (VII) when hydrolyzed with acids is cleaved at the C = N bond with a retention of the ring [6]. In contrast, the hydrolysis of the "dicarbomethoxyl analog" (VI) is accompanied by cleavage of the ring at the C – O bond; in addition, saponification of the ester group with subsequent decarboxylation* occurs in the hydrolysis of (VI), which in the final analysis leads to the cyclohexylamide of trifluorolactic acid (VIII).



(VII) (VI) (VIII)

The ester of trifluoropyruvic acid reacts with triethyl phosphite in the same manner as does hexafluoroacetone [8, 9]. The cyclic phosphorane (IX) was obtained as the result of the formation of a new C – C bond, the hydrolysis of which leads to the corresponding pinacol (X)(scheme at top of next page).

It is obvious, the same as in the case of the reaction of trialkyl phosphite with hexafluoroacetone [8, 9] or with the ester of the unfluorinated pyruvic acid [10], that in the case of the ester of trifluoropyruvic acid the intermediately formed addition product of 1 mole of the carbonyl compound to 1 mole of the trailkyl phosphite is very unstable – even the gradual addition of (I) to an equimolar amount of the phosphite gives only phosphorane (IX) and unconsumed phosphite.

As a result, the ester of trifluoropyruvic acid when reacted with nucleophilic reagents behaves mainly like hexafluoroacetone.

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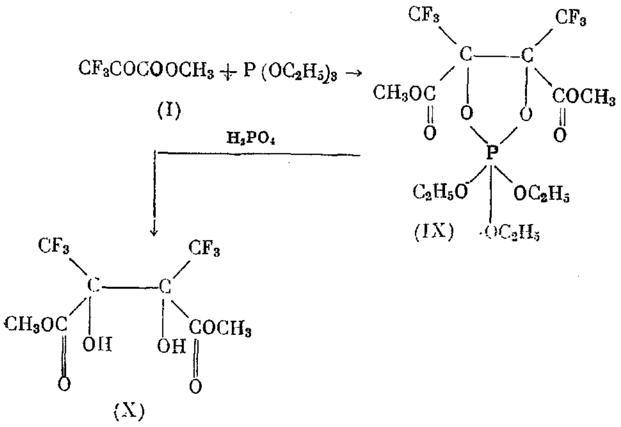
*In general, such decarboxylation is not characteristic for α-hydroxy acids and their derivatives, which are usually easily decarbonylated (and not decarboxylated) [7]. It is possible that in our case the presence of the electron-withdrawing trifluoromethyl and cyclohexylaminocarbonyl groups proves to be the determining factor in facilitating the decarboxylation.



EXPERIMENTAL

Methyl Ester of α-Hydroxy-α-methoxytrifluoropropionic Acid (II). To 7.8 g of methyl trifluoropyruvate, with cooling and stirring, was slowly added 1.6 g of methyl alcohol. Distillation gave 7.8 g (82% of theory) of polyketal (II), mp 132-133°; n_D^{20} 1.3625. Found: C 31.71; H 4.03; F 30.74%. $C_5H_7F_3O_2$. Calculated: C 31.21; H 3.19; F 30.32%.

β-Trifluoromethyl-β-carbomethoxy-β-propiolactone (III) and 2,4-Bis(trifluoromethyl)-2,4-bis(carbomethoxy)-1,3-dioxan-6-one (IV). Into an ether solution of 7.8 g of methyl trifluoropyruvate, contained in a flask fitted with a reflux condenser (∼ − 70°), was passed an excess of ketene, after which the mixture was allowed to stand overnight. Distillation gave lactone (III) and dioxanone (IV). The yield of (III) was 3.6 g (36% of theory), mp 68-70° (5 mm); n_D^{20} 1.3810. Found: C 36.17; H 2.40; F 29.17%. $C_6H_5F_3O_2$. Calculated C 36.36; H 2.52; F 28.78%. IR spectrum: 1770 and 1870 cm^{-1} (two C = O groups). The yield of (IV) was 3.5 g (40% of theory), mp 102-105° (5 mm); n_D^{20} 1.3860. Found: C 34.28; H 2.27; F 31.42%. $C_{10}H_8F_6O_7$. Calculated: C 33.80; H 2.26; F 32.21%. IR spectrum: 1770, 1835 and 1870 cm^{-1} (three C = O groups).

Lactone (III) was treated with an excess of aqueous dimethylamine solution to give the dimethylamide of β-hydroxy-β-carbomethoxy-γ,γ,γ-trifluorobutyric acid (Va), mp 110-112.5° (from heptane). Found: F 23.50; N 6.22%. $C_8H_{12}F_3NO_4$. Calculated: F 23.37; N 5.79%.

The treatment of dioxanone (IV) with excess aniline gave the anilide of β-hydroxy-β-carbomethoxy-γ,γ,γ-trifluorobutyric acid (Vb), mp 162-164° (from dichloroethane). Found: F 19.26; N 4.90%. $C_{12}H_{18}F_3NO$. Calculated: F 19.50; N 4.81%.

5-Cyclohexylamine-2,4-bis(trifluoromethyl)-2,4-bis(carbomethoxy)dioxolane (VI). To 3.3 g of cyclohexyl isocyanide, with strong cooling, was added 5 g of methyl trifluoropyruvate in drops. The next day the mixture was distilled to give 1.3 g of unreacted cyclohexyl isocyanide and 5.8 g (91% of theory) of iminedioxolane (VI), mp 117-118° (4 mm). Found: C 42.81; H 3.95; F 26.81; N 3.59%. $C_{15}H_{17}F_6NO_5$. Calculated: C 42.75; H 4.04; F 27.08; N 3.32%. IR spectrum: 1750 cm^{-1} (C = O group); 1780 cm^{-1} (C = N group).

Cyclohexylamide of Trifluorolactic Acid (VIII). A mixture of 1.9 g of iminedioxolane (VI) and 3 ml of concentrated HCl solution was heated for 6 h on the steam bath. The obtained crystals were filtered and washed with water. We obtained 0.86 g (85% of theory) of amide (VIII), mp 98-99°. Found: C 48.09; H 6.25; F 25.43; N 6.75%. $C_{19}H_{14}F_3NO_2$. Calculated: C 48.00; H 6.25; F 25.78; N 6.22%. IR spectrum: 1550 and 1650 cm^{-1} (CON$<$ group). In the NMR spectrum of the protons was detected the quadruplet

δ ($CF_3C<$ − H) 4.58 p.p.m. J (HF) 8 Hz.

Cyclic Phosphorane (IX). To an ether solution of 8.3 g of triethyl phosphite, with cooling in ice water, was gradually added an ether solution of 7.8 g of methyl trifluoropyruvate. The next day the mixture was distilled to give 3.8 g of unreacted triethyl phosphite and 8.4 g (70% of theory) of phosphorane (IX), bp 126-128° (3 mm). Found: C 34.90; H 4.15; F 24.01; P 6.76%. $C_{14}H_{21}F_6O_9P$. Calculated: C 35.15; H 4.39; F 23.85; P 6.49%. IR spectrum: 1770 cm^{-1} (C = O group).

Dimethyl Ester of α,α-Dihydroxy-α,α'-bis(trifluoromethyl)succinic Acid (X). A mixture of 9.56 g of phosphorane (IX) and 10 ml of concentrated phosphoric acid was heated for 15-20 min (bath temperature 180-200°). Then the mixture was cooled and the pinacol (X) was filtered, yield 2.85 g (65% of theory), mp 102-104° (from dichloromethane). Found: C 31.35; H 2.40; F 36.33%. $C_8H_8F_6O_6$. Calculated: C 30.68; H 2.56; F 36.31%. IR spectrum: 1750 cm^{-1} (C = O group); 3450-3530 cm^{-1} (OH group).

CONCLUSIONS

1. It was shown that the ketonic carbonyl group in the methyl ester of trifluoropyruvic acid is highly electrophilic.

2. Reaction with methanol gave the corresponding polyketal, while reaction with ketene, cyclohexyl isocyanide or triethyl phosphite gave cyclic adducts.

3. In the adducts, containing 2 moles of the trifluoropyruvic ester per mole of ketene or cyclohexyl isocyanide, the two moieties of the fluorinated keto ester are connected via the formation of a C – O bond, whereas a new C – C bond is formed between the moieties of the trifluoropyruvic ester in the adduct with triethyl phosphite, which leads to obtaining the pinacol derivative.

4. The reaction with ketene also gave the 1 : 1 adduct – the corresponding β-lactone.

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