Organic Chemistry

Free-radical reactions of methyl trifluoropyruvate with aldehydes

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Methyl trifluoropyruvate reacts with aldehydes in the presence of catalytic amounts of benzoyl peroxide at 130—140 °C to give β,β,β-trifluoro-α-(methoxycarbonyl)ethyl carboxylates. UV irradiation makes oligomerization of the initial ketoester predominant.

Key words: methyl trifluoropyruvate, reaction with aldehydes; benzoyl peroxide; UV irradiation; free-radical reactions; β,β,β-trifluoro-α-(methoxycarbonyl)ethyl carboxylates, synthesis.

The carbonyl group of trifluoropyruvates is extremely electrophilic, which makes these compounds highly reactive in many heterolytic and electrocyclic processes.[1—3] The behavior of alkyl trifluoropyruvates in free-radical reactions is less well understood. It is known[4] that UV irradiation of methyl trifluoropyruvate (**1**) in the presence of benzophenone or a mixture of ketoester **1** with an equimolar amount of isopropyl alcohol results in the corresponding pinacol (dimethyl 2,3-bis(trifluoromethyl)-2,3-dihydroxysuccinate) and an oligomer of ester **1** in nearly equal yields, *i.e.*, a photoexcited particle **1** forms the C—C and C—O bonds with an equal probability. When compound **1** is reduced with metallic sodium in the presence of trimethylchlorosilane, the formation of pinacol occurs more selectively.

With the goal of extending the area of application of ketoester **1** as a precursor of new compounds, we studied features of its free-radical reactions with aldehydes. Out of polyfluorocarbonyl compounds, hexafluoroacetone has been involved earlier[5] in such reactions. In this case, homolytic transformations mainly yield hexafluoroisopropyl carboxylates, while *C*-alkylation of aldehydes with hexafluoroacetone results in by-products.

Of the aliphatic aldehydes, acetaldehyde, butyraldehyde, and valeraldehyde were introduced by us into a free-radical reaction with ketoester **1**. Benzoyl peroxide (BP) was found to be the best catalyst and 130—140 °C the optimum temperature range. Ketoester **1** polymerizes to a large extent in the presence of *tert*-butyl peroxide, whereas UV irradiation allows polymerization alone.

The key feature of reactions of compound **1** with aliphatic aldehydes is due to the capability of reagents for soft [2+2] cycloaddition, which finally leads to trioxanes **2** (Scheme 1). Such a course of the reaction should be favorable for suppressing resinification processes in the mixture and increasing the selectivity of free-radical transformations, which was confirmed experimentally.

Thus, in a methyl trifluoropyruvate—acetaldehyde system, where, as shown earlier,[6] trioxane **2a** forms in quantitative yield immediately after mixing the reagents,

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[†] Deceased.

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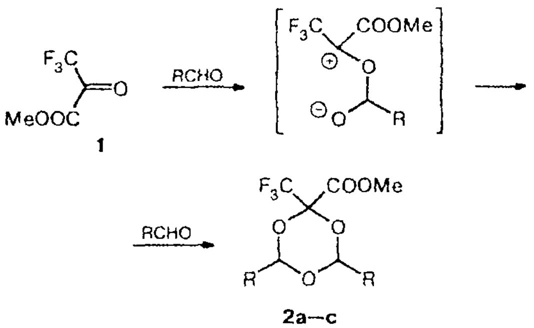
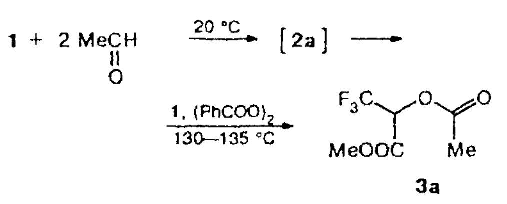
Scheme 1



R = Me (**a**), Pr^n (**b**), Bu^n (**c**)

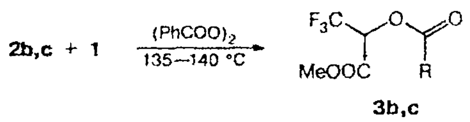
the reaction is completed in the presence of benzoyl peroxide at 130—135 °C over 10—12 h to give β,β,β-trifluoro-α-(methoxycarbonyl)ethyl acetate (**3a**) in ~60% yield (Scheme 2).

Scheme 2



It is much more difficult to obtain trioxanes **2b,c** from butyraldehyde and valeraldehyde. That is why the corresponding butyrate **3b** and valerate **3c** can be obtained in ~50% yields only by the reaction of ketoester **1** with trioxanes **2b,c** isolated in the individual state (Scheme 3).

Scheme 3

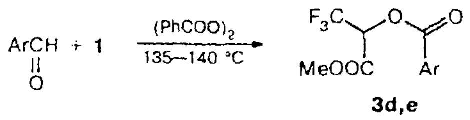


R = Pr^n (**b**), Bu^n (**c**)

When compound **1** is heated with butyraldehyde and valeraldehyde in the presence of BP, the yields of products **3b,c** do not exceed 20% because of intensive resinification of the mixture.

Unlike aliphatic aldehydes, aromatic aldehydes do not enter into [2+2] cycloaddition with ketoester **1**. However, the formation of the corresponding β,β,β-trifluoro-α-(methoxycarbonyl)ethyl carboxylates was rather highly selective in these reactions as well. Thus, heating of a mixture of compound **1** with benzaldehyde or anisaldehyde in the presence of BP affords the corresponding benzoate **3d** and *p*-methoxybenzoate **3e** in >50% yields (Scheme 4).

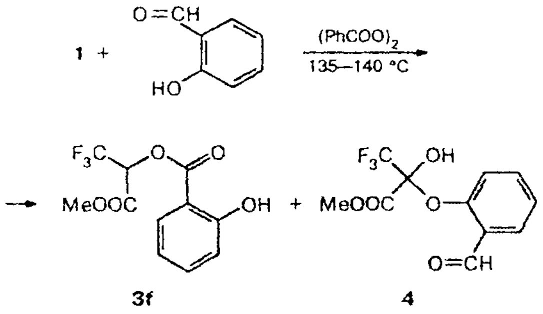
Scheme 4



Ar = Ph (**d**), 4-MeOC$_6$H$_4$ (**e**)

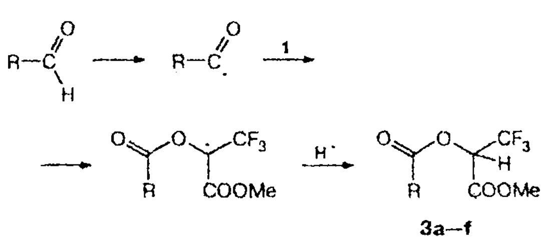
Only salicylaldehyde was extremely difficult to involve in this reaction. As a result, there was formed a mixture of compounds from which salicylate **3f** was isolated in 20% yield. Apparently, in this case, the formation of stable intermediate hemiacetal **4** hinders the reaction (Scheme 5).

Scheme 5



It follows from the results obtained that only one pathway is realized in the free-radical reactions of methyl trifluoropyruvate with aldehydes, *viz.*, *O*-alkylation of ketoester **1** with an acyl radical generated from aldehyde (Scheme 6). *C*-Alkylation of aldehydes with methyl trifluoropyruvate does not occur under the reaction conditions.

Scheme 6



Along with carboxylates **3a—f**, the reaction mixture contains oligomers of compound **1** and in addition, in the case of reactions with aliphatic aldehydes, trioxanes

Table 1. Data of elemental analysis and spectral parameters of compounds **2b,c**, **3a—f**

Compound	Found/Calculated (%)			Molecular formula	^{1}H NMR, δ (*J*/Hz)		^{19}F NMR, δ (*J*/Hz)	IR, ν(CO)/cm^{-1}
	C	H	F		OCH$_3$ (s)	Other protons		
2b	47.72 48.00	6.08 6.33	18.77 19.00	$C_{12}H_{19}F_3O_5$	3.89	1.7 (m, 4 H, CH$_2$); 1.56 (m, 4 H, CH$_2$); 0.9 (t, 6 H, CH$_3$); 5.10 (t, 2 H, CH)	−5.32 (s)	1770
2c	51.09 51.21	7.04 7.01	17.02 17.37	$C_{14}H_{23}F_3O_5$	3.87	1.36—2.66 (m, 12 H, CH$_2$); 0.9 (t, 6 H, CH$_3$); 5.10 (t, 2 H, CH)	−5.20 (s)	1770
3a	36.34 36.00	3.39 3.50	28.49 28.50	$C_6H_7F_3O_4$	3.77	2.16 (s, 3 H, CH$_3$); 5.39 (q, 1 H, OCH, J_{H-F} = 7.5)	−4.17 (d, J_{F-H} = 7.5)	1710, 1760
3b	42.43 42.10	5.00 4.82	25.29 25.00	$C_8H_{11}F_3O_4$	3.83	0.9 (t, 3 H, CH$_3$); 1.66 (m, 2 H, CH$_2$); 2.46 (m, 2 H, CH$_2$); 5.56 (q, 1 H, OCH, J_{H-F} = 5.0)	−4.17 (d, J_{F-H} = 5.0)	1710, 1760
3c	44.30 44.62	5.49 5.37	23.36 23.55	$C_9H_{13}F_3O_4$	3.80	0.9 (t, 3 H, CH$_3$); 1.4 (m, 2 H, CH$_2$); 1.63 (m, 2 H, CH$_2$); 2.53 (m, 2 H, CH$_2$); 5.55 (q, 1 H, OCH, J_{H-F} = 5.0)	−4.9 (d, J_{F-H} = 5.0)	1710, 1760
3d	50.66 50.38	3.41 3.43	21.60 21.75	$C_{11}H_9F_3O_4$	3.83	5.76 (q, 1 H, OCH, J_{H-F} = 7.5); 7.51—8.10 (m, C$_6$H$_5$)	−4.7 (d, J_{F-H} = 7.5)	1730, 1760
3e	49.63 49.32	3.90 3.76	19.77 19.52	$C_{12}H_{11}F_3O_4$	3.79	5.78 (q, 1 H, OCH, J_{H-F} = 5.0); 7.05 (d, 2 H, C—H, J_{H-H} = 8.0); 8.05 (d, 2 H, C—H, J_{H-H} = 8.0)	−5.17 (d, J_{F-H} = 5.0)	1735, 1770
3f	47.56 47.48	3.53 3.24	20.74 20.50	$C_{11}H_9F_3O_5$	3.86	5.90 (q, 1 H, OCH, J_{H-F} = 5.0); 7.05—8.10 (m, 4 H, C$_6$H$_4$); 10.93 (s, 1 H, OH)	−5.22 (d, J_{F-H} = 5.0)	1735, 1770

Note. The ^{1}H and ^{19}F NMR spectra of compounds **2b,c**, **3b,c**, and **3e,f** were recorded in CD$_3$CN, while the ^{1}H and ^{19}F NMR spectra of compounds **3a,d** were recorded in CDCl$_3$.

2a—c. These high-boiling admixtures can be easily decomposed by methanol to give volatile hemiacetal of ketoester **1**, which facilitates isolation of products **3a—f** by fractional distillation.

Trioxanes **2b,c** and carboxylates **3a—d** are thermally stable colorless liquids. Compounds **3e,f** are low-melting crystalline substances. Their compositions and structures were confirmed by data from elemental analysis and ^{1}H, ^{19}F NMR, and IR spectroscopy (Table 1). In the IR spectra of compounds **3a—f**, absorption bands at 1710—1735 and 1760—1770 cm^{-1} (νCO) are observed, and their ^{19}F NMR spectra exhibit signals as a doublet in the range δ −4.17 to −5.22 with spin-spin coupling constant J_{F-H} = 5.0—7.5 Hz characteristic of the CF$_3$CH group.

Experimental

Freshly distilled aldehydes and methyl trifluoropyruvate were used. Benzoyl peroxide was recrystallized before use. ^{1}H and ^{19}F NMR spectra were recorded on a Bruker WP-200 SY instrument (200.12 and 188.31 MHz, respectively) in CD$_3$CN and CDCl$_3$ (see Table 1), HMDS as the internal standard and CF$_3$COOH as the external standard. IR spectra were recorded on a UR-20 spectrometer (KBr pellets or a solvent-free thin film).

2-Methoxycarbonyl-4,6-di(*n*-propyl)-2-trifluoromethyltrioxane (2b). A mixture of methyl trifluoropyruvate (6.24 g, 0.04 mol) and butyraldehyde (5.76 g, 0.08 mol) was heated at 50—60 °C for 5 h, left at 20 °C for 15 h, and fractionated to give trioxane **2b** (9.84 g, 82%), b.p. 77—78 °C (1.2 Torr), n_D^{20} 1.4010.

4,6-Di(*n*-butyl)-2-methoxycarbonyl-2-trifluoromethyltrioxane (2c) was obtained by analogy with compound **2b** from methyl trifluoropyruvate (6.24 g, 0.04 mol) and valeraldehyde (6.88 g, 0.08 mol). Yield 9.97 g (76%), b.p. 99—101 °C (1.0 Torr), n_D^{20} 1.4105.

β,β,β-Trifluoro-α-(methoxycarbonyl)ethyl acetate (3a). A mixture of methyl trifluoropyruvate (7.8 g, 0.05 mol), acetaldehyde (4.4 g, 0.1 mol), and benzoyl peroxide (0.15 g) was heated in a sealed glass tube at 130—135 °C for 8 h. The tube was cooled and opened. After extra benzoyl peroxide (0.15 g) was added to the reaction mixture, the tube was re-sealed and heated anew at 130—135 °C for 8 h. The cooled mixture was dissolved in 10 mL of anhydrous MeOH and kept at 20 °C for 18 h. The product was purified from resinous substances using a column filled with silica gel (PKN-100, *h* = 10 cm, hexane (30 mL) as the eluent). The thus obtained light yellow solution was fractionated to give compound **3a** (6.4 g, 64%), b.p. 88—90 °C (20 Torr), n_D^{20} 1.3660.

β,β,β-Trifluoro-α-(methoxycarbonyl)ethyl butyrate (3b) was obtained by analogy with acetate **3a** from trioxane **2b** (6.0 g, 0.02 mol), methyl trifluoropyruvate (3.12 g, 0.02 mol), and benzoyl peroxide (0.2 g) at 135—140 °C. Yield 5.01 g (56%), b.p. 128—130 °C (20 Torr), n_D^{20} 1.3917.

β,β,β-Trifluoro-α-(methoxycarbonyl)ethyl valerate (3c) was obtained by analogy with acetate **3a** from trioxane **2c** (6.56 g, 0.02 mol), methyl trifluoropyruvate (3.12 g, 0.02 mol), and benzoyl peroxide (0.2 g) at 135—140 °C. Yield 4.84 g (51%), b.p. 146—147 °C (20 Torr), n_D^{20} 1.4022.

β,β,β-Trifluoro-α-(methoxycarbonyl)ethyl benzoate (3d) was obtained by analogy with acetate **3a** from methyl trifluoropyruvate (3.12 g, 0.02 mol), benzaldehyde (2.12 g, 0.02 mol), and benzoyl peroxide (0.3 g) at 135—140 °C. Yield 2.9 g (55%), b.p. 165 °C (3.0 Torr), n_D^{20} 1.4970.

β,β,β-Trifluoro-α-(methoxycarbonyl)ethyl *p*-methoxybenzoate (3e) was obtained by analogy with acetate **3a** from methyl trifluoropyruvate (3.12 g, 0.02 mol), anisaldehyde (2.72 g, 0.02 mol), and benzoyl peroxide (0.3 g) at 135—140 °C. Yield 2.9 g (50%), b.p. 190—191 °C (1.0 Torr), m.p. 52—53 °C.

β,β,β-Trifluoro-α-(methoxycarbonyl)ethyl salicylate (3f) was obtained by analogy with acetate **3a** from methyl trifluoropyruvate (4.59 g, 0.03 mol), salicylaldehyde (2.44 g, 0.02 mol), and benzoyl peroxide (0.3 g) at 135—140 °C. Yield 1.17 g (21%), b.p. 179—180 °C (1.0 Torr), m.p. 32—34 °C.

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