Organic Chemistry

Anodic perfluoroalkylation of the enol acetate of ethyl acetoacetate

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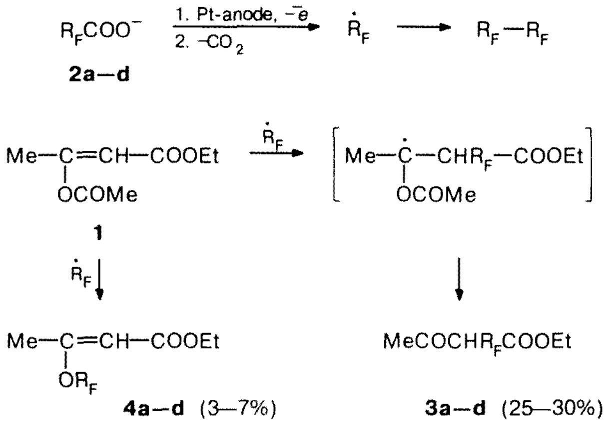
Electrochemical perfluoroalkylation of the enol acetate of ethyl acetoacetate was studied in the conditions of the Kolbe reaction. The yields of alkylation products depend on the competing adsorption of the enol acetate, the solvent, and perfluorocarboxylates on the surface of a platinum electrode.

Key words: enol acetate of ethyl acetoacetate, perfluoroalkyl radicals, ethyl 2-perfluoroalkylacetoacetates.

Previously,[1] it was demonstrated that anodic electrosynthesis of ethyl 2-trifluoromethylacetoacetate is feasible. Since ethyl 2-perfluoroalkylacetoacetates can be used as starting compounds in synthesis of fluoroamino acids,[2,3] we attempted to extend the preparative possibilities of this reaction and studied the reaction of enol acetate (**1**) with perfluoroalkyl radicals generated by anodic oxidation of anions of perfluorocarboxylic acids (**2a—d**) (Scheme 1). Anodic oxidation of perfluorocarboxylates **2a—d** in the presence of enol acetate **1** gave both the target ethyl 2-perfluoroalkylacetoacetates (**3a—d**) and the products of replacement of the acetyl group in the enol acetate by the perfluoroalkyl radical (**4a—d**).

Scheme 1



R_F = CF_3 (**a**); C_2F_5 (**b**); C_3F_7 (**c**); C_4F_9 (**d**)

The structures of compounds **3a—d** and **4a—d** were confirmed by the data of ^1H and ^{19}F NMR spectroscopy (Tables 1 and 2) and mass spectrometry. The fragmentation pathway of ethyl 2-perfluoroalkylaceto-

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Table 1. ^{1}H and ^{19}F spectral data of compounds **3a—d** (δ)

Compound	^{19}F NMR	^{1}H NMR
3a[a]	12.5 (3 F, $^3J_{HF}$ = 9.0 Hz)	1.44 (t, 3 H, CH_3(Et)); 2.48 (s, 3 H, CH_3CO); 4.37 (q, 2 H, CH_2(Et)); 4.66 (q, 1 H, CH, $^3J_{HF}$ = 9.0 Hz)
3b	8.4 (3 F); 42.3 (d, 2 F, $^3J_{HF}$ = 8.5 Hz)	1.43 (t, 3 H, CH_3(Et)); 2.50 (s, 3 H, CH_3CO); 4.35 (q, 2 H, CH_2(Et)); 4.68 (t, 1 H, CH, $^3J_{HF}$ = 8.5 Hz)
3c	5.3 (3 F); 32.5 (m, 2 F, $^3J_{HF}$ = 8.9 Hz, $^4J_{FF}$ = 8.5 Hz); 49.6 (2 F)	1.42 (t, 3 H, CH_3(Et)); 2.49 (s, 3 H, CH_3CO); 4.31 (q, 2 H, CH_2(Et)); 4.77 (t, 1 H, CH, $^3J_{HF}$ = 8.9 Hz)
3d	5.1 (3 F); 37.5 (m, 2 F, $^3J_{HF}$ = 9.1 Hz); 48.9 (2 F); 50.5 (2 F)	1.42 (t, 3 H, CH_3(Et)); 2.51 (s, 3 H, CH_3CO); 4.30 (q, 2 H, CH_2(Et)); 4.93 (t, 1 H, CH, $^3J_{HF}$ = 9.1 Hz)

[a] According to the spectral data, 2.8% enol was present. ^{1}H NMR, δ: 1.41 (t); 2.38 (s); 4.33 (q); 14.29 (s). ^{19}F NMR, δ: 11.0 (s).

Table 2. ^{1}H and ^{19}F NMR spectral data of compounds **4a—d**[a] (δ)

Compound	^{19}F NMR	^{1}H NMR
4a	−5.0 (s, 3 F)	1.48 (t, 3 H, CH_3(Et)); 2.35 (s, 3 H, CH_3CO); 4.65 (q, 2 H, CH_2(Et)); 5.71 (q, 1 H, CH)
4b	5.0 (t, 3 F); 25.6 (q, 2 F)	1.42 (t, 3 H, CH_3(Et)); 2.37 (s, 3 H, CH_3CO); 4.45 (q, 2 H, CH_2(Et)); 5.79 (t, 1 H, CH)
4c	5.3 (t, 3 F, $^4J_{FF}$ = 8.9 Hz); 22.0 (q, 2 F, $^4J_{FF}$ = 8.9 Hz); 50.1 (2 F)	1.41 (t, 3 H, CH_3(Et)); 2.38 (s, 3 H, CH_3CO); 4.30 (q, 2 H, CH_2(Et)); 5.78 (t, 1 H, CH)
4d	5.1 (t, 3 F, $^4J_{FF}$ = 7.5 Hz); 27.0 (t, 2 F, $^4J_{FF}$ = 9.0 Hz); 47.4 (q, 2 F, $^4J_{FF}$ = 7.5 Hz); 52.5 (t, 2 F, $^4J_{FF}$ = 9.0 Hz)	1.44 (t, 3 H, CH_3(Et)); 2.41 (s, 3 H, CH_3CO); 4.36 (q, 2 H, CH_2(Et)); 5.83 (t, 1 H, CH)

[a] For the major isomer (according to NMR spectroscopy and GLC, the ratio of *Z*/*E* isomers of **4** varied from 5 : 1 to 10 : 1).

acetates **3** and 3-perfluoroalkoxycrotonates **4** are shown in Schemes 2 and 3, respectively. A rather abundant molecular ion peak was observed in the mass spectra of all compounds. In all mass spectra, fragmentation ions of R_F are present: *m/z* 69, 119, and 169.

It should be noted that previously[1] ethyl 3,3,3-trifluoropropionate (**5**) was isolated, while formation of **4a** was not observed. However, when we reproduced the conditions reported in Ref. 1, we failed to detect even traces of compound **5**. In addition to compounds **3a—d** and **4a—d**, the enol acetate of ethyl 2-trifluoromethylacetoacetate, dehydrofluorination products, products of dimerization of perfluoroalkyl radicals, and several more compounds were identified in the reaction mixture by chromatomass spectrometry. However, these compounds were not isolated on the preparative scale and were not characterized by spectroscopy due to their low concentrations (less than 1—2%).

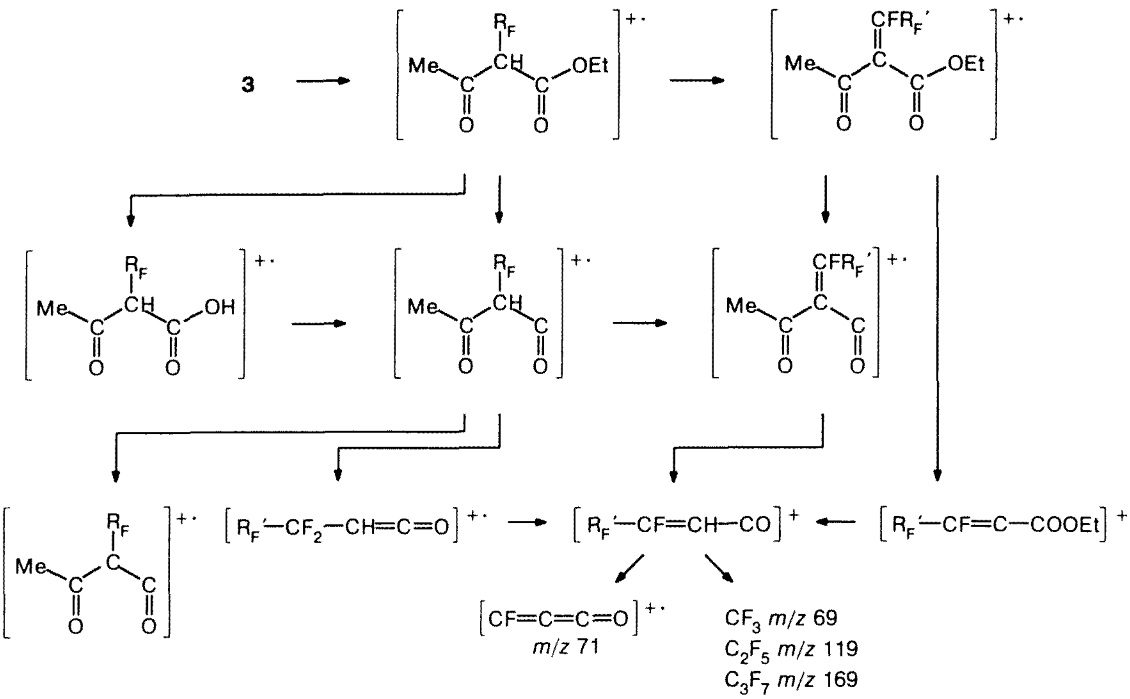
The nature of the solvent has a pronounced effect on perfluoroalkylation of **1**. Thus, in acetonitrile, the yields decreased gradually as the length of the perfluoroalkyl radical increased (Table 3), whereas in the case of C_4F_9COOH, product **3d** was not found, and only perfluorooctane was formed.

When electrochemical synthesis was carried out in acetone, the changes in the yields showed the opposite tendency (see Table 3). Previously,[4] an analogous tendency was observed in electrochemical synthesis of perfluoroalkylacetones from isopropenyl acetate in acetone. However, when we attempted to carry out the synthesis with the acid $C_6F_{13}COOH$, a film of $C_{12}F_{26}$

Table 3. Yields of perfluoroalkylation products

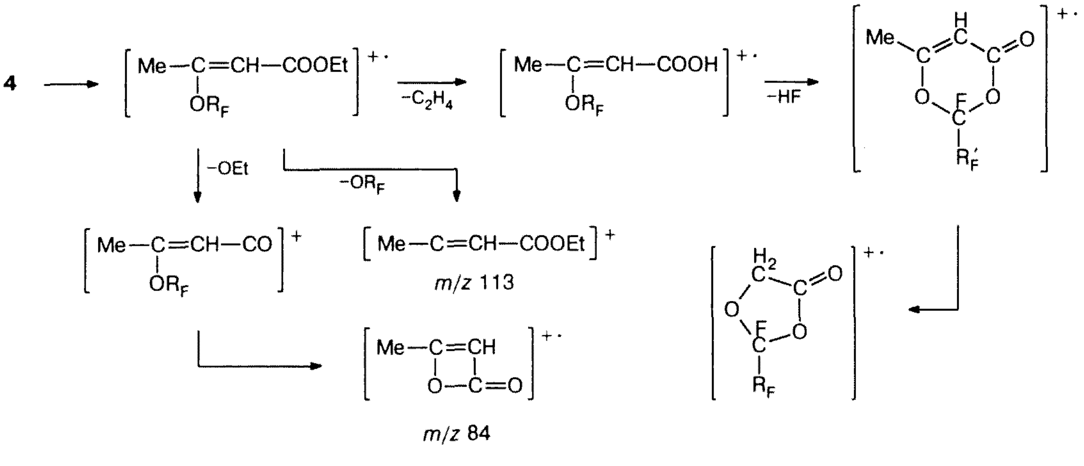
Product	B.p./°C (*p*/Torr)	Solvent	Yield (%)
3a	72 (20)	MeCN	31
		Me_2CO	15
3b	68 (12)	MeCN	19
		Me_2CO	22
3c	96 (15)	MeCN	9
		Me_2CO	25
3d	115 (25)	Me_2CO	27
4a	135 (750)	MeCN	7.1
4b	90 (100)	Me_2CO	5.1
4c	65 (20)	Me_2CO	4.9
4d	82 (20)	Me_2CO	3.4

Scheme 2



R_F = CF_3, C_2F_5, C_3F_7, C_4F_9; R_F' = F, CF_3, C_2F_5, C_3F_7

Scheme 3



R_F = CF_3, C_2F_5, C_3F_7, C_4F_9; R_F' = F, CF_3, C_2F_5, C_3F_7

(m.p. 64 °C [5]) formed on the anode surface, and the current decreased rapidly up to complete cessation.

Unlike other olefins, for example, ethene,[6] enol acetate **1** is weakly adsorbed on the surface of the platinum electrode. Therefore, acetonitrile, which is readily adsorbed, competes with the enol acetate over a wide range of potentials. Moreover, as a result of competitive adsorption of higher perfluorocarboxylates, the enol acetate is virtually displaced from the surface at high anodic potentials corresponding to the Kolbe reaction conditions. As a consequence, the yields of perfluoroalkylation products decrease in series **3a—d**.

Apparently, acetone, which is weakly adsorbed,[6] does not compete seriously with the enol acetate in adsorption on a platinum electrode. In this case, adsorption of R_FCOO^- anions plays a key role. An increase in the length of the perfluoroalkyl chain favors hydrophobization of the surface of the platinum electrode and hinders adsorption of water.[6] This leads to a decrease in the concentration of $OH^{\cdot}$ radicals and to suppression of side reactions (oxidation of enol acetate **1**, oligomerization, *etc.*), which enhances the yields of perfluoroalkylation products in series **3a—d**.

It was established that the use of a glassy-carbon anode results in a substantial decrease in the yields of perfluoroalkylation products. This confirms the key role of adsorption on the anode surface during perfluoroalkylation of the enol acetate of ethyl acetoacetate. It can be concluded that it is these adsorption effects that determine the influence of the solvent, the nature of the electrode material, and the length of the perfluoroalkyl radical on the yields of target products.

Experimental

Electrosynthesis was carried out in a 1-L diaphragmless cell with a cooling jacket equipped with a reflux condenser. Cooling was performed with a Medingen MK 70 apparatus. A platinum wire anode (750 cm^2) and a nickel wire cathode (23 cm^2) were used. The current density was maintained within 4—8 mA cm^{-2}. The current consumption was 2 F mol^{-1}. The ^{19}F NMR spectra were recorded on a Perkin—Elmer R-32 spectrometer (CF_3COOH as the external standard) and on a WM-250 instrument ($CFCl_3$) operating at 84.6 and 235.34 MHz, respectively. The chemical shifts are given relative to CF_3COOH. The ^1H NMR spectra were recorded on a Bruker WM-250 spectrometer (250.13 MHz) with Si_4Me as internal standard. The mass spectra were obtained on a Finnigan MAT instrument (EI, 70 eV). The enol acetate of ethyl acetoacetate was synthesized by the modified procedure.[7]

Ethyl 3-acetoxybut-2-enoate (1). Anhydrous pyridine (60 mL, 0.744 mol) was added with ice-cooling to a mixture of ethyl acetoacetate (50 mL, 0.4 mol) and AcCl (35 mL, 0.49 mol). Then the reaction mixture was heated to 120 °C, held for 15 min, cooled to ~20 °C, and poured into water (300 mL). The mixture was extracted with ether (3×50 mL) and dried with Na_2SO_4. The ether was evaporated, and the residue was distilled. B.p. 82—85 °C (8 Torr). The yield was 65.8 g (95.6%).

Electrochemical synthesis of ethyl 2-perfluoroalkylacetoacetates (3a—d) (general procedure). A solution of NaOH (0.2 g) in water (3 mL) was added to a solution of perfluorocarboxylic acid (0.02 g, 0.03 mol) in acetone or acetonitrile (45 mL), and then enol acetate **1** (~0.01 mol) was added. After electrolysis, the reaction mixture was concentrated to ~5 mL. Then ether (10 mL) was added, and the mixture was poured in water (80 mL). The ethereal layer was separated and dried with Na_2SO_4. The solvent was evaporated, and the residue was distilled (see Table 3).

Ethyl 2-trifluoromethylacetoacetate (3a) was obtained from trifluoroacetic acid (3.01 g, 26 mmol) and **1** (2.07 g, 12 mmol). Mass spectrum, m/z ($I_{rel}(\%)$): 198 $[M]^+$ (3.5), 170 $[M-C_2H_4]^+$ (2.7), 152 $[M-OEt-H]^+$ (4.0), 91 $[CF_2=CH-CO]^+$ (8.0), 43 $[CH_3CO]^+$ (100).

Ethyl 2-pentafluoroethylacetoacetate (3b) was obtained from perfluoropropionic acid (4.15 g, 25.3 mmol) and **1** (1.89 g, 11 mmol). Mass spectrum, m/z ($I_{rel}(\%)$): 248 $[M]^+$ (1), 228 $[M-HF]^+$ (2), 208 $[M-40]^+$ (8), 183 $[M-OEt-HF]^+$ (11), 141 $[M-107]^+$ (12), 43 $[CH_3CO]^+$ (100).

Ethyl 2-heptafluoropropylacetoacetate (3c) was obtained from perfluorobutyric acid (4.62 g, 21.6 mmol) and **1** (1.55 g, 9 mmol). Mass spectrum, m/z ($I_{rel}(\%)$): 298 $[M]^+$ (2), 270 $[M-C_2H_4]^+$ (0.5), 258 $[M-40]^+$ (7), 233 $[M-OEt-HF]^+$ (17), 191 $[M-107]^+$ (21), 43 $[CH_3CO]^+$ (100).

Ethyl 2-nonafluorobutylacetoacetate (3d) was obtained from perfluoropentanoic acid (8.58 g, 32.5 mmol) and **1** (2.2 g, 13 mmol). Mass spectrum, m/z ($I_{rel}(\%)$): 348 $[M]^+$ (10), 328 $[M-HF]^+$ (4), 303 $[M-OEt]^+$ (50), 43 $[CH_3CO]^+$ (100).

Isolation of perfluoroalkoxybut-2-enoates (4a—d). After the electrochemical synthesis (see above), the reaction mixture was placed in a Wurtz flask, and the solvent was distilled off under an atmospheric pressure. Then products **4a—d** were distilled slowly (see Table 3).

Ethyl 3-trifluoromethoxybut-2-enoate (4a) was obtained from trifluoroacetic acid (6.27 g, 55 mmol) and **1** (4.3 g, 25 mmol). Compound **3a** was also isolated in a yield of 1.24 g (25%). Mass spectrum of **4a**, m/z ($I_{rel}(\%)$): 198 $[M]^+$ (21), 170 $[M-C_2H_4]^+$ (19), 153 $[M-OEt]^+$ (100), 150 $[M-C_2H_4-HF]^+$ (18).

Ethyl 3-pentafluoroethoxybut-2-enoate (4b) was obtained from perfluoropropionic acid (11.70 g, 71.3 mmol) and **1** (5.34 g, 31 mmol). Compound **3b** was also isolated in a yield of 1.23 g (16%). Mass spectrum of **4b**, m/z ($I_{rel}(\%)$): 248 $[M]^+$ (31), 220 $[M-C_2H_4]^+$ (23), 203 $[M-OEt]^+$ (100), 200 $[M-C_2H_4-HF]^+$ (28).

Ethyl 3-heptafluoropropoxybut-2-enoate (4c) was obtained from perfluorobutyric acid (17.47 g, 81.6 mmol) and **1** (5.85 g, 34 mmol). Compound **3c** was also isolated in a yield of 1.72 g (17%). Mass spectrum of **4c**, m/z ($I_{rel}(\%)$): 298 $[M]^+$ (30), 270 $[M-C_2H_4]^+$ (12), 253 $[M-OEt]^+$ (95), 250 $[M-C_2H_4-HF]^+$ (22).

Ethyl 3-nonafluorobutoxybut-2-enoate (4d) was obtained from perfluoropentanoic acid (27.07 g, 103 mmol) and **1** (7.06 g, 41 mmol). Compound **3d** was also isolated in a yield of 2.71 g (19%). Mass spectrum of **4d**, m/z ($I_{rel}(\%)$): 348 $[M]^+$ (27), 320 $[M-C_2H_4]^+$ (8), 303 $[M-OEt]^+$ (81), 300 $[M-C_2H_4-HF]^+$ (24).

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