As is well known, benzoylacetic ester finds extensive application in organic synthesis. It was therefore of interest to work out a method for the synthesis of (pentafluorobenzoyl)acetic ester, which could serve as starting compound for the synthesis of a whole series of heterocycles, \( \beta \)- and \( \gamma \)-diketones, and other compounds containing a polyfluoro aromatic residue.

In an attempt to synthesize (pentafluorobenzoyl)acetic ester by the condensation of pentafluorobenzoyl chloride with enolates of acetoacetic ester, instead of the expected product, chromone derivatives were formed since the intermediately formed (pentafluorobenzoyl)acetoacetic ester was immediately cyclized with elimination of ortho fluorine [1].

Here we propose two methods for the preparation of (pentafluorobenzoyl)acetic ester. In the condensation of pentafluorobenzoyl chloride with the ethoxymagnesium derivative of malonic ester, (pentafluorobenzoyl) malonic ester is formed in 65% yield, and the partial hydrolysis of this gives (pentafluorobenzoyl)acetic ester (I) in 38% yield for the two stages:

\[
\text{CsF}_5\text{COCl} \xrightarrow{\text{Mg(OCH}_3\text{H})_2} \text{CsF}_5\text{COCH}(\text{COOCH}_2\text{H})_2 \xrightarrow{\text{H}_{2}\text{SO}_4} \text{CsF}_5\text{COCH}_2\text{COOCH}_2\text{H}_5.
\]  

The structure of (I) was confirmed by the analyses of its anilide and 2,4-dinitrophenylhydrazone, and also by spectral data. The ultraviolet spectra of (I) and unfluorinated benzoylacetic ester are similar, but the absorption maximum of (I) is shifted hypsochromically by 22 nm (Fig. 1), a phenomenon frequently met with polyfluoro aromatic compounds [2]. The PMR spectrum of (I) (Fig. 2; internal reference tetramethylsilane) is similar to that of benzoylacetic ester, but it contains one band less, and the missing band (Fig. 3, \( \delta_3 \) 9.6 p. p. m.) can correspond in its chemical shift, its area, the number of component peaks, and their splitting only to a phenyl group. The areas of the bands corresponding to the OH group (see Fig. 3, \( \delta_4 \) 16.6 p. p. m.) and to olefin hydrogen (\( \delta_4 \) 7.4 p. p. m.) in the spectrum of benzoylacetic ester are considerably less than in the spectrum of (I) (see Fig. 2, \( \delta_3 \) 17.0 and \( \delta_4 \) 7.6 p. p. m.), which points to a greater content of enol form in (I).

Unlike ethyl trifluoroacetate [3], ethyl pentafluorobenzoate (II) does not form the corresponding acylacetic ester in Claisen condensation in presence of sodium. However, when ester condensation is conducted in presence of bromo(diisopropylamino)magnesium (I) may be obtained in 43% yield:

\[
\text{CsF}_5\text{COOCH}_2\text{H}_5 + \text{CH}_3\text{COOCH}_2\text{H}_5 \xrightarrow{(i-\text{C}_3\text{H}_7)_2\text{NMgBr}} \text{CsF}_5\text{COCH}_2\text{COOCH}_2\text{H}_5
\]  

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\]  

* This article is published in accordance with a resolution of the Conference of Chief Editors of Journals of the Academy of Sciences of the USSR of July 12, 1962, as a dissertation paper by A. T. Prudchenko.
Fig. 2. PMR spectrum of (pentafluoro-benzoyl)acetic ester. Peak 1-$(\text{CH}_3)_4\text{Si}$; $\delta_1-\delta_5$ are, respectively, 1.7, 5.6, 7.6, and 17.0 p.p.m.

It is interesting that in the condensation of (II) with sodioacetoacetic ester, instead of the expected (I), the main product is diethyl tetrafluorohomoterephthalate [α-carboxy-2,3,5,6-tetrafluoro-p-toluic acid diethyl ester] (IV), whose structure was confirmed by analysis, its spectra, and its further transformations. The $^{19}$F NMR spectrum of (IV) contains two bands of complex structure at $\delta_1 65$ and $\delta_2 63$ p.p.m. (internal reference trifluoroacetic acid), which confirms the para disposition of the ester groupings; the calculated chemical shifts are 69 and 62 p.p.m., respectively [4].

It is probable that in the course of this reaction nucleophilic replacement of para fluorine* by the acetoacetic ester anion occurs with subsequent alcoholysis under the action of catalytic amounts of sodium ethoxide. Analogous alcoholysis was observed previously in the reaction of sodium o-bromobenzoate with sodioacetoacetic ester in presence of bronze [6]. We did not observe the cyclization of the ester (III) with elimination of ortho fluorine and formation of a benzofuran; such a transformation has been observed in the condensation of hexafluorobenzene with sodioacetoacetic ester [7]. The transformations described can be represented by the following scheme:

The hydrolysis of (IV) with an aqueous solution of potassium hydroxide leads to tetrafluorohomoterephthalic acid (V) in 77% yield; however, the latter is not oxidized to tetrafluoroterephthalic acid by treatment with a solution of potassium permanganate or dichromate in sulfuric acid. Heating of (V) in dimethylformamide gave (2,3,5,6-tetrafluorophenyl)acetic acid (VI). The ultraviolet absorption curve of (VI) is similar to those of phenyl- and (pentafluorophenyl)-acetic acids, but differs greatly both in the position of the maximum and in the extinction coefficient.

* In the literature we have found only one nucleophilic substitution reaction of pentafluorobenzoic acid—the formation of p-aminotetrafluorobenzoic acid [5].
from the curve for p-toluic acid (Fig. 4). Hence, as would be expected, when (V) is heated with dimethylformamide, it is the carboxyl group in the nucleus between two fluorine atoms which is eliminated (cf., \[8\]). Under these conditions neither phenylacetic acid nor (pentafluorophenyl)acetic acid is de-carboxylated.

**EXPERIMENTAL**

Infrared spectra were run on substances in the pure state and as pellets with KBr on a UR-10 instrument. Ultraviolet spectra were run on an SFD-2 instrument: solvent—ethanol; molar concentration $10^{-4}$; layer thickness 0.5 cm. NMR spectra were run on a JNM-3 instrument at a frequency of 40 MHz.

**Ethyl Pentafluorobenzoate (II).** A mixture of 12 g of pentafluorobenzoic acid, 86.4 ml of absolute alcohol, and 8.64 ml of concentrated sulfuric acid was boiled for 11 h. The reaction mixture was steam-distilled, the distillate was saturated with NaCl and extracted with ether, and the extracts were dried with MgSO$_4$.

Solvent was driven off, and vacuum fractionation gave 10.05 g (75.8%) of (II); b. p. 63 °C (5 mm); $n_D^20$ 1.4252. Found: C 44.98; 45.23; H 1.87; 2.13; F 39.38; 39.10%. C$_9$H$_8$F$_5$O$_2$. Calculated: C 45.03; H 2.10; F 39.56%. $\lambda_{\text{max}}$ (in alcohol) 270 ml$^{-1}$ (log $\varepsilon$ 3.065). Infrared spectrum (in pure state): 1005 s (C–F), 1235 s (C–O–C in esters), 1510 s (fluorinated aromatic ring), 1740 s (C = O in esters), 2880 w, 2910 w, 2940 w, 2985 m (CH$_2$ and CH$_3$).

**Diethyl (Pentafluorobenzoyl)malonate.** 6.5 g of malonic ester was taken, and about one-half of it was added to a mixture of 1.02 g of dry magnesium turnings, 4.9 ml of absolute alcohol, and 0.1 ml of CC$_4$H$_8$, which was contained in a three-necked flask fitted with stirrer, dropping funnel, and reflux condenser. Reaction set in after a few minutes and became vigorous; the rest of the malonic ester was then added dropwise. 14.2 ml of dry ether was added cautiously to the reaction mixture at room temperature, and the rate of reaction then increased appreciably. To dissolve the magnesium completely, the reaction mixture was heated for three hours in a boiling water bath and cooled. 10.03 g of pentafluorobenzoic chloride in 10 ml of dry ether was added slowly, and the mixture was boiled for ten minutes. It was cooled, and 10 ml of water and 5 ml of 20% sulfuric acid were added. The aqueous layer was extracted with ether, and the ether extracts were washed with sodium carbonate solution and water and then dried with MgSO$_4$. Ether was driven off, and distillation gave 10.07 g (65%) of diethyl (pentafluorobenzoyl)malonate; b. p. 137 °C (6 mm); $n_D^{25}$ 1.4620. Found: C 47.53; 47.46; H 2.79; 2.79; F 27.75; 27.09; OC$_2$H$_5$ 24.82; 24.73%; mol. wt. 368; 365. C$_{14}$H$_{12}$F$_5$O$_5$. Calculated: C 47.50; H 3.13; F 26.85; OC$_2$H$_5$ 25.42%; mol. wt. 354. $\lambda_{\text{max}}$ (in alcohol) 275 ml$^{-1}$ (log $\varepsilon$ 4.146). Infrared spectrum (in pure state): 1005 s (C–F), 1240 s (C–O–C in esters), 1510 s (fluorinated aromatic ring), 1665 s (C = O in ketones), 1730 s (C = O in esters), 2985 m, 2940 w, 2910 w, and 2875 w (CH$_2$ and CH$_3$).

**(Pentafluorobenzoyl)acetic Ester (I).** Crude (pentafluorobenzoyl)malonic ester was prepared as described above from 9.4 g of pentafluorobenzoic chloride. The reaction mixture was treated with 20% sulfuric acid, and the mixture was boiled for one hour at 145–150 °C. Found: N 4.39; 4.32; F 29.64; 29.35%.

The anilide corresponding to (I) was prepared by heating a mixture of 1 g of (I) and 0.44 g of aniline in 1.2 ml of dry xylene for one hour at 145–150 °C. Found: N 4.39; 4.32; F 29.64; 29.35%.

*G. S. Shchegoleva took part in the experimental work.*
C_{15}H_{14}F_{10}O_4. Calculated: N 4.29; F 28.9%. 2,4-Dinitrophenylhydrazone of (I), m. p. 118° (from alcohol). Found: N 12.44; 12.34; F 20.21; 20.40%. C_{11}H_{18}F_{14}NO_8. Calculated: N 12.14; F 20.55%.

Ethyl Pentafluorobenzoate (II) in the Claisen Reaction. Bromo(diisopropylamino)magnesium was prepared by a known method [9] from 3.06 g of magnesium, 13.8 g of ethyl bromide, and 12.84 g of diisopropylamine. A mixture of 14.9 g of ethyl pentafluorobenzoate (II) and 5.31 g of ethyl acetate was then added dropwise. The mixture was stirred for three hours and then poured into a mixture of 90 g of ice and 7.5 ml of concentrated sulfuric acid; after steam distillation and fractionation we obtained 7.55 g (43%) of (I). The infrared spectra of samples of (I) prepared in this way and prepared from (pentafluorobenzoyl)malonic ester were found to be identical, and a mixture of their anilides melted without depression.

Diethyl 2,3,5,6-Tetrafluorohomoterephthalate Sodioacetoacetic ester was prepared in the usual way from 0.96 g of sodium, 12.5 ml of absolute alcohol, and 5.55 g of acetoacetic ester. The reflux condenser was replaced by a low still head, and alcohol was driven off under the vacuum of a water pump with gentle warming until dryness was almost attained; the last traces of alcohol were driven off in the vacuum of an oil pump with rise in bath temperature to 100°. 10 g of (II) was added to the cooled residue; the reaction mixture was heated at 140°-145° (in the bath) for three hours, and the temperature was then raised gradually to 180°. The reaction mixture was cooled, 5 ml of water was added, and the mixture was acidified by the addition of a cooled solution of 1.2 ml of concentrated sulfuric acid in 4.4 ml of water. The ester layer was separated, and the aqueous layer was extracted with ether. The ether extracts were washed with sodium bicarbonate solution and water, and were dried with MgSO_4. Ether was driven off, and distillation of the residue gave 7.13 g (55.7%) of unpurified (IV); b. p. 141°-142° (5 mm); n_D^{25} 1.4590. Found: C 50.97; 50.93; H 4.04; 4.03; F 24.88; 24.76; OC_2H_5 28.98; 29.00%; mol. wt. 306; 303; hydrolysis value 361. C_{13}H_{16}F_4O_4. Calculated: C 50.69; H 3.92; F 24.67; OC_2H_5 29.24%; mol. wt. 308.2; hydrolysis value 364. λ_{max} (in alcohol) 372 and 326 μγ (log ε 3.634 and 2.756). Infrared spectrum (in pure state): 1020 s (C-F), 1195 s, 1230 s (C-O-C in esters), 1500 s (fluorinated aromatic ring), 1760 s (C = O in esters), 2990 m, 2945 m, 2910 w, and 2880 w (CH_2 and CH_3).

2,3,5,6-Tetrafluorohomoterephthalic Acid (V). 3 g of crude (IV) and a solution of 4.2 g of KOH in 150 ml of water was boiled for four hours. The mixture was acidified and extracted repeatedly with ether, and the extract was dried with MgSO_4. Ether was driven off, and distillation of the residue gave 1.9 g (77.2%) of unpurified (V); b. p. 220°-221° (from water). Found: C 42.87; 42.65; H 1.67; 1.57; F 30.49; 30.39%; acid value 440.2; 436.3. C_8H_4F_4O_4. Calculated: C 42.89 H 1.59; F 30.15%; acid value 444.0. λ_{max} (in alcohol) 272 μγ (log ε 3.182). Infrared spectrum (in KBr): 1020 s (C-O-C in esters), 1760 s (C = O in esters), 1500 s (fluorinated aromatic ring), 1715 s (C = O in esters), 2990 m, 2945 m, 2910 w, and 2880 w (CH_2 and CH_3).

(2,3,5,6-Tetrafluorophenyl)acetic Acid (VI). 3.6 g of (V) was dissolved in 27 ml of dry dimethylformamide, and the mixture was heated for one hour with stirring in an oil bath (130°-140°). The mixture was steam-distilled, the distillate was repeatedly extracted with ether, and the extracts were dried with MgSO_4. After the removal of ether we obtained 1.17 g (40.4%) of (VI); b. p. 140.5°-141.5° (from benzene). Found: C 45.80; 46.12; H 2.00; 1.92; F 36.34; 36.41; active hydrogen 0.44; 0.42%. C_8H_4F_4O_2. Calculated: C 46.19; H 1.94; F 36.54; active hydrogen 0.48%. λ_{max} (in alcohol) 226 and 228 μγ (log ε 2.384 and 3.14). Infrared spectrum (in KBr): 1000 s (C-F), 1520 s (fluorinated aromatic ring), 1715 s (C = O in acids).

The NMR spectra were determined by A. K. Petrov, whom the authors thank.

SUMMARY

1. Two methods were developed for the synthesis of (pentafluorobenzoyl)acetic ester: by the condensation of pentafluorobenzoyl chloride with the ethoxymagnesium derivative of malonic ester with subsequent partial hydrolysis and decarboxylation, and by the ester condensation of ethyl pentafluorobenzoate with ethyl acetate in presence of bromo(diisopropylamino)magnesium.

2. In the condensation of ethyl pentafluorobenzoate with sodioacetoacetic ester, as a result of nucleophilic substitution and subsequent hydrolysis, diethyl tetrafluorohomoterephthalate is formed. By the hydrolysis of the latter with partial decarboxylation, (2,3,5,6-tetrafluorophenyl)acetate acid was obtained.
LITERATURE CITED


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.