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Abstract

Full Text

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PREPARATION OF FLUORINATED HETEROCYCLIC COMPOUNDS FROM HEXAFLUOROBENZENE

In the reaction of hexafluorobenzene with acetoacetic ester, instead of the pentafluorophenylacetoacetic ester expected according to the patent (^{1}), we isolated as the main reaction product a substance of composition $C_{12}H_8F_4O_3$ (I). This compound does not show the reactions characteristic of acetoacetic ester derivatives. Thus, it did not react with 2,4-dinitrophenylhydrazine or hydroxylamine, and under the conditions of ketonic cleavage it was converted not into pentafluorophenylacetone but into an acid of composition $C_{10}H_4F_4O_3$ (II).

The IR spectrum of I has absorption bands in the region 2860-3000 cm^{-1} (methyl and methylene groups), 1740 cm^{-1} ($C = O$ of an ester group), 1500 cm^{-1} (fluorinated aromatic ring), and 1610, 1015, and 740 cm^{-1} (furan ring (^{2})).

Fig. 1. H^1 NMR spectrum of 2-methyl-3-carbethoxy-4,5,6,7-tetrafluorocoumarone (I). Peak **4** is benzene; peaks **1, 2, 3** are explained in the text.

The H^1 NMR spectrum (benzene internal standard) contains three peaks with an area ratio of 3 : 3 : 2 (Fig. 1). Peak 1 is a triplet with $\delta_1 5.6$ m.u.; peak 3 is a quartet with $\delta_3 2.9$ m.u. The structure of these peaks and the magnitude of their chemical shifts indicate that they belong to the $-CH_2CH_3$ group in the ester. Peak 2 ($\delta_2 4.6$ m.u.) belongs to a single methyl group. Such a value of the chemical shift of the methyl group is characteristic of furan derivatives (^{3}).

On the basis of these data we assign to compound I the structure of 2-methyl-3-carbethoxy-4,5,6,7-tetrafluorocoumarone.

The UV spectrum of (I) is somewhat simpler than the spectrum of its non-fluorinated analogue III (obtained by dehydration of 2-methyl-3-carbethoxy-4,5,6,7-tetrahydrocoumarone), but it retains the principal absorption maximum at about 250 mμ, characteristic of both compounds (for I $\lambda_{\max}$248–250 mμ ($\lg\varepsilon$3.92); for III $\lambda_{\max}$252–256 mμ ($\lg\varepsilon$3.92)). Simplification of the spectrum and a slight displacement of the absorption maximum to the short-wave region are characteristic of fluorinated aromatic compounds (^{4}).

The formation of I probably proceeds according to the scheme:

$$\text{hexafluorobenzene} + CH_3COCHCOOC_2H_5 \xrightarrow{Na} \text{[tetrafluorophenyl-substituted acetoacetic ester intermedia}$$
$$\rightleftharpoons \text{[hydroxy intermediate]} \longrightarrow \text{2-methyl-3-carbethoxy-4,5,6,7-tetrafluorocoumarone}$$

Closure of the furan ring also occurs under the action of acetoacetic ester on 2,3-dichloro-1,4-naphthoquinone (^{5}), which indirectly confirms the scheme for the formation of I proposed by us.

Ester I is readily hydrolyzed to acid II, which, on heating with copper in quinoline, is decarboxylated to form 2-methyl-4,5,6,7-tetrafluorocoumarone (IV). The structures of II and IV are confirmed by their IR and UV spectra, as well as by the NMR spectra of the H^1 and F^{19} nuclei.

Fluorine atoms in the aromatic nucleus apparently increase the stability of the furan ring in coumarones. According to preliminary data, in the coumarones obtained by us (I and II) the furan ring cannot be opened by known methods.

Elimination of ortho fluorine atoms in hexafluorobenzene under the action of various nucleophilic agents apparently constitutes a general method for obtaining fluorine-containing heterocyclic compounds. Thus, 2-pentafluorophenoxyethanol (V), with elimination of hydrogen fluoride, is readily converted into 5,6,7,8-tetrafluoro-1,4-benzodioxane (VI):

$$\mathrm{C_6F_6} \xrightarrow{\mathrm{HOCH_2CH_2OH}} \mathrm{C_6F_5OCH_2CH_2OH} \rightarrow 5,6,7,8\text{-tetrafluoro-}1,4\text{-benzodioxane}$$

V VI

After the present work had already been completed, an article by English chemists appeared (^{6}), in which the preparation of 5,6,7,8-tetrafluoro-1,4-benzodioxane by an analogous method was described.

Experimental Part

IR spectra were recorded on an IR-10 instrument in a solution of CCl_4 and in KBr pellets. UV spectra were recorded on an SFD-2 instrument; solvent–

methanol, molar concentration 10^{-4}, layer thickness 0.5 cm. NMR spectra were recorded on a JNM-3 instrument at a frequency of 40 MHz.

2-Methyl-3-carbethoxy-4,5,6,7-tetrafluorocoumarone (I). To 0.7 g of sodium hydride in 20 ml of dimethylformamide, 3.49 g of acetoacetic ester is added. After hydrogen evolution has ceased, 5 g of hexafluorobenzene is added, and the mixture is boiled for 5 h. It is diluted with water and extracted with chloroform. After removal of the solvents, 2.2 g (30%) of I is obtained, mp 69.7-70° (from methanol).

Found, %: C 51.6; 51.7; H 3.0; 2.9; F 28.2; 27.9
$C_{12}H_8F_4O_3$. Calculated, %: C 52.1; H 2.9; F 27.5

Mol. wt.: found 262, calculated 276.

2-Methyl-3-carboxy-4,5,6,7-tetrafluorocoumarone (II). To a suspension of 0.28 g of (I) in 4.3 ml of alcohol, a solution of 0.06 g of KOH in 1.4 ml of alcohol is added. After dissolution of the precipitate, the mixture is stirred for another 0.5 h. Then 1.5 ml of H_2O is added and the alcohol is distilled off. The residue is dissolved in water and acidified with HCl. The precipitate that separates is filtered off, washed with water, and dried. 0.22 g (88%) of II is obtained, mp 211° (from alcohol, in a sealed capillary).

Found, %: C 48.7; H 1.5; F 30.7; 30.9
$C_{10}H_4F_4O_3$. Calculated, %: C 48.4; H 1.6; F 30.7

$$\lambda_{\max} 246\text{–}248 \text{ m} \quad (\lg \varepsilon 3.98).$$

IR spectrum—a broad band at 3400-3600 cm^{-1} (OH).

2-Methyl-3-carbethoxycoumarone (III). 1 g of 2-methyl-3-carbethoxy-4,5,6,7-tetrahydrocoumarone and 0.4 g of 10% palladium on charcoal are heated for 4 h at 250-255°. Ether is added, the mixture is filtered, and the ether is distilled off. This gives 0.61 g (62%) of III, m.p. 31.5-32°.

Found, %:	C 71.3; H 6.1
$C_{12}H_{12}O_3$. Calculated, %:	C 71.3; H 5.9

On boiling III with 10% alcoholic KOH for 3 h, 2-methyl-3-carboxycoumarone is obtained in quantitative yield, m.p. 190°; according to data in [7], m.p. 191°. $\lambda_{\max}$ 248-252 mμ ($\lg \varepsilon$ 3.99).

2-Methyl-4,5,6,7-tetrafluorocoumarone (IV). 0.96 g of III, 0.45 g of copper powder, and 9 ml of quinoline are boiled for 1 h, then steam-distilled. The distillate is acidified with hydrochloric acid. The precipitate that separates is filtered off, washed with water, and dried. This gives 0.6 g (76%) of IV, m.p. 60.5-61° (from aqueous methanol).

Found, %: C 53.1; 53.2; H 2.1; 2.0; F 36.9
$C_9H_4F_4O$. Calculated, %: C 52.9; H 2.0; F 37.2

λ_{max} 236-238 mμ ($\lg\varepsilon$ 4.06). IR spectrum: 1625 cm^{-1}, 1015 cm^{-1}, 740 cm^{-1} (furan ring). In the ^{19}F NMR spectrum there are four bands of equal intensity (two doublets, two triplets); in the proton spectrum there are two bands with an intensity ratio of 1 : 3.

2-Pentafluorophenoxyethanol (V). A mixture of 6 g of KOH, 65 ml of ethylene glycol, and 20 g of C_6F_6 is heated for 3 h at 150°. It is poured into water and extracted with ether. Distillation gives 13.4 g (56%) of V, b.p. 80-81°/6 mm, n_D^{20} 1.4433.

Found, %: F 41.8; 42.0
$C_8H_5F_5O_2$. Calculated, %: F 41.7

5,6,7,8-Tetrafluoro-1,4-benzodioxane (VI). A mixture of 1.6 g of KOH, 40 ml of dimethylformamide, and 6.2 g of V is heated for 5 h at 135°. It is poured into water, acidified, and 2.73 g (48%) of VI is filtered off, m.p. 78-79° (after sublimation). According to data in [6], m.p. 78-79°.

Found, %: F 37.0; 37.3
$C_8H_4F_4O_2$. Calculated, %: F 36.6

Mol. wt.: found 210, calculated 208.

In the ^{19}F NMR spectrum there are two bands of equal intensity; in the proton spectrum, one band.

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Note: Figure translations are in progress. See original paper for figures.