POLYFLUORINATED HETEROCYCLIC COMPOUNDS

IV. The Interaction Between Sodium Acetoacetate Ester and Polyfluoroaromatic Compounds $\!$

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Khimiya Geterotsiklicheskikh Soedinenii, Vol. 5, No. 5, pp. 778-780, 1969

UDC 547.728.1'539.1

The condensation of sodium acetoacetate ester with polyfluoroaromatic compounds proceeds according to a type of S-arylation with subsequent ring formation or deacetylation depending on the condition employed.

It has previously been shown [1] that, during the interaction between hexafluorobenzene and sodium acetoacetate ester (Na-AAE) in dimethylformamide(DMF), 2-methyl-3-ethoxycarbonyl-4,5,6,7-tetrafluorocoumarone (I) is obtained as the main product. We have suggested that this reaction proceeds according to the scheme of S-arylation through the formation of the pentafluorophenylacetoacetate ester. In the enolic form the latter enters into the reaction of intramolecular nucleophilic substitution with the formation of the coumarone of compound I. Somewhat later during the study of the same reaction Young proposed that it proceeds according to the scheme of O-arylation through the formation of the ethyl ester of β -pentafluorophenoxycrotonic acid, with subsequent ring formation to produce the coumarone of compound I [2].

In order to reveal the mechanism of this reaction we synthesized the previously known ethyl ester of β pentafluorophenoxycrotonic acid by condensing sodium pentafluorophenolate with cis- β -chlorocrotonic ester in DMF. However, this ester does not undergo change in the conditions under which the coumarone of compound I is formed. It was impossible to produce ring formation of this ester in the presence of a number of other alkaline agents (NaH, K₂CO₃, KF, etc.) in DMF or in dioxane under different conditions. In all cases the original product either does not undergo change or is cleaved with the formation of pentafluorophenol. It has been shown in separate experiments that the coumarone of compound I does not change in similar conditions.

In order to determine the nature of the intermediate compound in the reaction between hexafluorobenzene and Na-AAE.



we synthesized 2-methyl-3-ethoxycarbonyl-4,5,7-trifluorocoumarone by condensation of pentafluorobenzene with Na-AAE in DMF. It is well known that the reaction between pentafluorobenzene and nucleophilic agents leads to the replacement of the fluorine atom in the para position by an atom of hydrogen [3]. Thus, during the reaction between Na-AAe and pentafluorobenzene, two intermediate products **IIa** and **IIb** may be formed, the cyclization of which must lead to the formation of two isomeric coumarones, **IIIa** and **IIb**.



We have shown that during this reaction only 2methyl-3-ethoxycarbonyl-4,5,7-trifluorocoumarone (IIIa) is formed. The structure of this compound was confirmed by oxidation to 2,3,5-trifluorosalicylic acid (IV) which by decarboxylation was converted into the known [4] 2,4,5-trifluorophenol (V).

The opening of the coumarone ring was conducted by a previously described method [5]. The coumarone of compound I described by us previously [1] gives rise to 2,3,4,5-tetrafluorosalicylic acid which is identical to the compound obtained by the method described by Prudchenko et. al [5]. The structure of the coumarone of compound IIIa and the acid of compound IV is also confirmed by the NMR spectra of F^{19} and IR spectra.

The condensation of Na-AAe with polyfluoroaromatic compounds through S- and not O-arylation is confirmed by a previous study of one of the authors [6] in which it was shown that, during the interaction between the ethyl ester of pentafluorobenzoic acid and Na-AAE in the absence of a solvent, the diethyl ester of tetrafluorohomoterephthalic acid was formed as the main product. In the latter case apparently alcoholysis of the intermediately formed S-arylated acetoacetic ester occurs in the presence of traces of sodium ethoxide.

In order to reveal the factors which are responsible for the cause of the subsequent transformation of the S-arylated acetoacetic ester, a study was made of the interaction between hexafluorobenzene and Na-AAE under different conditions.† It was found that the reaction between hexafluorobenzene and Na-AAE in the

*For part III, see [5].

[†]In all cases the reaction mixtures were analyzed by gas liquid chromatography.

presence of the sodium ethoxide as described previously [6] leads to the formation of the ethyl ester of pentafluorophenylacetic acid. During the interaction between hexafluorobenzene and Na-AAE in DMF with the addition of catalytic amounts of sodium ethoxide a mixture of the coumarone of compound I and the ethyl ester of pentafluorophenylacetic acid was formed. The latter is not formed when the reaction is conducted in DMF in the absence of sodium ethoxide.

Thus, the initially formed S-arylated derivative may be subjected to intramolecular cyclization and deacetylation depending on the medium and the presence of the alcoholate.

EXPERIMENTAL

IR spectra were determined in a CCl₄ solution in the UR-10 apparatus. UV spectra were recorded with an SFD-2 apparatus. The solvent was ethyl alcohol, at a molar concentration of 10^{-4} , and the thickness of the layer was 0.5 cm. NMR spectra were recorded in a JNM-4H-100 apparatus.

2-Methyl-3-ethoxycarbonyl-4,5,7-trifluorocoumarone (IIIa). A 7 g (0.05 mole) quantity of acetoacetic ester was added with vigorous stirring to 1.4 g (0.05 mole) sodium hydride in 45 ml of DMR. When hydrogen evolution had ceased 10 g (0.05 mole) pentafluorobenzene was added, the mixture was maintained for 5 hours at 140° C, diluted with water; and filtered. A 3.26 g (21%) quantity of compound IIIa was obtained with a mp of 111-112°C (from methanol). Found, %: C 56.12, 56.15; H 3.55, 3.35; F 22.37, 22.37. Calculated for $C_{12}H_9F_3O_3$,%: C 55.81; H 3.48; F 22.08%. IR spectrum: 1530 (fluorinated aromatic ring), 1720 (C==O complex ester group), 2860-2980 (CH₃ and CH₂), 3080 cm⁻¹ (C-H aromatic). UV spectrum: λ_{max} 250 nm (log ε 3.91). NMR spectrum of F¹⁹: three signals of equal intensity δ 18.3, 20.0, 20.7 ppm in a weak field from C₄F₆.

2,3,5-Trifluorosalicylic acid (IV). A solution of 0.85 g (0.003 mole) of compound IIIa and 1.03 g (0.006 mole) KMnO₄ in 45 ml of acetone was stirred for 16 hr at 20° C. The acetone was removed by distillation. The residue was boiled in water and filtered and washed several times with boiling water. The filtrate was evaporated, acidified, and extracted with ether. A 0.33 g (52%) quantity of compound IV was obtained with a mp of 173° C (from water in a sealed capillary). Found, %: C 44.32, 44.10; H 1.40, 1.59; F 29.83, 29.81. Calculated for $C_7H_3F_3O_3$, %: C 43.75; H 1.56; F 29.68. IR spectrum: 1510 (fluorinated aromatic ring), 1690 (C=O bond), 1710 (C=O free), 3100 (OH bond), 3510 cm⁻¹ (OH free). NMR spectra of F¹⁹: two signals with a ratio of areas of 2:1, with chemical displacements in a strong field from fluoroben-

zene 25 and 34.6 ppm. The values of the chemical displacements convincingly coincide with values calculated according to an additive scheme [7].

2,4,5-Trifluorophenol (V). A 0.05 g (0.0003 mole) quantity of the acid of compound IV was heated for 9 hr in an ampul at $270-300^{\circ}$ C. A 0.03 g (79%) quantity of the phenol of compound V was obtained with a mp of 39.5-40° C. According to the data in the literature [4] the mp is 42° C. IR spectrum: 1540 (fluorinated aromatic ring), 3085 (C-H aromatic), 3600 cm⁻¹ (OH).

Ethyl ester of β -pentafluorophenoxycrotonic acid (VI). A 1.8 g (0.012 mole) quantity of the cis- β -chlorocrotonic ester and 2.5 g (0.012 mole) of sodium pentafluorophenolate were heated at 140° C in DMF for 90 min, the mixture was poured into water, extracted with ether, and dried with MgSO₄. A 1.9 g (52%) quantity of compound VI was obtained with a mp of 40.5° C (from methanol). Found, %: C 49.27, 49.03; H 3.36, 3.16; F 31.81, 32.14. Calculated for C₁₂H₉F₅O₃, %: C 48.64; H 3.04; F 32.09. IR spectrum: 1040 (C-F); 1530 (fluorinated aromatic ring), 1660 (C=C), 1740⁻¹ (C=O complex ester group). UV spectrum: λ_{max} 238 nm (log ε 4.16), similar to the UV spectrum of the ethyl ester of β -phenoxycrotonic acid: λ_{max} 238 nm (log ε 4.09).

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16 April 1967

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