MECHANISM OF THE CLEAVAGE OF MIXED ANHYDRIDES OF α -HYDROHEXAFLUOROISOBUTYRIC ACID BY TRIETHYLAMINE

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Mixed anhydrides of α -hydrohexafluoroisobutyric acid are readily cleaved by Et₃N [1]. Low-temperature ¹⁹F NMR was used in the present investigation to study the mechanism of this reaction, as exemplified by the cleavage of the mixed anhydride of α -hydrohexafluoroisobutyric acid and benzoic acid (I) to PhCOF and the triethylammonium salt of trifluoromethylmalonyl difluoride.

$$(CF_3)_2CHCOOCOPh + Et_3N \rightarrow CF_3C(COF)_2 HNEt_3 + PhCOF$$

As previously suggested [1], the first step in this reaction is the removal of a proton from the anhydride (I) to form a triethylammonium salt containing the anion (II) (Fig. 1). This salt is stable up to -40 °C, but it decomposes at a moderate rate at -20° C. A typical feature of this decomposition is the intermediate formation of substantial amounts of the anion of α -hydrohexafluoroisobutyryl fluoride (III) (Fig. 2, cf [2]). At higher temperatures, the ion (III) also decomposes, and in the final analysis the spectrum contains only signals for PhCOF and the anion of trifluoromethylmalonyl difluoride (IV) (Fig. 3).

The intermediate formation of the anion (III) suggests the parallel formation of the anion of the mixed anhydride of benzoic and α -hydro- β -benzoyloxypentafluoroisobutyric acids (V). In contrast to the routes put forward in [1], decomposition of the anion of the mixed anhydride (II) occurs both by an intermolecular process comprising several reversible steps involving the elimination and addition of the fluoride and benzoate anions,* and by the irreversible cleavage of the mesomeric carbanions (V) and (VI), which contain the fragment 0

 $-C-O-CF_2-\overline{C}$ (cf. [4]). Suggested routes for the cleavage of the anion (II) into PhCOF and anion (IV) are shown in Scheme 1.

Cleavage of PhCOF from the anion (V) must afford the anion (VII). We have been unable to identify unambiguously this anion from the ¹⁹F NMR spectrum, since the signal for its CF_3 group is superimposed on other signals at -27 ppm. However, the poorly resolved signal at -96.5 ppm[†] is tentatively assigned to the COF group of the anion (VII) (cf. (Fig. 2).

Attempts to detect the presence of anions (V) and (VI) in the reaction mixture were unsuccessful. They could not be detected either in the ¹⁹F NMR spectra, nor as the corresponding CH-acids when the reaction was stopped by treatment with dry HCl. These anions are probably of low stability and, since they decompose as soon as they are formed, they do not accumulate in amounts large enough to be detected. The instability of the anion (VI) has been confirmed by independent synthesis from the acid fluoride (VIII). It has been found that the anion (VI), unlike the anion (II), decomposes very rapidly at -30° C, and slowly even at -78° C. Anions (V) and (VI) are probably of similar stability.

It is noteworthy that in the decomposition of the anion (VI), significant amounts of the intermediate anion (III) are formed, an observation which also supports Scheme 1.

^{*} This cleavage results in the formation of the corresponding ketenes and perfluoromethacrylic acid derivatives (cf. [3]), but in the presence of nucleophiles their concentrations must be vanishingly small, so that they are not recorded by NMR.

[†]For the signals of the COF group of anion (IV), see below.

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An interesting feature of the low-temperature ¹⁹F NMR spectra of the mixtures studied here, formed in the decomposition of anions (II) and (VI), is that even when the reaction is complete the spectra show signals both for CF₃ and COF (cf. Fig. 3). When the temperature is raised, the signals for both of these are broadened (except for that of PhCOF), at -30° C they merge, and above 10° C only a well-resolved triplet for CF₃ and a quartet for COF are seen, the corresponding spin – spin coupling constant decreasing from 25.2 to 20.8 Hz on heating from -70 to $+90^{\circ}$ C. On cooling to -70° C the original spectrum is restored.

The changes in the spectra on cooling are due to restriction of rotation around the partial double bonds $\sum_{C \neq \overline{C} \rightarrow C}$ in the anion (IV)



TABLE 1. ¹⁹F NMR Spectra of Mesomeric Fluorocarbanions

	т., °С	ð, ppm			J, Hz	
Carbanion		1	2	3	12	2-3
¹ CF ₃ ² CF ₃ (II)	-50	26,6 q.	27,6 q.	-	10,3 -	
$^{1}CF_{3}$ C $^{2}CF_{3}$ $^{2}CF_{3}$ $^{(11)}$ $^{(21)}$	-50	-27,2 d. q.	−28,3 d.q.	—77,6q.q.	9,911	,8 17,9
(III) (IVa) (IVb) (IVC)	80 80 80	—27,3 t. —26 6 d.d. —23,7 t.	94,0 q. 97,1 d.q. 95,5 q.	94,9 d.q. 	25,2 17,910 11,4	 ,3 10,9
$\frac{PhCOOCF_2}{^{2}CF_3} \xrightarrow{C^{2} \rightarrow C} F^3$ (VI)	—70	—29,6 br.d.q.	—28,4 br.d.t.	—74,7 br.t.q.	~12~	12 ~12



Fig. 1. $^{19}\mathrm{F}$ NMR spectrum of an equimolar mixture of the anhydride (L) and $\mathrm{Et}_3\mathrm{N}$ at $-50^\circ\mathrm{C}.$



Fig. 2. ¹⁹F NMR spectrum of an equimolar mixture of (I) and Et_3N after 5.5 h (-20°C), recorded at -50°C.



Fig. 3. ¹⁹F NMR spectrum of an equimolar mixture of (I) and Et₃N after 2 h (90°C), recorded at -70° C.



Fig. 4. ¹⁹F NMR spectrum of the triethylammonium salt of trifluoromethylmalonyl difluoride at -80°C in a mixture of ether and diglyme (1:1).

The anion (IV), obtained independently from the corresponding CH-acid, behaves in an identical way (Fig.

4).

$$CF_{3}CH(COF)_{2} \xrightarrow{+NEt_{3}} (IV)$$

EXPERIMENTAL

 19 F NMR spectra were obtained on a Perkin-Elmer R-32 spectrometer (84.6 MHz). Chemical shifts are given in parts per million from CF₃COOH (the internal standard used was CF₃COOEt, for which a chemical shift of -2.5 was assumed). All operations were carried out in an atmosphere of dry argon or in sealed ampuls. The solvents were dried by standard methods.

The parameters of the ¹⁹F NMR spectra for the mesomeric carbanions are given in Table 1.

Cleavage of the Mixed Anhydrides of α -Hydrohexafluoroisobutyric and Benzoic Acids (1) by Triethylamine. To 1.31 g (4.36 mmole) of freshly distilled (1) and 0.055 g (0.39 mmole) of CF₃COOEt in 1.5 ml of diglyme was added dropwise with stirring (~78°C) 0.46 g (4.55 mmole) of Et₃N in 1 ml of diglyme, and the mixture was stirred for 1 h. The ¹⁹F NMR spectrum at -50°C showed the anion (II) (cf. Fig. 1). After 5.5 h at -20°C, the anion (II) was not recorded in the spectrum, but PhCOF, anions (III), (IV), and, presumably (VII) were present in a ratio of ~3:3:2:2 (cf. Fig. 2). After 2 h (90°C), the mixture contained only PhCOF and anion (IV) (cf. Fig. 3).

Cleavage of α -Hydro- β -benzoyloxypentafluoroisobutyryl Fluoride (VIII) by Triethylamine. A mixture of 1.66 g (13.6 mmole) of PhCOOH, 2.49 g (14.0 mmole) of perfluoromethacrylyl fluoride, and 5 ml of diglyme was kept at 20°C for 15 h, to give a solution of the adduct (VIII). ¹H NMR spectrum: 4.9 t.q. (CH), 6.9-7.8 m (C₆H₅), JCH-CF₂=J_{CH-CF₃}=7.9 Hz. ¹⁹F NMR spectrum: -127.3 t.q. (COF), -13.7 d.d.t. (CF₃), -8.7 d.d.d.q (CF₂), JCF₃-CF₂=J_{CF₃-COF}=J_{CF₂-COF=9.8 Hz, J_{CF₃-CH=J_{CF₂-CH=7.8 Hz, J_{CF₂-o-H=2.4 Hz. Volatile products were pumped off in a vacuum (7 mm), and 0.16 g (1.3 mmole) of CF₃COOEt added. The mixture was cooled to -90 to -80°C, 1.50 g (14.8 mmole) of Et₃N in 4 ml of ether added dropwise with stirring, and stirring continued for 20 min. The ¹⁹F NMR spectrum at -70°C showed the anion (VI) and small amounts of its decomposition products. After 6 days at -78°C, the anion (VI) had decomposed to the extent of 70% (as assessed by the reduction in the intensity of the COF group signal at -74.7 ppm). The main products were PhCOF and the anions (III), (IV), and probably (VII), in a ratio of ~4:3:1:2. At -30°C, the anion (IV), together with trace amounts of impurities (-104.8 s; -102.4 s; -14.5 m; -13.4 m; +31.7 br. s).}}}}

Temperature Dependence of the ¹⁹F NMR Spectra of the Triethylammonium Salt of Trifluoromethylmalonyl Difluoride. To 0.9732 g (5.53 mmole) of $CF_3CH(COF)_2$ in 1 ml of diglyme at -30 to -20°C was added dropwise with stirring 0.56 g (5.5 mmole) of Et_3N in 1.5 ml of diglyme. The mixture was warmed to 20°C, the volatile products removed in vacuo (7 mm), and 0.1322 g (0.930 mmole) of CF_3COOEt in 0.5 ml of diglyme added. For the recording of the NMR spectra, the solution was diluted with an equal volume of ether. The ¹⁹F NMR spectrum at -80°C showed the isomeric anions (IVa-c) in a ratio of ~8:3:1 (cf. Fig. 4).

CONCLUSIONS

1. Reaction of triethylamine with the mixed anhydride of α -hydrohexafluoroisobutyric and benzoic acids results in cleavage of an α -proton to form a salt containing a mesomeric carbanion which is stable at temperatures below -40°C.

2. Cleavage of the triethylammonium salt of the mixed anhydride of α -hydrohexafluoroisobutyric and benzoic acids to benzoyl fluoride and a salt of trifluoromethylmalonyl difluoride involves several reversible elimination-addition steps of fluoride and triethylammonium benzoate, together with irreversible cleavage of the acid fluoride and mixed anhydride of α -hydro- β -benzoyloxypentafluoroisobutyric acid.

3. According to the ¹⁹F NMR spectrum, the triethylammonium salt of trifluoromethylmalonyl difluoride at temperatures below -50° C contains three isomers as a result of restricted rotation around the partial double bonds C⁻⁻C⁻⁻C in the mesomeric carbanion.

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REGIOSELECTIVITY IN THE REACTION

OF POLYFLUORINATED β -DIKETONES

WITH HYDROXYL-CONTAINING NUCLEOPHILES

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 β -Diketones containing a single fluoroalkyl substituent react with NH- and SH-nucleophiles at the carbonyl group bonded to the nonfluorinated substituent to form β -aminovinyl ketones and monothio- β -diketones respectively [1], although hydrolysis of the β -diketones in neutral and basic media occurs at the carbon bonded to the fluorinated substituent. We have previously put forward a mechanism to explain the regioselectivity of the reaction of β -diketones with nucleophiles in terms of the different stabilities of the adducts formed [2]. This mechanism is confirmed by the fact that reaction of unsymmetrical polyfluorinated β -diketones with MeOH gives predominantly the adduct at the carbon bonded to the fluorinated substituent [3].

This investigation concerns a ¹H, ¹⁹F, and ¹³C NMR study of the reaction of unsymmetrical polyfluorinated β -diketones with water in deuteroacetone, in order to elucidate the dependence of the course of the reaction on the structures of the fluorinated and nonfluorinated substituents



The PMR spectra of β -diketones containing fluoroalkyl and methyl substituents show signals characteristic of methyne and methyl protons (Table 1 (I) - (VII)). On adding water to a solution of the β -diketone in deuteroacetone, a signal appears for the methylene protons, at 2.86-3.06 ppm (cf. Table 1, (Ia)-(VIIa)). In addition, the PMR spectra of (I), (II), (IV), and (VIII) show resolved signals for the methyl groups of the original β -diketone and its hydrate. The ¹⁹F NMR spectra also show signals which may be assigned to the original β -diketone (I)-(VII) and their hydrates (Ia)-(VIIa). The amounts of the β -keto-gem-diols (Ia)-(VIIa), measured 24 h after the addition of water to a solution of the β -diketone in deuteroacetone, varies from 2 to 63% depending on the structure of the fluoroalkyl substituent (cf. Table 1).

The PMR spectra of solutions of β -diketones containing fluoroalkyl and phenyl substituents [Table 2, (IX)-(XV)] with water in deuteroacetone also show signals for methylene and methyne protons, although the amount of the hydrated form in this instance is less than in the case of β -diketones containing a methyl substituent [cf. Table

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