ORGANIC CHEMISTRY

HEXAFLUOROACETONE ALKOXYCARBONYLIMINES

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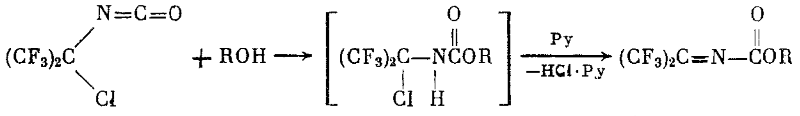
A convenient preparative method was developed for the preparation of hexafluoroacetone alkoxycarbonylimines by the reaction of α-chlorohexafluoroisopropyl isocyanate with alcohols in the presence of pyridine. The reaction of hexafluoroacetone benzyloxycarbonylimine with benzyl alcohol and 4-fluoro-3-chloroaniline affords the corresponding urethanes, products of addition at the azomethine bond.

The chemistry of N-substituted imines of polyfluoro ketones, which has been intensively developed during the last decade, is attracting the attention of investigators by the possibility of using these compounds for the synthesis of diverse organofluorine compounds, including physiologically active substances [1]. At the same time, the question of the synthesis and properties of these highly reactive representatives of N-substituted imines of polyfluoro ketones, i.e., hexafluoroacetone (HFA) alkoxycarbonylimines, remains unanswered because information on them is limited [1]. In the present paper, we consider a convenient preparative method, developed by us, for the synthesis of HFA alkoxycarbonylimines (III), based on the reaction of α-chlorohexafluoroisopropyl isocyanate (I) with alcohols in the presence of bases, and also some chemical conversions of (III).

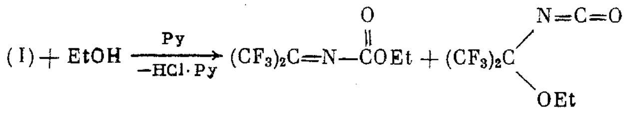
It has been shown that with successive addition of equimolar amounts of alcohols and Py to an ether solution of (I) at 20°C the corresponding HFA alkoxycarbonylimines (IIIa-d) are formed in 54-70% yield.



(I) (II) (IIIa-d)

R = Pr (IIIa), Bu (IIIb), *i*-Am (IIIc), CH_2Ph (IIId).

Apparently, the primary reaction products are urethanes (II), which are smoothly dehydrochlorinated by pyridine, being converted to imines (III). It should be noted that a distinctive feature of isocyanate (I), just as of other α-chloroalkyl isocyanates [2], is the presence of two centers in the molecule which are reactive with respect to nucleophilic reagents, namely, the isocyanate group and the chlorine atom. From this standpoint, an alternative direction of the studied conversions would be replacement of the chlorine atom by an alkoxy group with the formation of α-alkoxyhexafluoroisopropyl isocyanates, which we observed in the reaction of (I) with EtOH and Py



(IIIe) (IV)

The formation of a mixture of isomeric imine (IIIe) and α-ethoxyhexafluoroisopropyl isocyanate (IV) in a 3:2 ratio was determined by IR, PMR, and ^{19}F NMR spectroscopy. In all the other considered cases, products containing an isocyanate group were not observed.

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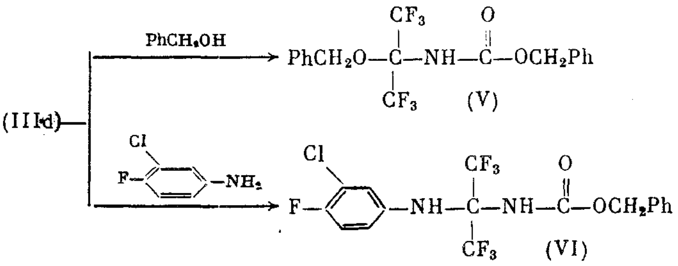
TABLE 1. Yield, Properties, and Data of Elemental Analysis Products

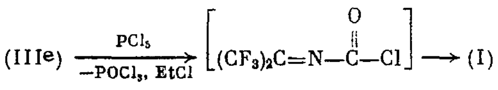
Compound	Yield, %	mp, °C; bp, °C (p, mm Hg)	n_D^{20}	Found, %			Empirical formula	Calculated, %		
				C	H	N		C	H	N
(IIIa)	55	67 (110)	1.3387	33,34	2.98	5,39	$C_7H_7F_6NO_2$	33.48	2.81	5.58
(IIIb)	62	46–48 (10)	1.3462	36,35	3.34	5,17	$C_8H_9F_6NO_2$	36.24	3.42	5.28
(IIIc)	57	53–56 (10)	1.3541	38,56	4.13	4,83	$C_9H_{11}F_6NO_2$	38,72	3.97	5.02
(IIId)	67	93–95 (10)	1,4200	44,17	2.14	4,52	$C_{11}H_7F_6NO_2$	44.18	2.36	4,68
(IIIe)	74	106,5 (760)	1,3296	30.47	2,26	5.75	$C_6H_5F_6NO_2$	30.38	2.11	5,91
(V)	64	74–75	–	52.95	3,99	3.74	$C_{18}H_{15}F_6NO_3$	53,07	3.69	3.44
(VI)	95	104–106	–	45,52	2,80	6,54	$C_{17}H_{12}ClF_7N_2O_2$	45.91	2,72	6,30
(VIII)	100	34–35	–	–	–	–	$C_6H_7F_6NO_3$	–	–	–

The HFA alkoxycarbonylimides (III) were colorless mobile liquids, the composition and structure of which were confirmed by data of elemental analysis, IR and ^1H and ^{19}F NMR spectra, and some chemical conversions typical both of N-substituted HFA imines and of urethanes.

Imine (IIId) reacts exothermically with benzyl alcohol and 4-fluoro-3-chloroaniline, forming products of addition at the C=N bond, i.e., urethanes (V) and (VI).

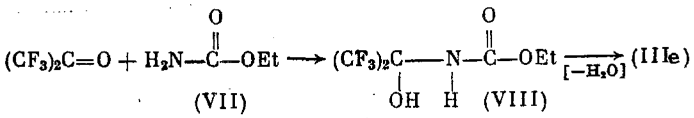


Boiling of imine (IIIe) with an equimolar amount of PCl_5 affords isocyanate (I),* i.e., in this case a direction of the reaction of the urethanes with the chlorinating agents is observed [4].



$$(IIIe) \xrightarrow[-POCl_3,\ EtCl]{PCl_5} \left[(CF_3)_2C{=}N{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}Cl\right] \longrightarrow (I)$$

Hexafluoroacetone ethoxycarbonylimine (IIIe), which is a convenient starting reagent for the preparation of (I), was also obtained by back synthesis, by dehydration of the adduct of HFA and urethane (VII) by trifluoroacetic anhydride in a quinoline medium in 74% yield.



$$(CF_3)_2C{=}O + \underset{(VII)}{H_2N{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OEt} \longrightarrow \underset{(VIII)}{(CF_3)_2\underset{OH}{\underset{|}{C}}{-}\underset{H}{\underset{|}{N}}{-}\overset{\overset{\displaystyle O}{\|}}{C}{-}OEt} \xrightarrow[{[-H_2O]}]{} (IIIe)$$

Heating of the reaction mixture to 120-130°C is required for completion of dehydration of adduct (VIII).

EXPERIMENTAL

The PMR and ^{19}F NMR spectra were recorded with a Bruker CXP-200 spectrometer in solutions in acetone-d_6 for all compounds. The IR spectra were obtained with a Specord IR-75 instrument (film or suspension in white mineral oil and KBr plates). The melting points were determined in a sealed capillary.

Hexafluoroacetone Propyloxycarbonylimine (IIIa). A solution of 1.2 g (0.02 mole) of PrOH in 10 ml of ether was added slowly dropwise to a solution of 4.8 g (0.021 mole) of iso-

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*For previous communication, see [3].

TABLE 2. ^1H and ^{19}F NMR and IR Spectra of Products

Compound	PMR δ, ppm	^{19}F NMR, δ, ppm (intensity)	IR spectrum ν, cm^{-1}
(IIIa)	0.99 t($3H, CH_3$), 1.76 m ($2H, CH_3\underline{CH_2}$), 4.31 t($2H, CH_2O$)	6.6 br. s, 9.3 br. s (1 : 1)	1764 (C=N) 1720 (C=O)
(IIIb)	0.97 t($3H, CH_3$), 1.42 m($2H, CH_3\underline{CH_2}$), 1.72 m ($2H, EtCH_2$), 4,36 t ($2H, CH_2O$)	7.2 br. s, 9.5 br.s (1 : 1)	1757 (C=N) 1730 (C=O)
(IIIc)	0.92 d [$6H, (CH_3)_2C$], 1.63 q ($2H, \underline{CH_2}CH$), 1,77 m (1H, CH), 4.39 t ($2H, CH_2O$)	6.4 br. s, 9.3 br. s (1 : 1)	1780 (C=N) 1730 (C=O)
(IIId)	5,31 s ($2H, CH_2$), 7,39 s (5H, Ph)	6.7 br. s, 9.8 br. s (1 : 1)	1790–1700 (C=N, C=O)
(IIIe)	1,38 t ($3H, CH_3$), 4,36 q ($2H, CH_2$)	7.0 br. s, 10.0 br. s (1 : 1)	1760 (C=N) 1730 (C=O)
(IV)	1,25 t ($3H, CH_3$), 4,22 q ($2H, CH_2$)	2.76 s	2290 (N=C=O)
(V)	4.77 s ($2H, CH_2O$), 5.21 s [$2H, CH_2OC(O)$], 7,30–7.60 m (10H, Ph), 8.25 s (1H, NH)	3.62 s	1740 (C=O)
(VI)	3.56 s (1H, NH), 5,03 s ($2H, CH_2$), 7.21 m (8H, CH-arom), 9.23 s [1H, NHC(O)]	−50.9 s, 4.8 s (1 : 6)	1727 (C=O)
(VIII)	1.27 t ($3H, CH_3$), 4.20 q($2H, CH_2$), 7,40 s (1H), 8,35 s (1H)	−3.44 s	–

cyanate (I) in 25 ml of ether at 20°C. After 1 h, a solution of 1.6 g (0.02 mole) of Py in 10 ml of ether was added dropwise at 20°C. The resulting precipitate was filtered, and the filtrate was fractionated. We obtained 1.9 g of (IIIa).

Hexafluoroacetone Alkoxycarbonylimines (IIIb-d). These compounds were obtained similarly to imine (IIIa) from 0.021 mole of isocyanate (I) and 0.02 mole of the corresponding alcohol in the presence of 0.02 mole of Py.

Hexafluoroacetone Ethoxycarbonylimine (IIIe). We kept 8.9 g (0.1 mole) of urethane (VII) and 18.2 g (0.11 mole) of HFA in a sealed ampul at room temperature for 3 days. The ampul was opened, and adduct (VIII) was dissolved in 30.3 g (0.235 mole) of quinoline. At 20°C, 21.0 g (0.1 mole) of trifluoroacetic anhydride was added dropwise to the obtained solution with stirring. A 45°C (60 mm) fraction was recovered by vacuum distillation from the reaction mixture, and 17.5 g (74%) of imine (IIIe) was obtained by distillation from this fraction.

Reaction of Isocyanate (I) with EtOH. A solution of 1.3 g (0.028 mole) of EtOH in 8 ml of ether was added dropwise to a solution of 6.9 g (0.03 mole) of isocyanate (I) in 15 ml of ether at 20°C, and after 1.5 h a solution of 2.24 g (0.028 mole) of Py was added dropwise at 20°C. The resulting precipitate was filtered, the ether was evaporated, and the residue was distilled. We obtained 3.94 g of an azeotropic mixture of substances (IIIe) and (IV) in a 3:2 ratio, bp 90°C, n_D^{20} 1.3296.

Benzyl N-[2-(Benzyloxy)hexafluoro-2-propyl]carbamate (V). To a solution of 0.7 g (2.3 mmoles) of imine (IIId) in 7 ml of hexane was added 0.25 g (2.3 mmoles) of benzyl alcohol at 20°C. The reaction mixture was left for 48 h. The resulting crystals were filtered and dried. We obtained 0.61 g of compound (V).

Benzyl N-[2-(4-Fluoro-3-chloroanilino)hexafluoro-2-propyl]carbamate (VI). A solution of 1.85 g (0.006 mole) of imine (IIId) in 5 ml of ether was added to a solution of 0.9 g (0.006 mole) of 4-fluoro-3-chloroaniline in 5 ml of ether at 20-30°C. After 10 h, the ether was evaporated, and the residue was recrystallized from hexane. We obtained 2.6 g of compound (VI).

The yield, properties, results of elemental analysis, and IR and ^1H and ^{19}F NMR spectra of the obtained compounds are given in Tables 1 and 2.

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FLUOROALKYL-CONTAINING β,β'-TRICARBONYL COMPOUNDS: TAUTOMERISM AND REACTION WITH N-NUCLEOPHILES

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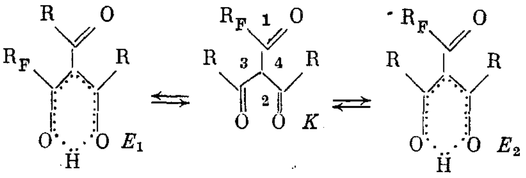
The tautomeric composition of α-polyfluoroacyl derivatives of acetylacetone and malonic ester has been established and it has been shown that with N-nucleophiles (ammonia, 1,2-ethylenediamine, o-phenylenediamine) these compounds undergo 'acid' decomposition with the elimination of the polyfluoroacyl group. With hydrazines, malonic ester derivatives react similarly but acetylacetone derivatives undergo cyclization into pyrazoles. The regiodirectivity of the interaction of fluoroalkyl-containing β,β'-tricarbonyl compounds with N-nucleophiles does not depend on their tautomeric composition and is determined by orbital control.

We have previously studied the structure and regiodirectivity of the interaction between α-polyfluoroacyl derivatives of acetic acid esters (I) and N-nucleophiles [1-3].

In the present work we have studied tautomers and reactions of α-polyfluoroacyl derivatives of acetylacetone (II) and malonic ester (III) (the synthesis of which was described in a previous communication [4]) with N-nucleophiles, and we have also carried out a qualitative examination of the regiodirectivity of the interaction between the fluoroalkyl-containing β,β'-tricarbonyl compounds (β,β-FTC) (I)-(III) mentioned above in a framework of perturbation of molecular orbitals.

Compounds (II), (IIIa, b) were obtained by acylation of acetylacetone and malonic ester by means of the acid fluorides of perfluorocarboxylic acids (PFA) – perfluoropropionic and perfluorovaleric – or α-hydroxyperfluoropropylene [4], and (IIIc) by acylation of malonic ester by the acid chloride of 3-hydroperfluoropropionic acid according to the method given in [1].

In the PMR spectra of compounds (IIa, b) there were singlets from the magnetically equivalent protons of the acetyl groups (2.18-2.20 ppm, 6H) and downfield, the enol proton (17.41-17.42 ppm, 1H), which is evidence of their existence exclusively in the form of the E_2 tautomer (Table 1)



(IIa, b) (IIIa—c)

R = Me(II); R = OEt(III); $R_F = C_2F_5$(a); C_4F_9(b); $H(CF_2)_2$(c).

At the same time, in the PMR spectra of compounds (IIIa-c), in addition to the double set of signals from the methyl and methylene protons of the ester group (1.20-1.45 ppm, m, 6H; 4.0-4.5 ppm, m, 4H), signals are detected from the α-protons of the triketo form (4.88-

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