2-ACETOXY-2-ACETYLAMINOHEXAFLUOROPROPANE AND ITS REACTIONS

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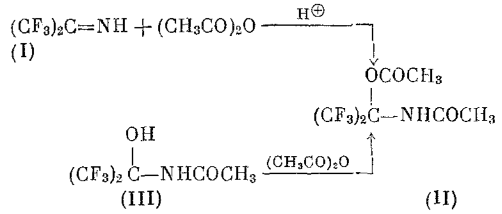
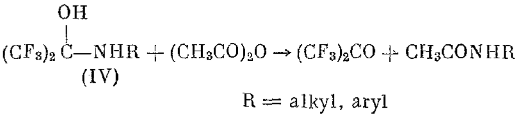
In general, imines not substituted on the nitrogen atom are fairly strong bases [1]. Accordingly, they readily form salts with various acids [2] and under mild conditions as a rule, at room temperature — they are acylated by acetic anhydride [3, 4], ketene [5], acyl halides [4, 5], and phenyl isocyanate [6]. The imine of hexafluoroacetone (I), the basicity of which is markedly lowered because of the electron-accepting action of the two trifluoromethyl groups, takes part in such reactions with great difficulty, if at all. Thus, the imine (I) does not form a hydrochloride with anhydrous hydrogen chloride in ether and does not react with ketene in the absence of a catalyst [7].* The imine (I) reacts with phenyl isocyanate only at 200°, giving N-hexafluoroisopropylidene-N'-phenylurea. The imine (I) also does not react with acetic anhydride on prolonged heating to 100°. However, in the presence of catalytic amounts of H_2SO_4 this reaction takes place even at 0°, giving a high yield of 2-acetoxy-2-acetylaminohexafluoropropane (II).



$$\underset{(I)}{(CF_3)_2C{=}NH} + (CH_3CO)_2O \xrightarrow{H^{\oplus}} \underset{(II)}{(CF_3)_2\overset{OCOCH_3}{\overset{|}{C}}{-}NHCOCH_3} \xleftarrow{(CH_3CO)_2O} \underset{(III)}{(CF_3)_2\overset{OH}{\overset{|}{C}}{-}NHCOCH_3}$$

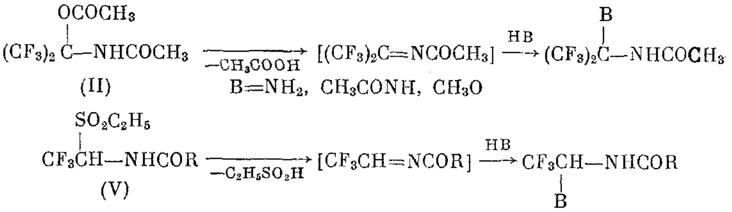
We have also obtained the acetoxyamide (II) by the acetylation of the geminal hydroxyamide (III) with acetic anhydride. The attempts of Newallis and Rumanowski [9] to carry out this reaction were unsuccessful. It is interesting, as we have shown previously [10], that in contrast to the hydroxyamide (III) the geminal hydroxyamines (IV) are not acetylated at the hydroxy group by acetic anhydride but decompose into hexafluoroacetone and the corresponding acetamide



$$\underset{(IV)}{(CF_3)_2\overset{OH}{\overset{|}{C}}{-}NHR} + (CH_3CO)_2O \rightarrow (CF_3)_2CO + CH_3CONHR$$

$$R = \text{alkyl, aryl}$$

This difference in the direction of the reaction is explained by the fact that in the hydroxyamide (III) the basicity of the nitrogen is reduced and the attack of the electrophilic agent is directed to the oxygen atom (cf. [11]). The acetoxyamide (III) reacts fairly readily with nucleophilic reagents with replacement of the acetoxy group, recalling in this respect the sulfonamide (V) [12]



$$\underset{(II)}{(CF_3)_2\overset{OCOCH_3}{\overset{|}{C}}{-}NHCOCH_3} \xrightarrow[-CH_3COOH]{} [(CF_3)_2C{=}NCOCH_3] \xrightarrow{HB} (CF_3)_2\overset{B}{\overset{|}{C}}{-}NHCOCH_3$$

$$B{=}NH_2,\ CH_3CONH,\ CH_3O$$

$$\underset{(V)}{CF_3\overset{SO_2C_2H_5}{\overset{|}{C}H}{-}NHCOR} \xrightarrow[-C_2H_5SO_2H]{} [CF_3CH{=}NCOR] \xrightarrow{HB} CF_3\underset{B}{\underset{|}{C}H}{-}NHCOR$$

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*The same result has been obtained by Middleton and Krespan [8]. In addition, they found that in the presence of boron trifluoride the reaction of the imine (I) with ketene leads to the acetylimine of hexafluoroacetone.

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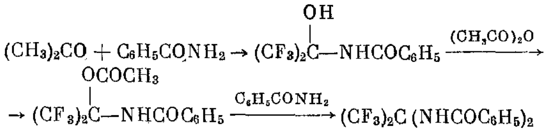
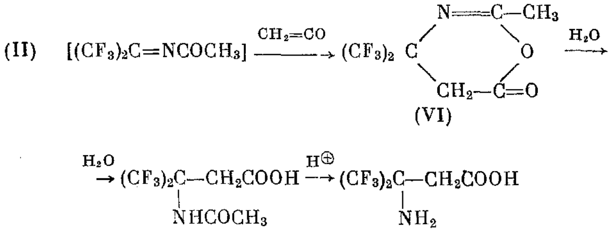
In particular, the reaction of (II) with acetamide leads to 2,2-bis-(acetamido)-hexafluoropropane. In view of this, and also the fact that the acetoxyamide (II) is formed from the hydroxyamide (III) and acetic anhydride, it must be considered that 2,2-bis-(benzamido)-hexafluoropropane, which we have recently obtained [13] by the reaction of hexafluoroacetone with benzamide in acetic anhydride is formed by the following route



$$(CH_3)_2CO + C_6H_5CONH_2 \rightarrow (CF_3)_2\underset{}{\overset{OH}{C}}\text{—}NHCOC_6H_5 \xrightarrow{(CH_3CO)_2O} (CF_3)_2\overset{OCOCH_3}{C}\text{—}NHCOC_6H_5 \xrightarrow{C_6H_5CONH_2} (CF_3)_2C(NHCOC_6H_5)_2$$

The reaction of the acetoxyamide (II) with ketene leads to the dihydrooxaginone (VI), the hydrolysis of which gives β-acetylamino-β,β-bis-(trifluoromethyl)-propionic acid and then hexafluoro-β-valine [14]



Thus, the acetoxyamide (II) is the source of the acetylimine of hexafluoroacetone.

EXPERIMENTAL

2-Acetoxy-2-acetylaminohexafluoropropane (II). At −78°, 4.7 g of the imine (I), 3 g of acetic anhydride, and a drop of H_2SO_4 were mixed in a glass tube. The tube was sealed and heated to 0°. After the end of the exothermic reaction, the solid mass was heated to 50° and was then cooled. After the product had been washed with a little ether, 6.4 g (83% of theoretical) of the amide (II) was obtained with m.p. 129-130° (in a sealed capillary, from acetone). Found %: C 31.61; H 2.51; F 42.72. $C_7H_7F_6O_3N$. Calculated %: C 31.5; H 2.62; F 42.65. IR spectrum: 1800 cm^{-1} (OC=O), 1695 cm^{-1} (NC=O), 1560 cm^{-1} (N—H). In the absence of sulfuric acid the imine (I) did not react with acetic anhydride on heating in the boiling water bath for 17 h.

A mixture of 4.6 g of hexafluoroacetone, 1.56 g of acetamide, 2.8 g of acetic anhydride, and two drops of H_2SO_4 was heated in a sealed tube for 2.5 h at 100°. The tube was opened, the mass was treated with a small amount of cold ether, and the solid matter was filtered off. This yielded 2.1 g (30% of theoretical) of the amide (II), identical with that described above.

2,2-Bis-(acetylamino)-hexafluoropropane. A mixture of 2 g of the amide (II), 0.5 g of acetamide, and 13 ml of dioxane was boiled for 6 h. The dioxane was distilled off and the residue was treated with ether. This yielded 1 g (50% of theoretical) of the bis-amide, m.p. 224-226° (from alcohol). Found %: F 42.75; N 10.65. $C_7H_8F_6O_2N_2$. Calculated %: F 42.9; N 10.62.

2-Methoxy-2-acetylaminohexafluoropropane. A mixture of 1 g of the amide (II), 1 ml of methanol, and 5 ml of dioxane was boiled for 4 h, and the residue after the distillation of the solvent was recrystallized from a mixture of benzene and heptane. This gave 0.4 g (45% of theoretical) of crystals with m.p. 95-97°. Found %: F 47.78; N 6.1. $C_6H_7F_6O_2N$. Calculated %: F 47.8; N 5.77.

N-Acetyl-2,2-diaminohexafluoropropane. A solution of 0.55 g of the amide (II) in 5 ml of acetonitrile was saturated with ammonia. The mixture was poured into water and extracted with ether. From the ether was obtained 0.27 g (60% of theoretical) of crystals with m.p. 89-90° (from heptane). Literature data [8]: m.p. 88-89°.

β-Acetylamino-β,β-bis-(trifluoromethyl)-propionic Acid. Over an hour, 10 ml (−78°) of ketene was passed into a solution of 14 g of the amide (II) in 20 ml of boiling acetonitrile. The acetonitrile was evaporated off and distillation of the residue gave a fraction boiling up to 110° (8 mm). The distillate was treated with water and after two days the crystals were filtered off and dried over P_2O_5 in vacuum. This yielded 5.8 g (41.5% of theoretical) of the acid, m.p. 149-150° (from benzene). Found %: F 42.58; N 5.22. $C_7H_7F_6O_3N$. Calculated %: F 42.65; N 5.25. IR spectrum: 1740 cm^{-1} (C=O), 1685 cm^{-1} (NC=O), 1570 cm^{-1} (N—H). A mixture of 3.06 g of the acetylaminoacid and 30 ml of hydrochloric acid (1 : 1) was boiled for 4.5 h, the solution was evaporated in vacuum, and the residue was treated with 30 ml of benzene and boiled in an apparatus with a Dean and Stark trap for 1.5 h. The hot mass was filtered. After evaporation, the filtrate yielded 1.5 g (56% of theoretical) of hexafluoro-β-valine, m.p. 69-71°. A mixture with an authentic sample [14] gave no depression of the melting point.

N-Hexafluoroisopropylidene-N'-phenylurea. A mixture of 0.76 g of the imine (I) and 0.46 g of phenyl isocyanate was heated in a sealed tube for 23 h at 190-200°. The solid mass was extracted with hot heptane. From the heptane 0.49 g (45% of theoretical) of the phenylurea, m.p. 190-192° (from benzene), was isolated. Found %: N 10.04. $C_{10}H_6F_6ON_2$. Calculated %: N 9.86. IR spectrum (ν_{max}, cm^{-1}): 1462 (v.s), 1515 (v.s), 1605 (w), 1720 (v.s), 1758 (v.s).

CONCLUSIONS

2-Acetoxy-2-acetylaminohexafluoropropane has been obtained and some of its reactions have been studied.

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