NEW REACTION OF ACID CHLORIDES OF PERHALO ACIDS WITH DIMETHYLFORMAMIDE

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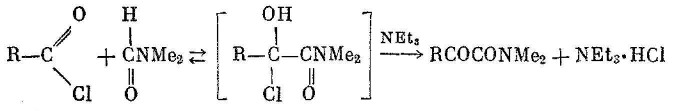
The distinctive traits of perhalo acyl chlorides in the reactions with dimethylformamide (DMF) [1] and with triethylamine (TEA) [2] were shown previously. Each of these reactions was studied separately. In the present paper we studied the reaction of perhalo acyl chlorides (I) simultaneously with DMF and TEA, which led to a new method for the preparation of a number of previously unknown dimethylamides of perhalo α-keto acids of the (II) type.* The reaction of acid chlorides (I) with DMF and TEA proceeds under mild conditions, at times even at −78°, by the following scheme:



(Ia—e) A (IIa—e)

R=CF_3 (a); C_2F_5 (b); C_3F_7 (c); i=C_3F_7 (d); CCl_3 (e); $(CF_3)_3C$ (f)

The reaction apparently begins with the formation of the unstable intermediate compound A, which loses hydrogen chloride and is converted to the α-ketoamide (II). Without the TEA the formation of the ketoamides (II) was not observed (however, see [1]).

Below are discussed the traits of various acid chlorides in the indicated reaction and the properties of the obtained ketoamides. Whereas acid chlorides (Id) and (Ie) react with DMF and TEA even at −78°, acid chloride (If), not containing halogen atoms α to the C=O group, reacts with DMF and TEA at 100°, giving only monohydroperfluoroisobutane – the hydrolysis product of the starting acid chloride

$$(CF_3)_3CCOCl \xrightarrow[2)\,H_2O]{1)\,NEt_3,\ DMF} (CF_3)_3CCOOH \xrightarrow{-CO_2} (CF_3)_3CH$$

α-Ketoamides (IIa-c) easily react with water to form the α,α-dihydroxyamides (IIIa-c), which, in turn, can be dehydrated with phosphorus pentoxide

$$\underset{(II)}{RCOCONMe_2} \underset{P_2O_5}{\overset{H_2O}{\rightleftarrows}} \underset{(III)}{RC(OH)_2CONMe_2}$$

R=CF_3 (a); C_2F_5 (b); C_3F_7 (c)

During dehydration, which at times requires substantial heating of the reaction mixture, a part of the ketoamide is converted to a tar, which apparently explains the comparatively low yield of dimethylamides (IIa-c) (in isolating the latter from the reaction mixture the mixture was first treated with water and the obtained α,α-dihydroxyamides (IIIa-c) then had to be dehydrated with P_2O_5). When the purpose of the experiment was to obtain the α,α-dihydroxyamide, as is shown on the example of (IIIc), the yield of product was high. The acid hydrolysis of α,α-dihydroxyamide (IIIc) gave the hydrate of α-ketoperfluorovaleric acid (IV),

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*Prior to our work the dimethylamides of perfluoro-α-ketovaleric acid [1], perfluoro-α-ketopropionic acid [3-5], and ω-hydroperfluoro-α-ketocaprylic acid [6], and their derivatives, were known.

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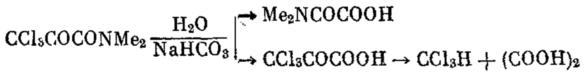
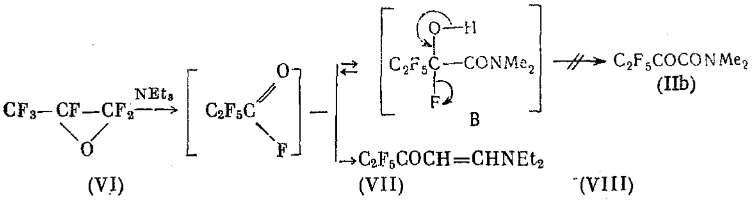
which was then converted to the methyl ester (V)

$$C_3F_7C(OH)_2CONMe_2 \xrightarrow[\text{[}H_2SO_4\text{]}]{H_2O} \underset{(IV)}{C_3F_7C(OH)_2COOH} \xrightarrow{MeOH} \underset{(V)}{C_3F_7COCOOMe}$$

α-Ketoamides (IIa-c) are stable toward aqueous $NaHCO_3$ solution, whereas in the case of ketoamide (IIe) haloform decomposition takes place, either of the amide or of the intermediately formed acid, leading to the formation of a mixture of dimethyloxamic and oxalic acids



It was interesting to check the possibility of obtaining the ketoamides from perfluoroolefin oxides, which are, as is known [7], potential sources of acid fluorides. It proved that the main reaction product of perfluoropropene oxide with DMF and TEA is the known [2] diethylaminoalkenone (VIII), and not the α-ketoamide (IIb), which is formed only in slight amount



This is probably explained by the fact that in the intermediate compound B, due to the higher strength of the C – F bond (when compared with the C – Cl bond in A), the decomposition toward the formation of the ketoamide is made difficult, in which connection the equilibrium is shifted toward the left, and the reaction of oxide (VI) with TEA proves to be the main reaction [2, 7]. The same result is also obtained with the authentic acid fluoride (VII), which distinguishes acid fluorides from acid chlorides in this reaction.

EXPERIMENTAL

The mixtures were analyzed and the obtained compounds were identified by the GLC method. The NMR-spectra were taken on a Perkin – Elmer R-12 instrument with an operating frequency of 60 MHz (the chemical shifts are given on the δ-scale with hexamethyldisiloxane as the reference). The F^{19} NMR-spectra were recorded on a Hitachi H-6013 instrument with an operating frequency of 56.6 MHz (the chemical shifts are given on the τ-scale using CF_3COOH as the external standard). The IR-spectra were taken on a UR-10 spectrophotometer.

Dimethylamide of Perfluoro-α-ketopropionic Acid (IIa). A mixture of 20 g of acid chloride (Ia), 42 g of DMF and 8.8 g of TEA was heated in a glass ampul at 100° for 5 h, after which it was diluted with water; the obtained oil was separated, and the aqueous solution was extracted with ether. The oil and ether extracts were combined, washed in succession with $NaHCO_3$ solution, dilute HCl solution, and water, and dried over $MgSO_4$ and P_2O_5. After distilling off the ether we obtained 3 g (15% of theory) of dimethylamide (IIa) with bp 69.5° (19 mm) and n_D^{20} 1.3910. Infrared spectrum (ν, cm^{-1}): 1670 and 1770 (C = O); 3300 (OH).* NMR spectrum: 2.97 and 2.99 ($2CH_3$); 6.17 (OH). Found: C 35.4; H 3.72; F 33.6; N 8.26%. $C_5H_6F_3NO_2$. Calculated: C 35.6; H 3.56; F 33.7; N 8.26%.

Dimethylamide of Perfluoro-α-ketobutyric Acid (IIb). In the same manner as before, from 38 g of acid chloride (Ib), 72 g of DMF and 23.2 g of TEA we obtained 8 g (20%) of dimethylamide (IIb) with bp 68.5-69° (14 mm); n_D^{20} 1.3652. Infrared spectrum (ν, cm^{-1}): 1675 and 1775 (C = O). NMR spectrum: 2.96 and 2.98 ($2CH_3$). Found: C 33.0; H 2.67; F 43.5; N 6.38%. $C_6H_6F_5NO_2$. Calculated: C 32.9; H 2.62; F 43.4; N 6.38%.

Dimethylamide of Perfluoro-α-ketovaleric Acid (IIc). In the same manner as before, from 15 g of acid chloride (Ic), 24 g of DMF and 6.5 g of TEA we obtained, at 0°, 5.7 g (33%) of dimethylamide (IIc) with bp 62-66° (7 mm). The compound is identical (GLC) with that obtained previously [1].

Dimethylamide of Perfluoro-α-ketoisobutyric Acid (IId). In the same manner as before, from 5 g of acid chloride (Id), 10 g of DMF and 2.6 of TEA (at first at – 78° for 10 h, and then at room temperature for 30 h) we obtained 1.8 g (30%) of dimethylamide (IId) with bp 76.5° (17 mm); n_D^{20} 1.3620. Infrared spectrum (ν, cm^{-1}): 1670 and 1760 (C = O). NMR spectrum: 2.94 and 3.12 ($2CH_3$). F^{19} NMR spectrum: 4 (doublet of

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*The band at 3300 cm^{-1} was attributed to the formation of the hydrate (IIIa) during the time of taking the spectrum.

CF_3 attached to CF, J 7.4 Hz); 90 (answering to the heptet of CF attached to $(CF_3)_2$). Found: C 31.1; H 2.21; F 49.6; N 5.34%. $C_7H_6F_7NO_2$. Calculated: C 31.2; H 2.23; F 49.5; N 5.21%.

Dimethylamide of Trichloro-α-ketopropionic Acid (IIe). With stirring, to 102 g of DMF was added in drops, at −78°, 42.2 g of acid chloride (Ie), and then 24 g of TEA was added in 20 min. The mixture was stirred for 5 h, with a gradual raising of the temperature up to room temperature, and then it was allowed to stand overnight, after which it was diluted with water and extracted with ether. The ether solution was dried over $MgSO_4$. Distillation gave 26 g (51.5%) of dimethylamide (IIe) with bp 95-96° (2 mm); n_D^{20} 1.4955. Infrared spectrum (ν, cm^{-1}): 1660 and 1745 (C=O). NMR spectrum: 3.0 (CH_3). Found: C 27.6; H 2.92; Cl 48.2%. $C_5H_6Cl_3NO_2$. Calculated: C 27.5; H 2.76; Cl 48.7%.

Reaction of Acid Chloride (If) with DMF and TEA. In the same manner as in the first experiment, from 9.5 g of acid chloride (If), 10 g of DMF and 3.6 g of TEA we obtained in a trap (−78°) 3.4 g (45%) of monohydroperfluoroisobutane, identical (GLC) with the authentic compound [8], and 1 g of an oil, which was not investigated further.

Dimethylamide of Perfluoro-α,α-dihydroxypropionic Acid (IIIa). Dimethylamide (IIa (0.5 g) was allowed to stand in the air. After 12 h we obtained 0.54 g (87%) of hydrate (IIIa) with mp 80-81° (from water), identical with the authentic compound [3]. Infrared spectrum (ν, cm^{-1}): 1665 (C=O); 3280 (OH). NMR spectrum: 2.87 and 2.94 ($2CH_3$); 5.8 (OH). Found: C 29.1; H 5.0%. $C_5H_{10}F_3NO_3$. Calculated: C 29.2; H 4.87%.

Dimethylamide of Perfluoro-α,α-dihydroxybutyric Acid (IIIb). A solution of 2.5 g of dimethylamide (IIb) and 0.6 g of water in 20 ml of acetone was evaporated at room temperature. After 12 h we obtained 2.35 g (88%) of hydrate (IIIb) with mp 39-40° (from heptane). Infrared spectrum (ν, cm^{-1}): 1670 (C=O); 3280 (OH). NMR spectrum: 3.0 ($2CH_3$); 5.8 (OH). Found: C 30.4; H 3.28%. $C_6H_8FN_5O_3$. Calculated: C 30.4; H 3.38%.

Dimethylamide of Perfluoro-α,α-dihydroxyvaleric Acid (IIIc). With stirring, to 15 g of DMF at 0° was added 9.6 g of acid chloride (Ic) in 5 min, and then 4.16 g of TEA was added in 10 min. The mixture was stirred for another hour at 20° and then diluted with water (150 ml). The separated oil crystallized on cooling. We obtained 7.0 g (60%) of hydrate (IIIc) with mp 58-59° (precipitated from DMF with water). Infrared spectrum (ν, cm^{-1}): 1674 (C=O); 3400 (OH). NMR spectrum: 3.06 and 3.35 (2 CH_3 triplets, J 1.5 Hz ($2CH_3$)); 6.36 (OH). Found: C 27.8; H 3.17; F 43.5%. $C_7H_{10}F_7NO_3$. Calculated: C 27.5; H 3.30; F 43.5%.

Perfluoro-α,α-dihydroxyvaleric Acid (IV). A mixture of 25 g of hydrate (IIIc) and 55 ml of 90% H_2SO_4 solution was heated at 100° for 7 h. From the mixture was distilled in vacuo, at 92-95° (15 mm), 16 g (76%) of acid (IV) with mp 112-113° (from benzene). Infrared spectrum (ν, cm^{-1}): 1640 and 1745 (CO); 3400 (OH). NMR spectrum: 7.05 (broad OH). Found: C 23.0; H 1.23. F 50.5%. $C_5H_3F_7O_4$. Calculated: C 23.0; H 1.16; F 51.1%.

Methyl Ester of Perfluoro-α-ketovaleric Acid (V). A mixture of 9.5 g of acid (IV), 30 ml of absolute methanol and 0.3 ml of H_2SO_4 was refluxed for 10 h, diluted with water, the organic layer was separated, and the aqueous layer was extracted with ether. The organic layer and ether extract were combined and dried over $MgSO_4$. Distillation at atmospheric pressure gave 6.95 g (yield 87% when based on reacted acid) of ester (V), and 0.9 g of acid (IV) as residue. Redistillation in vacuo over conc. H_2SO_4 gave ester (V) with bp 36-38° (55 mm); n_D^{20} 1.3170. Infrared spectrum (ν, cm^{-1}): 1760 (C=O). NMR spectrum: 3.94 (CH_3). Found: C 28.2; H 1.23; F 52.5%. $C_6H_3F_7O_3$. Calculated: C 28.1; H 1.15; F 51.9%.

Reaction of Oxide (VI) with DMF in the Presence of TEA. In the same manner as in the first experiment, the workup of a mixture of 12 g of oxide (VI), 25 g of DMF and 7.2 g of TEA gave traces (GLC) of dimethylamide (IIb) and 2.1 g (24%) of the diethylaminoalkenone (VIII), identical (TLC on Al_2O_3 and NMR) with the authentic compound [2, 7].

Reaction of Acid Fluoride of Perfluoropropionic Acid (VII) with DMF in the Presence of TEA. In the same manner as in the first experiment (heating at 100° for 3 h), the workup of a mixture of 6 g of acid fluoride (VII), 13 g of DMF and 5 g of TEA gave traces (GLC) of dimethylamide (IIb) and 1.3 g (25%) of the diethylaminoalkenone (VIII), identical (TLC on Al_2O_3 and NMR) with the authentic compound [2, 7].

Hydrolysis of Dimethylamide of Trichloro-α-ketopropionic Acid (IIe). A mixture of 2 g of amide (IIe), 12 ml of H_2O and 2.5 g of $NaHCO_3$ was heated at 40-50° for 10 h. When the evolution of CO_2 had ceased (identified by reaction with $Ba(OH)_2$ solution) the obtained solution was treated with 2 ml of conc. H_2SO_4, followed by extraction with ether to give 0.75 g of a crystalline mixture, which was composed of 0.19 g of oxalic acid (isolated by precipitation as the Ca salt) and 0.56 g of dimethyloxamic acid (74%) with mp 126-128° (decomp.) (from acetonitrile–benzene mixture). Found: C 39.5; H 6.03; N 11.4%. $C_4H_7NO_3$. Calculated: C 41.0; H 5.98; N 11.9%.

CONCLUSIONS

A study was made of a new reaction of perhalo acyl chlorides with dimethylformamide in the presence of triethylamine, leading to the formation of the dimethylamides of perhalo α-keto acids.

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