

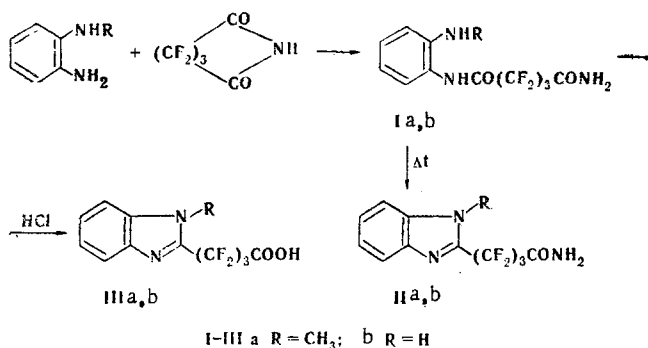
γ -(1-METHYL-2-BENZIMIDAZOLYL)PERFLUOROBUTYRIC ACID
AND ITS TRANSFORMATIONS

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UDC 547.785.5'221:543.226

γ -(1-Methyl-2-benzimidazolyl)perfluorobutyric acid was synthesized, and it was established that its chloride is converted by heating to the lactam of this acid with splitting out of a methyl group from the nitrogen atom.

ω -(1-Alkyl-2-benzimidazolyl)perfluorocarboxylic acids have not been described. We have synthesized the first representative of acids of this type — γ -(1-methyl-2-benzimidazolyl)-perfluorobutyric acid (IIIa) — and studied its transformations. Acid IIIa was obtained by the scheme previously used for the synthesis of the analogous IIIb [1].



Perfluoroglutarimide reacts with N-methyl-o-phenylenediamine in chloroform to give Ia, which melts in a capillary at 160–161°C. It has previously been shown that o-methylamino-acetanilide is obtained in the acetylation of N-methyl-o-phenylenediamine [2]. It is possible that acylation takes place at the primary amino group in our case also.

It might have been assumed that Ia, like its unmethylated analog, is converted to a benzimidazole derivative (IIa), which also melts at the indicated temperature, when it is heated in a capillary. In order to ascertain which transformations occur when Ia is heated we subjected it to thermal analysis. The differential thermal analysis (DTA), thermogravimetric (TG), and differential thermogravimetric (DTG) curves are presented in Fig. 1. Exothermic and endothermic peaks that can be associated with chemical or phase transformations are present on the DTA curve. The minimum at 110°C, which is due to melting of the compound, is followed immediately by a maximum at 130°C; this constitutes evidence for a process with heat liberation.

A 5.24% decrease in the mass of the sample is observed on the TG curve at 110–120°C; this is equivalent to the loss of one molecule of water. A peak that attests to chemical transformation of the compound at a maximum rate at 110°C is observed on the DTG curve over the same temperature range. Thus water is split out and a benzimidazole derivative is formed at 110–120°C. The structure of the latter was confirmed by IR spectroscopic data.

When the temperature is raised further, a minimum appears on the DTA curve at 160°C, which corresponds to the melting point of the amide (IIa). When Ia is refluxed in toluene, water is also split out, and toluene-insoluble amide IIa is formed. Mass loss is not observed for it on the TG curve at 110–120°C, and only one minimum at 160°C, which corresponds to its melting point, is present on the DTA curve. Acid IIIa was isolated when Ia was heated with

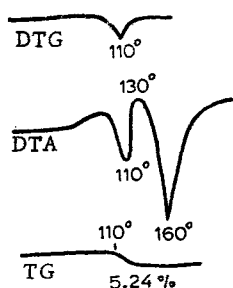
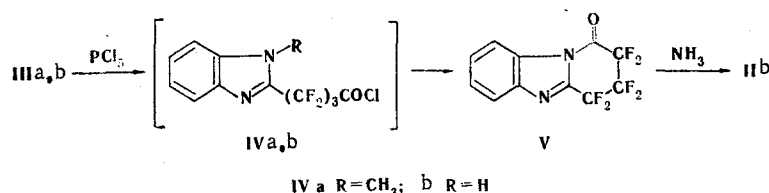


Fig. 1. Thermal analysis of the o-methylaminoanilide of perfluoroglutaramide (I).

20% hydrochloric acid. We were also able to obtain this acid by alkylation of the previously described [1] γ -(2-benzimidazolyl)perfluorobutyric acid (IIIb) with dimethyl sulfate. Alkylation with dimethyl sulfate proceeds exclusively at the nitrogen atom of the benzimidazole ring.

We attempted to obtain amide IIa by alternative synthesis by the action of ammonium hydroxide on the chloride of acid IIIa. However, we found that 1-oxo-2,2,3,3,4,4-hexafluoro-1,2,3,4-tetrahydropyrido[1,2-a]benzimidazole (V) is formed instead of the expected acid chloride (IVa) in the reaction of phosphorus pentachloride with acid IIIa.



The acid chloride evidently undergoes intramolecular cyclization with splitting out of a methyl group and the formation of methyl chloride. Lactam V was also obtained by heating acid IIIb with phosphorus pentachloride. The two samples have identical properties, and no melting-point depression is observed for a mixture of them. The structure of lactam V is confirmed by IR and mass-spectral data. The mass spectrum of lactam V contains a molecular ion with a mass of 294. Amide IIb is formed in the reaction of lactam V with ammonium hydroxide. We have previously [1] assumed that the reaction of phosphorus pentachloride with acid IIIb gives the chloride (IVb), which reacts with ammonia and is converted to amide IIb. On the basis of the data obtained in the present research it may be concluded that the acid chloride (IVb) formed in the reaction readily undergoes cyclization on heating to give lactam V, which is converted to amide IIb by the action of ammonia.

EXPERIMENTAL

Thermal analysis was carried out with an MOM derivatograph (Hungary) in platinum crucibles at a temperature-rise rate of 6 deg/min. The mass spectra were recorded with an MKh-1303 mass spectrometer. The IR spectra of KBr pellets of the compounds were recorded with a UR-10 spectrometer.

Perfluoroglutaramide o-Methylaminoanilide (Ia). A mixture of 7.95 g (0.031 mole) of perfluoroglutarimide, 4.4 g (0.036 mole) of N-methyl-o-phenylenediamine, and 100 ml of chloroform was maintained at 20°C for 30 min, after which the precipitate was removed by filtration, and dried to give 9.3 g (75.3%) of a product with mp 110°C (according to DTA, from methanol with benzene). IR spectrum: 1145, 1170 (C-F); 1700 (C=O); 3270, 3380 cm⁻¹ (NH₂). Found, %: N 12.1; F 33.3. C₁₂H₁₁F₆N₂O₂. Calculated, %: N 12.2; F 33.2.

γ -(1-Methyl-2-benzimidazolyl)perfluorobutyramide (IIa). A 0.44-g (1.2 mmole) sample of Ia was dissolved in 10 ml of toluene, and the solution was refluxed for 3 h. It was then cooled, and the precipitate was removed by filtration and dried to give 0.39 g (95%) of a product with mp 160-161°C (from methanol with benzene). IR spectrum: 1145, 1170 (C-F); 1710 (C=O); 3220, 3390 (NH₂); 980 cm⁻¹ (imidazole ring). Found, %: N 12.8. C₁₂H₉F₆N₃O. Calculated, %: N 12.9.

γ -(1-Methyl-2-benzimidazolyl)perfluorobutyric Acid (IIIa). A) A mixture of 5 g (14.5 mmole) of anilide Ia and 25 ml of 20% hydrochloric acid was refluxed for 3 h, after which it was cooled, and the precipitate was removed by filtration and dried to give 3.9 g (82%) of a

product with mp 193-194°C (from aqueous alcohol). Found, %: F 35.1. $C_{12}H_8F_6N_2O_2$. Calculated, %: F 34.9.

B) A 0.5-ml (5.2 mmole) sample of dimethyl sulfate was added dropwise with stirring at 60°C to a solution of 0.54 g (13.5 mmole) of sodium hydroxide and 1.5 g (4.8 mmole) of acid IIIb in 5 ml of water, the mixture was heated to the boiling point, and 0.1 ml (1.04 mmole) of dimethyl sulfate was added. The mixture was refluxed for 1.5 h, after which it was cooled and poured into 25 ml of water. The aqueous mixture was acidified with 20% hydrochloric acid, and the precipitate was removed by filtration, washed with water, and dried to give 1.17 g (78%) of a product with mp 193-194°C (from aqueous alcohol). Found, %: C 44.2; H 2.3; F 34.6; N 8.2. $C_{12}H_8F_6N_2O_2$. Calculated, %: C 44.1; H 2.4; F 34.9; N 8.5.

1-Oxo-2,2,3,3,4,4-hexafluoro-1,2,3,4-tetrahydropyrido[1,2-a]benzimidazole (V). A mixture of 3.12 g (0.01 mole) of acid IIIb and 2.1 g (0.01 mole) of phosphorus pentachloride was heated at 110°C until hydrogen chloride evolution ceased, after which the phosphorus oxychloride was removed by distillation, and the residue was vacuum distilled to give 2.7 g (92%) of a product with bp 121-122°C (12 mm). The product crystallized on cooling to give a solid with mp 92-93°C (after sublimation). Lactam V was similarly obtained in 72% yield from acid IIIa. IR spectrum, cm^{-1} : 1700 (C=O). Found, %: C 45.1; H 1.4; F 38.5; N 9.6; M by mass spectroscopy 294. $C_{11}H_4F_6N_2O$. Calculated, %: C 44.9; H 1.3; F 38.7; N 9.5; M 294.

γ -(2-Benzimidazolyl)perfluorobutyramide (IIb). A 1-ml (15 mmole) sample of 25% ammonium hydroxide was added with stirring at 20°C to a solution of 1.16 g (4 mmole) of V in 10 ml of benzene, and the mixture was allowed to stand for 30 min. The precipitate was removed by filtration, washed with water, and dried to give 1.05 g (96.3%) of a product with mp 231-232°C (from aqueous alcohol). IR spectrum: 1145, 1170 (C-F); 1710 (C=O); 3220, 3390 (NH₂); 981 cm^{-1} (imidazole ring). Found, %: N 13.4. $C_{11}H_7F_6N_3O$. Calculated, %: N 13.5.

LITERATURE CITED

1. N. A. Malichenko, A. P. Krasnoshchek, T. P. Medvedeva, and L. M. Yagupol'skii, *Khim. Geterotsikl. Soedin.*, No. 9, 1262 (1976).
2. C. H. Roeder and A. R. Day, *J. Org. Chem.*, **6**, 25 (1941).

INVESTIGATION OF CONDENSED PYRIMIDINE, PYRAZINE, AND PYRIDINE SYSTEMS.

XXVI.* REACTION OF 5-HYDROXY-6-AMINOPYRIMIDINES WITH HALOMALONIC ESTERS

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UDC 547.859'863'867.8'787

The reaction of 5-hydroxy-6-aminopyrimidines with chloromalononic ester in alcohol or with bromomalononic ester in dimethylformamide leads to 6-carbethoxypyrimido-7-oxazinones, whereas a mixture of 6-carbethoxypyrimido-7-oxazinones and 6,6'-spirodipyrimido-7-oxazinones is formed in the reaction with bromomalononic ester in alcohol. The latter oxazinones were obtained by reaction of 5-hydroxy-6-aminopyrimidines with dibromomalononic ester. Some of the properties of the synthesized compounds were studied.

In a continuation of our earlier research [2] we studied the reaction of 4-chloro-5-hydroxy-6-aminopyrimidine (I) and its 2-methyl derivative (II) with ethyl esters of halomalononic acid. *See [1] for communication XXV.

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