[CONTRIBUTION FROM THE RESEARCH INSTITUTE OF TEMPLE UNIVERSITY]

Addition Compounds of Perfluoro Fatty Acids with Ethers and Tertiary Amines[1]

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Perfluoro fatty acids have been found to react with ethers and tertiary amines to form stable addition compounds. Various physical and chemical properties of the representative examples $3CF_3CO_2H \cdot 2(C_2H_5)_2O$, $2C_3F_7CO_2H \cdot (C_2H_5)_2O$, $3C_3F_7CO_2H \cdot 2$dioxane, $3CF_3CO_2H \cdot 2C_6H_5N(CH_3)_2$ and $5C_3F_7CO_2H \cdot 3C_6H_5N(CH_3)_2$ are described.

The reaction of iodine with silver trifluoroacetate[2] in ethyl ether and the reaction of cyclopentyl iodide with silver *n*-heptafluorobutyrate in ethyl ether resulted in the formation of, besides the expected silver iodide, peculiar type compounds which merited special attention. Further studies revealed that trifluoroacetic acid and heptafluorobutyric acid reacted with substantial heat evolution with some ethers and tertiary amines forming stable addition compounds in other than 1:1 molar ratios.

In contrast to the complete inertness of acetic and *n*-butyric acids toward simple ethers such as ethyl ether and dioxane, the completely fluorinated analogs reacted readily, forming addition products of significantly higher boiling points than the original acids or ethers. Trifluoroacetic acid and heptafluorobutyric acid reacted with ethyl ether to form $3CF_3CO_2H \cdot 2(C_2H_5)_2O$ and $2C_3F_7CO_2H \cdot (C_2H_5)_2O$, respectively. When treated with water, the former compound at first formed a lower layer but was hydrolyzed very rapidly with formation of the free acid and an upper layer of ethyl ether. The latter addition product was only very slightly soluble in water, and could not be hydrolyzed appreciably in twice its volume of water even if heated to 100° for two hours in a sealed tube. It did, however, hydrolyze slowly in a large excess of water and more rapidly in a dilute alkaline solution. Heptafluorobutyric acid and dioxane formed $3C_3F_7CO_2H \cdot$ 2dioxane which hydrolyzed very rapidly. *n*-Butyl ether and heptafluorobutyric acid also formed an addition product, of undetermined composition, boiling at 158°, n^{30}_D 1.3478. In addition heptafluorobutyric acid reacted readily with Diethyl Carbitol, $(C_2H_5OC_2H_4)_2O$, to form a stable, only slightly water-soluble addition compound, b.p. 106° (24 mm.). Diethyl Cellosolve also yielded a slightly water-soluble addition compound. Preliminary experiments indicated that the poly-functional reactants, perfluoroglutaric acid and Diethyl Carbitol formed a viscous, only slightly water-soluble addition product. The striking affinity of perfluoro fatty acids for ethers was further demonstrated in the following manner. To a solution of heptafluorobutyric acid and water in 1:2 molar ratio, ethyl ether was added in 0.5 molar proportion. An exothermic reaction occurred and, in spite of the presence of the relatively large proportion of water, the ether addition product was formed just as in the case when no water was present.

Although carboxylic acids are known to react with amines by formation of salts, the above findings suggested the possibility of the reaction of perfluoro-acids with amines to form addition complexes in other than molar ratios. In order to eliminate the possibility of amide formation it was decided to study the reaction of tertiary amines with these acids. Trifluoroacetic acid and heptafluorobutyric acid reacted with dimethylaniline to form the distillable addition products $3CF_3CO_2H \cdot 2C_6H_5N(CH_3)_2$ and $5C_3F_7CO_2H \cdot 3C_6H_5N(CH_3)_2$ respectively. The former compound was soluble in water, while the latter was essentially insoluble in twice its volume of water although it did hydrolyze slowly in a large excess of water and more rapidly in an alkaline solution. A white, crystalline, water-soluble salt was formed when trifluoroacetic acid and dimethylaniline reacted in a 1:1 molar ratio. At this same ratio, however, heptafluorobutyric acid and dimethylaniline formed a slightly water-soluble liquid salt which could not be crystallized and which was readily soluble in benzene. Both of these salts reacted exothermally with additional perfluoro-acid to form the aforementioned addition products. On distillation of the 1:1 salts it is most significant that the only products isolated were the original amines and the same addition products. If excess acid were used in the original preparation, the only products that were found on fractionation were some unreacted acid and the identical addition product.

Various physical constants of these five representative addition compounds are summarized in Table I. With regard to the boiling points given, vapor density measurements indicate that these compounds are highly dissociated in the gaseous state at temperatures of the boiling point and above. Viscosity data are given in the experimental section.

Other tertiary amines such as trimethylamine and pyridine apparently form only water-soluble crystalline salts with these perfluoroacids and cannot be distilled without decomposition. Triethylamine, however, does form a slightly water-soluble product with heptafluorobutyric acid, which cannot be distilled at 1 mm. pressure without decomposition.

Preliminary experiments have been carried out which indicate that acetone forms a stable, water-soluble, addition product with heptafluorobutyric acid boiling at about 137°, and that acetonitrile may form a relatively weak addition compound also. Thus it appears that some ketones and nitriles form these peculiar addition compounds also.

Infrared spectra have been taken of all five well-characterized addition compounds and gave additional evidence that we were dealing with definite compound formation. As an example, the spectrum of the addition compound $3C_3F_7CO_2H \cdot 2$ dioxane showed definite absorption peaks at 12.1 and 12.9 microns which were not to be found in the

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[1] Presented at the 118th Meeting of the American Chemical Society, Chicago, Ill., September 3 to 8, 1950.

[2] M. Hauptschein and A. V. Grosse, THIS JOURNAL, **73**, 2461 (1951).

TABLE I

Formula[a]	B.p., °C.	d^{20}_4	d^0_4	$\Delta d/\Delta t$	n^{20}_D	Molar refraction Found[b]	Molar refraction Calcd.[c]
$3CF_3CO_2H \cdot 2(C_2H_5)_2O$	102	1.1529	1.1898	−0.00184	1.3180	84.1	84.7
$2n$-$C_3F_7CO_2H \cdot (C_2H_5)_2O$	130	1.4263	1.4644	− .00190	1.3073	67.4	68.6
$3n$-$C_3H_7CO_2H \cdot$2dioxane	153	1.4999	1.5353	− .00177	1.3294	111.2	112.8
$5n$-$C_3F_7CO_2H \cdot 3C_6H_5N(CH_3)_2$	*ca.* 90 (0.5 mm.)	1.4769	1.5016	− .00124	1.3901	230.0	234.0
$3CF_3CO_2H \cdot 2C_6H_5N(CH_3)_2$	127 (20 mm.)	1.3161	1.3393	− .00116	1.4284	114.4	119.1

[a] Composition of liquid phase at specified boiling point. [b] Calculated from Lorenz–Lorentz equation. [c] Calculated from the usual values for atomic refractions: C, 2.418; H, 1.100; O (in C═O), 2.211; O (in ethers), 1.643; O (in OH) 1.525; F, 1.23; N (in tertiary amines), 2.840; double bond, 1.733.

spectrum of either reactant. Similarly, an absorption peak at 13.05 microns was present for $5C_3F_7COOH \cdot 3C_6H_5N(CH_3)_2$ but not for either reactant.

A good deal of additional work will have to be done before it will be possible to determine the exact types of bonds and structural arrangements involved. A probable assumption is that the odd composition of these compounds can be explained by some sort of intermolecular hydrogen bonding between the fluorine atoms of the acids and the hydrogen atoms of the ethers or amines. But a prerequisite for this sort of hydrogen bonding is a much stronger primary bond such as an oxonium (salt) type linkage between the oxygen of ethers or the basic nitrogen of amines and the highly acidic proton of these strong acids. From these considerations it appears that whenever an organic hydrogen-containing compound possessing atoms with sufficient basicity in the Lewis sense is mixed with perfluorocarboxylic acids a reaction of the above type may be anticipated.

Experimental

Materials and Procedure.—Trifluoroacetic acid and heptafluorobutyric acid were obtained from Minnesota Mining and Manufacturing Co. Anhydrous ethyl ether, dioxane and dimethylaniline were obtained from Eimer and Amend Co., and were Reagent grade or C.P.

The experimental procedure was very simple. The ether or amine was simply mixed with the perfluoro-acid at room temperature. An immediate reaction ensued with substantial evolution of heat when the ether addition compounds were prepared, and even greater evolution of heat when the tertiary amine addition products were prepared. The reaction products were allowed to cool to room temperature and subsequently fractionally distilled at atmospheric pressure or at reduced pressures.

Reaction of Perfluoro-fatty Acids with Ethers.—Several reactions were carried out between trifluoroacetic acid, b.p. 71.1° at 734 mm., and anhydrous ethyl ether employing molar ratios (acid:ether) of 1:1 and 3:2. In the former case the only product formed besides unreacted ether in the forerun was the addition compound $3CF_3CO_2H \cdot 2(C_2H_5)_2O$, b.p. 102° at 760 mm. In the latter case essentially the entire product was this same addition compound; thus the composition was determined by synthesis. *Anal.*[3] Calcd. for $3CF_3CO_2H \cdot 2(C_2H_5)_2O$: C, 34.29; H, 4.73; F, 34.88; acid (as CF_3CO_2H), 69.77. Found: C, 34.18; H, 4.57; F, 35.21; acid (by titration), 68.54, 69.18.

Heptafluorobutyric acid, b.p. 120.0° at 735 mm., and ethyl ether reacted in 1:1 and 2:1 molar proportions (acid:ether). In the former case the only product formed besides 1 part of unreacted ether was 1 part of the addition compound $2C_3F_7CO_2H \cdot (C_2H_5)_2O$, b.p. 130°. In the latter case the entire product was found to boil essentially at 130° at 760 mm., and therefore corresponded to $2C_3F_7CO_2H \cdot (C_2H_5)O$. *Anal.*[3] Calcd. for $2C_3F_7CO_2H \cdot (C_2H_5)_2O$: C, 28.70; H, 2.41; acid (as $C_3F_7CO_2H$), 85.24. Found: C, 27.78; H, 2.53; acid (by titration), 85.82, 86.22.

In a similar manner the composition of the heptafluorobutyric acid–dioxane complex was demonstrated to be 3 acid:2 dioxane (b.p. 152.8°) both by synthesis and analysis. *Anal.*[3] Calcd. for $3C_3F_7CO_2H \cdot 2C_4H_8O_2$: C, 29.35; H, 2.34; acid (as $C_3F_7CO_2H$), 78.47. Found: C, 27.67; H, 2.28, 2.48; acid (by titration), 79.05.

Reaction of Perfluoro-fatty Acids with Dimethylaniline.—Trifluoroacetic acid reacted with dimethylaniline in the molar ratios (acid:amine) of 1:1, 3:2 and 2:1. Fractional distillation at 20 mm. pressure yielded, besides a forerun of dimethylaniline at the 1:1 ratio and a forerun of trifluoroacetic acid at the 2:1 ratio, an addition product boiling at 127° at 20 mm. and corresponding to $3CF_3CO_2H \cdot 2C_6H_5N(CH_3)_2$. At the 3:2 ratio the entire product boiled essentially at 127° at 20 mm. which indicated the proper composition. A 2.0-g. sample of the compound was treated with excess 5% potassium hydroxide and was easily hydrolyzed to form, in addition to CF_3CO_2K, 0.8 g. of an upper layer of dimethylaniline (theory for 2.0 g. of $3CF_3CO_2H \cdot 2C_6H_5N(CH_3)_2$ = 0.83 g.) which was converted to its picrate, m.p. 160–161° (lit. 163°).

Anal.[3] Calcd. for $3CF_3CO_2H \cdot 2C_6H_5N(CH_3)_2$: C, 45.21; H, 4.31; N, 4.79. Found: C, 44.63; H, 4.16; N, 5.08.

Heptafluorobutyric acid reacted with dimethylaniline in the molar ratios (acid:amine) of 1:1, 3:2 and 2:1. Fractional distillation of the products at 0.5 mm. pressure, yielded in all cases an addition product boiling at about 90° and corresponding most closely to $5C_3F_7CO_2H \cdot 3C_6H_5N(CH_3)_2$, f.p. *ca.* 8°, in addition to the stoichiometric amounts of either unreacted dimethylaniline (at the 1:1 and 3:2 ratios) or heptafluorobutyric acid (at the 2:1 ratio) as a forerun. A 2.0-g. sample of the addition compound hydrolyzed easily in excess 5% potassium hydroxide to form, in addition to $C_3F_7CO_2K$, 0.5 g. of an upper layer of dimethylaniline (theory for 2.0 g. of $5C_3F_7CO_2H \cdot 3C_6H_5N(CH_3)_2$ = 0.51 g.,) which was converted to its picrate, m.p. 159–160° (lit. 163°).

Anal.[3] Calcd. for $5C_3F_7CO_2H \cdot 3C_6H_5N(CH_3)_2$: C, 36.86; H, 2.67; N, 2.93. Found: C, 36.37, 36.57; H, 2.54, 2.72; N, 3.17.

Reaction of Silver Trifluoroacetate with Iodine and the Reaction of Silver *n*-Heptafluorobutyrate with Cyclopentyl Iodide Using Ethyl Ether as the Solvent in Both Cases.—The discovery of the perfluoro-fatty acid–ethyl ether addition compounds was actually first made quite unexpectedly when investigations were being carried out on the reactions of silver perfluoro-fatty acid salts with iodine and cyclopentyl iodide employing as a solvent a large quantity of ethyl ether. In each case it was established that the principal products obtained, besides theoretical amounts of silver iodide, were the appropriate ether addition products characterized above. The free perfluoro-acid was probably first formed in both cases by attack of the perfluoroacyl group on the solvent by abstraction of a hydrogen and also, when cyclopentyl iodide was used, by loss of hydrogen iodide and abstraction of that hydrogen. In this connection, it is of interest to note that *n*-amyl iodide reacted normally with silver heptafluorobutyrate in ethyl ether to give an 80% yield of *n*-amyl heptafluorobutyrate, b.p. 143–144°, $n^{25.5}_D$ 1.3340, d^{27}_4 1.2471 and d^0_4 1.2915. A more complete description of this ester is reserved for a future communication on the preparation of polyfluoro-esters by the silver salt–alkyl halide method.

Kinematic Viscosities of Two Perfluoro-fatty Acid Addition Compounds.—Viscosities were determined with standard Ostwald–Cannon–Fenske type viscosimeters, calibrated with water and pure *n*-cetane. Temperature control was established by using striped dewar flasks and thermoregula-

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(3) Microanalysis by Clark Microanalytical Laboratory, Urbana, Illinois. The compositions are given by the nearest simple *whole number* ratios. This does not preclude the possibility that the actual combination was more complex and fractional.

tor controlled heater baths. Temperatures were measured with a National Bureau of Standards calibrated thermometer.

The experimental values for $5C_3F_7COOH \cdot 3C_6H_5N(CH_3)_2$ were 43.85 centistokes (cts.) at 21.0°, and 6.867 cts. at 67.55°. After standing for 120 days the measured viscosity was 52.60 cts. at 17.7°. All these values lie on a straight line when plotted on an ASTM (D 341-39 and 43) viscosity chart, and the following values were read off this line in centistokes: 210 (0°), 35.0 (25°), 11.0 (50°), 5.1 (75°) and 2.9 (100°). The slope of this line, showing the temperature dependence of viscosity, *i.e.*, the so-called ASTM slope was 0.93.

The experimental values for $2C_3F_7COOH \cdot (C_2H_5)_2O$, in cts., were 1.318 at 21.0° and 0.634 at 67.55°. The viscosities for rounded temperature values were taken from the ASTM line: 2.20 cts. (0°), 1.22 (25°), 0.80 (50°), 0.58 (75°), 0.46 (100°). The ASTM slope was 1.19.

Acknowledgments.—The authors wish to express their gratitude to the U. S. Air Force, Air Materiel Command, for their financial support of this work, and to Mr. E. A. Nodiff for the density measurements here reported.

PHILADELPHIA, PENNA. RECEIVED JANUARY 12, 1951

[CONTRIBUTION FROM THE DIVISION OF BIOCHEMISTRY, MEDICAL SCHOOL, THE UNIVERSITY OF CALIFORNIA, BERKELEY]

A Phospho-tri-anhydride Formula for the Nucleic Acids

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A new structural formula for both ribo- and desoxyribo-nucleic acids is proposed, having as its core a $(P_2O_5)_n$ polymer chain of phospho-anhydride links. There are three such links per P atom. In addition, each P atom binds one hydroxyl group and one nucleoside (in a phospho-sugar ester bond). A unit cell, based on the proposed formula for the nucleic acids, is calculated. By means of a theoretical treatment, the formula is shown to be compatible with the available, factual data concerning the structure of the nucleic acids.

A careful examination of the available data concerning the structure and behavior of the nucleic acids leads to the conclusion that the facts are consistent with only *one* phospho-sugar ester bond per nucleotide and that the basic structure of the nucleic acids is a polymer core of phospho-anhydride links. There are three such links per phosphorus atom. In addition, each phosphorus atom binds one hydroxyl group and one nucleoside (phospho-sugar ester link) as shown diagrammatically in Fig. 1 for a ribose nucleic acid type (the difference between ribose and desoxyribose types will be discussed later.)

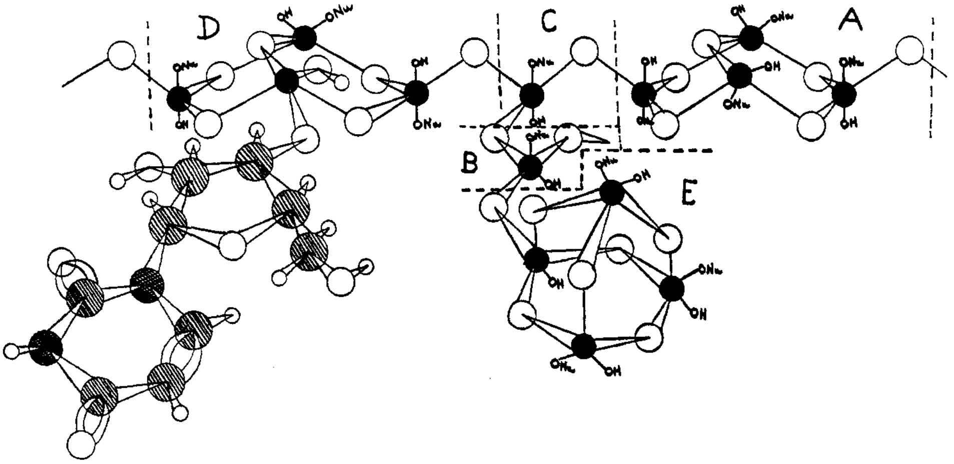

Fig. 1.—Proposed new structure for the nucleic acids: ●, phosphorus atoms; ○, oxygen atoms; ▨, carbon atoms; ●, nitrogen atoms; ONu, o-nucleoside (phospho-sugar ester link); °, hydrogen atoms. Bond distances, bond angles and relative atom and group sizes are not depicted exactly. To obtain proper perspective of the relationship between the polymer chain and the nucleoside, the uridine nucleoside should be considered as rotated 90°. The base of the nucleoside is to be imagined as parallel to the sugar moiety, but extending back toward the polymer core.

Section E, Fig. 1 represents an end group of the polymer chain. Its basic tetrahedral structure is identical with that of the hexagonal (monomeric) form of P_4O_{10}.[2–5] This can be visualized by mentally replacing all OH and ONu groups bound to each phosphorus atom by a single oxygen atom engaged in an "apical" P≡O.[3,6,7]

By cleavage of the proper P–O–P bond, section E can be opened to form a unit which is identical to the equivalent sections A and D. Sections B and

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(2) W. L. Hill, G. T. Faust and S. B. Hendricks, THIS JOURNAL, **65**, 794 (1943).

(3) G. C. Hampson and A. J. Stosick, *ibid.*, **60**, 1814 (1938).

(4) L. R. Maxwell, S. B. Hendricks and L. S. Deming, *J. Chem. Phys.*, **5**, 626 (1937).

(5) H. C. J. DeDecker and C. H. MacGillavry, *Rec. trav. chim.*, **60**, 159 (1941).

(6) The "apical" P to O bond in any of the forms of P_4O_{10} has been found to possess a bond distance of 1.39 Å.[3,7] Addition of the triple bonding radii for P and O yields 1.43 Å. Hence, this bond, having a calculated bond energy of 237.9 kcal./mole, may appropriately be referred to as a triple bond.

(7) H. C. J. DeDecker, *Rec. trav. chim.*, **60**, 413 (1941).