2,2-Diphenyl-4-bromo-5-cyclohexenone (XIII).—A solution of 2.15 g. of 2,2-diphenyl-5-cyclohexenone in 50 ml. of carbon tetrachloride was refluxed for 32 hours with 1.55 g. of N-bromosuccinimide. Crude succinimide separated in quantitative yield (0.85 g.) and a crude yield of 2.5 g. (85%) of the bromo ketone was left after evaporation of the solvent. Colorless needles were obtained from isoöctane–benzene, m.p. 135–136°, b.p. 135–138° (0.006 mm.). Its acetone solution decolorized 2% aqueous potassium permanganate.

Anal. Calcd. for $C_{18}H_{15}BrO$: C, 66.07; H, 4.62. Found: C, 66.02; H, 4.89.

2,2-Diphenyl-4,6-dibromo-5-cyclohexenone (XIV).—To a solution of 2 g. of 2,2-diphenyl-4-bromo-5-cyclohexenone in 50 ml. of carbon tetrachloride was added a solution of 0.31 ml. of bromine in 15 ml. of the same solvent. Decolorization required about 48 hours. After removal of the solvent a quantitative crude yield (2.5 g.) of colorless felted needles was obtained which, on recrystallization from isoamyl alcohol, melted at 165–166°. The product decolorized aqueous potassium permanganate.

Anal. Calcd. for $C_{18}H_{14}Br_2O$: C, 53.23; H, 3.47. Found: C, 53.18; H, 3.67.

Absorption Spectra.—A modified Beckman spectrophotometer was used for ultraviolet absorption measurements. Results are reported graphically in Fig. 1. Absolute ethanol solutions of the compounds were used in the following strengths: for 2,2-diphenylcyclohexanone, 0.009 molar; for the unsaturated ketones, 0.0001 molar.

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[CONTRIBUTION FROM THE RESEARCH INSTITUTE OF TEMPLE UNIVERSITY AND THE MATERIALS LABORATORY, WRIGHT AIR DEVELOPMENT CENTER]

Fluorinated Esters. I. Esters of Perfluoro Monocarboxylic and Dicarboxylic Acids with 1,1-Dihydroperfluoroalcohols and $\alpha,\alpha,\omega,\omega$-Tetrahydroperfluoroglycols

BY MURRAY HAUPTSCHEIN, JOSEPH F. O'BRIEN, CHARLES S. STOKES AND ROBERT FILLER

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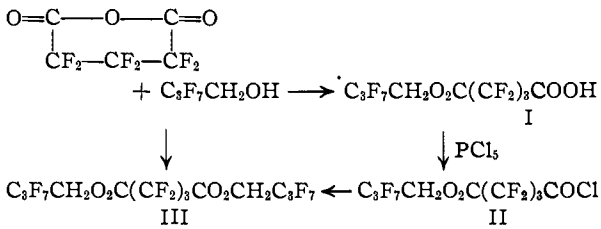
A general method for the synthesis of the almost completely fluorinated esters and diesters of 1,1-dihydroperfluoro alcohols and $\alpha,\alpha,\omega,\omega$-tetrahydroperfluoro glycols with perfluoromono- and dicarboxylic acids, by the action of perfluoro acid chlorides and anhydrides on the fluorinated alcohols and diols, is described. Several physical and chemical properties of these new compounds, as well as of certain intermediates, are given.

This is the introductory paper to studies which are being carried out for the purpose of relating and correlating various properties with the molecular structure and constitution of several series of fluorinated diesters. Since no general method is as yet available for the preparation of totally fluorinated esters,[1] it was decided to investigate first a series of esters of 1,1-dihydroperfluoro alcohols with perfluorocarboxylic acids, the only member of which to be reported is trifluoromethyl trifluoroacetate, obtained by Swarts.[2] It was found that the representative alcohol, 1,1-dihydroperfluorobutanol did not esterify at a practical rate *n*-perfluorobutyric acid either when the latter strong acid was employed in excess or when chloroform was used for the azeotropic removal of the water of esterification.[3] This chemically stable alcohol, however, did react slowly with the low boiling *n*-perfluorobutyryl chloride to form 1,1-dihydroperfluorobutyl perfluorobutyrate. In a similar manner, the higher boiling perfluoroöctanoyl chloride reacted more rapidly with 1,1-dihydroperfluorobutanol to give 1,1-dihydroperfluorobutyl perfluoroöctanoate. 1,1-Dihydroperfluoroethyl perfluorobutyrate was obtained on treating 1,1-dihydroperfluoroethanol with perfluorobutyryl chloride.

This method has been extended to the synthesis of $\alpha,\alpha,\omega,\omega$-tetrahydroperfluoroglycol esters of perfluoro acids. Excess perfluorobutyryl chloride reacted with 1,1,5,5-tetrahydro-1,5-perfluoropentanediol and with 1,1,6,6-tetrahydro-1,6-perfluorohexanediol to yield 1,1,5,5-tetrahydro-1,5-perfluoropentanediol di-*n*-perfluorobutyrate and 1,1,6,6-tetrahydro-1,6-perfluorohexanediol di-*n*-perfluorobutyrate, respectively.

The method is also applicable to the preparation of bis-1,1-dihydroperfluoroalkanol esters of perfluorodicarboxylic acids, although certain difficulties are still to be overcome in this case. These shortcomings arise from the fact that good methods are needed for the production of satisfactory yields of the intermediate acid chlorides of perfluorodicarboxylic acids. The difficulty in synthesizing perfluoroglutaryl chloride has been previously cited.[4] In the present study crude perfluoroadipyl chloride did form a diester with 1,1-dihydroperfluorobutanol, but its purity is questionable. On the other hand, the easily preparable perfluoroglutaric anhydride[4] made possible an excellent synthesis of bis-(*n*-1,1-dihydroperfluorobutyl) perfluoroglutarate in accordance with the scheme



Perfluoroglutaric anhydride was treated with *n*-1,1-dihydroperfluorobutanol in the molar ratio of 1:2, respectively. There was obtained 58.8% of the desired diester III and 26.1% of the half ester (I). I is readily converted into III by treating the acid chloride II with an equimolar quantity of the alcohol. The acidic monoester I was very stable

(1) See M. Hauptschein and A. V. Grosse, THIS JOURNAL, **74**, 4454 (1952).

(2) F. Swarts, *Bull. soc. chim. Belg.*, **43**, 476 (1934).

(3) E. E. Burgoyne and F. E. Condon, THIS JOURNAL, **72**, 3276 (1950).

(4) M. Hauptschein, C. S. Stokes and E. A. Nodiff, *ibid.*, **74**, 4005 (1952).

TABLE I

NEW COMPOUNDS

Compound	B.p., °C.	Mm.	n^tD	d^t_4	t, °C.	Carbon,[a] % Calcd.	Found	Hydrogen,[a] % Calcd.	Found	Mol. wt.[b] Calcd.	Found
$C_3F_7CO_2CH_2C_3F_7$	124	760	1.2875	1.6547	21.2	24.26	24.19	0.51	0.55	396	393
			1.2961	1.7057	0.0						
$C_7F_{15}CO_2CH_2C_3F_7$	81.5	35	1.2960	1.7565	25.0	24.18	24.09	.34	.35	596	598
			1.2997	....	15.0						
$C_3F_7CO_2CH_2(CF_2)_3CH_2O_2CC_3F_7$	131	30	1.3140	1.7085	23.0	25.84	25.75	.67	.61	604	603
			1.3222	1.7550	0.0						
$C_3F_7CO_2CH_2(CF_2)_4CH_2O_2CC_3F_7$[c]	85	1.5	1.3160	1.734	25.0	25.70	23.79	.62	.87	654	650
							24.04		1.03		
$C_3F_7CH_2O_2C(CF_2)_3CO_2CH_2C_3F_7$	129	30	1.3142	1.7090	24.0	25.84	26.00	.67	0.63	604	604
	105	8	1.3224	1.7551	0.0						
$C_3F_7CH_2O_2C(CF_2)_3COOH$	117	8	1.3285	....	22.0	25.61	25.84	.72	0.56	422	427
$C_3F_7CH_2O_2C(CF_2)_3COCl$	95	42	1.3299	....	21.0	8.05	8.01 (chlorine)				
$C_7F_{15}COCl$	129–130	744	1.3025	....	25.0	8.20	8.03 (chlorine)				

[a] Carbon and hydrogen analyses determined by Clark Microanalytical Laboratory, Urbana, Illinois. [b] Molcular weights determined from saponification equivalents. [c] This compound may be slightly impure as indicated by the carbon analysis. However, this analysis is quite difficult and results tend to be low at times due to incomplete decomposition of the stable fluorocarbon structure.

thermally, but was water-soluble and extensively hydrolyzed to perfluoroglutaric acid and 1,1-dihydroperfluorobutanol. No stable end-point, corresponding to the neutralization of the –COOH group, was obtained on titration with 0.1 *N* sodium hydroxide solution, but excellent results were obtained for complete saponification (see Table I).

By the interaction of perfluoroglutaric anhydride with $\alpha,\alpha,\omega,\omega$-tetrahydroperfluoro glycols, condensation polymers of the type $[-OCO(CF_2)_3COOCH_2-(CF_2)_nCH_2-]_n$ readily can be prepared.

The physical constants and analytical data for the new compounds prepared in these investigations are listed in Table I. All of the esters and diesters are non-flammable and insoluble in water. They are only very slowly hydrolyzed in 10% potassium carbonate solution, but are easily saponified in 10% potassium hydroxide solution. In general the rate of hydrolysis of these "fluorocarbon" esters is greater than that of less completely fluorinated esters.

The infrared absorption spectra of all of these esters and diesters have been taken. A complete description of these spectra as well as of other types of fluorine-containing esters will be published separately. It suffices to note here that the relatively large shift to lower wave lengths which has been observed previously[4] for the C=O stretching vibrations of esters in which only the acid portion is perfluorinated, is even further increased when the alcohol portion is also fluorinated. Quite naturally, however, the effect exerted by the perfluorinated cluster alpha to the carbonyl group (*i.e.*, in the acid portion) is much greater than the effect of fluorines in the alcohol portion of the molecule.

Experimental

Preparation of Perfluoroacyl Chlorides.—*n*-Perfluorobutyryl chloride[5] and *n*-perfluoroöctanoyl chloride were prepared in over 90 and 58% yields, respectively, by treating the perfluoro-fatty acids (Minnesota Mining and Manufacturing Company) with excess phosphorus pentachloride. Perfluoroöctanoyl chloride has not been reported previously (see Table I). When the two solids, perfluoroöctanoic acid (207 g., 0.5 mole) and phosphorus pentachloride (104.3 g.) were thoroughly shaken together to ensure adequate contact, the reaction mixture liquefied shortly with vigorous evolution of hydrogen chloride. After refluxing for four hours, the mixture was subjected to fractional distillation yielding as the first fraction, phosphorus oxychloride and finally 125 g. (58%) of the desired acid chloride, b.p. 129–130° (744 mm.). This yield, no doubt, can be increased considerably by allocating more effort to the recovery process.

Preparation of 1,1-Dihydroperfluoroalcohols and $\alpha,\alpha,\omega,\omega$-Tetrahydroperfluoroglycols. — 1,1-Dihydroperfluoroethanol was prepared using lithium aluminum hydride as described by Henne, *et al.*[6] In a similar manner, *n*-1,1-dihydroperfluorobutanol was prepared in 87–90% yields by treating perfluorobutyryl chloride with lithium aluminum hydride.

$\alpha,\alpha,\omega,\omega$-Tetrahydroperfluoropentanediol and -hexanediol were prepared in 86 and 85% yields by the lithium aluminum hydride reductions of diethyl perfluoroglutarate and diethyl perfluoroadipate, respectively, as previously described.[7] These diols boiled at 111.5° at 10 mm., and 100° at 3 mm., respectively, and their melting points checked with the previously reported values.[7]

Preparation of *n*-1,1-Dihydroperfluoroalkyl Perfluoroalkanoates.—*n*-Perfluorobutyryl chloride (51.15 g., 10% excess) was added dropwise to 40 g. (0.20 mole) of *n*-1,1-dihydroperfluorobutanol heated to the refluxing temperature. A slow reaction ensued which was followed by the rate of formation of hydrogen chloride gas. The reaction mixture was finally refluxed for two days. The product was then treated with 10% potassium carbonate solution until the upper aqueous layer gave a negative test for chloride ion. The lower layer was dried over anhydrous magnesium sulfate and was then rectified in a Podbielniak fractionating column. In addition to recovered 1,1-dihydroperfluorobutanol, there was isolated 31.7 g. (40% conversion) of 1,1-dihydroperfluorobutyl perfluorobutyrate, b. p. 123–124° (mostly 124° at 760 mm.). The net yield based on reacted alcohol was almost quantitative.

In a similar manner, 34 g. (20% excess) of perfluoroöctanoyl chloride reacted more rapidly than the above with 1,1-dihydroperfluorobutanol (13 g., 0.65 mole) to form 23.5 g. (61% conversion, net yield was almost quantitative) of 1,1-dihydroperfluorobutyl perfluoroöctanoate, b.p. 81.5° at 35 mm. In this case, the reaction mixture was refluxed for 10 hours and extracted as an ethereal solution.

Similarly, a 10% excess of perfluorobutyryl chloride was added to boiling 1,1-dihydroperfluoroethanol, which was heated under reflux for 2.5 days. In this case there was obtained only a 25% conversion to 1,1-dihydroperfluoroethyl perfluorobutyrate, $C_3F_7CO_2CH_2CF_3$, b.p. 92° at 737 mm., n^{25}D 1.278, d^{25}_4 1.565; mol. wt., calcd. 296; found (by saponification equivalent), 298.

(5) Minnesota Mining and Manufacturing Co., Brochure on Heptafluorobutyric Acid.

(6) A. L. Henne, R. M. Alm and M. Smook, THIS JOURNAL, **70**, 1968 (1948).

(7) E. T. McBee, W. F. Marzluff and O. R. Pierce, *ibid.*, **74**, 444 (1952).

Preparation of α,α,ω,ω-Tetrahydroperfluoroalkanediol Di-*n*-perfluorobutyrates.—*n*-Perfluorobutyryl chloride (10% excess) was added dropwise to 13.2 g. (0.0623 mole) of 1,1,5,5-tetrahydro-1,5-perfluoropentanediol heated to above the melting point. The reaction was carried out for two days, the mixture being finally heated to 150°, and was followed by the rate of formation of hydrogen chloride gas. The product was then treated with 10% potassium carbonate solution until the upper aqueous layer gave a negative test for chloride ion. The lower layer was dried over anhydrous magnesium sulfate and was finally fractionally distilled under vacuum. No unreacted glycol was detected, and there were isolated 23.25 g. (62% yield) of 1,1,5,5-tetrahydro-1,5-perfluoropentanediol di-*n*-perfluorobutyrate, b.p. 131° at 30 mm.

In a similar manner, 26.2 g. (0.1 mole) of 1,1,6,6-tetrahydro-1,6-perfluorohexanediol reacted with 5% excess of perfluorobutyryl chloride to give 20 g. of the desired diester, b.p. 82–85° (mostly 85°) at 1.5 mm., as well as 15 g. of recovered glycol, most of which precipitated out on cooling the reaction mixture. This represented a 30.6% conversion and a 71.6% yield of 1,1,6,6-tetrahydro-1,6-perfluorohexanediol di-*n*-perfluorobutyrate.

Preparation of Bis-(*n*-1,1-dihydroperfluorobutyl) Perfluoroglutarate.—Fifty-two grams (0.234 mole) of perfluoroglutaric anhydride prepared as previously described[4] was allowed to react with *n*-1,1-dihydroperfluorobutanol (93.6 g., 0.468 mole) at 180° for two days. Upon rectification there were isolated two compounds, namely, bis-(*n*-1,1-dihydroperfluorobutyl) perfluoroglutarate, III (83.2 g., 58.8%), which was washed and dried prior to analysis, and mono-*n*-1,1-dihydroperfluorobutyl perfluoroglutarate, I (25.8 g., 26.1%). Thus the total yield of the two products based on the anhydride was 84.9% of theory. The acid-ester, I, (20.0 g., 0.0474 mole) reacted with 10% excess phosphorus pentachloride to yield 14.4 g. (69.0%) of mono-*n*-1,1-dihydroperfluorobutyl perfluoroglutaryl chloride (II). This acid chloride-ester reacted with equimolar quantities of 1,1-dihydroperfluorobutanol in the previously described fashion to yield additional diester III.

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[CONTRIBUTION FROM THE SCHOOL OF PHARMACY, UNIVERSITY OF NORTH CAROLINA]

Palladium Catalysis. V.[1] The Hydrogenation of α-Oximino Ketones[2,3]

BY YEN-TSAI CHANG[4] AND WALTER H. HARTUNG

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A mechanism is proposed for the hydrogenation of α-oximino ketones which explains the stereospecificity of the reaction, whereby a single racemic modification is formed. The polar oxygen and nitrogen atoms of the substrate molecule adsorb on the catalyst to form a rigid ring-like structure. 1,4-Addition of hydrogen, followed by *cis*-addition of the second molecule of hydrogen, can give rise to only a single steric structure. Or, 1,2-addition to the same original ring-like complex forms an intermediate stage of which the steric structure determines the approach of the additional hydrogen molecule to the 3,4-double bond, giving rise to the same racemic modification.

The reduction of α-oximino ketones to the corresponding amino alcohols affords a convenient route to many compounds with pharmacological activity.[5] The mechanism by which these reactions proceed is of interest, first, because of the type of products that have been identified at the intermediate stages of hydrogenation and, second, because the amino alcohol is isolated always as a single racemic modification, although two diastereoisomeric racemates might be expected.

The character of the isolable intermediate stages, where more than one molecule of hydrogen is taken up, as well as of the final product itself, is a function of the catalytic process, as Linstead and co-workers have shown.[6] These authors, who reduced diphenic acid and phenanthrene derivatives over platinum oxide, explain the formation of perhydro products by postulating complete saturation at a single contact of the substrate molecule with the catalyst, that is, there is minimum desorption at partially hydrogenated stages; and they account for the predominant formation of a single racemic product on the basis of specific steric structure of the substrate–catalyst complex. Experimental results with α-oximino ketones suggest that somewhat analogous phenomena obtain; not all the hypothetical intermediate products have been obtained, and the final amino alcohol possesses a single steric structure.

The oximino ketones used in this study may be divided into three types, as in Table I, depending

TABLE I

α-OXIMINO KETONES

For types B and C the indicated likely pathways come into consideration.

Ar—CO—C—R
‖
NOH

	Ar =	R =	M.p. (uncor.), °C.	Ref.
Type A	C_6H_5	$COOC_2H_5$	118–119	5d
Type B	C_6H_5	H	124–126	7
	p-HOC_6H_4	CH_3	178–179	5a
	3,4-$(HO)_2C_6H_3$	CH_3	161–162	5a
Type C	C_6H_5	CH_3	113–114	8
	C_6H_5	$CH_2C_6H_5$	125–126	1

(1) For No. IV see W. H. Hartung and Y. T. Chang, THIS JOURNAL, **74**, 5927 (1952).

(2) Also No. XIX in Amino Alcohol Series; for No. XVIII see J. P. LaRocca and W. H. Hartung, *J. Am. Pharm. Assoc.*, **40**, 140 (1951).

(3) Presented before the Medicinal Chemistry Section, XIIth International Congress of Pure and Applied Chemistry, New York, September 12, 1951.

(4) Fellow, American Foundation for Pharmaceutical Education, 1948-1951.

(5) (a) W. H. Hartung, J. C. Munch, E. Miller and F. S. Crossley, THIS JOURNAL, **53**, 4149 (1931); (b) H. K. Iwamoto and W. H. Hartung, *J. Org. Chem.*, **9**, 513 (1944); (c) B. L. Zenitz and W. H. Hartung, *ibid.*, **11**, 444 (1946); (d) W. H. Hartung, T. T. Dittrich and Y. Chang, THIS JOURNAL, **75**, 238 (1953); (e) R. Baltzly and J. S. Buck, *ibid.*, **62**, 164 (1940).

(6) R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine and R. H. Whetstone, *ibid.*, **64**, 1985 (1942).

(7) W. M. Whaley, thesis, University of Maryland, 1947.

(8) Obtained from Sharp and Dohme through the courtesy of Dr. James M. Sprague.