better than acetone cyanohydrin nitrate as an nitrating agent for sterically hindered amines.

The reaction was studied to determine the optimum conditions for obtaining the maximum yield of product. In certain instances (*cf.* Table I), higher yields were obtained using ether or an ether–hexane mixture (2:1 by volume) as the solvent rather than pure hexane. Low temperatures and alternate additions of *n*-butyllithium and ethyl nitrate seemed to increase the yields of product. Maximum yields were obtained when the ratio of reactants of *n*-butyllithium-amine-ethyl nitrate was 2:1:1.

Experimental

Materials.—The hexane was mechanically stirred overnight with concentrated sulfuric acid, washed with aqueous sodium carbonate and water, and finally dried over sodium. For some of the reactions, the hexane was dried further by distillation over lithium aluminum hydride, but this seemed to make very little difference in the resultant yield. The ethyl ether was dried over sodium, and the liquid amines were either stored over sodium hydroxide pellets or distilled over calcium oxide to remove traces of water. The *n*-butyllithium reagent was a 15% solution in hexane (Foote Mineral Co., New Johnsville, Tenn.). Phenyllithium was prepared by treating bromobenzene with lithium in dry ether.[8]

Procedure.—The basic procedure for the preparation of the primary aliphatic nitramines is outlined as follows. The solvent (200–300 ml.) was placed in a flask equipped with a mechanical stirrer, Dry Ice condenser, and two dropping funnels containing ethyl nitrate and *n*-butyllithium reagent. The reaction mixture was vigorously stirred while immersed in a Dry Ice–acetone bath and was kept under a dry nitrogen atmosphere. The amine (0.33 mole) was added to the flask followed by rapid addition of 0.33 mole of the *n*-butyllithium reagent. Then 0.17 mole of ethyl nitrate was added dropwise during a 1-hr. period and the reaction mixture was stirred for an additional hour. Two more addition steps followed, both consisting of a rapid addition of 0.17 mole of *n*-butyllithium reagent and a dropwise addition of 0.083 mole of ethyl nitrate over a period of 0.5 hr., after which the reaction was stirred for an additional 0.5 hr. After the reaction mixture was allowed to come to room temperature, sufficient water was added to dissolve the lithium salt of the nitramine and any other solid material. The water layer was separated from the hexane layer, acidified at 0° to pH 1 with hydrochloric acid, and extracted with ether. The ether extract was dried over anhydrous magnesium sulfate and filtered and the solvent was removed by distillation. The crude product was distilled at 10-mm. pressure or less (see Table I for yields of purified product).

Acknowledgment.—The elemental analysis was performed by A. Bernhardt, Mülheim (Ruhr), Germany. We thank the National Science Foundation for support of D. B. L. and Drexel Institute of Technology for a faculty research grant.

[8] H. Gilman and J. W. Morton, *Org. Reactions*, **8**, 286 (1954).

Perfluorobiacetyl from the Oxidation of Perhalobutenes[1]

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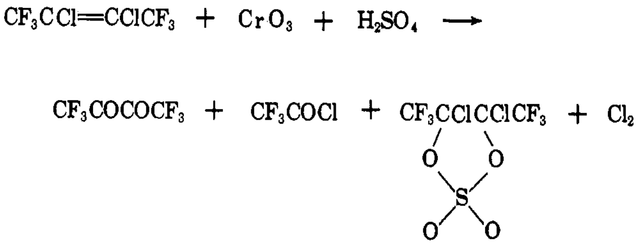
Only a limited number of perfluoro α,β-diketones have been described in the literature. The first member, perfluorobiacetyl (PFBA), has not been described before, although several attempts have been made in this direction.[2-4] Tucker and Whittle[5] recently indicated that they thought the reason PFBA had not been observed in the hexafluoroacetone photolysis was its instability. The only presently known examples of fluorinated open-chain α,β-diketones are those in which R of R–CO–CO–R is perfluoropropyl,[6] perfluoroisopropyl,[7] and octafluorobutyl.[6] The cyclic diketone, perfluorocyclobutane-1,2-dione, has also been described.[8] The straight-chain compounds were prepared by the condensation of polyfluoroacyl chlorides in the presence of nickel carbonyl to give enediol diesters which pyrolyzed to the α,β-diketones,[6] the perfluoroisopropyl compound was made by the addition of oxalyl fluoride to perfluoropropene catalyzed by fluoride ion,[7] and the cyclic member of this series was made by the hydrolysis of 1,2-dimethoxyhexafluorocyclobutane.[8]

We have now synthesized the first and simplest member of the series by a new and relatively simple method. PFBA was obtained from 2,3-disubstituted 1,1,1,4,4,4-hexafluoro-2-butenes and from perfluoro-2-butyne by oxidation with chromium trioxide in sulfuric acid. The best synthesis utilized 2,3-dichloro-1,1,1,-4,4,4-hexafluoro-2-butene which is the highest boiling of the starting materials tried and gave the best yield, about 35%. The three other compounds examined were low-boiling materials and were only partly oxidized when passed through a solution of chromium trioxide in sulfuric acid at 50°.



$$CF_3CCl{=}CClCF_3 + CrO_3 + H_2SO_4 \longrightarrow$$

$$CF_3COCOCF_3 + CF_3COCl + \underset{\substack{O\quad O\\ S\\ O\quad O}}{CF_3CClCClCF_3} + Cl_2$$

PFBA is a deep yellow liquid boiling at 20° and freezing at −20°. This boiling point is 68° lower than that of biacetyl, but such a difference is not unique; most perfluorinated compounds have a boiling point lower than their hydrocarbon analogs. Notably, the perfluorinated carbonyl compounds of two, three, four, and eight carbon atoms all boil about 70–80° lower than their hydrocarbon equivalents. The ultraviolet spectrum of PFBA is very close to that of biacetyl, having maxima at 422 mμ (ε 13.9) and 443 mμ (ε 13.0) and shoulders at 290 mμ (ε 19.4), 303 (ε 14.9), 415 (ε 13.7), and 450 (ε 11.8). Biacetyl has maxima at 280 and 420 mμ and a shoulder at 440 mμ. The infrared spectrum is, as expected, different from that of biacetyl, and has

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[1] Presented at the 2nd International Symposium on Fluorine Chemistry, Estes Park, Colo., July 1962.

[2] R. N. Haszeldine, *J. Chem. Soc.*, 584 (1951).

[3] R. N. Haszeldine, *Nature*, **168**, 1028 (1951); E. T. McBee, O. R. Pierce, H. W. Kilbourne, and J. A. Barone, *J. Am. Chem. Soc.*, **75**, 4090 (1953).

[4] S. J. W. Price and K. O. Kutschke, *Can. J. Chem.*, **38**, 2128 (1960), and references cited therein.

[5] B. G. Tucker and E. Whittle, *Proc. Chem. Soc.*, 93 (1963).

[6] J. J. Drysdale and D. D. Coffman, *J. Am. Chem. Soc.*, **82**, 511 (1960); J. J. Drysdale (to E. I. du Pont de Nemours and Co.), U. S. Patent 3,012,-069 (Dec. 5, 1961).

[7] R. D. Smith, F. S. Fawcett, and D. D. Coffman, *J. Am. Chem. Soc.*, **84**, 4285 (1962).

[8] D. C. England, *ibid.*, **83**, 2205 (1961); E. I. du Pont de Nemours and Co. (by D. C. England), British Patent 873,222 (July 19, 1961).

strong bands at 5.68, 7.88, 8.24, 8.46, 11.61, and 14.22 μ.

PFBA reacts readily with *o*-phenylenediamine in the typical identification reaction of α,β-diketones to produce 2,3-bis(trifluoromethyl)quinoxaline, and with strong bases it gives the expected haloform reaction of trihalomethyl ketones and aldehydes which in this case evolves fluoroform. However, unlike nonfluorinated ketones, it reacts readily and exothermically with water and with alcohols to give hydrates and hemiketals, of which both mono- and diaddition products can be isolated.

In addition to PFBA, oxidation of 2,3-dichloro-1,1,1,-4,4,4-hexafluoro-2-butene gives trifluoroacetyl chloride, 2,3-dichloro-1,1,1,4,4,4-hexafluorobutane-2,3-diol cyclic sulfate, and chlorine. The cyclic sulfate isolated in this work is the first example of a perhalogenated cyclic sulfate. It is quite stable thermally, but hydrolyzes rapidly in aqueous acetone or aqueous ethanol to PFBA hydrate (or alcoholate) and hydrochloric and sulfuric acids. It reacts directly with *o*-phenylenediamine to give 2,3-bis(trifluoromethyl)quinoxaline and with strong base to evolve fluoroform. Unlike hydrocarbon cyclic sulfates, which are solids, this compound is a liquid despite its high molecular weight.

Oxidation of perfluoro-2-butene, perfluoro-2-butyne, and 1,1,1,4,4,4-hexafluoro-2-butene, performed by bubbling these through a mixture of chromium trioxide in fuming sulfuric acid, because of the low boiling points, also yielded perfluorobiacetyl. The yields are given in Table I.

TABLE I

Compd.	B.p., °C.	PFBA, % yield
$CF_3CF{=}CFCF_3$	0	7.3, 2.7
$CF_3C{\equiv}CCF_3$	−24	15.2, 17.1
$CF_3CH{=}CHCF_3$	8.5	26.6

Sulfur trioxide concentration has a pronounced effect on the yield of the cyclic sulfate and trifluoroacetyl chloride, though little effect on that of PFBA (see Table II). Thus, the proportion of intermediate which loses chlorine leading to PFBA is independent of the sulfur trioxide concentration, but that portion which does not lose chlorine is open to competition for conversion to trifluoroacetyl chloride and the cyclic sulfate, the ratio of products depending on the concentration of sulfur trioxide. It appears, therefore, that at least two intermediates are involved. One being susceptible to attack by sulfur trioxide and the other not. They may be formed independently or one may be formed from the other. The yield of PFBA was greater at higher temperatures with a correspondingly lower yield of the cyclic sulfate. Thus the ratio of these two intermediates may be temperature dependent.

TABLE II

	Product yield, %			
SO_3, mole %	PFBA	CF_3COCl	Sulfate	Cl_2
23.8	35	8.6	42.3	51.5
4.0	17[a]	19.5	13.0	34.1[a]
0	34.7	26.2	7.0	62.6
1.8 (H_2O)	6.2	25.1[b]	0	76.8
58.0 (H_2O)	0	0[b]	0	32.8

[a] Some of these products were lost in the work-up of the experiment. [b] No attempt was made to isolate trifluoroacetic acid.

When chlorate was the oxidizing agent in fuming sulfuric acid no cyclic sulfate was isolated, and when perchlorate was the oxidizing agent no trifluoroacetyl chloride was found. This difference in products probably arises from intermediates similar to those in the chromium trioxide reaction but in which the intermediate formed with chlorate collapses possibly to a cyclic structure which forms trifluoroacetyl chloride and the intermediate formed with perchlorate remains open for attack by sulfur trioxide.

A strong stereochemical preference is shown in this reaction. When the oxidation of a 47:53 *cis-trans* mixture of 2,3-dichloro-1,1,1,4,4,4-hexafluoro-2-butene was stopped after two-thirds had reacted, the remaining butene contained 98% of the *cis* and 2% of the *trans* isomer. Also, partial oxidation in trifluoroacetic acid and in acetic acid left a greater concentration of *cis*- than *trans*-butene. This marked steric preference is unexpected since the difference in the molecular diameters of chlorine, 1.80 Å., and the trifluoromethyl group, 1.97 Å., is not large. The ratio of *cis* to *trans* isomers in the mixture of butene was determined by gas chromatography on a 20% silicone on Celite packed column.[9]

Additional work is expected to show the versatility of this reaction in the oxidation of related olefins, especially those of higher molecular weight and of cyclic structure. More information is also needed on the cause of the stereochemical effect. The heats and entropies of activation for each of the isomers should prove enlightening.

PFBA is a most interesting compound and is proving to be very reactive. We have started studies on its photochemical reactions, and its condensation reactions in the preparation of heterocyclic compounds. This work will be reported at a later date.

Experimental[10]

Chromic Acid Oxidation of 2,3-Dichloro-1,1,1,4,4,4-hexafluoro-2-butene.—To 110.0 g. (1.10 moles) of chromium trioxide in 532 g. of fuming sulfuric acid (20% sulfur trioxide) at 60–70° was added 116 g. (0.50 mole) of 2,3-dichloro-1,1,1,4,4,4-hexafluoro-2-butene[11] over a 1.5-hr. period. The mixture stood overnight at room temperature and and was then heated to 65° over a 6.5-hr. period with a nitrogen purge to remove the products from the oxidizing medium. There was collected 88.0 g. of products in a Dry Ice–acetone cooled trap. Distillation of the cold-trap material yielded 16 g. (0.23 mole), 45.2% of chlorine, b.p. −33 to −30°; 10 g. (0.08 mole), 24.0%, of trifluoroacetyl chloride, b.p. −20 to −15°; 30 g. (0.15 mole), 31.0%, of PFBA, b.p. 17–20°; and 14 g. (0.06 mole), 12.0%, of 2,3-dichloro-1,1,1,4,4,4-hexafluoro-2-butene, b.p. 65–70°. The material remaining in the kettle was green and on cooling formed a gel. Addition of water caused the separation of 61 g. (0.185 mole), 37.1%, of an oil layer. Distillation gave a colorless liquid, b.p. 67–68° (50 mm.), $n^{20}\mathrm{D}$ 1.3730, containing two components indicated by gas chromatography which analysis indicated to be stereoisomers of 2,3-dichloro-1,1,1,4,4,4-hexafluorobutane-2,3-diol cyclic sulfate.

Anal. Calcd. for $C_4Cl_2F_6O_4S$: C, 14.60; Cl, 21.59; S, 9.73. Found: C, 14.54, 14.65; Cl, 21.12; S, 10.10.

The infrared and mass spectra are consistent with the proposed structure.

On careful distillation the higher boiling isomer, b.p. 68° (50 mm.), $n^{20}\mathrm{D}$ 1.3740, was isolated in over 99% purity.

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[9] See F. Dickinson, R. Hill, and J. Murray, *J. Chem. Soc.*, 1441 (1958).

[10] All boiling and melting points are uncorrected.

[11] 2,3-Dichloro-1,1,1,4,4,4-hexafluoro-2-butene was prepared by the method of J. W. Clark and C. E. Rectenwald [(to Union Carbide Corp.), U. S. Patent 3,149,170 (Sept. 15, 1964)].

The starting material generally used was a mixture of 46.7% *cis*- and 53.3% *trans*-2,3-dichloro-1,1,1,4,4,4-hexafluoro-2-butene. One run was stopped when approximately 70% had reacted. The recovered butene contained 98% of the *cis* isomer and 2% of the *trans*.

A series of similar runs was made with varying amounts of SO_3 and water in the sulfuric acid to study the effect of varied concentrations of sulfur trioxide on the oxidation. The results are summarized in Table II.

To test the possible use of other acidic solvents, runs were made as described above but using acetic anhydride, acetic acid, trifluoroacetic acid, and phosphoric acid containing phosphorus pentoxide as solvents. In phosphoric acid there was only slight reaction, and the recovered starting material had a yellow color. However, neither PFBA nor chlorine could be positively identified. In runs using acetic anhydride, acetic acid, and trifluoroacetic acid, oxidation was very slow. PFBA was not detected in any of these runs, but the recovered butene from the acetic acid and trifluoroacetic acid runs was richer in the *cis* isomer than was the starting material.

A distillate, b.p. 62–71°, obtained from the run using trifluoroacetic acid was a mixture of chromyl chloride in trifluoroacetic acid.

Chromic Acid Oxidation of Hexafluoro-2-butyne, 1,1,1,4,4,4-Hexafluoro-2-butene, and Perfluoro-2-butene.—The fluorinated compound was bubbled through a stirred mixture of 44–50 g. (0.44 to 0.50 mole) of chromium trioxide in 400–500 g. of fuming sulfuric acid at 60–70°. The products were collected in Dry Ice–acetone cooled traps and then distilled or analyzed by gas chromatography. The results are shown in Table I.

Perchlorate Oxidation of 2,3-Dichloro-1,1,1,4,4,4-hexafluoro-2-butene.—Potassium perchlorate (40 g., 0.29 mole) was added in four portions to 600 g. of fuming sulfuric acid at 60–65° while also adding 61 g. (0.26 mole) of 2,3-dichloro-1,1,1,4,4,4-hexafluoro-2-butene. Yellow liquid collected in Dry Ice–acetone cooled traps and the kettle material became orange. Distillation of the material from the traps gave 2 g., 7%, of PFBA, and dilution of the kettle material gave 13 g., 15%, of the cyclic sulfate.

A smaller run in which the kettle was heated at 75–95° yielded 35.6% of PFBA, isolated as 2,3-bis(trifluoromethyl)quinoxaline, and a very small amount of cyclic sulfate.

Chlorate Oxidation of 2,3-Dichloro-1,1,1,4,4,4-hexafluoro-2-butene.—To 500 g. of fuming sulfuric acid at 25–50° were added 13.5 g. (0.11 mole) of potassium chlorate and 25 g. (0.11 mole) of 2,3-dichloro-1,1,1,4,4,4-hexafluoro-2-butene in three portions each. After standing over the weekend the mixture was heated to 96° with a slow nitrogen purge, and the products were collected in a Dry Ice–acetone cooled trap. Distillation gave 1.5 g. (0.01 mole), 5%, of trifluoroacetyl chloride and 0.5 g. (0.003 mole), 3%, of PFBA. No cyclic sulfate was isolated.

2,3-Bis(trifluoromethyl)quinoxaline.—Addition of PFBA to excess *o*-phenylenediamine at 0° caused an exothermic reaction. Recrystallization from an ethanol–water mixture gave white crystals, m.p. 117–118°. The same product was obtained from PFBA hydrate or 2,3-dichloro-1,1,1,4,4,4-hexafluorobutane-2,3-diol cyclic sulfate with *o*-phenylenediamine by heating in water.

Anal. Calcd. for $C_{10}H_4F_6N_2$: C, 45.1; H, 1.60; N, 10.52. Found: C, 44.93, 44.87; H, 1.59, 1.56; N, 10.32.

Steroids. XX.[1] Some 2-Aza- and 3-Aza-5α-cholestanes[2–5]

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The synthesis of 2-aza- and 3-azasteroids for biological evaluation was of interest to us as an extension of the work on azasteroids.[8–12] Hara[13] had prepared 2-aza- and 3-azacholanes by a Beckmann rearrangement of methyl 2-oximino-A-nor-5β-cholanate and was able to separate the lactams formed by chromatography. Shoppee[14] reported the preparation of 3-aza-A-homo-5α-cholestan-4-one by the Beckmann rearrangement of 5α-cholestan-3-one oxime. Later, after preparing this lactam by a more rigorous route, he recognized that the original product was a mixture and stated ". . . it now appears that this reputed compound is an inseparable mixture, or a molecular compound, of the 3-aza-A-homo-5α-cholestan-4-one and the isomeric Beckmann rearrangement product 4-aza-A-homo-5α-cholestan-3-one."[15] Although Hara and Shoppee employed the Beckmann rearrangement in the preparation of azasteroids, our experience indicates that the Schmidt reaction conducted in polyphosphoric acid usually gives superior yields and fewer purification problems.[12,16]

The reaction of A-nor-5α-cholestan-2-one (I) with hydrazoic acid in polyphosphoric acid gave a mixture of lactams (III), 2-aza-5α-cholestan-3-one (IIIa) and 3-aza-5α-cholestan-2-one (IIIb), in 77% yield. The Beckmann rearrangement of A-nor-5α-cholestan-2-one oxime (II) in polyphosphoric acid gave the same mixture, but in lower yield (30%). The product appeared to exist as a uniform, homogeneous material, m.p. 220–221°, after purification. Attempts to separate these isomers from this mixture were unsuccessful, but their presence was established by the preparation and separation of some derivatives.

Treatment of III with phosphorus pentachloride[17] yielded a mixture of dichloro lactams which were separated into two fractions, m.p. 227–229 and 209–211°, in a 1:1 ratio. The carbonyl absorption in these products was shifted 0.18 μ toward a smaller wave length as for α,α-dichloroamides.[18] The higher melting fraction yielded 4-chloro-2-aza-4-cholesten-3-one (VI) on treatment with collidine establishing that it was 4,4-dichloro-2-aza-5α-cholestan-3-one (IV). The lower melting fraction, 1,1-dichloro-3-aza-5α-cholestan-2-one (V), which is unable to eliminate HCl, was unchanged by this treatment.

N-Methylation of III with methyl iodide in the presence of sodium hydride resulted in the recovery of two crystalline products, fraction I, m.p. 137–138°, and

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[1] For paper XIX, see N. J. Doorenbos and K. A. Kerridge, *J. Heterocyclic Chem.*, in press.

[2] Presented at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept. 1963.

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[7] Noxzema Foundation Fellow, 1958–1960; Dunning Foundation Fellow, 1960; National Institutes of Health Fellow, 1961–1962.

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[16] N. J. Doorenbos and M. T. Wu, *J. Org. Chem.*, **26**, 2548 (1961).

[17] W. Francis, J. Thornton, J. Werner, and T. Hopkins, *J. Am. Chem. Soc.*, **80**, 6238 (1958).

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