melting point determination, analysis by t.l.c., as well as comparison of infrared spectra.

20β-Acetoxy-4,16-pregnadien-3-one (IId).—20β-Hydroxy-4,16-pregnadien-3-one (150 mg.) was dissolved in 1 ml. of dry pyridine and cooled in ice. Acetic anhydride (1 ml.) was added, and the solution was allowed to stand at room temperature for 18 hr. It was then poured into 30 ml. of ice slush and stirred for 10 min., and the resulting white precipitate was filtered and air-dried. Crystallization from acetone–isopropyl ether gave a first crop of 82 mg., m.p. 155–156°. An analytical sample had m.p. 156–157°; $[\alpha]^{24}D$ +160°; $\Delta\nu$ 52.5 (18-H), 79.5, and 86 (21-H) c.p.s.

Anal. Calcd. for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.16; H, 9.48.

Oxidation of IIa and IIb with Manganese Dioxide.—In each case, 50 mg. of the respective 20-ol was dissolved in 10 mg. of chloroform. Manganese dioxide, 1 g., was added and the suspension was stirred for 24 hr. Filtration and concentration gave a crystalline residue matching the R_f of 16-dehydroprogesterone (0.6 in the ligroin–propylene glycol system). Crystallization from isopropyl ether in each case gave this compound (V), as verified by the usual criteria.

Reduction of 20α-Hydroxy-5,16-pregnadien-3-one Ethylene Ketal (IIIa).—A solution of ketal IIIa in ethanol was shaken in the presence of palladium on charcoal. Approximately 1 molar equiv. of hydrogen was taken up in 20 min. Spectral analysis of the crude crystalline product indicated a mixture of the expected 16,17-dihydro-20α-hydroxy ketal and about 15% of a material judged to be a saturated 20-carbonyl compound resulting from isomerization of the allylic alcohol. Thus, the n.m.r. spectrum showed major peaks at 41 (18-H), 70.5, and 76.5 (21-H) c.p.s. as expected of the desired product and much weaker signals at 38.5 (18-H) and 127 (21-H) c.p.s., together with a weak band at 5.85 μ in the infrared, pointing to the presence of a minor amount of a saturated ketone.

The ketal group was removed by warming the compound in 80% acetic acid for 30 min., diluting with water, and collecting the precipitate by filtration. A brief sublimation at 85° (0.01 mm.) effectively removed the more volatile 20-carbonyl impurity and the residue was then crystallized from ethyl acetate–petroleum ether. The product had m.p. 147° and 159–162° and did not depress the melting point of an authentic sample of 20α-hydroxy-4-pregnen-3-one, lit.[6b] m.p. 161–162°. The infrared spectra of the samples were identical.

Reduction of 20β-Hydroxy-5,16-pregnadien-3-one Ethylene Ketal (IIIb).—The reduction of the 20β-isomer was carried out in the same manner as described for the 20α-compound. The crude solid had m.p. 182–186° and appeared to be free of any saturated carbonyl by-product. The n.m.r. spectrum had peaks consistent with a saturated 20β-hydroxypregnane derivative[5]: 47 (18-H), 65, and 71 (21-H) c.p.s. Cleavage of the ketal function by warming in dilute acetic acid followed by recrystallization of the product from acetone–petroleum ether gave pure 20β-hydroxy-4-pregnen-3-one, m.p. 175.5–178°, mixture melting point with an authentic sample showed no depression, lit.[6b] m.p. 174–175°.

Preparation and Reactions of Fluoro Ketone Cyanohydrins

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Fluorinated aldehydes and ketones are strong Lewis acids, forming stable hydrates, hemiketals and acetals, and amine addition products. Strong nucleophiles such as alkoxide ion react with fluorinated carbonyl compounds giving both addition and cleavage of the carbon–carbon bond.[2]

We have found that perfluoroacetone and several chlorofluoroacetones react smoothly with both potassium and sodium cyanide in tetrahydrofuran (THF) or ether–THF to give the THF-soluble salts of the acetone cyanohydrins. Acidification of the salts gives the cyanohydrins. This method is a new and simple laboratory procedure for the preparation of these compounds. Neither 1,2-dichlorotetrafluorocyclopentenone-3 nor trichloroacetaldehyde gave the corresponding cyanohydrin salts when treated with sodium cyanide in THF; the cyclopentenone gave a glassy trimeric product and trichloroacetaldehyde gave only tar.[3]

Yields of cyanohydrin salts decreased with increasing numbers of chlorine atoms in the ketone. Cyanide ion was consumed in other ways which must reflect both the greater ease of cleavage of the carbon–carbon bond and the ease of displacement of chlorine by cyanide ion.

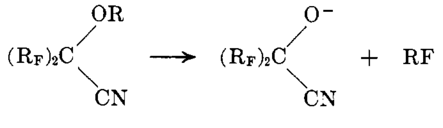
Several esters of dichlorotetrafluoroacetone cyanohydrin were prepared by adding the appropriate acyl, sulfur or phosphorus chloride, or anhydride to the cyanohydrin or the cyanohydrin sodium salt in THF. Table I summarizes these results.

Dichlorotetrafluoroactone cyanohydrin was degraded by a variety of reagents that normally effect replacement of hydroxyl groups. Treatment of the cyanohydrin with either sulfur tetrafluoride[4] or diethylaminotrifluorochloroethane[5] gave only tar.

None of the desired chloronitrile was found in reactions of the cyanohydrin or its sodium salt with the sulfur or phosphorus chlorides. Long heating of the dichlorotetrafluoroacetone cyanohydrin tetrachloro phosphate ester at 250° gave a complex mixture of high-boiling products and starting material.

Probably these reactions failed because of the repression by neighboring fluorine of carbonium ion character in the transition states for reaction. For this same reason, fluoro alcohols fail to give the corresponding chlorides with these same reagents. However, Knunyants has reported the conversion of α,α-bis(trifluoromethyl)-p-hydroxybenzyl alcohol to the corresponding chloride using thionyl chloride.[6] In this case, repression of carbonium ion character in the transition state by the trifluoromethyl groups is off-set by the enhanced stability of the benzyl carbonium ion.

Several of the esters were treated with potassium or sodium fluoride in a variety of solvents. The reactions were rapid even at room temperature and in each case the only product isolated corresponded to displacement of 1,3-dichlorotetrafluorocyanoisopropoxy anion by fluoride ion. Thus, p-nitrobenzenesulfonyl fluoride and p-nitrobenzoyl fluoride were isolated from reactions of potassium fluoride with the corresponding esters. No product was isolated from reaction of the bisulfite ester; double displacement by fluoride ion here would have



$$(R_F)_2C(OR)(CN) \longrightarrow (R_F)_2C(O^-)(CN) + RF$$

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(1) Allied Chemical Corp.

(2) C. Woolf, Abstracts of Papers presented at 132nd National Meeting of the American Chemical Society, New York, N. Y., Sept., 1957, p. 23-M.

(3) Aqueous cyanide ion readily reacts with α-haloaldehydes giving acids; see F. D. Chattaway and H. Irving, *J. Chem. Soc.*, 1038 (1929).

(4) Sulfur Tetrafluoride, Technical Information Bulletin, Organic Chemicals Department, E. I. du Pont de Nemours and Co., 1959.

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TABLE I

1,3-DICHLOROTETRAFLUOROACETONE CYANOHYDRIN ESTERS

Reagent used	Ester $(\mathrm{ClCF_2})_2\mathrm{C}<^{\mathrm{OR}}_{\mathrm{CN}}$	M.p. or b.p. (mm.), °C.	% yield
p-Nitrobenzoyl chloride	*p*-Nitrobenzoate	112–113	65
p-Nitrobenzenesulfonyl chloride	*p*-Nitrobenzenesulfonate	105–107	94
Trifluoroacetic anhydride	Trifluoroacetate	31 (23)	30 crude, 19 pure
Phosphorus trichloride	Tris(1,3-dichlorotetrafluorocyanoisopropyl) phosphite	53–55 (0.1)	15
Phosphorus pentachloride	1,3-Dichlorotetrafluorocyanoisopropyl tetrachlorophosphate	115 (25)	28

afforded thionyl fluoride, and, while some gas was evolved in this reaction, no evidence was adduced for the presence of thionyl fluoride. A careful search for volatile fragments was made in each case, using gas chromatography, and none was detected.

Experimental

1,3-Dichlorotetrafluoroacetone Cyanohydrin Sodium Salt.—In a 250-ml. three-necked flask, fitted with stirrer and dropping funnel, were placed 100 ml. of tetrahydrofuran and 4.9 g. (0.10 mole) of sodium cyanide. 1,3-Dichlorotetrafluoroacetone (20 g., 0.10 mole) was added dropwise to the stirred, cold (5°) suspension. The sodium cyanide dissolved within 1 hr., giving an orange solution. Evaporation of the solution at the water pump, followed by trituration with ether, afforded 19.5 g. of white powder (79% yield).

Anal. Calcd. for $C_4Cl_2F_4NNaO$ (248): N, 5.65; Na, 9.32. Found: N, 6.03, 5.76; Na, 9.49.

Similar experiments using perfluoroacetone, 1,1,3-trichlorotrifluoroacetone, and 1,1,3,3-tetrachlorodifluoroacetone afforded 87, 49, and 32% yields, respectively, of the cyanohydrin sodium salts of these ketones. Potassium cyanide was found to react more readily with all of the ketones but gave lower yields in tetrahydrofuran than did sodium cyanide. A suspension of potassium cyanide in ether containing 5 vol. % of tetrahydrofuran reacted rapidly and cleanly with all of the ketones, giving white slurries of the potassium salts.

1,3-Dichlorotetrafluoroacetone Cyanohydrin *p*-Nitrobenzoate.—A solution of 4.8 g. (0.026 mole) of *p*-nitrobenzoyl chloride in 10 ml. of dry tetrahydrofuran was added to a stirred solution of 6.5 g. (0.026 mole) of the cyanohydrin sodium salt in 50 ml. of dry tetrahydrofuran at 0°. The mixture was heated at 50° for 3 hr. and the solvent was removed at the water pump. The residue was triturated with 100 ml. of boiling heptane. The suspension was filtered hot and the filtrate was cooled in ice and filtered to give 7.5 g. (65% yield) of the benzoate ester, m.p. 112–113°, $\lambda_{\max}^{\mathrm{CCl_4}}$ 5.60 μ. A sample was recrystallized in good yield from heptane: m.p. 112–113°.

Anal. Calcd. for $C_{11}H_4Cl_2F_4N_2O_4$ (375.1): C, 35.2; H, 1.08; Cl, 18.9. Found: C, 35.4; H, 1.43; Cl, 18.8.

1,3-Dichlorotetrafluoroacetone Cyanohydrin *p*-Nitrobenzenesulfonate Ester.—*p*-Nitrobenzenesulfonyl chloride (45 g., 0.20 mole) (Eastman White Label) in 60 ml. of THF was added dropwise to 0.20 mole of the cyanohydrin sodium salt in 100 ml. of THF. The mixture was heated to 50° for 3 hr., then evaporated on the steam bath. The crystalline residue was dissolved in hot heptane–benzene (1:1) and filtered. A total of 61 g. (74% yield) of sulfonate ester was obtained in two crops (47 and 14 g.): m.p. 106–108°; $\lambda_{\max}^{\mathrm{CCl_4}}$ 6.5, 7.1, and 8.3 μ.

Anal. Calcd. for $C_{10}H_4Cl_2F_4N_2O_5S$ (411): C, 29.2; H, 0.975; Cl, 17.5; N, 6.83; S, 7.74. Found: C, 29.4; H, 1.20; Cl, 16.8; N, 6.85; S, 7.37.

1,3-Dichlorotetrafluoroacetone Cyanohydrin Trifluoroacetate Ester.—Distilled trifluoroacetic anhydride (21 g., 0.10 mole) was added slowly to a chilled, fine suspension of 0.10 mole of cyanohydrin sodium salt in 50 ml. of ether. The mixture was refluxed 1 hr., distilled on a 15-in. spinning-band column at 1 atm. to remove ether, and then distilled at 45 mm. to give 8.7 g. of a mixture of the desired ester (5.4 μ) and trifluoroacetic acid (5.6 μ). Careful redistillation at 23 mm. gave five fractions containing decreasing amounts of free acid. The last two fractions (very moisture sensitive) were taken for characterization: 4.19 g. (13%); b.p. 30.5–31° (23 mm.); $\lambda_{\max}^{\mathrm{neat}}$ 5.43, 7.52, and 8–9 μ.

Anal. Calcd. for $C_6Cl_2F_7NO_2$ (323): C, 22.4; Cl, 22.0; N, 4.34. Found: C, 23.1; Cl, 20.0; N, 4.02.

Tris(1,3-dichlorotetrafluorocyanoisopropyl) Phosphite.—A mixture of 9.4 g. (0.066 mole) of distilled phosphorus trichloride and 49.8 g. (0.20 mole) of cyanohydrin sodium salt in 100 ml. of THF was stirred at 25° for 40 hr., then filtered. The filtrate was stripped of solvent at the water pump, then distilled through a 15-in. spinning-band column. A fraction boiling at 95° (1 mm.) was taken: 7.3 g. (15%); $\lambda_{\max}^{\mathrm{CCl_4}}$ 6.0, 7.8, and 8.5–9.5 μ.

Anal. Calcd. for $C_{12}Cl_6F_{12}N_3O_3P$ (706): C, 20.4; Cl, 30.2; N, 5.95; P, 4.33. Found: C, 20.0; Cl, 31.0; N, 5.81; P, 4.09.

Bis(1,3-dichlorotetrafluorocyanoisopropyl) Sulfite.—A mixture of 11.9 g. (0.10 mole) of thionyl chloride and 24.9 g. (0.10 mole) of cyanohydrin sodium salt in 60 ml. of THF was stirred at 25° for 15 hr. After removal of solvent at the water pump, the residual liquid was filtered from the sodium chloride using ether solvent. Distillation of the mixture, ultimately at *ca.* 0.01 mm., gave 4.19 g. (19%) of a fuming liquid: b.p. 51–53° (0.01 mm.); $\lambda_{\max}^{\mathrm{CCl_4}}$ 6.0, 7.7, and 8–9.5 μ.

Anal. Calcd. for $C_8Cl_4F_8N_2O_3S$ (498): C, 19.3; Cl, 28.5; N, 5.62; S, 6.44. Found: C, 19.5; H, 0.3; Cl, 28.5; N, 5.66; S, 6.54.

1,3-Dichlorotetrafluorocyanoisopropyl Tetrachlorophosphate.—1,3-Dichlorotetrafluoroacetone cyanohydrin was prepared *in situ* by vigorously stirring 10 g. (0.050 mole) of dichlorotetrafluoroacetone with 2.45 g. (0.050 mole) of dry sodium cyanide in 50 ml. of ether containing 5 ml. of THF. A bulky precipitate of the cyanohydrin sodium salt formed, replacing the granular sodium cyanide after 12–15 hr. at 25°. Anhydrous hydrogen chloride was bubbled through the mixture until an excess was present (*Caution, use hood*). The mixture was filtered, stripped of solvent at the water pump, then heated with 11 g. (0.053 mole) of phosphorus pentachloride for 3 hr. at 100°. A clear, colorless liquid formed. Distillation gave a colorless, viscous, fuming liquid: 5.2 g. (28%); b.p. 114–115° (14 mm.); $\lambda_{\max}^{\mathrm{CCl_4}}$ 6.45, 6.9, and 7.8 μ.

Anal. Calcd. for $C_4Cl_6F_4NOP$ (398): C, 12.05; Cl, 51.4; N, 3.52; P, 7.79. Found: C, 13.1; Cl, 52.5; N, 3.38; P, 7.84.

Electron Paramagnetic Resonance Studies of Homolytic Carbon–Oxygen and Oxygen–Oxygen Fission in Symmetrical Biscyclohexadien-4-one Peroxides

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Evidence has been presented that (a)[1] bis(1-phenyl-3,5-di-*t*-butyl-2,5-cyclohexadien-4-one) peroxide (I) and (b)[2,3] bis(1,3,5-tri-*t*-butyl-2,5-cyclohexadien-4-one) per-

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