operated glass circulation pump, a manometer, and a mercury cutoff. Earlier attempts were made to observe the luminescence in a cell designed for measurements of the photo-excited fluorescence. These attempts consumed reagent wastefully since about 75% of the cell system was heated to the decomposition temperature whereas only a small volume could be observed by the photocell.

Measurements of the luminescent intensity were made at several temperatures in the range 56 to 72° C; these yield an apparent activation energy of about 30 kcal/mole. This may be interpreted, following Vasil'ev *et al.* (1), as the activation energy for the decomposition of the ester. At least one alternative explanation involving the reactions

$$R + R \rightarrow R_2^*$$
$$R_2^* + B \rightarrow B^*$$
$$B^* \rightarrow B + h\nu$$
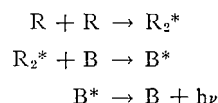
cannot be eliminated on the basis of measurements made thus far. Here R_2^* represents the initially excited dimer of the radicals R (which might be acetyl), and B and B^*, the unexcited and excited states of the product biacetyl. Much more intensive study is required, including identification of the emitting species, before a mechanism can be considered seriously.

The hyponitrite is a difficult compound with which to work and very little is known of the mechanism of its decomposition. The kinetics of the pyrolysis of ditertiarybutyl peroxide are well known. First trials with this initiator were unsuccessful, however, presumably because of the instability of acetyl radicals at the temperature necessary for its rapid decomposition (above 150° C), or because of the instability of the triplet state of biacetyl at that temperature (3).

It is hoped to follow this preliminary investigation with a more complete study in an attempt to determine the mechanism of the phenomenon.

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THE SYNTHESIS OF 17α-FLUOROPROGESTERONE

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The biological activity of progesterone can be enhanced by the presence of appropriate substituents in positions α to the 20-carbonyl group. Thus 21-fluoro- and 17α-bromo-progesterone were shown to be twice as active as the natural hormone (1, 2). It was of interest therefore to prepare 17α-fluoroprogesterone and to compare its activity with that of the chloro and bromo analogues.

A previous attempt to introduce a fluorine in position 17 by opening a suitable 16,17-epoxypregnane with hydrogen fluoride, was reported to be unsuccessful (3); we chose, therefore, to investigate the reaction of a 20-cyano-17,20-epoxypregnane (I) with hydrogen halides. The latter pathway was recently used for the preparation of 17α-fluoro-11-dehydrocorticosterone acetate (4). Starting from 17α-bromopregnenolone we prepared readily the corresponding cyanoepoxide (I, R = H) by the action of alcoholic potassium cyanide at room temperature (5, 6). A proof of structure of (I) was obtained by its conversion to the known (7) 17α-chloropregnenolone acetate (III, R = Ac).
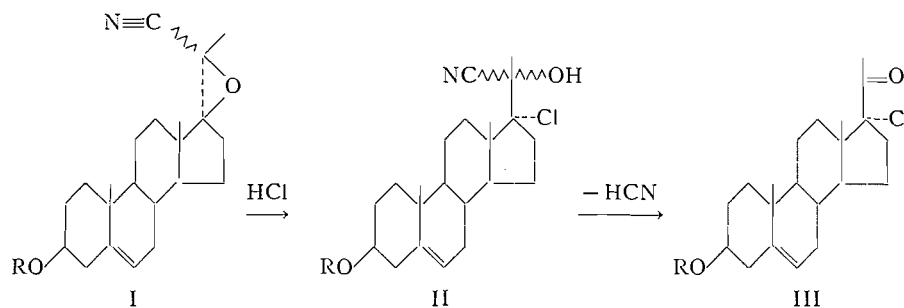
When 17α-bromoprogesterone was similarly allowed to react with potassium cyanide, a crystalline cyanoepoxide was obtained in high yield, the α,β-unsaturated 3-ketone being inert under our reaction conditions. This cyanoepoxide (IV), however, proved to be remarkably stable towards the action of anhydrous HF under the reaction conditions previously described in the 11-oxygenated series (4). It would seem that an 11-oxygen function facilitates the acid-catalyzed opening of the epoxide ring in 17,20 by anhydrous HF. In our case we found that treatment of IV with aqueous HF in a heterogeneous system resulted in the formation of the desired 17α-fluoro-20-cyanohydrin (V), smoothly and in good yield.

The resulting cyanohydrin (V) was found to be stable in non-hydroxylated solvents like ether, but it readily lost the elements of hydrogen cyanide when dissolved in an aqueous alcohol. Alternatively the regeneration of the 20-ketone function was effected by heating the cyanohydrin in organic bases, such as collidine, in a more conventional but less satisfactory manner. A proof of structure for the resulting 17α-fluoroprogesterone was obtained by removal of hydrogen fluoride upon prolonged treatment with refluxing dimethylformamide in the presence of LiBr and Li₂CO₃ (8), providing the known 16-dehydroprogesterone.
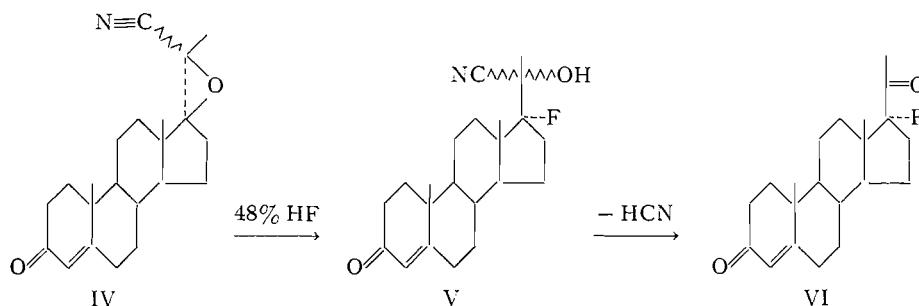
It was interesting to note that a substitution of fluorine at position 17α causes a positive increment in the rotation[1] (see Table I), contrary to the effect of a chlorine or bromine substituent. A hypsochromic displacement of the 20-ketone frequency in the infrared was observed due to the axial fluorine atom. There is only a slight shift with a 17α-chloro substituent, and no effect at all with a 17α-bromine atom. These shifts parallel those observed for an 11-ketone in the 9α-halogenated series (9). 17α-Fluoroprogesterone is slightly less active, in the Clauberg subcutaneous test, than the parent natural hormone.

TABLE I

	$[\alpha]_D$ CHCl$_3$	M_D	ΔM_D	$\Delta\nu$ 20-C=O CHCl$_3$ (cm^{-1})
Progesterone	+202°	+635	—	—
17α-Br-progesterone (2)	+ 20°	+ 80	−555	—
17α-Cl-progesterone (7)	+ 51°	+180	−455	+ 5
17α-F-progesterone	+196°	+650	+ 15	+20

EXPERIMENTAL[2]

Reaction between 17α-Bromopregnenolone and KCN

17α-Bromopregnenolone (5.00 g) (m.p. 158–159° C) was dissolved in 310 ml of 95% ethanol. A solution of 1.50 g of KCN and 2.20 g potassium acetate in 40 ml water was added and the resulting clear solution was stirred at room temperature for 19 hours. The product (4.0 g) was isolated by pouring the solution into 2 l. of ice water and filtering.

A 2-g portion of the crude bromine-free precipitate was suspended in benzene and chromatographed over 100 g of silica gel. Ethyl acetate – benzene 10:90 eluted 1 g of amorphous material, the infrared spectrum of which was consistent with the *cyanoepoxide* structure I (R = H): ν_{nujol} 3350 cm^{-1} (OH), 2240 cm^{-1} (—CN).

Increasing quantities of EtOAc in benzene eluted crystalline substances whose infrared spectra indicated the presence of a cyanohydrin group, m.p. 250–255° decomp., raised by crystallization from ethanol to 267–298° decomp. A sample was crystallized for analysis, m.p. 290° decomp. According to Barton's suggestions in the corresponding 11-oxygenated series (4) we assign to this substance the structure of a cyclopropanone cyanohydrin VII (or its epimer), intermediate in a Favorski rearrangement. Calc. for

VII
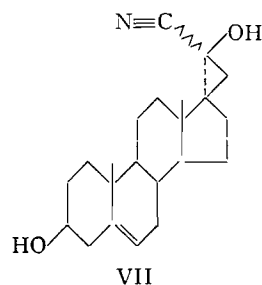
$C_{22}H_{31}O_2N$: C, 77.37; H, 9.15; N, 4.10%. Found: C, 77.67; H, 8.98; N, 3.91%. ν_{nujol} 3440 and 3240 cm^{-1} (OH), 2240 cm^{-1} (C≡N), 1053 cm^{-1} (C—O). Both hydroxyl groups were acetylated by acetic anhydride in pyridine at room temperature.

[1]*Professor Carl Djerassi kindly informed us that he observed a positive Cotton effect for 17α-fluoropregnenolone, prepared independently by Dr. Jensen of the University of Chicago.*
[2]*Melting points were determined in evacuated capillaries and corrected.*

17α-Chloropregnenolone Acetate (III, R = Ac)—Proof of Structure I

The amorphous cyanoepoxide I (0.500 g) was dissolved in 10 ml acetic acid. Anhydrous HCl was bubbled through the solution at room temperature for 30 minutes. A reddish-brown color developed. Ice water was added and the precipitate was collected on a filter and air-dried to give 0.514 g of a solid with a positive Beilstein test. One-half gram of this precipitate (II, R = Ac) was refluxed for 1 hour with 10 ml of toluene and 1 ml of a toluene solution containing 2.3% of collidine. The cooled solution was extracted with CH_2Cl_2, washed with iced dilute HCl, $NaHCO_3$ solution, and water, dried, and the solvent removed to give 0.495 g of a yellow oil which was reacetylated overnight at room temperature with 10 ml of pyridine and 2 ml of acetic anhydride. The usual working up gave 0.472 g of a crude product which was chromatographed on silica gel. EtOAc–benzene 3:97 eluted crystalline fractions (300 mg) which were recrystallized from ether–methanol for analysis, m.p. 142–144° C (III, R = Ac). Calc. for $C_{23}H_{33}ClO_3$: C, 70.30; H, 8.46; Cl, 9.02%. Found: C, 70.52; H, 8.01; Cl, 9.54%. This substance did not depress the melting point of an authentic sample of 17α-chloropregnenolone acetate (7). The infrared spectra were identical.

20-Cyano-17β,20-epoxy-4-pregnene-3-one (IV)

To 17α-bromoprogesterone (20.0 g) in 1200 ml commercial ethanol, there was added a mixture of 5.8 g KCN and 8.5 g CH_3COOK in 150 ml of water. The resulting solution was stirred at room temperature for 24 hours. At the end of this time 3.0 g of 20-cyano-17β,20-epoxy-4-pregnene-3-one crystallized out and was collected on a filter. The alcoholic filtrate was poured into ice water and the precipitate collected on a filter and washed with water. The combined dried precipitate weighed 17.0 g representing crude cyano-epoxide IV, m.p. 230–240° C. A sample was crystallized three times for analysis, m.p. 246–250° C (methanol). $[\alpha]_D^{25}$ +21.3 (CHCl$_3$ 1%); λ_{max} 241 mμ, ε 17,400. Calc. for $C_{22}H_{29}O_2N$: C, 77.84; H, 8.61; N, 4.13%. Found: C, 77.81; H, 8.46; N, 4.06%. ν_{CHCl_3} 2250 cm^{-1} (C≡N), 1665 and 1620 cm^{-1} (3-ketone-Δ^4). The structure of this substance was proved by conversion to the known 17α-chloroprogesterone (7), m.p. 165–167° C. The infrared spectra were identical and no depression of the melting point with an authentic sample was observed.

17α-Fluoroprogesterone (VI)

20-Cyano-17β,20-epoxy-4-pregnene-3-one (IV), 2.4 g, was slurried with 30 g of 48% aqueous HF at room temperature for 1 hour. The resulting oily substance was taken up in ether and washed to neutrality with $NaHCO_3$ solution and water. Evaporation of the solvent gave 2.45 g of a white solid, which crystallized from ether, m.p. 210–211° decomp. ν_{CHCl_3} 3360 cm^{-1} (OH), 2240 cm^{-1} (C≡N), 1663 and 1619 cm^{-1} (3-keto-Δ^4). When this substance, representing crude 17α-fluoro-4-pregnene-3-one-20-cyanohydrin, was refluxed in aqueous methanol overnight, HCN gas was evolved and crude 17α-fluoro-progesterone was recovered by evaporation of the solvent. Alternatively the cyano-hydrin, 1.0 g, was refluxed for 1 hour in 5 ml of collidine. After the usual working up, 0.98 g of a yellow oil was obtained which was chromatographed on neutral alumina (Woelm III). The petroleum ether – benzene eluates contained 0.450 g of 17α-fluoro-progesterone, m.p. 170–174° C. A sample was recrystallized from acetone–hexane for analysis, m.p. 177–179° C, $[\alpha]_D$ +195.7° (CHCl$_3$). Calc. for $C_{21}H_{29}O_2F$: C, 75.87; H, 8.79; F, 5.71%. Found: C, 76.08; H, 8.85; F, 5.90%. ν_{CHCl_3} 1718 cm^{-1} (20-ketone, 17α-fluoro), 1665 and 1620 cm^{-1} (3-ketone-Δ^4).

Dehydrofluorination

To 17α-fluoroprogesterone, 130 mg, dissolved in 10 ml of dimethylformamide, there was added 130 mg of LiBr and 130 mg Li₂CO₃. The mixture was refluxed under N_2 for 24 hours. Usual working up gave 80 mg of a yellow oil which crystallized from acetone. The melting point did not depress upon admixture with an authentic sample of 16-dehydroprogesterone, m.p. 184–186° C. The infrared spectrum showed the characteristic Δ^{16} band at 1591 cm⁻¹.

Attempted Reaction of IV with Anhydrous HF

The cyanoepoxide IV, 5.0 g, was dissolved in 100 ml of dry tetrahydrofuran. To this solution, cooled into a dry ice – acetone bath, there was added 20 g of anhydrous HF. The resulting solution was stirred at room temperature for 18 hours. The usual working up (4) gave 5.0 g of a solid which crystallized from ether, m.p. 225–236° decomp. The infrared spectrum was identical with that of IV.

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SOME REMARKS ON AGGREGATION OF POLYTHENE IN SOLUTION

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INTRODUCTION

In a recent article Trementozzi (1) noted serious differences in the weight-average molecular weights, $\overline{M_w}$, obtained for high- and low-pressure polythene samples from light scattering in α-chloronaphthalene (α-CN) and tetralin solutions. He suggested that these differences were due to association of polythene molecules in α-CN solutions at the temperatures in question (~100–140° C). Thus, the α-CN data presumably gave the dimension of aggregates of polythene chains, rather than that of the average molecular chain. The suggested association was supported by data showing a decrease in $\overline{M_w}$ values obtained for one high-pressure polythene as the temperature of the α-CN solutions rose from 95–141° C. Subsequently Tung (2) noted similar differences in $\overline{M_w}$ values