with 2-ethylhexyldimethylamine, m.p. 57–57.5°. Other tertiary amines such as benzyldimethylamine, dimethylaniline and pyridine reacted vigorously, but no attempt was made to isolate the liquid reaction products.

We have found also that a similar type adduct, m.p. 48–49°, was formed from the reaction of hexachloroacetone hydrate with triethylamine at Dry Ice–acetone temperature. This adduct was much less stable than the perfluoroheptane-4,4-diol·triethylamine compound. It decomposed after standing for only one hour at room temperature, but could be stored at 0° without change.

With certain primary and secondary amines, *i.e.*, ethanolamine, diisobutylamine and dicyclohexylamine, cleavage of the perfluoro ketone or ketone hydrate occurred with formation of the corresponding amides of perfluorobutyric acid and C_3F_7H. The less basic aromatic amines such as aniline and *p*-chloroaniline failed to react with the ketone. Anhydrous ammonia formed a crystalline adduct thought to be perfluoroheptan-4-amino-4-ol which, however, decomposed on standing at room temperature to the amide and C_3F_7H.

A related reaction was carried out involving the synthesis of $C_3F_7COCH_2COOC_2H_5$ by the condensation of ethyl perfluorobutyrate and ethyl acetate in the presence of sodium ethoxide.

Experimental[12]

Perfluoroheptan-4-one.—In an atmosphere of dry nitrogen, 109.0 g. (0.45 mole) of ethyl perfluorobutyrate (Columbia Organic Chemicals) was added over a period of two hours with stirring to sodium shot (10.36 g., 0.45 mole) in 150 ml. of anhydrous ether. Reaction was indicated by the immediate change in color to yellow (later dark red). After stirring overnight at room temperature there was no unreacted sodium. The reaction mixture was acidified with 3 *N* sulfuric acid, the ether layer separated and the aqueous layer exhaustively extracted with ether. The combined ether extracts were dried over anhydrous magnesium sulfate. The ether was removed by distillation and the residue was fractionated in a Podbielniak column. Perfluoroheptan-4-one (49 g., 60%) boiled at 73–76° (lit. 75°[4–6]). A central cut, b.p. 75°, was warmed with P_2O_5; mol. wt., calcd. for $C_7F_{14}O$: 366; found (gas density balance) 364. The infrared spectrum[13] was identical to that reported by Henne[4] for $C_3F_7COC_3F_7$.

The temperature of this reaction is critical, since at higher temperatures (*ca.* 60° bath temp.) the yield of ketone was considerably lower and two other products were formed in significant amounts. In a 0.3-mole run, 13 g. of product I (b.p. 83°, $n^{26}D$ 1.3030; C, 30.93; H, 2.00) was obtained along with 7.5 g. of product II, b.p. 147°, $n^{23}D$ 1.3252; C, 31.76; H, 2.96. Compound I contained perfluoroheptan-4-one and II, which reduced cupric acetate, was not characterized further.

The use of sodium dispersion in toluene is not recommended since the perfluoro ketone forms a homogeneous azeotrope containing approximately 20% by weight of toluene, b.p. *ca.* 80°, $n^{23}D$ 1.3540.

The reaction of sodium with methyl perfluorobutyrate gave $C_3F_7COC_3F_7$ in about 50% yield.

Perfluoroheptan-4,4-diol.—To a 1-g. sample of pure perfluoroheptan-4-one (b.p. 75°) a slight deficiency of water was added. The product was evacuated at 0.1 mm. A white crystalline solid, m.p. 35–35.5°,[14] $n^{20}D$ 1.293 (for super-cooled sample), remained. The solid is $C_3F_7C(OH)_2C_3F_7$.

Anal. Calcd. for $C_7H_2F_{14}O_2$: C, 21.88; H, 0.52. Found: C, 21.70; H, 0.57.

The dihydroxy structure for the ketone hydrate was further confirmed by examination of its infrared spectrum. It has a broad band around 3.0 μ which is attributed to the associated hydroxyl group. The carbonyl band at 5.6 μ was only very slight, while in the ketone spectrum there is an intense carbonyl band at 5.6 μ.[15]

Reaction of Perfluoroheptan-4-one with Primary and Secondary Amines.—N-(2-Hydroxyethyl)-perfluorobutyramide, m.p. 56.5–57.5°; N,N-diisobutylperfluorobutyramide, m.p. 155°; and N,N-dicyclohexylperfluorobutyramide, m.p. 179.5–180° (all recryst. from benzene) were obtained in nearly quantitative yield by the reaction at room temperature of $C_3F_7COC_3F_7$ with excess ethanolamine, diisobutylamine and dicyclohexylamine, respectively. These amines also were prepared from $C_3F_7COOC_2H_5$.

Perfluoroheptane-4,4-diol–Triethylamine Adduct.—Perfluoroheptane-4,4-diol (2.34 g., 0.006 mole) was treated with an excess of anhydrous triethylamine (1.13 g., 0.01 mole). At room temperature there was a vigorous exothermic reaction and a white crystalline product formed immediately. The product may be purified by recrystallization from benzene or by sublimation at 100°. The yield of $C_3F_7C(OH)_2C_3F_7\cdot N(C_2H_5)_3$ was 2.8 g. (95%), m.p. 87.5–88.5°.

Anal. Calcd. for $C_{13}H_{17}F_{14}NO_2$: C, 32.16; H, 3.50. Found: C, 32.06; H, 3.70.

The infrared spectrum showed a hydroxyl band at 2.85 μ. The carbonyl band at 5.6 μ is absent. It is of interest to note that there was no reaction between dry perfluoroheptan-4-one and dry triethylamine at room temperature. However when a drop of water was added there was a vigorous reaction resulting in the formation of the previously described adduct. The ketone hydrate was regenerated by treatment with sulfuric acid.

Ethyl *n*-Heptafluorobutyroacetate (By Charles S. Stokes).—$C_3F_7COCH_2COOC_2H_5$, b.p. *ca.* 150°, $n^{24}D$ 1.355, was prepared by the method identical to that used by Henne[16] for the preparation of $CF_3COCH_2COOC_2H_5$.

Copper(II) Chelate of Ethyl *n*-Heptafluorobutyroacetate.—The chelate was prepared by treating a sample of $C_3F_7COCH_2COOC_2H_5$ with an aqueous solution of copper(II) acetate. After shaking at room temperature a crystalline solid was obtained. The product was recrystallized from ethanol to give bright blue-green crystals, m.p. 105–105.5° in nearly quantitative yield.

Anal. Calcd. for $C_{16}H_{12}F_{14}O_6Cu$: Cu, 10.1. Found: Cu (electrolytic), 10.3.

Acknowledgment.—The financial support of the Research Corporation is gratefully acknowledged.

(12) Microanalyses by Clark Microanalytical Laboratory.

(13) Determined with a Baird Associates Infrared Recording Spectrophotometer of Samuel P. Sadtler and Sons, Inc., Phila., Pa.

(14) It "boiled" near 75° which indicates that the reaction of the ketone with water is probably an equilibrium reaction, and that at higher temperatures the equilibrium is shifted in the direction of the individual components.

(15) It is predicted that this small carbonyl band would disappear entirely at temperatures considerably below 30°, at which temperature the present spectrum was taken. At lower temperatures the equilibrium would be displaced entirely toward the hydrate.

(16) A. L. Henne, *et al.*, THIS JOURNAL, **69**, 1819 (1947).

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The Treatment of Arachin with Terephthalyl Dichloride

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Mann[1] showed that the intrinsic viscosity of peanut protein (measured in 10 *M* urea solution) was increased by treatment of the protein with terephthalyl dichloride. It was suggested that the increase was the result of cross-linking of protein molecules.

Following Mann's method for the preparation of the modified protein (using the arachin fraction of peanut protein instead of the whole protein) an examination of the modified arachin has been made in the ultracentrifuge and by viscosity determina-

(1) G. E. Mann, THIS JOURNAL, **75**, 3526 (1953).

tions in two solvents. The viscosity results confirmed that the intrinsic viscosity of the arachin was increased and the ultracentrifugal examination gave evidence that cross-linking of molecules had occurred as a result of the treatment.

Experimental

The arachin fraction of peanut protein was prepared by extracting defatted peanut meal with 10% (w./v.) sodium chloride and precipitating the arachin at 32% saturation with ammonium sulfate. Purification of the arachin was achieved by a similar reprecipitation. After removing the ammonium sulfate by dialysis, the protein was dried with alcohol and acetone.

The terephthalyl dichloride was supplied by Imperial Chemical Industries, Ltd., Dyestuffs Division. Buffer salts and urea were A.R. or of equivalent purity.

Ultracentrifuge measurements were made in a Spinco model E ultracentrifuge at 50,700 r.p.m. (190,000 g.). Viscosity measurements were made in an Ostwald viscometer at 25°.

For the preparation of the modified arachin, 1.6 g. of terephthalyl dichloride per 20 g. of protein was used, the reaction being carried out at *p*H 9.5 and 0°. These conditions were found by Mann[1] to give the maximum intrinsic viscosity of the modified protein. After the reaction, the protein solution was dialyzed with stirring against phosphate buffer (ionic strength $I = 0.2$, *p*H 7.8) for 48 hours. No attempt was made to estimate the amount of terephthalyl dichloride which had reacted with the protein.

Results and Discussion

In Table I the intrinsic viscosities $[\eta]$ (deciliters per gram) of native and modified arachin in two solvents are shown.

TABLE I

Solvent	η Native arachin	η Modified arachin
Phosphate buffer $I = 0.2$, *p*H 7.8	0.055	0.094
Phosphate buffer $I = 0.2$, *p*H 7.8-7.2 *M* urea	.23	.37

Although Mann's viscosities were measured in 10 *M* urea and the values above obtained in 7.2 *M* urea, there does not appear to be as large an increase attained in this work as was obtained by Mann.

Figure 1 (a) shows the sedimentation diagram of native arachin in phosphate buffer (ionic strength $I = 0.2$, *p*H 7.8) while Fig. 1(b) gives the sedimentation diagram for the modified arachin in the same solvent. From the presence of the faster sedimenting peaks in Fig. 1(b) it is evident that some type of aggregation of the arachin molecules has occurred. (The alternative possibility that the increased sedimentation constant is the result of combination of terephthalyl groups with the protein without cross-linking is unlikely. Mann's figures showed that the maximum terephthalic acid content was 0.052 g. per g. of protein which would be insufficient to increase the sedimentation constant to the values shown.)

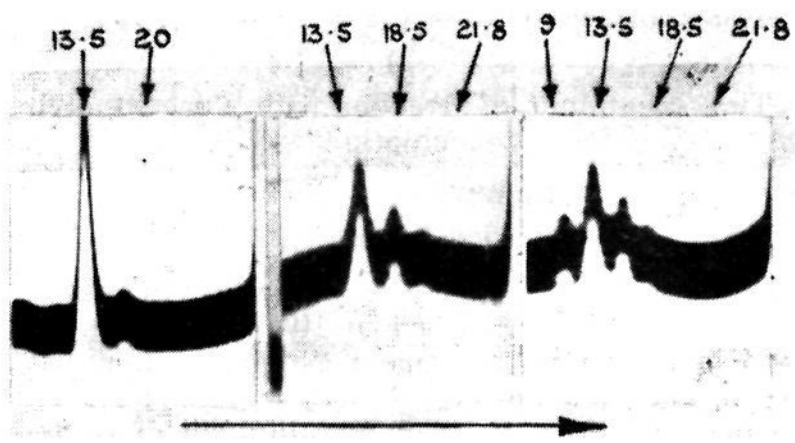

Fig. 1.—Sedimentation diagrams of (a) native arachin, (b) arachin treated with terephthalyl dichloride, (c) arachin treated with terephthalyl dichloride showing dissociated component; in phosphate buffer $I = 0.2$, *p*H 7.8, protein concn. *ca.* 1 g./100 ml. Numbers above peaks refer to rounded sedimentation constants in Svedberg units.

In the absence of diffusion data, accurate determinations of molecular weights are impossible. If, however, a value of 1.3 is assumed for the frictional ratio (f/f_0) then the molecular weights corresponding to the sedimentation constants 13.5, 18.5 and 21.8 of Fig. 1(b) are in the ratio 320,000:500,000:660,000 or very approximately 2:3:4. The value of 500,000 which is *ca.* 1.5 times the molecular weight of arachin could be arrived at if the arachin dissociated into halves at *p*H 9.5 (which it does readily, *cf.* Johnson and Shooter[2]) and three of the dissociated molecules were then linked together with terephthalyl dichloride. In some cases the dissociation product was visible in the ultracentrifuge diagram (Fig. 1(c)).

(2) P. Johnson and E. M. Shooter, *Biochim. Biophys. Acta*, **5**, 361 (1950).

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The C-20 Epimers of 4-Pregnene-11β,17α,20-triol-3-one

BY G. I. POOS

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Among various metabolites of the adrenal hormones, a substance recently detected on paper chromatograms by DeCourcy, Bush, Gray and Lunnon[1] appears to hold particular biological interest. Excretion of this substance in the urine of non-pregnant females was reported[1] to reach a high level in the week prior to menstruation. The material also could be detected in the urine of pregnant women, although in appreciably lower concentration. On the basis of R_f values and color reactions, the authors advanced the structure 4-pregnene-11β,17α,20-triol-3-one for the new metabolite.

As an aid in the identification of the compound, authentic samples of 4-pregnene-11β,17α,20-triol-3-one, both in the 20β V and 20α VIII stereoisomeric modification, have been synthesized. It is the purpose of the present communication to present a synthetic route to V and VIII, and also to record the physical properties of the pure crystalline materials.

Although a variety of methods are available for the synthesis of the 4-pregnene-11,17,20-triol-3-ones, a route involving lithium aluminum hydride reduction of the 3-dioxolane of 21-desoxycortisone

(1) C. DeCourcy, I. E. Bush, C. H. Gray and J. N. Lunnon, *J. Endocrinology*, **9**, 401 (1953).