performed per day by a single operator. Although the method had been utilized only in conjunction with carbon blacks, it should be broadly applicable to any adsorbent.

Some further aspects of the data merit brief discussion. Table II shows that k changes only slightly from the butane to the ethyl chloride system. This is reasonable; the apparent surface area is not likely to vary greatly when the probe molecules are approximately equal in size, as is the case here. In the case of water adsorption, the k value is sensitive to differences between channel and furnace blacks, but seems constant in each group. The absence of pore structure in the furnace blacks doubtless lowers the effective number of sites for water adsorption, thus raising the value of k. The water molecule is, presumably, sufficiently small to gain entry into some of the pores of the channel blacks, resulting in a relatively large heat of adsorption, hence a low k value. The apparent constancy of k for ethyl chloride and butane adsorption suggests that little penetration of the pore structure of the channel blacks occurs with these adsorbates.

The proportionality parameter k' is considerably greater for butane than for ethyl chloride. Since the "reaction areas" in these cases are approximately equal (see Table I), a given surface region of the black seems to accommodate greater amounts of butane than ethyl chloride prior to bulk liquefaction. In view of the polar nature of the ethyl chloride molecule, this result seems reasonable.

1. Brunauer, S., Emmett, P. H., and Teller, E. J. Am. Chem. Soc. **60**, 309 (1938).
2. Anderson, R. B. and Emmett, P. H. J. Appl. Phys. **19**, 367 (1948).
3. Starkweather, F. M. and Palumbo, D. T. J. Electrochem. Soc. **104**, 287 (1957).

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STEROIDS. CXV. THE SYNTHESIS OF HALOGENATED STEROID HORMONES, 4-CHLORO-19-NOR HORMONE ANALOGS*

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In an earlier paper (1) we noted that halogenation of progesterone at C-4 virtually eliminates progestational activity. It was thus of considerable interest to convert the extremely potent progestational agents (2), 19-nor: 17α-methyl- (3), 17α-ethynyl- (3), 17α-vinyl- (4), and 17α-ethyltestosterone (5) as well as 19-norprogesterone (6) into their 4-chloro analogs for evaluation of gestational activity. This transformation was readily accomplished by converting the parent steroids I into their 4,5-oxides (II) by reaction with alkaline hydrogen peroxide followed by hydrochloric acid treatment to yield directly the 4-chloro-Δ^4-3-ketones (III). This sequence is one first described in the cholesterol series by Shaw and Stevenson (7) and later described in the hormones series by ourselves (1) and by Camerino *et al.* (8). An alternate synthesis involving direct halogenation has been described by Petrow and co-workers (9) while a later paper by a Schering group (10) describes the synthesis of 4-halo hormone analogs by the addition of hypohalous acid to Δ^4-3-ketones.

In the case at hand 17α-methyl-19-nortestosterone (I*a*), 17α-ethynyl-19-nortestosterone (I*b*), and 19-norprogesterone (I*e*) were each reacted for periods of 35 minutes to 1 hour

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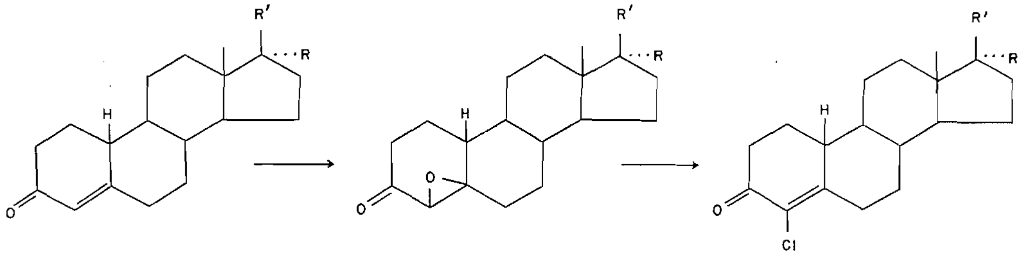
*Paper CXIV, Kincl, F. A. and Garcia, M. Ber. **92**, 595 (1959).*

with alkaline hydrogen peroxide in cold methanol solution to give a mixture (1) of the corresponding 4β,5β- and 4α,5α-epoxides. Without purification the epoxide mixtures were treated for 1 hour with concentrated hydrochloric acid in acetone solution (1), thus giving a high yield of the 4-chloro-Δ^4-3-keto compounds II*a*, II*b*, and II*e*.



(I) (II)

(*a*) R = CH_3; R' = OH
(*b*) R = C≡CH; R' = OH
(*c*) R = CH=CH_2; R' = OH
(*d*) R = CH_2CH_3; R' = OH
(*e*) R = H; R' = $COCH_3$

Hydrogenation of 4-chloro-17α-ethynyltestosterone (II*b*) in pyridine (11) over a palladium – calcium carbonate catalyst and interrupted at 1.1 equivalents hydrogen uptake gave 4-chloro-17α-vinyltestosterone (II*c*) in 70% yield, while hydrogenation of II*b* in dioxane (12) with palladium – barium sulphate, interrupted at 2.1 moles uptake, gave the 17α-ethyl compound (II*d*) in 60% yield. When tested* in the Clauberg assay by either the oral or subcutaneous route, compounds II exhibited only a relatively low order of progestational activity.

EXPERIMENTAL

Melting points are uncorrected. Rotations were determined in chloroform and ultraviolet absorption spectra in 96% ethanol.

4-Chloro-17α-methyl-19-nortestosterone (II*a*).—A solution of 17α-methyl-19-nortestosterone (I*a*) (10 g) in methanol (250 ml) was cooled to 0° and then treated dropwise and successively with 35% hydrogen peroxide (40 ml) and 10% sodium hydroxide (16 ml). After it had been left to stand for 35 minutes at 0–5° the solution was poured into water and extracted with ethyl acetate. Evaporation of the washed extract gave 11 g of crude epoxide as a semicrystalline product exhibiting no selective absorption in the ultraviolet. The epoxide without further purification was dissolved in acetone (100 ml), and concentrated hydrochloric acid (10 ml) was added. The solution, after being kept for 1 hour at room temperature, was poured into salt water and the product extracted with methylene chloride. The extract was washed successively with water, sodium carbonate solution, water, and then evaporated. The residue in 200 ml of benzene–hexane (1:1) was adsorbed on 300 g of neutral alumina, whereupon acetone–hexane crystallization of the benzene eluate gave 6.32 g of 4-chloro-17α-methyl-19-nortestosterone (II*a*), m.p. 145–148°. The analytical specimen from acetone–ether exhibited m.p. 148–151°, λ_{max} 255 mμ, log ε 4.12, $[\alpha]_D$ +42°.† Anal. Calc. for $C_{19}H_{27}ClO_2$: C, 70.67; H, 8.43; Cl, 10.98. Found: C, 70.68; H, 8.39; Cl, 10.61.

**Bio-assays by The Endocrine Laboratories, Madison, Wisc.*

†After completion of our work this compound was reported by Camerino et al. (ref. 8b) with m.p. 151–152°, λ_{max} *255 mμ, log ε 4.14.*

4-Chloro-17α-ethynyl-19-nortestosterone (II*b*).—17α-Ethynyl-19-nortestosterone (I*b*) (10 g) was epoxidized and then treated with acid as described above for the 17-methyl analog. The residue was chromatographed on neutral alumina and the benzene and benzene–ether 4:1 fractions crystallized from acetone–hexane to yield 5.54 g of II*b*, m.p. 186–188°, λ_{max} 225 mμ, log ϵ 4.11, $[\alpha]_D$ +7°. Anal. Calc. for $C_{20}H_{25}ClO_2$: C, 72.16; H, 7.57; Cl, 10.65. Found: C, 72.49; H, 7.46; Cl, 10.69.

4-Chloro-19-norprogesterone (II*e*).—19-Norprogesterone (0.8 g) in methanol (100 ml) at 0° was treated with 3.5 ml of 35% hydrogen peroxide and 1.4 ml of 10% sodium hydroxide and stirred for 1 hour at 0–5°. A small amount of insoluble material was removed and the filtrate poured into salt water. The crude epoxide mixture (0.83 g) was isolated by ethyl acetate extraction and then dissolved in 40 ml of acetone, and 1 ml of concentrated hydrochloric acid was added. After the solution had stood for 1 hour at room temperature, water, salt, and ice were added, the precipitate was collected, washed, dried, and recrystallized from acetone–hexane, yielding 0.61 g of II*e*, m.p. 169–172°. Recrystallization from the same solvents afforded the analytical sample, m.p. 174–177°, λ_{max} 256 mμ, log ϵ 4.11, $[\alpha]_D$ +127°. Anal. Calc. for $C_{20}H_{27}O_2Cl.\frac{1}{2}C_3H_6O$: C, 70.96; H, 8.31; Cl, 9.74%. Found: C, 71.01; H, 7.93; Cl, 9.68.

4-Chloro-17α-vinyl-19-nortestosterone (II*c*).—4-Chloro-17α-ethynyl-19-nortestosterone (5 g) in pyridine (100 ml) was hydrogenated at 25° and 580 mm over 2 g of pre-reduced 2% palladium – calcium carbonate catalyst. When hydrogen uptake reached 1.1 equivalents (2 to 3 hours in general) the reduction was interrupted, the catalyst removed, and the solvent concentrated *in vacuo*. The oily residue was taken up in ethyl acetate, the solution washed with dilute acid, carbonate solution, and then water. Evaporation and crystallization of the product from acetone–hexane gave 3.54 g of the vinyl compound (II*c*), m.p. 115–118°. Two recrystallizations from the same solvent pair produced the analytical specimen, m.p. 124–126°, λ_{max} 255 mμ, log ϵ 4.13, $[\alpha]_D$ +51°. Anal. Calc. for $C_{20}H_{27}ClO_2$: C, 71.69; H, 8.15; Cl, 10.59. Found: C, 71.42; H, 8.05; Cl, 10.71.

4-Chloro-17α-ethyl-19-nortestosterone (II*d*).—The reduction at 25° and 580 mm of 2 g of 4-chloro-17α-ethynyl-19-nortestosterone (II*b*) in 160 ml of dioxane over 0.8 g of prehydrogenated 10% palladium – barium sulphate catalyst was stopped after the uptake of 2.1 equivalents of hydrogen (ca. 3 hours). The catalyst was filtered and the solution concentrated to dryness, whereupon acetone–hexane crystallization of the reduced product gave 1.20 g of 17α-ethyl compound (II*d*), m.p. 122–125°. Repeated crystallization yielded the pure substance, m.p. 126–128° (mixture melting point depression with II*c*), λ_{max} 256 mμ, log ϵ 4.14, $[\alpha]_D$ +47°. Anal. Calc. for $C_{20}H_{29}O_2Cl$: C, 71.34; H, 8.68; O, 9.50. Found: C, 71.30; H, 8.69; O, 9.58.

1. RINGOLD, H. J., BATRES, E., MANCERA, O., and ROSENKRANZ, G. J. Org. Chem. **21**, 1432 (1956).
2. MCGINTY, D. and DJERASSI, C. Ann. N. Y. Acad. Sci. **71**, 500 (1958).
3. DJERASSI, C., MIRAMONTES, L., ROSENKRANZ, G., and SONDHEIMER, F. J. Am. Chem. Soc. **76**, 4092 (1954).
4. SANDOVAL, A., MIRAMONTES, L., ROSENKRANZ, G., and SONDHEIMER, F. J. Am. Chem. Soc. **75**, 4117 (1953).
5. COLTON, F. B., NYSTED, L. N., RIEGEL, B., and RAYMOND, A. L. J. Am. Chem. Soc. **79**, 1123 (1957).
6. MIRAMONTES, L., ROSENKRANZ, G., and DJERASSI, C. J. Am. Chem. Soc. **73**, 3540 (1951).
7. SHAW, J. I. and STEVENSON, R. J. Chem. Soc. 3549 (1955).
8. (*a*) CAMERINO, B., PATELLI, B., and VERCELLONE, A. J. Am. Chem. Soc. **78**, 3540 (1956). (*b*) CAMERINO, B., MODELLI, R., and PATELLI, B. Farmaco, (Pavia), **13**, 52 (1958); Chem. Abstr. **52**, 13768 (1958).
9. KIRK, D. N., PATEL, D. K., and PETROW, V. J. Chem. Soc. 1184 (1956).
10. OLIVETO, E. P., GEROLD, C., and HERSHBERG, E. B. J. Am. Chem. Soc. **79**, 3596 (1957).

11. RUZICKA, L. and MÜLLER, P. Helv. Chim. Acta, **22**, 755 (1939).
12. HERSHBERG, E. B., OLIVETO, E. P., GEROLD, C., and JOHNSON, L. J. Am. Chem. Soc. **73**, 5073 (1951).

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THE STREAMING BIREFRINGENCE OF CELLULOSE MICELLES: A CONFIRMATION OF THE THEORY FOR RIGID RODS

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INTRODUCTION

Theories of streaming birefringence have been reviewed by Edsall (1) and by Cerf and Scheraga (2). Peterlin and Stuart (3, 4) have developed a theory for the orientation of rigid ellipsoids of revolution which permits the calculation of particle lengths from streaming birefringence data. Donnet (5) has made a comparison of the lengths of tobacco mosaic virus particles measured directly from electron micrographs and those calculated from flow birefringence measurements using the theory of Peterlin and Stuart. Good agreement between the two methods was obtained.

This note deals with similar measurements on a cellulose sol.

EXPERIMENTAL

Apparatus

The streaming birefringence apparatus, used in this work, is the concentric cylinder type with rotating outer cylinder. A longitudinal section of the cylinders and optical system is shown in Fig. 1.

The outer cylinder, made of stainless steel, has an internal diameter of 3.40 cm and an inside length of 6.35 cm. Four interchangeable stainless steel inner cylinders, 6.30 cm long and having different diameters, make it possible to vary the annular gap from 1.5 mm to 0.2 mm and the velocity gradient up to 10^4 sec^{-1}.

The light source is a General Electric A-H4 100-watt mercury arc with a filter combination to isolate the 546-mμ mercury line.

Cellulose Sol

The sol was prepared (6) by boiling 10 g bleached sulphite wood pulp in 5 *N* sulphuric acid for 3.5 hours, and the residue, after it was washed, was dispersed in 2 l. of distilled water.

To narrow the distribution of particle sizes the sol was then centrifuged at 3500 *g* for 1 hour in a Spinco preparatory ultracentrifuge and the supernatant sol was used for the measurements.

Electron micrographs of the rod-like cellulose particles were made using palladium-shadowed specimens.

RESULTS AND DISCUSSION

The distribution of particle lengths from the electron micrographs is given in Table I. The experimental values of the extinction angle χ over a range of gradients *G* and using three different stators are plotted in Fig. 2.

The electron micrographs indicate that the cellulose particles range in length from 1500 Å to 6500 Å. From this information a theoretical extinction angle curve, character-

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