

Steroids. XI.^{1a} 17-Ethynylandrostan-17 β -ol and Androstane-2,17-dione^{1b}

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In connection with certain biological experiments, it was necessary to synthesize several hitherto undescribed androstane derivatives and the present note deals briefly with the preparation of these substances.

A toluene solution of androstan-17-one, obtained by hydrogenation of $\Delta^{3,5}$ -androstadien-17-one,² readily reacted with acetylene in the presence of potassium *t*-butoxide affording after acidification nearly 90% of 17-ethynylandrostan-17 β -ol. This substance differs from 17-ethynyltestosterone,³ the most potent orally active, progestational hormone, only in the absence of the Δ^4 -3-keto moiety, and proved ineffective when tested in rabbits by oral administration in five times the threshold dose of 17-ethynyltestosterone. This further demonstrates the importance of an α,β -unsaturated keto grouping in ring A for progestational activity.³ Partial reduction of the ethynyl group was readily accomplished with palladium-on-calcium carbonate catalyst in pyridine solution⁴ while complete reduction to the 17-ethyl derivative was effected in ethyl acetate solution.

The most facile approach to the preparation of androstane-2,17-dione appeared to be Kröhnke's nitron synthesis⁵ which had already been applied successfully by Ruzicka and co-workers⁶ to the conversion of cholestan-3-one to cholestan-2-one. The pyridinium salt⁷ of 2-bromoandrostan-3,17-dione on treatment with *p*-nitrosodimethylaniline afforded the reddish-orange nitron, which on decomposition with dilute hydrochloric acid led to Δ^3 -androstene-2,17-dione-3-ol (enol form of androstane-2,3,17-trione), characterized by an enol acetate and enol tosylate. The structure assignment of the enol and its derivatives rests on analogy to the proved case in the cholestanone series^{6,8} and the typical ultraviolet absorption maximum at 272 μ . Raney nickel reduction⁶ of the enol tosylate produced the desired androstane-2,17-dione.

Experimental⁹

17-Ethynylandrostan-17 β -ol.—To a solution of 5.0 g. of potassium in 70 cc. of *t*-butyl alcohol was added in a current of nitrogen 5.18 g. of androstan-17-one in 50 cc. of toluene.

(1) (a) Paper X, Romo, Rosenkranz and Djerassi, *J. Org. Chem.*, **15**, November (1950). (b) Taken from part of a thesis submitted by Srta. Rosa Yashin to the Facultad de Química Universidad Motolinia.

(2) Rosenkranz, Kaufmann and Romo, *THIS JOURNAL*, **71**, 3693 (1949).

(3) Cf. Ehrenstein, *Chem. Revs.*, **42**, 457 (1948).

(4) Ruzicka and Müller, *Helv. Chim. Acta*, **23**, 755 (1939); cf. Djerassi and Scholz, *THIS JOURNAL*, **71**, 3962 (1949).

(5) Kröhnke, *Ber.*, **69**, 2006 (1936) and later papers.

(6) Ruzicka, Plattner and Furrer, *Helv. Chim. Acta*, **27**, 524 (1944).

(7) Ruzicka, Plattner and Aeschbacher, *ibid.*, **21**, 866 (1938).

(8) Stiller and Rosenheim, *J. Chem. Soc.*, 353 (1938).

(9) All melting points are corrected and were determined on the Kofler block. All rotations were carried out in chloroform solution. We are indebted to Srta. Amparo Barba of our Microanalytical Department for the analyses and to Srta. Dora Hernández for technical assistance.

The reaction vessel was protected from moisture and a slow current of acetylene gas was passed overnight through the mechanically stirred mixture. The reddish solution was diluted with ca. 500 cc. of water, neutralized with hydrochloric acid and the now nearly colorless solution was steam distilled for 1.5 hours. On cooling, the residue crystallized and was filtered and washed well with water; yield 5.0 g. (88%), m. p. 144–150°. Recrystallization from hexane gave colorless crystals with m. p. 155–157°, $[\alpha]^{20D}$ -34.8° .

Anal. Calcd. for $C_{21}H_{32}O$: C, 83.94; H, 10.74. Found: C, 83.51; H, 11.03.

17-Vinylandrostan-17 β -ol.—The hydrogen uptake corresponded to exactly one mole when a solution of 7.68 g. of the 17-ethynyl derivative in 120 cc. of C. p. pyridine was shaken in an hydrogen atmosphere with 0.5 g. of 2% palladium-on-calcium carbonate catalyst. Filtration of the catalyst, evaporation of the solvent to dryness under reduced pressure and trituration with hexane afforded 6.94 g. (90%) of the 17-vinyl analog with m. p. 124–126°. Further recrystallization from the same solvent raised the m. p. to 129.5–130°, $[\alpha]^{20D}$ $+2^\circ$.

Anal. Calcd. for $C_{21}H_{34}O$: C, 83.38; H, 11.33. Found: C, 83.54; H, 11.48.

17-Ethylandrostan-17 β -ol.—The 17-vinyl derivative rapidly consumed one mole of hydrogen in ethyl acetate solution with 5% palladium-on-barium sulfate catalyst (American Platinum Works, Newark, N. J.). The analytical sample had m. p. 116–117.5°, $[\alpha]^{20D}$ -3° after recrystallization from hexane.

Anal. Calcd. for $C_{21}H_{36}O$: C, 82.83; H, 11.92. Found: C, 82.81; H, 11.80.

Androstane-3,17-dione-2-(*p*-dimethylaminophenyl)-nitron.—A mixture of 21 g. of 2-bromoandrostan-3,17-dione pyridinium salt,⁷ 250 cc. of ethanol, 250 cc. of chloroform, 7.1 g. of *p*-nitrosodimethylaniline and 47 cc. of 1 N NaOH solution, initially at 0°, was stirred mechanically at room temperature for 3.5 hours and then concentrated under reduced pressure to incipient crystallization. After cooling in ice, the crystals were collected and washed with a mixture of hexane and acetone. Concentration of the filtrate furnished a small second crop of equal purity yielding a total of 15 g. (69%) with a m. p. 185–187°. Further crystallization from acetone-hexane produced shiny, reddish-orange plates of the nitron with m. p. 187–188°.

Anal. Calcd. for $C_{27}H_{36}O_3N_2$: C, 74.29; H, 8.31. Found: C, 74.42; H, 8.57.

Δ^3 -Androstene-2,17-dione-3-ol.—The above nitron (15 g.) was decomposed by shaking it vigorously several times in ethereal suspension with 5% hydrochloric acid. The ether extract was washed with bicarbonate solution, cooled in ice and treated for a few minutes with stirring with 400 cc. of 20% potassium hydroxide solution. The milky aqueous suspension of the potassium salt of the enol was separated, the enol liberated by acidification and extracted with ether. After washing until neutral, drying and evaporating, the residue was crystallized from hexane; yield, 5.2 g. (46%), m. p. 165–175°, $[\alpha]^{20D}$ $+149.8^\circ$, ultraviolet maximum at 272 μ , log *E* 3.98 (ethanol). Since the product did not crystallize well, it was characterized in the form of two esters.

The enol acetate was prepared by heating 1 g. of the enol with 5 cc. of pyridine and 3 cc. of acetic anhydride for one-half hour and then pouring into cold dilute hydrochloric acid; yield 0.95 g. (84%), m. p. 189–195°. Several crystallizations from ethanol afforded the analytical sample with m. p. 208–210°, $[\alpha]^{20D}$ $+164.5^\circ$, ultraviolet maxima at 236 μ (log *E* 4.13) and 296 μ (log *E* 1.90).

Anal. Calcd. for $C_{21}H_{36}O_4$: C, 73.22; H, 8.19. Found: C, 73.21; H, 8.22.

The enol tosylate was synthesized in an analogous fashion, except that the reaction was carried out at room temperature; yield 89%, m. p. 203–208°. Recrystallization from acetone-hexane raised the m. p. to 206–208°, $[\alpha]^{20D}$ $+133.4^\circ$, ultraviolet maxima at 228 μ (log *E* 4.30), and 294 μ (log *E* 1.95).

Anal. Calcd. for $C_{26}H_{38}O_2S$: C, 68.39; H, 7.06. Found: C, 68.61; H, 7.00.

Androstane-2,17-dione.—The reduction of 4.0 g. of the enol tosylate with 2 g. of W-4 Raney nickel catalyst¹⁰ in 400 cc. of ethanol was carried out exactly as described for the analogous reaction in the cholestane series⁶ including re-oxidation and chromatography; yield 0.88 g. (35%), m. p. 150–154°. The analytical sample was obtained from acetone–pentane with m. p. 152.5–154.5°, $[\alpha]_D^{20} +119.9^\circ$, ultraviolet maximum at 290 m μ (log E 1.87).

Anal. Calcd. for C₁₉H₂₈O₂: C, 79.12; H, 9.79. Found: C, 79.03; H, 9.79.

(10) Adkins and Pavlic, *THIS JOURNAL*, **69**, 3039 (1947).

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The Infrared Spectrum of P₄

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Phosphorus in both the liquid and vapor state is known to be tetraatomic.¹ The molecular structure of P₄ has been investigated in electron² and X-ray³ diffraction experiments which eliminate a plane square model in favor of a tetrahedral² or near tetrahedral³ configuration. The Raman spectrum⁴ is also compatible⁵ with tetrahedral symmetry, T_d, but by itself is not conclusive. This investigation of the infrared spectrum of phosphorus confirms the tetrahedral structure for P₄. In addition, selection rule violations in the infrared spectra of solid yellow phosphorus and carbon disulfide solution are reported.

Experimental

The absorption spectrum of yellow phosphorus was observed from 400 to 1300 cm.⁻¹ with a Perkin-Elmer Model 12B spectrometer. Pieces of the solid, from 0.5 to 1.5 mm. thick, were mounted between potassium bromide plates. Carbon disulfide solutions, ranging from 10 to 50% phosphorus by volume, were observed in a 1.6 mm. liquid cell. Considerable difficulty was experienced in obtaining a satisfactory spectrum of the vapor. The results included herein were observed upon heating⁶ to 230° a sealed, evacuated 90 cm. Pyrex cell, 4.5 cm. in diameter, with potassium bromide windows, and containing 3.8 g. of solid yellow phosphorus in a side arm. The primary optics of the spectrometer were modified to accommodate this cell and heating jacket by placing a globar at the focus of the 3" diameter, 6" focal length, spherical mirror removed from the spectrometer, and passing the reflected parallel light through the cell. A 3" by 2" flat mirror and another identical spherical mirror were used to bring the light along the optical axis of the monochromator and focus the image of the source upon the

(1) See Yost and Russell, "Systematic Inorganic Chemistry," Prentice-Hall, Inc., New York, N. Y., 1944, p. 155 *et seq.*, for a general survey of the data and literature.

(2) Maxwell, Hendricks and Mosley, *J. Chem. Phys.*, **3**, 699 (1935).

(3) Thomas and Gingrich, *ibid.*, **6**, 659 (1938).

(4) Venkateswaran, *Proc. Indian Acad. Sci.*, **4A**, 345 (1946), and prior work cited therein.

(5) The details of the discussion are summarized by Herzberg, "Infrared and Raman Spectra of Polyatomic Molecules," D. Van Nostrand Co., Inc., New York, N. Y., 1945, p. 299.

(6) The general details of the heating arrangement were similar to a shorter cell described by Miller and Koch, *THIS JOURNAL*, **70**, 1890 (1948). A separately controlled heating coil at each end was necessary to compensate for radiation losses which otherwise caused phosphorus to condense on the windows.

entrance slits. Figure 1 gives a schematic diagram of the arrangement.

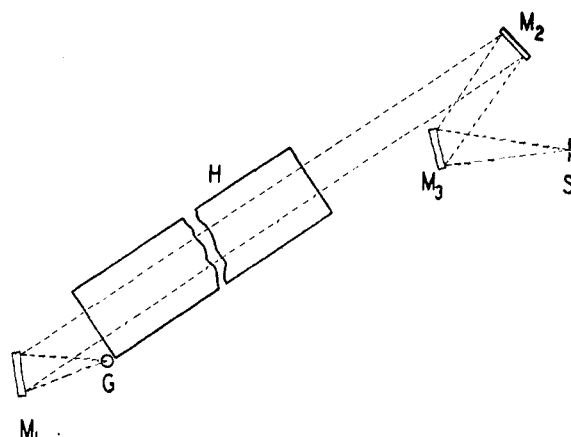


Fig. 1.—Schematic diagram of apparatus: G, globar; H, heater and cell; M₁, spherical mirror; M₂, flat mirror; M₃, spherical mirror; S, entrance slit.

Results and Discussion

The observed spectrum of the vapor is given in Fig. 2 and the spectral data are summarized in Table I, which includes frequency assignments.

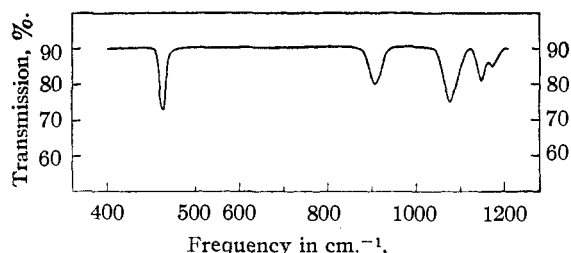


Fig. 2.—The infrared spectrum of P₄ vapor.

In the case of tetrahedral symmetry, P₄ has three fundamentals of species A₁, E and F₂, all of which are Raman active; the A₁ fundamental is polarized. In addition, the F₂ fundamental is infrared active. In all of the infrared spectra there was no indication of absorption at 363 cm.⁻¹, the lowest fre-

TABLE I
THE INFRARED AND RAMAN SPECTRA OF P₄

Solid	Infrared CS ₂ soln., ν cm. ⁻¹	Vapor	Raman ⁴ Liquid, Δν cm. ⁻¹	Assign- ment
a	a	a	363 (2, 0.85)	ν ₂
465 vw?	461 w	464.5 m	465 (6, 0.87)	ν ₃
602 ms	604 ^b m		606 (10, 0.05)	ν ₁
811 vw				ν ₂ + ν ₃
911 w	916 w	910 mw		2ν ₃
959 ^b w				ν ₁ + ν ₂
1053 m, b		1075 m		ν ₁ + ν ₃
		1150 } mw		2ν ₂ + ν ₃
		1173 }		

^a Too low for observation with KBr optics. ^b Should be infrared inactive for tetrahedral symmetry.