

mg., m.p. 317–319°) which crystallized from chloroform-methanol to give the dione enol benzoate as fine needles, m.p. 317–319°,  $[\alpha]_D +35^\circ$  (c, 1.6),  $\lambda$  231  $\mu$ m (16,900),  $\lambda$  5.77, 5.97, 6.13  $\mu$ .

*Anal.* Calcd. for  $C_{37}H_{52}O_3$ : C, 81.57; H, 9.62. Found: C, 81.4; H, 9.7.

*Huang-Minton reduction of friedelane-2,3-dione.* The dione (104 mg.) was suspended in diethylene glycol (14 cc.), potassium hydroxide (1 g.) and hydrazine hydrate (99–100%; 1.5 cc.) added. The mixture was heated under reflux for 30 min., the condenser removed until the reaction mixture temperature reached 210° and refluxing continued for a further 5 hr. Water (30 cc.) was added, the mixture extracted with chloroform, the extract washed with water, dried (sodium sulfate) and evaporated to give a solid, which crystallized from chloroform-methanol to give friedelane as needles, m.p. and mixed m.p. 251–252°,  $[\alpha]_D +22^\circ$  (c, 0.62).

*Anal.* Calcd. for  $C_{36}H_{52}$ : C, 87.30; H, 12.70. Found: C, 87.5; H, 12.6.

*Friedelane-2,3-dione quinoxaline derivative.* A mixture of the dione (50 mg.), *o*-phenylenediamine hydrochloride (100 mg., freshly sublimed) and sodium acetate (150 mg.) in acetic acid (50 cc.) was refluxed for 2 hr., cooled, poured into water, and the product collected by filtration. Three recrystallizations from chloroform-methanol gave the quinoxaline as slightly yellow small needles, m.p. 248–251°,  $\lambda$  239 (19,950) and 322  $\mu$ m (7,100), lit.,<sup>10</sup> m.p. 244–246°.

*Anal.* Calcd. for  $C_{36}H_{52}N_2$ : C, 84.32; H, 10.22. Found: C, 83.8; H, 9.9.

*Friedelane-2,3-dione methyl ether.* Boron trifluoride etherate (3.5 cc.) was added to a suspension of the dione (50 mg.) in methanol (80 cc.), the mixture refluxed for 2 hr., the resultant solution diluted with water, and the product collected by filtration. Three recrystallizations from chloroform-methanol gave the methyl ether as needles, m.p. 248–251°,  $[\alpha]_D +27^\circ$ ,  $+32^\circ$  (c, 1.4, 1.0),  $\lambda$  255  $\mu$ m (6200),  $\lambda$  6.00, 6.21  $\mu$ .

*Anal.* Calcd. for  $C_{31}H_{50}O_2$ : C, 81.88; H, 11.08. Found: C, 81.6; H, 11.1.

*Conversion of friedelane-2,3-dione to friedelin (friedelan-3-one).* A solution of the dione (55 mg.) in ether (35 cc.) was

added to lithium aluminum hydride (200 mg.) in ether (50 cc.), the mixture heated under reflux for 15 min. and allowed to stand overnight at room temperature. Working up in the usual way yielded a hydroxy ketone, m.p. 218–221°, from chloroform-methanol,  $\lambda$  2.90, 5.85  $\mu$ . Acetylation by treatment with acetic anhydride and pyridine at 100° gave an acetoxy ketone, m.p. 218–221°,  $[\alpha]_D -50^\circ$  as needles from methanol.

*Anal.* Calcd. for  $C_{32}H_{52}O_3$ : C, 79.28; H, 10.81. Found: C, 79.1; H, 10.7.

Zinc dust (10 g.) was added portionwise to a solution of the acetoxy ketone (80 mg.) in acetic acid (50 cc.) and the mixture heated under reflux for 22 hr. After filtration and evaporation of the solvent, the residue was extracted with chloroform and the extract washed with water and dried (sodium sulfate). On removal of the chloroform, the residue was dissolved in benzene and chromatographed on alumina (5 g. Woelm, Grade I). Elution with benzene (4 × 50 cc.) gave fractions 14 mg. (m.p. 235–242°), 9 mg. (m.p. 248–255°), 9 mg. (m.p. 248–255°) and 40 mg. (m.p. 244–252°). The last three were combined, recrystallized once from chloroform-methanol and once from ethyl acetate to give friedelin, m.p. and mixed m.p. 255–260° (capillary), 268–270° (vacuum).

It yielded friedelin oxime which, after recrystallization once from benzene and once from dioxane, melted at 287–290°, melting point and mixed melting point with authentic sample, m.p. 297–300° (vacuum).

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WALTHAM, MASS.

[CONTRIBUTION FROM THE EASTERN REGIONAL RESEARCH LABORATORY<sup>1</sup>]

## Steroidal Sapogenins. LIX. Conversion of 3 $\beta$ -Acetoxy-5,16-pregnadiene-11,20-dione to Intermediates in the 5-Androstene Series<sup>2</sup>

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Beckmann rearrangement of the monoxime of 3 $\beta$ -acetoxy-5,16-pregnadiene-11,20-dione, III, gave 17-acetamino-3 $\beta$ -acetoxy-5,16-androstadiene-11-one, IV. Conditions were found for selective borohydride reduction of the 11-ketone group without attack at the *N*-acetyl enamine function to form, after hydrolysis and reacetylation, 3 $\beta$ -acetoxy-11 $\beta$ -hydroxy-5-androstene-17-one.

There is currently great interest in steroidal compounds which combine the structural features of C-11 oxygenation and the C-5 olefinic bond. This interest arises from the high degree of bioactivity

shown by many compounds (in particular 6-fluoro and 6-methyl derivatives) potentially derivable from precursors possessing the  $\Delta^5$  and C-11 oxygenation functions.<sup>3</sup> Previously such derivative types were usually prepared by the process of 3-ketalation of 11-oxygenated  $\Delta^4$ -3-ketones,<sup>3</sup> the

(1) Eastern Utilization Research and Development Division, Agricultural Research Service, United States Department of Agriculture.

(2) Previous paper in this series, Steroidal Sapogenins. LVIII, A. M. Woodbury, *et al.*, *J. Econ. Bot.*, in press. Presented at 137th national ACS meeting, Cleveland, Ohio, April 1960.

(3) See for example formulation III of A. Bowers, L. Cuéllar Ibanez, and H. J. Ringold, *Tetrahedron*, **7**, 138 (1959) and the many references cited by A. Bowers, E. Denot, M. B. Sanchez, L. M. Sanchez-Hidalgo, and H. J. Ringold, *J. Am. Chem. Soc.*, **81**, 5234 (1959).

$\Delta^4$  bond migrating to the 5,6 position during the ketalation. The 11-oxygenation of these compounds typically derives from microbiological hydroxylation.<sup>4</sup>

In view of the importance of these derived synthetic hormones, we wish to report the preparation of several  $\Delta^5$ -11-oxygenated precursor androstene compounds derived by chemical procedures from the steroidal sapogenin, gnetrogenin, (botogenin). These derivatives possess the special feature of a  $3\beta$ -hydroxy-5-ene system as well as 11-oxygenation. Direct microbiological C-11 hydroxylative procedures for preparing such compounds could not have been applied since, in general, an already formed  $\Delta^4$ -3-ketone system is probably prerequisite for C-11 direct hydroxylation.<sup>4</sup>

In previous papers from this laboratory we had described the preparation of the 12-ketone, gnetrogenin,<sup>5,6</sup> its conversion to 11-keto diosgenin, I,<sup>7</sup> and the side-chain degradation of I to yield the key intermediate  $3\beta$ -acetoxy-5,16-pregnadiene-11,20-dione, II.<sup>8</sup> More recently the degradation of 11-ketodiosgenin to the 11-oxo-16-dehydro pregnene, II, was carried out using several modifications of our previously described procedure. These variations are presented in detail, as they seem to be generally applicable to degradation of C-ring oxygenated sapogenins.

Conversion of I to the corresponding pseudo-sapogenin diacetate was carried out by heating in acetic anhydride at 180°. Oxidation of the latter without isolation was accomplished in a one-phase acetic acid-ethylene chloride aqueous chromium trioxide mixture at -5°. For best yields it was necessary to conduct the oxidation at this temperature and to maintain low temperature during the reduction of excess chromic ion with sodium metabisulfite. The oxidation intermediate, 11-ketodiosone, was not isolated. On treatment with refluxing acetic acid,<sup>10</sup>  $3\beta$ -acetoxy-5,16-pregnadiene-11,20-dione, II, was obtained in 60% yield. The Beckmann rearrangement of  $\Delta^{16}$ -20 ketosteroid oximes discovered by Tendick and Lawson in 1943, U.S. Patent 2,335,616, and utilized by Rosenkranz, Mancera, Sondheimer, and Djerassi<sup>11</sup>

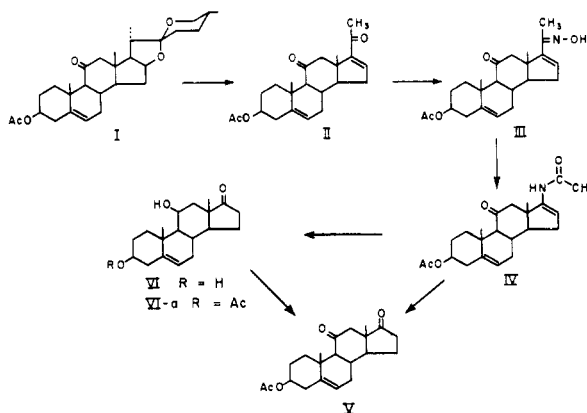


Fig. 1.

in unsubstituted C-ring compounds was applied to compound II. Treatment of II with hydroxylamine hydrochloride as in the procedure of Rosenkranz, Mancera, Sondheimer, and Djerassi<sup>11</sup> gave the monoxime,  $3\beta$ -acetoxy-5,16-pregnadiene-11,20-dione 20-monoxime, III, in 61% yield. On treatment with p-acetamidobenzenesulfonyl chloride, Beckmann rearrangement occurred.<sup>11</sup> The intermediate *N*-acetyl enamine, IV, was obtained in an impure light yellow-orange crystalline form from which a small sample of the pure colorless material was obtained by recrystallization. The impure substance was used without purification in the subsequent steps, as its infrared and ultraviolet spectra were quite similar to those of the pure substance. The ultraviolet maximum of the *N*-acetyl enamine IV,  $\lambda_{\text{max}}^{\text{CH}_3\text{OH}}$  237 m $\mu$ ,  $\epsilon = 7640$ , was similar to the absorption values for unacylated enamines reported by Leonard and Locke<sup>12</sup> and similar to that of the 11-desoxy analog of the present compound described by Rosenkranz, Mancera, Sondheimer, and Djerassi.<sup>11</sup> The infrared spectrum of IV with bands at 3450, 1720, 1686, and 1493  $\text{cm}^{-1}$  was in reasonable agreement with published values for the corresponding 11-desoxyamide.<sup>11</sup> On hydrolysis of IV<sup>11</sup> followed by reacetylation,  $3\beta$ -acetoxy-5-androstene-11,17-dione, V, was obtained in 70% yield. The structure of V is based on analogy with the 11-desoxy compound,<sup>11</sup> on the elemental analysis, and on the infrared absorption spectrum which showed bands at 1707 (11-ketone) and 1740  $\text{cm}^{-1}$  (acetate and 17-ketone).<sup>13</sup>

We became interested in preparing the intermediate,  $3\beta,11\beta$ -dihydroxy-5-androstene-17-one,

(12) N. J. Leonard, and D. M. Locke, *J. Am. Chem. Soc.*, **77**, 437 (1955).

(13) After the researches reported in this paper were completed, we noted a report by M. Martin-Smith, *J. Chem. Soc.*, 523 (1958), in which was reported the preparation of V by an unusual route. This worker observed that  $3\beta$ -acetoxy-17 $\alpha$ -hydroxy-5 $\alpha$ -pregnane-11,20-dione on chromic acid oxidation gave  $3\beta$ -acetoxy-5 $\alpha$ -androstane-11,17-dione which on further oxidation gave, in low yield, the corresponding 5 $\alpha$ -hydroxy derivative. On dehydration the latter gave a compound identical in all physical properties and infrared spectrum with V.

(4) S. H. Eppstein, *et al.*, *J. Am. Chem. Soc.*, **76**, 3174 (1954).

(5) H. A. Walens, S. Serota, and M. E. Wall, *J. Org. Chem.*, **22**, 182 (1957).

(6) M. E. Wall, J. J. Willaman, T. Perlstein, D. S. Correll, and H. S. Gentry, *J. Am. Pharm. Assoc. (Sci. Ed.)*, **46**, 155 (1957).

(7) E. S. Rothman and M. E. Wall, *J. Am. Chem. Soc.*, **79**, 3228 (1957).

(8) E. S. Rothman and M. E. Wall, **81**, 411 (1959). See also O. Halpern and C. Djerassi, *J. Am. Chem. Soc.*, **81**, 439 (1959) for the 11 $\alpha$  hydroxy congener of the compound II.

(9) M. E. Wall and S. Serota, *J. Am. Chem. Soc.*, **79**, 6481 (1957).

(10) A. F. B. Cameron, *et al.*, *J. Chem. Soc.*, 2807 (1955).

(11) G. Rosenkranz, O. Mancera, F. Sondheimer, and C. Djerassi, *J. Org. Chem.*, **21**, 520 (1956).

VI. From VI one could prepare 11 $\beta$ -hydroxy-4-androstene-3,17-dione<sup>14</sup> which is the starting point for the synthesis of 9 $\alpha$ -fluoro-17 $\alpha$ -methyl-11 $\beta$ ,17 $\beta$ -dihydroxy-4-androstene-3-one, (halotestin).<sup>15</sup> Hitherto the latter steroids have been available only through the microbiological oxidation of 4-androstene-3,17-dione.<sup>4</sup> Although compound VI might have been prepared from V by forming the 17-monoketal or monoenamine followed by lithium aluminum hydride reduction of the 11-ketone and removal of the protective group, we felt that it might be preferable to retain and utilize the enamine grouping in IV as an already existing blocking group thereby saving two reaction steps. Reasoning that it might be possible to reduce the 11-ketone group without attacking the unsaturated amide linkage, several reduction systems were investigated. Lithium aluminum hydride, in the several solvents tried, seemed to reduce the  $\Delta^{16}$  double bond, as did sodium borohydride in isopropanol or diethylene glycol dimethyl ether. In these cases the products showed infrared amide, hydroxyl, and NH bands but did not show selective ultraviolet absorption near 238  $\mu$ . However, use of sodium borohydride in methanol gave the desired VI, after hydrolysis, in 35% yield. The hydrolysis could be carried out in either acid or basic media but in the latter case was difficult to drive to completion. Structure proof was based on observation of correct analytical values; the infrared absorption spectrum showing a single carbonyl band at 1740  $\text{cm}^{-1}$  (17-ketone); and the fact that monoacylation at C-3 followed by oxidation of VI gave the 11,17-diketone V identical with the diketone directly derived from hydrolysis of IV. Acetylation of VI under mild conditions gave the 3 $\beta$ -acetoxy-11 $\beta$ -hydroxy derivative VIa. In the course of chromatography of the acetylated mother liquors of VIa, 11 $\beta$ -hydroxy-3,5-androstadiene-17-one, VII, was isolated as a by-product. Structure assignment of VII was based on correct analytical values, characteristic ultraviolet spectrum<sup>16</sup> with maxima at 230, 236, and 245  $\mu$ ,  $\lambda_{\text{max}}^{\text{CH}_3\text{OH}}$  236  $\mu$ ,  $\epsilon = 21,900$ , and infrared spectrum showing bands at 3600 (hydroxyl), and 1743  $\text{cm}^{-1}$  (17-ketone) as well as bands at 3060, 865, 821, and 811  $\text{cm}^{-1}$  characteristic of the conjugated system. Other acid-induced dehydration by-products may have been formed but could not be isolated.

#### EXPERIMENTAL<sup>17</sup>

3 $\beta$ -Acetoxy-5,16-pregnadiene-11,20-dione, II. One hundred grams of 11-keto-diosgenin acetate,<sup>7</sup> I, were heated with

(14) M. E. Herr and F. W. Heyl, *J. Am. Chem. Soc.*, **75**, 5927 (1953).

(15) M. E. Herr, J. A. Hogg, and R. H. Levin, *J. Am. Chem. Soc.*, **78**, 500 (1956).

(16) L. Dorfman, *Chem. Rev.*, **53**, 47 (1953).

(17) We wish to thank S. Serota for determination of optical rotations, R. Kelly for elemental analyses, and C. Leander and A. Smith for spectral determinations.

250 ml. of acetic anhydride containing 0.1% v/v glacial acetic acid for 21 hr. at 180°. After cooling, sufficient water was added to decompose all the acetic anhydride. The volume was brought to 1500 ml. with acetic acid and an equal volume of ethylene chloride was added. The solution was cooled to -8° in an ice-salt bath. To this solution was added a solution of 50.0 g. of chromic acid in 1500 ml. of 90% acetic acid, precooled to +7°. The oxidant was added over a period of 30 min. at such a rate that the temperature did not rise above -2°. The reaction was then allowed to proceed another 30 min. Excess chromium trioxide was then reduced with a solution of 50 g. of sodium metabisulfite in 400 ml. of water, precooled to -4°, and added at such a rate that the temperature did not exceed -2°. To the reduced solution was added 5 l. of 20% sodium chloride solution, and the lower layer consisting of ethylene chloride was drawn off. The aqueous solution was then repeatedly extracted with ether; the combined organic layers were washed with sodium bicarbonate solution until neutral and dried with anhydrous sodium sulfate. The solvents were removed *in vacuo* and the residual glassy 11-keto-diosone refluxed 2 hr. with 1 l. of glacial acetic acid. The acid was removed *in vacuo*, the residue taken up in heptane; the last traces of acetic acid were removed by washing with sodium bicarbonate solution and the heptane was dried with anhydrous sodium sulfate. The crude heptane solution of II was passed through a Florisil<sup>18</sup> column; elution with benzene followed by evaporation of solvent and crystallization from methanol gave 47 g. of II, m.p. 183°,  $[\alpha]_D^{25} -1.7^\circ$ .

Conversion of 3 $\beta$ -acetoxy-5,16-pregnadiene-11,20-dione, II, to its monoxime, III. A mixture of 6.89 g. of II, 35 ml. of absolute ethanol, 10 ml. of pyridine, and 2.34 g. of hydroxylamine hydrochloride was refluxed for 35 min. On cooling crystals formed and were collected. Dilution of the filtrate with water gave additional crystalline material. The combined crops, after recrystallization from methanol, gave 4.34 g. (61%) of C-20 monoxime, m.p. 214-217°. The analytical sample melted at 217° to a pink liquid  $\lambda_{\text{max}}^{\text{CH}_3\text{OH}}$  234.5  $\mu$ ,  $\epsilon = 15,200$ ,  $[\alpha]_D^{25} -24.7^\circ$ .

Anal. Calcd. for C<sub>23</sub>H<sub>31</sub>O<sub>4</sub>N: N, 3.63. Found: N, 3.58.

17-Acetamino-3 $\beta$ -acetoxy-5,16-androstadiene-11-one, IV. The monoxime III, 4.31 g. in 12.3 ml. of dry pyridine, was treated with 5.27 g. of *p*-acetamidobenzenesulfonyl chloride in 12.3 ml. of pyridine at 0°, and was stirred at 10° for 2 hr. and at 26° for 2 additional hr. The mixture was then stirred into crushed ice whereupon a thick emulsion separated. Extraction with methylene chloride-hexane was carried out, and solid matter collecting at the interface was collected with the organic layer. Evaporation of the solvent *in vacuo* gave an orange syrup which on repeated re-evaporation *in vacuo* with a little methanol was freed of pyridine traces, whereupon the residue spontaneously crystallized. Recrystallization from methanol gave needles, m.p. 220-225° (dark red melt),  $[\alpha]_D^{25} \pm 0$ ;  $\nu_{\text{max}}^{\text{CHCl}_3}$  3450 (NH), 1721 (acetate); 1690 (amide + ketone), 1492  $\text{cm}^{-1}$  (NH),  $\lambda_{\text{max}}^{\text{CH}_3\text{OH}}$  237  $\mu$ ,  $\epsilon = 7,640$ .

Anal. Calcd. for C<sub>23</sub>H<sub>31</sub>NO<sub>4</sub>: C, 71.66; H, 8.11; N, 3.63. Found: C, 71.60; H, 8.10; N, 3.61.

3 $\beta$ ,11 $\beta$ -Dihydroxy-5-androsten-17-one, VI. The enamine amide, IV, 2.15 g., in 20 ml. of dry methanol (distilled from magnesium turnings) was treated with 235 mg. of sodium borohydride at room temperature for 20 hr. A fresh charge of 225 mg. of sodium borohydride was added and the mixture was again let stand for 20 hr. The suspension was then diluted with methylene chloride and hexane and was shaken with dilute aqueous sodium dihydrogen phosphate to destroy excess reagent. The organic layer was separated and dried with sodium sulfate. An aliquot refluxed with 5% methanolic-aqueous potassium hydroxide for 1 hr. showed persisting infrared bands at 1735 and 1665  $\text{cm}^{-1}$  although their intensity was reduced relative to an untreated aliquot.

(18) Specification of brand names of materials used does not imply endorsement over similar commercial products.

The remainder of the material was evaporated to dryness, redissolved in 45 ml. of methanol, 18 ml. of 6N aqueous hydrochloric acid was added and the mixture was refluxed 1.5 hr. The cooled mixture was extracted with methylene chloride-hexane which on concentration gave 720 mg. of crystalline product, m.p. 173–190°. Recrystallization from ether gave blades, m.p. 192–197°. The analytical sample from hexane gave rosettes, m.p. 190–192°,  $[\alpha]_D^{25} -20$ .

*Anal.* Calcd. for  $C_{19}H_{28}O_2$ : C, 74.96; H, 9.27. Found: C, 74.62; H, 9.41.

*11 $\beta$ -Hydroxy-3,5-androstadiene-17-one*, VII. The mother liquors from the preceding preparations were evaporated to dryness, dissolved in benzene, and placed on a short column of Florisil. Elution with benzene gave a noncrystalline orange glassy material followed by 39 mg. of a crystalline fraction. Recrystallization of the latter from methanol and from aqueous methanol gave broad blades having a high vapor pressure near the melting point. The melting point under very slow temperature-rise conditions was 161.5–165°, but a moderate rate of heating on open microscope slide gave the value 178–179°,  $[\alpha]_D^{25} +52.1^\circ$ ,  $\nu_{max}^{CS_2}$  3600 (single sharp), 1743 (v. strong), 821, 811, 865  $cm^{-1}$ , ultraviolet absorption bands occurred at 230, 237, 245  $m\mu$ ,  $\lambda_{max}^{CH_3OH}$  237  $m\mu$ ,  $\epsilon = 21,900$ .

*Anal.* Calcd. for  $C_{19}H_{28}O_2$ : C, 79.68; H, 9.15. Found: C, 79.61; H, 9.30.

Further elution of the column with ether gave 60 mg. of VI.

*3 $\beta$ -Acetoxy-11 $\beta$ -hydroxy-5-androstene-17-one*, VIa. The 3 $\beta$ -11 $\beta$ -dihydroxy-17-ketone, VI, 100 mg., was let stand 16 hr. in a mixture of 2 ml. of pyridine and 1 ml. of acetic anhydride. Dilution with water, extraction with ether, and washing the ether free of acetylation mixture with dilute hydrochloric acid and with dilute sodium bicarbonate gave, after evaporation, the required monoacetate. Recrystallization from hexane gave spindles undergoing transition beyond 200°. At 216° the primary crystal forms began to melt before transition of crystal form was completed. Decomposition and reddening supervened, the last crystal of the stable phase disappearing at 231°,  $[\alpha]_D^{25} -17.1^\circ$ . The

analytical sample melted cleanly at 232°, after undergoing transition, but did not decompose.

*Anal.* Calcd. for  $C_{21}H_{30}O_4$ : C, 72.80; H, 8.73. Found: C, 72.71; H, 8.61.

*3 $\beta$ -Acetoxy-5-androstene-11,20-dione*, V. (a) From VIa. 3 $\beta$ -Acetoxy-11 $\beta$ -hydroxy-17-ketone, VIa, 500 mg., was dissolved in 6 ml. of pyridine at 10° and treated with a slurry of 500 mg. of chromium trioxide in 6 ml. of cold pyridine.<sup>19</sup> After standing 16 hr. at room temperature the mixture was diluted with ice water and with ether. Dilute hydrochloric acid was added to make the aqueous phase distinctly acid, and enough dilute sodium bisulfite was added to reduce chromium to the trivalent state. At this point emulsified solid brown matter went into solution and the phases separated cleanly. The organic layer was separated and washed with water, dilute sodium bicarbonate, and saturated sodium chloride. The residue on evaporation gave 500 mg. of colorless crystalline residue, m.p. 163–167°. After crystallizing from methyl acetate and from methanol, the product melted from 172–174°,  $[\alpha]_D^{25} +38^\circ$ ; Martin-Smith<sup>18</sup> gives m.p. 171°,  $[\alpha]_D +38^\circ$ .

*Anal.* Calcd. for  $C_{21}H_{30}O_4$ : C, 73.22; H, 8.19. Found: C, 72.81; H, 8.37.

(b) From IV. A 5-g. sample of the *N*-acetyl enamine, IV, was dissolved in 110 ml. of 5% ethanolic potassium hydroxide and refluxed for 1 hr. The cooled flask contents were diluted with water and extracted with ether. The organic layer was washed with 2*N* hydrochloric acid to remove yellow coloration, with dilute sodium bicarbonate, and with saturated sodium chloride. An aliquot of this material did not show persisting acetate infrared bands. The solvent was evaporated and the residue was acetylated with acetic anhydride-pyridine mixture at room temperature overnight. The product, crystallized from methanol, was obtained in 74% yield and was identical with the sample described in part (a).

PHILADELPHIA 18, PA.

(19) G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Am. Chem. Soc.*, **75**, 422 (1953).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

## The Relative Stabilities of *cis* and *trans* Isomers. IX. A Study of the Importance of Conformational Transmission in Determining the Relative Stabilities of Hydrindanones in Steroidal Systems<sup>1</sup>

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A-nor-5 $\beta$ -androstan-3-one (VIII) and A-nor-D-homo-5 $\beta$ -androstan-3-one (XIV) have been prepared. A comparison of their rotatory dispersion curves, together with the corresponding curves obtained from the epimeric mixtures which resulted when they were treated with base, showed that the strain induced in VIII by the *trans*-C/D fusion and conformationally transmitted to the A/B fusion was not of importance in determining the position of equilibrium at the latter juncture.

The hydrindane and hydrindanone systems, because of their apparent relative simplicity and wide occurrence in nature, have furnished a challenge to conformational analysis to interpret the relative stabilities of the *cis* and *trans* junctures. Although a large amount of work directed at such an interpretation has been carried out,<sup>2</sup> even a qualitative

understanding of these systems is lacking in certain cases.

One effect which must in principle influence the stability of a hydrindanone juncture as in the A/B rings of a compound such as VIII and which has not previously been considered in this connection, is the effect of the strained *trans* C/D fusion as relayed

(1) Paper VIII, N. L. Allinger, R. B. Hermann, and C. Djerassi, *J. Org. Chem.*, **25**, 922 (1960).

(2) See ref. 1 for summary and references.