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STUDIES ON C-NOR-D-HOMOSTEROIDS—I[1]

SYNTHESIS OF A NITROGEN-FREE DERIVATIVE OF JERVINE

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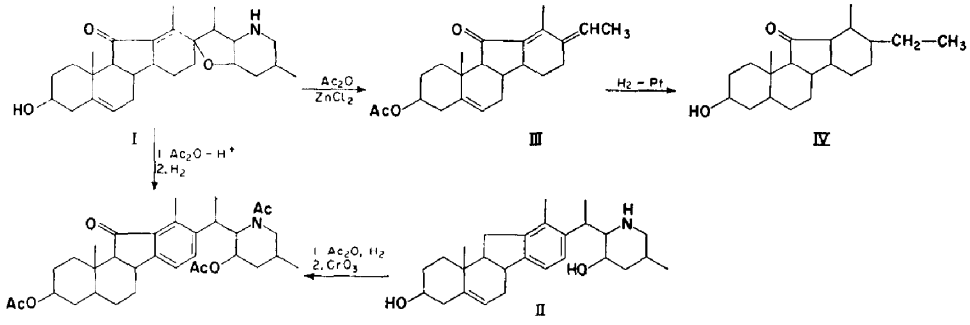
Abstract—The synthesis of some C-nor-D-homopregnane derivatives and a nitrogen-free derivatives of jervine and veratramine from hecogenin are described. It provides final confirmation of the C-nor-D-homoskeleton and correlation with the normal steroids.

THE tentative structure for jervine and veratramine presented by Jacobs *et al.* was later corrected by Wintersteiner *et al.* who as a result of their study of the problem published the correct structures and the first examples of the unusual C-nor-D-homosteroids.[2] This was followed by the structural determination of the ceveratrum alkaloids, but no synthetic proof for the peculiar ring system has been reported. Moreover, some of the C_{21} aglycones of the ester glycosides isolated from Asclepiadaceae plants were shown to give Jacobs hydrocarbon on selenium dehydrogenation[3] and could possibly have a C-nor-D-homopregnane skeleton.[4]



From the acetolysis of jervine (I), which had been given the C-nor-D-homoskeleton structure by Wintersteiner *et al.*,[5] Fried *et al.* obtained a nitrogen-free compound

[1] This paper represents Part X of *Studies on the Constituents of Asclepiadaceae Plants*, Part IV *Chem. Pharm. Bull., Japan* **10**, 818 (1962).

[2] L. F. Fieser and M. Fieser, *Steroids* p. 870–895. Reinhold, New York (1959).

[3] R. E. Winkler and T. Reichstein, *Helv. Chim. Acta* **38**, 721 (1954).
F. Korte and J. Ripphahn, *Liebigs Ann.* **621**, 1527 (1959), **8**, 738 (1960).
H. Mitsuhashi and Y. Shimizu, *Chem. Pharm. Bull., Japan* **7**, 749 (1959); **8**, 738 (1960).
J. M. Nascimento, H. Jaeger, Ch. Tamm and T. Reichstein, *Helv. Chim. Acta* **42**, 661 (1959).

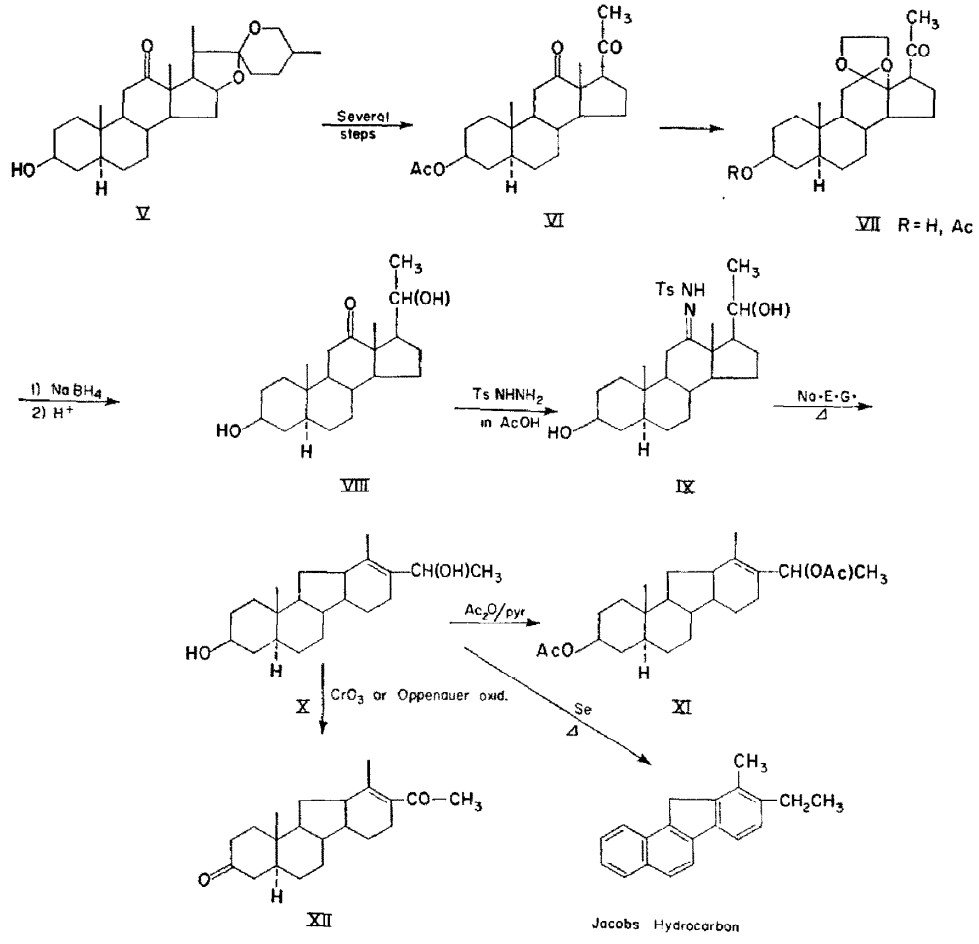
[4] J. W. Cornforth, *Chem. Ind.* 602 (1959).
H. Mitsuhashi and Y. Shimizu, *Chem. Pharm. Bull., Japan* **7**, 949 (1959). For convenience, in the term, C-nor-D-homopregnane, we mean the compound which biogenetically corresponds to the normal pregnane and should be called 17a-methyl-D-homo-12,18-bisnorpregnane by the IUPAC system.

[5] J. Fried, O. Wintersteiner, M. Moore, B. M. Iselin and A. Klinsberg, *J. Amer. Chem. Soc.* **73**, 2970 (1951).

which was given the structure III.[6] This substance can be hydrogenated to the 3-hydroxy-11-keto derivative (IV),[7] which is the most simple C-nor-D-homopregnane derivative of natural origin. A preliminary report on the synthesis of IV was recently published.[8]

The conversion of a normal steroid to a C-nor-D-homosteroid has been reported in the spirostane series[9] but not in the pregnane series.

In an attempt to synthesize a C-nor-D-homopregnane with no oxygen function at C-11, hecogenin (V) was degraded to 3β-acetoxy-5α-pregnane-12,20-dione (VI),[10] ketalized at C-12 to 3β-hydroxy-12,12-ethylenedioxy-5α-pregnan-20-one which on sodium borohydride reduction followed by deketalization, gave 3β,20β-dihydroxy-



[6] J. Fried and A. Klinsberg, *J. Amer. Chem. Soc.*, **75**, 4929 (1953).

[7] J. Fried *et al.* describe this compound as 17-ethyletiojervane-3β-ol-11-one acetate.[6]

[8] Preliminary communication, *Tetrahedron Letters* NO. 21, 777 (1961).

[9] [a]R. Hirschmann, C. S. Snoddy, Jr., C. F. Hiskey and N. L. Wendler, *J. Amer. Chem. Soc.* **76**, 4013 (1954); [b]J. Elks, G. H. Phillipps, D. H. A. Taylor and L. J. Wyman, *J. Chem. Soc.* 1739 (1954).

[10] R. E. Marker and E. Rohmann, *J. Amer. Chem. Soc.* **62**, 518 (1940); R. B. Wagner, J. A. Moore, R. E. Forker, *Ibid.* **72**, 1856 (1950); A. F. B. Cameron, R. M. Evans, J. C. Hamlet, J. S. Hunt, P. G. Jones and A. G. Long, *J. Chem. Soc.* 2807 (1955).

5α-pregnan-12-one (VIII).[11] The tosylhydrazone of VIII, (IX) was prepared in acetic acid and subjected to the pyrolytic decomposition in sodium ethylene glycolate. Crystallization of the reaction mixture gave X, m.p. 196–198°, with the molecular formula, $C_{21}H_{34}O_2$ and a strong tetranitromethane reaction. The I.R. spectra of X shows neither a ketone group nor a vinyl hydrogen. Acetylation of X yields diacetate (XI), $C_{25}H_{38}O_4$, m.p. 138°; with two oxygens as secondary hydroxyl groups. The chromic acid oxidation of X gives an amorphous product (XII) which shows a strong U.V. maximum at 247 mμ suggesting the occurrence of α,β-unsaturated ketone group.[12] The selenium dehydrogenation of X affords Jacobs hydrocarbon in excellent yield.[13] Based on these data, X is given the structure as cited in Chart II.

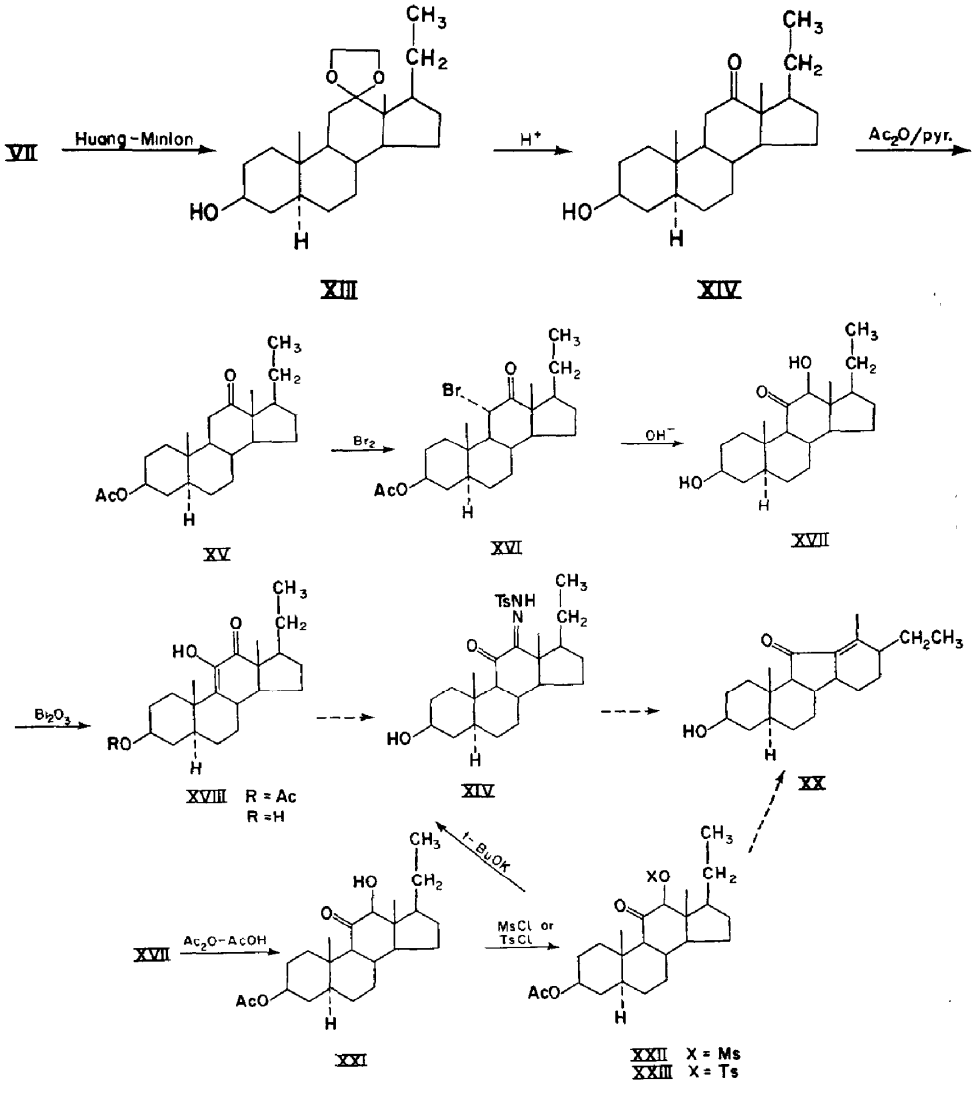
In order to synthesize IV, the introduction of an oxygen function at C-11 is necessary. Such a synthesis has already been reported in the spirostane series by Hirschmann *et al.*[9a] They prepared the tosylhydrazone of 11-keto-hecogenin and submitted it to alkaline decomposition to afford an enone compound, which has a U.V. max at 255 mμ as found also in jervine. They also reported that the I.R. spectra of the enone and jervine resemble each other. After several attempts to prepare the 11-oxygenated C-nor-D-homopregnane, this method was applied to the pregnane series.

The reduction of the C-20 ketone to a methylene group preceded the modification of the C-11-oxygenation and ring rearrangement. The Huang–Minlon reduction of VII gave 3β-hydroxy-12,12-ethylenedioxy-5α-pregnane (XIII) in 86% yield. The ketal group was then removed to give 3β-hydroxy-5α-pregnan-12-one (XIV), the acetate of which (XV), m.p. 140° was found to be identical with the compound reported by Wall *et al.*[14] and identified by its I.R. spectrum. The bromination of the acetate yielded the 11α-bromo derivative (XVI) which yielded the 11,12-ketol (XVII) on treatment with alkali. The 11α-bromo-orientation of XVI was deduced from the I.R. absorption of the 12-ketone (1740 cm^{-1}). The oxidation of (XVII) yielded only the 3β-acetoxy-11,12-enol-diketo (XVIII) and no α-diketo derivative was isolated from the mother liquors. The compound (XVIII) resists tosylhydrazone formation. It is very probable that the conjugated system protects the addition of the reagent to the ketone group, since the ease of the hydrazone formation decreases with the formation of a conjugated system. This difficulty might have been avoided by using the keto isomer which we were unable to isolate.

The rearrangement by solvolysis of the 11-keto-12-mesylate was studied next. Partial acetylation of XVII followed by mesylation gave 3β-acetoxy-12β-mesylate (XXII). The mesylate is so resistant to solvolysis that the starting material was recovered even under such conditions as refluxing methanol or acetic anhydride containing several salts.[15] If more vigorous condition such as refluxing with potassium t-butoxide in t-butanol was applied, the resulting product, in rather good yield, was the enol compound (XVIII, R = H). The tosylate (XXIII) which was prepared in the same manner as the mesylate behaves similarly. The formation of the enol

[11] D. N. Kirk, D. K. Patel and V. Petrow, *J. Chem. Soc.*, 1046 (1957).
[12] The calculated value is 249 mμ.
[13] H. Mitsuhashi and Y. Shimizu, *Tetrahedron Letters* NO. 20, (1962).
[14] M. E. Wall, T. Perlstein and S. G. Levine, *J. Org. Chem.* **26**, 159 (1961). The identity was confirmed only by the I.R. spectra, due to the lack of a sample for comparison.
[15] S. Winstein, D. Smith, J. Paravish, *Amer. Chem. Soc.* **81**, 5511 (1959).

compound (XVIII) in potassium t-butoxide can be explained by the utilization of molecular oxygen. This reaction can be compared with the ketol formation in potassium t-butoxide reported by Barton *et al.*[16] As the mesylate or tosylate of rockogenin acetate undergoes solvolysis very easily, the resistance of the mesylate or tosylate of XXII to solvolysis must be attributed to the effect of the neighbouring



ketone group. Electron withdrawal by the keto group causes a more positive charge near the C-12, so that the C—O bond is strengthened and the decrease of $SN1_i$ reactivity and increase of SN2 reactivity occur.

[16] [a] E. J. Bailey, J. Elks and D. H. R. Barton, *Proc. Chem. Soc.* 214 (1960).
[b] E. J. Bailey, D. H. R. Barton, J. Elks and J. F. Templeton, *J. Chem. Soc.* 1578 (1962)

The third method considered is the rearrangement of the 11-hydroxy-12-tosylhydrazo-compound to the C-nor-D-homosteroid. The α-bromo ketone (XVI) was hydrolyzed to 11,12-ketol (XVII), which should be a thermodynamically more stable form, but it was noticed that in the initial stage of hydrolysis, crystals appeared and then gradually dissolved. The crystals were filtered when the amount seemed to be at a maximum and recrystallized from methanol to give pure 12,11-ketol (XXIV), m.p. 193°. The overall yield was raised to 50% by successive treatment without the purification of the bromine compound. The action of tosylhydrazine on XXIV in acetic acid at room temperature produced the crystalline tosylhydrazone (XXV) in a few minutes. The hydrazone was added to an ethylene glycol solution of sodium and heated at 170°. From about 140°, the evolution of N_2 gas was observed, and the reaction mixture yielded crystals of XXIV, m.p. 190° with the molecular formula, C_{21}

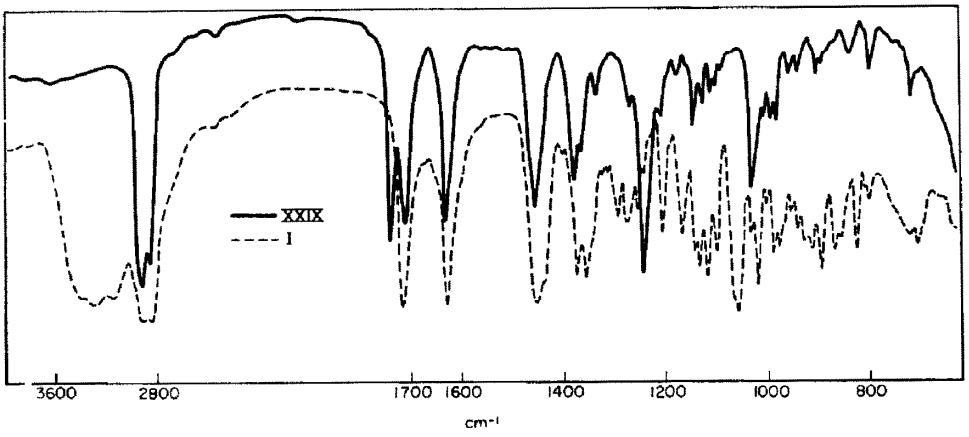


FIG. 1. Infrared spectra of I and XXIX

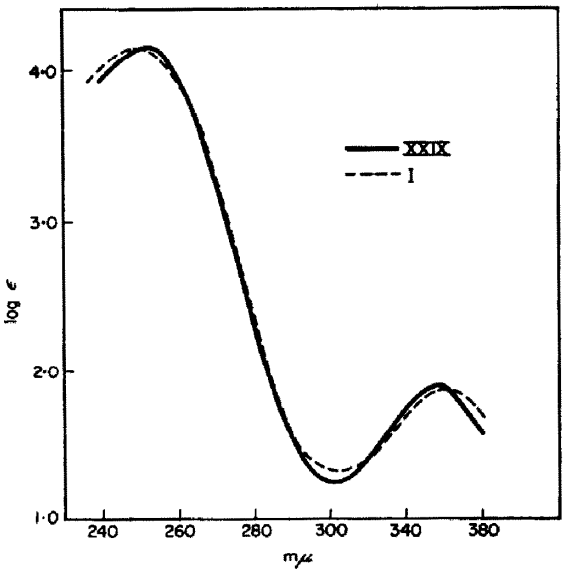
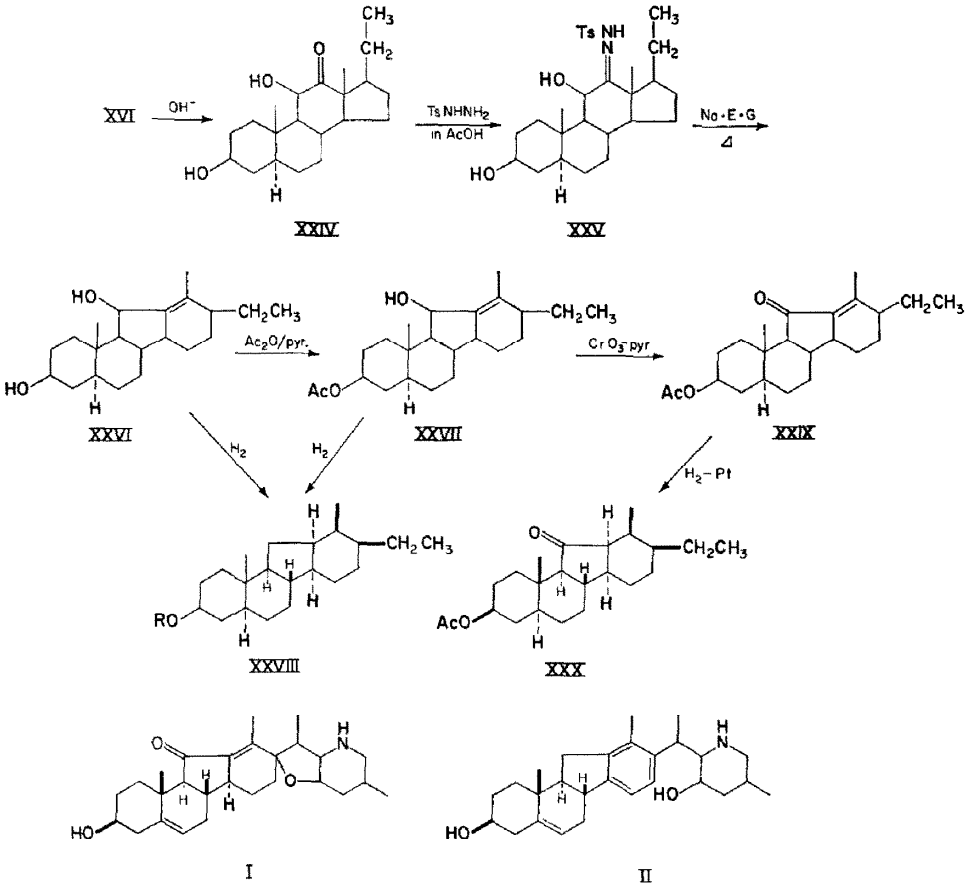


FIG. 2. Ultraviolet spectra of I and XXIX in ethanol

$H_{34}O_2$ and a strong positive tetranitromethane reaction. The I.R. spectrum shows no carbonyl absorption, but relatively strong distinctive absorption at 1678 cm^{-1}, characteristic of an exocyclic bond to a five membered ring and was later proved to be the case. Catalytic hydrogenation of the compound gave a mono-ol (XXVIII) with loss of a hydroxyl group suggesting the presence of an allyl alcohol type structure.

The acetylation of XXVII gave a monoacetate, $C_{23}H_{36}O_3$ with absorption at 1678 cm^{-1}, indicating a double bond. Oxidation of the acetate by several of the normal reagents were unsuccessful, but mild oxidation with chromic oxide–pyridine at room temperature gave the corresponding enone compound (XXIX), m.p. 143·5° in good yield. This compound shows I.R. absorption maximum at 1710 cm^{-1} (Fig. 1) and U.V. maxima at 255 mμ and 340 mμ. This absorption resembles that of jervine which has a similar chromophore. Catalytic hydrogenation of XXIX gave the dihydro derivative (XXX), m.p. 118°–119°, identical with IV prepared from jervine (I) by mixed m.p. and I.R. spectral comparison.

Since jervine and veratramine have been correlated, the C-nor-D-homo ring system of both compounds has been confirmed conclusively. Moreover, considering the configuration of hecogenin and the reactions used, the stereochemistry of jervine and veratramine can be expressed as shown in chart IV.



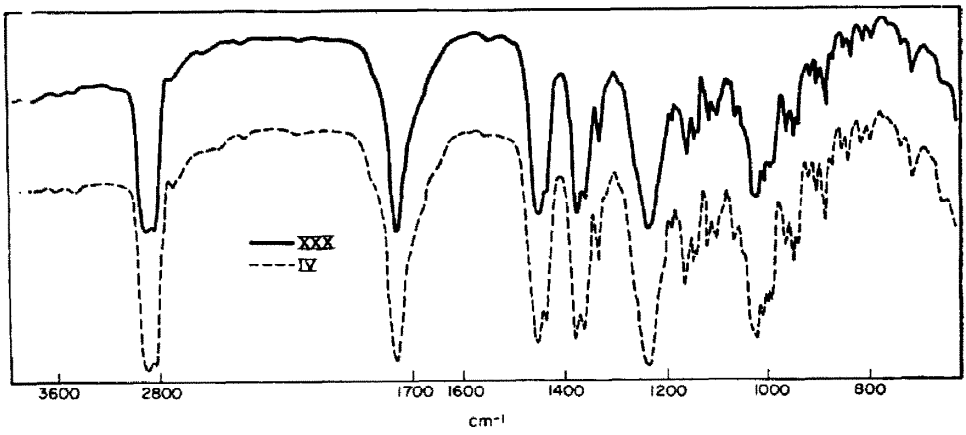


FIG. 3. Infrared spectra of IV and XXX

EXPERIMENTAL

The m.p.'s are uncorrected unless otherwise specified. The I.R. spectra were taken in a Shimazu infrared spectrophotometer type I.R. Compounds VI, VII, and VIII were prepared from hecogenin (V) by methods based mainly on known procedures.[10,11] The yield exceeded 30% by the successive treatment without purification at each stage. The constants of these compounds are as reported.

Tosylhydrazone of 3β,20β-*dihydroxy*-5α-pregnan-12-*one*, (IX). 3β,20β-Dihydroxy-5α-pregnan-12-one (VIII; 1·0 g) and tosylhydrazine (1·0 g) were dissolved in acetic acid (10 cc) and allowed to stand overnight at room temp. and water added. Recrystallization of the product from methanol–water gave prisms, m.p. 225° (dec.) (1·25 g, 84%). (Found: C, 64·78; H, 8·33, N. 4·87; S, 6·14. $C_{28}H_{42}O_4N_2S \cdot H_2O$ requires: C, 64·59; H, 8·52; N, 5·38; S, 6·25%).

Alkaline decomposition of (IX). The above tosylhydrazine (IX; 1.2 g) was suspended in a solution prepared by dissolving Na (1·0 g) in 40 cc ethylene glycol, and heated. The nitrogen evolution started at 140° and the solution was kept at 170° for 1·5 hr. After cooling, water was added to the mixture followed by extraction with methylene chloride. The organic layer was washed with water and dried. After evaporation, the residue was crystallized from ethyl acetate to give a pure crop of X (240 mg; 30%), m.p. 198°. (Found: C, 79·02; H, 10·57. $C_{21}H_{34}O_2$ requires: C, 79·19; H, 10·76%).

This compound shows no distinctive I.R. absorption but has a strong tetranitromethane reaction. Chromatography of the mother liquors after crystallization gave a small additional amount of X and two other compounds of m.p. 138° and m.p. 254°. The structure of the former is unknown but the latter proved to be 3β,12β,20β-trihydroxy-5α-pregnane.[13]

Acetylation of diol (X). The diol (X; 70 mg) was heated with the mixture of pyridine (1·5 cc) and acetic anhydride (1·0 cc) for 3° min on a water-bath. After pouring into ice-water, the mixture was extracted with ether and treated according to the usual procedures. Recrystallization of the product from hexane-ether gave fine plates (XI; 70 mg), m.p. 138°. (Found: 74·65; H, 9·38; $C_{25}H_{38}O_4$ requires: C, 74·59; H, 9·52%); ν_{max} 1740 cm^{-1} (acetyl).

Chromic acid oxidation of the diol (X). The diol (X; 50 mg) was dissolved in 90% acetic acid (1·5 cc) and added to a solution of CrO_3 (25 mg) in 90% AcOH (1·5 cc). After standing 16 hr at room temp., the reaction mixture was taken up in ether and washed with water, $NaHCO_3$ solution and water respectively and dried. After evaporation, attempted crystallization of the residue gave only a amorphous powder (XII), which had a strong absorption at 247 mμ; (not analysed). Oppenauer-oxidation gave similar results.

3β-*Hydroxy*-12,12-*ethylenedioxy*-5α-*pregnane* (XIII). 3β-Hydroxy-12,12-ethylenedioxy-5α-pregnane-20-one (2·3 g) was added to the solution of NaOH (3·7 g) in diethylene glycol (37 cc) containing hydrazine hydrate (6 cc), and refluxed for 1 hr. After cooling, the reaction mixture was heated, equipped with a take-off condenser to remove water until the temperature was 195°, and maintained

[17] O. Wintersteiner and M. Moore, *J. Amer. Chem. Soc.* **75**, 4938 (1953); Ch. Tamm and O. Wintersteiner *Ibid.* **74**, 3842 (1952); O. Wintersteiner and N. Kosansky, **74**, 4474 (1952).

at that temperature for 8 hr. Water was added to the mixture and the crystalline mass which separated crystallized from methanol-water in prisms (1·9 g; 87%), m.p. 165° (Found: C, 76·00; H, 10·54. $C_{23}H_{38}O_3$ requires: C, 76·19; H, 10·57%). ν_{max} 3520 (OH), 840, 950, cm^{-1}.

3β-Hydroxy-5α-pregnan-12-one (XIV). 3β-Hydroxy-12,12-ethylenedioxy-5α-pregnane (XIII; 1·8 g) was heated in 90% AcOH (20 cc) on a water-bath for 2 hr. Then the mixture was concentrated under red. press. and addition of water precipitated a crystalline product which recrystallized from methanol–water in needles (quantitative yield), m.p. 186° (partially solvated), (Found: C, 78·91; H, 10·55. $C_{21}H_{34}O_2$ requires: C, 79·19; H, 10·76%), ν_{max} 3300 (OH), 1700 (C=O) cm^{-1}.

3β-Acetoxy-5α-*pregnan*-12-*one* (XV). 3β-Hydroxy-5α-pregnan-12-one (1·4 g) was heated with the mixture of pyridine (10 cc) and Ac_2O (7 cc) at 90° for 40 min. The product was crystallized from EtOH—H_2O to give needles (1·45 g), m.p. 139–140°, (Found: C, 76·82; H, 10·03. $C_{23}H_{36}O_3$ requires: C, 76·62; H, 10·07), ν_{max} 1740 (acetyl), 1717 (C=O), 1243 (acetyl) cm^{-1}.

3β-Acetoxy-12α-*bromo-5α-pregnan*-12-*one* (XVI). 3β-Acetoxy-5α-pregnan-12-one (1·4 g) was dissolved in benzene (20 cc) and brominated with bromine (0·7 g) in benzene (5 cc). The first few drops of the bromine solution were discoloured, after 5 min the rest was added and the mixture kept at room temp for 1 hr. The benzene solution was washed with Na_2CO_3 solution and water, dried and evaporated to dryness under red. press. Crystallization from n-hexane gave prisms (1·0 g; 50%), m.p. 148° (dec), (Found: C, 63·84; H, 8·11. $C_{23}H_{35}O_3Br$ requires: C, 62·84; H, 8·02%), ν_{max} 1740 (acetyl and C=O) cm^{-1}.

3β,12β-Dihydroxy-5α-pregnan-11-*one* (XVII). 3β-Acetoxy-12α-bromo-5α-pregnan-12-one (1·0 g) was dissolved in t-BuOH (10 cc) and 5% NaOH solution (10 cc). The two-phase solution was refluxed for 6 hr. The initial appearance of crystals disappeared on prolonged boiling. After addition of water, the product was isolated by filtration and recrystallized from EtOH–H_2O in needles or plates (quantitative yield), m.p. ca, 200°, (Found: C, 75·35; H, 10·10. $C_{21}H_{34}O_3$ requires: C, 75·40; H, 10·25%), ν_{max} 3400 (OH), 1715 (C=O).

3β-Acetoxy-11-*hydroxy*-12-*keto*-$\Delta^{9(11)}$-*pregnene* (XVIII). 3β,12β-Dihydroxy-5α-pregnan-11-one (700 mg) was heated in AcOH with Bi_2O_3 under reflux for 30 hr. The solution gradually became black. The mixture was extracted with benzene and the benzene extracts evaporated to dryness. Crystallization from methanol gave a fine crop of the enol compound (280 mg) and the diacetate of starting material (300 mg), m.p. 155–158°, (Found: C, 73·42; H, 8·86. $C_{23}H_{34}O_4$ requires: C, 73·76; H, 9·15%), ν_{max} 3450 (OH), 1740 (acetyl), 1670 (C=O), 1690 (C=C).

Attempted tosylhydrazone formation of the enol compound (XVIII). The enol compound was treated with the same amount of tosylhydrazide in AcOH at room temp or 80°. The starting material was recovered. Conc. HCl was also used as a catalyst without success.

3β-Acetoxy-12β-*hydroxy-5α-pregnan*-11-*one* (XXI). 3β,12β-Dihydroxy-5α-pregnan-11-one (1·4 g) was refluxed in the mixture of AcOH (15 cc) and Ac_2O (1·5 cc) for 1 hr and water (8 cc) was added gradually and the solution boiled a further 10 min. During this period, white prisms crystallized out. After addition of 10 cc more of water, the crystals were filtered and recrystallized from CH_2Cl_2–MeOH to give needles (70%), m.p. 206–207°, (Found: C, 73,64; H, 9·62. $C_{23}H_{36}O_4$ requires: C, 73·36; H, 9·64%), ν_{max} 3550 (OH), 1745 (acetyl), 1718 (C=O) cm^{-1}.

3β-Acetoxy-12β-*mesyloxy-5α-pregnan*-11-*one* (XXII). 3β-Acetoxy-12β-hydroxy-5α-pregnan-11-one (800 mg) was dissolved in anhydrous pyridine (7 cc) and mesylchloride (0·7 cc) added under ice-cooling and kept overnight at room temp. The mixture was poured into ice water and extracted with ether. The ethereal layer was washed with dilute HCl, $NaHCO_3$ solution and water and dried (Na_2SO_4). After evaporation of the solvent, the residue was crystallized from methanol in prisms (770 mg, 80%), m.p. 173°, (Found: C, 61·94; H, 8·20. $C_{24}H_{38}O_6S \cdot 1/2\ H_2O$ requires: C, 62·20; H, 8·40%).

Attempted solvolysis of the above mesylate. Solvolysis of the mesylate was attempted under several conditions by heating in acetic acid containing several salts at 90°. In all cases the starting material was recovered in rather good yield.

3β-Acetoxy-12β-*tosyloxy-5α-pregnan*-11-*one.* 3β-Acetoxy-12β-hydroxy-5α-pregnan-11-one was treated as described as in the case of the above mesylate to give prisms, m.p. 194–195°, (Found: C, 67·56; H, 8·13. $C_{30}H_{42}O_6S$ requires: C, 67·97; H, 7·98%).

Action of t-BuOK *on* (XXII) *and* (XXIII). The mesylate (XXII) or the tosylate (XXIII); 100 mg) was refluxed in a solution of 1·5 g potassium in t-BuOH (10 cc) for 6 hr. After addition of water, the solution was acidified to give a crystalline mass which was highly solvated. Acetylation gave a compound which was identical with XVIII.

3β,11β-Dihydroxy-5α-pregnan-12-one (XXIV). 3β-Acetoxy-11α-bromo-5α-pregnan-12-one (XVI; 1·6 g) was refluxed in 10 cc each of 5%NaOH and t-BuOH for 2·5 hr. After cooling, the silky needles were separated by filteration, washed several times with water and crystallized from methanol (500 mg) m.p. 192–193°, (Found: C, 75·20; H, 10·34. $C_{21}H_{34}O_3$ requires: C, 75·40; H, 10·25%), ν_{max} 3550 (OH), 1700 (C=O).

The mother-liquor, after extraction with ether followed by the action of Girard P gave a ketonic fraction (140 mg), which was the impure 12,11-ketol (m.p. 185°).

The tosylhydrazone of 3β,11β-dihydroxy-5α-pregnan-12-one (XXV). 3β,11β-Dihydroxy-5α-pregnan 12-one (XXIV; 250 mg) was dissolved in the mixture of 5 cc of EtOH and 7 cc of AcOH and tosylhydrazide (300 mg) added. Immediate appearance of crystals was observed at room temp. After standing overnight, the crystals were filtered and recrystallized from ethanol to give needles (290 mg), (Found: C, 62·83; H, 8·05; N, 5·27. $C_{28}H_{42}O_4S{\cdot}2H_2O$ requires: C, 62·43; H, 8·61; N, 5·20%).

Rearrangement of the tosylhydrazone (XXV) to (XXVI). The tosylhydrazone (XXV; 270 mg) was suspended in sodium ethylene glycolate which was made by dissolving sodium (80 mg) in ethylene glycol (5·0 cc) and heated for 2 hr. at 170°. After cooling, the reaction mixture was poured into water. The crystals were recrystallized from methylene chloride-isopropyl ether to give fine prisms (110 mg; 60%) m.p. 180–190°, $[\alpha]_D$ +34·0° (*c*, 0·95 $CHCl_3$), (Found: C, 79·25; H, 10·85. $C_{21}H_{34}O_2$ requires: C, 79·19; H, 10·76%), ν_{max} 3480 (OH), 1678 (C=C) cm^{-1}, tetranitromethane (+).

Acetylation of (XXVI). Compound XXVI (100 mg) was warmed with pyridine (1·0 cc) and acetic anhydride (0·5 cc) on a water-bath for 30 min. The cooled solution was poured into ice-water; crystals separated which were recrystallized from methanol–water to give needles (XXVII; 650 mg; 65%), m.p. 152°, $[\alpha]_D$ +31·2° (*c*, 1·09 $CHCl_3$), (Found: C, 76·50; N, 9·78. $C_{23}H_{36}O_3$ requires C, 76·62; H, 10·07%), ν_{max} 3500 (OH), 1740 (acetyl), 1678 (C=C) cm^{-1}.

Catalytic hydrogenation of the acetate (XXVII). The acetate of (XXVII; 100 mg) was shaken with PtO_2 (100 mg) in acetic acid under H_2 atmosphere for 6 hr, the catalyst was then filtered off and the solvent evaporated to dryness under red. press. The residue was a colorless oil and behaved as a pure substance on chromatography, (Found: C, 79·30; H, 10·91. $C_{23}H_{38}O_2$ requires: C, 79·71; H, 11·05%), ν_{max} 1740 (acetyl) cm^{-1}. The hydrolysis of this acetate gave a waxy mono-ol m.p. ca 70°, (not analyzed). The hydrogenation of XXVI gave the same waxy substance, the acetate of which is identical with the prepared compound.

Chromic-oxidation of the acetate XXVII). To a solution of CrO_3 (300 mg) in anhydrous pyridine (10 cc), the acetate (XXVII; 200 mg) in pyridine (5 cc) was added with ice-cooling; then the mixture allowed to stand for 2 hr at 37°. After addition of water, the solution was extracted with ether. The organic layer was washed with dil. HCl, water and dried. Evaporation of the solvent deposited crystals, which recrystallized from MeOH to give plates (XXVIII; 150 mg, 75%), m.p. 143·5°, (corrected) $[\alpha]_D$ −34·2° (*c*, 1·35 $CHCl_3$), (Found: C, 77·01; H, 9·55. $C_{23}H_{34}O_3$ requires: C, 77·05; N, 9·65%), I.R.: see Fig. 1, U.V. 255 mμ (log ε 1·89).

Catalytic hydrogenation of the enone compound (XXIX). After PtO_2 (100 mg) was reduced in acetic acid (5 cc), the enone XXIX in acetic acid (5 cc) was added. The hydrogen up-take ceased within 10 min. (7 cc at 20°). The catalyst was filtered off and the solution evaporated to dryness under red. press. to give material which was recrystallized to give prisms (XXX; 80 mg; 80%), m.p. 118·2–118·9° (corrected), $[\alpha]_D$ −15·5° (*c*, 1·55 $CHCl_3$), (Found: C, 76·95; H, 10·03. $C_{23}H_{36}O_3$ requires. C, 76·62; H, 10·07%), I.R. see Fig. 3. This compound proved to be identical with IV derived from jervine by direct comparison (I.R. and mixed m.p.).

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