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Investigations on Steroids. XI.[1] Synthesis of Steroidal Oxazole, Imidazole, and Triazole

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Steroidal oxazoles, imidazoles, and triazoles were synthesized for biological studies. 2α–Acetoxy– or 2α–bromo–3–ketones of androstane and cholestane series were converted into 2′–methylsteroidal[3,2–*d*]oxazoles (III) by reaction with ammonium acetate. Reductive acetylation of 2–hydroxyimino–3–oxo steroids (V) gave 2α–acetamido–3–ketones (VI) which were cyclized by the use of sulfuric acid to 2′–methyl–steroidal[2,3–*d*]oxazoles (XI). 2′–Methyl–steroidal[2,3–*d*]imidazoles (XII) were prepared from VI by reaction with ammonium acetate. 2α–Amino–3–ketone hydrochlorides, obtained by catalytic hydrogenation of V, were converted by reaction with thiocyanate into steroidal [2,3–*d*]imidazoline–2′–thiones which were desulfurized to afford imidazoles (XIV). Androst–4–eno[2,3–*d*]–triazoles (XX) were prepared from the 2–acetoxymethylene–3–ketone *via* the 2–hydroxyimino–3–one hydrazone by application of the established procedures.

The ORD (and CD) data of VI and the corresponding 3β–alcohol (VIIId) are presented.

Previous parts of this series described the preparation of androstano[3,2–*b*]pyridines[3] and [2,3–*c*]furazans.[4] Certain members of the latter class were found to have high anabolic androgenic ratios as those of the androstano[3,2–*c*]pyrazole[5] and [2,3–*d*]isoxazole derivatives.[6] The analogous steroidal heterocycles have been synthesized in several laboratories and the compounds fused with a five–membered aromatic heterocycle include various androstano [2,3–*c*]pyrazole,[7] [2,3–*c*],[7a] [3,2–*d*][8a] and [3,2–*c*]isoxazole,[8b] [2,3–*d*][9a] and [3,2–*d*]thiazole,[9b] [2,3–*d*]triazole,[10] [3,2–*b*]pyrrole,[11] [3,2–*b*]furane,[12] and [2,3–*c*]thiophene derivatives.[13] The

1) Part X: *Chem. Pharm. Bull.* (Tokyo), **16**, 1460 (1968).
2) Location: *Minamifunabori, Edogawa–ku, Tokyo.*
3) *a*) M. Shimizu, G. Ohta, K. Ueno, and T. Takegoshi, *Chem. Pharm. Bull.* (Tokyo), **12**, 77 (1964); *b*) *cf.* T.C. Miller, *J. Heterocyclic Chem.*, **3**, 338 (1966).
4) *a*) G. Ohta, T. Takegoshi, K. Ueno, and M. Shimizu, *Chem. Pharm. Bull.* (Tokyo), **13**, 1445 (1965); *b*) A. Kasahara, T. Onodera, M. Mogi, Y. Oshima, and M. Shimizu, *ibid.*, **13**, 1460 (1965); *c*) *cf.* R.E. Havraneck, G.B. Hoey, and D.H. Baeder, *J. Med. Chem.*, **9**, 326 (1966).
5) R.O. Clinton, A.J. Manson, F.W. Stonner, H.C. Neumann, R.G. Christiansen, R.L. Clarke, J.H. Ackerman, D.F. Page, J.W. Dean, W.B. Dickinson, and C. Carabateas, *J. Am. Chem. Soc.*, **83**, 1478 (1961).
6) A.J. Manson, F.W. Stonner, H.C. Neumann, R.G. Christiansen, R.L. Clarke, J.H. Ackerman, D.F. Page, J.W. Dean, D.K. Phillips, G.O. Potts, A. Arnold, A.L. Beyler, and R.O. Clinton, *J. Med. Chem.*, **6**, 1 (1963).
7) *a*) R.L. Clarke and S.J. Daum, *J. Org. Chem.*, **30**, 3786 (1965); *b*) U.S. Patent 3144447 [*C.A.*, **61**, 10746 (1964)].
8) *a*) U.S. Patent 3144449 [*C.A.*, **61**, 13384 (1964)]; *b*) *cf.* references cited in ref. 4a).
9) *a*) U.S. Patent 3076801 [*C.A.*, **59**, 12874 (1963)]; *b*) J.A. Zderic, H. Carpio, A. Ruiz, D.C. Limon, F. Kincl, and H.J. Ringold, *J. Med. Chem.*, **6**, 195 (1963), see also the references cited therein.
10) *a*) G. Nathansohn, E. Testa, and N. DiMola, *Experientia*, **18**, 57 (1962); *b*) N.J. Doorenbos and C.P. Dorn, *J. Pharm. Sci.*, **54**, 1219 (1965); *c*) U.S. Patent 3280112 (1966).
11) *a*) T.C. Miller and R.G. Christiansen, *J. Org. Chem.*, **29**, 3612 (1964); *b*) U.S. Patent 3032551 [*C.A.*, **58**, 8006 (1963)].
12) *a*) J.C. Orr, M.L. Franco, A.D. Cross, and F. Sondheimer, *Steroids*, **3**, 1 (1964); *b*) D.L. Storm and T.A. Spencer, *Tetrahedron Letters*, **1967**, 1865.
13) H. Kaneko, Y. Yamato, T. Kon, and M. Kurokawa, Abstracts of the 24th Meeting of Japan Pharm. Soc., 1967, p. 347.

anabolic activities reported for some of these compounds are generally in a lower order.

In order to examine the relationship between biological activities and the structure of heterocycle, a number of related compounds have been synthesized in this laboratory. The present paper reports observations obtained in the preparation of steroidal[3,2-*d*]oxazoles (III), [2,3-*d*]oxazoles (XI), and [2,3-*d*]imidazoles (XII, XIV) of androstane and cholestane series, and androst-4-eno[2,3-*d*]triazoles (XX). During progress of this study, the oxazole (IIIb)[14] and the dihydro derivatives of the triazole (XX)[10c] have been synthesized and the synthesis and inactivity of certain androstano[3,2-*d*]oxazoles and [2,3-*d*]imidazoles have been briefly noted.[15]

The 2′-methyl-steroidal[3,2-*d*]oxazoles (III) wereprepared from 3-keto steroids (I) *via* 2-acetoxy- or 2-bromo-3-ketones. Acetoxylation of 17β-acetoxyandrostan-3-one (Ib) with lead tetraacetate in the presence of boron trifluoride gave the 2α-acetoxy-3-ketone (IIb). The configuration assignment of the 2α-acetoxy group was based on the method of formation[16] and on the nuclear magnetic resonance (NMR) spectrum which showed the signal of the C-2 proton possessing a similar splitting pattern (τ 4.7, quartet, J=13.0 and 6.5 cps) as that of 2α-acetoxycholestan-3-one.[17] Treatment of the acetoxy ketone (IIb) with ammonium acetate in refluxing acetic acid[18] gave the 2′-methyl[3,2-*d*]oxazole (IIIb). The same sequence has been reported by Fürer, *et al.*[14] Hydrolysis of IIIb gave the 17β-hydroxy derivative (IIIa) which was also obtained by condensation of the 2α-bromo-3-ketone (IVb) with ammonium acetate[18] and subsequent hydrolysis. The 17α-methyl derivative (IIIc) and the cholestano derivative (IIId) were prepared similarly.

The [3,2-*d*]oxazole structure for III was presumed from the analogous ring formation reactions[18] and further confirmed by non-identity with the corresponding [2,3-*d*]oxazole (XI) described below. The 2α-acetoxy-3-ketone isomerizes into the 3β-acetoxy-2-ketone[16] but the above ring formation proved to take place without the isomerization, as reported in the preparation of steroidal[3,4-*d*] or [4,3-*d*]oxazoles.[14]

For the synthesis of the [2,3-*d*]oxazole (XI), the 2-acetamido-3-ketone (VI) was required. Reductive acetylation of the 2-hydroxyimino-3-ketone (Vb,d) with zinc and an acetic acid–acetic anhydride mixture gave the 2α-acetamido-3-ketone (VIb,d).[19] The 17β-acetoxy group of VIb was selectively hydrolyzed to give the 17β-alcohol (VIa). Hydrogenation of Va with palladium in the presence of hydrochloric acid, followed by partial acetylation of the amine hydrochloride (VIIa) furnished the same compound (VIa). The α configuration was assignable to the C-2 amino and amido groups since the products were believed to take the more stable conformation during the reduction procedure which involved heating in acetic acid or treatment with hydrochloric acid, a procedure which should be equilibrating.[20] In the infrared (IR) and UV spectra, the shifts of position of the C-3 carbonyl absorption caused by substitution of the amido group ($\Delta\gamma$ +9 cm^{-1}, $\Delta\lambda$ −6 mμ) were comparable with those given by the C-2 equatorial acetate.[16] In the NMR spectrum of VId, after deuteration, the resonance of the C-2 proton appeared as quartet (τ 5.42) due to the X part of ABX system.

14) B. Fürer, S. Julia, and C, P. Papantoniou, *Bull. Soc. Chim. France*, **1966**, 3407.
15) P. de Ruggieri and C. Gandolfi, *Proceedings of the First Congress on Hormonal Steroids*, **2**, 69 (1965).
16) H.B. Henbest, D.N. Jones, and G.P. Slater, *J. Chem. Soc.*, **1961**, 4472.
17) K.L. Williamson, and W.S. Johnson, *J. Am. Chem. Soc.*, **83**, 4623 (1961).
18) *cf. a)* G. Theilig, *Chem. Ber.*, **86**, 96 (1953); *b)* J.W. Cornforth and R.H. Cornforth, *J. Chem. Soc.*, **1953** 93.
19) 2α-Acetamidocholestan-3-one (VId) was reported earlier without proof for the 2α-configuration to be obtainable by oxidation of the corresponding 2ξ-acetamido-3ξ-ol. Its melting point and ultraviolet (UV) absorption data are not in complete agreement with those observed in the present study. *cf.* O.E. Edwards and K.K. Purushothaman, *Can. J. Chem.*, **42**, 712 (1964).
20) *cf.* A. Hassner and P. Catsoulacos, *J. Org. Chem.*, **32**, 549 (1967).

Coupling constants (J=13.0 and 6.0 cps), obtained from the 60 Mc and 100 Mc spectra, accorded with those observed for the 2α-acetoxy-3-ketone (II), being compatible with the equatorial conformation (2α) of the amido group attached to the chair form of ring A.[21] However, the twisted ring A conformation with an equatorial amido group (2β), which is possible to give the similar coupling constants,[22] is not strictly excluded by these data.

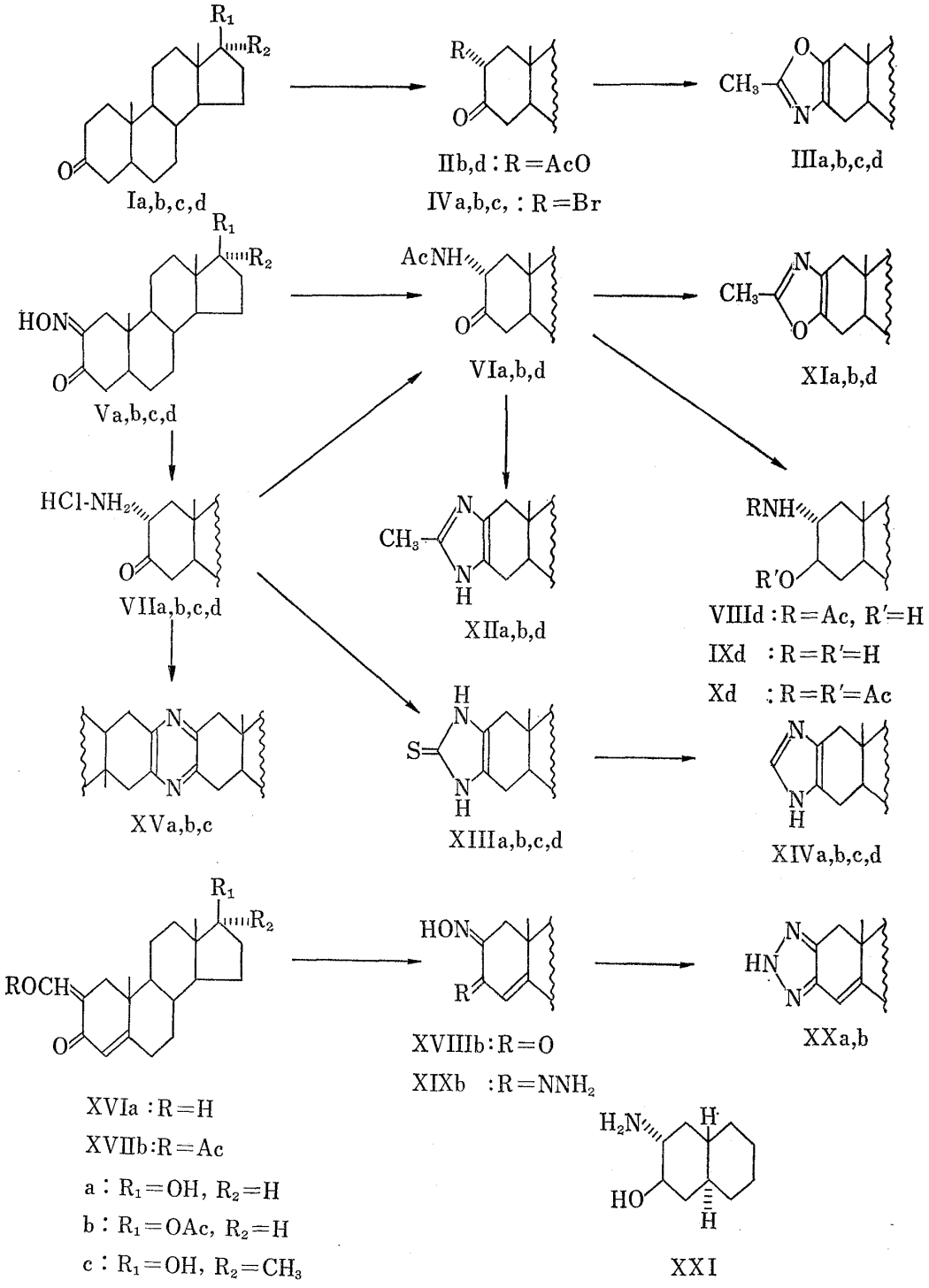

Chart 1

21) *cf. a*) R.J. Abraham and J.S.E. Holker, *J. Chem. Soc.*, **1963**, 806; *b*) T. Komeno, K. Tori, and K. Takeda, *Tetrahedron*, **21**, 1635 (1965).

22) *cf. a*) T. Kuriyama, S. Kondo, and K. Tori, *Tetrahedron Letters*, **1963**, 1485; *b*) S. Burstein and H.L. Kimball, *Steroids*, **2**, 1 (1963).

Convincing evidence for the configuration of the 2α–acetamido–3–ketone (VI) was provided by the amino alcohol (IXd) derived from VId *via* the amido alcohol (VIIId). The ketone (VId) was reduced with sodium borohydride and the main product (VIIId) was hydrolyzed with alkali to give IXd. Acetylation of VIIId and IXd gave the same diacetate (Xd), thus showing that no inversion occurred during hydrolysis. In the NMR spectrum of IXd, the chemical shifts and broad peak width at half–height (W_h) of $C_{(2)}$–proton (τ 7.38, W_h 25 cps) and $C_{(3)}$–proton (τ 6.87, W_h 23 cps) were in excellent agreement with those reported for the axial protons at positions 2 and 3, respectively, of the diequatorial 2–amino–3–alcohol (XXI) of *trans*–decahydronaphthalene series. The compound (XXI) is distinguishable from its stereo isomers by their NMR spectra[23] and hence the configurations of compounds VI, VIIId and IXd were proved. Furthermore, the amino alcohol (IXd) and its diacetate (Xd) were distinct from the corresponding 2β–amino–3α–ol[24a,b] or 2β–amino–3β–ol[24c] and their acetates, respectively.

Ring closure of the amido ketone (VIb,d) with sulfuric acid in acetic anhydride[25] gave the 2′–methyl[2,3–*d*]oxazole (XIb,d). Both the [3,2–*d*] and [2,3–*d*]oxazoles exhibited the UV absorption at 225 mμ and the IR spectrum similar to each other, but direct comparison (mp, IR and gas chromatography) of the corresponding compounds proved the non–identity.

The 2′–methyl[2,3–*d*]imidazole (XIIb,d) was obtained by heating the amido ketone (VIb,d) with ammonium acetate in acetic acid.[26] Reaction of the amino ketone hydrochloride (VII) with thiocyanate yielded the imidazolinethione (XIII),[27] which was desulfurized with Raney nickel to afford the imidazole derivative unsubstituted at the 2′–position (XIV). Treatment of VII with alkali, accompanied by concurrent air–oxidation,[28a] furnished the dimeric compound (XV), whose UV absorption at 290 mμ is attributable to the tetrasubstituted pyrazine structure.[28b] The synthesis of the corresponding disubstituted steroidal pyrazines has been already reported.[10b,29]

The 4,5–unsaturated androstano[2,3–*d*]triazole (XX) was synthesized according to the method used for the preparation of the corresponding cortisol derivative.[30] The diacetate (XVIIb) of the 2–hydroxymethylene–3–ketone (XVIa) was converted into the 2–hydroxyimino derivative (XVIIIb) by nitrosation with sodium nitrite in acetic acid and the hydrazone (XIXb) of XVIIIb was dehydrated with phosphorous pentachloride to give the triazole (XXb), from which the 17β–alcohol(XXa) was obtained by hydrolysis.

The optical rotation of the amido ketone (VI) should be noted. The molecular rotation difference of the amido ketone from the parent ketone is strongly negative ($\Delta[M]_D$ −361° for VIa and −364° for VId) and seems exceptional when compared with the increments (+95° ——134°) effected by various other 2α–substituents.[31] Comparison of the optical rotatory dispersion (ORD) curves of the parent ketone (Ia), the acetoxy ketone (IIb) and the amido ketones(VIa, d), as shown in Fig. 1 and 2, revealed that the amido ketones have a negative background dispersion which is inferred to give rise to the above anomalous $\Delta[M]_D$ –value and which also obscures the C–3 carbonyl Cotton effect at about 290 mμ. This background

23) A. Pavia, F. Winternitz, and R. Wylde, *Bull. Soc. Chim. France*, **1966**, 2506.
24) *a*) K. Ponsold, *Chem. Ber.*, **96**, 1411 (1963); *b*) A. Hassner and C. Heathcock, *J. Org. Chem.*, **30**, 1748 (1965); *c*) A. Hassner, M.E. Lorber, and C. Heathcock, *ibid.*, **32**, 540 (1967).
25) *cf.* A. Treibs and W. Sutter, *Chem. Ber.*, **84**, 96 (1951).
26) *cf.* H. Bredereck and G. Theilig, *Chem. Ber.*, **86**, 88 (1953).
27) *cf.* G. de Stevens and A. Halamandaris, *J. Am. Chem. Soc.*, **79**, 5710 (1957).
28) *cf. a*) H.E. Baumgarten and F.A. Bower, *J. Am. Chem. Soc.*, **76**, 4561 (1954); *b*) B. Klein and J. Berkowitz, *ibid.*, **81**, 5160 (1959).
29) U.S. Patent 3280113 (1966).
30) H. Mrozik, P. Buchschacher, J. Hannah, and J.H. Fried, *J. Med. Chem.*, **7**, 584 (1964).
31) *cf. a*) L.F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp. N.Y. 1959, p. 287; *b*) R. Gardi, P.P. Castelli, and A. Ercoli, *Tetrahderon Letters*, **1962**, 497; *c*) S.S. Stradling and D.S. Tarbell, *J. Org. Chem.*, **29**, 1170 (1964); *d*) J.F. Pelletto, G.R. Allen, and M.J. Weiss, *J. Med. Chem.*, **10**, 106 (1967).

effect is attributable to the negative Cotton effect associated with the amido group which appears as a trough at 225 mμ in the curve of VId in methanol and at 230 mμ in dioxane. The assignment of the trough to the amido Cotton effect was based on its position which is similar to those of the extrema observed in the cases of L-3-aminopyrrolid-2-one (about 245 mμ),[32a] the N-acetyl-11-azasteroid (238 mμ),[32b] and (−)-cotinine, a naturally occurring lactam (222 mμ).[32c] In addition, the red shift of the position of the trough with the change of decreasing solvent polarity can be interpreted as indicating the Cotton effect due to the n–π^* transition of the amido group,[32a] although the shift of the amido absorption in the UV spectrum was not detectable. The occurrence of the amido Cotton effect in VI is the result of the restricted rotation about the C–N–$C_{(2)}$ bond caused by the steric requirements, the intramolecular hydrogen-bonding or solvation.[33] Generally in amides, the partial double-bond character of the C–N bond is considered to restrict the rotation, for which evidences have been given by NMR studies.[34]

The circular dichroism (CD) measurement of the amido ketone (VId) disclosed the C-3 carbonyl Cotton effect at 290 mμ, which was found to be markedly solvent-dependent. The compound VId in methanol shows a positive CD maximum at 290 mμ, and in dioxane a double-humped curve with a positive maximum at 300 mμ and a negative one at 273 mμ. The curve taken in dichloromethane is intermediate between those in methanol and dioxane (Fig. 3). The positive sign of VId in methanol, where the intramolecular hydrogen-bond seems to be broken, is the same as that of the 2α-acetoxy-3-ketone which follows the octant rule.[35] This parallels with the case of the amido ketones substituted in ring D of D-homo-steroids which in methanol give the same sign of the carbonyl Cotton effect as that of the corresponding ketols,[36] although anomaly to octant rule is known in certain amino ketones[37]

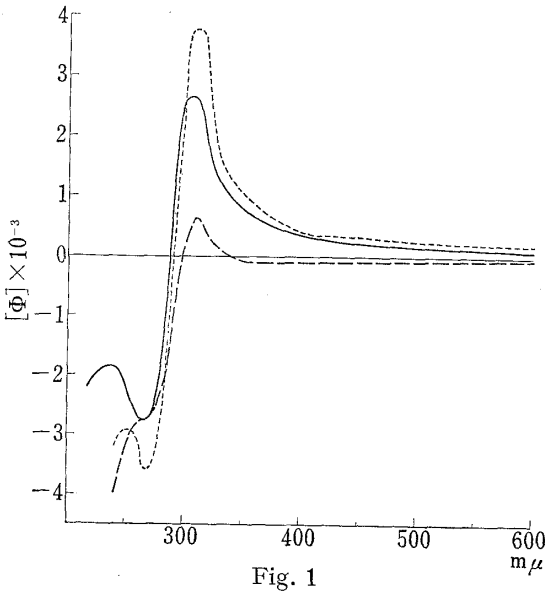

Fig. 1

ORD curves of 17β-hydroxyandrostan-3-one (Ia) in MeOH (————), 2α,17β-diacetoxyandrostan-3-one (IIb) in dioxane (·····), and 2α-acetamido-17β-hydroxyandrostan-3-one (VIa) in MeOH (– – – – –)

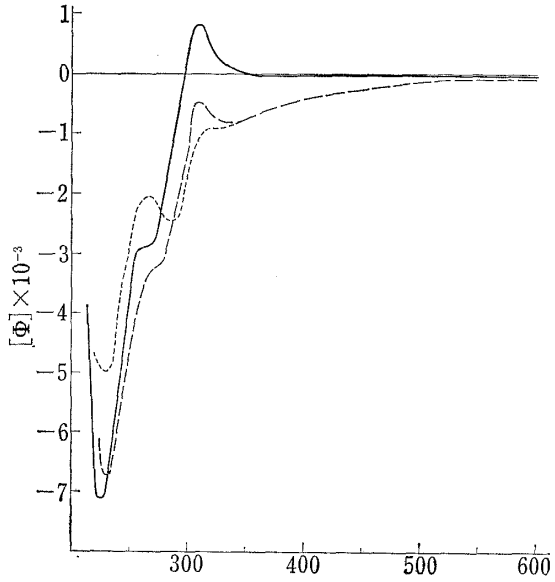

Fig. 2

ORD curves of 2α-acetamidocholestan-3-one (VId) in MeOH (————), in dioxane (·····), and in dichloromethane (– – – – –)

32) *a*) B.J. Litman and J.A. Schellman, *J. Phys. Chem.*, **69**, 978 (1965); *b*) J.P. Kutney, G. Eigendorf, and J.E. May, *Chem. Commun.*, **1966**, 59; *c*) J.C. Craig and S.K. Roy, *Tetrahedron*, **21**, 401 (1965).
33) L. Skulski, G.C. Palmer, and M. Calvin, *Tetrahedron Letters*, **1963**, 1773.
34) *cf.* J.A. Pople, W.S. Schneider, and H.J. Bernstein, "High Resolution Nuclear Magnetic Resonance," McGraw Hill, 1959, p. 366.
35) W. Klyne, *Tetrahedron*, **13**, 29 (1961).
36) D.F. Morrow, M.E. Brokke, G.W. Moersch, M.E. Butler, C.F. Klein, W.A. Neuklis, and E.C. Huang, *J. Org. Chem.*, **30**, 212 (1965).
37) *cf.* S. Yamada and T. Kunieda, *Chem. Pharm. Bull.* (Tokyo), **15**, 490(1967) and the references cited therein.

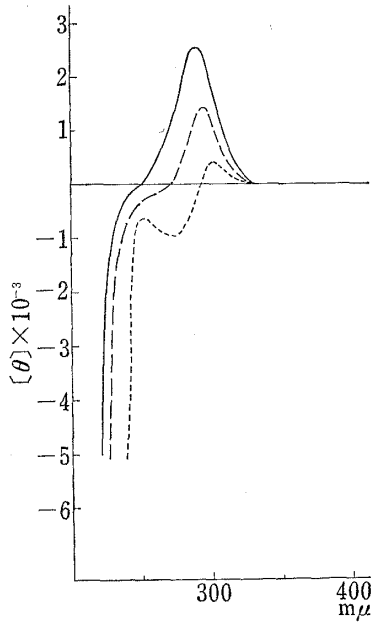

Fig. 3

CD curves of 2α-acetamidocholestan-3-one (VId) in MeOH (————), in dioxane (·····), and in dichloromethane (– – – – –)

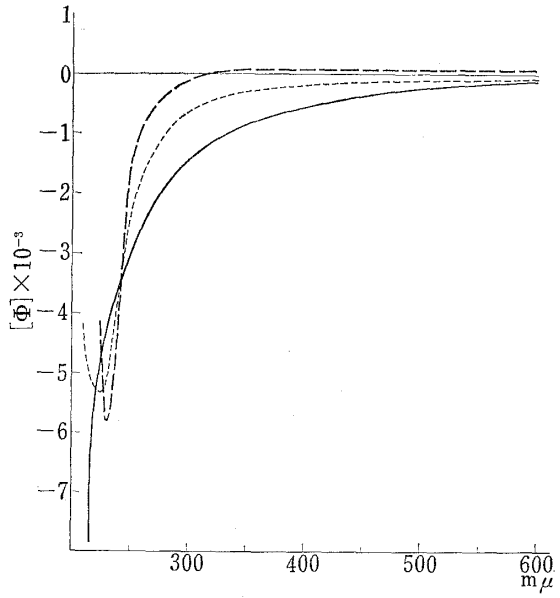

Fig. 4

ORD curves of 2α-acetamidocholestan-3β-ol (VIIId) in MeOH (————), in dioxane (·····), and in dichloromethane (– – – – –)

and D-homo ketols.[35] The double-humped curve of VId in dioxane with maxima separated by 27 mμ indicates the existence of solvational and conformational equilibria, separated or combined.[38a,b,c] Since the chair form of ring A is unlikely to be changeable even by intramolecular hydrogen-bonding, the negative maximum at the shorter wave-length can be interpreted as being due to the solvated species, the intramolecular hydrogen-bonded species and/or the rotational isomers possessing the acetamido group located in the front negative octant.[39] Differentiation of these factors is difficult. A 5α-acetamido-6-keto steroid in dioxane has been shown recently to give double CD maxima near 290 mμ.[38d]

In connection with these results, the ORD curve of the corresponding amido alcohol (VIIId) was of interest (Fig. 4). The plain curve of VIIId in methanol indicates the free rotation of the amido group, whereas in the curves taken in dichloromethane and in dioxane, there appears a trough at about 230 mμ, indicative of the restricted rotation. As for the sign of the amido Cotton effect of VId and VIId, further studies are necessary to establish the relationship with the conformation of the amido group.

In a preliminary biological assay,[40] the compound IIIc showed weak myotrophic and androgenic activities with favourable ratios, but other androstano derivatives described above revealed considerably diminished activities when compared with testostereone propionate given by subcutaneous injection.

38) *a*) K.M. Wellman, P.H. Laur, W.S. Briggs, A. Moscowitz, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 66 (1966); *b*) G.C. Barret, *J. Chem. Soc.* (C), **1967**, 1; *c*) E. Bach, A. Kjaer, R. Dalbohm, T. Walle, B. Sjöberg, E. Bunnenborg, C. Djerassi, and R. Records, *Acta Chem. Scand.*, **20**, 2781 (1966); *d*) G. Snatzke and A. Veithen, *Ann.*, **703**, 159 (1967).

39) *cf.* K.M. Wellman, W.S. Briggs, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 73 (1965).

40) The biological activities were evaluated by Mr. A. Kasahara and his associtates in this Laboratory. Details will be reported elsewhere.

Experimental[41]

2α,17β-Diacetoxyandrostan-3-one (IIb)——To a suspension of 17β-acetoxyandrostan-3-one (Ib, 5.0 g) in AcOH (220 ml) containing $Pb(OAc)_4$ (8.0 g), was added BF_3-etherate (13.0 g) and the mixture was stirred at 25° under N_2. After 3 hr, the starch-iodide test for $Pb(OAc)_4$ was negative and the reaction mixture was poured into ice-water (800 g). The precipitated solid was collected and the dried solid was extracted with benzene to remove insoluble materials. The solvent was evaporated and the residue was fractionally recrystallized from MeOH to yield IIb (**0.92** g), mp 197—199°, $[\alpha]_D$ +39.0° (c=1.70), (lit., mp 200—201°, $[\alpha]_D$ +40.5°[31b]; mp 190—192°, $[\alpha]_D$ +45°[14]). UV λ_{max} mμ (ε): 285 (64.4). IR ν_{max} cm^{-1}: 1753 (2α-acetoxy), 1738 (17β-acetoxy), 1729 (3-ketone); $\nu_{max}^{CHCl_3}$ cm^{-1}: 1724 (3-ketone). ORD (dioxane, c=0.51 at 20°): $[\phi]_{589}$ +182°, $[\phi]_{310}$ +3860°, $[\phi]_{268}$ −3550°, $[\phi]_{260}$ −3240°. *Anal.* Calcd. for $C_{23}H_{34}O_5$: C, 70.74; H, 8.78. Found: C, 70.66; H, 8.77.

17β-Hydroxy-2′-methylandrostano[3,2-*d*]oxazole (IIIa)——a) A solution of IIb (100 mg) and $AcONH_4$ (100 mg) in AcOH (3.0 ml) was refluxed for 3 hr. After cooling, the reaction mixture was diluted with H_2O and the precipitate was filtered, washed with H_2O and dried. The crude product (95 mg, mp 94—105°) was crystallized from MeOH to give the 17-acetate (IIIb, 80 mg), mp 108—110°, $[\alpha]_D$ +42.2° (c=0.81), (lit.,[14] mp 106—107°, $[\alpha]_D$ +83°). UV λ_{max} mμ (ε): 225 (7200). IR ν_{max} cm^{-1}: 1773, 1672, 1573. Gas chromatography (retention time): 4.8 min. *Anal.* Calcd. for $C_{23}H_{33}O_3N$: C, 74.36; H, 8.95; N, 3.77. Found: C, 74.02; H, 8.91; N, 3.57.

A mixture of IIIb (75 mg) in MeOH (3.0 ml) and $KHCO_3$ (100 mg) in H_2O (1.0 ml) was refluxed for 2 hr. After cooling, the mixture was diluted with H_2O and the separated crystals (55 mg) were collected and recrystallized from MeOH to give IIIa, mp 209—211°, $[\alpha]_D$ +61.8° (c=0.68). UV λ_{max} mμ (ε): 225 (6900). IR ν_{max} cm^{-1}: 3260, 1688, 1575. Gas chromatography (retention time): 3.6 min. *Anal.* Calcd. for $C_{21}H_{31}O_2N$: C, 76.55; H, 9.48; N, 4.25. Found: C, 76.41; H, 9.49; N, 4.43.

b) A solution of 17β-acetoxy-2α-bromoandrostan-3-one (IVb, 500 mg) and $AcONH_4$ (500 mg) in AcOH (10 ml) was refluxed for 5 hr. The reaction mixture was diluted with H_2O and extracted with benzene. The benzene solution was evaporated and the resulting crude acetate (IIIb) was hydrolyzed in the same manner as described above to give IIIa (30 mg), mp and mixed mp 209—210°.

17β-Hydroxy-17α,2′-dimethylandrostano[3,2-*d*]oxazole (IIIc)——A solution of 2α-bromo-17β-hydroxy-17α-methylandrostan-3-one (IVc, 2.00 g) and $AcONH_4$ (2.00 g) in AcOH (40 ml) was refluxed for 5 hr. The reaction mixture was concentrated *in vacuo* and diluted with H_2O. The precipitate was collected, dissolved in benzene and chromatographed on alumina (40 g). The product (1.20 g) eluted with ether (250 ml) was recrystallized from acetone and then from MeOH to give IIIc (0.25 g), mp 229—230°. $[\alpha]_D$ +30.4° (c=1.23). UV λ_{max} mμ (ε): 225 (6900). IR ν_{max} cm^{-1}: 3400 (OH), 1667, 1573. *Anal.* Calcd. for $C_{22}H_{33}O_2N$: C, 76.92; H, 9.68; N, 4.08. Found: C, 76.96; H, 9.99; N, 4.10.

2′-Methylcholestano[3,2-*d*]oxazole (IIId)——A solution of 2α-acetoxycholestan-3-one (IId, 1.00 g) and $AcONH_4$ (1.70 g) in AcOH (30 ml) was refluxed for 3 hr. After removal of the solvent *in vacuo*, the residue was diluted with H_2O to separate a crystalline mass which was collected, dissolved in petr. ether and chromatographed on Florisil (20 g). The product (0.71 g, mp 115—126°) eluted with petr. ether–bezene (1:9, 200 ml) and benzene (400 ml) was crystallized from acetone to afford IIId (0.56 g), mp 130—131°, $[\alpha]_D$ +57.7° (c=1.04). UV λ_{max} mμ (ε): 225 (5570). IR ν_{max} cm^{-1}: 1662, 1570. NMR (τ): 7.62 (2′-C$\underline{H}_3$), 9.21 (19-C$\underline{H}_3$), 9.23 (18-C$\underline{H}_3$). *Anal.* Calcd. for $C_{29}H_{47}ON$: C, 81.82; H, 11.13; N, 3.29. Found: C, 82.13; H, 10.87; N, 3.50.

2α-Acetamido-17β-acetoxyandrostan-3-one (VIb)——To a suspension of 2-hydroxyimino-17β-acetoxyandrostan-3-one (Vb, 3.85 g) in AcOH—Ac_2O (1:1, 75 ml) containing anhydrous AcONa (0.35 g) and $HgCl_2$ (35 mg), was added Zn-dust (7.7 g) in small portions with shaking at room temperature and the mixture was refluxed for 30 min. The insoluble material was removed by filtration and washed with AcOH (20 ml). The filtrate and washings were combined, diluted with H_2O and extracted with benzene (100 ml×3). The benzene solution was washed with H_2O, dried and concentrated. The residue in the same solvent (60 ml) was chromatographed on alumina (100 g) and eluted with benzene, benzene—ether (9:1), ether, ether—AcOEt (1:1) and AcOEt. The crystals (2.50 g) eluted with ether—AcOEt (1:1) were recrystallized from MeOH to afford VIb (1.85 g), mp 222—231°, $[\alpha]_D$ −78.8° (c=1.12). UV λ_{max} mμ (ε): 281(27.6). IR ν_{max} cm^{-1}: 3260, 3070, 1731, 1669, 1664. NMR (τ): 3.55 (N$\underline{H}$, doublet J=7.0), 5.40 (2β-H, 17α-H, multiplet), 7.69

41) Melting points are uncorrected. Unless otherwise stated, specific rotations were taken in $CHCl_3$, IR spectra in a KBr disc, and UV spectra in EtOH. NMR spectra were measured in $CDCl_3$ at 60 Mc with JEOL, JNM-3H spectrometer or, where noted, at 100 Mc with JEOL, JNM-4H spectrometer. ORD and CD measurements were carried out with JASCO ORD/UV-5 spectropolarimeter and gas chromatography with Barber-Coleman Model 10 Unit packed with 1% SE-30-Anakrom ABS. Conditions used for gas chromatography were as follows: column temperature 240°, detector temperature 215°, flash heater temperature 255°, argon gas flow rate 100 ml/min. Microanalyses were performed by Mr. B. Kurihara and his staff in this Laboratory.

($C\underline{H}_3COO$–), 8.01 ($C\underline{H}_3CON\langle$), 8.82 (19–$C\underline{H}_3$), 9.20 (18–$C\underline{H}_3$). ORD (MeOH, $c=0.25$ at 20°): $[\phi]_{589}$ −124°, $[\phi]_{360-350}$ −380°, $[\phi]_{310}$ +422°, $[\phi]_{270}$ −3190° (inflexion), $[\phi]_{230}$ −7450°. *Anal.* Calcd. for $C_{23}H_{35}O_4N$: C, 70.92; N, 9.06; N, 3.60. Found: C, 70.81; H, 9.10; N, 3.83.

2α-Acetamido-17β-hydroxyandrostan-3-one (VIa)——a) To a solution of the amine hydrochloride (VIIa, see below; 1.71 g) in tetrahydrofuran (20 ml), were added portionwise at 3° Ac_2O (8.5 ml) and then $NaHCO_3$ (0.42 g) with stirring. After stirring for 20 min, excess Ac_2O was decomposed below 10° by adding a saturated aqueous solution of $NaHCO_3$ (7.0 g). The mixture was concentrated *in vacuo* and extracted with $CHCl_3$. The $CHCl_3$ solution was washed with H_2O, dried and evaporated. The product (1.80 g) was dissolved in $CHCl_3$ and chromatographed on Florisil (30 g). The compounds (1.37 g) eluted with $CHCl_3$ and $CHCl_3$–AcOEt (9:1) were crystallized from acetone to give VIa (1.01 g), mp 209—217°, $[\alpha]_D$ −75.3° ($c=0.96$). UV λ_{max} mμ (ε): 279 (48.4). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3410, 1715, 1663, 1510, 1505. NMR (after deuteration with D_2O and 35% HCl) (τ): 5.42 (2β–H, quartet, $J=12.3$, 5.8), 6.32 (17α–H), 8.01 ($C\underline{H}_3CON\langle$). ORD (MeOH, $c=0.63$ at 20°): $[\phi]_{589}$ −67.4°, $[\phi]_{375-365}$ −92.0°, $[\phi]_{309}$ +625°, $[\phi]_{271}$ −2700° (inflexion), $[\phi]_{240}$ −3010°. *Anal.* Calcd. for $C_{21}H_{33}O_3N$: C, 72.58; H, 9.57; N, 4.03. Found: C, 72.49; H, 9.49; N, 4.10.

b) A solution of VIb (100 mg) and $KHCO_3$ (100 mg) in MeOH (4.0 ml) and H_2O (1.0 ml) was refluxed for 4 hr, the solvent was removed *in vacuo* and the residue was diluted with H_2O to separate a solid. Crystallization from acetone gave VIa, mp 209—217°, identical (mixed mp and IR) with that described above.

2α-Acetamidocholestan-3-one (VId)——As described for VIb, a mixture of 2–hydroxyiminocholestan–3–one (Vd, 2.00 g), AcONa (0.10 g) and $HgCl_2$ (30 mg) in Ac_2O—AcOH (1:1, 40 ml) was treated with Zn (3.00 g). The reaction mixture was filtered, the filtrate was diluted with H_2O and the precipitate was collected. Crystallization from MeOH gave a product (1.54 g), mp 186—190°. Recrystallization from the same solvent gave an analytical sample of VId, mp 191—193°, $[\alpha]_D$ −49.8° ($c=1.26$). UV λ_{max} mμ (ε): 283 (30.3). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3410, 1713, 1664,. (Lit.,[19] mp 184—186°, UV λ_{max}^{EtOH} mμ (ε): 279 (130). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3370, 1710, 1665). NMR (after deuteration with D_2O and 35% HCl; 100 Mc) (τ): 5.41 (2β–H, quartet, $J=13.0$, 6.0). ORD and CD (MeOH, $c=0.57$ at 19°): $[\phi]_{700}$ −15.2°, $[\phi]_{589}$ −37.8°, $[\phi]_{400}$ −68.0°, $[\phi]_{310}$ +832°, $[\phi]_{266}$ −2800 °(inflexion), $[\phi]_{225}$ −7180°, $[\phi]_{215}$ −3970°; $[\theta]_{330}$ 0, $[\theta]_{290}$ +2560, $[\theta]_{250}$ 0, $[\theta]_{215}$ −9660 (dichloromethane, $c=0.53$ at 21.5°): $[\phi]_{700}$ −126°, $[\phi]_{589}$ −185°, $[\phi]_{336}$ −700°, $[\phi]_{311}$ −505°, $[\phi]_{272}$ −3190° (inflexion), $[\phi]_{230}$ −6720°, $[\phi]_{225}$ −6300°; $[\theta]_{330}$ 0, $[\theta]_{294}$ +1415, $[\theta]_{270}$ 0, $[\theta]_{256}$ −222 (inflexion), $[\theta]_{225}$ −6940 (dioxane, $c=0.58$ at 16.5°): $[\phi]_{700}$ −130.5°, $[\phi]_{589}$ −184°, $[\phi]_{317}$ −921° (peak), $[\phi]_{285}$ −2419°, $[\phi]_{267}$ −2035°, $[\phi]_{230}$ −5000°, $[\phi]_{220}$ −4750°; $[\theta]_{330}$ 0, $[\theta]_{300}$ +380.3, $[\theta]_{292}$ 0, $[\theta]_{273}$ −684.5, $[\theta]_{250}$ −329.4, $[\theta]_{240}$ −509.3. *Anal.* Calcd. for $C_{29}H_{49}O_2N$: C, 78.50; H, 11.13; N, 3.16. Found: C, 78.80; H, 10.89; N, 3.31.

2α-Amino-3-oxo Steroid Hydrochloride (VII)——A suspension of 2–hydroxyimino–17β–hydroxyandrostan–3–one (Va, 2.00 g) in MeOH (130 ml) containing 35% HCl (0.70 ml) was hydrogenated with 40% Pd on carbon (1.00 g) for 10 min, during which 2 molar equivalent H_2 was absorbed. The catalyst was removed by filtration, the solvent was evaporated *in vacuo* below 40°, and the residue was dissolved in MeOH (16 ml). Addition of ether (80 ml) separated crystals (1.28 g) of 2α–amino–17β–hydroxyandrostan–3–one hydrochloride (VIIa), mp above 300°, $[\alpha]_D$ +117.3° ($c=1.26$). The compound was unstable in warm solutions, IR ν_{max} cm^{-1}: 3600, 3200, 1728, 1590. *Anal.* Calcd. for $C_{19}H_{32}O_2NCl$: C, 66.79; H, 9.43; N, 4.10. Found: C, 66.49; H, 9.50; N, 3.88.

2α–Amino–17β–acetoxyandorstan–3–one hydrochloride (VIIb), mp above 300° and 2α–amino–17β–hydroxy–17α–methylandrostan–3–one hydrochloride (VIIc), mp 249—250° (decomp.) were prepared similarly. The analyses were unsatisfactory and the crude compounds were used for further reactions.

A mixture of VId (1.00 g) suspended in MeOH (200 ml), 30% Pd on carbon (0.50 g) and an anhydrous methanolic HCl solution (0.10 g in 3.0 ml) was shaken under H_2 for 8 hr. The uptake of H_2 was 95% of the theoretical amount. Treatment of the reaction mixture below 25° as described for VIIa gave a crude product (0.93 g). Two crystallizations from MeOH afforded a pure sample of 2α–aminocholestan–3–one hydrochloride (VIId), mp 245—250° (decomp.), $[\alpha]_D$ +63.4° ($c=0.35$, MeOH). IR ν_{max} cm^{-1}: 3400—2300, 1725. *Anal.* Calcd. for $C_{27}H_{48}ONCl$: C, 74.01; H, 11.05; N, 3.20. Found: C, 74.21; H, 10.82; N, 3.44.

2α-Acetamidocholestan-3β-ol (VIIId)——To a solution of VId (1.00 g) in tetrahydrofuran (100 ml) was added $NaBH_4$ (0.40 g) in H_2O (3.0 ml) and the mixture was allowed to stand at room temperature overnight. The mixture was concentrated *in vacuo* and the residue was neutralized with aqueous AcOH to separate a precipitate. This (1.00 g, mp 217—222°) was dissolved in benzene and chromatographed on silica gel (30 g). After elution with benzene, benzene—ether (9:1, 1:1, 1:9) and ether, elution with ether—$CHCl_3$ (1:1, 1.2 liler) gave a mixture (0.30 g), mp 212—218° which has not been examined in detail. Further elution with the same solvent mixture (1.6 liters) and recrystallization of the product from acetone gave VIIId (0.50 g), mp 228—230°, $[\alpha]_D^{23}$ +14.6° ($c=0.96$), $[\alpha]_D^{50}$ +12.1° ($c=0.34$, CCl_4), $[\alpha]_D^{19}$ −13.7° ($c=0.52$, dioxane), $[\alpha]_D^{23}$ −47.2 ($c=0.51$, MeOH). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3645, 3410, 3300, 1654, 1513. NMR (100 Mc) (τ): 4.25 (NH, multiplet), 6.18 (3α–H, multiplet, W_h 25 cps), 6.68 (2β–H, multiplet, W_h 25 cps). ORD (MeOH, $c=0.40$ at 23.5°): $[\phi]_{700}$ −144°, $[\phi]_{589}$ −200°, $[\phi]_{210}$ −10600° (dichlorometnane, $c=0.49$ at 23°): $[\phi]_{700}$ +43.4°, $[\phi]_{589}$ +61.7°, $[\phi]_{415-405}$ +98°, $[\phi]_{230}$ −5800°, $[\phi]_{225}$ −4350°. (Dioxane, $c=0.53$ at 19°): $[\phi]_{700}$ −37.3°, $[\phi]_{589}$ −61.0°, $[\phi]_{226}$ −5300°, $[\phi]_{220}$ −4800°. *Anal.* Calcd. for $C_{29}H_{51}O_2N$: C, 78.14; H, 11.53; N, 3.14. Found: C, 77.94; H, 11.30; N, 3.29.

2α-Aminocholestan-3β-ol (IXd)——A mixture of VIIId (0.20 g) in MeOH (9.0 ml) and KOH (4.0 g) in H_2O (1.0 ml) was refluxed for 27 hr. The reaction mixture was poured into H_2O and the precipitate was filtered, washed with H_2O and dried. Recrystallization from MeOH gave IXd (0.16 g), mp 162—164°, $[\alpha]_D$ +7.0° (c=1.06). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3345, 3130, 1582. NMR (100 Mc) (τ): 6.87 (3α-H, multiplet, W_h 23 cps), 7.38 (2β-H, multiplet, W_h 25 cps). *Anal.* Calcd. for $C_{27}H_{49}ON$: C, 80.33; H, 12.24; N, 3.47. Found: C, 80.03; H, 12.27; N, 3.49.

2α-Aminocholestan-3β-ol O,N-Diacetate (Xd)——a) Acetylation of VIIId (70 mg) in pyridine (1.0 ml) with Ac_2O (0.50 ml) at room temperature for 5 hr gave Xd. Recrystallization from MeOH gave a pure sample (40 mg), mp 164—165°, $[\alpha]_D$ −10.6° (c=0.54). IR ν_{max} cm^{-1}: 1722, 1666, 1516. *Anal.* Calcd. for $C_{31}H_{53}O_3N$: C, 76.33; H, 10.95; N, 2.87. Found: C, 76.58; H, 10.84; N, 3.16.

b) Acetylation of IXd in a similar manner gave Xd, mp 164—165°, identical (mixed mp and IR) with that described above.

17β-Acetoxy-2′-methylandrostano[2,3-*d*]oxazole (XIb)——To a stirred suspension of VIb (1.48 g) in Ac_2O (20 ml), was added dropwise a mixture of conc. H_2SO_4 (0.20 ml) and Ac_2O (10 ml). After being kept at room temperature overnight, the mixture was heated at 80° for 3 hr. The cooled mixture was diluted with H_2O and the separated crystals were collected (1.37 g), dissolved in benzene and chromatographed on alumina (30 g). Elution with benzene and benzene—ether (9:1) gave a solid (1.16 g, mp 133—135°) which was recrystallized from MeOH to afford XIb (1.04 g), mp 134—135°, $[\alpha]_D$ +45.3° (c=1.67). UV λ_{max} mμ (ε): 225 (6000). Gas chromatography (retention time): 5.9 min. *Anal.* Calcd. for $C_{23}H_{33}O_3N$: C, 74.36; H, 8.95; N, 3.77. Found: C, 74.58; H, 8.80; N, 4.00.

17β-Hydroxy-2′-methylandrostano[2,3-*d*]oxazole (XIa)——Hydrolysis of the acetate (XIb) as described for IIIb gave XIa. The product was crystallized from AcOEt to afford solvated crystals, mp 57—58°, $[\alpha]_D$ +50.3° (c=1.10). *Anal.* Calcd. for $C_{21}H_{31}O_2N \cdot CH_3COOC_2H_5$: C, 71.89; H, 9.41; N, 3.36. Found: C, 71.75; H, 9.42; N, 3.36. After prolonged drying *in vacuo* at 45°, XIa melted at 88—90°, $[\alpha]_D$ +59.6° (c=1.69). UV λ_{max} mμ (ε): 225 (6200). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3600, 3300, 1738, 1675, 1571, 1274. The very weak absorption at 1738 cm^{-1} was indicative of the incomplete removal of the crystalline AcOEt. NMR (τ): 7.61 (2′-C$\underline{H}_3$). Gas chromatography (retention time): 4.1 min. *Anal.* Calcd. for $C_{21}H_{31}O_2N$: C, 76.55; H, 9.48; N, 4.25. Found: C, 76.32; H, 9.53; N, 4.22.

2′-Methylcholestano[2,3-*d*]oxazole (XId)——As described for VIIIb, VIa (1.30 g) in Ac_2O (20 ml) was treated with a mixture of conc. H_2SO_4 (0.15 ml) and Ac_2O (6.0 ml). The product (1.25 g, mp 115—123°) in petr. ether (15 ml) was chromatographed on alumina (30 g). Elution with petr. ether—benzene (19:1, 100 ml; 1:1, 200 ml) gave a crystalline solid (1.07 g) which was recrystallized from acetone to give XId (0.97 g), mp 132—133°, $[\alpha]_D$ +60.5° (c=1.27). UV λ_{max} mμ (ε): 225 (5600). IR ν_{max} cm^{-1}: 1666, 1577. NMR (τ): 7.60 (2′-C$\underline{H}_3$). *Anal.* Calcd. for $C_{29}H_{47}ON$: C, 81.82; H, 11.13; N, 3.29. Found: C, 81.27; H, 11.09; N, 3.42.

The mp was depressed on admixture with IIId and the IR curve was different in finger print region with that of IIId but gas chromatography failed to distinguish XId from IIId.

17β-Acetoxy-2′-methylandrostano[2,3-*d*]imidazole (XIIb)——A solution of VIb (0.975 g) and $AcONH_4$ (1.92 g) in AcOH (15 ml) was refluxed for 6 hr. The solvent was removed *in vacuo*. To the residue were added small pieces of ice and a 5% aqueous NH_4OH solution to separate a solid, which was collected, dissolved in benzene and chromatographed on alumina (25 g). The materials eluted with benzene—ether (4:1, 1:1), ether, and AcOEt were combined (0.90 g) and recrystallized from acetone to yield XII (0.68 g), mp 248—251° (decomp.), $[\alpha]_D$ +43.2° (c=0.95). UV λ_{max} mμ (ε): 223 (7300). IR ν_{max} cm^{-1}: 3600—2350, 1737, 1629, 1534, 1242. *Anal.* Calcd. for $C_{23}H_{34}O_2N_2$: C, 74.55; H, 9.25; N, 7.56. Found: C, 74.26; H, 9.14; N, 7.80.

17β-Hydroxy-2′-methylandrostano[2,3-*d*]imidazole (XIIa)——Hydrolysis of the acetate (XIIb) by the similar procedure as described for IIIb gave XIIa, which was crystallized from MeOH—AcOEt (1:1), mp 272—277° (decomp.), $[\alpha]_D$ +64.3° (c=1.34, MeOH). UV λ_{max} mμ (ε): 223 (6900). IR ν_{max} cm^{-1}: 3600—2200, 3270, 3080, 1627, 1536. *Anal.* Calcd. for $C_{21}H_{32}ON_2$: C, 76.78; H, 9.82; N, 8.53. Found: C, 76.94; H, 9.77; N, 8.61.

2′-Methylcholestano[2,3-*d*]imidazole (XIId)——As described for XIIb, XIId was prepared from VId (1.50 g). A pure sample (0.97 g) was obtained after chromatography of the crude product on Florisil, followed by crystallization from MeOH–acetone, mp 239—240° (decomp.), $[\alpha]_D$ +60.2° (c=0.99). UV λ_{max} mμ (ε): 223 (6100). IR ν_{max} cm^{-1}: 1624, 1532. *Anal.* Calcd. for $C_{29}H_{48}N_2$: C, 82.01; H, 11.39; N, 6.60. Found: C, 81.99; H, 11.37; N, 6.53.

Steroidal[2,3-*d*]imidazoline-2′-thione (XIII)——A solution of VIIa (1.00 g) and KSCN (0.85 g) in EtOH (60 ml) was refluxed for 2 hr. The solvent was removed *in vacuo*, H_2O was added to the residue and the separated product was collected. The product was mixed with acetone (3.0 ml) to give a crystalline solid (0.74 g) which was recrystallized from MeOH—acetone to yield 17β-hydroxyandrostano[2,3-*d*] imidazoline-2′-thione (XIIIa, 0.61 g), mp above 300°, $[\alpha]_D$ +66.5° (c=0.73, pyridine). UV λ_{max} mμ (ε): 271 (19400). IR ν_{max} cm^{-1}: 3350, 3100, 1678, 1502. *Anal.* Calcd. for $C_{20}H_{30}ON_2S$: C, 69.33; H, 8.73; N, 8.09; S, 9.25. Found: C, 69.03; H, 8.54; N, 7.76; S, 9.52.

17β-Acetoxyandrostano[2,3-*d*]imidazoline-2′-thione (XIIIb) was prepared similarly from the crude amine hydrochloride (VIIb, 0.50 g). Crystallization from EtOH gave a pure sample (0.26 g), mp above

300°, $[\alpha]_D$ +54.7° (c=1.72, pyridine). UV λ_{max} mμ (ε): 271 (19700). IR ν_{max} cm^{-1}: 3090, 1730, 1675, 1507, 1243. *Anal.* Calcd. for $C_{22}H_{32}O_2N_2S$: C, 68.00; H, 8.30; N, 7.21. Found: C, 68.13; H, 8.57; N, 7.05.

17β-Hydroxy-17α-methylandrostano[2,3-*d*]imidazoline-2'-thione (XIIIc) was prepared similarly from the crude amine hydrochloride (VIIc, 1.50 g). Crystallization from acetone gave a pure sample (0.78 g), mp above 300°, $[\alpha]_D$ +57.8° (c=1.08, pyridine). UV λ_{max} mμ (ε): 271 (19200). IR ν_{max} cm^{-1}: 3480, 3100, 1670, 1500. *Anal.* Calcd. for $C_{21}H_{32}ON_2S$: C, 69.97; H, 8.95; N, 7.77. Found: C, 70.10; H, 8.80; N, 7.76.

Cholestano[2,3-*d*]imidazoline-2'-thione (XIIId) was prepared similarly from VIId (2.00 g). The crude product (1.86 g) in $CHCl_3$ (200 ml) was chromatographed on alumina (50 g) and the materials (0.91 g) eluted with $CHCl_3$–acetone (1:1) and MeOH were crystallized from EtOH to give a pure sample (0.70 g), mp above 300°, $[\alpha]_D$ +75.0° (c=0.67, pyridine). UV λ_{max} mμ (ε): 271 (20800). IR ν_{max} cm^{-1}: 3070, 1673, 1500. *Anal.* Calcd. for $C_{28}H_{46}N_2S$: C, 75.97; H, 10.48; N, 6.33; S, 7.24. Found: C, 76.14; H, 10.50; N, 6.36; S, 6.98.

Steroidal[2,3-*d*]imidazole without a 2'-Methyl Group (XIV)——A mixture of XIIIa (0.50 g) and Raney Ni (W-5, 2.50 g) in EtOH (100 g) was refluxed for 3 hr. After removal of Ni, the solvent was evaporated *in vacuo* and the residue was crystallized from acetone to afford 17β-hydroxyandrostano[2,3-*d*]imidazole (XIVa, 0.22 g), mp 228—230° (decomp.), $[\alpha]_D$ +65.7° (c=1.09). UV λ_{max} mμ (ε): 223 (7200). IR ν_{max} cm^{-1}: 3400—2200, 3120, 1620, 1600, 1447. *Anal.* Calcd. for $C_{20}H_{30}ON_2$: C, 76.39; H, 9.26; N, 8.91. Found: C, 76.22; H, 9.64; N, 8.79.

By desulfurization in the same way the following compounds were prepared.

17β-Acetoxyandrostano[2,3-*d*]imidazole (XIVb); yield, 47.5%, crystallized from MeOH, mp 278—280°, $[\alpha]_D$ +39.4° (c=0.71, MeOH). UV λ_{max} mμ (ε): 223 (6600). IR ν_{max} cm^{-1}: 3400—2200, 1735, 1620, 1237. *Anal.* Calcd. for $C_{22}H_{32}O_2N_2$: C, 74.12; H, 9.05; N, 7.86. Found: C, 74.45; H, 9.12; N, 7.73.

17β-Hydroxy-17α-methylandrostano[2,3-*d*]imidazole (XIVc); yield, 65.7%, crystallized from MeOH, mp 260—262°, $[\alpha]_D$ +32.7° (c=1.47, MeOH). UV λ_{max} mμ (ε): 223 (6500). IR ν_{max} cm^{-1}: 3600—2200, 3160, 1620, 1580, 1450. *Anal.* Calcd. for $C_{21}H_{32}ON_2$: C, 76.78; H, 9.82; N, 8.53. Found: C, 76.95; H, 9.65; N, 8.25.

Cholestano[2,3-*d*]imidazole (XIVd); yield 66.2%, purified by chromatography on Florisil with elution with $CHCl_3$—acetone (1:1) and acetone and by crystallization from benzene, mp 258—260°, $[\alpha]_D$ +62.4° (c=0.98). UV λ_{max} mμ (ε): 223 (7900). IR ν_{max} cm^{-1}: 1620, 1596. *Anal.* Calcd. for $C_{28}H_{46}N_2$: C, 81.89; H, 11.29; N, 6.82. Found: C, 81.88; H, 11.00; N, 6.85.

Bis(steroidal[3,2-*e*,3',2'-*b*])pyrazine (XV)——A solution of VIIa (0.60 g) in ice-water (30 ml) was basified with a 10% aqueous NaOH solution to give a solid which was collected (0.53 g), dissolved in EtOH (10 ml) and warmed gently on a steam-bath for a few minutes to separate a crystalline mass. Recrystallization from a large amount of EtOH gave bis(androstano[3,2-*e*,3',2'-*b*])pyrazine-17β,17'β-diol (XVa, 0.24 g), mp above 300°, $[\alpha]_D$ +80.3° (c=0.70). UV λ_{max} mμ (ε): 290 (14000), shoulder 310 (6900). IR ν_{max} cm^{-1}: 1470, 1400, 938. *Anal.* Calcd. for $C_{38}H_{56}O_2N_2$: C, 79.67; H, 9.85; N, 4.89. Found: C, 79.49; H, 9.73; N, 5.01.

The following compounds were prepared similarly.

Bis(androstano[3,2-*e*,3',2'-*b*]pyrazine-17β,17'β-diol diacetate (XVb), mp above 300°, $[\alpha]_D$ +54.1° (c=1.25). UV λ_{max} mμ (ε): 290 (15000) shoulder 310 (7300). *Anal.* Calcd. for $C_{42}H_{60}O_4N_2$: C, 76.79; H, 9.21; N, 4.26. Found: C, 76.94; H, 9.50; N, 4.44.

17α,17'α-Dimethylbis(androstano[3,2-*e*,3',2'-*b*]pyrazine-17β,17'β-diol (XVc), mp above 300°, $[\alpha]_D$ +54.9° (c=0.75). UV λ_{max} mμ (ε): 290 (14500), shoulder 310 (6800). *Anal.* Calcd. for $C_{40}H_{60}O_2N_2$: C, 79.95; H, 10.06; N, 4.66. Found: C, 79.65; H, 9.92; N, 4.73.

17β-Acetoxy-2-acetoxymethyleneandrost-4-en-3-one (XVIIb)——A solution of 17β-hydroxy-2-hydroxymethyleneandrost-4-en-3-one (XVIa, 0.50 g) in Ac_2O (3.0 ml) and pyridine (3.0 ml) was allowed to stand at room temperature for 24 hr. The reaction mixture was poured into H_2O and the separated product was collected, dissolved in benzene and purified by chromatography on Florisil. Crystallization from MeOH gave an analytical sample, mp 163—165°, $[\alpha]_D$ +49.2° (c=1.02). UV λ_{max} mμ (ε): 264 (14000). IR ν_{max} cm^{-1}: 1765, 1735, 1685, 1625, 1615, 1250, 1190. *Anal.* Calcd. for $C_{24}H_{32}O_5$: C, 71.97; H, 8.05. Found: C, 71.89; H, 7.95.

17β-Acetoxy-2-hydroxyiminoandrost-4-en-3-one (XVIIIb)——To a mixture of XVIIb (0.25 g) in MeOH (5.0 ml) and $NaNO_2$ (0.20 g) in H_2O (0.5 ml), was added dropwise AcOH (0.23 g) and the mixture was stirred at room temperature for 2 hr. The reaction mixture was poured into H_2O (50 ml) and the precipitated product was collected and crystallized from MeOH to give a crude product (0.11 g), mp 210—216° (decomp.). Recrystallization from the same solvent gave an analytical sample of XVIIIb, mp 222—225° (decomp.), $[\alpha]_D$ +122° (c=0.85). UV λ_{max} mμ (ε): 263 (15000). IR ν_{max} cm^{-1}: 3180—3120, 1732, 1695, 1615, 1240. *Anal.* Calcd. for $C_{21}H_{29}O_4N$: C, 70.17; H, 8.13; N, 3.90. Found: C, 69.98; H, 8.20; N, 3.99.

17β-Acetoxy-2-hydroxyiminoandrost-4-en-3-one 3-Hydrazone (XIXb)——A solution of XVIIIb (0.85 g) and 80% $NH_2NH_2 \cdot H_2O$ (0.45 g) in MeOH (60 ml) was refluxed for 30 min. The solvent was removed, H_2O was added, and the separated product (0.56 g) was crystallized from MeOH to afford XIXb, mp 230—240° (decomp.), $[\alpha]_D$ +225° (c=0.80, pyridine). UV λ_{max} mμ (ε): 235 (9000), 305 (10100). IR ν_{max} cm^{-1}: 3410, 3320, 3260, 3170, 3040, 1738, 1620, 1590, 1530, 1255, 1035, 960. *Anal.* Calcd. for $C_{21}H_{31}O_3N_3$: C, 67.53; H, 8.37; N, 11.25. Found;: C, 67.60; H, 8.52; N, 11.51.

17β-Hydroxyandrost-4-eno[2,3-*d*]triazole (XXa)——To an ice-cooled solution of XIXb (1.50 g) in pyridine (20 ml) and $CHCl_3$ (50 ml), was added PCl_5 (5.0 g). The mixture was stirred for 20 min and then poured into ice–water. The $CHCl_3$–layer was separated, washed with a 5% aqueous HCl soluton, and the H_2O, dried and evaporated. The residue (1.30 g) in benzene was chromatographed on Florisil (30 g). The products eluted with benzene (250 ml), benzene—ether (4:1, 650 ml; 2:1, 200 ml; 1:1, 100 ml) and ether (100 ml) were combined and crystallized from MeOH to give the 17–acetate (XXb, 0.27 g). Further recrystallization from the same solvent gave a pure sample, pale yellow, mp 187—188°, $[\alpha]_D$ +139° (c=0.79). UV λ_{max} mμ (ε): 259—260 (13300). IR ν_{max} cm^{-1}: 1730, 1630, 1250, 1120, 1115, 985 (triazole).[42] *Anal.* Calcd. for $C_{21}H_{29}O_2N_3 \cdot H_2O$: C, 67.53; H, 8.37; N, 11.25. Found: C, 67.68; H, 8.60; N, 11.43. The anhydrous sample was obtained after drying *in vacuo* at 140—150° for 6 hr. *Anal.* Calcd. for $C_{21}H_{29}O_2N_3$: C, 70.95; H, 8.22; N, 11.82. Found: C, 70.28; H, 8.18; N, 11.64.

Hydrolysis of the acetate (XXb, 100 mg) in MeOH (15 ml) with NaOH (100 mg) in H_2O (2.0 ml) at reflux temperature for 15 min and crystallization of the product from ether–acetone gave XXa (80 mg), mp 250—254°, $[\alpha]_D$ +153° (c=0.57, pyridine). UV λ_{max} mμ (ε): 259—260 (13300). IR ν_{max} cm^{-1}: 3300, 3150, 3050, 1630, 1520, 1110, 1100, 978. *Anal.* Calcd. for $C_{19}H_{27}ON_3$: C, 72.80; H, 8.68; N, 13.41. Found: C, 72.59; H, 8.64; N, 13.65.

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42) H. Rapaport and W. Nilssen, *J. Am. Chem. Soc.*, **83**, 4262 (1961).