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Katsujiro Ueno and Genkichi Ohta : Investigations on Steroids. Ⅶ.*1 Derivatives of 17β-Hydroxyandrostano[2,3-*c*]furazan substituted at Position 16.

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In androgenic and anabolic steroids related to testosterone, substitution at the 16-position with a methyl or hydroxyl group generally decreases their biological activities[1] but certain 16-methylene compounds are claimed to retain anabolic activity.[2] Since 17β-hydroxyandrostano[2,3-*c*]furazan (I) and its 17α-methyl derivative were found to have high anabolic/androgenic ratios,[3] the derivatives of I with the 16-methylene, methyl and hydroxyl group were prepared to determine their biological activities.

The preparation of these compounds was based on the known methods of synthesis and the configurations at positions 16 and 17 were assigned by analogy with the corresponding reported compounds.

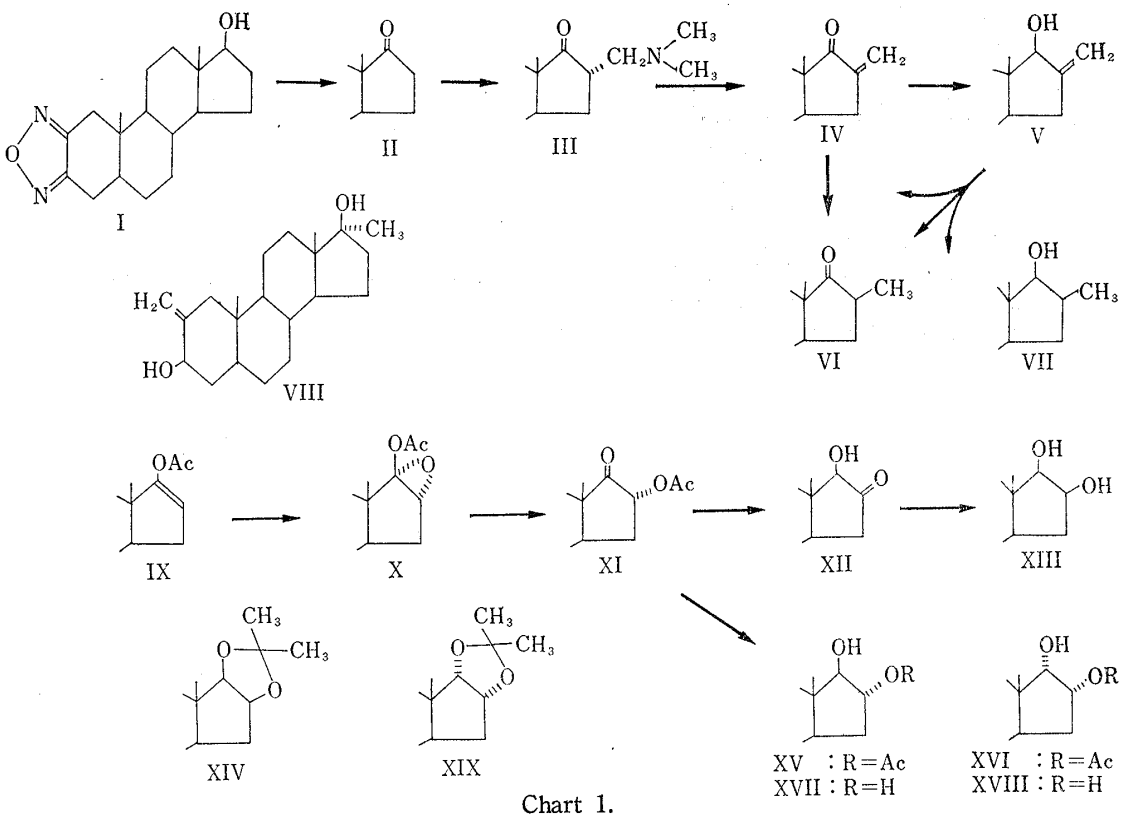

Chart 1.

*1 Part Ⅵ : This Bulletin, **14**, 285 (1966).

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1) *a*) A. Butenandt, J. Schmidt-Thomé, T. Weiss : Ber., **72**, 417 (1939). *b*) P. L. Julian, E. W. Meyer, H. C. Printy : J. Am. Chem. Soc., **70**, 3872 (1948). *c*) S. Bernstein, E. W. Cantrall : J. Org. Chem., **26**, 3560 (1961). *d*) A. Bowers, P. G. Holton, E. Necoechea, F. A. Kincl : J. Chem. Soc., **1961**, 4057. *e*) J. H. Fried, A. N. Nutile, G. E. Arth, L. H. Sarett : J. Org. Chem., **27**, 682 (1962). *f*) P. de Ruggieri, C. Gandolfi, U. Guzzi, D. Chiaramonti, C. Ferrari : Farmaco, **20**, 280 (1965).

2) U. S. Pat. : 3,117,060 (C. A., **61**, 12060 (1964)).

3) A. Kasahara, T. Onodera, M. Mogi, Y. Oshima, M. Shimizu : This Bulletin, **13**, 1460 (1965).

Mannich reaction of 17-oxoadrostano[2,3-*c*]furazan (II)[4] with formaldehyde and dimethylamine in acetic acid afforded the 16α-dimethylaminomethyl-17-ketone (III) and the 16-methylene-17-ketone (IV).[5] The former was converted to IV by heating in acetic acid and acetic anhydride. Reduction of IV with sodium borohydride gave the 16-methylene-17β-ol (V).[6] Hydrogenation of IV with palladium afforded the 16β-methyl-17-ketone (VI), which was reduced with sodium borohydride to give the 16β-methyl-17β-ol (VII).[6] It has been shown that the above reactions are stereospecific and the configuration assignment of compounds (III, V, VI and VII) was made in accordance with the precedents.[1d,5,6]

In an attempted hydrogenation of the 16-methylene-17β-ol (V) with palladium, the 16β-methyl-17-ketone (VI) was obtained as the main product along with the 16β-methyl-17β-ol (VII). Since the 17-ketone (VI) appeared to be yielded by rearrangement of V and similar rearrangement of the allylic secondary alcohol was described in the literature,[7] V was treated with palladium in refluxing tetrahydrofuran and also with hydrochloric acid in tetrahydrofuran at room temperature. In both of the above treatment, the product was shown by gas chromatography and spectral data to consist of three compounds, *i.e.*, the rearrangement product (VI), the oxidation product (IV), and the reduction product (VII), although the former two were not separated by usual column chromatography. The reaction of 17α-methyl-2-methyleneandrostane-3β,17β-diol (VIII) with palladium was reported to give the rearrangement product and the oxidation product, but the reduction product was not reported.[7c] Apparently, the formation of IV and VII resulted from the hydrogen transfer of V, which is similar to the reaction of cholest-2-en-1α-ol benzoate with alumina yielding cholestan-3β-ol and cholest-1-en-3-one.[8]

For preparation of the 16α- and 16β-hydroxy derivatives, the method of Leeds, Fukushima and Gallagher[9] was employed. The enol acetate (IX) of II was oxidized with perbenzoic acid giving the 17β-acetoxy-16α,17α-epoxide (X) which was rearranged by the use of perchloric acid into the 16α-acetoxy-17-ketone (XI). Treatment of XI with alkali afforded the 17β-hydroxy-16-ketone (XII) which was reduced with sodium borohydride to give the 16β,17β-diol (XIII). The *cis*-dihydroxy structure was characterized by formation of the acetonide (XIV).

Reduction of XI with sodium borohydride gave a mixture of the epimers, 16α-acetoxy-17β-ol (XV) and -17α-ol (XVI) which, without separation, was hydrolyzed to furnish the mixture of the corresponding diols (XVII and XVIII). By treatment of the mixture with acetone and perchloric acid, the unaffected 16α,17β-diol (XVII) was readily separated from the 16α,17α-isopropylidenedioxy compound (XIX). The latter was hydrolyzed to recover the 16α,17α-diol (XVIII).

The assignment of configurations of the 16- and 17-substituents followed from that referred in the above method.[9] The molecular rotation differences of XI from IX (+162°) and of the acetate of XII from IX (−547°) are consistent with the corresponding reported values (+162 and −528°),[9] respectively. The assignment is further supported by the formation of two acetonides (XIV and XIX).

4) G. Ohta, T. Takegoshi, K. Ueno, M. Shimizu : This Bulletin, **13**, 1445 (1965).
5) Cf. K. Brückner, K. Irmscher, F. v. Werder, K.-H. Bork, H. Metz : Chem. Ber., **94**, 2897 (1961), and ref. 1*b*).
6) Cf. *a*) F. Neumann, O. Mancera, G. Rosenkranz, F. Sondheimer : J. Am. Chem. Soc., **77**, 5676 (1955). *b*) F. A. Kincl, M. Garcia : Chem. Ber., **92**, 595 (1959).
7) *a*) A. S. Dreiding, J. H. Hartman : J. Am. Chem. Soc., **78**, 1216 (1956). *b*) S. Sakai : This Bulletin, **7**, 50 (1959). *c*) J. A. Edwards, M. C. Calzada, A. Bowers : J. Med. Chem., **6**, 178 (1963).
8) H. Mühle, E. Orsz, Ch. Tamm : Helv., **49**, 939 (1966).
9) N. S. Leeds, D. K. Fukushima, T. F. Gallagher : J. Am. Chem. Soc., **76**, 2943 (1954).

In biological assay, compounds (V, VI, XIII, and XVII) did not exhibit anabolic activity comparable to that of the parent compound (I).*3

Experimental*4

16α-Dimethylaminomethyl-17-oxoandrostano[2,3-*c*]furazan (III) and 16-Methylene-17-oxoandrostano-[2,3-*c*]furazan (IV)——A mixture of II[4] (6.10 g.), dimethylamine hydrochloride (19.4 g.), a 37% HCHO-solution (15.9 ml.) and AcOH (200 ml.) was heated at 100° for 10 hr. The reaction mixture was concentrated *in vacuo*, diluted with a 10% HCl-solution (20 ml.) and water, and extracted with benzene. The benzene solution was washed with water, dried and evaporated. Crystallization of the residue from acetone–MeOH gave the crude product of IV (1.40 g.) melting at 199~203°. The acidic aqueous solution was basified with Na_2CO_3 and extracted with ether. The ethereal solution was washed with water, dried and evaporated to give the Mannich base (III) as a syrup; the base was characterized as its hydrochloride (see below). The syrup was dissolved in AcOH (60 ml.) and Ac_2O (100 ml.) and heated at 100° for 3 hr. The reaction mixture was concentrated *in vacuo*, water was added and the separated product was collected and crystallized from acetone–MeOH to give an additional crop of IV (3.9 g.) melting at 200~202°. Total yield was 83.5%. Recrystallization from acetone–MeOH gave a pure sample, m.p. 204~206°, $[\alpha]_D$ +75.7°(c=1.03). UV λ_{max} mμ (ε): 223~227 (10500). IR ν_{max} cm^{-1}: 1722 (C=O); 1495, 1000 (furazan); 3080, 1641 (>C=CH_2). *Anal.* Calcd. for $C_{20}H_{26}O_2N_2$: C, 73.59; H, 8.03; N, 8.58. Found: C, 73.55; H, 8.02; N, 8.87.

Addition of an ethanolic HCl solution to an ethereal solution of the Mannich base gave the hydrochloride of III. Crystallization from ether–MeOH and from acetone–MeOH afforded a pure sample (solvated), m.p. 197~198°. UV λ_{max} mμ (ε): 217 (4750). IR ν_{max} cm^{-1}: 3580, 1632 (H_2O); 3460, 1045 (CH_3OH); 2660~2470 (+NH); 1734 (C=O); 1003 (furazan). *Anal.* Calcd. for $C_{22}H_{33}O_2N_3 \cdot HCl \cdot \frac{1}{2}CH_3OH \cdot \frac{1}{2}H_2O$: C, 62.41; H, 8.61; N, 9.71. Found: C, 62.34, 62.61; H, 8.47, 8.42; N, 9.72.

17β-Hydroxy-16-methyleneandrostano[2,3-*c*]furazan (V)——To a solution of IV (1.00 g.) in tetrahydrofuran (80 ml.) and MeOH (40 ml.) was added a solution of $NaBH_4$ (0.50 g.) in H_2O (15 ml.). After standing overnight, the mixture was concentrated *in vacuo*, diluted with water, and acidified with AcOH. The separated solid was collected and crystallized from acetone to give V (0.88 g.) of m.p. 243~245°. Further recrystallization gave a pure sample, m.p. 244~247°, $[\alpha]_D$ −24.6°(c=0.66, tetrahydrofuran). UV: no maximum above 210 mμ. IR ν_{max} cm^{-1}: 3485, 1069 (OH); 3075, 1657 (>C=CH_2); 1495, 1002 (furazan). *Anal.* Calcd. for $C_{20}H_{28}O_2N_2$: C, 73.13; H, 8.59; N, 8.53. Found: C, 72.85; H, 8.82; N, 8.69.

16β-Methyl-17-oxoandrostano[2,3-*c*]furazan (VI)——A solution of IV (0.65 g.) in tetrahydrofuran (50 ml.) was hydrogenated over 20% Pd-C (100 mg.) at room temperature. Removal of the catalyst by filtration, evaporation of the solvent and crystallization of the residue from acetone–MeOH gave VI (0.54 g.) of m.p. 203~205°. Recrystallization gave a pure sample, m.p. 205.5~208°, $[\alpha]_D$ +126.5°(c=1.25). UV λ_{max} mμ (ε): 217 (4230). IR ν_{max} cm^{-1}: 1730 (C=O); 1496, 1002 (furazan). *Anal.* Calcd. for $C_{20}H_{28}O_2N_2$: C, 73.13; H, 8.59; N, 8.53. Found: C, 73.40; H, 8.66; N, 8.49.

17β-Hydroxy-16β-methylandrostano[2,3-*c*]furazan (VII)——A mixture of VI (1.58 g.) in tetrahydrofuran (120 ml.) and MeOH (64 ml.) and $NaBH_4$ (0.79 g.) in H_2O (24 ml.) was kept at room temperature overnight. The mixture was neutralized with AcOH, concentrated *in vacuo*, and diluted with water to separate crystals (1.30 g.), m.p. 256~260°. Recrystallization from acetone gave VII, m.p. 261~263°, $[\alpha]_D$ +52.3°(c=0.67, tetrahydrofuran). UV λ_{max} mμ (ε): 217 (4290). IR ν_{max} cm^{-1}: 3520, 1065, 1043 (OH); 1584, 1495, 1003 (furazan). *Anal.* Calcd. for $C_{20}H_{30}O_2N_2$: C, 72.69; H, 9.15; N, 8.48. Found: C, 72.61; H, 8.96; N, 8.35.

Reactions of the 16-Methylene-17β-ol (V)——a) A solution of V (0.27 g.) in tetrahydrofuran (20 ml.) was shaken with 20% Pd-C (50 mg.) under H_2 at room temperature. The absorption of H_2 stopped after 13 min., while 0.3 equimolar H_2 was consumed. The catalyst was filtered, the filtrate was concentrated *in vacuo*, and the residue (λ_{max}: 217 mμ) in benzene was chromatographed over alumina (10 g.). Elution with benzene gave crystals (0.14 g.; 52%) which was recrystallized from acetone–MeOH to afford the 16β-methyl-17-ketone (VI, 110 mg.), m.p. 204~206°, identical with that described above (mixed m.p. and IR). After an intermediate fraction (25 mg.), a fraction of the 16β-methyl-17β-ol (VII, 80 mg.) was eluted with benzene–ether (1:1). Crystallization from acetone gave VII (50 mg.), m.p. 256~260°, identical with that described above (mixed m.p. and IR).

b) A mixture of V (0.10 g.) in tetrahydrofuran (20 ml.) and 20% Pd-C (50 mg.) was heated under reflux for 8 hr. The mixture was filtered, the filtrate was concentrated and the residue (λ_{max}: 221 mμ) in benzene

*3 The biological activities were assayed by Mr. A Kasahara and his associates in this Laboratory; details will be given elsewhere.

*4 Melting points are uncorrected. Unless otherwise stated, IR spectra were taken in a KBr disc, UV spectra in EtOH and optical rotations in $CHCl_3$. The microanalyses were performed by Mr. B. Kurihara and Miss K. Hanawa in this Laboratory.

was chromatographed over alumina (4 g.). Elution with benzene gave a product (40 mg.; λ_{max} : 221 mμ) whose IR spectrum contained the bands corresponding to Ⅳ and Ⅵ. Gas chromatography*5 showed two peaks due to Ⅳ (retention time : 16.2 min.) and Ⅵ (retention time : 15.1 min.). Elution with benzene–ether (1:1) gave a fraction of Ⅶ (20 mg.; λ_{max} : 217 mμ), from which Ⅶ, m.p. 255~258° was obtained by crystallization from acetone and identified with an authentic sample described above.

c) To a solution of Ⅴ (0.28 g.) in tetrahydrofuran (30 ml.) was added a 35% HCl solution (3 ml.) and the mixture was allowed to stand at room temperature for 40 hr. The mixture was concentrated *in vacuo*, diluted with water and extracted with benzene. Evaporation of the benzene solution and chromatography of the residue as described in b) afforded a fraction of the mixture of Ⅳ and Ⅵ (140 mg.) and a fraction of Ⅶ (70 mg.). The IR spectrum and gas chromatogram of the mixture were identical with those described in b). A pure sample of Ⅶ (50 mg.) was obtained by crystallization of the fraction of Ⅶ.

17-Acetoxyandrost-16-eno[2,3-*c*]furazan (IX)——A mixture of H_2SO_4 and isopropenyl acetate (1:50, 2 ml.) was added to Ⅱ (2.00 g.) in isopropenyl acetate (20 ml.) and the mixture was heated at 100~125° for 2 hr., while the distillate (5 ml.) was removed. Isopropenyl acetate (10 ml.) and a mixture of H_2SO_4 and isopropenyl acetate (1:50, 2 ml.) were added, the mixture was again heated for 2.5 hr. and the distillate (10 ml.) was removed. The reaction mixture was diluted with ether, washed with an aqueous 5% Na_2CO_3 solution and water, dried and concentrated. The residue in benzene was filtered through alumina (10 g.) and the filtrate was concentrated *in vacuo*. Crystallization of the residue from acetone gave Ⅸ (1.52 g.) of m.p. 156~161°. The second crop (90 mg.), m.p. 159~162° was obtained from the mother liquor. Recrystallization gave a pure sample, m.p. 162~163.5°, $[\alpha]_D$ +67.6°(c=1.20). M_D=241°. UV λ_{max} mμ (ε) : 217 (6610). IR ν_{max} cm^{-1} : 1618, 809 (⊿16); 1756, 1205 (ester); 1586, 1497, 1001 (furazan). *Anal.* Calcd. for $C_{21}H_{28}O_3N_2$ (mol. wt., 356.5) : C, 70.76; H, 7.92; N, 7.86. Found : C, 70.70; H, 7.82; N, 7.95.

17β-Acetoxy-16α,17α-epoxyandrostano[2,3-*c*]furazan (X)——To a solution of Ⅸ (7.1 g.) in benzene (50 ml.) was added a 0.2*M* solution (250 ml.) of perbenzoic acid in benzene and the mixture was allowed to stand at room temperature for 26 hr. The mixture was shaken with a dil. Na_2CO_3 solution containing small pieces of ice, and the benzene layer was washed with water, dried and evaporated *in vacuo*. Crystallization of the residue from acetone–MeOH gave Ⅹ (5.3 g.), m.p. 175~176°; from the mother liquor was obtained an additional crop (0.50 g.), m.p. 176°. Recrystallization gave a pure sample, m.p. 175~176°, $[\alpha]_D$ +76.7° (c=1.17). UV λ_{max} mμ (ε) : 217~218 (4280). IR ν_{max} cm^{-1} : 3045, 1056 (epoxide ring); 1748, 1214, 1196 (ester), 1582, 1495, 1001 (furazan). *Anal.* Calcd. for $C_{21}H_{28}O_4N_2$: C, 67.72; H, 7.58; N, 7.52. Found: C, 67.93; H, 7.41; N, 7.68.

16α-Acetoxy-17-oxoandrostano[2,3-*c*]furazan (XI)——To a mixture of Ⅹ (5.8 g.) in AcOH (75 ml.) was added 70% $HClO_4$ (1.7 g.) in AcOH (6 ml.) and the mixture was kept at room temperature for 3 hr. The mixture was diluted with ether (1.2 L.) and shaken with an aqueous 10% Na_2CO_3 solution (1 L.) and small pieces of ice. The ethereal solution was washed with water, dried and concentrated *in vacuo*. Crystallization of the residue from MeOH gave Ⅺ (4.9 g.), m.p. 202~204°. The second crop (0.30 g.) from the mother liquor melted at 195~200°. Recrystallization gave an analytical sample, m.p. 202~204°, $[\alpha]_D$ +108.2°(c=1.34). M_D=403°. UV λ_{max} mμ (ε) : 217 (4380). IR ν_{max} cm^{-1} : 1745 (broad, carbonyl); 1235 (ester); 1500, 1000 (furazan). *Anal.* Calcd. for $C_{21}H_{28}O_4N_2$ (mol. wt., 372.5) : C, 67.72; H, 7.58; N, 7.52. Found : C, 67.90; H, 7.50; N, 7.54.

17β-Hydroxy-16-oxoandrostano[2,3-*c*]furazan (XII)——A mixture of Ⅺ (2.60 g.) and a methanolic 4% KOH solution (100 ml.) was refluxed under N_2 for 1 hr. The mixture was concentrated *in vacuo* and diluted with water to separate a precipitate which was collected. Crystallization from acetone–MeOH gave Ⅻ (1.75 g.), m.p. 231~236°. Recrystallization from acetone gave a pure sample, m.p. 232~236°, $[\alpha]_D$ −91.7° (c=1.04). UV λ_{max} mμ (ε) : 217 (4560). IR ν_{max} cm^{-1} : 3540, 1050 (OH); 1740 (C=O); 1491, 996 (furazan). *Anal.* Calcd. for $C_{19}H_{26}O_3N_2$: C, 69.06; H, 7.93; N, 8.48. Found : C, 69.20; H, 7.82; N, 8.35.

Acetylation of Ⅻ with Ac_2O and pyridine at room temperature gave the 17-acetate which was crystallized from acetone–MeOH, m.p. 210~212°, $[\alpha]_D$ −82.3°(c=1.28). M_D=−306°. *Anal.* Calcd. for $C_{21}H_{28}O_4N_2$ (mol. wt., 372.5) : C, 67.72; H, 7.58; N, 7.52. Found : C, 67.77; H, 7.46; N, 7.62.

16β,17β-Dihydroxyandrostano[2,3-*c*]furazan (XIII)——A mixture of Ⅻ (0.86 g.) in tetrahydrofuran-MeOH (63:34, 97 ml.) and $NaBH_4$ (0.40 g.) in H_2O (13 ml.) was kept at room temperature for 5 hr. Treatment of the reaction mixture as described for Ⅴ and crystallization of the product from MeOH gave XIII (0.72 g.), m.p. 188~190/199~200°, $[\alpha]_D$ +55.9°(c=1.10, dioxane). UV λ_{max} mμ (ε) : 217~218 (4430). IR ν_{max} cm^{-1}: 3340, 1053 (OH); 1630 (H_2O); 1585, 1500, 1006 (furazan). *Anal.* Calcd. for $C_{19}H_{28}O_3N_2 \cdot \frac{1}{3}H_2O$: C, 67.42; H, 8.54; N, 8.28. Found : C, 67.48; H, 8.39; N, 8.31.

Acetylation of XIII with Ac_2O and pyridine at room temperature overnight gave the 16,17-diacetate of XIII, which was crystallized from MeOH, m.p. 206~207°, $[\alpha]_D$ +51.5°(c=1.02). *Anal.* Calcd. for $C_{23}H_{32}O_5N_2$: C, 66.32; H, 7.74; N, 6.73. Found : C, 66.57; H, 7.76; N, 6.91.

*5 Gas chromatography was performed by using a Barber-Colman Model 10, with a column packed with 1% SE-30 silicon polymer (G. E.) on Anakrom ABS. The conditions used were : column temperature 220° and argon gas flow 80 ml./min.

16β,17β-Isopropylidenedioxyandrostano[2,3-*c*]furazan (XIV)——To a solution of XIII (0.15 g.) in acetone (10 ml.) was added 2 drops of 70% $HClO_4$. After 2 hr., the mixture was diluted with water and extracted with ether. The ethereal solution was washed with an aqueous 5% $NaHCO_3$ solution and water, dried and evaporated. After chromatography of the residue in benzene solution over alumina, the product was crystallized from acetone-MeOH to give XIV (0.13 g.), melting at 201~209°. Recrystallization gave a pure sample, m.p. 206~208.5°, $[\alpha]_D$ +77.3°(c=1.34). UV λ_{max} mμ (ε): 217 (4500). IR ν_{max} cm^{-1}: 1381, 1373 (*gem.* dimethyl); 1059 (ether); 1495, 1000 (furazan). *Anal.* Calcd. for $C_{22}H_{32}O_3N_2$: C, 70.93; H, 8.66; N, 7.52. Found: C, 70.98; H, 8.87; N, 7.71.

Reduction of the 16α-Acetoxy-17-ketone (XI) with Sodium Borohydride——a) To an ice-cooled solution of XI (2.5 g.) in tetrahydrofuran (162 ml.) and MeOH (87 ml.) was added dropwise a solution of $NaBH_4$ (1.1 g.) in H_2O (35 ml.) and the mixture was stirred for 1.75 hr. The mixture was then heated under reflux for 30 min. to hydrolyze the acetoxyl group, concentrated *in vacuo*, diluted with water and neutralized with AcOH to separate a precipitate which was collected, washed thoroughly with water and dried. This (2.2 g.) was dissolved in acetone (100 ml.), a few drops of 70% $HClO_4$ was added and the solution was kept at room temperature for 2 hr. The solvent was removed *in vacuo*, water was added and the separated product was collected, washed with water and dried. Benzene (10 ml.) was added to the product and mixed and the insoluble material was filtered to give the crude 16α,17β-diol (XVII) (see below). The benzene solution was filtered through a column of alumina (10 g.) and the column was washed with benzene. The solvent was removed and the residue was crystallized from acetone-MeOH to yield 16α,17α-isopropylidenedioxyandrostano-[2,3-*c*]furazan (XIX) (0.46 g., 18.4%) melting at 195~197.5°. Recrystallization gave a pure sample, m.p. 196~198°, $[\alpha]_D$ +46.4°(c=0.93). UV λ_{max} mμ (ε): 218 (4050). IR ν_{max} cm^{-1}: 1380, 1374, 1223, 1201 (*gem.* dimethyl); 1493, 1002 (furazan). *Anal.* Calcd. for $C_{22}H_{32}O_3N_2$: C, 70.93; H, 8.66; N, 7.52. Found: C, 71.11; H, 8.70; N, 7.61.

The above crude diol was crystallized from acetone to afford 16α,17β-dihydroxyandrostano[2,3-*c*]furazan (XVII, 1.20 g.) melting at 221.5~224°. An additional crop (0.28 g.) of m.p. 220~223° was obtained from the mother liquor. Total yield was 66.4%. Recrystallization gave an analytical sample, m.p. 222~224°, $[\alpha]_D$ +41.1°(c=1.53, dioxane). UV λ_{max} mμ (ε): 217~218 (4510). IR ν_{max} cm^{-1}: 3350~3220, 1042 (OH); 1498, 1005 (furazan). *Anal.* Calcd. for $C_{19}H_{28}O_3N_2$: C, 68.84; H, 8.49; N, 8.43. Found: C, 68.57; H, 8.56; N, 8.36.

Acetylation of the diol (XVII) gave the 16α,17β-diacetoxy derivative, which was crystallized from MeOH, m.p. 137~138/165~166.5°, $[\alpha]_D$ −25.0°(c=1.08). *Anal.* Calcd. for $C_{23}H_{32}O_5N_2$: C, 66.32; H, 7.74; N, 6.73. Found: C, 66.32; H, 7.79; N, 6.92.

b) As described in a), XI (1.0 g.) in tetrahydrofuran-MeOH (65:35, 100 ml.) was reduced with $NaBH_4$ (0.45 g.) in H_2O (14 ml.). The cold reaction mixture was neutralized with AcOH, concentrated *in vacuo* and diluted with water to separate a solid; this is a mixture of the 16α-acetoxy-17β-ol (XV) and 17α-ol (XVI). Oxidation of the solid (50 mg.) with 8*N* CrO_3-H_2SO_4 in acetone[10] regenerated the 16α-acetoxy-17-ketone (XI, 30 mg.), m.p. and mixed m.p. 202~204°, identified also by comparison of the IR spectrum.

The solid (1.0 g.) was mixed with a small volume of warm benzene and the insoluble material was collected (0.30 g.). Repeated crystallization from acetone gave 16α-acetoxy-17β-hydroxyandrostano[2,3-*c*]furazan (XV), m.p. 214~217°, $[\alpha]_D$ +81.3°(c=1.23). UV λ_{max} mμ (ε): 217~218 (4520). IR ν_{max} cm^{-1}: 3460, 1034 (OH); 1708, 1253 (ester); 1495, 1002 (furazan). *Anal.* Calcd. for $C_{21}H_{30}O_4N_2$: C, 67.35; H, 8.08; N, 7.48. Found: C, 67.37; H, 8.06; N, 7.74.

Acetylation of XV gave the 16α,17β-diacetate of XVII, whose IR spectrum was identical with that described in a), m.p. and mixed m.p. 137~138/165~166.5°.

16α,17α-Dihydroxyandrostano[2,3-*c*]furazan (XVIII)——A mixture of the isopropylidenedioxy derivative (XIX, 0.33 g.), AcOH (25 ml.) and H_2O (15 ml.) was heated under reflux for 1.25 hr. The mixture was concentrated *in vacuo* and diluted with water. The separated solid was collected and dissolved in $CHCl_3$. The solution was filtered through a column of alumina (9.3 g.) and fractions eluted after 30 ml. of forerun was collected. Evaporation of the solvent and crystallization of the residue from acetone gave XVIII (0.24 g.) melting at 231~234°. Recrystallization furnished a pure sample, m.p. 232~234°, $[\alpha]_D$ +19.8°(c=1.51, dioxane). UV λ_{max} mμ (ε): 217~218 (4420). IR ν_{max} cm^{-1}: 3450, 3290, 1072, 1042 (OH); 1497, 1000 (furazan). *Anal.* Calcd. for $C_{19}H_{28}O_3N_2$: C, 68.64; H, 8.49; N, 8.43. Found: C, 68.62; H, 8.51; N, 8.71.

Acetylation with Ac_2O and pyridine at room temperature afforded the diacetate, which was crystallized from acetone, m.p. 189.5~190.5°, $[\alpha]_D$ +19.8°(c=1.15). *Anal.* Calcd. for $C_{23}H_{32}O_5N_2$: C, 66.32; H, 7.74; N, 6.73. Found: C, 66.05; H, 7.56; N, 6.83.

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