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Chemical Modifications of Androsta-1,4-diene-3,17-dione. I. The Synthesis of 2β- and 1α-Hydroxy Derivatives of 3β-Hydroxyandrosta-5,7-diene-3,17-dione 17-Ethylene Ketal[1]

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Using androsta-1,4,6-triene-3,17-dione 17-ethylene ketal as starting material, 2β- and 1α-monohydroxylated analogues of 3β-hydroxyandrosta-5,7-dien-3-one ethylene ketal have been prepared *via* (i) deconjugation of the 3-keto-4,6-diene to the 3-keto-5,7-diene, (ii) calcium borohydride reduction to the 3β-hydroxy derivative, (iii) selective epoxidation of the 1,2-double bond to the 1β,2β- and 1α,2α-epoxides and (iv) lithium aluminum hydride reduction of these epoxides to the title compounds.

Stereo-selectivities existed in these transformations are discussed.

In recent years numerous kinds of the modified steroids have been presented for the chemotherapeutic purpose. Androsta-1,4-diene-3,17-dione readily obtained from cholesterol by microbiological oxidation using *Arthrobacter simplex*[3] has suitable functions for the chemical modification at A, B, and D rings. Thus, the 1,4-dien-3-one system gives a clue for the modification of A and B rings, while the 17-keto group for the introduction of a substituent to and the modification of D ring. Furthermore, the former function can in general be introduced into cholesterol and the related steroids by the dehydrogenation with high potential quinones (*e.g.*, 2,3-dichloro-5,6-dicyanobenzoquinone).[4] Therefore, any method of conversion used for this steroid might be expected to be applicable to the other steroids.

As the first target in this series of work, the transformation of androsta-1,4-diene-3,17-dione to 2β-hydroxy and 1α-hydroxy derivatives of 3β-hydroxyandrosta-5,7-diene without affecting the 17-keto function was attempted. Since ergosterol has been converted to ecdysone,[5] the former product can be the direct intermediate for the synthesis of rubrosterone[6] and the method described herein might provide a new synthetic method for the insect moulting hormones from the related steroids. Furthermore, since recent studies indicate that vitamin D must be hydroxylated at 1α-position in the body before it produces its characteristic physiological effects,[7] 17-nor-17-ketovitamin D (the compound upon irradiation of the latter product)

1) This work was presented at the 94th Annual Meeting of the Pharmaceutical Society of Japan, Sendai, April 1974. Abstract of papers, p. 71.

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3) *a*) M. Nagasawa, M. Bae, G. Tamura, and K. Arima, *Agr. Biol. Chem.*, **33**, 1644 (1969); *b*) J. Ewart R.H., *Pure Appl. Chem.*, 33, 39 (1973).

4) A.B. Turner, *J. Chem. Soc.* (*C*), **1968**, 2568.

5) *a*) D.H.R. Barton, P.G. Feakins, J.P. Poyser, and P.G. Sammes, *J. Chem. Soc.* (*C*), **1970**, 1584; *b*) A. Furlenmeier, A. Furst, A. Langeman, G. Waldvogel, P. Hocks, U. Kerb, and R. Wiechert, *Helv. Chim. Acta*, **50**, 2387 (1967); *c*) For a review of existing syntheses, see D.H.S. Horn, in "Naturally Occurring Insecticides," ed. by M. Jacobson and D.G. Crosby, M. Dekker, Inc., New York, 1971.

6) *a*) H. Hikino, Y. Hikino, and T. Takemoto, *Tetrahedron Letters*, **1968**, 4255; *b*) P. Hocks, U. Kerb, R. Wiechert, A. Furlenmeier, and A. Furst, *Tetrahedron Letters*, **1968**, 4281; *c*) K. Shibata and H. Mori, *Chem. Pharm. Bull.* (Tokyo), **16**, 1404 (1968); *d*) A convenient procedure for the introduction of the 7-en-5-ol function into 7-dehydrocholesterol was described: L. Caglioti, G. Cainelli, and G. Maina, *Tetrahedron*, **19**, 1057 (1963).

7) *a*) M.F. Holick, H.K. Schnoes, H.F. DeLuca, T. Suda, and R.J. Cousins, *Biochemistry*, **10**, 2799 (1971); *b*) D.E.M. Lawson, D.R. Fraser, E. Kodicek, H.R. Morris, and D.H. Williams, *Nature*, **230**, 228 (1971).

seems to be an important compound both for its physiological test and as a synthetic precursor for the analogues of the active metabolites of vitamin D.

Very recently, two of the present authors and their collaborators have succeeded in the introduction of 5,7-diene function as well as 2β- or 1α-hydroxy function into cholesterol using cholesta-1,4,6-trien-3-one (Ib) as starting material.[8]

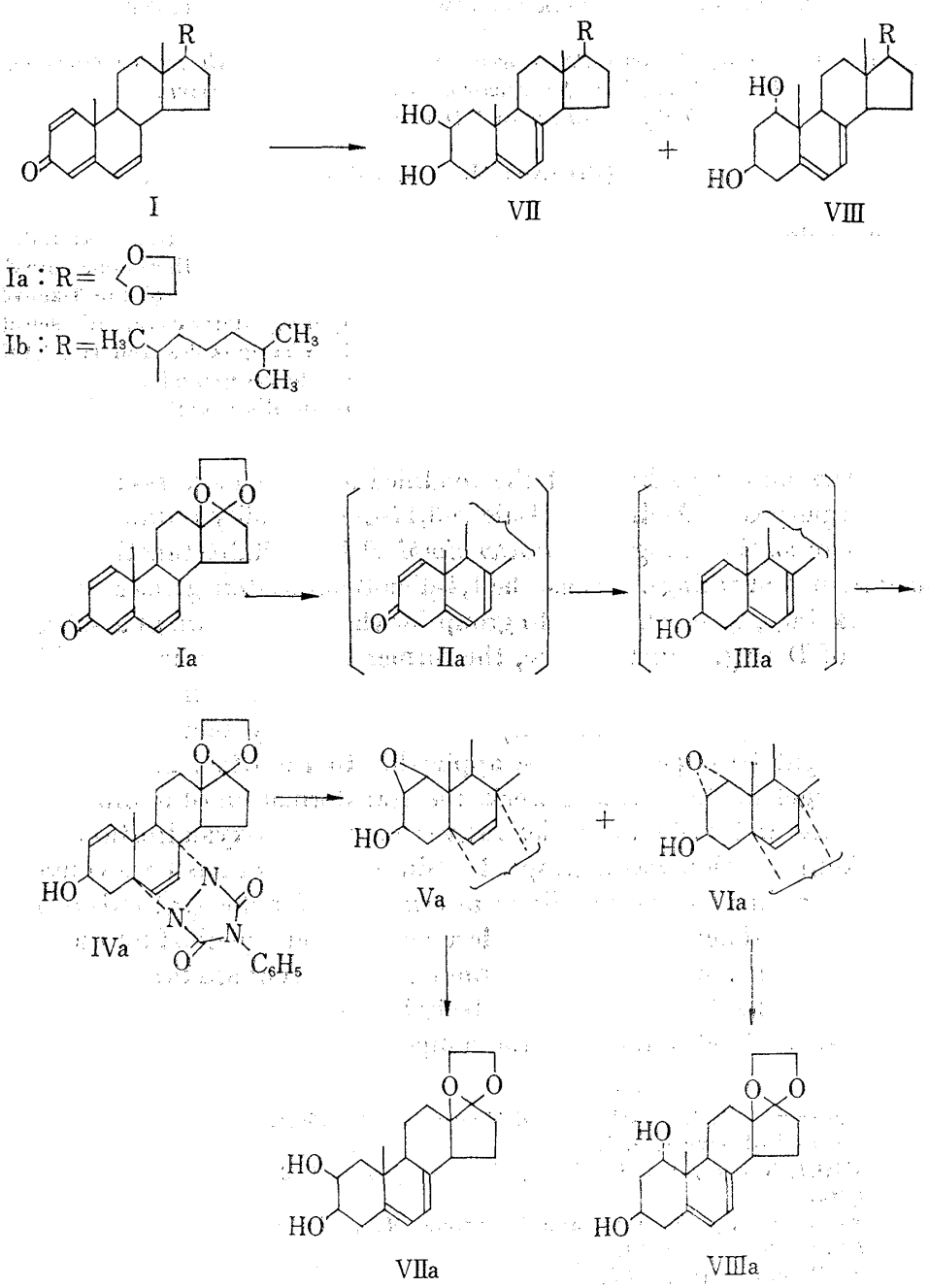


Chart 1

The reaction sequence leading to both 2β- and 1α-hydroxy derivatives (VIIb and VIIIb) of 7-dehydrocholesterol did not use any acidic condition in its steps which would hydrolyse a ketal function. Thus, it is expected that the method is especially fitted to the present trans-

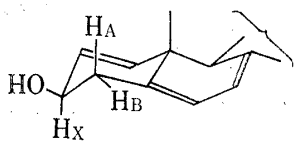
8) C. Kaneko, A. Sugimoto, Y. Eguchi, S. Yamada, M. Ishikawa, S. Sasaki, and T. Suda, *Tetrahedron*, **30**, 2701 (1974).

formation, since androsta-1,4-diene-3,17-dione can easily be converted to androsta-1,4,6-triene-3,17-dione 17-ethylene ketal (Ia) by the known method.[9,10]

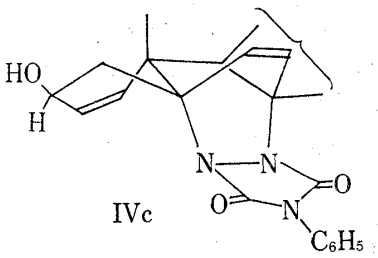
The preparation of 2β- or 1α-hydroxy derivatives (VIIa or VIIIa) of 3β-hydroxy-17,17-ethylenedioxyandrosta-5,7-diene was accomplished by five steps from Ia. However, since the conversion of Ia to IVa can be carried out without any purification of the intermediate compounds (IIa and IIIa), the actual steps needed to accomplish these transformations were three for each product (VIIa or VIIIa). The entire scheme for these transformations is shown in Chart 1. In this Chart, the compounds shown in the parenthesis are the ones whose purifications not only were unnecessary, but also caused the decrease in overall yields of the final products (VIIa and VIIIa).

Treatment of Ia with an excess of *t*-BuOK followed by a rapid addition into ice-water and extraction with benzene-ethyl acetate afforded an oily residue, whose ultraviolet (UV) spectrum showed maximum at 234 nm together with shoulder peaks at 265, 276, and 288 nm. The positions of these shoulder peaks were fitted well to those (268, 277, and 288 nm) of cholesta-1,5,7-trien-3-one (an unstable crystalline compound obtained from Ib under the same deconjugation reaction in the previous work).[8] However, all attempts for the direct isolation and purification of 17,17-ethylenedioxyandrosta-1,5,7-trien-3-one (IIa) have failed. Therefore, the direct reduction of the whole deconjugation product was attempted. Reduction with $NaBH_4$ under a variety of condition was examined, however, none of them gave a satisfactory result. We therefore employed calcium borohydride as the reducing reagent. The choice of this reagent was based on the following two reasons: (i) the instability of the 1,5,7-trien-3-one system obviously required near neutrality and low temperature in the reaction condition,[11] and (ii) this reagent afforded cholesta-1,5,7-trien-3β-ol (IIIa) in 80% yield from IIb.[8]

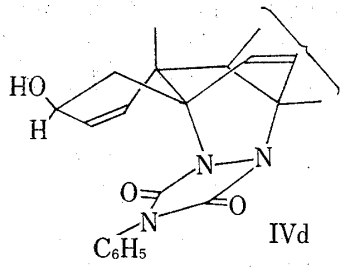
The reduction of the crude deconjugation product with this reagent in ethanol below $-10°$ resulted in the formation of the desired product (IIIa). If purification was carried out at this stage by the use of silica gel column chromatography, IIIa was obtained in *ca.* 15% yield from Ia. This compound (mp 144—146°) had typical homoannular diene absorptions (λ_{max}^{EtOH}: 260 (sh.), 270, 280, and 291 nm) and an acceptable mass spectrum (M^+ at 328). The nuclear magnetic resonance (NMR) spectrum showed one proton signal centered at 5.74τ consisted of approximately equal intensity assignable as X part of ABX system whose coupling constants being 10 (J_{AX}) and 6 Hz (J_{BX}), respectively. Since the signal assignable to both H_1 and H_2 appeared as a singlet (4.38τ as a broad singlet), the AB part of the system should be the two protons on C_4. From the reasonable assumption that rings A and B adopts conformation (IIIc), an axial-bond (α-configuration) of the H_3 of IIIa (H_x in the stereoformula IIIc) can be deduced.



IIIc



IVc (*endo*-addition product)



IVd (*exo*-addition product)

9) St. Kaufmann, J. Pataki, G. Rosenkranz, J. Romo, and C. Djerassi, *J. Am. Chem. Soc.*, **72**, 4531 (1950). See also T. Wolff and H. Dannenberg, *Chem. Ber.*, **103**, 917 (1970).
10) P. Wieland and G. Anner, *Helv. Chim. Acta*, **50**, 289 (1967).
11) M. Fieser and L. Fieser, "Reagents for Organic Synthesis," Vol. 2, Wiley-Interscience, New York 1969, p. 57 and references cited therein.

The trien-3β-ol (IIIa) reacted with 4-phenyl-1,2,4-triazoline-3,5-dione at room temperature to give only one kind of 1,4-addition product (mp 219—219.5°) in 85% yield. The NMR spectrum of this addition product (IVa) is quite complex. However, since the pattern and position of the two proton-signal at C_1 and C_2 of IVa (4.28τ as a broad singlet) are almost the same with those of IIIa, it is concluded that IVa is the ordinary endo-addition product, IVc (endo or exo is defined by relative relationship between the urazole and the newly formed double bond).[12] As can be understood by the stereo-formulae (IVc for endo-product and IVd for exo-product), the nearby existed 4-phenylurazole moiety may affect seriously the vinylic protons (H_1 and H_2) in the NMR spectrum. The endo-structure (IVc) is also in good accordance with the inertness of its 6,7-double bond to the following epoxidation reaction,[13] because the two faces of the double bond are sterically shielded; the β-face by the angular methyl group and the α-face by the urazole ring as illustrated in the stereo-structure (IVc).

More conveniently, the addition product (IVa) was obtained in the following way. Thus, the whole calcium borohydride reduction product obtained as above was treated with 4-phenyl-1,2,4-triazoline-3,5-dione (addition was continued until discharge of the red color terminated) and IVa was separated easily from the other reduction products by column chromatography on silica gel. Thus, the addition product (IVa) can be obtained without any purification of the intermediate compounds (IIa and IIIa) in the yield of 25% from Ia.

The addition product (IVa) was then treated with 2 mole equivalent of *m*-chloroperbenzoic acid in $CHCl_3$ at room temperature for 2 days and the epoxides (Va and VIa) were separated by chromatography on silica gel with benzene–ether.

The fraction more strongly adsorbed on silica gel was the 1α,2α-epoxide (VIa), mp 222—224°, whose yield was 20—25%. The other fraction (the less polar fraction) afforded the 1β,2β-epoxide (Va), mp 219.5—220.5° in the yield of 55—60%. Though the NMR spectra clearly show that both compounds are 1,2-epoxides, the exact stereochemistry of the epoxide function in each compound can not be determined by spectroscopic methods at this stage, except that if one product is the α-epoxide the other one must be the β-epoxide and *vice versa*. The structure determinations of these epoxides (Va and VIa) rest entirely upon the structures of their lithium aluminum hydride-reduction products (*vide infra*).

Lithium aluminum hydride reduction of these two epoxides (Va and VIa) in refluxed THF for 1 hr resulted in both the reproduction of the 5,7-diene function and the regio-selective fission of the epoxide ring in Va and VIa, respectively.[13] Thus, Va gave VIIa, mp 190—192°, in *ca.* 50% yield as a predominant product, while VIa afforded VIIIa, mp 192—198°, exclusively in *ca.* 40% yield.

Since in general the ring opening of an epoxide function by nucleophiles (including hydride ion) should give a product (at least in predominance) having both the hydroxyl group and the entering nucleophile in a diaxial-*trans*-relationship,[14] it is probable to expect that the β-epoxide (Va) should give 2β-hydroxy derivative, while the α-epoxide (VIa) give 1α-hydroxy derivative. The comparison of the C_{19}-methyl signals in the NMR spectra of these two hydroxy compounds (VIIa and VIIIa) revealed actually that the signal of VIIa appeared at 8.96τ whose position is lower than that (9.07τ) of VIIIa by 11 cps. This difference can be attributed to the 1,3-diaxial-*cis*-relationship between the 2β-hydroxy group and the angular methyl group in the former compound (VIIa).[15]

12) For Alder's endo rule, see: *a*) K. Alder and G. Stein, *Angew. Chem.*, **50**, 510 (1937); *b*) G. Desimoni, G. Colombo, P.P. Righetti, and G. Tacconi, *Tetrahedron*, **29**, 2635 (1973).

13) The inertness of the 6,7-double bond to the oxidation reaction in the related cyclo-adducts was also noted by the other research groups: *a*) D.H.R. Barton, T. Shioiri, and D.A. Widdowson, *J. Chem. Soc.* (*C*), **1971**, 1968; *b*) D.R. Crump, D.H. Williams, and B. Pelc, *J.C.S. Perkin I*, **1973**, 2731.

14) D.N. Kirk and M.P. Hartshorn, "Steroid Reaction Mechanisms," Elsevier Pub. Co., Amsterdam, 1968, p. 112.

15) N.S. Bhacca and D.H. Williams, "Applications of NMR spectroscopy in Organic Chemistry; Illustration from the Steroid Field," Holden-day, Inc., San Francisco, 1964, p. 13.

Table I. PMR Chemical Shifts (τ Values) and Coupling Constants (J c/s) of IIIa—VIIIa and the related Compounds[a]

Compound	H-1 and H-2	H-3	H-6 and H-7	C_6H_5	CH_3	C-17 substituent	Other signals
IIIa	4.38 (2H) (br. s)	5.74 (d.d, J=10 and 6)	4.20—4.70 (2H, m)		9.03 (3H, s) 9.23 (3H, s)	6.13 (4H) (br. s)	
IVa	4.28 (2H) (br. s)	6.60 (1H)[b] (d.d, J=15 and 8)	3.54 (1H, d) 3.74 (1H, d) [J=8]	2.64 (5H, m)	8.90 (3H, s) 9.02 (3H, s)	6.10 (4H) (br. s)	4.96 (1H)[b] (t, J=6)
Va	6.48 (1H) (t, J=4) 6.82 (1H) (d, J=4)	6.96 (1H)[b] (m)	3.62 (1H, d) 3.84 (1H, d) [J=8]	2.68 (5H, m)	9.00 (3H, s) 9.08 (3H, s)	6.12 (4H) (m)	5.04 (1H)[b] (m)
VIa	6.76 (2H) (s) or 6.78 (2H) (m)	6.78 (2H)[b] (m) or 6.76 (2H)[b] (s)	3.54 (1H, d) 3.80 (1H, m) [J=8]	2.65 (5H, m)	8.80 (3H, s) 8.98 (3H, s)	6.10 (4H) (m)	4.98 (1H)[b] (t, J=8)
VIIa	6.38 (1H) (m, $W_{1/2}$ =8)	6.04—6.36 (1H) (m, $W_{1/2}$ =18)	4.40 (1H) (d) 4.75 (1H) (m) [J=6]		8.96 (3H, s) 9.22 (3H, s)	6.12 (4H) (br. s)	
2-OH-7-dehydrocholesterol (VIIb)	6.10—6.60 (2H, m)		4.40 (1H) (d) 4.70 (1H) (d) [J=6]				
VIIIa	6.28 (1H) (m, $W_{1/2}$ =8)	5.80—6.15 (1H) (m, $W_{1/2}$ =25)	4.30 (1H) (d) 4.66 (1H) (d) [J=6]		9.07 (3H, s) 9.22 (3H, s)	6.12 (4H) (br. s)	
1-OH-7-dehydrocholesterol (VIIIb)	6.30 (1H) (m, $W_{1/2}$ =8)	6.05 (1H) (m, $W_{1/2}$ =25)	4.36 (1H) (d) 4.66 (1H) (d) [J=6]				

a) The spectra were recorded in $CDCl_3$. TMS was used as an internal standard.
b) The assignments of these signals are tentative.

Finally, the structures of these dihydroxy compounds (VIIa and VIIIa) were determined unequivocally by the comparison of their NMR spectra with those of the corresponding 7-dehydrocholesterols whose structures were determined in our previous work.[8,16] The NMR spectra of these and some related compounds are listed in the Table.

The lithium aluminum hydride reduction step corresponds to the final step in the present synthesis and also demonstrates the correctness of the stereo-structures of the two epoxides (Va and VIa). Substantial formation of the α-epoxide (VIa) upon the peroxide oxidation of IVa seems to indicate that there exists some interaction between the reacting peracid and the lone pair of nitrogen atom in the urazole ring with a relative lowering of the energy of the

16) C. Kaneko, S. Yamada, A. Sugimoto, Y. Eguchi, M. Ishikawa, T. Suda, M. Suzuki, S. Kakuta, and S. Sasaki, *Steroids*, **23**, 75 (1974).

α-face-epoxidation transition state,[17] since *cis*-epoxidation is usually observed in the epoxidation of allylic alcohols.[18]

Concomitant introduction of 2β-hydroxy and 5,7-diene functions into the 17,17-ethylenedioxy-androstane skeleton is thus achieved in *ca.* 7.5% overall yield from Ia with essentially three steps (Ia→IVa→Va→VIIa) without affecting the 17-ethylene ketal function. In these conversions, only the second step is non-stereoselective to give VIa whose relative yield-ratio to Va is 1/3—1/2. This minor product affords VIIIa upon reduction by $LiAlH_4$. The overall yield of VIIIa from Ia is *ca.* 2.5%.

Though the overall yields of the final products are not satisfactory, the shortness of the required steps in this method would overcome this disadvantage. Furthermore, it should be noted that the present method can be applied to the related compounds having a labile function especially to an acidic condition as exemplified by the 17,17-ethylenedioxy function, because this method uses neither acidic nor pyrolytic condition in any of its steps.

The further transformation of VIIa and VIIIa to rubrosterone and 17-nor-17-ketovitamin D are under current investigation.

Experimental

All melting points were determined in capillary tube and are uncorrected. The infrared spectra were recorded in KBr pellets on DS-403G JASCO and IR-S JASCO spectrometers. The UV absorption spectra were determined on a Hitachi Model-323 spectrometer in 95% EtOH. The NMR spectra were obtained using either a C-60 JEOL (60 Mcps) or JNM PS-100 (100 Mcps) spectrometer and the chemical shifts are given in τ-units (see Table). Mass spectra were recorded on a Hitachi Model RMU-7M double focus mass spectrometer using all cases a direct sample insertion into the ion source. Optical rotations were measured in dioxane by Yanagimoto Model OR-10 direct reading polarimeter or by JASCO ORD/UV-5 spectrometer.

Purification of the Solvents used in the Deconjugation Reaction——*t*-Butanol was dried with $MgSO_4$, filtered and distilled: bp 82.5°. Dimethyl sulphoxide was dried with CaH_2, filtered and distilled under reduced pressure: bp 86°/18 mm.

Preparation of 3β-Hydroxy-17,17-ethylenedioxyandrosta-1,5,7-triene (IIIa)——To the solution of 17,17-ethylenedioxyandrosta-1,4,6-trien-3-one (Ia) (10 g) in 100 ml of DMSO (distilled before use) was added finely powdered *t*-BuOK (prepared from 5 g of potassium) and the solution was stirred for 14 min at 15°. The whole process was carried out under argone atmosphere. The reaction mixture was poured into ice-water containing *ca.* 1.2 mole equivalent (to the potassium used) of acetic acid and extracted rapidly with benzene–ethyl acetate mixture (1: 2 v/v). The organic layer was washed with ice-water several times. After dried over Na_2SO_4 and evaporation of the solvent under reduced pressure below 35°, 9.5 g of residue was obtained.

To a finely powdered $CaCl_2$ (7.5 g) in 230 ml of methanol was added 3.7 g of $NaBH_4$ dissolved in 300 ml of ethanol under stirring at 0°. After the addition was completed, the solution was cooled below −10°. To this solution, the crude deconjugation product obtained as above in 120 ml of THF was added slowly under stirring between −10— −15° and the whole was stirred for 3 hr at the same temperature and then for 1 hr under ice-cooling. The excess of $Ca(BH_4)_2$ was decomposed by adding 100 ml of 50% aqueous acetone and the whole was kept stirring at room temperature overnight. The solution was concentrated *in vacuo* at about 50 ml. The concentrated reaction mixture was poured into water and inorganic materials were dissolved by addition of acetic acid. Extraction with CH_2Cl_2, washing with water several times and drying over $MgSO_4$ afforded 9.4 g of the residue. The residue was chromatographed over silica gel. From the fraction eluted with benzene–CH_2Cl_2 (9: 1 v/v), 2.0 g of semi-crystalline product was obtained. Recrystallization of this product from ether–hexane afforded 1.55 g of 3β-hydroxy-17,17-ethylenedioxyandrosta-1,5,7-triene (IIIa), mp 144—146°. IR cm^{-1}: 3400, 1620. UV nm(ε): 260, 270, 280 (13000), 291. $[\alpha]_D$: −135°. Mass Spectrum *m/e*: 328 (M^+). *Anal.* Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.56; H, 8.55.

Preparation of the 1,4-Adduct (IVa) of 3β-Hydroxy-17,17-ethylenedioxyandrosta-1,5,7-triene with 4-Phenyl-1,2,4-triazoline-3,5-dione from 3β-Hydroxy-17,17-ethylenedioxyandrosta-1,5,7-triene (IIIa)——To the solution of IIIa (500 mg) in 20 ml of distilled tetrahydrofuran (THF) was added under stirring 4-phenyl-1,2,4-triazoline-3,5-dione (freshly sublimed before use) in a small portion (270 mg) until discharge of the red

17) We thank Dr. T. Shibata, Pharmaceutical Laboratory of Keio-gijuku University, for valuable discussions concerning this point.

18) Ref. 14, p. 74.

color terminated. After stirring for 1 hr at room temperature, solvent was evaporated and the residue (770 mg) was recrystallized from acetone–ether to give 640 mg of IVa, mp 219—219.5°. IR cm^{-1}: 3410, 3200, 1750, 1687. UV nm(ε): 259 (3400). $[\alpha]_D$: 0°. Mass Spectrum *m/e*: 328 (parent peak). *Anal.* Calcd. for $C_{29}H_{33}O_5N_3$: C, 69.16; H, 6.60; N, 8.34. Found: C, 68.54; H, 6.56; N, 8.33.

Direct Preparation of the 1,4-Adduct (IVa) from 17,17-Ethylenedioxyandrosta-1,4,6-trien-3-one (Ia)——To the solution of Ia (6 g) in dimethylsulfoxide (DMSO) (60 ml) was added finely powdered *t*-BuOK (prepared from 3 g of potassium) and the solution was stirred for 14 min at 15° under argon atmosphere. The reaction mixture was poured into ice-water containing acetic acid. After extraction followed by $Ca(BH_4)_2$ reduction described as above, the crude fraction of IIIa was obtained, which without purification was used for the subsequent addition reaction. Thus, the residue was dissolved in 200 ml of THF and to this solution was added 4-phenyl-1,2,4-triazoline-3,5-dione under stirring until discharge of the red color terminated. After stirring for 1 hr at room temperature, the solvent was evaporated and the residue (6.5 g) was chromatographed on silica gel. Elution with benzene–ether (8: 2 v/v) gave 2.25 g of IVa, which was sufficiently pure for subsequent reaction. Recrystallization from acetone–ether afforded the analytically pure IVa as colorless needles, mp 219—219.5°. The mixed melting point determination with the sample obtained as above assured their identity.

Epoxidation of the 1,4-Cyclo-adduct (IVa) with *m*-Chloroperbenzoic Acid——To the solution of IVa (1.29 g) in 80 ml of $CHCl_3$ was added under stirring 1.02 g of *m*-chloroperbenzoic acid and the whole was stirred at room temperature for 40 hr. The reaction mixture was poured into 10% aqueous potassium carbonate and extracted with $CHCl_3$. The organic layer was separated, washed with water and dried over $MgSO_4$. Evaporation of the solvent gave 1.48 g of the residue, which was chromatographed over silica gel. Elution with benzene–ether (88: 12—84: 16 v/v) gave the crystaline fraction (917 mg) which after recrystallization from acetone–hexane afforded the 1β,2β-epoxide (Va) (820 mg), mp 219.5—220.5°. IR cm^{-1}: 3480, 1744, 1680. UV nm(ε): 259 (4000). $[\alpha]_D$: −50°. Mass Spectrum *m/e*: 344 (parent peak). *Anal.* Calcd. for $C_{29}H_{33}O_6N_3$: C, 67.03; H, 6.40; N, 8.09. Found: C, 66.70; H, 6.17; N, 8.14.

Elution with benzene–ether (82: 18 v/v) gave the crude 1,2-epoxide fraction (352 mg). Recrystallization from acetone–hexane gave pure 1α,2α-epoxide (VIa) (245 mg), mp 222—224°. IR cm^{-1}: 3440, 1745, 1680. UV nm(ε): 255 (3000). $[\alpha]_D$: −50°. Mass Spectrum *m/e*: 344 (parent peak). *Anal.* Calcd. for $C_{29}H_{33}O_6N_3$: C, 67.03; H, 6.40; N, 8.09. Found: C, 66.51; H, 6.44; N, 8.11.

Preparation of 2β,3β-Dihydroxy-17,17-ethylenedioxyandrosta-5,7-diene (VIIa)——The solution of the 1β,2β-epoxide (Va) (400 mg) in 80 ml of THF was added to the solution of $LiAlH_4$ (480 mg) in 160 ml of THF under stirring and the whole was refluxed for 90 min. After cooling, the excess of the reagent was decomposed by adding aqueous sodium sulfate and the solution was dried over Na_2SO_4. Evaporation of the solvent afforded 377 mg of the crude diol, which was chromatographed over silica gel. Elution with 2% methanol–$CHCl_3$ (v/v) gave 230 mg of fraction which after recrystallization from acetone–hexane gave pure 2β,3β-dihydroxy-17,17-ethylenedioxyandrosta-5,7-diene (VIIa) (175 mg), mp 190—192°. IR cm^{-1}: 3490, 3300. UV nm(ε): 263, 272, 282.5 (10100), 294.5. $[\alpha]_D$: 0°. Mass Spectrum *m/e*: 346 (M^+). *Anal.* Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.67; H, 8.97.

Preparation of 1α,3β-Dihydroxy-17,17-ethylenedioxyandrosta-5,7-diene (VIIIa)——The solution of the 1α,2α-epoxide (VIa) (200 mg) in THF (40 ml) was added to the solution of $LiAlH_4$ (240 mg) in 80 ml of THF under stirring and the whole was refluxed for 90 min. After cooling, the excess of the reagent was decomposed by adding aqueous sodium sulfate and the solution was dried over anhydrous sodium sulfate. Evaporation of the solvent afforded 200 mg of the residue which was then chromatographed over silica gel. The fractions eluted from 2% methanol–$CHCl_3$ (v/v) were collected (101 mg) and recrystallized from acetone–hexane to give 60 mg of VIIIa, mp 192—198°. IR cm^{-1}: 3410. UV nm(ε): 262, 270, 281 (11000), 293. $[\alpha]_D$: −141°. Mass Spectrum *m/e*: 346 (M^+). *Anal.* Calcd. for $C_{21}H_{30}O_4$: C, 72.80; H, 8.73. Found: C, 72.39; H, 8.77.

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