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25. Kikuo Yasuda and Hiromu Mori: Synthesis of Some 3,5-Diene-2,7-dioxosteroids.

(*Research Laboratory, Teikoku Hormone Mfg. Co., Ltd.*[*1])

tert-Butyl chromate oxidation of some steroidal 3,5-dienes was examined. The oxidation proceeded first at C-7 and then at C-2 irrespective of what substituent was at C-3. Thus some 3,5-diene-2,7-diones were obtained by reoxidation of 3,5-dien-7-one. 1,6-Addition of methylmagnesium iodide to 17β-acetoxyandrosta-3,5-dien-7-one afforded 17β-hydroxy-3α-methylandrost-4-en-7-one, which was converted to 17β-acetoxy-3α-methylandrost-5-en-7-one by treatment with acetic acid and concentrated hydrochloric acid. Similarly 17β-acetoxy-3,3-dimethylandrost-5-en-7-one was obtained from 17β-acetoxy-3-methylandrosta-3,5-dien-7-one.

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It was reported[1] from this laboratory that oxidation of 3,5-dien-3-ol acetates with *tert*-butyl chromate gave the corresponding 7-oxo-derivatives. Further study on the oxidation of some 3,5-dienes is described in the present paper.

Androsta-3,5-dien-17β-ol acetate (Ia)[2] was treated with *tert*-butyl chromate[3] in carbon tetrachloride in the presence of acetic anhydride for 7 hours under reflux to give 17β-acetoxyandrosta-3,5-dien-7-one (IIa),[4] which was identical with an authentic sample prepared from 3β,17β-diacetoxyandrost-5-en-7-one (VII)[3] by the method of Marshall and his co-workers.[5] Further oxidation of IIa with the same reagent by 20 hours reflux gave 17β-acetoxyandrosta-3,5-diene-2,7-dione (IIIa). IIIa was also obtained by the following reaction sequence: sodium borohydride reduction of IIa followed by acetylation to 3,5-dien-7β,17β-diol diacetate (IV), *tert*-butyl chromate oxidation of IV to the corresponding 2-one (V), hydrolysis of V with alkali to the 7β,17β-diol (VI), and partial oxidation of VI with manganese dioxide in chloroform for 10 hours at room temperature followed by acetylation to IIIa. These observations indicate that the newly introduced carbonyl group of IIIa obtained by one step from IIa is located in C-2. The 3,5-dieno-structure of IV and the 3,5-dien-2-oxo-strutcure of V were confirmed by their ultraviolet and infrared spectra. The assignment of the configuration of the 7-acetoxy groups in IV and V was based upon the following evidences mainly from the nuclear magnetic resonance spectral data and partly from the molecular rotation differences. The nuclear magnetic resonance spectra of Ia, IIa, IIIa, IV and V were measured in deuteriochloroform and their data are summarized in Table I. i) The coupling constant between 7- and the adjacent 8β-proton in V was found to be 8.5 c.p.s. Such a large value should be observed, when the dihedral angle between two protons in question is near 0° or 180°. Therefore, the orientation of 7-proton in V should be considered as axial in relation to the axial one of the adjacent 8β-proton. Accordingly, the configuration of the 7-acetoxy group in V must be β (equatorial). Rufer and his co-workers[6] have recently reported that no coupling between 7β- and 8β-proton is observed in the nuclear magnetic resonance spectrum of 7α-bromocholest-5-ene-3β,4β-

*1 1604, Shimosakunobe, Kawasaki (安田喜久男, 森 弘).

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2) L. H. Knox, V. S. Berger, D. Cuadriello, P. W. Landis, A. D. Cross: J. Am. Chem. Soc., **85**, 1851 (1963).
3) K. Heusler, A. Wettstein: Helv. Chim. Acta, **35**, 289 (1952).
4) A. Butenandt, E. Hausmann, J. Paland: Ber., **71**, 1316 (1938).
5) C. W. Marshall, R. E. Ray, I. Laos, B. Riegel: J. Am. Chem. Soc., **79**, 6308 (1957).
6) C. Rufer, H. Hoffmeister, H. Schairer, M. Traut: Chem. Ber., **98**, 2383 (1965).

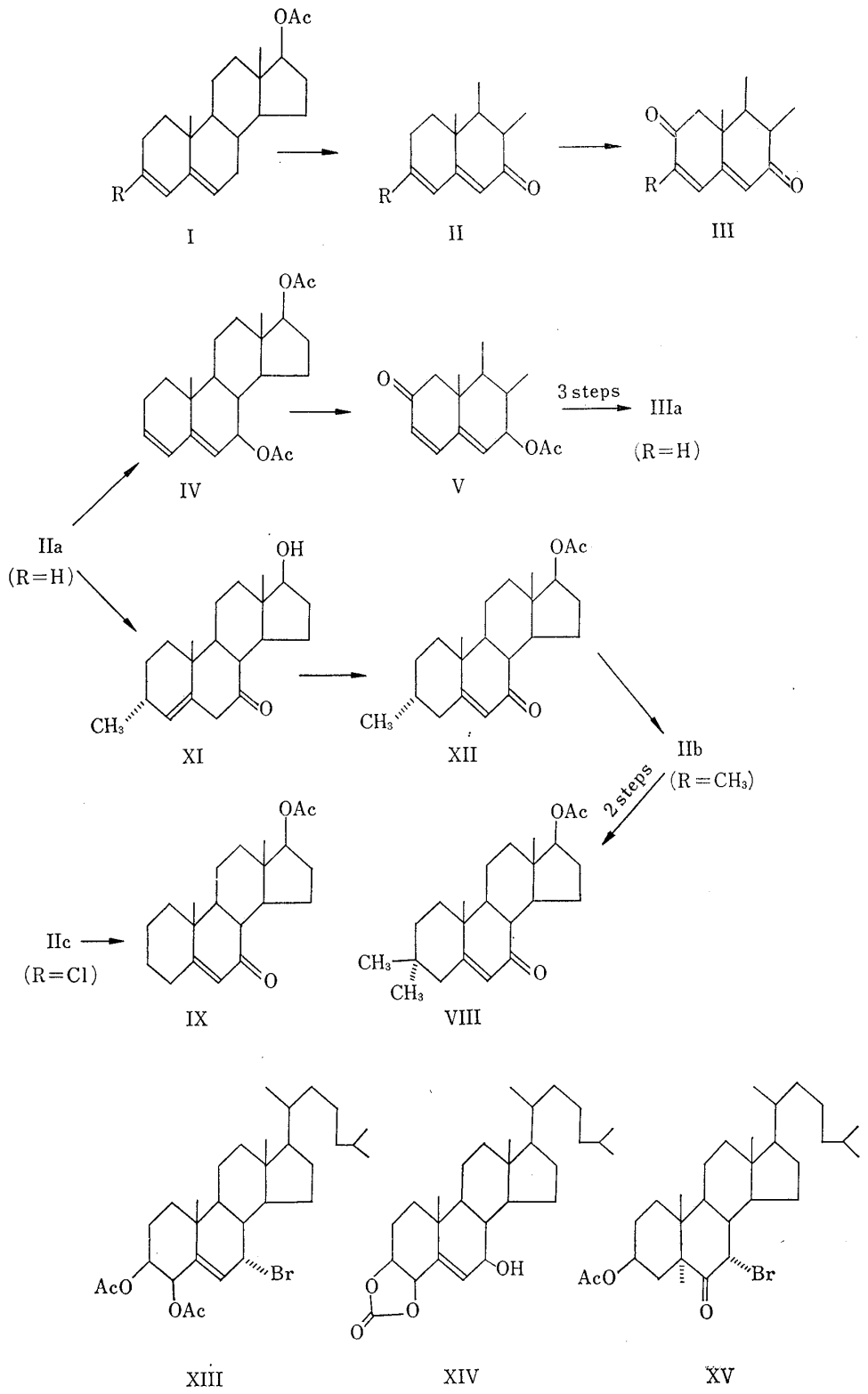


Chart 1.

diol diacetate (XIII), while a large coupling constant between 7α- and 8β-proton is observed in the case of cholest-5-ene-3β,4β,7β-triol 3,4-carbonate (XIV). In addition, no coupling between 7β- and 8β-proton was observed in the spectrum of the known compound, 3β-acetoxy-7α-bromo-5α-cholestan-6-one (XV)[7] (the data is shown in experimental). These observations also support our conclusion. When theoretically

TABLE I. Nuclear Magnetic Resonance Spectral Data[a] of 3,5-Dienes

Compound	13β-CH_3	10β-CH_3	17β-OAc	7β-OAc	3-H	4-H	6-H	7-H
Ia	0.83	0.98	2.05		5.65 5.86 6.03 (m) (m) (m)		5.40 (m)	
IV	0.87	1.04	2.03	2.03	5.80 (m)	5.80 (m)	5.25 (d) J=3.1	5.15 (q?) J=3.1(6H:7H) J=8.6(7H:8H)
V	0.87	1.18	2.04	2.06	5.92 (AB q) J=10.3	6.85	5.80 (d) J=2.6	5.22 (q) J=2.6(6H:7H) J=8.5(7H:8H)
IIa	0.87	1.15	2.05		6.15 (m)	6.15 (m)	5.63 (s)	
IIIa	0.87	1.30	2.06		6.20 (AB q) J=9.4	7.05	6.02 (s)	

a) The spectra were obtained at 60 Mc.p.s., on a Hitachi H-60 spectrometer, in $CDCl_3$ containing $(CH_3)_4Si$ as an internal standard. Chemical shifts are quoted as p.p.m. downfield from $(CH_3)_4Si$ (0.00 p.p.m.). Coupling constants J are given in c.p.s.
Abbreviations used are s=singlet, d=doublet, q=quartet and m=multiplet.

derived Karplus' equation[8] is applied to the case of V, the calculated values of the coupling constants are 6.76 (7β:8β) and 8.17 c.p.s. (7α:8β), respectively, on the basis of the dihedral angles (54° (7β-H); 174° (7α-H)) measured by the Dreiding-model. Although the calculation*2 directs us to the same conclusion, it should be also noted that the observed coupling constants between 7β- and 8β-proton in XIII and XV (0 c.p.s.) are very different from the values expectable from the equation. The signal of 7α-proton in IV did not show such a clear pattern as in V because of overlapping with that of 6-vinylic proton, but the coupling constant under consideration appeared approximately as 8.6 c.p.s., supporting also the β-orientation of the 7-acetoxy group. ii) It has been reported[9] that the introduction of 7β-acetoxy group causes low-field shift (0.042 p.p.m.) of both 18- and 19-methyl group, while no shift is observed by the introduction of 7α-acetoxy group. The low-field shifts of the signals of 18- (0.04 p.p.m.) and 19-methyl group (0.06 p.p.m.) in IV due to the 7-acetoxy group are apparent from comparison of the data of Ia and IV. Although the shifts are too small to infer the configuration only from this observation, the β-orientation of the 7-acetoxy group in IV seems to be more likely. Comparison of IIa and IIIa informs that the shift of 19-methyl group in IIIa due to the 2-carbonyl group is 0.15 p.p.m. Supposing this value is applicable to the case of V, both the shifts of its angular methyl groups due to the 7-acetoxy group can be defined as 0.04 (18-methyl) and 0.05 p.p.m. (19-methyl). This result also prefers the 7β-substitution. iii) As pointed out early in the exploring time,[10,11a] the molecular rotation difference between cholesteryl acetate and its

*2 The earlier equation (M. Karplus : J. Chem. Phys., **30**, 11 (1959)) are also well consistent with the found (the calculated values : 5.28 snd 9.26).

7) *a*) I. M. Heilbron, E. R. H. Jones, E. S. Spring : J. Chem. Soc., **1937**, 801. *b*) E. J. Corey : J. Am. Chem. Soc., **76**, 175 (1954). *c*) E. J. Corey, R. A. Sneen : *Ibid.*, **78**, 6269 (1956).
8) M. Karplus : *Ibid.*, **85**, 2870 (1963).
9) Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, K. Tsuda : This Bulletin, **10**, 338 (1962).
10) *a*) A. E. Bide, H. B. Henbest, E. R. H. Jones, P. A. Wilkinson : J. Chem. Soc., **1948**, 1788 (as inferred by the authors, the assignment of the 7-ols in the lit. should be reversed). *b*) H. J. Ringold, G. Rosenkranz, C. Djerassi : J. Am. Chem. Soc., **74**, 3318 (1952).
11) *a*) L. F. Fieser, M. Fieser : "Steroids," 154～157 (1959). Reinhold Publishing Corp., New York. Maruzen Asian Edition, Maruzen Co., Ltd., Tokyo. *b*) *Ibid.*, 268～271. *c*) *Ibid.*, 18～21.

7-hydroxy derivative or the ester is very characteristic of the configuration of the substituent at C-7, that is, the molecular rotation differences due to the 7α- and 7β-substituent are negative and positive, respectively. In analogy to this relationship, the molecular rotation difference between Ia and Ⅳ as shown in Table Ⅱ serves to deny the α-orientation of the 7-acetoxy group in Ⅳ. Thus the β-orientation of the 7-acetoxy groups of Ⅳ and Ⅴ was adopted, though we failed to obtain their 7α-isomers to be compared. This conclusion is also favorably consistent with the known behavior of metal hydride reduction.[11a)]

The similar oxidation of 3-methylandrosta-3,5-dien-17β-ol acetate (Ib)[12)] and 3-chloroandrosta-3,5-dien-17β-ol acetate (Ic)[13)] gave the corresponding 7-ones, Ⅱb and Ⅱc, respectively. Ic was prepared in good yield from testosterone acetate by the method of Westphal and his co-workers.[14)] Structural assignment of Ⅱ was achieved as follows. i) 1.6-Addition of methylmagnesium iodide[15)] to Ⅱb in the presence of cupric acetate[16)] followed by acetylation afforded 17β-acetoxy-3,3-dimethylandrost-5-en-7-one (Ⅷ). Its ultraviolet and infrared spectra showed the presence of an α,β-unsaturated ketone and its nuclear magnetic resonance spectrum showed no vinylic methyl group but additional two tertiary ones. In case that the oxidation of Ib occurred first at C-2, the product expectable from such a Grignard reaction must be a 3,6- or 3,4-dimethyl derivative with which the result is incompatible. Thus the other possible structure, 17β-acetoxy-3-methylandrosta-3,5-dien-2-one, was excluded. ii) Ⅱc was readily hydrogenated on palladium black in ethanol to the known 17β-acetoxyandrost-5-en-7-one (Ⅸ).[17)] This result allowed to deny the other possible structure, 17β-acetoxy-3-chloroandrosta-3,5-dien-2-one (X). Fortunately, in the recent work[18)] there has been prepared the compound X, whose physical constants are evidently different from those of Ⅱc.

As the other route to structural assignment of Ⅱb, 1,6-addition of methylmagnesium iodide to Ⅱa was also performed. It gave 17β-hydroxy-3α-methylandrost-4-en-7-one (Ⅺ), which was treated with acetic acid and concentrated hydrochloric acid to afford 17β-acetoxy-3α-methylandrost-5-en-7-one (Ⅻ). Dehydrogenation of Ⅻ by chloranil in *tert*-buthanol[15)] afforded Ⅱb in very low yield. These observations are sufficient for structural proof of Ⅱb. The 4-en- and 5-en-7-oxo-structure of Ⅺ and Ⅻ were readily concluded by their ultraviolet and infrared spectra. The α-orientation of the 3-methyl groups of Ⅺ and Ⅻ depended upon analogy to the relationship between 7α,17α- and 7β,17α-dimethyltestosterone.[15)]

Further oxidation of Ⅱb and Ⅱc as well as Ⅱa gave the corresponding 2,7-diones, Ⅲb and Ⅲc, respectively. Structural assignment of Ⅲb and Ⅲc was based upon analogy to Ⅲa.

The yields of Ⅱ from Ⅰ by *tert*-butyl chromate oxidation were around 30% (Ⅱa: 23%, Ⅱb: 26%, Ⅱc: 42%) and it was shown from the ultraviolet and infrared spectra that each mother liquor contained mainly the starting material with only a small amount of the 2-oxo-compound. From these observations it is evident that *tert*-butyl chromate oxidation of the 3,5-dienes (Ⅰ) afforded first the corresponding 7-ones (Ⅱ) and then 2,7-diones (Ⅲ) irrespective of what substituent was at C-3. The ultraviolet

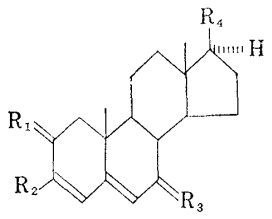
12) B. Pelc : Collection Czechoslov. Chem. Commun., **25** 1624 (1960).
13) R. Deghuenghi, R. Gaudy : Can. J. Chem., **40**, 818 (1962).
14) U. Westphal, Y. L. Wang, H. Hellmann : Ber., **72B**, 1233 (1939).
15) J. A. Campbell, J. C. Babcock : J. Am. Chem. Soc., **81**, 4069 (1959).
16) A. J. Birch, M. Smith : Proc. Chem. Soc., **1962**, 356.
17) *a*) S. Kuwada, K. Tsuchihashi : Yakugaku Zasshi, **59**, 352 (1939). *b*) R. E. Marker, E. L. Wittle, B. F. Tullar : J. Am. Chem. Soc., **62**, 223 (1940).
18) G. W. Moersch, T. P. Culbertson, D. F. Morrow. E. L. Wittle, R. R. Humphrey, W. A. Neuklis, M. E. Butler, M. M. Creger : J. Med. Chem., **7**, 741 (1964).

Table II. Molecular Rotations of Androsta-3,5-diene-7β,17β-diol Diacetate (IV) and Its Related Compounds

Compound	7-Substituent	M_D	Difference
Cholesteryl acetate		−184[a]	0
	7β-OAc	+263[a]	+447
	7α-OAc	−852[a]	−668
Androsta-3,5-dien-17β-ol acetate (Ia)		−522[b]	0
IV	7β-OAc	+ 37	+559

a) The value is calculated by "Constantes Selectiones, Pouvoir Rotatoire Naturel. I. Steroides." (by J.-P. Mathieu, A. Petit; Masson et Cie, Paris (1956)).
b) The value is calculated by our experimental data of Ia (m.p. 132~133.5°, $[\alpha]_D^{20}$ −166° (c=0.97, $CHCl_3$). UV λ_{max}^{MeOH} mμ (ε): 228 (17,200), 235.5 (18,300), 244 (11,800). In the lit., m.p. 126~127°, $[\alpha]_D$ −173° ($CHCl_3$);[2] m.p. 128°, $[\alpha]_D$ −155° ($CHCl_3$).[c]
c) G. Rosenkranz, S. Kaufmann, J. Romo: J. Am. Chem. Soc., **71**, 3689 (1949).

Table III. Ultraviolet Spectra of 3,5-Diene-2,7-diones (III) and Their Related Compounds

Compound		Substituent				λ_{max} mμ (Solvent)	
		R_1	R_2	R_3	R_4	Calcd.	Found
	IIa	H_2	H	=O	OAc	280	280 (MeOH)
	IIb	〃	CH_3	〃	〃	298	292~293 (〃)
	IIc	〃	Cl	〃	〃		284~285 (〃)
		=O	H	H_2	C_8H_{17}	286	290[a] (EtOH)
	X	〃	Cl	〃	OAc	301	306[18] (b)
	IIIa	〃	H	=O	〃	286	286 (MeOH)
	IIIb	〃	CH_3	〃	〃	296	296 (〃)
	IIIc	〃	Cl	〃	〃	301	299 (〃)

a) B.R. Davis, T.G. Halsall: J. Chem. Soc., **1962**, 1833.
b) Solvent is not stated in the lit.

spectra of the 3,5-diene-2,7-diones (III) and their related compounds are listed in Table III. Fieser and Fieser[11c] regarded the chromophores of cholest-4-ene-3,6-dione, -8-ene-7,11-dione and -8(14)-ene-7,15-dione as a kind of cross conjugation to calculate their absorption maxima by a more powerful chromophore with no increment for the second carbonyl function. Analogously, the calculated values of III based upon the 3,5-dien-7-oxo-system with no accounting for the 2-oxo-function are well consistent with the values found.

Experimental*3

17β-Acetoxyandrosta-3,5-dien-7-one (IIa)——A solution of androsta-3,5-dien-17β-ol acetate (Ia)[2] (900 mg.) in CCl_4 (27 ml.) was refluxed with *tert*-butyl chromate solution in CCl_4[3] (9 ml.) and Ac_2O (0.9 ml.) for 7 hrs. Excess of the reagent was decomposed by addition of oxalic acid (4.5 g.) and hot water. After stirring 1 hr., the whole was extracted with CH_2Cl_2. The organic layer was washed with water, 4% NaOH and water, dried over Na_2SO_4 and evaporated to dryness. Recrystallization of the residue from acetone gave IIa (220 mg., m.p. 200~215°). Two recrystallizations from the same solvent afforded an analytical sample as colorless needles, m.p. 220~223°, which was identical with an authentic sample prepared from 3β,17β-diacetoxyandrost-5-en-7-one (VII)[3] by the method of Marshall and his co-workers.[5]

The IR spectra of the mother liquors showed the presence of a small amount of the 2,7-dione (IIIa).

17β-Acetoxyandrosta-3,5-diene-2,7-dione (IIIa)——a) By one step from IIa. A solution of IIa (5 g.) in CCl_4 (150 ml.) was refluxed with *tert*-butyl chromate solution in CCl_4[3] (50 ml.) and Ac_2O (5 ml.) for 10 hrs. Successively, CCl_4 (150 ml.), *tert*-butyl chromate solution (50 ml.) and Ac_2O (5 ml.) were added to the reaction

*3 Melting points are uncorrected. Rotations were measured in $CHCl_3$ at 20°, UV spectra in MeOH, IR spectra as KBr-disk, and NMR spectra (ref. Table I) at 60 Mc.p.s. in $CDCl_3$ containing $(CH_3)_4Si$ as an internal standard.

mixture for additional 10 hrs reflux. Then the whole was treated similarly as described above. Recrystallization from acetone gave the crude IIIa (1.1 g., m.p. 245~255°). Several recrystallization from the same solvent afforded an analytical sample as yellow needles, m.p. 265~267°, $[\alpha]_D$ −292° (c=1.05). UV λ_{max} mμ (ε): 286 (23,500). IR ν_{max} cm^{-1}: 1680, 1658 (2- and 7-C=O), 1620, 1595 (-C=C-), 1730, 1246 (ester). *Anal.* Calcd. for $C_{21}H_{26}O_4$: C, 73.66; H, 7.66. Found: C, 73.85; H, 7.84.

b) *via* 7β-Acetoxy derivatives. i) $NaBH_4$ reduction of IIa. To a suspension of IIa (3.3 g.) in MeOH (33 ml.) was added $NaBH_4$ (2.3 g.) in a water-bath. After 1 hr., the mixture become homogeneous and was kept stirring for additional 2 hrs. Excess of the reagent was decomposed by acetone and then poured into water. The precipitate was collected, washed with water, and dried in vacuum. The crude 7β-ol (3.1 g.) was acetylated by Ac_2O (6.2 ml.) and pyridine (9.3 ml.) at room temperature overnight. Recrystallization from ether-MeOH gave androsta-3,5-diene-7β,17β-diol diacetate (IV) (2.8 g., m.p. 128~131°). One more recrystallization from the same solvent afforded an analytical sample as colorless needles, m.p. 132~133.5°. $[\alpha]_D$ +10° (c=1.14). UV λ_{max} mμ (ε): 231 as inflection (21,000), 236.5 (22,100), 244 as inflection (14,600). IR ν_{max} cm^{-1}: 1655, 1612 (-C=C-), 1730, 1250, 1240 (ester). *Anal.* Calcd. for $C_{23}H_{32}O_4$: C, 74.16; H, 8.66. Found: C, 73.95; H, 8.33. ii) *tert*-Butyl chromate oxidation of IV. A solution of IV (2 g.) in CCl_4 (60 ml.) was treated in a similar way as described in a). Recrystallization of the crude product from MeOH-H_2O gave 7β,17β-diacetoxyandrosta-3,5-dien-2-one (V) (350 mg., m.p. 182~189°). Several recrystallization from the same solvent afforded an analytical sample as colorless needles, m.p. 191~193.5°, $[\alpha]_D$ +93° (c=1.17). UV λ_{max} mμ (ε): 283 (14,200). IR ν_{max} cm^{-1}: 1675 (-C=O), 1643, 1585 (-C=C-), 1731, 1250, 1236 (ester). *Anal.* Calcd. for $C_{23}H_{30}O_5$: C, 71.48; H, 7.82. Found: C, 71.16; H, 7.82. iii) Conversion of V into IIIa by MnO_2 oxidation. A solution of V (100 mg.) in MeOH (10 ml.) was gently refluxed with 4% NaOH (1 ml.) for 20 min. and then evaporated to dryness in vacuum. The ethereal solution of the residue was washed with water, dried over Na_2SO_4 and evaporated to dryness. The crude product, without any purification, was dissolved into $CHCl_3$ (10 ml.) and treated with MnO_2 (1 g.) at room temperature for 10 hrs. Then MnO_2 was removed by filtration. The residue from the filtrate was acetylated by Ac_2O (0.5 ml.) and pyridine (1 ml.) at room temperature overnight. The ethereal solution of the crude product was washed with 10% HCl, water, 5% Na_2CO_3, and water, dried over Na_2SO_4, and evaporated to dryness. Recrystallization from acetone gave IIIa as yellow needles (27 mg., m.p. 246~255°), which was identical with the sample obtained from IIa by one step as described above.

17β-Acetoxy-3-methylandrosta-3,5-dien-7-one (IIb)——a) From 3-methylandrosta-3,5-dien-17β-ol acetate (Ib).[11] A solution of Ib (3 g.) in CCl_4 (90 ml.) was refluxed with *tert*-butyl chromate solution in CCl_4[3] (30 ml.) and Ac_2O (3 ml.) for 6 hrs. Then the reaction mixture was worked up in a similar way as described in the preparation of IIa. The crude product was subjected to chromatography on Florisil by benzene. From the earlier eluent was obtained IIb (637 mg., m.p. 196~202°) and the further crop of IIb (180 mg., m.p. 197~204°) from the middle eluent. Several recrystallization from acetone afforded an analytical sample as colorless needles, m.p. 203~204.5°, $[\alpha]_D$ −399° (c=1.01). UV λ_{max} mμ (ε): 292~293 (19,100). IR ν_{max} cm^{-1}: 1634 (7-C=O), 1659, 1598 (-C=C-), 1730, 1240 (ester). *Anal.* Calcd. for $C_{22}H_{30}O_3$: C, 77.15; H, 8.83. Found: C, 76.98; H, 8.86.

A small amount of the 2,7-dione (IIIb) was given from the later eluent.

b) From 17β-acetoxy-3α-methylandrost-5-en-7-one (XII). A solution of XII (140 mg.) in *tert*-BuOH (4 ml.) was treated with chloranil (130 mg.) under reflux for 5 hrs. in the N_2 atmosphere. The reaction mixture was diluted with ether. The ethereal solution was washed with water, 4% NaOH and water, dried over Na_2SO_4, and evaporated to dryness. Chromatography of the residue on Florisil with benzene furnished IIb (8 mg.) as amorphous solid, whose UV and IR spectra showed no defect in comparison with a sample obtained from Ib.

17β-Acetoxy-3-methylandrosta-3,5-diene-2,7-dione (IIIb)——In a similar way as described in a) of the preparation of IIIa was treated IIb (5 g.). The solution of the crude product in CH_2Cl_2 was passed through Florisil. Recrystallization from ether-MeOH gave IIIb (580 mg., m.p. 222~225°). Two recrystallizations from the same solvent afforded an analytical sample as yellow needles, m.p. 227~229°, $[\alpha]_D$ −269° (c=1.78). UV λ_{max} mμ (ε): 296 (26,300). IR ν_{max} cm^{-1}: 1670, 1658 (2- and 7-C=O), 1620, 1592 (-C=C-), 1730, 1249 (ester). *Anal.* Calcd. for $C_{22}H_{28}O_4$: C, 74.13; H, 7.92. Found: C, 73.81; H, 7.86.

The mother liquor resulted in a troublesome mixture containing a considerable amount of unreacted IIb.

17β-Acetoxy-3-chloroandrosta-3,5-dien-7-one (IIc)——To a solution of testosterone acetate (10 g.) in $CHCl_3$ (40 ml.) was slowly added PCl_5 (10 g.) (well crashed) with stirring in an ice-water bath. Immediately the whole become violet with generation of heat. Being kept below room temperature for 30 min., the reaction mixture was concentrated in vacuum to a small volume and then diluted with ether. The ethereal solution was washed with cold water, 4% NaOH and water, dried over Na_2SO_4, and evaporated to dryness. Recrystallization of the residue from acetone gave 3-chloroandrosta-3,5-dien-17β-ol acetate (Ic) (6.5 g., m.p. 153~158°). Further crop from the mother liquor, 1.3 g., m.p. 147~153°. Several recrystallization from the same solvent afforded an analytical sample as colorless needles, m.p. 154~160°, $[\alpha]_D$ −169° (c=0.92). UV λ_{max} mμ (ε): 235.5 (22,200), 242.5 (24,600), 250 as inflection (17,300). IR ν_{max} cm^{-1}: 1622 (-C=C-, Δ^3 and Δ^5 were superimposed), 1729, 1243 (ester) (in the lit.,[12] m.p. 148~152°, $[\alpha]_D^{23}$ −172° (c=1 in $CHCl_3$), UV λ_{max}^{MeOH} 242 mμ (log ε 4.4)). *Anal.* Calcd. for $C_{21}H_{29}O_2Cl$: C, 72.29; H, 8.38. Found: C, 72.42; H, 8.10.

In a similar way as described in a) of the preparation of IIIa was treated Ic (13 g). Recrystallization of the crude product from acetone gave IIc (5.7 g., m.p. 190~194°). Several recrystallization from the same solvent afforded an analytical sample as colorless needles, m.p. 196.5~197.5°, $[\alpha]_D$ −370° (c=1.03). UV λ_{max} mμ (ε): 284~285 (28,000). IR ν_{max} cm^{-1}: 1651 (7-C=O), 1616 (-C=C-, Δ^3 and Δ^5 were superimposed), 1729, 1238 (ester). *Anal.* Calcd. for $C_{21}H_{27}O_3Cl$: C, 69.50; H, 7.50. Found: C, 69.28; H, 7.48.

From the mother liquor was obtained the crude 2,7-dione (IIIc) (400 mg., m.p. 180~209°), whose IR spectrum showed about 70~80% purity.

17β-Acetoxy-3-chloroandrosta-3,5-diene-2,7-dione (IIIc)——In a similar way as described in a) of the preparation of IIIa was treated IIc (4 g.). The oily residue was subjected to reoxidation with the same system because the IR spectrum of an aliquot showed a very poor content of the 2,7-dione. Recrystallization from acetone gave the crude IIIc (530 mg., m.p. 206~225°). After laborious recrystallization from the same solvent was obtained an analytical sample as yellow needles, m.p. 247~254°, $[\alpha]_D$ −335° (c=1.12). UV $_{max}$ mμ (ε): 299 (24,700). IR ν_{max} cm^{-1}: 1695, 1659 (2- and 7-C=O), 1618 (-C=C-, Δ^3 and Δ^5 were superimposed), 1730, 1241 (ester). *Anal.* Calcd. for $C_{21}H_{25}O_4Cl$: C, 66.92; H, 6.68. Found: C, 67.31; H, 6.85.

1,6-Addition of CH_3MgI to IIb——To a solution of IIb (400 mg.) and $Cu(OAc)_2$ (40 mg.) in tetrahydrofurn (24 ml.) was added CH_3MgI solution (prepared from Mg (340 mg.), CH_3I (0.8 ml.) and ether (9 ml.)) dropwise over 10 min. in an ice-water bath. After stirring for additional 3½ hrs. at room temperature, the reaction mixture was worked up in the usual way. The solution of the crude product in AcOH (16 ml.) and conc. HCl (0.8 ml.) was stayed overnight in an ice-box and then poured into water. The whole was extracted with ether. The ethereal solution was washed with water, 4% NaOH and water, dried over Na_2SO_4, and evaporated to dryness. The residue was chromatographed on alumina by benzene-hexane (1:1). From the earlier fraction was recovered the crude raw material (200 mg.), which was easily recognized by its UV and IR spectra. From the middle and later fraction was obtained 17β-acetoxy-3,3-dimethylandrost-5-en-7-one (VIII) (63 mg., m.p. 226~230°). Recrystallization from acetone afforded an analytical sample as colorless scales, m.p. 229~231°, $[\alpha]_D$ −121° (c=1.27). UV λ_{max} mμ (ε): 240 (14,200). IR ν_{max} cm^{-1}: 1670 (7-C=O), 1630 (-C=C-), 1730, 1265 (ester). NMR (in $CDCl_3$) p.p.m.: 0.80 (3α-CH_3 and 13β-CH_3), 0.99 (3β-CH_3), 1.13 (10β-CH_3), 2.01 (17β-OAc), 5.60 (6-H, broad), *Anal.* Calcd. for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 76.93; H, 9.48.

Hydrogenation of IIc——A solution of IIc (285 mg.) in EtOH (30 ml.) was hydrogenated on Pd-black (30 mg.) at room temperature. After 18 min., the UV absorption of an aliquot at 285 mμ disappeared. The catalyst was removed. The filtrate was diluted with ether. The ethereal solution was washed with 4% NaOH and water, dried over Na_2SO_4, and evaporated to dryness. Recrystallization from ether gave 17β-acetoxyandrost-5-en-7-one (IX) (163 mg., m.p. 211~213°). One more recrystallization from MeOH afforded an analytical sample as colorless needles, m.p. 212~213°, $[\alpha]_D$ −184° (c=0.98). UV λ_{max} mμ (ε): 239.5 (13,100). IR ν_{max} cm^{-1}: 1665 (7-C=O), 1620 (-C=C-), 1730, 1248 (ester). In the lit., m.p. 212~213°,[17a] m.p. 215~217°.[17b] *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.21; H, 9.19.

17β-Hydroxy-3α-methylandrost-4-en-7-one (XI)——In a similar way as described on VIII was treated IIa (2 g.) with CH_3MgI. Excess of the reagent was decomposed with ice-water. The whole was extracted with ether. The ethereal solution was washed with cold 10% NH_4Cl, 5% Na_2CO_3 and water, dried over Na_2SO_4, and evaporated to dryness below 30°. Recrystallization from acetone-hexane gave XI (1.07 g., m.p. 163~169°). Two recrystallizations from the same solvent afforded an analytical sample as colorless needles, m.p. 163~169°, $[\alpha]_D$ +54° (c=0.99). IR ν_{max} cm^{-1} 1711 (-C=O), 1660 (-C=C-), 3570 (-OH). *Anal.* Calcd. for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.14; H, 9.88.

17β-Acetoxy-3α-methylandrost-5-en-7-one (XII)——A solution of XI (600 mg.) in AcOH (24 ml.) and conc. HCl (1.2 ml.) was stayed overnight in an ice-box and then poured into water. The precipitate was collected by filtration and dissolved into ether. The ethereal solution was washed with 4% NaOH and water, dried over Na_2SO_4, and evaporated to dryness. Recrystallization from ether-MeOH gave XII (430 mg., m.p. 146.5~149.5°). One more recrystallization afforded an analytical sample as colorless needles, m.p. 149.5~150.5°, $[\alpha]_D$ −166° (c=0.91). UV λ_{max} mμ (ε): 241 (13,400). IR ν_{max} cm^{-1}: 1666 (7-C=O), 1620 (-C=C-), 1724, 1253 (ester). *Anal.* Calcd. for $C_{22}H_{32}O_3$: C, 76.70; H, 9.36. Found: C, 76.78; H, 9.39.

3β-Acetoxy-7α-bromo-5α-cholestan-6-one (XV)——The compound XV was prepared by the procedure which E. J. Corey and R. A. Sneen employed.[7c] NMR (in $CDCl_3$) p.p.m.: 0.70 (13β-CH_3), 0.79 (10β-CH_3), 2.02 (3β-OAc), 3.28 (5-H, quartet: J=6 c.p.s. (5α:4α); J=10 c.p.s. (5α:4β)), 4.18 (7-H), 4.70 (3-H, broad).

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