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Preparation of the Steroidal 1,4,11-Trien-3-ones and a Surprisingly Rapid Dienone-phenol Rearrangement*

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25D-Spirosta-1,4,11-trien-3-one (**5a**) and androsta-1,4,11-trien-17β-ol-3-one acetate (**16b**) were prepared from hecogenin and 5β-androstane-3α,12α,17β-triol, respectively. The dienone-phenol rearrangements of these compounds were carried out and the structures of all reaction products were clarified.

Rates of the rearrangement of **16b** were determined in a 95 : 5 (w/w) mixture of acetic acid and acetic anhydride containing *p*-toluenesulfonic acid at 20° and varying acidity function H_0. Comparison with a reference compound, androsta-1,4-dien-17β-ol-3-one acetate (**36**), indicated for **16b** a reactivity enhanced by a factor of 180 at 20° and $H_0=0$. Products were found to be four kinds of the A-aromatic B-seco allyl acetates (at 20° and $H_0=-0.80$; $\Delta^{9(11)}$-12α-OAc (**25c**) 75%, $\Delta^{9(11)}$-12β-OAc (**25d**) 2%, and $\Delta^{11(12)}$-9(α and β)-OAc (**26c**) 23%) with the A-aromatic B/C *cis* $\Delta^{11(12)}$-steroid (**27c**) (3%). The results suggest important participation of the C-11 (12) double bond in the rearrangement of **16b**. Treatment of the B-seco $\Delta^{9(11)}$-12α-allyl alcohol (**25b**) with the acid of $H_0=-1.86$ at 80° led to the B/C *cis* steroid (**27c**) with a concurrent isomerization to an intermediate, B-seco $\Delta^{9(11)}$-12β-allyl acetate (**25d**), which is interpreted as a result of electrophilic aromatic substitution of an allyl cation formed from the B-seco $\Delta^{9(11)}$-12α-allyl alcohol.

During the course of our past investigation on the acetolyses of several A-ring substituted 11α-*p*-toluenesulfonyloxy steroidal sapogenins, it was found that the 11α-*p*-toluenesulfonyloxy-1,4-dien-3-one, besides the expected main product, 1,4,9(11)-trien-3-one, gave a new type of B-seco steroid (a) and a styrene derivative (b) (Chart 1). And it was assumed that this B-seco steroid was produced from the Hofmann olefin, which has a double bond at C-11, as an intermediate by the acid catalyzed isomerization processes (Chart 2).[2]

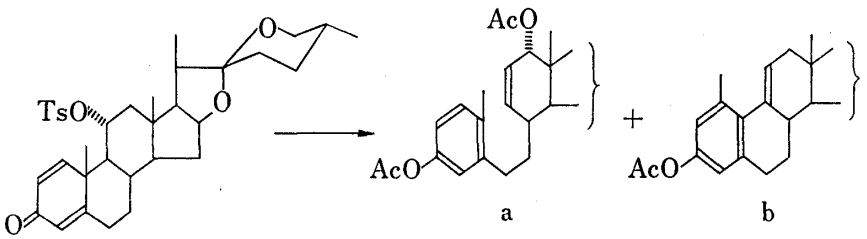


Chart 1

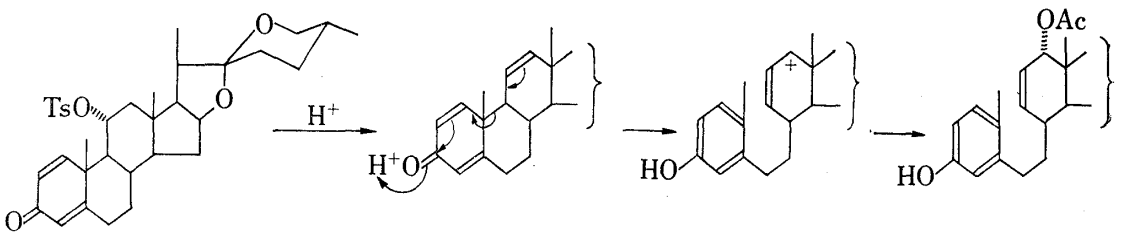


Chart 2

* Dedicated to the memory of Prof. Eiji Ochiai.

1) Location: *Fukushima-ku, Osaka, 553, Japan.*

2) K. Takeda, H. Tanida, and K. Horiki, *J. Org. Chem.*, 31, 734 (1966).

Recently, Kropp[3] reported on the acid catalyzed isomerization reaction of 4α,β,8α-dimethyl-5,6,7,8-tetrahydro-2(4αH)-naphthalenone where a 8,8α-seco derivative was obtained along with the normal isomerization product.

Here we wish to report syntheses of derivatives of the above-assumed Hofmann olefin, 25D-spirosta-1,4,11-trien-3-one and 17β-acetoxyandrosta-1,4,11-trien-3-one, and kinetic investigations of unusually facile isomerization by acid.

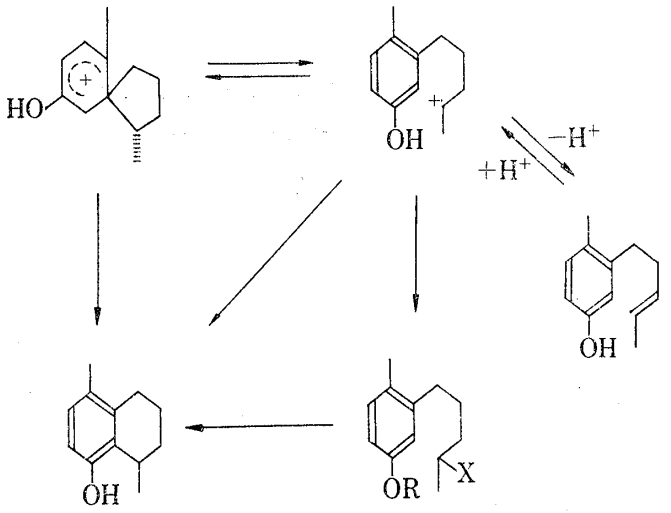


Chart 3

1. Preparation of Materials

a. Spirostane Series——Engel and his co-workers[4] reported that when treated with the basic alumina 17α-methylated 12α-tosyloxy steroids gave unsaturated compounds with the double bond located at C-11 in high yield. On the other hand as reported by Chen,[5] when 12α-methanesulfonyloxycholane was treated with collidine it gave a chol-11-ene derivative together with a 18-methyl migrated steroid. In our case, treatment of 12α-tosyloxy spirostane (**1c**) or its 1,4-dien-3-one derivative (**4c**) with basic alumina or with lithium carbonate (Li_2CO_3) in dimethylformamide (DMF) always gave mainly a 18-methyl migrated compound, tentatively assigned as **3** or **6** and a small amount of Δ^{11}-unsaturated sapogenin (**2** or **5**) was detected from nuclear magnetic resonance (NMR). Difference in products obtained by elimination of the sulfonyloxy group may be due to a slight variation of the C-ring conformation caused by the side chain on the steroidal nucleus.

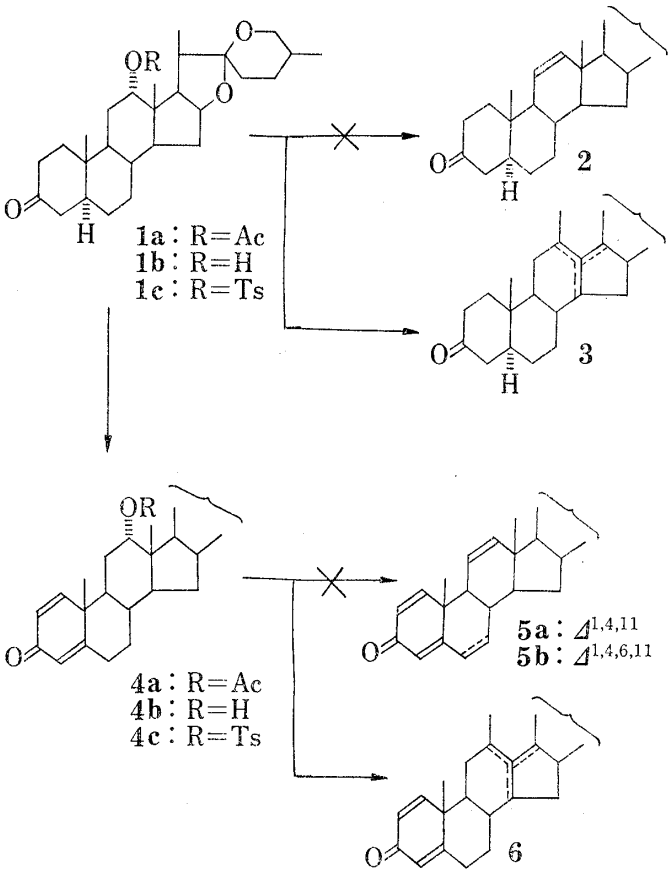
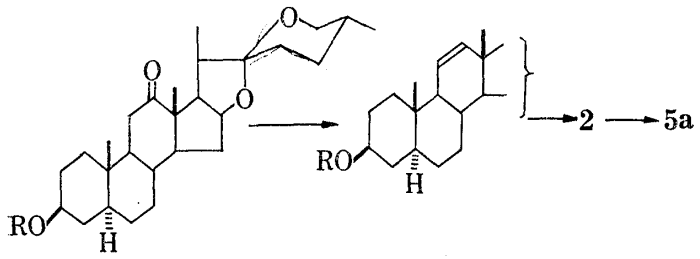


Chart 4

As this elimination reaction of the 12α-sulfonyloxy group was not suitable to obtain the Δ^{11}-unsaturated spirostanes, hecogenin was used as a starting material. According to the

3) P.J. Kropp, *J. Am. Chem. Soc.*, **85**, 3280 (1963).
4) Ch. R. Engel, K.F. Jennings, and G. Just, *J. Am. Chem. Soc.*, **78**, 6153 (1956); G. Just and Ch. R. Engel, *J. Org. Chem.*, **23**, 12 (1958).
5) F.C. Chen, *Tetrahedron Letters*, **1963**, 2057.



Hecogenin

Chart 5

slightly modified procedures reported by Conforth, *et al.*[6] and Sondheimer, *et al.*,[7] hecogenin was converted to 5α,25D-spirost-11-en-3β-ol 3-acetate *via* the bromohydrin intermediate.

Spirost-11-en-3-one (**2**), obtained by the chromic acid oxidation of spirost-11-en-3β-ol, was treated with 2,3-dichloro-5,6-dicyanobenzoquinone (DDQ) and the desired 25D-spirosta-1,4,11-trien-3-one (**5a**) was obtained. However, this trienone was contaminated with a very small amount of tetraenone (**5b**) and due to the difficulty of the complete separation, the impure trienone (**5a**) was supplied to examine the following acetolysis reaction without further purification.

b. Androstane Series——3α,12α,17β-Trihydroxy-5β-androstane (**7a**)[8] was chosen as a starting material to synthesize 17β-acetoxy-androst-1,4,11-trien-3-one (**16b**). In order to protect the hydroxyl group at C-3 and C-17 in **7a** selectively, we attempted acylation reactions such as carbethoxylation and benzoylation, the latter of which was found to be a preferable method. 3α,17β-Dibenzoyloxy-5β-androstan-12α-ol (**7b**) was then oxidized to its 12-ketone (**8b**) by the Jones reagent. Bromination of this ketone gave a mixture of 11α- and 11β-bromo-ketone (**9b**).[9] Reduction of the bromo-ketone with sodium borohydride ($NaBH_4$) followed by treatment with zinc in boiling acetic acid provided the C-11 unsaturated derivative (**11b**), which was converted to the diacetate (**11d**) and hydrolyzed with sodium carbonate in aqueous methanol to obtain 17-monoacetate (**11e**) according to the method reported by Immer, *et al.*[10] Oxidation of **11e** with Jones reagent gave 17β-acetoxy-5β-androst-11-en-3-one (**12a**), identical with the physical data reported by the same authors[10] in all respects.

Although several procedures were reported in the literature concerning bromination of the steroidal A-ring in the 5β-series,[11,12] bromination of **12b** was carried out using trimethylphenylammonium perbromide according to the method recently reported by Jacques, *et al.*,[12] mainly because this bromination occurred on the carbon next to the ethyleneketal moiety without affecting a double bond. During the course of ketalization of **12a** with ethylene glycol and *p*-toluenesulfonic acid, as acid hydrolysis of the 17β-acetoxyl group was also induced simultaneously, it was reacetylated by the usual way. The thus obtained ketal compound (**12b**) was brominated by trimethylphenylammonium perbromide followed by deketalization with perchloric acid in acetic acid to obtain the bromo-ketone (**13**). Treatment of **13** with Li_2CO_3 in DMF gave a mixture of the unsaturated compound (**14** and **15**). In some cases the trienone (**16b**) was also obtained as a by-product, which means that **13** is a mixture of monobromo- and 2,4-dibromo-3-one (**13c**).

Although dehydrogenation of **15a** with DDQ gave the desired 1,4,11-trien-3-one (**16b**), this trienone was always contaminated with a small amount of 1,4,6,11-tetraen-3-one (**17**). Elimination of the contaminated tetraenone (**17**) was almost impossible by the usual method as mentioned earlier.

6) *a*) J.W. Conforth, J.M. Osbond, and G.H. Phillips, *J. Chem. Soc.*, **1954**, 907; *b*) J. Elks, G.H. Phillips, D.A.H. Taylor, and L.J. Wyman, *J. Chem. Soc.*, **1954**, 1739.
7) M. Nussim, Y. Mazur, and F. Sondheimer, *J. Org. Chem.*, **29**, 1120 (1964).
8) C.H. Hassall, *Organic Reactions*, **9**, 93 (1957).
9) P. Krauth, *J. Org. Chem.*, **32**, 3626 (1967).
10) H. Immer, M. Lj. Mihailovic, K. Schaffner, D. Arigoni, and O. Jeger, *Helv. Chim. Acta*, **45**, 753 (1962).
11) J.P. Dusza, J.P. Joseph, M. Heller, and S. Bernstein, *J. Med. Chem.*, **6**, 364 (1963).
12) A. Marquet and J. Jacques, *Bull. Soc. Chim. France*, **1962**, 90.

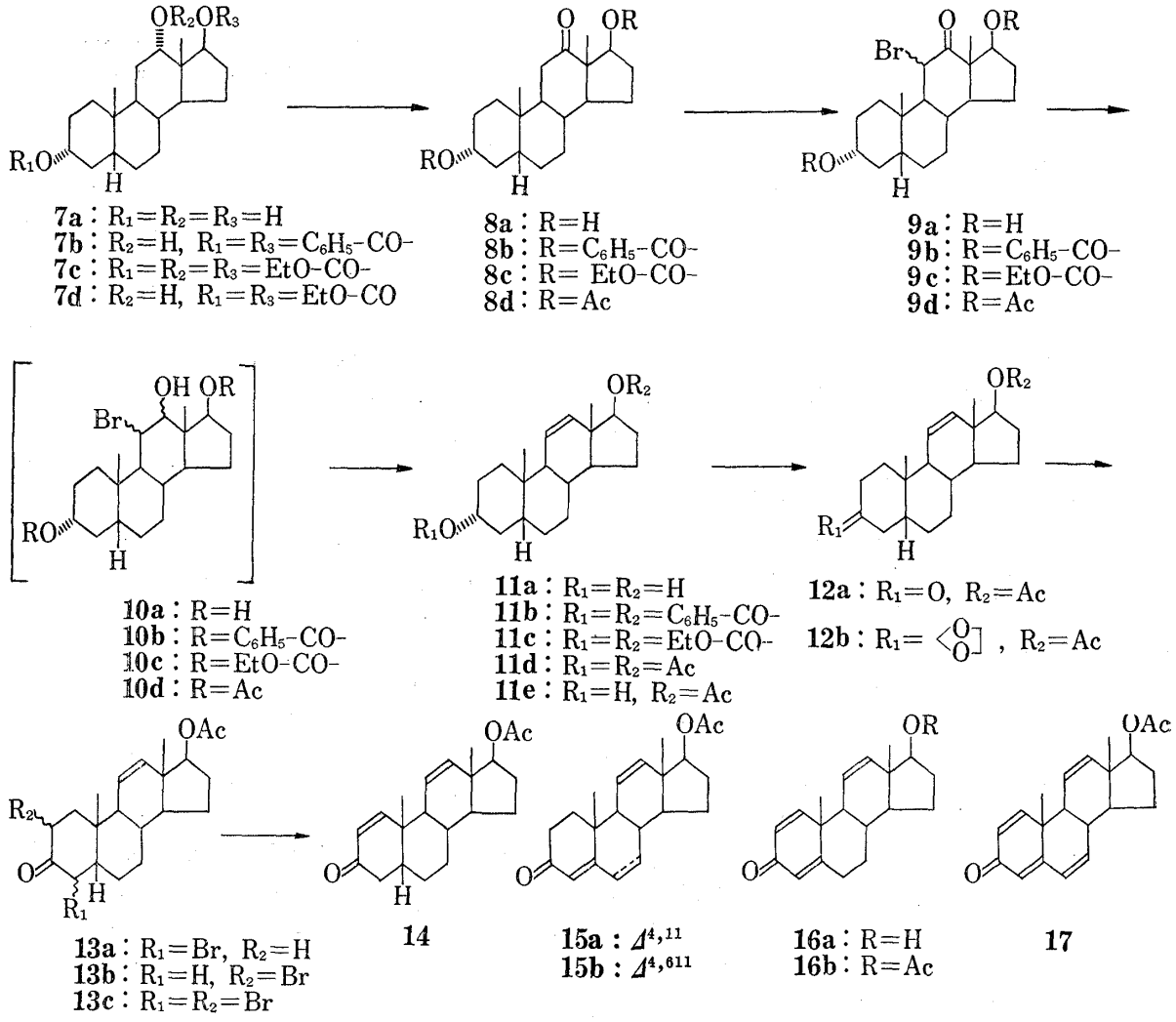


Chart 6

Selenium dioxide dehydrogenation of **14** or **15a** also gave a pure 17β-acetoxyandrosta-1,4,11-trien-3-one (**16b**) without any tetraenone (**17**) as impurity, but the yield was considerably low.

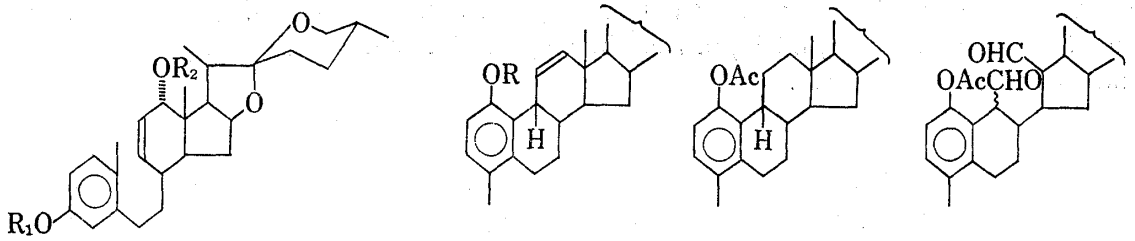
II. Structure Determination of the Products from Dienone-phenol Rearrangements

a. Spirostane Series——After trienone (**5a**) was heated at 90° for 96 hr in acetic acid solution containing *ca.* 1% acetic anhydride, the products were separated by preparative thin layer chromatography (TLC) to give **18c** in 67% yield together with a small amount of **19b**.

i) Structure of **18c**: Hydrolysis of **18c** with lithium aluminum hydride ($LiAlH_4$) followed by acetylation under very mild conditions in order to acetylate the phenolic hydroxyl group selectively, provided a monoacetate (**18b**). This compound was identical with the B-seco A-ring aromatic steroidal sapogenin obtained previously by acetolysis of 11α-*p*-tosyloxy-25D-spirosta-1,4-dien-3-one in all respects. From this result it is confirmed that the B-seco steroid (**18c**) was derived from the Δ^{11}-unsaturated sapogenin (**5a**), the intermediate which we proposed earlier.

A further detailed examination of this B-seco steroid was carried out on the androstane derivatives.

ii) Structure of B/C *cis* Steroid (**19**): When trienone (**5a**) was treated with lithium perchlorate in acetic acid it also gave **19a** in 52% yield. Infrared (IR) spectrum of this compound showed the hydroxyl group and absorption band corresponding to the aromatic nucleus.

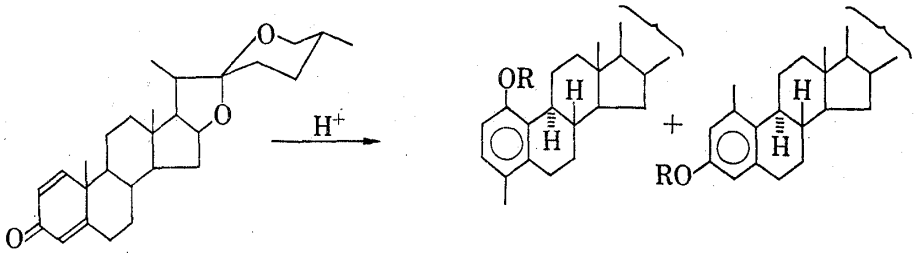


18 a : $R_1=R_2=H$
18 b : $R_1=Ac$, $R_2=H$
18 c : $R_1=R_2=Ac$

19 a : R=H
19 b : R=Ac

20

21



22

23 a : R=H
23 b : R=Ac

24 a : R=H
24 b : R=Ac

Chart 7

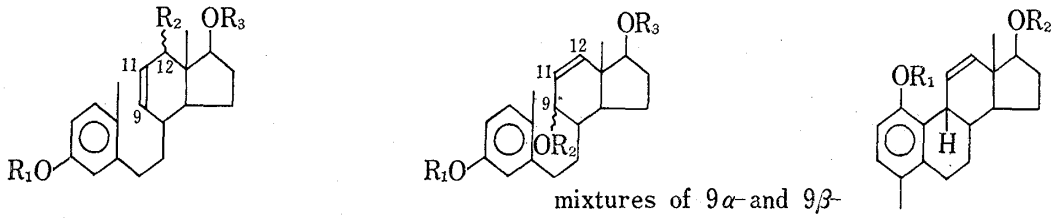
Following signals were observed in NMR[13] of **19a**: one methyl on benzene ring (δ 2.16, s), two proton signals on benzene with an *ortho* coupling as an AB type doublet of doublets (J=8.0 Hz), unseparable two vinyl protons at δ 5.93 and a benzyl allyl proton at δ 3.83. Oxidation of **19b** with ruthenium tetroxide[14] gave an oily aldehyde, the structure of which was tentatively assigned as **21** from IR. In NMR of the acetate (**19b**), the appearance of vinyl protons at δ 5.93 and 5.70 was assigned to the AB part of an ABX pattern. This signal pattern suggests that the acetoxyl substituent on the benzene ring and the double bond are located very near to each other, according to the effects of acetylation upon neighboring protons and hydroxyl groups advocated by Okamoto and Kawazoe.[15] Ultraviolet spectrum (UV) of the acetate (**19b**) showed absorptions at 265.5 (ε 360) and 274.4 nm (ε 280) and this indicated that the double bond was not conjugated with the benzene ring. Summarizing the above results, it is deduced that the position of the acetoxyl group on the benzene ring should be C-1 and the double bond at C-11. Configuration of the benzyl allyl proton in **19b** was examined by the 100 Hz proton decoupling technique. Upon irradiation of this proton the vinyl proton signal becomes an AB type quartet and on the other hand irradiation at both vinyl protons led the benzyl allyl proton to an approximate doublet of a coupling constant of J=8 Hz with the C-8 proton. These facts imply that the configuration of the hydrogen at C-9 is β, that is B/C ring *cis*-fused, from the modified Karplus equation.[16]

Catalytic hydrogenation of **19b** gave a saturated compound (**20**). When compared with molecular rotation ($[M]_D$), circular dichroism (CD) and optical rotatory dispersion (ORD) data of this **20** with those of the natural B/C *trans*-fused phenolic compound (**23**), the results also indicated that the B and C rings in **20** are *cis*-fused[17] (*cf.* Table I).

b. Androstane Series——Treatment of the trienone (**16b**) with 0.5 N sodium acetate in acetic acid gave four kinds of isomerization products when the reaction mixture was separated

13) Abbreviation used: s=singlet, d=doublet, t=triplet, q=quartet and m=multiplet.
14) G. Snatzke and H.W. Fehlhaver, *Ann.*, **663**, 123 (1963).
15) T. Okamoto and Y. Kawazoe, *Chem. Pharm. Bull.* (Tokyo), **11**, 643 (1963).
16) K. Kuriyama, E. Kondo, and K. Tori, *Tetrahedron Letters*, **1963**, 1485 and references cited therein.
17) *a*) G. Snatzke, M. Majtár, and F. Werner-Zamojska, *Tetrahedron*, **28**, 281 (1972); *b*) E.J. Bailey, J. Elks, J.F. Oughton, and L. Stephenson, *J. Chem. Soc.*, **1961**, 4535.

with preparative TLC together with the unchanged product which consisted mainly a $\Delta^{1,4,6,11}$-tetraen-3-one (**17**): namely, i. **25c**, ii. **26c**, iii. **27c**, and iv. **25d**. The exact yield of each compound was cited in Table III.



25a: $R_1=R_3=H$, $R_2=\alpha$-OH
25b: $R_1=Ac$, $R_3=H$, $R_2=\alpha$-OH
25c: $R_1=R_3=Ac$, $R_2=\alpha$-OAc
25d: $R_1=R_3=Ac$, $R_2=\beta$-OAc

26a: $R_1=R_2=R_3=H$
26b: $R_1=Ac$, $R_2=R_3=H$
26c: $R_1=R_2=R_3=Ac$

27a: $R_1=R_2=H$
27b: $R_1=H$, $R_2=Ac$
27c: $R_1=R_2=Ac$

Chart 8

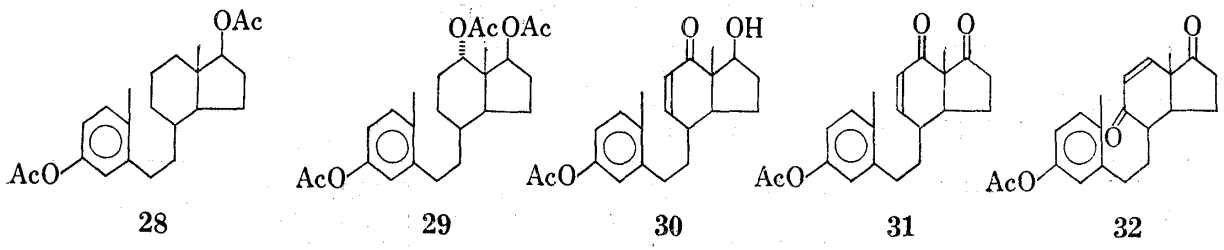
i) Structures of **25c** and **25d**: The IR spectrum of **25c** showed a phenolic acetate band at 1761 and an acetate band at 1740 cm^{-1}. NMR showed three acetyl methyls (δ 1.99, 2.04, and 2.24), one methyl on benzene ring (δ 2.24), two vinyl protons (δ 5.84), one proton attached to a carbon bearing acetoxyl group (δ 4.97) and ABK type three aromatic protons (δ 6.69—7.18) characteristic of the B-seco phenolic steroid. The main parts of this NMR signal pattern are similar to those of the B-seco sapogenin (**18c**).

DDQ oxidation[18] of the 3-monoacetate (**25b**), in which the phenolic hydroxyl group was acetylated, gave an α,β-unsaturated ketone (**30**). Catalytic hydrogenation of **25c** afforded a small amount of the hydrogenolysis product (**28**) together with the saturated compound (**29**) and this fact indicated that the second hydroxyl group should be located at the allylic position of the disubstituted double bond. Chromium trioxide oxidation of **25b** gave a diketone (**31**), and signals of the AB part of the two olefinic protons belonging to the ABX pattern were detected in the NMR of this **31**. From these results the double bond should be located between C-9 and C-11 and the acetoxyl group at C-12.

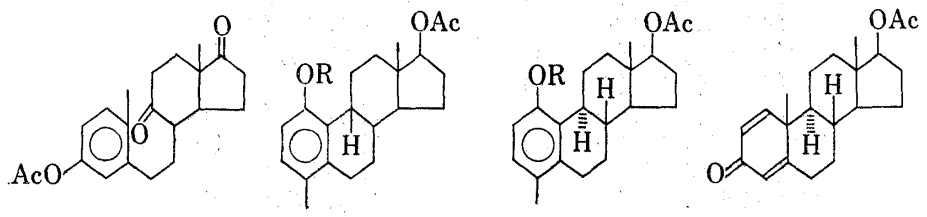
Since in **29** the proton signal corresponding to a hydrogen atom attached to a carbon bearing acetoxyl group was observed at δ 4.83 as a triplet (J=2.5 Hz), the configuration of the acetoxyl group was assumed to be α.[19] We observed an $[M]_D$ difference of 705° between the epimeric pair of **25c** ($[M]_D$ +326.1°) and **25d** ($[M]_D$ −378.4°), which were obtained from the conjugated ketone (**30**) by $NaBH_4$ reduction followed by acetylation. When Mills' rule[20] is applied for these data, it is predicted that **25c** has an axial acetoxyl group while **25d** has an equatorial one. A similar observation would be +976° for methyl chol-9(11)-ene-3α,12α-diol-ate 12-acetate and +15° for 12β-acetate epimer, so that the $[M]_D$ difference is +961°: Therefore, the assignment based on the NMR data is consistent with this prediction. Main product of the $NaBH_4$ reduction of **30** followed by acetylation was identical with **25d**, obtained directly by the isomerization of **16b** with acetic acid as mentioned above while the minor one was the epimeric 12α-acetoxy derivative (**25c**).

ii) Structure of **26c**: As a characteristic signal pattern corresponding to the aromatic B-seco steroid was observed in the NMR spectrum of the triacetate (**26c**), the structure of **26** was easily assumed to be very similar to that of **25**. Hydrolysis of **26c** with $LiAlH_4$ followed by acetylation under very mild conditions provided a monoacetate (**26b**).

18) S.H. Burstein and H.J. Ringold, *J. Am. Chem. Soc.*, **86**, 4952 (1964).
19) *cf.* Y. Kawazoe, Y. Sato, T. Okamoto, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **11**, 328 (1963).
20) J.A. Mills, *J. Chem. Soc.*, **1952**, 4976.



28 29 30 31 32



33 34a : R=H 34b : R=Ac 35a : R=H 35b : R=Ac 36

Chart 9

VPC examination showed that **26c**, obtained from **26b**, was a mixture of almost equal amount of the two substances. When **26b** was oxidized with chromium trioxide it gave only a pure unsaturated diketone **32** in high yield. These results suggested that both of **26b** and **26c** are mixtures of the epimeric allylic 9α and 9β alcohols.

The position of the double bond and the acetoxyl group in **26c** are deduced by the NMR spectrum. AB type quartet (J=10.0 Hz) corresponding to two vinyl protons appeared at δ 5.93 and 7.26 in **32** which indicates that the double bond should be located between C-11 and C-12 and the acetoxyl group at C-9. This structure was further confirmed by direct comparison of the saturated ketone (**33**), which was obtained by catalytic hydrogenation of **32**, with the compound obtained from androst-4-ene-3,17-dione by oxidative cleavage using microorganisms.[21]

iii) Structure of **27c**: **27c** was also obtained by similar treatment of **16b** with lithium perchlorate as in the case of sapogenin, or with p-toluenesulfonic acid in dioxane.

Analogous signal pattern **27c** was also observed in NMR when compared with that of **19b**. Examination of $[M]_D$, ORD and CD of the saturated derivative (**34**), and its 9α-epimer (**35**), having a natural estrane nucleus derived from **36**,[22] showed similar physical properties to those of the above-mentioned sapogenin series, **20** and **23**. Thus the structure of **27** was assigned as a B/C *cis*-fused A-ring aromatic steroid corresponding to **19**.

III. Kinetics

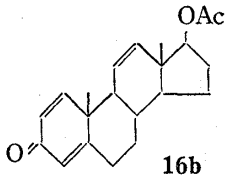
The dienone-phenol rearrangements of the trienone (**16b**) were carried out in a 95: 5 (w/w) mixture solvent of acetic acid and acetic anhydride containing p-toluenesulfonic acid and the rates were determined at three different low temperatures and varying acidity function H_0. The results were summarized in Table II with those of reference compound (**36**). Plotting logarithms of the rates at 20° against $-H_0$ yields a straight line with a slope of 1.15 (determined by least square method) and an intercept value of -4.543 (Fig. 1), from which k_{obs} at H_0=0 and 20° was obtained as 2.87×10^{-5} sec^{-1}. On the other hand, rates of **36** were determined at 40°, 50°, and 60° and varying H_0.[22] The rates of **36** at H_0=0 were calculated similar

21) E. Kondo and K. Tori, *J. Am. Chem. Soc.*, **86**, 736 (1964).
22) Dienone-phenol rearrangement of the reference compound (**36**) will be published in a forthcoming paper.

TABLE I. Spectral Data (MeOH)

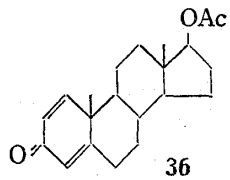
Compound	Physical data		
	$[M]_D$ ($CHCl_3$)	ORD λ(nm)([ϕ])	CD λ(nm)([θ])
19 b	−1514	400(−4340), 277.5(−14940) 274(−14340), 250(−21400) 225(−50480), 215(−68150)	294(0), 275(−2080) 268(−1999) 247(−475)
20	−639.5	325(−3420), 278(−5860) 273.5(−5580), 269(−5720) 250(−7310), 230(−13960)	300(0), 275.5(−850) 269(−720), 240(0) 225(−4640), 210(0)
23 b	+312.8	400(+866), 350(+1440) 300(+2870), 279(+4490) 273(+4290), 233(+11270)	286(0), 274(+810) 266(+760), 243(0)
27 b	−990	400(−3870), 290(−23720) 268(+1100), 230(−25140) 215(−43990)	302(0), 282(−18920) 244(−518), 229(−9950) 220(−16070)
34 b	−288.3	400(−1090), 300(−2280) 279(−3520), 274(−3070) 270.5(−3150), 230(−10090) 217(−7440), 210(−15090)	300(0), 275(−1010) 260(−578), 256(−456) 245(0)
35 b	+497.6	400(+1850), 300(+4270) 280(+5890), 275(+5360) 270(+5610), 240(+10490)	290(0), 276(+910) 272(+673), 268(+794) 261(+384), 259(+484) 256(+331), 248(0)
34 a	−233.5	400(−1210), 291.5(−10.220) 267.5(+5210), 248(−2260) 227(+5290)	303(0), 282(−9170) 247(−366), 231.5(−4670) 225(0)
35 a	+490.3	400(+1660), 292(+11240) 271(−1840), 238(+7250) 225(−2650)	305(0), 283(+8780) 248(+365), 231.5(+8900) 223(0), 220(−3070)

TABLE II. Rates and H_0 of 17β-Acetoxoyandrosta-1,4,11-trien-3-one (**16b**) and -1,4-dien-3-one (**36**)



16b

Temp., °C[a]	Acid conc. [N][b]	H_0	k_{obs}, sec^{-1}
20.0	0.01120	−0.87	2.90×10^{-4}
	0.01120	−0.87	2.91×10^{-4}
	0.00540	−0.62	1.46×10^{-4}
	0.00540	−0.62	1.52×10^{-4}
	0.00804	−0.80	2.35×10^{-4}
30.0	0.00540	−0.62	3.40×10^{-4}
40.0	0.00540	−0.62	8.17×10^{-4}



36

20.0		0	1.58×10^{-7}

a) Temperatures for **16b** were controlled within ±0.03° at 20° and within ±0.02° at 30° and 40°.
b) *p*-Toluenesulfonic acid in 95.0% acetic acid–5.0% acetic anhydride (w/w).

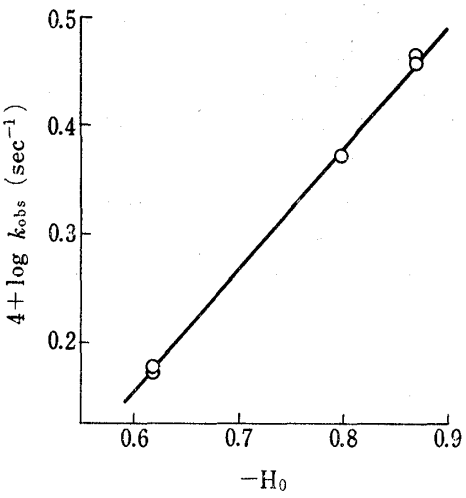


Fig. 1. Plots of Logarithmic Rate Constants at 20° against $-H_0$ Function; Slope=1,15 (r: 0.9979)

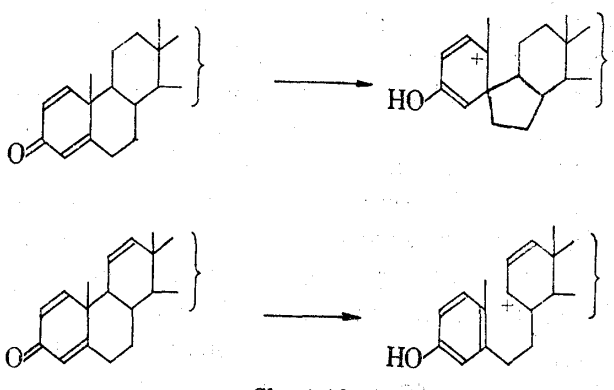


Chart 10

to the above. Arrhenius plots of the thus calculated rates at three different temperatures give a rate (1.58×10^{-7} sec^{-1}) at 20° and $H_0=0$, which was used for comparison of reactivities. The unusually high reactivity of **16b** is seen here; the relative ratio of **16b** to **36** is calculated as 180. It should be noted that the present results are in sharp contrast with the reported ones;[17b] the presence of a carbonyl group at C-11 position greatly retards the dienone-phenol rearrangement, although both the Δ^{11}-olefin group and the carbonyl group have a similar effect on the ground state energy of molecules in a sense that their introduction transforms the tetrahedral carbon configuration into a strained trigonal one. The slope of approximate unity, obtained from plotting of the rates of **16b** at 20° against H_0, suggests on the basis of the Zucker-Hammett hypothesis that as in the case of **36** the reaction proceeds by the Hammett A-1 mechanism which consists of a pre-equilibrium of proton transfer followed by a rate-determining unimolecular decomposition. Applying a mechanism generally accepted for the dienone-phenol rearrangement, the reaction of **36** is considered to proceed through consecutive 1,2-alkyl shifts and involve a cationic species of a cyclohexadiene type of high energy level. On the other hand, combination of the present rate enhancement and the data on the below-mentioned products indicate that the reaction of **16b** takes place with formation of a stable cation of an allyl type as a result of participation of the C-11 double bond.

IV. Products Distribution

The products from **16b** were found to be a mixture of compounds resulting from intermolecular trapping of the intermediate allylic cation by acetic acid solvent and compounds resulting from intramolecular trapping by the phenol which was formed from the A-ring together with the allyl cation. The intermolecular trapping gave four kinds of isomeric allyl

Table III. Product Distribution from **16b**[a]

Temp., °C	H_0	**27c**	**25c**	**26c**[b]	**25d**
20.0	−0.87	3.0	74.7(71.0)	20	1.9
	−0.80	3.0	75.1(71.0)	23	2.3
	−0.62	2.6	73.4(69.4)	24	2.1
30.0	−0.62	3.4	75.6	21	1.9
40.0	−0.62	2.7	75.4	24	2.3

a) presented by % theory
b) As **26c** was not isolated in a pure form, the yields were not corrected for the sensitivity flame detector of VPC, so that they involve some errors.

acetates and the intramolecular trapping gave a steroid of the phenol acetate type. Structures and distribution of the observed products are presented in Table III and Chart 8. However, the allyl acetates are not stable enough under the reaction conditions. It was observed that **26c** underwent an allylic isomerization and was converted into **25c** and a minor amount of **27c**. Furthermore, the pseudo-first-order rate constants calculated from the formation of **25c** were found to deviate from the real constants obtained from the reacting **16b**, These results show that the data in Table III, strictly speaking, are not of kinetic control. In the absence of a thermodynamic control, plotting logarithms of amounts of either the decreasing reactant (A–At) or the forming product (A∞–At) against time gives an identical rate constant. In the present plotting of forming **25c**, no thermodynamic control involves for an initial short time. Adapting a value near the yield observed at the end of reaction as A∞, the rate constant was calculated and this calculation was repeated with a slight change of A∞ to obtain a rate constant, identical with that calculated from the decreasing reactant (trial and errors). When the identity was attained, the A∞ value is the yield of kinetic control and presented in parentheses in Table III.

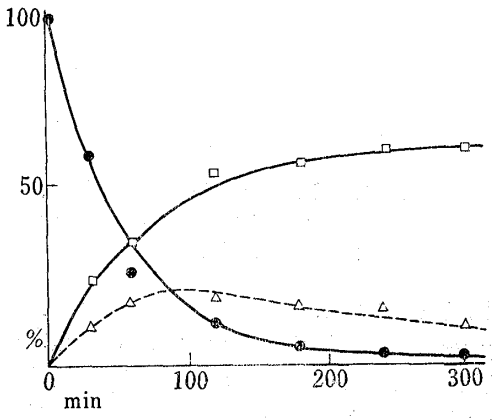


Fig. 2. Disappearance of **25b** (●), Formation of **27c** (□), and **25d** (△) as a Function of Time. The Yield of **27c** was 70% at an Infinity Time.

The allyl alcohol (**25b**) was treated by a stronger acid ($H_0=-1.86$) and higher temperature (80°). As shown in Fig. 2, the formation of B/C *cis*-fused phenol (**27c**) was observed with the decrease of **25b** and the isomeric acetate (**25d**) was increasingly formed for a time, and then gradually disappeared. These results are understood in view that an allyl cation derived from **25b** undergoes an electrophilic aromatic substitution to form **27c**

$$12\alpha\text{-OAc (25c)} \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \text{allyl}^+ \underset{k_{-2}}{\overset{k_2}{\rightleftharpoons}} 12\beta\text{-OAc (25d)}$$

$$\text{allyl}^+ \xrightarrow{k_3} \text{B/C } \textit{cis} \text{ phenol} \qquad (k_1 > k_{-2})$$

and, in part, internally returns to **25d** which is less reactive because the OAc substituent has a quasi-equatorial arrangement. The B/C *cis*-fusion in **27** would result from an attack of the allyl cation in a sterically less hindered side.

After all, the present investigation clearly demonstrates that, in accord with the previous suggestion,[2] if steroidal 1,4,11-triene-3-one is resulted from acetolysis of the 11α-*p*-toluenesulfonyloxy-1,4-dien-3-one as an elimination product (Chart 2), it immediately rearranges into the B-seco steroid under the reported acetolysis conditions.

Experimental

Melting points were determined with Yanagimoto Micromelting Point Apparatus and uncorrected. Unless otherwise noted, optical rotations were taken in $CHCl_3$ solution with Perkin-Elmer 141 Polarimeter; CD and ORD in MeOH solution with JASCO ORD/UV-6; UV spectra in 95% EtOH solution with Hitachi EPS-3T Spectrophotometer; IR with JASCO DS403G; and NMR in $CDCl_3$ solution with Varian A-60 using TMS as internal reference and chemical shifts are shown as δ. Gas–liquid phase chromatography (VPC) analysis was carried out on a Yanagimoto Gas Chromatograph GCG 550F equipped with a flame ionization detector.

I. Preparation of Materials

12α-Tosyloxy-25D,5α-spirostan-3-one (1c)——To a solution of the 12α-hydroxy-3-one[23] (**1b**), mp 257°, $[\alpha]_D^{24}$ −26.2 ±2° (c=1.069), (4.5 g) in pyridine (70 ml) was added *p*-toluenesulfonyl chloride (7.0 g) and the

23) Lit. 6*b*) mp 254—257°.

reaction mixture was kept to stand at room temperature for 2 days. The reaction mixture was poured onto crushed ice and extracted with a mixture of ether and CH_2Cl_2. The extract was washed successively with dil. HCl, aqueous NaOH solution, H_2O, and dried over Na_2SO_4. Evaporation of the solvent yielded 5.7 g of a crude tosylate (**1c**). Recrystallization of the crude product from *n*-hexane–acetone gave fine needles, mp 186.5—187.5°, $[\alpha]_D^{22.5}$ −8.3±2° (*c*=0.997). *Anal.* Calcd. for $C_{34}H_{48}O_6S$: C, 69.83; H, 8.27. Found: C, 69.77; H, 8.30. IR ν_{max}^{Nujol} cm^{-1}: 3046, 1597, 1716, 1174.

Treatment of 1c with Basic Al_2O_3——A solution of **1c** (2.6 g) in benzene (130 ml) was heated at *ca.* 80° for 8 hr with E. Merck standardized basic Al_2O_3 (104 g). After filtration of Al_2O_3, the filtrate was removed *in vacuo*. The residue which showed small peaks of vinyl protons at 5.43 and 5.85 in NMR was purified by recrystallization from *n*-hexane–acetone to afford **3** (1.19 g) as prisms, mp 147.5—151°, $[\alpha]_D^{22.5}$ −29.3±2° (*c*=1.060). No material corresponding to **2** was isolated after recrystallization. *Anal.* Calcd. for $C_{27}H_{40}O_3$: C, 78.59; H, 9.77. Found: C, 78.42; H, 9.91. IR ν_{max}^{Nujol} cm^{-1}: 1713, 1643.

Treatment of 1c with Li_2CO_3——To a solution of **1c** (5.5 g) in DMF (80 ml) was added Li_2CO_3 (4.0 g) and the mixture refluxed with stirring for 5 hr under N_2 atmosphere. The solution was diluted with dil. HCl and extracted with CH_2Cl_2. After evaporation of the solvent, the residue was purified by Al_2O_3 chromatography followed by recrystallization from *n*-hexane–acetone to give 1.9 g of **3**, mp 143—147°, identical with the compound yielded by the above-mentioned procedure.

12α-Hydroxy-25D-spirosta-1,4-dien-3-one (**4b**)——To a solution of 12α-acetoxy-3-one[24] (**1a**) (8.8 g) in anhydrous dioxane (250 ml) was added DDQ (15 g) and the mixture was refluxed for 18 hr. After the usual work-up the resulting material was purified by Al_2O_3 chromatography followed by recrystallization from *n*-hexane–$CHCl_3$ to give **4a** (2.8 g), mp 256—258°, $[\alpha]_D^{23.5}$ −5.6±2° (*c*=1.063). *Anal.* Calcd. for $C_{29}H_{40}O_5$: C, 74.32; H, 8.60. Found: C, 74.40; H, 8.77. IR ν_{max}^{Nujol} cm^{-1}: 3028, 1628, 1604, 1740 (1245), 1665. The above acetate (**4a**) (2.7 g) was saponified with 5% methanolic KOH (70 ml) by heating on a steam bath for 1 hr and a crude product (2.5 g) was purified by recrystallization from *n*-hexane–$CHCl_3$ to yield **4b** (2.13 g), mp 234—237°, $[\alpha]_D^{23.5}$ −53.6±2° (*c*=1.112). *Anal.* Calcd. for $C_{27}H_{38}O_4$: C, 76.02; H, 8.98. Found: C, 76.02; H, 9.01. UV λ_{max} nm (ε): 246.5 (13800).

12α-Tosyloxy-25D-spirosta-1,4-dien-3-one (**4c**)——To a solution of **4b** (2.1 g) in pyridine (20 ml) was added *p*-toluenesulfonyl chloride (3.5 g) and the mixture was heated on a water bath (40—50°) for 5 hr, then allowed to stand overnight at room temperature. After the usual work-up the resultant gum was crystallized from *n*-hexane–acetone to afford **4c** (1.5 g), mp 197—198° (decomp.), as needles, $[\alpha]_D^{23}$ −0.6±2° (*c*=1.151). *Anal.* Calcd. for $C_{34}H_{44}O_6S$: C, 70.31; H, 7.64. Found: C, 70.20; H, 7.71. UV λ_{max} nm (ε): 228.5 (22100), 244 (15100); IR ν_{max}^{Nujol} cm^{-1}: 3020, 1631, 1606, 1671, 1191, 1175.

Treatment of 4c with Al_2O_3——Treatment of **4c** (500 mg) by basic Al_2O_3 (20 g) in 25 ml of benzene at 60—70° for 9.5 hr followed by working up as above gave an oily substance (243 mg), which was not crystallized after purification with TLC. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3042, 1671, 1633, 1608, 891.

Treatment of 4c with Li_2CO_3——Under the above-mentioned conditions, **4c** (130 mg) was heated with Li_2CO_3 (100 mg) in DMF (5 ml) solution under N_2 atmosphere for 4 hr and the mixture was worked up as usual. IR of thus obtained oily substance (50 mg) after purification with TLC was identical with that of the product obtained above.

25D,5α-Spirost-11-en-3-one (**2**)——To a solution of the already known spirost-11-en 3β-ol[25] (100 mg) in acetone (10 ml) was added Jones reagent (1.2 eq CrO_3) and the reaction mixture was stirred for 2 min under cooling. The mixture was worked up as usual to yield a crude ketone (**2**) (100 mg). The crude product was dissolved in benzene and passed through a short Al_2O_3 column and the eluate was crystallized from *n*-hexane–acetone to afford plates, mp 170—172°, $[\alpha]_D^{24}$ −26.4±4° (*c*=0.394). *Anal.* Calcd. for $C_{27}H_{40}O_3$: C, 78.59; H, 9.77. Found: C, 78.52; H, 10.02. IR ν_{max}^{Nujol} cm^{-1}: 2996, 1719.

25D-Spirosta-1,4,11-trien-3-one (**5a**)——To a solution of **2** (3.5 g) in anhydrous dioxane (100 ml) was added DDQ (8.0 g) and the mixture was refluxed for 21 hr. After filtration of the precipitated DDH, the solvent was removed *in vacuo*. The residue was purified by Al_2O_3 chromatography (eluted from benzene–ether=9: 1 fraction) followed by a further purification with preparative TLC to yield 0.52 g of **5a**. Almost pure **5a** (mp 188—190°) was obtained by recrystallization from a mixture of petroleum ether–CH_2Cl_2 as prisms, $[\alpha]_D^{24}$ −60.3±2° (*c*=1.106). *Anal.* Calcd. for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88;. Found: C, 79.57; H, 9.03. UV λ_{max} nm (ε): 246 (15300), 302.5. IR ν_{max}^{Nujol} cm^{-1}: 3033, 1627, 1607, 1667. A very weak absorption at 302.5 nm in UV suggested that this **5a** was contaminated with a small amount of **5b**. Purification with column chromatography, preparative TLC *etc.* were unable to remove completely the contaminated **5b** from above **5a**.

Partial Benzolyation of 5β-Androstan-3α,12α,17β-triol (**7a**)——To a solution of **7a**[8] (10 g) in a mixture of dry pyridine (120 ml) and dioxane (60 ml) was added benzoyl chloride (9.5 ml) slowly at 0° under ice cooling. The solution was left to stand for 17 hr at 0°, then at room temperature for additional 6 hr. After worked up as usual, the product was purified by Al_2O_3 chromatography followed by recrystallization from *n*-hexane

24) mp 220—221°, $[\alpha]_D^{23.5}$ −1.0±2° (*c*=1.033). (Lit. 6*b*). mp 214—217°).
25) mp 190—192°, $[\alpha]_D^{24.5}$ −40.9±2° (*c*=1.103). (Lit. 6*b*). mp 192—194°).

to give **7b** (9 g), mp 156—158°, as colourless prisms, $[\alpha]_D^{24}$ +88.6±1.1° (c=0.979). *Anal.* Calcd. for $C_{33}H_{40}O_5$: C, 76.71; H, 7.80. Found: C, 76.75; H, 7.72. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500, 1703.

5β-Androstan-3α,17β-diol-12-one (8a)——To a solution of **7b** (796 mg) in acetone (16 ml) was added Jones reagent (1.2 eq) at room temperature with stirring. After the usual work-up, oxidation product (762 mg) was recrystallized from *n*-hexane–acetone to give pure **8b**, mp 292—293° as fine needles, $[\alpha]_D^{24}$ +160.8 ±1.9° (c=0.965). *Anal.* Calcd. for $C_{33}H_{38}O_5$: C, 77.01; H, 7.44. Found: C, 76.89; H, 7.57. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1711. Saponification of **8b** was carried out with 5% methanolic KOH under reflux to give **8a**, mp 261—262° (recrystallized from MeOH–ether), $[\alpha]_D^{23.5}$ +96.7±2° (c=0.971). *Anal.* Calcd. for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.47; H, 9.92. IR ν_{max}^{Nujol} cm^{-1}: 3363, 1701.

Cathylation of 7a and Preparation of 8c——To an ice-cooled of **7a** (500 mg) in a mixture of dry pyridine (6 ml) and dioxane (3 ml) was added ethyl chloroformate (1 ml) dropwise and the mixture was left to stand for 18 hr at 0° and worked up as usual. Two kinds of oily substances, **7c** (280 mg) and **7d** (360 mg), were separated by preparative thick layer chromatography from the reaction products. The compound of 280 mg must be the 3,12,17-tricathylate (**7c**) because of no hydroxyl IR band, while the compound of 360 mg was assigned to the 3,17-dicathylate (**7d**) because it showed hydroxyl IR band at ~3600 cm^{-1} and an axial 12-hydroxyl group in steroids is belived to resist cathylation. Then, **7d** was oxidized with Jones reagent to give **8c**, mp 146—148°, as needles, $[\alpha]_D^{23.5}$ +106.4±2° (c=1.013). *Anal.* Calcd. for $C_{25}H_{38}O_7$: C, 66.64; H, 8.50. Found: C, 66.93; H, 8.62. IR ν_{max}^{Nujol} cm^{-1}: 1742 (1273), 1705. Hydrolysis of **8c** with 5% methanolic KOH afforded **8a**, mp 261—262°, identical with an authentic sample described above.

5β-Androst-11-ene-3α,17β-diol (11a) and Its Derivatives——a) *via* 12-Keto-3,17-dicathylate (**8c**): To a solution of **8c** (2 g) in $CHCl_3$ (16 ml) was added a solution of Br_2 (0.9 g) in $CHCl_3$ (4 ml) at room temperature and then the mixture was heated up to *ca.* 50° and left at the same temperature for 30 min. Solvent was removed *in vacuo* and the residue (**9c**) was dissolved in 95% EtOH (30 ml) and a 7% aqueous $NaHCO_3$ (10 ml) was added to this solution to keep alkaline. $NaBH_4$ (0.5 g) was added to the solution and the mixture was kept for 3 hr at room temperature with stirring. After worked up in the usual manner, a non-crystalline crude bromohydrin (**10c**) (2.1 g) was obtained. A solution of the crude **10c** in AcOH (30 ml) was refluxed for 4 hr with 10 g of Zn dust. After Zn was filtered and washed with CH_2Cl_2, the filtrate was diluted with H_2O and extracted with CH_2Cl_2. These CH_2Cl_2 extract and washings were combined, washed with aqueous NaOH solution, H_2O, dried over Na_2SO_4, and evaporated. Since crystallization of this crude **11c** was unsuccessful, saponification was carried out with 5% methanolic KOH to obtain 11-ene-diol (**11a**), mp 221—223° as colourless needles, after recrystallization from *n*-hexane–acetone, $[\alpha]_D^{24}$ +25.0±0.8° [MeOH–$CHCl_3$ (1:1)] (c=0.663). *Anal.* Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 79.07; H, 10.12. IR ν_{max}^{Nujol} cm^{-1}: 3293, 3007, 1628.

b) *via* 12-Keto-3,17-dibenzoate (**8b**): To a solution of **8b** (5 g) in $CHCl_3$ (50 ml) containing two drops of 4N HBr–AcOH was added a solution of Br_2 (2 g) in $CHCl_3$ (10 ml) dropwise with heating at 40—50° and the mixture was left to stand at the same temperature for 2 hr. After the solvent was removed *in vacuo*, the residue was dissolved in a mixture of ether and $CHCl_3$ and the solution was washed with aqueous Na_2CO_3, H_2O, dried over Na_2SO_4, and evaporated to give 6.65 g of **9b**, mp 207—210° (recrystallized from EtOH), $[\alpha]_D^{22}$ +71.7±6° (c=0.364). *Anal.* Calcd. for $C_{33}H_{37}O_5Br$: Br, 13.46. Found: Br, 12.14. This crude **9b** (6.6 g) was reduced with $NaBH_4$ (2.5 g) as in (a) to give an oily bromohydrin (**10b**) (5.6 g). Crude **10b** (4.3 g) was treated with Zn dust by the procedure described above to give 565 mg of crystalline **11b** (eluted from petroleum ether–ether on Al_2O_3 chromatography), mp 139—140° (recrystallized from *n*-hexane–ether), $[\alpha]_D^{24}$+96.1±1.2° (c=1.128). *Anal.* Calcd. for $C_{33}H_{38}O_4$: C, 79.17; H, 7.65. Found: C, 79.37; H, 7.74. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3070, 3007, 1723 (1277), 1603, 1584.

Saponification of **11b** in the usual manner afforded **11a** which was purified by recrystallization from *n*-hexane–$CHCl_3$ and melted at 229—230°.

c) *via* 12-Keto-3,17-diacetate (**8d**)[9]: Twenty grams of the diacetate (**8d**),[26] mp 194—197° obtained from **8a** by an action of Ac_2O in pyridine, was dissolved in a mixture of AcOH (320 ml) and a few drops of 4N HBr–AcOH and to this added a solution of Br_2 (10 g) in 80 ml of AcOH at 50° according to the above described manner and the mixture was left to stand for 3 hr with stirring. The mixture was worked up as usual to give 30 g of a crude bromo-ketone **9d**. A portion of this was recrystallized from EtOH and showed mp 139—145°. ORD of this bromo-ketone indicated that this substance was a mixture of the epimeric α- and β-bromo-ketones.[9] (*Anal.* Calcd. for $C_{23}H_{33}O_5Br$: Br, 17.02. Found: Br, 17.73). $NaBH_4$ reduction of the remainder of crude **9d** followed by treatment with Zn as described in the case of **9b** or **9c** gave *ca.* 20 g of a crude olefin (**11d**). It was chromatographed on Al_2O_3 (E. Merck standardized) to give an oily **11d** (6.5 g). Recrystallization of this from *n*-hexane–ether gave colourless prisms, mp 102—105°,[27] $[\alpha]_D^{23}$+42.0±2° (c= 1.047). *Anal.* Calcd. for $C_{23}H_{34}O_4$: C, 73.61; H, 9.15. Found: C, 74.20; H, 9.20.

5β-Androst-11-en-17β-ol-3-one 17-Acetate (12a)——To a solution of **11d** (17 g) in MeOH (800 ml) was added at 0° Na_2CO_3 saturated in a mixture of MeOH (280 ml) and H_2O (40 ml) and the mixture was kept at

26) $[\alpha]_D^{23}$ +125.1±1.7° (c=0.985), IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1723. (Lit. 9). mp 193—194°).
27) Lit. 10). mp 96°.

room temperature for 2 days. This solution was poured into a saturated aqueous NaCl solution and extracted with $CHCl_3$ and the extract was worked up as usual. Separation of the reaction mixture by Al_2O_3 chromatography afforded **11d** (6.5 g) from benzene fraction, the desired 17-monoacetate **11e** (6 g) from benzene–ether fraction, and **11a** (2 g) from benzene–MeOH fraction. Pure **11e** melted at 153—155° and was identical with the data reported in the literature,[10] $[\alpha]_D^{24}+21.9\pm0.5°$ ($c=1.704$). *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 76.02; H, 9.96. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3595, 1729. NMR: 0.85 (s, 3H), 0.88 (s, 3H), 2.04 (s, 3H), 3.57 (m, 1H), 4.22 (m, 1H), 5.44 (q, $J=10$ and 2 Hz), 5.88 (q, $J=10$ and 3 Hz).

11e (1.0 g) was oxidized with Jones reagent in the usual manner to give **12a** (1.0 g). This was recrystallized from *n*-hexane–CH_2Cl_2 to give pure **12a**, mp 109—110°, as prisms, $[\alpha]_D^{24}+23.8\pm0.5°$ ($c=0.973$). *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.04; H, 9.15. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3023, 1742 (1244), 1722.

3-Ethyleneketal Derivative (12b)——To a suspension of **12a** (8.1 g) in 700 ml of ethylene glycol was added *p*-TsOH·H_2O (0.5 g) and ethylene glycol was distilled slowly *in vacuo* during 7 hr at 88°. The residue was poured into 5% aqueous Na_2CO_3 solution under cooling and extracted with ether–CH_2Cl_2. Since IR of the residue (9.0 g), after evaporation of the solvent, showed no acetyl band, it was again acetylated with Ac_2O (20 ml) in pyridine (50 ml) and worked up as usual. The resulting oil was chromatographed on Al_2O_3 to give 9.7 g of **12b**. Crystallization from petroleum ether–ether gave pure **12b**, mp 93—95° as colourless needles, $[\alpha]_D^{24}+22.2\pm0.5°$ ($c=1.055$). *Anal.* Calcd. for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.91; H, 9.01. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3016, 1741 (1245), 1099.

Bromination of 12b——To a solution of **12b** (900 mg) in anhydrous THF (9 ml), trimethylphenylammonium perbromide (1.1 g) was added at room temperature. After standing for 5 min, the reaction mixture was poured into 5% aqueous $NaHCO_3$ and extracted with ether and worked up as usual. A resultant oily bromide (1.305 g), without further purification, was treated with 70% $HClO_4$ (1.5 ml) in a mixture of AcOH (20 ml) and H_2O (5 ml) and the reaction mixture left to stand for 16 hr at room temperature to remove the protecting group. The crystalline product was recrystallized from *n*-hexane–acetone to give **13**, mp 152—155°, $[\alpha]_D^{23}+22.6\pm0.3°$ ($c=0.982$). *Anal.* Calcd. for $C_{21}H_{29}O_3Br$: Br, 19.52. Found: Br, 19.33. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3012, 1739 (1244).

Dehydrobromination of 13——To a stirred solution of **13** (700 mg) in DMF (15 ml) was added Li_2CO_3 (1.0 g) and the mixture was heated at 90—100° for 20 hr under N_2 atmosphere. The mixture was poured onto H_2O and extracted with CH_2Cl_2–ether. The extract was washed with dil. HCl, H_2O, and dried over Na_2SO_4. The residue, after evaporation of the solvent, was separated by preparative TLC with benzene–ether (4: 1) to give two fractions: one of which was recrystallized from *n*-hexane–CH_2Cl_2 to give $\Delta^{1,11}$-dienone (**14**) (fine needles, 64 mg), mp 156—159°, $[\alpha]_D^{23}+143.9\pm1.7°$ ($c=1.001$). *Anal.* Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.43; H, 8.43. UV λ_{max} nm (ε): 226.5 (9720). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3031, 1744 (1245), 1689, 1619. The other was recrystallized from the same solvent to give $\Delta^{4,11}$-dienone (**15**) (prisms, 168 mg), mp 160—162°, $[\alpha]_D^{23}+109.0\pm1.3°$ ($c=1.035$). *Anal.* Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.76; H, 8.38. UV λ_{max} nm (ε): 239.5 (16100). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3018, 1742 (1242), 1679, 1620.

In another run using 9.65 g of **13**, the following three fractions were separated by preparative thick layer chromatography: **14** (1.303 g), crude **15** (2.50 g) and $\Delta^{1,4,11}$-trienone (**16b**, 0.833 g).

UV absorptions of the crude **15** at 238 and 287 nm suggested that this material was contaminated with $\Delta^{4,6,11}$-trienone (**15b**). To eliminate the impurity, 100 ml of aqueous $Na_2S_2O_5$ (15 g) solution was added to a solution of the crude **15** (2.4 g) in MeOH (150 ml) and the solution was refluxed for 4 hr and extracted with CH_2Cl_2. After working up as usual, UV of the thus obtained **15a** (1.88 g) indicated that the contaminated trienone (**15b**) absorbing at 287 nm was almost removed.

Purification of the 3rd fraction (**16b**) shown above by Al_2O_3 chromatography and TLC followed by recrystallization from *n*-hexane–acetone gave pure trienone (**16b**), mp 144—145°, $[\alpha]_D^{23}+52.7\pm4.5°$ ($c=0.205$). *Anal.* Calcd. for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 77.14; H, 8.07. UV λ_{max} nm (ε): 245 (15700).

Dehydrogenation of 14 or 15a with SeO_2——i. To a solution of **14** (400 mg) in a mixture of *t*-BuOH (20 ml) and pyridine (0.2 ml), SeO_2 (244 mg) was added and the mixture was refluxed for 14.5 hr under N_2 atmosphere and worked up as usual. Since the crude product was not crystallized, it was hydrolyzed with methanolic KOH to give crystalline **16a** (40 mg). A pure sample melted at 147—149°. *Anal.* Calcd. for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.17; H, 8.46. UV λ_{max} nm (ε): 245 (14100).

Reacetylation of **16a** with Ac_2O in pyridine gave the acetate **16b**, mp 140—142° (needles) which was identical with an authentic sample.

ii. Preparation of **16b** was also carried out from **15a** (50 mg) with SeO_2 (30 mg) by the procedure described as above. The reaction product was purified by Al_2O_3 chromatography followed by recrystallization from petroleum ether–ether to give **16b** (8 mg), mp 140°, identified with an authentic sample.

Dehydrogenation of 15a with DDQ——**15a** (1.85 g) was dehydrogenated with DDQ (1.4 g) as described in the case of the spirost-11-en-3-one (**2**) to give a crude **16b** (1.172 g), mp 150—152°. As UV of this crude material indicated that it was contaminated with a considerable amount of the tetraenone (**17**), **17** was removed by repeated crystallization from *n*-hexane–acetone as far as possible. The residue of the mother liquor was purified by Al_2O_3 chromatography followed by recrystallization from petroleum ether–ether to give almost pure **16b** (485 mg), mp 137—140°.

II. Structure Determination of the Acetolysis Products

Acetolysis of 5a——A solution of **5a** (100 mg) in 5 ml of AcOH containing 1% Ac_2O was heated at 90° in a sealed tube for 96 hr. The solution was poured onto ice water and extracted with CH_2Cl_2. After working up as usual the residue was separated by preparative TLC (KG. benzene: ether=9: 1) to obtain 2 mg of oily **19b** (2%) and 49.5 mg of oily **18c** (40%) with recovery of 41 mg of crystalline **5a** (41%) contaminated with **5b**.

Yields on Text were corrected for the recovered **5a**.

Structure of 18c——After $LiAlH_4$ (5 mg) was added to a stirring solution of **18c** (40 mg) in anhydrous ether (5 ml) at room temperature, excess of $LiAlH_4$ was decomposed with AcOEt under ice cooling. After H_2O was added and the organic layer was separated, and aqueous layer was extracted with CH_2Cl_2–ether. The combined extracts were washed with dil. HCl. H_2O, dried over Na_2SO_4 and evaporated to give 40 mg of a colorless oil **18a**. This oil showed no absorption corresponding to an acetoxyl group in IR.

To a solution of **18a** (35 mg) in pyridine (1.3 ml) and $CHCl_3$ (1.3 ml) was added Ac_2O (0.33 ml) at 0° and the mixture left to stand for 3.5 hr at the temperature. The solution was worked up as usual and the acetylated substance was separated by preparative TLC (KG. benzene: ether=4: 1) to give an oily **18c** (13 mg) and crystalline **18b** (15 mg). Recrystallization of crude **18b** from *n*-hexane–acetone gave fine needles, **18b**, mp 88—90°. This monoacetate was identical with that obtained by acetolysis of 11α-tosyloxy-25D-spirosta-1,4-dien-3-one in all respects.

Structure of 19a——a. Reaction of **5a** with $LiClO_4$: To a solution of **5a** (192 mg) in AcOH (10 ml) containing 1% Ac_2O was added $LiClO_4$ (0.532 g) and the mixture heated at 90° for 19.5 hr and worked up as described above to give an oily residue (230 mg). Purification by preparative TLC gave crystalline **19a** in a yield of 52%, mp 204—206° (from petroleum ether–ether), $[\alpha]_D^{24}$ −343.7±7.3° [MeOH–$CHCl_3$ (1: 1)] (c=0.490). *Anal.* Calcd. for $C_{27}H_{36}O_3$: C, 79.37; H, 8.88. Found: C, 79.56; H, 8.94. UV λ_{max} nm (ε): 280—286 (2480): IR ν_{max}^{Nujol} cm^{-1}: 3340, 3028, 1588. NMR: 0.94 (s, 3H), 2.16 (s, 3H), 3.83 (d-t, J=8 Hz, 1H), 5.93 (2H), 6.47 (d, $J\fallingdotseq$8 Hz, 1H), 6.80 (d, $J\fallingdotseq$8 Hz, 1H).

Treatment of **19a** with Ac_2O and pyridine gave an acetate (**19b**), mp 174—176° (prisms, from acetone), $[\alpha]_D^{24}$ −336.0±7.2° (c=0.475). *Anal.* Calcd. for $C_{29}H_{38}O_4$: C, 77.30; H, 8.50. Found: C, 77.27; H, 8.42. UV λ_{max} nm (ε): 265.5 (360); 274.4 (280). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3003, 1762, 1203, NMR: 0.92 (s, 3H), 2.21 (s, 3H), 2.28 (s, 3H), 3.65 (1H), 5.70 (q, J=10 and 2 Hz), 5.93 (q, J=10 and 1 Hz), 6.78 (d, $J\fallingdotseq$8 Hz, 1H), 6.98 (d, $J\fallingdotseq$8 Hz, 1H).

b. Oxidation of **19b** with RuO_4: To a RuO_4 solution prepared from RuO_2 (8 mg) suspended in CCl_4 (2 ml) by an action of $NaIO_4$ (21 mg)–H_2O (2 ml), a solution of **19b** (12 mg) in CCl_4 (2 ml) was added at room temperature with stirring and the mixture stood for 1 hr. The black percipitate was filtered off after addition of 3 drops of MeOH, and the solvent was evaporated without heating. Since an oily residue obtained was very labile, it was dissolved in CCl_4 and examined by the IR. IR of this crude **21** showed absorptions corresponding to an aldehyde group. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1765, 1723, 2766.

c. Hydrogenation of **19b**: **19b** was reduced catalytically with 10% Pd-C in acetone at room temperature. The product was recrystallized from petroleum ether to give **20**, mp 142—144°, $[\alpha]_D^{24}$ −141.3±2.4° (c=0.741). *Anal.* Calcd. for $C_{29}H_{40}O_4$: C, 76.95; H, 8.91. Found: C, 76.63; H, 8.86. UV λ_{max} nm (ε): 267 (287), 273 (239). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3080, 1766 (1207).

Dienone-phenol Rearrangement of 22——To a solution of **22** (500 mg) in dioxane (10 ml) was added conc. HCl (20 ml) and the solution was refluxed for 2 hr. H_2O was added and the organic substance extracted with ether. The ether extract was washed, dried and evaporated *in vacuo* to give an oily residue (500 mg). The resulting residue was separated by preparative TLC (KG. benzene: ether=4: 1) into two fractions: yellow oily substance (**23a**) (180 mg) and yellow oil (**24a**) (110 mg). As both substances were very unstable, each of them was acetylated with Ac_2O in pyridine. The former was purified by TLC followed by recrystallization from petroleum ether–ether to give pure **23b**, mp 182—184°, $[\alpha]_D^{25}$ +69.1±5° (c=0.320). *Anal.* Calcd. for $C_{29}H_{40}O_4$: C, 76.95; H, 8.91. Found: C, 76.70; H, 9.01. UV λ_{max} nm (ε): 268 (345), 276 (277). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1762, 1209.

From the latter, crystalline **24b**, mp 214—216°, was obtained by recrystallization from *n*-hexane–$CHCl_3$, then from *n*-hexane–AcOEt. **24b** was identified with an authentic sample.

Acetolysis of 16b——Into a 0.5N AcONa–AcOH solution containing 5% Ac_2O was dissolved **16b** and the solution heated at 90±5° for 190 hr. The reaction mixture was poured into a saturated NaCl solution and extracted with CH_2Cl_2. The extract was washed with 5% $NaHCO_3$ solution, H_2O, dried and evaporated.

The residue was separated by preparative TLC to give four products; oily **27c**, oily **26c**, oliy **25c**, and crystalline **25d**, with recovery of some **17**. Yields in total were quantitative and ratios of theoretical yields of the products were 5.2: 21.3: 67.8: 5.7, respectively. *Rf* values on TLC (KG. benzene: ether=5: 1) were 0.68 for **27c**, 0.45 for **26c**, 0.38 for **25c**, 0.30 for **25d**, and 0.19 for **17**; retention time on VPC (1.5% XE-60 on 80—100 mesh Gas Chrom Q packed in stainless steel (0.75 m×3 mm) column, oven temperature at 205° with a flow rate of N_2 in 79 ml/min) were 3.4 min for **27c**, 5.2 for **17**, 6.1 for **25c**, 7.5 and 8.5 for **26c** and 13.0 for **25d**, respectively.

Structure of 25c——Oil, $[\alpha]_D^{23}$ +76.1±1.2° (c=1.012). UV λ_{max} nm (ε): 267.5 (626), 274 (608). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3023, 1761 (1210, 1193), 1740 (1243), 1611, 1586. NMR: 0.85 (s, 3H), 1.99 (s, 3H), 2.04 (s, 3H), 2.24

(s, 6H), 4.97 (m, 1H), 5.84 (m, 2H), 6.69—7.18 (ABK, 3H).

a. Conversion of **25c** to **25b**: A solution of **25c** (250 mg) in anhydrous ether (15 ml) was added to a ether solution (25 ml) of $LiAlH_4$ (50 mg) at room temperature and stirred for 3 hr. AcOEt was then added to decompose the excess $LiAlH_4$ under ice cooling. After addition of a saturated aqueous NaCl solution, the mixture was extracted with CH_2Cl_2. The extract was washed, dried, and evaporated *in vacuo* to give an oil, **25a** (170 mg), which was acetylated with Ac_2O in a mixture of pyridine and CH_2Cl_2 (1: 1). The solution was worked up as usual and products were separated by preparative TLC (KG. 750 μ, benzene: AcOEt=1: 3) to give 91 mg of **25b** and 100 mg of a mixture of di- and triacetate. Recrystallization of **25b** from *n*-hexane–ether gave fine needles, mp 70—72°, $[\alpha]_D^{23}-5.9\pm1°$ ($c=0.461$). *Anal.* Calcd. for $C_{21}H_{28}O_4\cdot1/2H_2O$: C, 71.36; H, 8.27. Found: C, 71.33; H, 8.55. UV λ_{max} nm (ε): 267 (605), 273.7 (585). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3670, 3610, 3430, 1754, 1635, 1611, 1589.

b. Oxidation of **25b** with CrO_3–pyridine Complex: A solution of **25b** (27 mg) in pyridine (1 ml) was added to CrO_3 (40 mg)–pyridine (1 ml) complex and the mixture left to stand at room temperature for 2 days. This was extracted with AcOEt and worked up as usual. The residue was purified by preparative TLC (GF_{254}, 750 μ, benzene: ether=2: 3) to give two fractions. The less polar fraction was an oily **30** (8 mg) which was identified by IR with that resulted from **25b** by the following DDQ oxidation. The more polar fraction was a diketone (**31**) (14 mg) which was recrystallized from *n*-hexane–ether to give prisms (4 mg), mp 125—126.5°, $[\alpha]_D^{23}+62.9\pm1.2°$ ($c=0.855$). *Anal.* Calcd. for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 73.94; H, 6.92. UV λ_{max}nm (ε): 218 (16800). NMR: 1.17 (s, 3H), 2.27 (s, 3H), 2.31 (s, 3H), 5.95 (q, $J=$ 10.0 and 2.5 Hz), 6.85 (1H), 6.75—7.25 (3H).

c. DDQ Oxidation of **25b**: A mixture of **25b** (10 mg) and DDQ (10 mg) in anhydrous dioxane (1 ml) was heated at 95° for 8.5 hr. The residue was purified by TLC to give 4 mg of an oily **30**. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3500, 3600, 1765 (1190), 1685, 1645.

d. $NaBH_4$ Reduction of **30**: The α,β-unsaturated ketone (**30**) (25 mg) was reduced with $NaBH_4$ (20 mg) in MeOH (1 ml) at room temperature with stirring for 2 hr. The reaction mixture was poured into an aqueous NaCl solution and extracted with CH_2Cl_2. The extract was washed with H_2O and evaporated to give 21 mg of an oily substance. This oil was acetylated with Ac_2O (0.5 ml) in pyridine (1 ml). The acetylated substance was purified with TLC (KG. benzene: ether=5: 1) to give an oily **25c** (2 mg) and a crystalline **25d** (18 mg). The former was identical with the product obtained from the acetolysis of **16b** when compared with IR, TLC and VPC. The latter was recrystallized from *n*-hexane–ether to give pure **25d** (13 mg) mp 128.5—129.5°, identical with the acetolysis product of **16b**, $[\alpha]_D^{23}-88.3\pm2.8°$ ($c=0.452$). *Anal.* Calcd. for $C_{25}H_{32}O_6$: C, 70.07; H, 7.53. Found: C, 70.00; H, 7.72.

e. Hydrogenation of **25c**: **25c** (120 mg) was hydrogenated with 10% Pd-C (100 mg) in AcOEt (25 ml). The reduced substance was separated by preparative TLC (GF_{254}, 750 μ, benzene: ether=6: 1) to give three fractions. The less polar substance (2 mg) was deduced as **28** from IR, in which intensities of the bands corresponding to a phenyl acetate and to an aliphatic acetate are almost equal. **28** was not further investigated due to insufficiency of the material. From the middle fraction a mixture (37 mg) of the starting material (**25c**) and a saturated product (**29**) was obtained. From the polar fraction 66 mg of an oily **29** was yielded. $[\alpha]_D^{23}+24.2\pm0.7°$ ($c=0.906$). UV λ_{max}nm (ε): 267 (591), 273.8 (575). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3012, 1762 (1191), 1740 (1244), 1614, 1588. NMR: 0.88 (s, 3H), 1.99 (s, 3H), 2.06 (s, 3H), 2.26 (s, 6H), 4.83 (t, $J\fallingdotseq2.5$ Hz, 1H), 4.96 (m, 1H), 6.69—7.19 (ABK, 3H).

Structure of 25d——Needles, from *n*-hexane–ether, mp 127.5—130.5°. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1767, 1750, 1245, 1210, 1192. NMR: 0.91 (s, 3H), 1.99 (s, 3H), 2.02 (s, 3H), 2.26 (s, 6H), 4.75—5.37 (m, 2H), 5.52—5.90 (m, 2H), 6.72—7.27 (ABK, 3H). This substance was identical with the substance obtained by $NaBH_4$ reduction of α,β-unsaturated ketone (**30**) followed by acetylation.

Structure of 26c——Oil, $[\alpha]_D^{23}-3.7\pm0.6°$ ($c=0.764$). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1766 (1211), 1743 (1234). NMR: 0.87 (s), 0.96 (s), 2.05, 2.25, 6.68—7.18.

a. Saponification of **26c** with $LiAlH_4$: To a stirred suspension of $LiAlH_4$ (100 mg) in ether (25 ml), **26c** (106 mg) in anhydrous ether (10 ml) was added at room temperature and the mixture was stirred for 3.5 hr and worked up. The saponified substance (84 mg) was partially acetylated with Ac_2O (0.9 ml) in a mixture of pyridine (3.5 ml) and CH_2Cl_2 (3.5 ml) under cooling at 0° during 40 min. After worked up, an oily residue was purified by preparative TLC to give an oily phenylacetate (**26b**) (58 mg) and a mixture of di- and triacetate (24 mg). For **26b**, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3520—2960, 1753. A portion of the phenylacetate (**26b**) was again led to a triacetate which was subjected to vpc examination (*cf.* page 263). VPC showed that the oily triacetate was a mixture of two isomers in almost equal amount. The following oxidation clarified that this mixture is C-9 configurational epimers.

b. Oxidation of **26b** with CrO_3: To a solution of the phenylacetate (**26b**) (55 mg) in pyridine (2 ml) was added with CrO_3 (80 mg)–pyridine (2 ml) complex at room temperature and the mixture left to stand for 2 days. The product was purified with preparative TLC (GF_{254}, 750 μ, benzene: ether=1: 2) followed by recrystallization from *n*-hexane–ether to give diketone (**32**) (41 mg, prisms), mp 141—143°, $[\alpha]_D^{23}+34.9\pm$ 1.3° ($c=0.551$). *Anal.* Calcd. for $C_{21}H_{24}O_4$: C, 74.09; H, 7.11. Found: C, 74.08; H, 7.04. UV λ_{max}nm (ε): 213 (17400). NMR: 1.11 (s, 3H), 2.26 (s, 3H), 2.31 (s, 3H), 5.93 (d, $J=10.0$ Hz), 7.26 (d, $J=10$ Hz), 6.70 —7.18 (ABK, 3H).

c. Hydrogenation of **32**: A mixture of diketone (**32**) (15 mg) and 10% Pd-C (50 mg) in acetone (20 ml) was shaken with H_2. After working up as usual, the residue was recrystallized from *n*-hexane–acetone to give **33** (12 mg), mp 145.5—147.5°. This compound was identical with that of the authentic sample (mp 144.5—148°) obtained from androst-4-en-3,17-dione by microbial transformation, reported by E. Kondo, *et al.*[21]

Structure of 27c——Oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1758, 1739, 1239, 1204.

a. Partial Saponification of **27c**: To a solution of an oily **27c** (22 mg) in benzene (5 ml) was added Al_2O_3 (E. Merck standardized) (5 g) and the mixture left overnight at room temperature. After filtrarion of Al_2O_3, the mixture was treated with preparative TLC followed by recrystallization from *n*-hexane–acetone to give pure **27b** (2.5 mg) mp 165.5—168° (fine needles), $[\alpha]_D^{23}$ −303.3±6.3° (c=0.552). *Anal.* Calcd. for $C_{21}H_{26}O_3$: C, 77.27; H, 8.03. Found: C, 76.73, 76.55; H, 7.77, 8.04. (Calcd. for $C_{21}H_{26}O_3 \cdot 1/2CH_3COCH_3$: C, 76.02; H, 8.22). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3610, 3450, 3020, 1736, 1718 (acetone?), 1590, 1264, 1242. NMR: 0.96 (s, 3H), 2.06 (s, 3H), 2.15 (s, 3H), 3.86 (1H), 4.71 (m, 1H), 5.93 (q, J=10.0 and 1.5 Hz), 6.16 (q, J=10.0 and 2.1 Hz), 6.48 (d, J=8 Hz), 6.81 (d, J=8 Hz).

b. Rearrangement of **16b**: With $LiClO_4$: To a solution of **16b** (50 mg) in glacial AcOH (5 ml) was added $LiClO_4$ (100 mg) and the mixture heated at 90±2° for 19 hr. The mixture was poured into H_2O and extracted with CH_2Cl_2. The extracts were washed with 5% $NaHCO_3$, H_2O, and dried over Na_2SO_4. The solvent was removed and the oily residue was purified by preparative TLC (KG. 750 μ, benzene: ether=7: 1) to give 30 mg (60%) of **27b**. Recrystallization from *n*-hexane–acetone gave pure **27b**, mp 160—162° (fine needles).

With *p*-TsOH: To a solution of **16b** (50 mg) in dioxane (5 ml) was added *p*-TsOH·H_2O (790 mg) and the mixture heated at 95° for 1 hr. The mixture was poured into a saturated aqueous NaCl solution and extracted with CH_2Cl_2. The extracts were washed with 5% $NaHCO_3$, H_2O, dried over Na_2SO_4, and evaporated to dryness. The residual oil without purification was acetylated with Ac_2O (2 ml) in pyridine (5 ml), and worked up in the usual manner. To a solution of acetylated substance in benzene (8 ml) was added 5.0 g of Al_2O_3 and the mixture left to stand at room temperature for 31 hr. After removal of the solvent, the residue was purified by preparative TLC (KG. 750 μ, benzene: ether=7: 1) to give **27b** (20 mg). Recrystallization from *n*-hexane–acetone afforded pure **27b**, mp 164—165°, identical with the specimen obtained by the above-mentioned procedure.

c. Conversion of B-seco Steroids into A-aromatic B/C *cis* Steroid: From A-aromatic B-seco $\Delta^{9(11)}$-12α-Allyl Acetate (**25c**): To a solution of **25c** (43 mg) in glacial AcOH (4.0 ml) was added 88 mg of $LiClO_4$ and the mixture heated at 90±2° for 19 hr. Working up as described in the case of **16b** with $LiClO_4$ gave 22 mg of an oily residue. The residue was treated with Al_2O_3 as above to give **27b** (10 mg), mp 165—167°.

From A-aromatic B-seco $\Delta^{11(12)}$-9-Allyl Acetate (**26c**): To a solution of an oily **26c** (40 mg) in glacial AcOH (5 ml) was added 80 mg of $LiClO_4$ and the mixture treated as described in the case of **16b**. The crude resulting product was separated by preparative TLC (KG. 750 μ, benzene: ether=5: 1) into two fractions. From the less polar fraction was obtained **27c** (14 mg). From the more polar fraction was yielded **27b** (9 mg), mp 164—166° (from *n*-hexane–acetone).

d. Hydrogenation of **27b**: **27b** (41 mg) was hydrogenated with 10% Pd-C (100 mg) in acetone (20 ml) to give **34a**. Recrystallization from *n*-hexane–acetone yielded pure **34a** (25 mg), mp 203—204.5°, $[\alpha]_D^{25}$ −71.1 ±1.2° (c=0.959). *Anal.* Calcd. for $C_{21}H_{28}O_3$: C, 76.79; H, 8.59. Found: C, 76.95; H, 8.61. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3594, 3424, 2994, 1724, 1589. **34a** was acetylated with Ac_2O in pyridine to give crystalline **34b**. Recrystallization from *n*-hexane–ether yielded pure **34b**, mp 114—116° (prisms), $[\alpha]_D^{23}$ −77.8±1.9° (c=0.636). *Anal.* Calcd. for $C_{23}H_{30}O_4$: C, 74.56; H, 8.16. Found: C, 74.66; H, 8.19.

Androsta-1,4,6,11-tetraen-3-one (17)——A product from DDQ dehydrogenation of **15a** was purified by recrystallization from *n*-hexane–acetone to give pure **17**, mp 166—169°, $[\alpha]_D^{20}$ +5.7±0.5° (c=0.990). *Anal.* Calcd. for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46. Found: C, 77.62; H, 7.61. UV λ_{max}nm (ε): 224 (11000), 256.5 (9450), 302.5 (11500).

III. Kinetics on 16b

Approximate 25 mg of the sample (**16b**) was weighed into a 25 ml volumetric flask and filled with a 95.0: 5.0 (w/w) mixture of glacial AcOH and Ac_2O containing a definite amount of anhydrous *p*-TsOH. The flask was immersed in a constant temperature bath and aliquots, 2 ml portions of the reaction solution at a reaction temperature, were withdrawn from the flask avoiding the moisture under N_2 stream at an appropriate time interval. A given amount of 17β-acetoxyandrost-4-en-3,11-dione (internal reference for vpc analyses) was added to the aliquots and extracted with CH_2Cl_2. The extract was washed with a saturated aqueous NaCl solution, dried over Na_2SO_4, and evaporated. The resultant residue was acetylated with Ac_2O and pyridine as usual and the acetylated products were examined with vpc.

1% Diethylene glycol succinate on Gas Chrom Q packed in a stainless steel column (0.75 m×3 mm) was used and the oven temperature maintained at 205° during the analyses. Retention times were as follows; 2.9 min for **27c**, 4.3 for **16b**, 5.7 for **25c**, 6.8 and 7.7 for **26c**, 11.6 for **25d** and 10.2 for the internal reference. The peak areas were estimated with the usual half-width method. Plots of log (A-At) (A and At represent the peak areas at the initial and any times) *vs* time showed a straight line. Rate constants were obtained with the least square method by using FACOM 270-30 and listed in Table II.

Isomerization of 26c in Acid——To 2 ml of a 95.0: 5.0 (w/w) mixture of AcOH and Ac_2O containing *p*-TsOH in the concentration of 0.0054N was added **26c** (2.0 mg) and the mixture allowed to stand at 20.0± 0.03° in a constant temperature bath for 10 half-lives, during which almost complete isomerization of **16b** takes place. The material, extracted with CH_2Cl_2 from the reaction mixture, was acetylated and examined with vpc. A product (**25c**) was observed which corresponds to *ca.* 9% isomerization.

In another run, 0.0112N *p*-TsOH was used and the reaction products were treated as above. Formation of **25c** in about 17% yield was observed.

IV. Intramolecular Aromatic Substitution of 25b

Approximate 25 mg of the sample **25b** was weighed into a 25 ml volumetric flask and filled with a 95.0: 5.0 (w/w) mixture of glacial AcOH and Ac_2O containing 0.1951N *p*-TsOH ($H_0 = -1.86$).

The flask was allowed to stand in a bath maintained at 80.0° and 2 ml portions of the reaction mixture was withdrawn. To each of aliquots was added a given amount of 3α,17β-diacetoxy-5β-androstan-12-one (internal reference for vpc), extracted, and the extract was acetylated before analyses. Amounts of **25c**, **25d**, and **27c** were estimated from vpc by using a calibration curve and the results were shown in Fig. 2.