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Linear Steroid Analogues. II.[1] Syntheses of Linear Progesterone and Testosterone Analogues

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The syntheses of linearly disposed progesterone and testosterone analogues are described.

On the way of the syntheses, a plausible reaction path for the catalytic hydrogenation of the α,β-unsaturated ketone (**11a**) to the saturated ketone (**20a**) is discussed.

The stereochemistry of the alumina catalysed condensation products of 3β,20β-diacetoxy-8,9-*seco*-5α-pregnane-8,9,11-trione, not fully established in the previous paper, has been determined in the light of accumulated nulear magnetiə rlsonanel (NMR) data.

In the preceding paper[1] we determined the frameworks of some linear steroid analogues and proposed the likely stereochemistry of these compounds, though the configuration of position 7 was still mainly in question.

A series of compounds are presented here and the substituent effects on the chemical shift of the angular methyl groups have made determination of the stereochemistry possible.

Finally, the transformation of these compounds into linear analogues of progesterone and testosterone has been achieved.

We are also interested in the hormonal activities of these linear type steroids in comparison with their natural analogues, and these results will be presented elsewhere.

3β, 20β-Diacetoxy-9(8→7), 8(9→11)-diabeo-5α, 7α, 11β, 14β-pregnane (8)

The keto-diol-monoacetate (**2**), obtained from the diketo–ol (**1**) in three steps,[1] was dehydrated by thionyl chloride in pyridine to give the enone–ol-acetate (**3**). Refluxing compound (**3**) in acetic acid resulted in epimerization at C-14, giving the 14β-epimer (**4**).

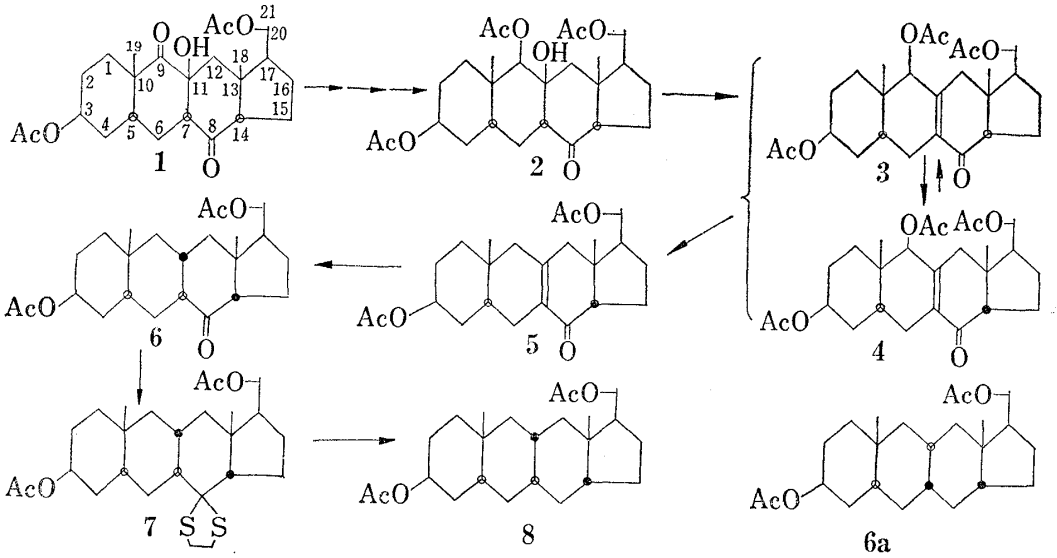


Chart 1

1) Part I: S. Aoyama and K. Sasaki, *Chem. Pharm. Bull.* (Tokyo), **18**, 481 (1970).
2) Location: *Fukushima-ku, Osaka.*

Thus, the hydrogenolysis of (**3**) with zinc powder in acetic acid gave the enone (**5**) in about 60% yield.

The signals of the 18-methyl protons for the epimers (**3**) and (**4**) are distinctly different; τ 9.32 for the 14α-, τ 9.03 for the 14β-epimer. The enone (**5**) exhibits an 18-methyl signal at τ 9.03 and should therefore have the 14β-configuration. On reduction with lithium in liquid ammonia, a reaction generally expected to give a thermodynamically stable product, **5** gave the presumably BC *trans*–product (**6**) which was not epimerized by alkali treatment. The alternative structure (**6a**) would have a boat or twist system for ring B, and this seems improbable from a model inspection. The ketone (**6**) exhibited a positive Cotton effect (**a**, +128°), consistent with the value expected from the octant diagrams[3] (**6-i**), (**6-ii**), and (**6-iii**) (*cf.* Fig. 1).

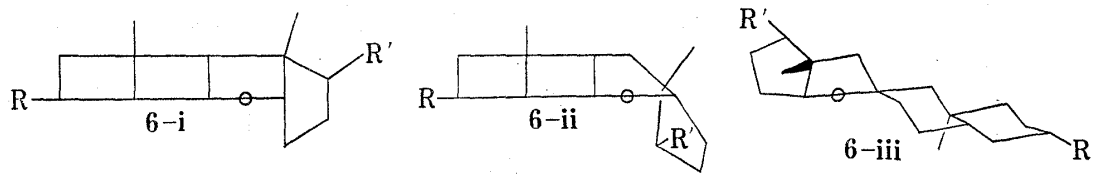


Fig. 1

Treatment of **6** with ethanedithiol and boron trifluoride–etherate gave the thioketal (**7**) which was reduced with Raney nickel to **8**, in which the 14β-configuration is preserved. The final structure determination for **8** was done by an independent synthesis described in the following section.

3β, 20β-Diacetoxy-9(8→7), 8(9→11)-diabeo-5α, 7α, 11β, 14α-pregnane

In the course of the preparation of linear progesterone, the 14α-epimer of the compound (**8**) was made: The mono–trichloroacetate (**9**)[1] was dehydrated with thionyl chloride in pyridine to **10**, which on hydrogenolysis with zinc in acetic acid gave the enone (**11a**), certainly a 14α-compound.

For the preparation of the enone (**11a**) a more convenient path was devised, starting with the diketo–ol (**1**). This was converted to the monothioketal (**12**), which was either dehydrated to **13** followed by desulfurization, or dehydrated after the desulfurization step, to give in both cases **11a**.

The 9-carbonyl group is considerably hindered by the rings A and C[4] as well as by the 19-methyl group. When treated with ethanedithiol and boron trifluoride–etherate, the diketo–ol (**1**) gave the monothioketal (**12**). This compound, (**12**), was reduced with Raney nickel under two different conditions; refluxing for some minutes afforded the ketol (**14a**), while with prolonged reaction time, the 9-carbonyl group was also reduced giving the glycol (**15a**), which was acetylated with acetic anhydride in pyridine to **15c**. In either case a small amount of the respective C-14 epimer (**14b**) or (**15b**) occurred as a minor product. Two reactions led to **11a** in good yield; the dehydration of **14a** with thionyl chloride, and desulfurization of **13** with Raney nickel. The 14β-enone (**11b**) was obtained similarly by dehydration of **14b**. Sodium borohydride reduction of the ketol (**14a**) gave a mixture of epimeric glycols (**15a**) and (**16a**) in the ratio of 1:2. Both glycols on oxidation with Jones reagent regenerated the parent ketol (**14a**). In the infrared (IR) spectra in diluted carbon tetrachloride (**15a**) shows a hydrogen-bonded hydroxyl band at 3585 cm^{-1}, but **16a** shows only free hydroxyl bands at 3647 cm^{-1} (*sec*-hydroxyl) and 3612 cm^{-1} (*tert*-hydroxyl) and therefore the former has a *cis* and the latter a *trans* glycol moiety in its structure.

3) C. Djerassi and W. Klyne, *J. Chem. Soc.*, **1962**, 4929; *idem*, *ibid.*, **1963**, 2390.
4) R.L. Clarke, *J. Am. Chem. Soc.*, **83**, 965 (1961).

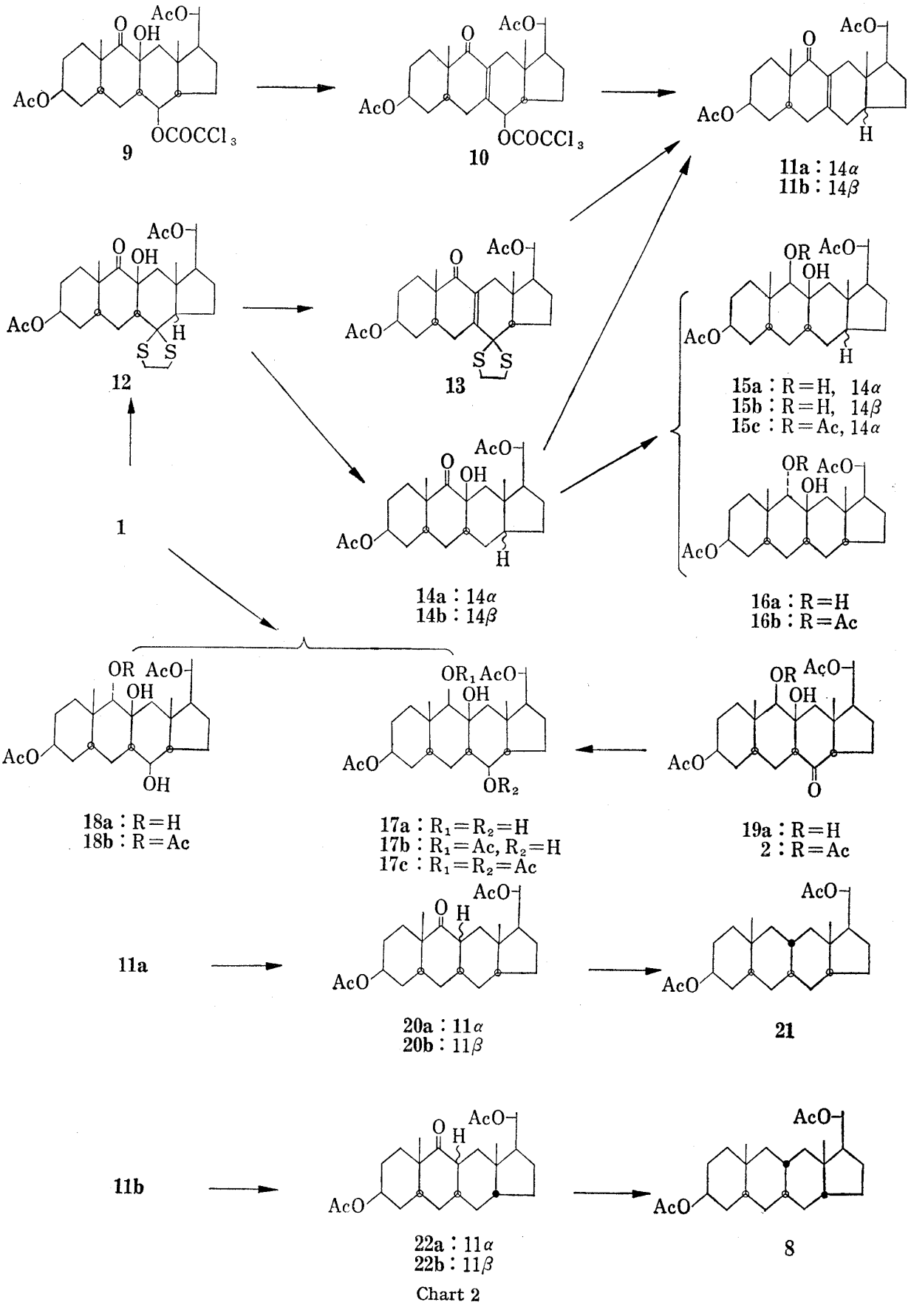


Chart 2

Similarly the diketo–ol (**1**) on reduction with sodium borohydride gave a mixture of epimeric triols (**17a**) and (**18a**), the former was identical with the triol obtained previously by hydrogenation of **1**. Acetylations of triols (**17a**) and (**18a**) with acetic anhydride in pyridine at room temperature afforded triol-monoacetates (**17b**) and (**18b**) respectively. That the 8-carbonyl function is reduced exclusively to 8β-alcohol in this reduction was demonstrated by the reduction of **19**[1] and **2**[1] with sodium borohydride to single **17a** and **17b** respectively. Hydrogenation of **11b** with rhodium-platinum oxide[5] as a catalyst in acetic acid afforded a saturated alcohol, which was oxidized to the ketone (**22a**). Treatment of **22a** with potassium hydroxide in methanol and subsequent acetylation gave the isomeric ketone (**22b**).

As was stated before, the 9-carbonyl group in this series of compounds did not readily give the hydrazone therefore the Wolff–Kishner reduction was carried out according to the modification of Nagata.[6] The product was identical with **8** prepared from **7** by desulfurization.

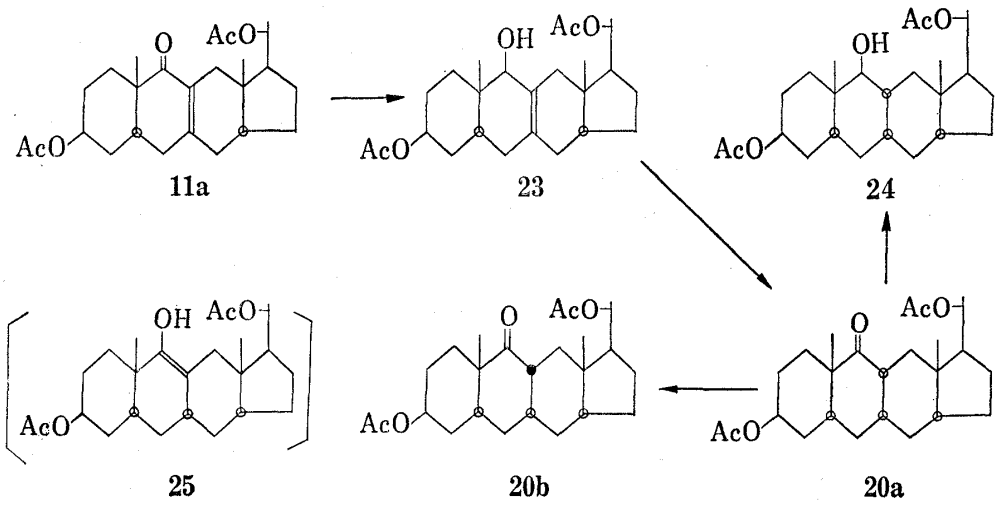


Chart 3

Table I. Product Ratios[a,b] in Hydrogenation of Enone (**11a**)

% Yields of the product	Reaction time				
	4 min	10 min	2 hrs	2.5 hrs	2.5 hrs Starting with **23**
11a[c]	16	10	6	5	4
20a[c]	19	41	72	69	66
24	3	7	19	23	25
23	62	41	3	3	5
20b	—	—	<1	<1	<1

a) based on TLC analysis
b) The realtive error in composition is estimated to be ±3%.
c) The ratio of these two products were determined by UV analysis because **11a** and **20a** were obtained in the same fraction and could not be separated by TLC.

Similarly, hydrogenation of **11a** gave the ketone (**20a**) in high yield. A kinetic study of this reaction revealed that the formation of **20a** was not a direct reduction of the double bond. Within a few minutes, 1 mole of hydrogen was absorbed but the main product was

5) *a*) S. Nishimura, *Bull. Chem. Soc. Japan*, **34**, 32 (1961); *b*) *Idem*, *ibid.*, **34**, 1544 (1961).
6) W. Nagata and H. Itazaki, *Chem. Ind.*, **1964**, 1194.

the allyl alcohol (**23**) besides some **20a**. Under the reaction condition **23** is gradually and almost completely converted into **20a** and **24**. Further hydrogenation of the 9-ketone formed is slow enough to allow time for this migration of the double bond.

After careful protonation with ammonium chloride and acetylation, lithium–ammonia reduction of the enone (**11a**) also afforded the ketone (**20a**) as a main product.[7] The BC-*trans* epimer (**20b**) was formed from **20a** in quantitative yield in a strongly alkaline medium. This epimerization accounts for the small amount of **20b** which accompanied **20a** in all reactions. The alcohol (**24**), the amount of which increased with reaction time, was probably formed by reduction of the ketone (**20a**), though its formation from the allyl alcohol (**23**) could not be excluded. The course of the conversion of the enone (**11a**) to the ketone (**20a**), *via*, the allylalcohol (**23**), needs some explanation. The steric hindrance of the tetrasubstituted double bond favors the hydrogenation of the 9-keto group as the first step. This allyl alcohol (**23**) is then converted into **20a**, probably through an intermediate enol (**25**). Ketonization of the enol under rather mild reaction condition gave the kinetic product (**20a**) exclusively, because the steric hindrance of 18- and 19-methyl groups favor protonation from the less hindered α-side.

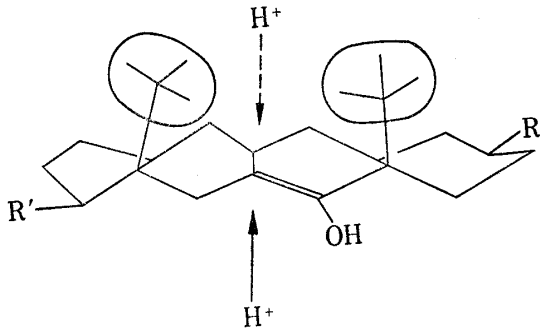


Fig. 2

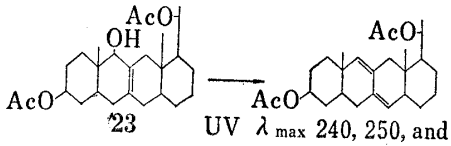
In strongly alkaline condition, however, an equilibration was observed and the thermodynamically stable product (**20b**) predominated.

Dreiding and Hartman[8] demonstrated the rearrangement in acid medium of the allyl alcohol moiety of monocyclic compounds and similar rearrangements have been observed in diterpene alkaloids.[9] However in our case attempted rearrangement of **23** in acetic acid led to the recovery of the starting material (**23**) and with forcing condition (1% $HClO_4$ in acetic acid) allyl alcohol (**23**) was converted to diene[10] almost exclusively. These observation led us to propose a plausible major pathway of the reaction as follows; i) formation of allyl alcohol (**23**) in the first step, ii) double bond migration from C_{11}-C_7 to C_9-C_{11} [(**23**)→(**25**)], iii) ketonization of the enol (**25**) forming the kinetically controlled product, the ketone (**20a**).

Linear Progesterone Analogues

The linear pregnane (**21**), obtained in a manner similar to that used for its 14β-epimer (**8**), was partially hydrolysed with potassium carbonate in aq. methanol to the 3-hydroxy compound (**26**), the structure of which was ascertained by Optical rotatory dispersion (ORD) (see Experimental). Oxidation of **26** with Jones reagent gave the 3-ketone (**27**). The usual method for introducing an olefinic function into position 1 and/or 4 in a 3-keto steroid was employed. Bromination of **27** with 1 mole of bromine gave the 2α-bromo-3-ketone (**28**), and with 2 moles of bromine the 2α, 4α-dibromo-3-ketone (**29**), as the main products respectively. The 2α-bromo-3-ketone (**28**) on treatment with lithium chloride in dry dimethyl formamide afforded 52% of the Δ^1-3-ketone (**30**) and 22% of the Δ^4-3-ketone (**32**). Dehydrobromination

7) A.J. Birch, H. Smith, and R.E. Thornton, *J. Chem. Soc.*, **1957**, 1339.
8) A.S. Dreiding and J.A. Hartman, *J. Am. Chem. Soc.*, **78**, 1216 (1956).
9) M.F. Barnes and J. MacMillan, *J. Chem. Soc.* (*C*), **1967**, 362.
10)



23 UV λ_{max} 240, 250, and 260mμ

of 2α,4α-dibromo-3-ketone (**29**) with lithium bromide and lithium carbonate in dry dimethyl formamide afforded the $\Delta^{1,4}$-3-ketone (**34**) in 81% yield. Hydrolysis of the 20-acetate (**30**), (**32**), (**34**), followed by oxidation, finally led to the linear progesterone analogues (**31**), (**33**), (**35**). The physical properties of these compounds are in excellent agreement with the given structures.

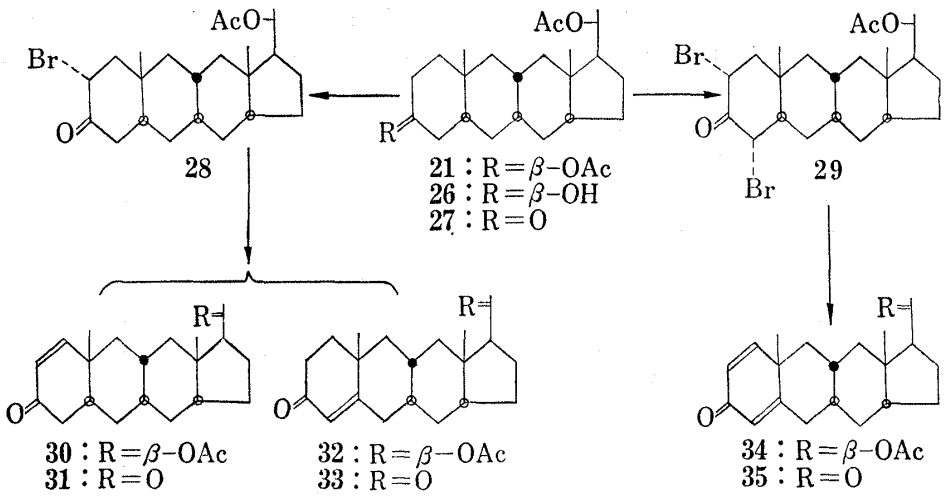


Chart 4

Linear Testosterone Analogues

Linear testosterone derivatives also were prepared from **26** by the Baeyer Villiger reaction. After protection of the 3-hydroxyl group in compound (**26**) as the tertiary butyl ether, achieved by reaction with iso-butene in the presence of a boron trifluoride etherate–phosphoric acid mixture, the 20β-acetoxyl group was converted to a 20-keto function *via* 20β-hydroxyl. The 3-*tert*-butoxy-20-keto compound (**38**) on treatment with refluxing benzene in the presence of trichloroacetic acid afforded the 3β-hydroxy-20-ketone (**39**), which on Baeyer Villiger oxidation gave 3β,17β-dihydroxy-linear androstan-17-acetate (**40**). Oxidation of **40** with Jones

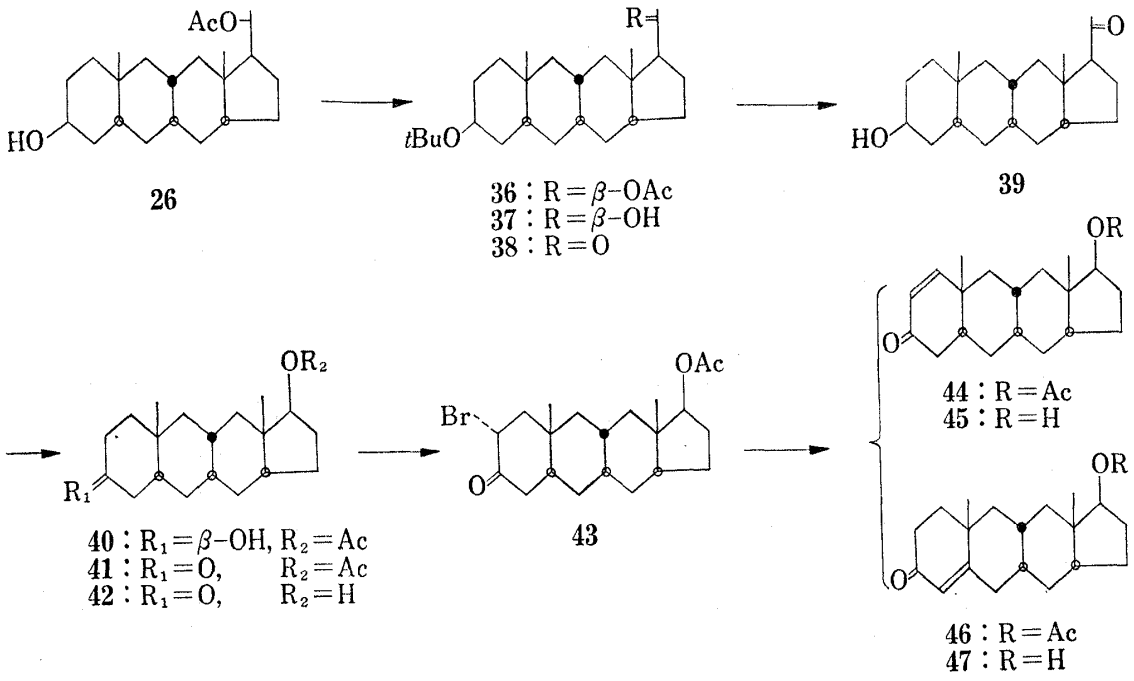


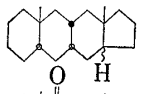
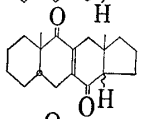
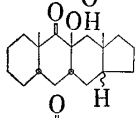
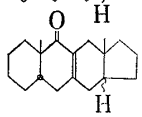
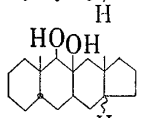
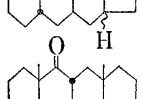
Chart 5

reagent and subsequent hydrolysis gave the 3-keto-17β-ol (**42**). From the 3-keto-17β-acetate (**41**), linear testosterone analogues were prepared by means of a bromination-dehydrobromination procedure, in a manner similar to that described for the linear progesterone analogues. Physical constants are in good agreement with the proposed structures.

Stereochemistry

So far as the A/B junction is concerned, 5α-configuration is maintained throughout the transformation of the steroid into its linear analogue. In the course of the conversion of the diketo–ol (**1**) to the linear pregnane (**21**) *via* **9**, **10**, **11a**, the reactions proceeded with retention of the 14-hydrogen configuration. As further support, many pairs of epimers (Table II), prepared here and previously,[1] show clear differences in the chemical shifts of their 18-methyl protons between the 14α-and 14β-epimers for each couple. These observations are in good agreement with the differences found in steroid series[11] where one can observe the difference of 0.3 ppm for 18-methyl protons between 14α and 14β.

Table II. Effects of the Configurations of 14-Hydrogen upon 18-Methyl Protons in τ Scale ($CDCl_3$)

Epimers[a] at C-14 position	18-Methyl chemical shifts		Δ[b] 14α-14β
	14α-H	14β-H	
	9.35	9.03	+0.32
	9.37	8.98	+0.38
	9.18	8.88	+0.30
	9.48	9.18	+0.30
	9.18	8.90	+0.28
	9.40	9.05	+0.35

a) 3β-Acetoxy and pregnane side chain (20β-acetoxy) are abbreviated for simplicity in all compounds.
b) A positive value denotes a downfield shift.

Consequently, the C/D junction has also been clarified. Finally, the stereochemistry of position 7 was deduced from NMR data on the series of compounds.

In Table III are shown the chemical shifts of 18- and 19-methyl protons of fourteen 14α-linear pregnane analogues. The substituent effects of the hydroxyl and acetoxyl groups are shown in Table IV. The 11-hydroxyl group has a marked effect upon both angular methyl groups (0.15—0.22 ppm). When an axial hydroxyl group is introduced at position 8, in addition to a 11-hydroxyl in these compounds, further downfield shift (0.22—0.25 ppm), in good additivity, of the 18-methyl signal is observed. Acetylation of the 8-hydroxyl group causes

11) R.F. Zürcher, *Helv. Chim. Acta*, **232**, 2055 (1963).

Table III. Chemical Shifts of C-18 and C-19 Protons of a Series of Linear Pregnane Analogues

Compds No.		Substituents			Chemical shifts (ppm)	
		9	11-β	8-β	19H	18H
1	(21)	H	H	H	9.13	9.35
2[a]		β-OH	H	H	9.15	9.37
3	(15a)	β-OH	OH	H	8.99	9.13
4[b]		β-OH	OH	OH	8.96	8.96
5[a]		β-OAc	H	H	9.08	9.37
6	(15c)	β-OAc	OH	H	8.93	9.21
7[b]		β-OAc	OH	OH	8.85	8.96
8	(17c)	β-OAc	OH	OAc	8.88	9.00
9	(16b)	α-OAc	OH	H	8.82	9.17
10	(18b)	α-OAc	OH	OH	8.75	8.92
11	(20b)	K[c]	H	H	8.90	9.40
12	(14a)	K	OH	H	8.69	9.18
13[b]		K	OH	OH	8.63	8.95
14[b]		K	OH	OAc	8.67	8.98

a) *cf.* experimental, preparation of (20b) *b*) previous paper *c*) ketone

Table IV. Effects of Some Axial Hydroxyl and Acetoxyl Groups on C-19 and C-18 Protons of Linear Pregnane Analogues

Substituents	Diff. between each couple of compds[a]	19H[b]	18H[b]
11β-OH	2→ 3	0.16	0.19
	5→ 6	0.15	0.16
	11→12	0.21	0.22
8β-OH	3→ 4	0.03	0.22
	6→ 7	0.08	0.25
	12→13	0.06	0.23
8β-OAc	6→ 8	0.05	0.21
	12→14	0.02	0.20

a) compound number from Table III *b*) downfield shift

a 0.03—0.04 ppm highfield shift in the 18-methyl signal. These observations are in good agreement with other data reported[12] in the steroid field. This fact establishes that the 11-hydroxyl group in these compounds is in a 1,3-diaxial position to both the 18- and the 19-methyl groups, and the 8-hydroxyl also keeps a 1,3-diaxial relationship with the 18-methyl group.

From these results, it is concluded that the alumina catalysed condensation products, the diketo-ol and its derived compounds, have a *trans-syn-trans-syn-trans* skeleton configuration as depicted in Fig. 3.

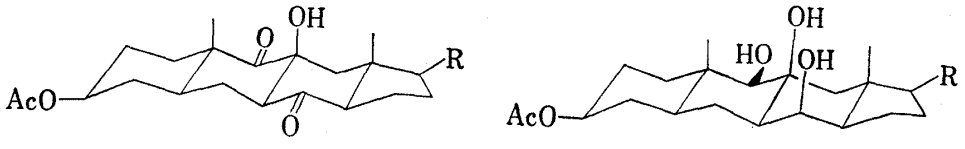


Fig. 3

12) Y. Kawazoe, Y. Sato, M. Natsume, H. Hasegawa, T. Okamoto, and K. Tsuda, *Chem. Pharm. Bull.* (Tokyo), **10**, 338 (1962).

Experimental

General Methods

All melting points were determined on Yanagimoto Micromelting apparatus and are uncorrected. Optical rotations were measured in 1% EtOH–$CHCl_3$ with a Perkin Elmer Polarimeter type 141 (c=1.0—0.6, l =1cm). Unless otherwise stated, UV spectra were recorded in 95% EtOH with a Hitachi EPE-2 spectrophotometer and IR spectra in CCl_4 by using a Koken DS-201B spectrophotometer. CD and ORD were measured with a Jasco Model ORD/UV-5 equipped with CD. NMR spectra were taken in $CDCl_3$ solution with a Varian A-60 spectrometer, TMS Serving as internal standard. Chemical shifts were reported in τ value and apparent coupling constants and bandwidths at half heights were obtained from the 1st order analysis in Hz. For preparative and analytical TLC, silica gel G or GF (E. Merck Co.) was used as an adsorbent.

3β,9β,20β-Triacetoxy-9(8→7),8(9→11)-diabeo-5α,14α-pregn-7(11)-en-8-one (3)——To a stirred solution of (2) (910 mg) in pyridine (10 ml) at −10° was added dropwise $SOCl_2$ (1 ml) and the solution was stirred for 15 min while the temperature was raised to 10°. The solution was taken up in ether and washed with 10% HCl, 10% aq. Na_2CO_3 and water and dried. Evaporation of the solvent gave crystalline solid (3) (744 mg), mp 195—201°. Recrystallization from acetone–n-hexane gave a sample with mp 202—204.5°, $[\alpha]_D^{24.5}$ −1.7°. UV λ_{max} mμ (ε): 243 (9985), 326 (55). IR ν_{max} cm^{-1}: 1738, 1685, 1635, 1245. NMR τ: 9.31 (3H, s, 18-Me), 9.13 (3H, s, 19-Me), 8.83 (3H, d, J=6.0, 21-Me), 7.97 (6H, s, 2×OAc), 7.87 (3H, s, OAc), 5.23 (2H, m, $C_{3,20}$–H), 4.62 (1H, broad s, $W^h/_2$=4, C_9-H). *Anal.* Calcd. for $C_{27}H_{38}O_7$: C, 68.33; H, 8.07. Found: C, 68.46; H, 8.08.

3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-5α,14β-pregn-7(11)-en-8-one (5)——A solution of 3 (785 mg) in AcOH (22 ml) was refluxed and to the solution was added zinc powder (3 g) in 10 portions and stirred for 5 hr under reflux. Zinc was removed by decantation and the solution was poured into cold aq. Na_2CO_3 and made neutral. The product was extracted with ether, washed with water and dried. After evaporation of the solvent the residue was crystallized from ether–n-pentane to afford 5 (145 mg), mp 153—160°. The mother liquor, a mixture of three components judging from TLC, was separated by preparative TLC (ether: petr. ether=2:1). The first fraction (from top) gave the additional 5 (270 mg) (collective yield, 60%). Recrystallization from ether–n-pentane gave a sample with mp 160—162°, $[\alpha]_D^{22}$ −41.8°. UV λ_{max} mμ (ε): 248.5 (10293). NMR τ: 9.20 (3H, s, 19-Me), 9.03 (3H, s, 18-Me), 8.85 (3H, d, J=6.0, 21-Me), 7.97 (3H, s, OAc), 7.96 (3H, s, OAc), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71. Found: C, 72.21; H, 8.83. The second fraction (183 mg) on crystallization from ether–n-pentane afforded 4 (94 mg), mp 153—156°. Recrystallization from the same solvent gave a sample with mp 154.5—155.5°, $[\alpha]_D^{24}$ −15.8°. UV λ_{max} mμ (ε): 248 (12300). IR ν_{max} cm^{-1}: 1736, 1670, 1650, 1245. NMR τ: 9.13 (3H, s, 19-Me), 9.03 (3H, s, 18-Me), 8.87 (3H, d, J=6.0, 21-Me), 7.97 (6H, s, 2×OAc), 7.88 (3H, s, OAc), 5.23 (2H, m, $C_{3,20}$-H), 4.53 (1H, broad s, $W^h/_2$=5, C_9–H). *Anal.* Calcd. for $C_{27}H_{38}O_7$: C, 68.33; H, 8.07. Found: C, 68.18; H, 8.03.

The last fraction (40 mg, crystallized from ether–n-pentane mp 196—202.5°) was found to be the starting material.

Equilibration of 3 in Refluxing AcOH——A solution of 3 (20 mg) in AcOH (3 ml) was refluxed under N_2 for 4 hr, then worked up similarly as above. The residue showing two spots on TLC, was separated by TLC (ether–petr: ether=2:1) to give 3 (3.5 mg, 19%) and 4 (15 mg, 81%). These compounds were identified by TLC and IR comparison.

3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14β-pregnan-8-one (6)——Freshly cut lithium metal (30 mg) was dissolved in distilled ammonia (6 ml) and into the solution under effective stirring was added dropwise a solution of 5 (225 mg) in abs. THF (tetrahydrofuran) (1.5 ml) over 5 min at refluxing temperature (−34°). After stirring additional 10 min dry NH_4Cl (100 mg) was added portionwise into the solution and ammonia was evaporated at room temperature. The residue was taken up in ether, washed with water and dried and evaporated. The residual product, after acetylation with Ac_2O–pyridine, gave the crude product, which was separated by preparative TLC (on Al_2O_3 Woelm, benzene: ether=5:3). The main fraction afforded 6 (155 mg, 63% yield). Recrystallization from ether–n-pentane gave a sample with mp 147.5—151°, $[\alpha]_D^{24}$ +64.5°. IR ν_{max} cm^{-1}: 1735, 1705, 1245. ORD (c=0.757, $CHCl_3$) [ϕ] (mμ): +6843 (318) (peak), −5990 (276) (trough) (a+128). NMR τ: 9.12 (3H, s, 19-Me), 8.98 (3H, s, 18-Me), 8.82 (3H, d, J=6.0, 21-Me), 7.98 (6H, s, 2×OAc), 5.22 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.96; H, 9.19.

3β,20β-Diacetoxy-9(8→7), 8 (9→11)-diabeo-5α,7α,11β,14β-pregnane (8) ***via*** **Thioketal** (7)——A mixture of 6 (100 mg), ethanedithiol (1 ml) and BF_3·etherate (1 ml) was stirred for 1 hr at room temperature. After addition of MeOH (0.5 ml), the mixture was taken up in ether and the ethereal solution was washed 3 times with 10% aq. NaOH and with water and dried. After evaporation of the solvent the residue (110 mg) was dissolved in abs. EtOH (5 ml). To the solution was added freshly prepared Raney nickel (W-2, *ca.* 1 g) and the mixture was refluxed for 2.5 hr under stirring. The catalyst was filtered off and washed several times with MeOH and the combined filtrate was evaporated. The residue (90 mg) was crystallized from MeOH to afford 8 (65 mg), mp 98—100°. Recrystallization from MeOH gave a sample with mp 99—

101°, $[\alpha]_D^{28.3}$ +13.4°. IR ν_{max} cm^{-1}: 1733, 1240. NMR τ: 9.13 (3H, s, 19-Me), 9.03 (3H, s, 18-Me), 8.87 (3H, d, J=6.0, 21-Me), 7.98 (6H, s, 2×OAc), 5.20 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{40}O_4$: C, 74.21; H, 9.97. Found: C, 74.20; H, 10.13.

3β,20β-Diacetoxy-8β-trichloroacetoxy-9(8→7),8(9→11)-diabeo-5α,14α-pregn-7(11)en-9-one (10)——To a solution of **9** (430 mg) in pyridine (6 ml) at −10° was added dropwise $SOCl_2$ (0.3 ml) and the mixture was stirred for 30 min then the temperature was raised to 5° and stirred for 15 min. The reaction mixture was worked up as usual and the product was crystallized from ether–*n*-pentane to give **10** (370 mg), mp 185—188°. Concentrations of the mother liquor gave additional **10** (34 mg), mp 183—188° (collective yield, 97%). Recrystallization from ether–*n*-pentane gave a sample with mp 186—188°, $[\alpha]_D^{27}$ +70.9°. UV λ_{max} mμ (ε): 242 (10650). IR ν_{max} cm^{-1}: 1766, 1736, 1679, 1639, 1240, 914. NMR τ: 9.27 (3H, s, 18-Me), 8.97 (3H, s, 19-Me), 8.82 (3H, d, J=6.0, 21-Me), 7.98 (3H, s, OAc), 7.92 (3H, s, OAc), 5.23 (2H, m, $C_{3,20}$–H), 4.41 (1H, d, J=3.0, C_8–H). *Anal.* Calcd. for $C_{27}H_{35}O_7Cl_3$: C, 56.06; H, 6.10; Cl, 18.40. Found: C, 55.95; H, 6.21; Cl, 18.58.

3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-5α,14α-pregn-7(11)en-9-one (11a)——A solution of **10** (405 mg) in AcOH (10 ml) was refluxed under stirring. To the solution was added zinc powder (1.5 g) in 4 portions over 2 hr and refluxed for additional 2 hr under stirring. After cooling, zinc was removed by decantation and the solution was poured into cold 10% aq. Na_2CO_3 and made neutral. The product was extracted with ether, washed with water, dried and evaporated. The residue was crystallized from iso-propyl ether–*n*-hexane to afford **11a** (150 mg), mp 150—153°. Purification of the mother liquor was effected by preparative TLC (CH_2Cl_2:AcOEt=10:1) and afforded additional **11a** (71 mg) (collective yield, 76%). Recrystallization from iso-propyl ether–*n*-hexane gave a sample with mp 153—155°, $[\alpha]_D^{27}$ +55.6°. UV λ_{max} mμ (ε): 245 (10284), 320 (180). IR ν_{max} cm^{-1}: 1733, 1671, 1628, 1247. NMR τ: 9.48 (3H, s, 18-Me), 9.03 (3H, s, 19-Me), 8.82 (3H, d, J=6.0, 21-Me), 8.00 (3H, s, OAc), 7.92 (3H, s, OAc), 5.22 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71. Found: C, 72.21; H, 8.60.

3β,20β-Diacetoxy-11β-hydroxy-9(8→7),8(9→11)-diabeo-5α,7α,14ξ-pregnane-8,9-dione-8-thioketal (12)——A mixture of **1** (448 mg), ethanedithiol (1.5 ml) and BF_3–etherate (1.5 ml) was stirred at room temperature for 1.5 hr then MeOH (3 ml) was added and the mixture was poured into cold 5% aq. NaOH solution. The product was extracted with ether, and the ethereal solution was washed 3 times with 5% aq. NaOH solution and with water. To the ether extract was added 10 ml of xylene and the mixture was evaporated to dryness *in vacuo* to remove remaining sulfur smell. Five times repetition of this procedure could remove the smell to considerable extent. The residue was crystallized from ether–petr. ether to give **12** (120 mg), mp 153—160°. Concentration of the mother liquor gave additional **12** (180 mg) as amorphous solid. Recrystallization from ether–petr. ether gave a sample with mp 152—155°, $[\alpha]_D^{22}$ −8.7°. IR ν_{max} cm^{-1}: 3550, 3420, 1736, 1715, 1236. *Anal.* Calcd. for $C_{27}H_{40}O_6S_2 \cdot H_2O$: C, 59.75; H, 7.43; S, 11.81. Found: C, 59.72; H, 7.72; S, 11.86.

3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-5α,14α-pregn-7(11)-ene-8,9-dione-8-thioketal (13)——This reaction was undertook to raise the yield of desulfurization step since the crystallization (as a purification) of **12** was rather difficult and with remaining sulfur smell the desulfurization of **12** proceeded with difficulty.

To a stirred solution of **12** (5.8 g) in pyridine (35 ml) at −5° was added dropwise $SOCl_2$ (9 g), and the mixture was stirred for 10 min while the temperature was raised to 20°. Usual work-up gave 10.7 g of the crude product, which was crystallized from ether–petr. ether giving **13** (9.7 g, 91% yield). Recrystallization from ether–petr. ether gave a sample with mp 195—197°, $[\alpha]_D^{25}$ +26.7°. UV λ_{max} mμ (ε): 249 (11276). IR ν_{max} cm^{-1}: 1736, 1675, 1607, 1245. *Anal.* Calcd. for $C_{27}H_{38}O_5S_2$: C, 64.00; H, 7.56; S, 12.66. Found: C, 64.15; H, 7.24; S, 12.42.

Desulfurization of 12

With Short Reaction Time——To a suspended solution of freshly prepared Raney nickel (W-2, *ca.* 10 g) in abs. EtOH (80 ml) was added **12** (1.65 g, crystalline form) in abs. EtOH (20 ml) and the mixture was stirred for 10 min under reflux. The nickel was filtered off and washed several times with MeOH. The combined filtrate was evaporated to dryness. The residue was chromatographed over silica gel column (150 g) using CH_2Cl_2: AcOEt=5:1 as an eluant (20 ml/fraction). The fraction 31—40 (90 mg) afforded a mixture of the starting material and the ketol (**14a**). The fraction 41—70 (1.28 g) was crystallized from ether–petr. ether to give **14a** (1.23 g, 81% yield), mp 120—127°. Recrystallization from MeOH gave a sample with mp 123—127°, $[\alpha]_D^{22}$ +52.2°. IR ν_{max} cm^{-1}: 3570, 3445, 1733, 1713, 1240. NMR τ: 9.18 (3H, s, 18-Me), 8.88 (3H, d, J=6.0, 21-Me), 8.69 (3H, s, 19-Me), 8.00 (3H, s, OAc), 7.95 (3H, s, OAc), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{38}O_6$ (434.55): C, 69.09; H, 8.81. Found[13]: C, 69.88; H, 9.32.

13) The difference between the calcd. value and the found one is not fully understandable since 5 times elemental analyses from different batch of the ketol and crystallized from different solvent fell into the same value within the error of ±0.3% and the elemental analyses of the enone (**11a**) and the glycol (**15a**) derived from this ketol agreed well with their calcd. values. But the measurement of mass spectrum of the compound (**14a**) shows the parent peak at *m/e* 434, a normal molecular weight. Therefore it probably comes from a stuborn solvation.

The mother liquor of **14a** (50 mg) and fraction 71—90 (87 mg) was a mixture of two components, one of them is the ketol (**14a**). Separation of the mixture by preparative TLC (CH_2Cl_2:AcOEt=10:1, duplicate development) afforded 70 mg of **14a** and 65 mg of the epimeric ketol (**14b**), which was crystallized from ether–petr. ether giving a sample with mp 119—121°, $[\alpha]_D^{22}$ +25.0°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3540, 1725, 1708. NMR τ: 8.88 (3H, s, 18-Me), 8.85 (3H, d, J=6.0, 21-Me), 8.70 (3H, s, 19-Me), 8.00 (6H, s, 2×OAc), 5.27 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{38}O_6$: C, 69.09; H, 8.81. Found: C, 69.02; H, 8.96.

With Long Reaction Time——In case the starting material (12) was a crude product and not purified by crystallization the desulfurization needs much longer reaction time. A mixture of **12** (2.27 g) and Raney nickel (freshly prepared W-2, *ca.* 12 g) in abs. EtOH (120 ml) was refluxed for 1 hr with stirring. The catalyst was filtered off and washed 10 times with MeOH, and the combined filtrate was evaporated. To the residue (1.89 g) (more than a half of the starting material was remained) was added new catalyst (*ca.* 10 g) in abs. EtOH (100 ml) and the mixture was refluxed for 2 hr with stirring. Work up similarly as before gave 1.70 g of the product mixture, which was chromatographed over silica gel (70—325 mesh, 300 g) with ether–petr. ether (3:1) (20 ml/fraction). The fraction 1—10 gave 711 mg of the ketol (**14a**) which accompanied a small amount of the starting material. Fraction 16—32 gave a mixture of the epimeric glycol (**15a**) and (**15b**) (611 mg). The fraction 33—42 gave 400 mg of the glycol (**15a**), which was crystallized from ether–petr. ether to afford a sample with mp 186—188°, $[\alpha]_D^{22}$ +38.4°. IR ν_{max} cm^{-1}: 3560, 1730, 1240. H-bonding measurement in CCl_4 using 20 mm cell ($c=6.8\times10^{-3}$ mole/liter) shows bands at 3636 cm^{-1} (free *sec.* OH) and 3585 cm^{-1} (bonded *tert.* OH). NMR τ: 9.18 (3H, s, 18-Me), 8.99 (3H, s, 19-Me), 8.85 (3H, d, J=6.0, 21-Me), 8.42 (1H, s, C_{11}–OH), 8.01 (1H, d, J=7.0, C_9–OH), 7.98 (3H, s, OAc), 7.97 (3H, s, OAc) 7.19 (1H, d, J=7.0, C_9–H), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{40}O_6$: C, 68.77; H, 9.24. Found: C, 68.89; H, 9.29.

The mixture of the epimeric glycols was separated by preparative TLC (ether–petr. ether=2:1, duplicate development) to give **15a** (340 mg) and **15b** (245 mg). Recrystallization of **15b** from ether–petr. ether gave a sample with mp 173—174°. IR ν_{max} cm^{-1}: 3558, 1732, 1240. NMR τ: 9.00 (3H, s, 19-Me), 8.90 (3H, s, 18-Me), 8.87 (3H, d, J=6.0, 21-Me), 8.42 (1H, s, C_{11}–OH), 8.00 (6H, s, 2×OAc), 5.22 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{40}O_6$: C, 68.77; H, 9.24. Found: C, 68.95; H, 9.19. These glycols, (**15a**) and (**15b**,) on oxidation with Jones reagent afforded the respective glycol (**14a**) and (**14b**).

Acetylation of the Glycol (15a)——The glycol (**15a**) (100 mg) was treated with Ac_2O–pyridine at room temperature overnight. Work up gave **15c**, crystallized from ether–petr. ether to afford a sample with mp 165—168°, $[\alpha]_D^{22}$ +49.3°. IR ν_{max} cm^{-1}: 3550, 1733, 1241. NMR τ: 9.21 (3H, s, 18-Me), 8.93 (3H, s, 19-Me), 8.80 (3H, d, J=6.0, 21-Me), 8.04 (3H, s, OAc), 8.02 (3H, s, OAc), 7.90 (3H, s, OAc), 5.62 (1H, s, C_9–H), 5.27 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{27}H_{42}O_7$: C, 67.75; H, 8.85. Found: C, 67.78; H, 8.86.

The Enone (11a) by Desulfurization of the Ene-dione-monothioketal (13)——A mixture of **13** (200 mg) and freshly prepared Raney nickel (*ca.* 2 g) in abs. EtOH (10 ml) was refluxed for 30 min with stirring. The catalyst was filtered off and washed 5 times with MeOH. The combined filtrate was evaporated to dryness. The residue was crystallized from ether–petr. ether to give **11a** (150 mg, 90% yield), mp 152—155°.

The Enone(11a)by Dehydration of the Ketol (14a)——To a stirred solution of **14a** (930 mg) in pyridine (10 ml) at −10° was added dropwise $SOCl_2$ (1.6 g). The solution was kept stirring at the temperature for 10 min. Work up as usual and crystallization from ether–petr. ether gave **11a** (650 mg, 76% yield), mp 150—153°.

The Enone (11b) by Dehydration of the Ketol (14b)——The ketol (**14b**) (65 mg) was similarly dehydrated with $SOCl_2$ in pyridine to give **11b** accompanied by a small amount of a material. Separation of the product by preparative TLC (CH_2Cl_2:acetone=25:1) afforded (**11b**) (45 mg), crystallized from ether–petr. ether to a sample with mp 143—146°, $[\alpha]_D^{23}$ −79.6°. IR ν_{max} cm^{-1}: 1737, 1674, 1640 (infl.), 1240, 1027. UV λ_{max} $m\mu$ (ε): 248 (10087). NMR τ: 9.18 (3H, s, 18-Me), 8.98 (3H, s, 19-Me), 8.83 (3H, d, J=6.0, 21-Me), 7.98 (3H, s, OAc), 7.91 (3H, s, OAc), 5.17 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{36}O_5$: C, 72.08; H, 8.71. Found: C, 72.06; H, 8.80.

Sodium Borohydride Reduction of the Ketol(14a)——To an ice-cooled solution of $NaBH_4$ (70 mg) in abs. MeOH (3 ml) under stirring was added **14a** (160 mg) in abs. MeOH (4 ml) and the solution was stirred for 1 hr, then poured into ice water. The product was extracted with ether and the ethereal solution was washed with water and the solvent was evaporated. The residue was a mixture of two components, which was separated by preparative TLC (benzene:MeOH=20:3, duplicate development). The faster-fraction amounted to 66 mg, and crystallized from ether–petr. ether to give **15a**. The slower fraction amounted to 100 mg, and crystallized from ether–petr. ether to give **16a**. Recrstallization of **16a** from the same solvent gave a sample with mp 214—216°, $[\alpha]_D^{22}$ +31.2° IR ν_{max} cm^{-1}: 3590 (infl.), 3505, 1730, 1240. H-bonding measurement in CCl_4 using 20 mm cell ($c=6.8\times10^{-3}$ mole/liter) shows bands at 3647 cm^{-1} (free *sec.* OH) and 3612 cm^{-1} (free *tert.* OH). *Anal.* Calcd. for $C_{25}H_{40}O_6$: C, 68.77; H, 9.24. Found: C, 68.88; H, 9.26. Jones oxidation of this glycol (**16a**) afforded the parent ketol (**14a**).

Acetylation of the Glycol (16a)——The glycol (**16a**) (100 mg) was treated with Ac_2O–pyridine at 80° for 1 hr. Work up gave **16b**, which was crystallized from ether–petr. ether to afford a sample, mp 239—243°, $[\alpha]_D^{22}$ +48.3°. IR ν_{max} cm^{-1}: 3470, 1734, 1240. NMR τ: 9.17 (3H, s, 18-Me), 8.88 (3H, d, J=6.0,

21-Me), 8.82 (3H, s, 19-Me), 8.00 (6H, s, 2×OAc), 7.92 (3H, s, OAc), 5.52 (1H, s, C_9-H), 5.23 (2H, m, $C_{3,20}$-H). *Anal.* Calcd. for $C_{27}H_{42}O_7$: C, 67.75; H, 8.85. Found: C, 67.86; H, 8.71.

Sodium Borohydride Reduction of 3β,20β-Diacetoxy-11β-hydroxy-9(8→7), 8(9→11)-diabeo-5α,7α,14α-pregnane-8,9-dione (1)——To an ice-cooled solution of $NaBH_4$ (80 mg) in abs. MeOH (10 ml) was added **1** (180 mg) in abs. MeOH (4 ml) and the mixture was stirred for 1.5 hr. Work up similarly as above gave the product mixture, which was separated by preparative TLC (benzene:MeOH=20:3). The faster fraction gave the triol (**17a**) (114 mg), identified by mixed melting point and comparison of the IR spectrum. The slower fraction gave the epimeric triol (**18a**) (62 mg), which was crystallized from ether–*n*-pentane to afford a sample with mp 229—231°, $[\alpha]_D^{25.5}$ +20.4°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3610, 3505, 1726, 1005. NMR τ: 9.15 (3H, s, 18-Me), 8.88 (3H, s, 19-Me), 8.83 (3H, d, J=6.0, 21-Me), 8.58 (1H, s, C_{11}-OH), 7.98 (3H, s, OAc), 7.95 (3H, s, OAc), 7.68 (1H, d, J=5.0, C_9-OH), 6.88 (1H, d, J=5.0, C_9-H), 5.27 (2H, m, $C_{3,20}$-H). *Anal.* Calcd. for $C_{25}H_{40}O_7$: C, 66.34; H, 8.91. Found: C, 66.12; H, 8.81.

Acetylation of 17a——The triol(**17a**) (200 mg) was acetylated with Ac_2O (1 ml) and pyridine (3 ml) at reflux for 3 hr. Work up gave a mixture of the triol-monoacetate(**17b**)and the triol-diacetate(**17c**)which was separated by TLC (CH_2Cl_2:AcOEt=10:1) to each component. The triol-monoacetate (**17b**) (370 mg) was crystallized from MeOH mp 222—224°, identified by mixed melting point and comparison of the IR spectrum. The triol-diacetate (**17c**) (131 mg) was crystallized from ether–*n*-pentane to a sample with mp 169—171°, $[\alpha]_D^{22}$ +25.4°. IR ν_{max} cm^{-1}: 3595, 1733, 1234, 1023. NMR τ: 9.00 (3H, s, 18-Me), 8.90 (3H, d, J=6.0, 21-Me), 8.88 (3H, s, 19-Me), 8.03 (3H, s, OAc), 8.00 (3H, s, OAc), 7.93 (3H, s, OAc), 7.87 (3H, s, OAc), 5.60 (1H, s, C_9–H), 5.20 (2H, m, $C_{3,20}$–H), 4.70 (1H, broad s, $W^h/_2$=5, C_8–H). *Anal.* Calcd. for $C_{29}H_{44}O_9$: C, 64.90; H, 8.26. Found: C, 64.75; H, 8.34.

Acetylation of 18a——The epimeric triol (**18a**) (37 mg) was acetylated with Ac_2O–pyridine at room temperature overnight. Work up gave the triol-monoacetate (**18b**), which was crystallized from acetone–*n*-hexane to give a sample with mp 296—297°, $[\alpha]_D^{23.5}$ +28.9°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3458, 1725, 1008. NMR τ: 8.92 (3H, s, 18-Me), 8.87 (3H, d, J=6.0, 21-Me), 8.75 (3H, s, 19-Me), 8.00 (3H, s, OAc), 7.98 (3H, s, OAc), 7.91 (3H, s, OAc), 7.38 (1H, d, J=6.0, C_8–OH), 6.93 (1H, s, C_{11}–OH), 6.03 (1H, d, J=6.0, C_8–H), 5.45 (1H, s, C_9–H), 5.22 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{27}H_{42}O_8$: C, 65.56; H, 8.56. Found: C, 65.71; H, 8.70.

Sodium Borohydride Reduction of 19a to 17a——To an ice-cooled solution of $NaBH_4$ (35 mg) in abs. MeOH (10 ml) was added **19a** (80 mg) in abs. MeOH (10 ml) and the mixture was stirred for 1.5 hr. Work up gave the product (82 mg), crystallized from MeOH to **17a** (70 mg), mp 219—221°. Identification was made by mixed melting point and comparison of the IR spectrum.

Sodium Borohydride Reduction of 2 to 17b——The keto-diol-monoacetate (**2**) (50 mg) was treated with $NaBH_4$ (30 mg) similarly as above and gave **17b** (45 mg), mp 221—224°. This was identified by mixed melting point and comparison of the IR spectrum.

Hydrogenation of the Enone (11a)

Preparation of 20a——The enone(**11a**) (870 mg) in AcOH (25 ml) was hydrogenated over $Rh_2O_3 \cdot PtO_2$[5] (275 mg) at room temperature for 2.5 hr and 1.2 mole eq. of hydrogen was consumed The reaction mixture was poured into cold aq. Na_2CO_3 and made neutral. The product was extracted with $CHCl_3$, washed with water and dried. After evaporation of the solvent, the residue, showing 3 spots on TLC, was separated by preparative TLC (CH_2Cl_2:AcOEt=10:1). The faster fraction (644 mg, 74%) was crystallized from MeOH to afford (**20a**) (570 mg), mp 138—143°. Recrystallization from MeOH gave a sample with mp 140—143°, $[\alpha]_D^{23}$ +84.6°. IR ν_{max} cm^{-1}: 1739, 1707, 1237. UV λ_{max}^{MeOH} $m\mu$ (ε): 298 (65). ORD (c=0.48, MeOH) [ϕ] ($m\mu$): +6368 (317) (peak), 0 (295), −2580 (280) (trough) (a +89). NMR τ: 9.60 (3H, s, 18-Me), 8.95 (3H, s, 19-Me), 8.84 (3H, d, J=6.0, 21-Me), 7.98 (3H, s, OAc), 7.88 (3H, s, OAc), 5.27 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.48; H, 9.23. The ketone(**20a**) and the starting material (**11a**) have the same *Rf* value on TLC but can easily be distinguished under UV light using silica gel GF, thus the mother liquor was found to be contaminated with a small amount of the starting material.

The middle fraction (209 mg, 23%) was crystallized from ether–petr. ether to give **24** with double mp 140—141°, 144—146°, $[\alpha]_D^{23}$ +31.7°. IR ν_{max} cm^{-1}: 3560, 3480, 1732, 1241. NMR τ: 9.25 (3H, s, 18-Me), 9.08 (3H, s, 19-Me), 8.85 (3H, d, J=6.0, 21-Me), 7.98 (6H, s, 2×OAc), 6.70 (1H, d, J=6.0, C_9–H), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{40}O_5$: C, 71.39; H, 9.59. Found: C, 71.14; H, 9.73. The slower fraction (27 mg, 3%) was characterized as **23** in the next run.

Preparation of 23——The enone (**11a**) (416 mg) in AcOH (15 ml) was hydrogenated over Rh_2O_3–PtO_2 (130 mg) at room temperature. Right after the uptake of 1 eq. mole of hydrogen (5 min), the reaction mixture was neutralized by pouring into cold aq. Na_2CO_3. The product was extracted with $CHCl_3$, washed with water, dried and evaporated. The residue was crystallized from ether–petr. ether to give **23** (200 mg), mp 157—160°. Recrystallization from the same solvent gave a sample with mp 159—161°. IR ν_{max} cm^{-1}: 3600, 3510, 1735, 1237. NMR τ: 9.43 (3H, s, 18-Me), 9.22 (3H, s, 19-Me), 8.82 (3H, d, J=6.0, 21-Me), 7.97 (3H, s, OAc), 7.95 (3H, s, OAc), 5.22 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.94; H, 9.42. The mother liquor shows on TLC 3 spots corresponding to those in the previous run but in different proportions. This was separated by preparative TLC (CH_2Cl_2:AcOEt=10:1). The faster fraction (148 mg) was a mixture of **11a** and **20a**. The mixture, upon treatment with KOH in MeOH

under reflux and subsequent acetylation with Ac_2O–pyridine, could be separated by preparative TLC to **11a** and **20b** in a ratio of 1:1. Characterization of **20b** will be described later. The middle fraction gave additional **23** (66 mg, collective yield 64%). The slower fraction (15 mg) was identified as **24** by comparison of the IR spectrum.

Oxidation of the Alcohol (24) to 20a——At room temperature, Jones oxidation of the alcoho l(**24**) gave a mixture of the saturated ketone (**20a**) and the enone (**11a**), the ratio of which was about 3:2 judging from the IR spectrum. In the cold run (0°) the saturated ketone (**20a**) was a sole product. The identification was made by mixed melting point and the comparison of IR spectrum.

Procedure for Kinetic Run——Hydrogenation was carried out at room temperature and atmospheric pressure using rhodium–platinum (7:3) oxide[5b] as a catalyst and AcOH as a solvent. The substrate (**11a**) (82 mg, 0.1 mmole) was added after the oxide (26 mg) was reduced to black with hydrogen in the solvent (8 ml). The hydrogenation of the compound in AcOH proceeded very rapidly as was seen previously and within 10 min. 1 mole eq. of hydrogen was absorbed then the absorption curve gave a plateau. In each run, as soon as the reaction time was up, the mixture was poured into cold aq. Na_2CO_3 solution and made neutral, and extracted with $CHCl_3$. Separation attempt of the compounds (**20a**) and (**11a**) by TLC with different solvent systems failed. Therefore the ratio of these compounds was determined by quantitative UV analysis, measuring the extinction at 245 mμ (this is the absorption maximum of enone (**11a**)). A calibration curve for this determination was obtained from artificial mixture in the usual manner. The results are shown in Table I in the subject.

3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregnan-9-one (20b)——A mixture of **20a** (680 mg) and KOH (250 mg) in MeOH (20 ml) was refluxed for 45 min under N_2, then poured into water. The product was extracted with $CHCl_3$, washed with water and dried and evaporated. The residue was acetylated in the usual manner with Ac_2O–pyridine to give **20b** (650 mg). Recrystallization from MeOH gave a sample with double mp 145—146°, 162—163°, $[\alpha]_D^{24}$ +18.0°. UV λ_{max} mμ (ε): 292 (45). IR ν_{max} cm^{-1}: 1735, 1708, 1247, 1027. NMR τ: 9.40 (3H, s, 18-Me), 8.90 (3H, s, 18-Me), 8.88 (3H, d, J=6.0, 21-Me), 8.05 (3H, s, OAc), 8.02 (3H, s, OAc), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.72; H, 8.99.

Hydrogenation of 20b——The ketone (**20b**) (100 mg) in AcOH (9 ml) was hydrogenated over $Rh_2O_3 \cdot PtO_2$ (50 mg) for 2 hr at room temperature. After work up the product was crystallized from MeOH to give 3β,20β-diacetoxy-9β-hydroxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregnane, mp 175—176°, $[\alpha]_D^{27.8}$ +5.6°. IR ν_{max} cm^{-1}: 3440, 1728, 1248. NMR τ: 9.37 (3H, s, 18-Me), 9.15 (3H, s, 19-Me), 8.85 (3H, d, J=6.0, 21-Me), 8.60 (1H, broad s, C_9–OH), 8.00(6 H, s, 2×OAc), 7.21 (1 H, α, I=9.0, C_9-H) 5.22 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{40}O_5$: C, 71.39; H, 9.59. Found: C, 71.58; H, 9.62

Acetylation of the alcohol (50 mg) obtained above, with Ac_2O–pyridine in the usual manner gave 3β, 9β,20β-triacetoxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregnane, mp 141—143°, $[\alpha]_D^{25.3}$ +23.8°. IR ν_{max} cm^{-1}: 1720, 1241. NMR τ: 9.37 (3H, s, 18-Me), 9.08 (3H, s, 19-Me), 8.87 (3H, d, J=6.0, 21-Me), 8.03 (3H, s, OAc), 8.00 (3H, s, OAc), 7.97 (3H, s, OAc), 5.58 (1H, d, J=10.0, C_9–H), 5.22 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{27}H_{42}O_6$: C, 70.10; H, 9.15. Found: C, 70.09; H, 9.34.

Hydrogenation of the 14β-Enone (11b)——The enone (**11b**) (200 mg) i nAcOH (25 ml) was hydrogenated over $Rh_2O_3 \cdot PtO_2$ (100 mg) at room temperature for 1 hr and 2.5 mole eq. (26 ml) of hydrogen was absorbed. Work up in a manner similar to that of the 14α-enone (**11a**) gave a saturated alcohol, which was crystallized from ether–petr. ether to give crystals, mp 173—175°. Its IR spectrum shows OH bands at 3560 cm^{-1} and 3510 cm^{-1} and its NMR spectrum exhibits signals at 8.50 τ (1H, s, C_9–OH) and 6.74 τ (1H, d, J=5.0, C_9–H). This alcohol (180 mg) in acetone (5 ml) was treated with Jones reagent at 0° for 10 min and worked up as usual. The product (181 mg), homogeneous on TLC, failed to give crystals from a variety of solvents therefore proceeded to the next step without purification. Treatment of the product (considered to be a BC-*cis*-ketone (**22a**)) with KOH (100 mg) in MeOH (10 ml) at reflux for 45 min followed by acetylation with Ac_2O–pyridine afforded the epimeric ketone (**22b**) (175 mg). Recrystallization from MeOH gave a sample with mp 203—205°, $[\alpha]_D^{23}$ −12.9°. IR ν_{max} cm^{-1}: 1733, 1710, 1244. ORD (c=2.078, $CHCl_3$) [φ] (mμ): −4229 (315) (trough), 0 (298), +4900 (274) (peak), (a −91). NMR τ: 9.05 (3H, s, 18-Me), 8.86 (3H, s, 19-Me), 8.85 (3H, d, J=6.0, 21-Me), 8.01 (3H, s, OAc), 7.99 (3H, s, OAc), 5.23 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{38}O_5$: C, 71.74; H, 9.15. Found: C, 71.79; H, 8.85.

3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregnane (21), Modified Huang Minlon Reduction——A mixture of the ketone (**20b**) (900 mg), NH_2NH_2 (28 ml, 98% up) $NH_2NH_2 \cdot 2HCl$ (7 g) and TEG (triethylene glycol, 45 ml) was heated at 135° for 1 hr. After addition of solid KOH (14 g, 85%), the temperature was gradually raised to 190° by distilling the low boiling material out and the mixture was heated for 1 hr at this temperature. After cooling the mixture was poured into water, extracted with $CHCl_3$ and the $CHCl_3$ solution was washed with water, dried and evaporated. The residue was acetylated with Ac_2O–pyridine in the usual manner and afforded the product, crystallized from MeOH giving **21** (807 mg, 90% yield), double mp 98—100°, 124—126°. Recrystallization from MeOH gave a sample with double mp 98—101°, 125—127°, $[\alpha]_D^{25}$ +27.4°. IR ν_{max} cm^{-1}: 1735, 1240. NMR τ: 9.35 (3H, s, 18-Me), 9.12 (3H, s, 19-Me), 8.85 (3H, d, J=6.0, 21-Me), 7.99 (6H, s, 2×OAc), 5.17 (2H, m, $C_{3,20}$–H). *Anal.* Calcd. for $C_{25}H_{40}O_4$: C, 74.21; H, 9.97. Found: C, 74.26; H, 10.00.

3β,20β-Diacetoxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14β-pregnane (8)——A mixture of the 14β-ketone (22b) (110 mg), $NH_2 \cdot NH_2$ (4 ml, 98% up), $NH_2 \cdot NH_2 \cdot 2HCl$ (860 mg) and TEG (6 ml) was treated similarly as above, and gave the product (108 mg). Judging from the NMR spectrum of the crude product it was found to be a 7:3 mixture of two components, the major corresponding to **8**. The mixture could be freed from the minor by crystallization from MeOH and gave 62 mg of crystalline **8**, mp 98—100°. Recrystallization from MeOH gave a sample with mp 99—101°. This compound was identified with the one prepared previously from the 8-keto compound (**6**) by mixed melting point and comparison of the IR and the NMR spectra.

20β-Acetoxy-3β-hydroxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregnane (26)

Partial Hydrolysis of 21——To a stirred solution of **21** (830 mg) in MeOH (40 ml) at 47° was added K_2CO_3 (750 mg) in H_2O (5 ml) and kept stirring for 30 min at this temperature. Then the mixture was poured into water and extracted with $CHCl_3$. The $CHCl_3$ solution was washed with water, dried and evaporated. The residue (740 mg) was crystallized from MeOH to give **26** (240 mg). The mother liquor was chromatographed over silica gel (500 g) (CH_2Cl_2:AcOEt=10:1) and gave additional **26** (466 mg, collective yield, 95%). Recrystallization from MeOH gave a sample with double mp 113—115°, 144—145°, $[\alpha]_D^{24}$ +38.4°. IR ν_{max} cm^{-1}: 3600, 1732, 1240. ORD[14] (c=0.637, MeOH) [ϕ] (mμ): +1098 (290), +4236 (225) (peak), −1883 (204). CD [θ] (mμ): +4089 (210) (max). *Anal.* Calcd. for $C_{23}H_{38}O_3$: C, 76.19; H, 10.57. Found: C, 75.81; H, 10.50.

20β-Acetoxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregnan-3-one (27)——To a solution of **26** (660 mg) in acetone (20 ml) was added Jones reagent (0.6 ml, 1.2 eq.) and the mixture was stirred for 10 min at room temperature, then worked up as usual. The product was crystallized from ether–petr. ether to give **27** (580 mg, 91% yield), mp 132—133°. Recrystallization from the same solvent gave a sample with mp 133—134°, $[\alpha]_D^{24}$ +74.9°. IR ν_{max} cm^{-1}: 1730, 1717, 1238. ORD (c=0.948, $CHCl_3$) [ϕ] (mμ): +5665 (312) (peak), 0 (292), −3764 (274) (trough) (a −94). NMR τ: 9.32 (3H, s, 18-Me), 8.95 (3H, s, 19-Me), 8.85 (3H, d, J=6.0, 21-Me), 7.98 (3H, s, OAc), 5.13 (1H, m, C_{20}–H). *Anal.* Calcd. for $C_{23}H_{36}O_3$: C, 76.62; H, 10.07. Found: C, 76.62; H, 9.97.

20β-Acetoxy-2α-bromo-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregnan-3-one (28)——To a cooled solution of the 3-ketone **27** (360 mg) in AcOH (15 ml) and 3 drops of 30% HBr–AcOH under stirring was added dropwise Br_2–AcOH (Br_2 content 176 mg 1.1 eq.) and the solution was stirred for 30 min and stored overnight at room temperature. The reaction mixture was poured into ice water and extracted with CH_2Cl_2. The CH_2Cl_2 layer was washed with 10% aq. Na_2CO_3 and water and dried. After the solvent was evaporated under reduced pressure at room temperature, the residue was crystallized from ether–petr. ether to give the 2α-bromoketone **28** (352 mg, 80% yield), mp 162—166°. Recrystallization from the same solvent gave a sample with mp 165—167°, $[\alpha]_D^{24}$ +75.5°. IR ν_{max} cm^{-1}: 1733, 1240. ORD (c=0.482, $CHCl_3$) [ϕ] (mμ): +6819 (311) (peak), 0 (291), −6363 (270) (trough) (a +132). NMR τ: 9.33 (3H, s, 18-Me), 8.87 (3H, s, 19-Me), 8.85 (3H, d, J=6.0, 21-Me), 7.98 (3H, s, OAc), 7.61 (C_1–βH, d of d, $J_{1\beta,2\beta}$=6.5, $J_{1\beta,1\alpha}$=−13.5), 5.20 (C_2–βH, q, $J_{2\beta,1\beta}$=6.5, $J_{2\beta,1\alpha}$=13.0). *Anal.* Calcd. for $C_{23}H_{35}O_3Br$: C, 62.88; H, 8.01; Br, 18.19. Found: C, 62.71; H, 7.99; Br, 17.95.

20β-Acetoxy-2α, 4α-dibromo-9(8→7),8(9→11)-diabeo-5α, 7α, 11β, 14α-pregnan-3-one 29——To a cooled solution of **27** (360 mg) in AcOH (3 ml) and 30% HBr–AcOH (0.3 ml) under stirring was added dropwise a solution of Br_2 (336 mg, 2.1 eq.) in AcOH (0.6 ml) and the solution was stored in refrigerator overnight then poured into ice water. The product was extracted with ether and the ethereal layer was washed with 5% aq. Na_2CO_3 and water and dried. After evaporation of the solvent under reduced pressure at room temperature, the residue was crystallized from CH_2Cl_2–ether–petr. ether to give the 2α,4α-dibromoketone (**29**) (432 mg, 83% yield), mp 178—182°. Recrystallization from CH_2Cl_2 ether gave a sample with mp 180—183° (decomp.), $[\alpha]_D^{24}$ +20.6°. IR ν_{max} cm^{-1}: 1750 (sh), 1730, 1240. ORD (c=1.032, $CHCl_3$) [ϕ] (mμ): +4440 (307) (peak), 0 (285), −3767 (235) (trough). NMR τ: 9.15 (3H, s, 18-Me), 8.85 (3H, d, J=6.0, 21-Me), 8.80 (3H, s, 19-Me), 8.00 (3H, s, OAc), 7.61 (C_1–βH, d of d, $J_{1\beta,2\beta}$=6.5, $J_{1\beta,1\alpha}$=−13.0), 5.41 (C_4–H, d, J=13.0), 5.11 (C_2–βH, q, $J_{2\beta,1\beta}$=6.5, $J_{2\beta,1\alpha}$=13.0). *Anal.* Calcd. for $C_{23}H_{34}O_3Br_2$: C, 53.29; H, 6.61; Br, 30.83. Found: C, 53.48; H, 6.48; Br, 30.94.

20β-Acetoxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregn-1-en-3-one (30) **and 20β-Acetoxy-9(8→7),8(9→11)-diabeo-7α,11β,14α-pregn-4-en-3-one** (32)

Dehydrobromination of the 2α-Bromoketone (28)——To a solution of **28** (370 mg) in DMF (dimethylformamide, 20 ml) was added LiCl (1.2 g) and the mixture was heated at 150° for 2.5 hr under stirring, then poured into water. The product was extracted with ether, washed with 5% aq. Na_2CO_3 and water and dried. Evaporation of the solvent gave the product, a mixture of 4 components, which was separated

14) I.P. Jennings, W.P. Mose, and P.M. Scopes[15] reported that the ORD of the compound containing the carboxyl chro mophor shows Cotton effect with a first extremum at about 227 mμ and in steroidal acetate the sign and the magnitude of its Cotton effect is much differing depending on the position of the substituent. Ex. 3β-Acetoxy5α-cholestane [ϕ] +772, 20β-Acetoxy-5α-pregnane [ϕ] +*ca.* 3000. Refering to these data it is reasonably deduced that the compound (**26**) has 3β-hydroxy-20β-acetoxy groups.

15) J.P. Jennings, W.P. Mose, and P.M. Scopes, *J. Chem. Soc.* (*C*), **1967**, 1104.

by preparative TLC (CH_2Cl_2:AcOEt=20:1). The first fraction (from the top) amounted to 28 mg (9.3%), and was supposed to possess a 2-bromo-Δ^1-3-ketone partial structure from its IR and NMR spectra but was not studied further. The second fraction amounted to 157 mg (52.3%) and crystallized from MeOH to give **30**, mp 126—130°. Recrystallization from MeOH gave a sample with mp 129—131°, $[\alpha]_D^{24}$ +60.6°. UV λ_{max} mμ (ε): 230 (10562). IR ν_{max} cm^{-1}: 1733, 1684, 1240. NMR τ: 9.35 (3H, s, 18-Me), 8.97 (3H, s, 19-Me), 8.88 (3H, d, J=6.0, 21-Me), 7.98 (3H, s, OAc), 5.15 (1H, m, C_{20}–H), 4.20 (C_2–H, d, J=10.0), 3.25 (C_1–H, d, J=10.0). *Anal.* Calcd. for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 76.96; H, 9.51. The third fraction amounted to 68 mg (22.2%) and crystallized from MeOH to give **32**, mp 173—176°. Recrystallization from MeOH gave a sample with mp 175—178°, $[\alpha]_D^{24}$ +152°. UV λ_{max} mμ (ε): 241 (17340). IR ν_{max} cm^{-1}: 1732, 1679, 1620, 1244. *Anal.* Calcd. for $C_{23}H_{34}O_3$: C, 77.05; H, 9.56. Found: C, 77.33; H, 9.59. The last fraction (25 mg, 8%) was later found to be the dienone (**34**), probably stemed from a dibromo compound contaminated in the starting material. Characterization of the dienone (**34**) is described in the following.

20β-Acetoxy-9(8→7),8(9→11)-diabeo-7α,11β,14α-pregna-1,4-dien-3-one (34)——A mixture of **29** (300 mg), LiBr (500 mg), Li_2CO_3 (500 mg) and DMF (3 ml) was heated at 120° for 30 min under stirring, then filtered and the residue washed with CH_2Cl_2. The combied filtrate was taken up in CH_2Cl_2, washed with water, dried and evaporated. The residue was chromatographed over silica gel (CH_2Cl_2:AcOEt=10:1) and gave the dienone (**34**) (166 mg, 81% yield). Recrystallization 2 times from ether–petr. ether gave a sample with mp 151—153°, $[\alpha]_D^{24}$ +49.8°. IR ν_{max} cm^{-1}: 1731, 1669, 1633, 1610, 1240. UV λ_{max} mμ (ε): 243.5 (16334). NMR τ: 9.28 (3H, s, 18-Me), 8.87 (3H, d, J=6.0, 21-Me), 8.74 (3H, s, 19-Me), 8.00 (3H, s, OAc), 5.10 (1H, m, C_{20}–H), 3.92 (C_4–H, broad s), 3.83 (C_2–H, d of d, $J_{2,1}$=9.5, $J_{2,4}$=1.5), 3.22 (C_1–H, d, $J_{1,2}$=9.5). *Anal.* Calcd. for $C_{23}H_{32}O_3$: C, 77.49; H, 9.05. Found: C, 77.29; H, 9.00.

9(8→7),8(9→11)-Diabeo-5α,7α,11β,14α-pregn-1-ene-3,20-dione (31)——A mixture of **30** (66 mg) and KOH (150 mg) in MeOH (3 ml) was refluxed for 1 hr under N_2, then poured into water, extracted with CH_2Cl_2.

The organic layer was washed with water, dried and evaporated. After checking the absence of the carbonyl band due to the acetoxyl group in IR spectrum, the residue (55 mg) was dissolved in acetone (2 ml) and oxidized with Jones reagent. After usual work up the product (50 mg) was crystallized from MeOH to give **31** (40 mg), mp 215—218°. Recrystallization from MeOH gave a sample with mp 217.5—218°, $[\alpha]_D^{24}$ +126.2°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1695, 1670, 1604. UV λ_{max} mμ (ε): 230 (10418). NMR τ: 9.33 (3H, s, 18-Me), 8.94 (3H, s, 19-Me), 7.90 (3H, s, 21-Me), 4.16 (1H, d, $J_{2,1}$=10, C_2–H), 3.22 (1H, d, $J_{1,2}$=10.0, C_1–H). *Anal.* Calcd. for $C_{21}H_{30}O_2$: C, 80.20; H, 9.62. Found: C, 79.95; H, 9.65.

9(8→7),8(9→11)-Diabeo-7α,11β,14α-pregn-4-ene-3,20-dione (33) (Linear Progesterone)——A mixture of **32** (32 mg) and KOH (100 mg) in MeOH (3 ml) was refluxed for 1 hr under N_2. Work up gave a 20-alcohol, which was oxidized with Jones reagent in the usual manner. The product was crystallized from MeOH to give **33** (25 mg) mp 183—186°. Recrystallization from MeOH gave a sample with mp 185—188°, $[\alpha]_D^{24}$ +226.3°. IR ν_{max} cm^{-1}: 1709, 1681, 1623. UV λ_{max} mμ (ε): 240.5 (17978). NMR τ: 9.32 (3H, s, 18-Me), 8.76 (3H, s, 19-Me), 7.88 (3H, s, 21-Me), 4.28 (1H, broad s, $W^h/_2$=2.5, C_4–H). *Anal.* Calcd. for $C_{21}H_{30}O_2$: C, 80.20; H, 9.62. Found: C, 80.07; H, 9.58.

9(8→7),8(9→11)-Diabeo-7α,11β,14α-pregna-1,4-diene-3,20-dione (35)——The dienone (**34**) (100 mg) was treated similarly as above. Hydrolysis followed by oxidation gave **35**, which was crystallized 2 times from MeOH to give a sample, mp 194—196°, $[\alpha]_D^{24}$ +104.6°. IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1700, 1664, 1611, 1606 (infl). UV λ_{max} mμ (ε): 243 (16459). NMR τ: 9.27 (3H, s, 18-Me), 8.72 (3H, s, 19-Me), 7.88 (3H, s, 21-Me), 3.92 (1H, s, C_4–H), 3.82 (C_2–H), 3.25 (C_1–H, $J_{1,2}$=10.0, $J_{2,4}$=2.0). *Anal.* Calcd. for $C_{21}H_{28}O_2$: C, 80.73; H, 9.03. Found: C, 80.46; H, 9.19.

20β-Acetoxy-3β-*tert*-butoxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregnane (36)——A mixture of **26** (1 g), BF_3·ether (0.5 ml), 100% H_3PO_4 (0.2 ml) and CH_2Cl_2 (10 ml) was placed in a Pyrex tube and cooled by dry ice–acetone. Into the mixture was distilled isobutylene (liquefied, 10 ml). The tube was sealed and shaken for two days at room temperature. Then the tube was opened and excess isobutylene was evaporated at room temperature. The mixture was taken up in CH_2Cl_2 and washed with 10% Na_2CO_3 and water. The solvent evaporated and the residue was crystallized from ether–petr. ether to give **36** (1.1 g, 96% yield), mp 143—146°. Recrystallization from the same solvent gave a sample with mp 146—149°, $[\alpha]_D^{28}$ +32.0°. IR ν_{max} cm^{-1}: 1732, 1244, 1200, 1078, 1052. *Anal.* Calcd. for $C_{27}H_{46}O_3$: C, 77.46; H, 11.08. Found: C, 77.37; H, 11.07.

3β-*tert*-Butoxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregnan-20-one (38)——A mixture of **36** (1 g) and KOH (500 mg) in MeOH (20 ml) was refluxed for 6 hr under N_2 and poured into water. The product was extracted with $CHCl_3$ and washed with water. The solvent was evaporated and the residue, after checking the homogeniety on TLC, was dissolved in acetone (20 ml) and treated with Jones reagent (0.1 ml, 1.5 eq.). The reaction mixture was worked up as usual and the product was chromatographed over silica gel (CH_2Cl_2:AcOEt=10:1) to give **38** (720 mg). Recrystallization from MeOH gave a sample with mp 146—148°, $[\alpha]_D^{22}$ +102.1°. IR ν_{max} cm^{-1}: 1708, 1195, 1075, 1050. *Anal.* Calcd. for $C_{25}H_{42}O_2$: C, 80.15; H, 11.30. Found: C, 80.05; H, 11.47.

3β-Hydroxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-pregnan-20-one (39)——A mixture of **38** (200 mg) and *p*-TsOH (40 mg) in benzene (20 ml) was refluxed for 30 min. Then the mixture was taken up in $CHCl_3$ and

washed with 10% aq. Na_2CO_3 and water, dried and evaporated. The residue (175 mg) was crystallized from MeOH to give **39** (100 mg), mp 157—161°. Recrystallization from MeOH gave a sample with mp 161—164°, $[\alpha]_D^{23}$ +110.8°. IR ν_{max} cm^{-1}: 3580, 1710. NMR τ: 9.35 (3H, s, 18-Me), 9.13 (3H, s, 19-Me), 7.90 (3H, s, 21-Me), 6.40 (1H, m, C_3-OH).

17β-Acetoxy-3β-hydroxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-androstane (40)

Baeyer Villiger Oxidation of 39——A mixture of **39** (100 mg), *m*-chloroperbenzoic acid (160 mg) and *p*-TsOH (4 mg) in dry $CHCl_3$ (4 ml, passed through Al_2O_3 column) was stirred for 15 min and stored at room temperature for 4 days. Then the mixture was taken up in $CHCl_3$ and washed with 10% aq. K_2CO_3 solution containing a small amount of $NaHSO_3$, and with water, dried and evaporated. The residue was chromatographed over silica gel (*n*-hexane:AcOEt=3:1, 20 ml/fraction). The fraction 50—100 gave **40** (83 mg). Recrystallization from ether–petr. ether afforded a sample with mp 179—181°, $[\alpha]_D^{23}$ +4.1°. IR ν_{max} cm^{-1}: 3592, 3400, 1738, 1245. *Anal.* Calcd. for $C_{21}H_{34}O_3$: C, 75.40; H, 10.25. Found: C, 75.24; H, 10.30.

17β-Acetoxy-9(8—7),8(9—11)-diabeo-5α,7α,11β,14α-androstan-3-one(41)——A solution of **40** (334 mg) in acetone (4 ml) was treated with Jones reagent (0.3 ml, 1.2 eq.) at room temperature and worked up as usual. The product was crystallized from ether to give **41** (280 mg, 84% yield), mp 168—171°. Recrystallization from ether gave a sample with mp 170—173°, $[\alpha]_D^{23}$ +39.6°. IR ν_{max} cm^{-1}: 1738, 1715, 1240. CD (c=1.8077 $\times 10^{-2}$ mole/liter, $CHCl_3$) $[\theta]$ (mμ): +6572 (293) (max). NMR τ: 9.16 (3H, s, 18-Me), 8.94 (3H, s, 19-Me), 7.96 (3H, s, OAc), 5.33 (1H, t, J=7.5, C_{17}-H). *Anal.* Calcd. for $C_{21}H_{32}O_3$: C, 75.86; H, 9.70. Found: C, 75.95; H, 9.68.

17β-Hydroxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-androstan-3-one (42)——A mixture of **41** (100 mg), KOH (100 mg), dioxane (3 ml), MeOH (2 ml) and water (1 ml) was refluxed for 30 min. Usual work up gave **42** (87 mg). Recrystallization twice from ether gave a sample with mp 170—173°, $[\alpha]_D^{23}$ +57.8°. IR ν_{max} cm^{-1}: 3570, 3450, 1715. NMR τ: 9.20 (3H, s, 18-Me), 8.93 (3H, s, 19-Me), 8.45 (1H, s, C_{17}-OH), 6.33 (1H, t, J=7.5, C_{17}-H). *Anal.* Calcd. for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.74; H, 10.51.

17β-Acetoxy-2α-bromo-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-androstan-3-one (43)——To a solution of **41** (66.5 mg) in THF (2.5 ml) at 0° was added trimethylphenyl ammonium perbromide (80 mg, 1.05 eq.) and the mixture was stirred for 15 min at the temperature. Yellow color of the solution, emerged by adding the reagent, gradually disappeared and instead colorless crystalline solids deposited. The mixture was poured into water and the product was extracted with CH_2Cl_2, washed with 5% Na_2CO_3 and water. After evaporation of the solvent the residue was crystallized from ether–petr. ether to give **43** (64 mg), mp 125—130°. Recrystallization from the same solvent gave a sample with mp 128—130°, $[\alpha]_D^{22}$ +38.3°. IR ν_{max} cm^{-1}: 1737, 1242. ORD (c=0.177, $CHCl_3$) $[\phi]$ (mμ): +4423 (308) (peak), 0 (290), −7484 (265) (a +119). NMR τ: 9.18 (3H, s, 18-Me), 8.88 (3H, s, 19-Me), 8.15 (3H, s, OAc), 7.62 (C_1-βH, d of d, $J_{1\beta,2\beta}$=6.5, $J_{1\beta,1\alpha}$=−13.0), 5.37 (1H, t, J=8.0, C_{17}-H), 5.27 (C_2-βH, q, $J_{2\beta,1\beta}$=6.5, $J_{2\beta,1\alpha}$=13.0). *Anal.* Calcd. for $C_{21}H_{31}O_3Br$: C, 62.84; 11)-H, 7.79; Br, 19.91. Found: C, 62.91; H, 7.66; Br, 20.20.

17β-Acetoxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-androst-1-en-3-one(44)and 17β-Acetoxy-9(8→7),8(9→ diabeo-7α,11β,14α-androst-4-en-3-one (46)

Dehydrobromination of 43——To a stirred solution of **43** (235 mg, crude material) in DMF (15 ml) was added LiCl (750 mg) and the mixture was stirred for 3 hr at 150° under N_2, then poured into water. The product was extracted with ether, washed with 5% aq. Na_2CO_3 and water and dried and evaporated. The residue was a mixture of four components and separated by preparative TLC (CH_2Cl_2–AcOEt=30:1). The first fraction amounted to 9 mg and identified as the starting material by comparison of IR and TLC. The second fraction amounted to 117 mg which was crystallized from ether–petr. ether to give **44**. mp 183—188°. Recrystallization from the same solvent gave a sample with mp 185—188°, $[\alpha]_D^{25.6}$ +33.7°. UV λ_{max} mμ (ε): 241 (17728). IR ν_{max} cm^{-1}: 1738, 1682, 1610, 1240. NMR τ: 9.17 (3H, s, 18-Me), 8.93 (3H, s, 19-Me), 7.98 (3H, s, 17-OAc), 5.35 (1H, t, J=8.0, C_{17}-H), 4.18 (C_2-H), 3.23 (C_1-H, d of d, J=10.0). *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.56; H, 9.26.

The third fraction amounted to 33 mg and crystallized from ether–*n*-hexane to give **46** (21 mg), mp 163—165°. Recrystallization from the same solvent gave a sample with mp 164—165°, $[\alpha]_D^{27.2}$ +118.7°. UV λ_{max} mμ (ε): 241 (17728). IR ν_{max} cm^{-1}: 1736, 1677, 1619, 1240. NMR τ: 9.13 (3H, s, 18-Me), 8.75 (3H, s, 19-Me), 7.97 (3H, s, OAc), 5.35 (1H, t, J=8.0, C_{17}-H), 4.28 (1H, broad, s, $W^h/_2$=2.5, C_4-H). *Anal.* Calcd. for $C_{21}H_{30}O_3$: C, 76.32; H, 9.15. Found: C, 76.51; H, 8.92.

The last fraction (16 mg) was presumed to have $\Delta^{1,4}$-3-ketone partial structure judging from the behavior on TLC and IR spectrum (ν_{max} cm^{-1}: 1668 (s), 1631 (m), 1609 (w)) but was not studied further.

17β-Hydroxy-9(8→7),8(9→11)-diabeo-5α,7α,11β,14α-androst-1-en-3-one(45)——A mixture of **44** (136 mg) and K_2CO_3 in 80% aq. MeOH (15 ml) was refluxed for 1.5 hr under N_2 then poured into water. The product was extracted with $CHCl_3$, washed with water and dried and evaporated. The residue (120 mg) was crystallized from ether–*n*-hexane to give **45**, mp 154—156°. Recrystallization from the same solvent gave a sample with mp 156—157.5°, $[\alpha]_D^{27.8}$ +39.4°. UV λ_{max} mμ (ε): 230 (10019). IR ν_{max} cm^{-1}: 3550, 3450, 1680, 1610. NMR τ: 9.20 (3H, s, 18-Me), 8.90 (3H, s, 19-Me), 8.27 (1H, s, C_{17}-OH), 6.48 (1H, t, J=7.5, C_{17}-H), 4.14 (C_2-H), 3.21 (C_1-H, d of d, J=10.0). *Anal.* Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found: C, 79.41; H, 9.78.

17β-Hydroxy-9(8→7),8(9→11)-diabeo-7α,11β,14α-androst-4-en-3-one (47) Linear Testosterone——A mixture of **46** (60 mg) and K_2CO_3 (100 mg) in 80% aq. MeOH was refluxed for 2 hr under N_2. Work up similarly as above gave the product (50 mg) which was crystallized from ether–*n*-hexane to give **47** (39 mg), mp 163—166°. Recrystallization from the same solvent gave a sample with mp 165—167°, $[\alpha]_D^{25.5}$ +147.7°. UV λ_{max} mμ (ε): 242 (17427). IR ν_{max} cm^{-1}: 3570, 3440, 1680, 1622. NMR τ: 9.18 (3H, s, 18-Me), 8.75 (3H, s, 19-Me), 8.33 (1H, s, C_{17}–OH), 6.30 (1H, t, J=7.0, C_{17}–H), 4.28 (1H, broad s, $W^h/_2$=2.5, C_4–H). *Anal.* Calcd. for $C_{19}H_{28}O_2$: C, 79.12; H, 9.79. Found: C, 79.10; H, 10.00.

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