üblichen Kriterien identisch mit XIII aus XI; ebenso war das Di-HBr-Salz identisch mit dem entsprechenden Salz von XIII aus XI.

Die Analysen wurden im mikroanalytischen Labor (Leitung: Herr *H. Egli*) ausgeführt; die Aufnahme der UV.- und IR.-Spektren sowie die Bestimmung der p*K*-Werte verdanken wir dem physikalisch-chemischen Labor (Leitung: Herr Dr. *W. Michaelis*).

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231. Steroid Total Synthesis, Part II[1]); (−)-17β-Hydroxy-des-A-androst-9-en-5-one[2])

by **G. Saucy** and **R. Borer**

Chemical Research Department, *Hoffmann-La Roche Inc.*
Nutley, New Jersey 07110, USA

(31. VIII. 71)

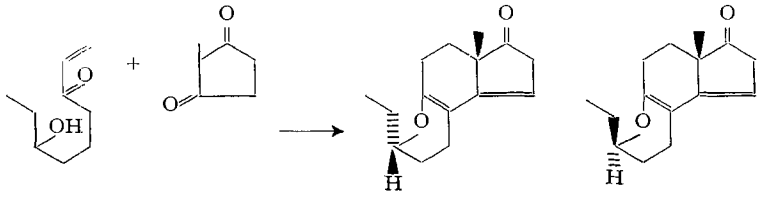
Summary. Based on the results obtained in the racemic series (part I), (−)-17β-hydroxy-des-A-androst-9-en-5-one has been synthesized, starting with (*S*)-(−)-5-heptanolide. The key step, *viz.* the condensation of (*S*)-(−)-7-hydroxy-1-nonen-3-one (or its amine adduct) with 2-methylcyclopentane-1,3-dione involves an asymmetric induction. Model experiments with (*R*)-(+)-5-decanolide leading to the enantiomeric homolog of the BCD-tricyclic compound are also described.

Recently we described [1] a new and efficient total synthesis of racemic 17β-hydroxy-des-A-androst-9-en-5-one. The present report deals with the synthesis of its optically active form[3]). The stereoselective synthesis involves a novel asymmetric induction step which we encountered [1] in the racemic series.

Stereochemistry of the key intermediate. In our work [1] with racemic material, we were not able to determine unambiguously the stereochemistry (**2** or **3**?) of the major product obtained from 2-methylcyclopentane-1,3-dione and the vinyl ketone **1** (reflux in pyridine-toluene). The problem was readily solved by carrying out an analogous sequence (see scheme 1) comprising as the key step the condensation of the optically active vinyl δ-hydroxy-ketone **7** with 2-methylcyclopentane-1,3-dione to afford the

[1]) Part I, *cf.* [1].
[2]) Presented in part at the Third International IUPAC Congress on the Chemistry of Natural Products (Steroids and Terpenes), Mexico City, Mexico, D.F., April 21–25, 1969; Program 14A.
[3]) *Cf.* [2] for related investigations and literature references.

diene **8a** and thence the *optically active* BCD-tricyclic compounds **9** and **10**. Availability[4]) of optically active (*R*)-(+)-5-decanolide (**4**) [3] was the prime reason for selecting this particular model. In addition, it was felt that it should be useful for projected syntheses of 19-norsteroids. The vinyl ketone **7** was readily prepared as follows. The (*R*)-(+)-*δ*-lactone **4** ($[\alpha]_D^{25} = +51°$, methanol)[5]) was first reduced with diisobutyl-

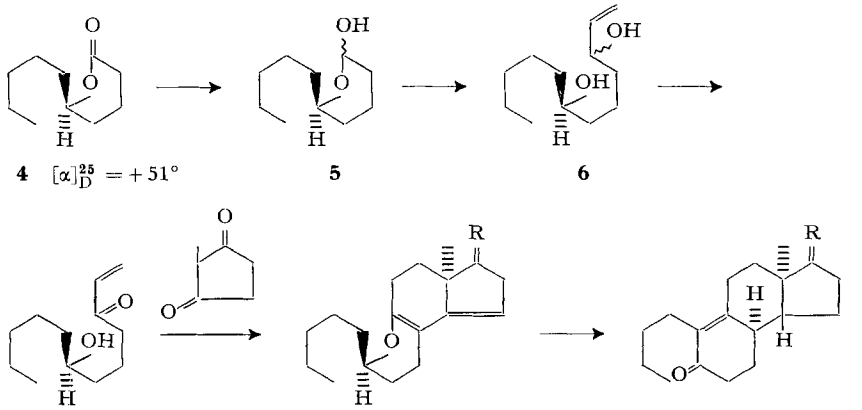


1 **2** **3**

(racemic compounds)

aluminium hydride [5] ('Dibal-H') in toluene at −70° to afford a nearly quantitative yield of lactol **5**, $[\alpha]_D^{25} = +39°$. Upon reaction with excess vinylmagnesium chloride in tetrahydrofuran, the vinyl alcohol **6** was obtained in excellent yield as a mixture of two diastereo-isomers which, on standing at 0°, slowly solidified. Although crystallization readily gave a product ($[\alpha]_D^{25} = -6°$) which was probably a pure diastereo-

Scheme 1



4 $[\alpha]_D^{25} = +51°$ **5** **6**

7

8a R = O, $[\alpha]_D^{25} = +170°$
8b R = β-H, α-OH

9 R = O, $[\alpha]_D^{25} = -60.5$
10 R = $^{\beta\text{-H},}_{\alpha\text{-OH}}$ $[\alpha]_D^{25} = +40.3$

isomer, no attempt was made to completely separate the mixture. Rather it was directly oxidized with activated manganese dioxide in 1,2-dichloroethane at room temperature to afford the relatively unstable vinyl ketone **7** in good yield. Boiling crude **7** with 2-methylcyclopentane-1,3-dione in acetic acid – xylene gave directly the dienol ether **8a** which was chromatographed on alumina. The pure fractions

[4]) We are indebted to Dr. *W. G. Jackson* of *Burdick and Jackson Laboratories, Inc.*, Muskegon, Michigan 49442, for supply of this material.

[5]) $[\alpha]_D = +53.5°$ (in ethanol) as well as CD. and ORD. data have recently been reported [4] for this compound, which was obtained [3] by microbiological reduction of 5-oxo-decanoic acid.

(TLC. analysis; 67% from crude **7**) were crystallized to afford pure **8a** (*'trans'*-isomer; $[\alpha]_D^{25} = +170°$)[6] in 35% yield (from crude **7**). The structure **8a** followed from the spectral data (see Experimental) and comparison with **2**. As regards the asymmetry at C-13, the negative *Cotton*-effect ($[\Theta] = -8950$ at 278 nm)[7] observed for the

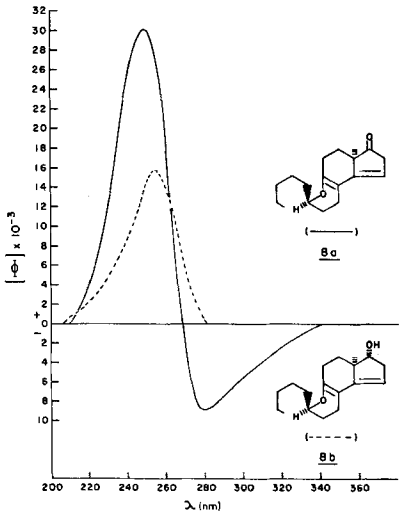
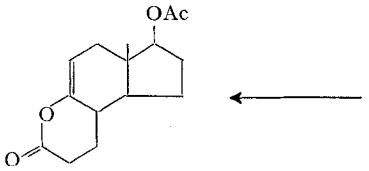
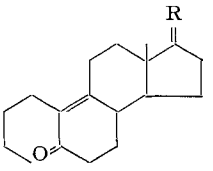


Fig. 1. *CD. Spectra of* **8a** *and* **8b** *in dioxane*

17-carbonyl group was strong evidence that we were dealing with a 13α-methyl compound[8]). This was confirmed by chemical conversion of **8a** into the 'unnatural' tricyclic enone **9** using the following sequence[9]): reduction with lithium aluminium hydride, hydrogenation, hydration, oxidation and cyclization.



11



12 R = α—H, β—OH; $[\alpha]_D^{25} = -41.6°$
13 R = O, $[\alpha]_D^{25} = +59.6°$

The enantiomeric 'natural' isomer **13** was prepared from the commercially available enol lactone **11**, using a published [7] procedure. The two non-crystalline products

[6]) This is the predominant isomer. The corresponding *'cis'*-isomer, which was probably present in the mother liquor, was not isolated. TLC. analysis did not resolve the (hypothetical) mixture.

[7]) CD. spectrum in dioxane (see Fig. 1). Compound **8a** exhibits a second, positive *Cotton* effect at 249 nm $[\Theta] = +30100$, which is due to the diene chromophore. The position of the carbonyl *Cotton* effect at 278 nm, rather than at 290 nm, results from overlap of the two different *Cotton* curves.

[8]) A positive *Cotton* effect (CD. spectrum in dioxane: $[\Theta] = +10800$ at 290 nm) has been recorded [6] for D-(–)-3-methoxy-17-oxo-estra-1, 3, 5(10), 8, 14-pentaene.

[9]) For details, see the analogous transformation **20** → **26**.

9 and **13** gave identical TLC., IR., UV., and NMR. data and opposite rotations ($[\alpha]_D^{25} = -60.5°$ and $+59.6°$, resp.). Selective reduction of the 17-ketone **9** with lithium tri-*t*-butoxy-aluminium hydride afforded the corresponding 17α-alcohol **10**, again as an oil; $[\alpha]_D^{25} = +40.3°$. The enantiomeric 17β-alcohol **12**, a precursor in the synthesis of **13**, had $[\alpha]_D^{25} = -41.6°$. The ORD. curves of the ketone pair **9**, **13** and of the alcohol pair **10**, **12** were found to be exact mirror images within the limits of the method (see Fig. 2 and 3). It follows that the crystalline diene **8a** and the oily products **9** and **10** are optically pure. This is the result of a stereoselective process starting with the optically active lactone **4** and involving a high degree of asymmetric induction in the formation of the diene **8a** from the vinyl ketone **7**.

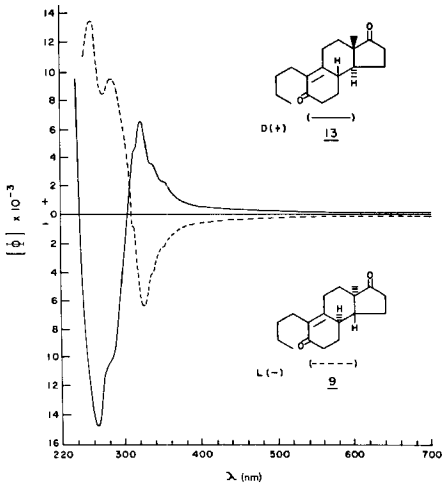


Fig. 2. *ORD. Spectra of* **9** *and* **13** *in dioxane*

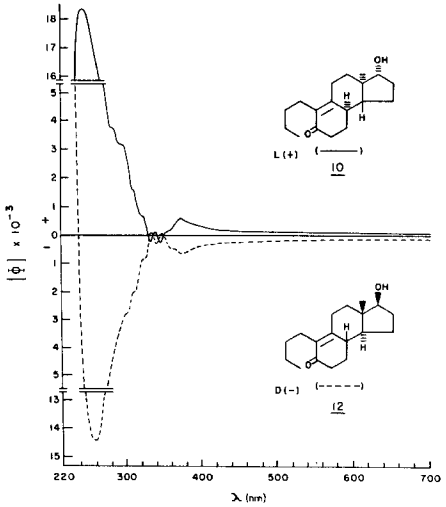


Fig. 3. *ORD. Spectra of* **10** *and* **12** *in dioxane*

Total synthesis of (−)-17β-hydroxy-des-A-androst-9-en-5-one (**28**). With the information gained in the model experiment (**4** → **9**, **10**), we could now synthesize the desired BCD-tricyclic compound **28**, starting with the novel (*S*)-(−)δ-lactone **15** (see scheme 2). This lactone was prepared[10]) by microbiological reduction [3] of the known [8] keto-acid **14**, using *Cladosporium butyri* (55% yield). The rotation ($[\alpha]_D^{25} = -58°$) observed for the lactone **15** indicated an optical purity of approx. 85%, based on comparison with homologous δ-lactones [3] [4]. The lactone **15** showed a tendency to 'polymerize'[11]) upon standing at room temperature. Reduction of **15** with diisobutylaluminium hydride [5] in toluene at $-70°$ gave the cyclic hemiacetal **16** in nearly quantitative yield. The product **16** had no aldehyde carbonyl absorption in the IR. and was shown by NMR. to be a mixture of the two possible diastereoisomers (*cf.* [1]). Reaction of the crude lactol **16** with excess vinylmagnesium chloride in tetrahydrofuran at 30° gave the vinyl alcohol **17** in excellent yield as a mixture of two diastereo-isomers. Selective oxidation of crude **17** with activated manganese

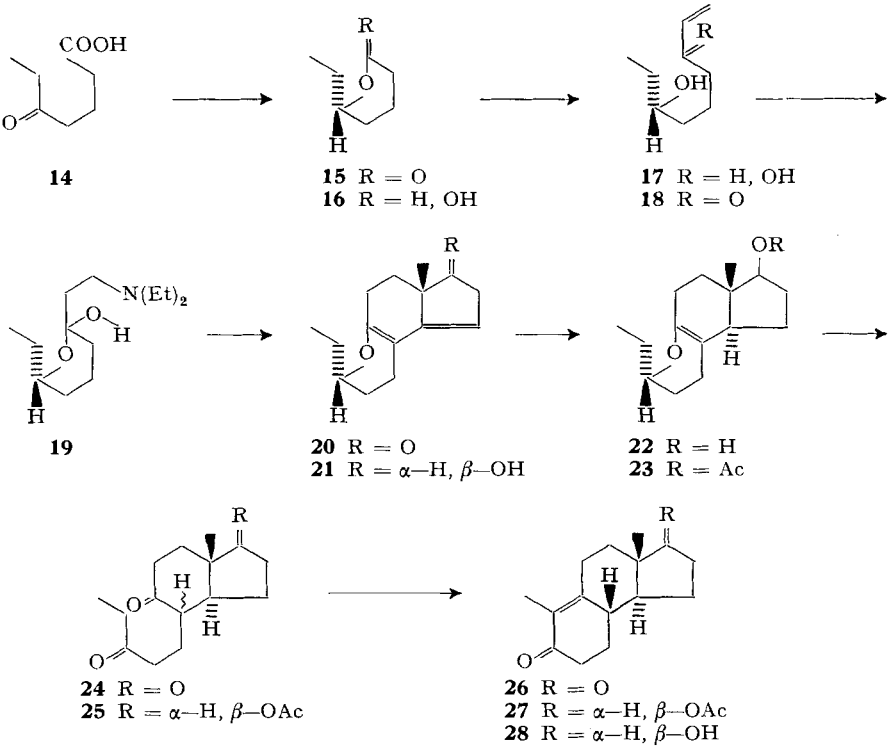
[10]) We would like to thank Dr. *J. Berger* and his staff of our Microbiology Department for this preparation.

[11]) A similar behaviour has been reported for other δ-lactones; see [9].

dioxide in 1,2-dichloroethane afforded crude vinyl ketone **18**, UV.-max. (ethanol) at 208 nm, ε = 8570, in about 54% yield. This yield was considered unsatisfactory, especially since it diminished on scale up.

Subsequently we were able to develop two more satisfactory procedures, the first of which consists of oxidizing the diol **17** with manganese dioxide *in the presence of diethylamine*[12]). This converts the relatively unstable vinyl ketone formed *in situ* directly to the considerably more stable '*Mannich* base' **19**, which exists mostly as its cyclic hemiacetal (IR.-analysis). The base **19** is quite stable towards acid and can conveniently be purified by extraction with aqueous acids. To our knowledge, the combination of MnO_2-oxidation with *Mannich* addition has hitherto not been

Scheme 2



14

15 R = O
16 R = H, OH

17 R = H, OH
18 R = O

19

20 R = O
21 R = α–H, β–OH

22 R = H
23 R = Ac

24 R = O
25 R = α–H, β–OAc

26 R = O
27 R = α–H, β–OAc
28 R = α–H, β–OH

described. In fact, some reports [10] seemed to indicate that both the amine reagent as well as the product **19** might suffer oxidative attack. Using the new oxidation process, the amine **19** could conveniently be prepared in substantially better yield (85% crude **19** from **17**)[13]). The advantage of the new method is particularly apparent when working on a larger scale.

The second, and in our hands most convenient procedure for the preparation of the amine **19** from the lactone **15**, is based on the direct reaction of the latter with

[12]) Other amines, *e.g. n*-butylamine and pyrrolidine, may be used with similar success.

[13]) Similarly, MnO_2-oxidation of 3-hydroxy-1-nonene in benzene in presence of diethylamine gave 1-(N,N-diethylamino)-3-oxo-nonane in 78% yield.

vinylmagnesium chloride in tetrahydrofuran at $-50°$, followed by addition of diethylamine to the vinyl ketone **18** formed initially. To our knowledge, this is the first successful example of the direct conversion of a δ-lactone to the corresponding vinyl ketone. Literature data suggested that the desired product **18** would undergo a second vinyl *Grignard* reaction (1,4-addition) leading eventually to a γ,δ-unsaturated ketone. A product of this type had been observed in the reaction of vinylmagnesium chloride with a carboxylic ester [11] and a steroid γ-lactone [12]. Our experiments indicate that the success of the transformation **15** → **18** is primarily due to conducting the reaction at a sufficiently low temperature, *i.e.* around $-50°$. Higher reaction temperatures led to rather complex mixtures, in line with the earlier reports [11] [12]. A 74% overall yield of pure[14]) base **19** could be obtained from the lactone **15**, using the new procedure.

In order to produce the diene **20**, the crude vinyl ketone **18** was condensed with 2-methylcyclopentane-1,3-dione in boiling acetic acid/toluene [1]. A good yield (65% from **18**, 32% from **15**) of crystalline product **20**, $[\alpha]_D^{25} = -165°$, was obtained after chromatography on alumina. A substantially better yield (89% from **19**, 60% from **15**) of chromatographed **20**, $[\alpha]_D^{25}$ $-165°$, resulted when the *Mannich* base **19** was used. Later work[15]) showed that this product also contained the corresponding 13α-methyl isomer (*'cis'* isomer) and probably some racemic material.

A complete purification of the product **20** was fortunately found to be unnecessary, since the desired enone **28** can readily be obtained in optically pure form by crystallization. This enabled us to use the total crude material **20** for the transformations described below.

First, the ketone **20** was reduced with lithium aluminium hydride in tetrahydrofuran at 0° to give a nearly quantitative yield of the 17-alcohol **21**. A chromatographed, crystalline sample had a wide melting point range (68–95°) and $[\alpha]_D^{25} = -177°$; no attempt was made to isolate optically pure **21**.

Selective hydrogenation of crude **21** in toluene over a palladium catalyst, followed by acetylation, gave the cyclic enol ether **23** in excellent overall yield. The analysis of the hydrogenation product **22** and its acetate **23** with respect to the asymmetric center at C-14 was complicated by the fact that the starting material **21** was not uniform. However, using the pure racemate of **21**, we had found [1] that the desired CD.-*trans* product is formed to the extent of 85% or more (GC. analysis). Hydration of the enol ether **23** with 1 N sulfuric acid in acetone, followed by addition of a solution of chromium trioxide in 6 N sulfuric acid, smoothly afforded the diketone **25**. Upon treatment with *p*-toluenesulfonic acid in boiling benzene followed by base hydrolysis, the cyclic enone **28** was produced in optically impure form. Simple crystallization of the crude product from benzene finally afforded optically pure **28**, $[\alpha]_D^{25} = -40°$. This material was found to be identical in all respects with an authentic sample[16]). No chromatography was required throughout. The overall yield of pure **28** from the lactone **15** (optically impure!) was 13%.

In an alternate and slightly inferior process, the crude hydrogenation product **22**

[14]) Purification *via* extraction with acid. No attempt was made to raise the optical purity, which was presumably in the order of 85%, as estimated for the lactone **15**.

[15]) *Cf.* Part III [13].

[16]) Obtained from *Roussel-UCLAF*, Paris, France.

was directly 'hydrated' and oxidized to form the triketone **24**. The crude product, upon treatment with *p*-toluenesulfonic acid in benzene, afforded the optically impure tricyclic compound **26**. Chromatography and repeated crystallization from benzene-hexane yielded an optically pure sample of **26**, $[\alpha]_D^{25} = +89°$. This material was found to be identical with a standard prepared from **28**[16]) by oxidation. Selective reduction of **26** (optically impure) with lithium tri-*t*-butoxyaluminium hydride in tetrahydrofuran at 0°, followed by chromatography and crystallization from benzene readily gave optically pure **28**.

Additional results related to the formation of the diene **20** and a discussion of the possible mechanism regarding the asymmetric induction will be presented in part III [13].

Experimental

General. M.p.'s were taken on a *Thomas-Hoover* apparatus and are uncorrected. IR. spectra were recorded on a *Beckman* Model IR-9 instrument, UV. spectra on a *Cary* Model 14 spectrophotometer. NMR. spectra were measured on a *Varian* HA-100 or A-60A spectrometer, using tetramethylsilane as an internal standard. ORD. and CD. spectra were measured on a *Jasco* Model ORD/UV-5 instrument. Optical rotations were measured on a *Perkin-Elmer* Model 141 polarimeter. – All reactions and chromatograms were routinely monitored by thin-layer chromatography (TLC.) (*Brinkman* silica gel GF 254 plates), using 1:1 benzene-ethyl acetate as eluent. The spots were developed by spraying with 50% aqueous *p*-toluenesulfonic acid followed by heating to 150°. *Woelm* neutral aluminium oxide, activity grade III, and silica gel 0.2–0.5 mm were used for column chromatography. Usual working up means 3 extractions with benzene, washing with brine, saturated $NaHCO_3$ solution and brine, drying over Na_2SO_4, filtration and evaporation at 40° in vacuo.

1. *6(R)-Pentyl-tetrahydropyran-2-ol* (**5**). A solution of 5(*R*)-hydroxydecanoic acid lactone **4** [3][4]), [4] (5.0 g, 29.4 mmoles) in toluene (50 ml) was cooled to −70° and treated with a 20% solution of diisobutylaluminium hydride in toluene (31.4 ml; 44.2 mmoles) during 30 min. The reaction mixture was stirred at −70° for 1 h and then slowly poured into a mixture of acetic acid (25 ml) and ice (50 g). The usual working up gave crude **5** (5.0 g) as an oil. A sample was distilled for analysis; b.p. 99–100°/1 Torr; $[\alpha]_D^{25} = +38.7°$ ($c = 1.4$, $CHCl_3$). IR. ($CHCl_3$): 3600 cm^{-1}. NMR. ($CDCl_3$): δ 0.88 (*t*, 3H, $J = 7$ Hz, CH_3), 3.00–4.10 (*m*, 2H, CH + OH), 4.65 (*d*, 0.6H, $J = 7$ Hz, $H(2)_{ax}$), 5.18 (*s*, 0.4 H, $H(2)_{eq}$).

$C_{10}H_{20}O_2$ (172.27) Calc. C 69.72 H 11.70% Found C 70.08 11.45%

2. *3(R, S),7(R)-Dihydroxy-1-dodecene* (**6**). A solution of crude lactol **5** (5.0 g, 29.1 mmoles) in tetrahydrofuran (THF) (20 ml) was added within 15 min at 30° to a stirred 1.9 M solution of vinylmagnesium chloride in THF (46 ml, 87.1 mmoles). The mixture was stirred overnight at room temperature and then poured onto a mixture of ice and saturated ammonium chloride solution. The usual working up gave crude **6** (5,7 g), semi-crystalline. A sample was recrystallized twice from isopropyl ether-pentane at 0° for analysis; colorless crystals, m.p. 65.5–67.5°; $[\alpha]_D^{25} = -5.9°$ ($c = 1.0$, $CHCl_3$). IR. ($CHCl_3$): 3615, 3450, 1646, 993, 930 cm^{-1}. NMR. ($CDCl_3$): δ 0.87 (*t*, 3H, $J = 7$ Hz, CH_3), 3.58 (*m*, 1H, H(7)), 4.08 (*m*, 1H, H(3)), 4.98, 5.12 (*m*, 2H, $=CH_2$), 5.89 (*m*, 1H, $J_{cis} = 10$, $J_{trans} = 16$, $J_{vic} = 6$ Hz, H(2)).

$C_{12}H_{24}O_2$ (200.32) Calc. C 71.95 H 12.08% Found C 71.63 H 12.35%

3. *7(R)-Hydroxy-1-dodecen-3-one* (**7**). A solution of crude diol **6** (5.22 g, 26.1 mmoles) in 1,2-dichloroethane (260 ml, dried over K_2CO_3) was vigourously stirred at room temperature with activated manganese dioxide[17]) (63 g) for 1 h. The suspension was filtered through a suction funnel and the residue was thoroughly washed with dichloroethane (2 × 50 ml) and ether (2 × 50 ml). The combined filtrate was evaporated at 30° to give crude **7** (3.98 g) as an oil. UV.$_{max}$ (EtOH): 208 nm ($\varepsilon = 7940$).

[17]) Obtained from *Winthrop Laboratories*; New York, N.Y. 10016.

4. L-*6aα-Methyl-3β-pentyl-1,2,3,5,6,8-hexahydro-cyclopenta*[f]*chromene-7(6aH)-one* (**8a**). A mixture of crude vinyl ketone **7** (3.98 g, 20.1 mmoles), 2-methylcyclopentane-1,3-dione (2.25 g, 20.1 mmoles), xylene (50 ml) and acetic acid (25 ml) was refluxed under nitrogen for $1^1/_2$ h and then evaporated to dryness. The residue was triturated with benzene and the crystals were filtered and washed with benzene. Thus, 400 mg (3.57 mmoles) of unreacted 2-methylcyclopentane-1,3-dione were recovered. The combined filtrate was evaporated and the residue (5.56 g) chromatographed on alumnia (278 g). Elution with hexane and hexane-ether-(19:1) afforded a total of 2.98 g crystalline **8a**. Recrystallization from methanol-water gave 1.75 g of pure **8a**: m.p. 55–60°, $[\alpha]_D^{25} = +159.5°$ ($c = 0.5$, $CHCl_3$). Recrystallization from pentane at $-70°$ gave an analytical sample: colorless crystals, m.p. 62.5–63.5°, $[\alpha]_D^{25} = +170°$ ($c = 0.5$ $CHCl_3$). UV.$_{max}$ (EtOH) at 252 nm ($\varepsilon = 18300$). IR. ($CHCl_3$): 1738, 1638 cm^{-1}. NMR. ($CDCl_3$): δ 0.92 (*t*, 3H, $J = 7$ Hz, CH_3CH_2), 1.13 (*s*, 3H, CH_3), 3.03 (*m*, 2H, H(8)), 3.72 (*m*, 1H, H(3)), 5.40 *t*, 1H, $J = 2.5$ Hz, H(9)). ORD. ($c = 0.282$, dioxane, 23°): $[\Phi]_{700}$ 0°, $[\Phi]_{589} + 213°$, $[\Phi]_{263} + 27400°$, $[\Phi]_{248}$ 0°, $[\Phi]_{228} - 15300°$ and $[\Phi]_{210\,(last)} - 7300°$. CD. ($c = 0.0103$ M, dioxane): $[\Theta]_{340}$ 0, $[\Theta]_{278} - 8950$, $[\Theta]_{268}$ 0, $[\Theta]_{249} + 30116$ and $[\Theta]_{210\,(last)}$ 0 (see Fig. 1).

$C_{18}H_{26}O_2$ (274.41) Calc. C 78.80 H 9.55% Found C 78.55 H 9.70%

5. *Conversion of diene* **8a** *to tricyclic enone* **9**. – *Reduction* (→**8b**). A solution of diene **8a** (1.37 g, 5 mmoles) in anhydrous THF (25 ml) was added slowly to a mixture of lithium aluminium hydride (137 mg, 3.62 mmoles) and THF (25 ml) at 0° with stirring (N_2). The reaction mixture was stirred at 0° for 30 min and then carefully treated with sufficient water to produce a white precipitate which was filtered and washed with THF and ether. The filtrate was dried (Na_2SO_4) and the solvent removed to give crude **8b** (1.39, crystalline), suitable for the next step. A sample was recrystallized from pentane for analysis: colorless crystals, m.p. 103–105°, $[\alpha]_D^{25} = +130°$ ($c = 0.52$, $CHCl_3$). IR. ($CHCl_3$): 3610, 1643 cm^{-1}. UV.$_{max}$ (EtOH) at 252 nm ($\varepsilon = 18500$). NMR. ($CDCl_3$): δ 0.90 (*t*, 3H, $J = 7$ Hz, CH_3CH_2), 0.97 (*s*, 3H, CH_3), 3.84 (*m*, 1H, H(3)), 4.02 (*m*, 1H, H(7)), 5.05 (*m*, 1H, H(9)). ORD. ($c = 0.320$, dioxane, 23°): $[\Phi]_{700} + 295°$, $[\Phi]_{589} + 381°$, $[\Theta]_{275} + 13800°$, $[\Phi]_{254}$ 0°, $[\Phi]_{238} - 12.500°$, $[\Phi]_{228\,(last)} - 10.800°$. CD. ($c = 0.0116$ M, dioxane, 23°): $[\Theta]_{280}$ 0, $[\Theta]_{254} + 15.800$, $[\Theta]_{205\,(last)}$ 0 (see Fig. 1).

$C_{18}H_{28}O_2$ (276.42) Calc. C 78.21 H 10.21% Found C 78.33 H 10.43%

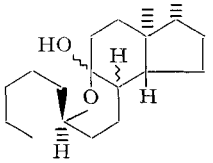
Hydrogenation. A solution of crude 17-hydroxy-diene **8b** (1.39 g, 5 mmoles) in toluene (50 ml) was hydrogenated at room temperature using a 5% palladium on carbon catalyst (378 mg). The uptake (111 ml) of hydrogen stopped after 6 h. The catalyst was filtered and washed with toluene. The solvent was removed to give crude *monoenol-ether* (1.3 g) as an oil.

Hydration. A solution of crude hydrogenation product (1.25 g, 4.5 mmoles) in acetone (25 ml) and 1 N H_2SO_4 (12.5 ml) was left at room temperature for 1 h after which it was diluted with brine and extracted with ether. The organic layers were washed with saturated $NaHCO_3$ solution and brine. The extract was dried (Na_2SO_4) and the solvent removed to give crude hemiacetal (1.2 g). A sample was chromatographed on alumina. Elution with hexane-ether-(1:1), -(1:2) and pure ether gave pure *hemiacetal*[18]) as an amorphous colorless material; $[\alpha]_D^{25} = +30.9°$ ($c = 0.50$, $CHCl_3$). IR. ($CHCl_3$): 3620 cm^{-1}. NMR. ($CDCl_3$): δ 0.87 (*t*, 3H, $J = 6$ Hz CH_3CH_2), 3.69 (*t*, 1H, $J = 6$ Hz, H(7)), 3.82 (*m*, 1H, H(3)).

Oxidation. A solution of crude hemiacetal[18]) (1.2 g, 4.05 mmoles) in acetone (40 ml) was treated at 20° with a mixture of chromium trioxide (2.0 g, 20 mmoles), in 6 N H_2SO_4 (10.2 ml). The mixture was stirred at room temperature for $2^1/_2$ h. The usual working up gave crude *triketone* (910 mg) as an oil.

Cyclization to L-*6-Butyl-3aα-methyl-1,2,3a,4,5,7,8,9,9aα,9bβ-decahydro-3*H*-cyclopenta*[a]*-naphthalene-3,7-dione* (**9**). A mixture of crude triketone (910 mg, 3.12 mmoles), toluene (50 ml)

[18])



(mixture of isomers)

and *p*-toluenesulfonic acid (205 mg) was refluxed for 3 h. The usual working up gave crude **9** (790 mg) as an *oil*, which after chromatography on silica gel (39.5 g) and elution with hexane-ether-(1:2) and -(1:4) afforded **9** (515 mg). A middle fraction of the chromatogram had a UV.$_{max}$ (EtOH) at 248 nm (ε = 14300) and a second maximum at 312 nm (ε = 1530), indicating the presence of an unknown by-product which was difficult to separate. A second chromatography on alumina failed to completely eliminate this by-product.

The best fraction had $[\alpha]_D^{25} = -60.5°$ (c = 2.0, $CHCl_3$). UV.$_{max}$ (EtOH) at 248 and 310 nm (ε = 13350 and 1330 resp.). IR. ($CHCl_3$); 1737, 1657, 1600 cm^{-1}. NMR. ($CDCl_3$): δ 0.90 (*t*, 3H, J = 7 Hz, CH_3CH_2), 1.03 (*s*, 3H, CH_3). ORD. (c = 0.1021, dioxane, 25°): $[\Phi]_{700}$ −101°, $[\Phi]_{589}$ −162°, $[\Phi]_{350}$ −2330° (shoulder (*sh*)), $[\Phi]_{336}$ −4170° (*sh*), $[\Phi]_{325}$ −6590°, $[\Phi]_{311}$ −823° (*sh*), $[\Phi]_{287}$ + 9600°, $[\Phi]_{274}$ + 8500°, $[\Phi]_{260}$ + 13710°, $[\Phi]_{250\,(last)}$ + 11000° (see Fig. 2).

$C_{18}H_{26}O_2$ (274.40) Calc. C 78.78 H 9.55% Found C 78.57 H 9.45%

6. L-*6-Butyl-3α-hydroxy-3aα-methyl-1,2,3a,4,5,8,9,9aα,9bβ-decahydro-7*H-*cyclopenta*[a]-*naphthalene-7-one* (**10**). To a solution of pure **9** (200 mg, 0.73 mmoles) in THF (10 ml) lithium tri-*t*-butoxyaluminium hydride (334 mg, 1.31 mmoles) was added at 0° in one portion. The mixture was stirred at 0° for 45 min and then treated with a mixture of acetone-water-(1:1) (3.0 ml) and 1 N H_2SO_4 (15 ml). The usual working up gave crude **10** (200 mg) which was chromatographed on alumina (20 g). Elution with benzene and benzene-ether-(9:1) and -(4:1) afforded a total of 182 mg **10** as an oil; $[\alpha]_D^{25} = +40.3°$ (c = 2.0, $CHCl_3$). UV.$_{max}$ (EtOH) at 249 nm (ε = 14580). IR. ($CHCl_3$): 3620, 1660, 1605 cm^{-1}. NMR. ($CDCl_3$): δ 0.92 (*t*, 3H, J = 7 Hz, CH_3CH_2), 0.91 (*s*, 3H, CH_3). ORD. (c = 0.1043, dioxane, 25°): $[\Phi]_{700}$ + 58°, $[\Phi]_{589}$ + 105°, $[\Phi]_{376}$ + 600°, $[\Phi]_{364-60}$ + 221° (*sh*), $[\Phi]_{350}$ − 221°, $[\Phi]_{343}$ + 110°, $[\Phi]_{336}$ − 193°, $[\Phi]_{327-25}$ + 719° (*sh*), $[\Phi]_{313}$ + 1685° (*sh*), $[\Phi]_{307}$ + 2485° (*sh*), $[\Phi]_{303-294}$ + 3320° (*sh*), $[\Phi]_{290-85}$ + 3865° (*sh*), $[\Phi]_{250}$ + 18500°, $[\Phi]_{240\,(last)}$ + 10790° (see Fig. 3).

$C_{18}H_{28}O_2$ (276.42) Calc. C 78.21 H 10.21% Found C 78.06 H 10.19%

7. D-*6-Butyl-3β-hydroxy-3aβ-methyl-1,2,3,3a,4,5,8,9,9aβ,9bα-decahydro-cyclopenta*[a]-*naphthalene-7*H-*7-one* (**12**). A solution of *n*-pentylmagnesium bromide, prepared in the usual manner from magnesium (2.88 g, 0.119 mole), 1-bromopentane (15.1 g, 0.1 mole) and ether (50 ml), was treated with a solution of enol lactone **11**[19] (27.6 g, 0.097 mole) in THF (200 ml) at −70° during 30 min. The mixture was stirred at −60° for 2 h, allowed to warm up to 0°, and then poured onto a mixture of ice and ammonium chloride. The mixture was extracted with ether, the combined ether extracts were washed with water and brine, the extract dried (Na_2SO_4) and the solvent removed to give 31 g of oil. This was dissolved in methanol (300 ml) and poured into a solution of NaOH (30 g; 100%) in H_2O (300 ml). After standing at room temperature for 20 h the mixture was extracted with ether (3 times). The combined ether extracts were washed with water and brine, dried (Na_2SO_4) and the solvent removed to give crude **12** (13.6 g) which was chromatographed on alumina (408 g). Elution with hexane-ether-(2:1) and -(1:1) afforded pure **12** (5.43 g) as an oil, $[\alpha]_D^{25} = -41.6°$ (c = 1.20, $CHCl_3$). UV.$_{max}$ (EtOH) at 250 nm (ε = 14600). IR. ($CHCl_3$): 3620, 1660, 1605 cm^{-1}. NMR. ($CDCl_3$): δ 0.92 (*t*, 3H, J = 7 Hz, CH_3CH_2), 0.91 (*s*, 3H, CH_3), 2.17 (*s*, 1H, OH). ORD. (c = 0.1040, dioxane, 25°): $[\Phi]_{700}$ −80°, $[\Phi]_{589}$ −124°, $[\Phi]_{377}$ −591°, $[\Phi]_{367-63}$ −456° (*sh*), $[\Phi]_{352}$ +96°, $[\Phi]_{345}$ −279°, $[\Phi]_{338}$ +132°, $[\Phi]_{330-323}$ −856° (*sh*), $[\Phi]_{318-14}$ −1990° (*sh*), $[\Phi]_{306-302}$ −2790° (*sh*), $[\Phi]_{260}$ −14630°, $[\Phi]_{240\,(last)}$ +10500° (see Fig. 3).

$C_{18}H_{28}O_2$ (276.42) Calc. C 78.21 H 10.21 Found C 78.08 H 10.02%

8. D-*6-Butyl-3aβ-methyl-1,2,3a,4,5,7,8,9,9aβ,9bα-decahydro-3*H-*cyclopenta*[a]-*naphthalene-3,7-dione* (**13**). A solution of **12** (552 mg, 2 mmoles) in acetone (22 ml) was treated with a solution of chromium trioxide (1.0 g, 10 mmoles) in 6 N H_2SO_4 (5 ml) at 20°. The mixture was stirred for $2^1/_2$ h at room temperature. The usual working up gave crude **13** (430 mg) as an oil which was chromatographed on silica gel (43 g). Elution with hexane-ether-(1:1) and -(1:2) afforded pure **13** (380 mg) as an oil; $[\alpha]_D^{25} = +59.6°$ (c = 1.465, $CHCl_3$). UV.$_{max}$ (EtOH) at 249 nm (ε = 14500). IR. ($CHCl_3$): 1740, 1660, 1605 cm^{-1}. NMR. ($CDCl_3$): δ 0.88 (*t*, 3H, J = 6.5 Hz, CH_3CH_2), 1.03 (*s*, 3H, CH_3). ORD. (c = 0.1011, dioxane, 25°): $[\Phi]_{700}$ + 85°, $[\Phi]_{589}$ + 140°, $[\Phi]_{354-47}$ + 2360° (*sh*), $[\Phi]_{338-34}$ + 3562° (*sh*), $[\Phi]_{323}$ + 6560°, $[\Phi]_{315}$ + 4530° (*sh*), $[\Phi]_{280}$ − 10580°, $[\Phi]_{260}$ − 15100°, $[\Phi]_{240}$ − 9600° (see Fig. 2).

$C_{18}H_{26}O_2$ (274.4) Calc. C 78.78 H 9.55 Found C 78.81 H 9.83%

[19]) Available from *Roussel-UCLAF*, Paris, France; *cf.* [7].

9. *6(S)-Ethyl-tetrahydropyran-2-ol* (**16**). A solution of (–)-5-hydroxyheptanoic acid lactone **15**[10]) (30.0 g, 0.235 mole) in toluene (300 ml) was cooled to –70° and treated with a 20% solution of diisobutylaluminum hydride in toluene (250 ml, 0.35 mole). The reaction mixture was stirred for 1 h at –70° and then slowly poured onto a mixture of acetic acid (90 ml) and ice (360 g). The usual working up gave crude **16** (32.0 g). A sample was chromatographed on silica gel. Elution with hexane-ether-(4:1), -(2:1) and -(1:1) gave analytically pure **16** as an oil, $[\alpha]_D^{25} = -40.0°$ (c = 2.5, dioxane). IR. ($CHCl_3$): 3605 cm^{-1}. NMR. ($CDCl_3$): δ 0.91 (t, 3H, J = 8 Hz, CH_3CH_2), 3.34 (broad, 1H, OH), 3.95 (m, 1H, H(2)) 4.75 (m, 0.65H, $H(6)_{ax}$), 5.30 (s, 0.35H, $H(6)_{eq}$).

$C_7H_{14}O_2$ (130.19) Calc. C 64.58 H 10.84% Found C 64.83 H 10.97%

10. *3(R,S),7(S)-Dihydroxy-1-nonene* (**17**). A solution of crude lactol **16** (32 g, 0.246 mole) in THF (150 ml) was added during 30 min at 30° to a 2.45 M solution of vinylmagnesium chloride in THF (315 ml, 0.77 mole). The reaction mixture was stirred at room temperature for 15 h, then poured onto a mixture of ice and saturated ammonium chloride solution. The mixture was extracted with ether, the combined ether extracts washed with brine, dried (Na_2SO_4) and the solvent removed to give the crude diol **17** (37.0 g) as an oil. A sample was chromatographed on silica gel, eluted with hexane-ether-(1:4) and pure ether, and then distilled (shortpath) for analysis: colorless oil; $[\alpha]_D^{25} = +10.8°$ (x = 2.13, $CHCl_3$). IR. ($CHCl_3$): 3615, 995, 935 cm^{-1}. NMR. ($CDCl_3$): δ 0.93 (t, 3H, J = 7 Hz, CH_3CH_2), 2.12 (broad, 2H, 2×OH), 3.53 (m, 1H, H(7)), 4.12 (m, 1H, H(3)), 5.08, 5.20 (m, 2H, $=CH_2$), 5.92 (m, 1H, J_{cis} = 10, J_{trans} = 16, J_{vic} = 6 Hz, H(2)).

$C_9H_{18}O_2$ (158.24) Calc. C 68.31 H 11.46% Found C 68.36 H 11.51%

11. *7(S)-Hydroxy-1-nonene-3-one* (**18**). A solution of crude diol **17** (7.1 g, 4.5 mmoles) in 1,2-dichloroethane (355 ml) was stirred vigorously at room temperature with activated manganese dioxide[17]) (85 g) for 1 h. The suspension was filtered through a suction funnel and the residue was thoroughly washed with dichloroethane (2×75 ml) and ether (2×75 ml). The solvent was removed to give crude vinylketone **18** (3.8 g) as an oil. UV.$_{max}$ (EtOH) at 208 nm (ε = 8570).

12. *6(S)-Ethyl-2-diethylaminoethyl-tetrahydropyran-2-ol* (**19**). – a) *From lactone* **15**[10]). To a solution of lactone **15** (32.0 g, 0.25 mole) in THF (160 ml), cooled under nitrogen to –75° in a dry ice-acetone bath, a solution of 3 M vinylmagnesium chloride in THF (171 ml, 0.51 mole) was added within 10 min at a temperature of –50 to –60°. The reaction mixture was stirred for an additional 10 min at –55°. After cooling to –60°, methanol (10 ml) was added carefully to the reaction mixture at –60°. Next, it was poured onto a mixture of ice (500 g), acetic acid (30 g), ammonium chloride (100 g) and ether (400 ml) The aqueous phase was separated and extracted with ether (2×350 ml) and the combined ether was washed with brine and dried over Na_2SO_4. Diethylamine (32 ml) was added to the solution, and after filtration and evaporation the crude '*Mannich* Base' **19** (51.5 g) was obtained as an oil. This was dissolved in ether (500 ml) and extracted with 1 N HCl (1×200 ml, 2×70 ml). The combined HCl extract was cooled and treated with 10 N NaOH (37 ml). The mixture was extracted with ether (3 times). The combined extract was washed with brine, dried (Na_2SO_4) and the solvent removed to give pure **19** (42.4 g) as an oil. A sample was chromatographed on alumina. Elution with hexane afforded the analytical sample: $[\alpha]_D^{25} = +45.09°$ (c = 2.2, benzene). IR. ($CHCl_3$): 3140 cm^{-1}. NMR. ($CDCl_3$): δ 0.90 (t, 3H, J = 7 Hz, CH_3CH_2), 1.05 (t, 6H, J = 7 Hz, 2×CH_3CH_2), 3.83 (m, 1H, H(3)).

$C_{13}H_{27}NO_2$ (229.36) Calc. C 68.08 H 11.87% Found C 68.26 H 11.71%

b) *From diol* **17**. A solution of crude diol **17** (35 g, 0.22 mole) in benzene (1050 ml) and diethylamine (70 ml) was stirred vigorously at room temperature with activated manganese dioxide[17]) (280 g) for 18 h. The suspension was filtered through a suction funnel and the residue washed with benzene (2×150 ml) and ether (2×150 ml). The solvent was removed to give crude **19** (43.7 g) as an oil, which was identical (TCL.-IR.) with the sample described above.

13. *3(S)-Ethyl-6a(S)-methyl-1,2,3,5,6,8-hexahydro-cyclopenta-*[f]*chromene-7(6aH)-one* (**20**)[15]). – a) *From* Mannich *base* **19**. A mixture of **19** (2.24 g, 10 mmoles), 2-methylcyclopentane-1,3-dione (1.35 g, 12 mmoles), toluene (45 ml) and acetic acid (15 ml) was carefully degassed, placed under nitrogen and heated to 110° for 1 h, using a *Dean-Stark* trap (there was slight reflux, but not enough for water to distill). The temperature was then raised to 130° for 1 h. The usual working up gave crude **20** (2.3 g, pink-colored crystals) which was chromatographed on alumina (230 g). Elution with hexane gave pure **20** (1.89 g; beige crystals). A sample was re-chromatographed as

described above to give the analytical sample[15]): colorless crystals, m.p. 70–98°, $[\alpha]_D^{25} = -165.8°$ ($c = 2.33$, $CHCl_3$). UV.$_{max}$ (EtOH) 253 nm ($\varepsilon = 18200$). NMR. ($CDCl_3$): δ 0.96 (*t*, 3H, $J = 7$ Hz, CH_3CH_2), 1.11 (*s*, 3H, CH_3), 3.68 (*m*, 1H, H(3)), 5.39 (*t*, 1H, $J = 2.5$ Hz, H(9)).

$C_{15}H_{20}O_2$ (232.32) Calc. C 77.55 H 8.68% Found C 77.26 H 8.83%

b) *From vinyl ketone* **18**. A mixture of **18** (3.8 g, 24.3 mmoles), xylene (50 ml), 2-methylcyclopentane-1,3-dione (2.96 g, 26.4 mmoles) and acetic acid (25 ml) was refluxed under nitrogen for $1^1/_2$ h. The reaction mixture was worked up as usual to give crude diene **20** (5.0 g), which was chromatographed as above to give pure **20** (3.69 g); m.p. 68–100; $[\alpha]_D^{25} = -164.7°$ ($c = 1.0$, $CHCl_3$).

14. *Conversion of diene* **20** *to* (–)-*17β-hydroxy-des-A-androst-9-en-5-one* (**28**). – *Reduction of* **20** (→**21**). A solution of crude **20** (42.0 g), 0.181 mole) in anhydrous THF (420 ml) was added at 0–5° within 15 min to a mixture of lithium aluminium hydride (4.2 g, 0.11 mole) in anhydrous THF (420 ml), with stirring and under nitrogen. The reaction mixture was stirred at room temperature for 30 min and then worked up by careful addition of water (20 ml), filtration and evaporation to give crude **21** (39.5 g, crystals). A sample was chromatographed on silica gel. Elution with benzene-ether-(4:1) and -(2:1) afforded the analytical sample, m.p. 68–100., $[\alpha]_D^{25} = -177.1°$ ($c = 1.88$, $CHCl_3$). UV.$_{max}$ (EtOH) 253 nm ($\varepsilon = 17800$). IR. ($CHCl_3$): 3620, 1644 cm^{-1}. NMR. ($CDCl_3$): δ 0.96 (*t*, 3H, $J = 7$ Hz, CH_3CH_2), 0.96 (*s*, 3H, CH_3), 3.63 (*m*, 1H, H(3)), 4.98 (*m*, 1H, H(9)). $C_{15}H_{22}O_2$ (234.32) Calc. C 76.88 H 9.46% Found C 76.74 H 9.73%

Hydrogenation of **21** (→**22**). A solution of crude **21** (39.5 g, 0.169 mole) in toluene (790 ml) was hydrogenated at room temperature using a 5% palladium on carbon catalyst (5.9 g). The uptake of hydrogen (3.8 l) stopped after 7 h. The catalyst was filtered, washed with benzene and the combined filtrate evaporated to give crude **22** (39.5 g) as an oil.

Acetylation of **22** (→**23**). A solution of crude **22** (39.5 g, 0,167 mole) in pyridine (39.5 ml) was treated with acetic anhydride (39.5 ml) at 0° with stirring. The resulting solution was stirred at room temperature for 15 h. For working up the mixture was diluted with benzene, cooled to 0° and then treated with methanol (17 ml). After 2 h at room temperature, the mixture was evaporated to dryness, the residue dissolved in benzene and the solution washed with 2N HCl, saturated $NaHCO_3$ solution and water. The aqueous phases were re-extracted with benzene. The combined extracts were dried (Na_2SO_4) and evaporated to give crude **23** (46.7 g) as an oil.

Hydration and oxidation of **23** (→**25**). A mixture of crude **23** (46.7 g, 0.167 mole), acetone (277 ml) and 1N H_2SO_4 (92.5 ml) was left at room temperature for 1 h. Acetone (185 ml) was added and the mixture was cooled, treated with a solution of CrO_3 (21.2 g) in 6N H_2SO_4 (106 ml) at 10–15° and then stirred at room temperature for 2 h. The usual working up gave crude diketone **25** (45.1 g) as an oil.

Cyclization of **25** (→**27**). A mixture of crude **25** (45.1 g, 0.153 mole), benzene (450 ml) and *p*-toluenesulfonic acid monohydrate (4.5 g) was refluxed (*Dean-Stark* trap) for 2 h with stirring. The usual working up gave crude **27** (41.2 g) as an oil.

(–)*17β-Hydroxy-des-A-androst-9-en-5-one* (**28**). A mixture of crude **27** (41.2 g, 0.149 mole), methanol (206 ml) and 2N NaOH (82 ml) was left at room temperature for 15 h. The usual working up gave crude **28** (32.2 g) as an oil which was chromatographed on alumina (322 g). Elution with hexane-benzene-(1:1) and -(1:2) and benzene-ether-(4:1) aftorded 18.7 g of chemically pure **28**. Recrystallization from benzene (100 ml) at room temperature afforded 7.55 g of optically pure **28**: m.p. 167–170°, $[\alpha]_D^{25} = -40.6°$ ($c = 1.0$, $CHCl_3$). UV.$_{max}$ (EtOH) at 248 nm ($\varepsilon = 15400$). A sample of the above material was recrystallized 4 times from benzene for analysis: colorless crystals, m.p. 168–170°, $[\alpha]_D^{25} = -39.6°$ ($c = 1.0$, $CHCl_3$). UV.$_{max}$ (EtOH) at 249 nm ($\varepsilon = 15900$). IR. ($CHCl_3$): 3625, 1660, 1610 cm^{-1}. NMR. ($CDCl_3$): δ 0.89 (*s*, 3H, 13-CH_3), 1.78 (*m*, 3H, 10-CH_3), 1.88 (*s*, 1H, OH), 3.68 (*m*, 1H, H(17)). ORD. ($c = 0.2344$, dioxane, 23°): $[\Phi]_{700}$ –58°, $[\Phi]_{589}$ –91°, $[\Phi]_{375}$ –950°, $[\Phi]_{366}$ –810°, $[\Phi]_{362}$ –850°, $[\Phi]_{350}$ –150°, $[\Phi]_{346}$ –220°, $[\Phi]_{342}$ 0°, $[\Phi]_{337}$ +450°, $[\Phi]_{330}$ +60°, $[\Phi]_{321}$ 0°, $[\Phi]_{317}$ –280°, $[\Phi]_{314}$ –260°, $[\Phi]_{257}$ –8748°, $[\Phi]_{243}$ 0°, $[\Phi]_{224}$ +11747°, $[\Phi]_{210(last)}$ +5998°. CD. ($c = 0.10$M, dioxane, 23°): $[\Theta]_{402}$ 0, $[\Theta]_{366}$ (*sh*) –580, $[\Theta]_{355}$ –1100, $[\Theta]_{347}$ –860, $[\Theta]_{341}$ –1040, $[\Theta]_{331}$ –320, $[\Theta]_{327}$ –400, $[\Theta]_{322}$ 0, $[\Theta]_{319}$ +140, $[\Theta]_{314}$ +40, $[\Theta]_{308}$ +200, $[\Theta]_{302}$ +80, $[\Theta]_{280}$ –40, $[\Theta]_{274}$ 0, $[\Theta]_{270}$ +60, $[\Theta]_{268}$ 0, $[\Theta]_{241}$ –13600, $[\Theta]_{222}$ 0, $[\Theta]_{210(last)}$ +6000. $C_{15}H_{22}O_2$ (234.34) Calc. C 76.88 H 9.48% Found C 76.65 H 9.56%

15. *Alternative synthesis of* **28** via **22** → **24** → **26**. – *Hydration and oxidation of* **22** (→ **24**). A mixture of crude **22** (48.2 g, 0.204 mole), acetone (485 ml) and 1N H_2SO_4 (242 ml) was left at room temperature for 1 h. The mixture was concentrated at 30° to half its volume and then extracted with ether (3 times). The combined ether extract was washed with brine, saturated $NaHCO_3$ solution and brine, then dried (Na_2SO_4) and evaporated to give 50.4 g of oil. This was dissolved in acetone (800 ml), treated at 5–10° with a solution of CrO_3 (52.7 g) in 6N H_2SO_4 (264 ml), and the mixture stirred at room temperature for 2 h. The usual working up gave crude triketone **24** (46.3 g) as an oil.

(+)*Des-A-androst-9-ene-5,17-dione* (**26**). A mixture of crude triketone **24** (46.3 g, 0.185 mole), benzene (463 ml) and *p*-toluenesulfonic acid monohydrate (4.6 g) was refluxed for 3 h. The usual working up gave crude **26** (42.0 g, crystals) which was chromatographed on silica gel (420 g). Elution with benzene-ether-(9:1), -(4:1) and -(1:1) gave 37.6 g of purified **26**. A second chromatogram on alumina (350 g) (elution with hexane-benzene-(4:1), -(1:1) and -(1:4)) finally afforded a total of 32.4 g of still purer **26**. A sample was recrystallized from ether-hexane to give chemically pure **26**: m.p. 100–117°, $[\alpha]_D^{25} = +58.3°$ ($c = 1.0$, $CHCl_3$). UV.$_{max}$ (EtOH) at 248 nm ($\varepsilon = 15100$). Further recrystallizations from benzene-hexane gave an optically pure sample: colorless crystals, m.p. 124–126°, $[\alpha]_D^{25} = +88.9°$ ($c = 1.0$, $CHCl_3$). UV.$_{max}$ (EtOH) at 247 nm ($\varepsilon = 15700$). IR. ($CHCl_3$): 1744, 1665, 1610 cm^{-1}. ORD. ($c = 0.292$, dioxane, 23°): $[\Phi]_{700}$ +96°, $[\Phi]_{589}$ +175°, $[\Phi]_{390}$ +613°, $[\Phi]_{376}$ +501°, $[\Phi]_{364}(sh)$ +835°, $[\Phi]_{350}(sh)$ +232°, $[\Phi]_{334}(sh)$ +4656°, $[\Phi]_{322}$ +8119°, $[\Phi]_{312}(sh)$ +5851°, $[\Phi]_{282}(sh)$ −7960°, $[\Phi]_{258}$ −9154°, $[\Phi]_{230}$ 0°, $[\Phi]_{210\,(last)}$ −7960°.

$C_{15}H_{20}O_2$ (232.32) Calc. C 77.55 H 8.68% Found C 77.24 H 8.67%

(−)*17β-Hydroxy-des-A-androst-9-en-5-one* (**28**). To a stirred solution of chromatographed **26** (32.3 g, 0.139 mole) in THF (960 ml), lithium tri-*t*-butoxy aluminum hydride (63,6 g, 0.25 mole) was added at 0° within 10 min. The reaction mixture was stirred at 0° for 30 min and then carefully treated with a mixture of acetone-water [200 ml (1:1)]. After addition of 3N H_2SO_4 (650 ml) the mixture was extracted with $CHCl_3$. The combined extracts were washed with water, saturated $NaHCO_3$ solution and water, dried (Na_2SO_4) and evaporated to give crude **28** (32.0 g, crystals), which was chromatographed on silica gel (640 g). Elution with benzene-ether-(4:1), -(2:1) and -(1:1) afforded chemically pure **28** (28.5 g) which was recrystallized from benzene (150 ml) at room temperature to give pure **28** (14.4 g), m.p. 165–168°, $[\alpha]_D^{25} = -42.7°$ ($c = 1.0$, $CHCl_3$).

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