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Synthesis of 2-Methyl-3-oxa-A-norestra-1,5(10)-dien-17β-ol and 2-Methyl-3-oxa-4,19-bisnorpregna-1,5(10)-dien-20-one[1]

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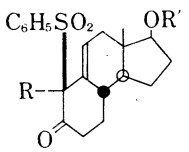
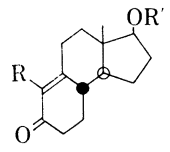
The titled compounds were synthesized from the corresponding 10-propargyl-des-A-9(10)-en-5-one derivatives through the 3,5-*seco*-4-nor-dioxo steroids. The preparation of des-A-19-norpregn-9(10)-ene-5,20-dione involving the condensation of phenyl methyl sulfone or dimethyl sulfone with methyl 1β-methoxycarbonyl-5,5-ethylenedioxy-7a-methyl-3aα, 7aβ-hexahydroindan-4α-yl propionate is also described.

In the preceding paper of this series,[1] A-furanosteroids with or without a methyl substituent at the β position in the furan ring were synthesized through 10β-phenylsulfonyl-17β-hydroxy-des-A-ester-9(11)-en-5-one (**1**) derived from 7a-methyl-1,5-dioxo-3aα,7aβ-hexahydroindan-4α-yl propionic acid. The present paper deals with synthesis of both an estrane and a pregnane system of A-furanosteroids having a methyl group at the α position in the furan ring.

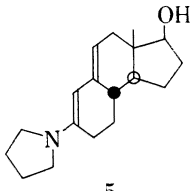
Since it is well known that a γ-diketone upon treatment with acid gives a furan, a starting material suitable for synthesizing α-methylfuranosteroids was considered to be a 3,5-seco-4-nor-2,5-dioxo steroid and such a compound can be prepared for example from the product of alkylation of 5-pyrrolidyl-17β-hydroxy-des-A-estra-5-(10),9(11)-diene(**5**) with 1,2-dichloro-2-propene as described by Nominé, *et al.*[3] who have used this compound for the preparation of 17β-hydroxy-A-norester-3-en-2-one. Recently, Pandit, *et al.*[4] have reported the reaction of a conjugated enamine with α-haloketone leading to the direct formation of a



1: R=R'=H
2: R=$CH_2C{\equiv}CH$, R'=Ac



3: R=$CH_2C{\equiv}CH$, R'=Ac
4a: R=CH_2COCH_3, R'=Ac
4b: R=CH_2COCH_3, R'=H



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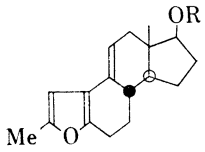
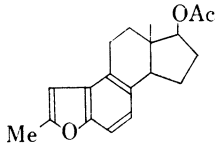


6a: R=Ac
6b: R=H
7: R=H,8α-H



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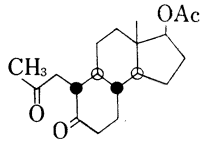

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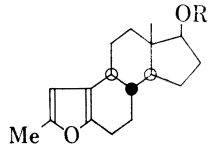


10a: R=H
10b: R=Ac

Chart 1

1) This work is Part XXXIV of "Thiosteroids"; Part XXXIII: T. Komeno, S. Ishihara, and H. Itani, *Tetrahedron*, **28** 4719 (1972).
2) Location: *Fukushima-ku, Osaka, 553, Japan.*
3) G. Nominé, J. Mathieu, R. Bucourt, L. Nédélec, M. Vignau, and J.C. Gasc, *C.R. Acad. Sc., Paris*, **264**, 1396 (1967).
4) U.K. Pandit, H.R. Reus, and K. de Jonge, *Rec. Trav. Chim. Pays-Bas*, **89**, 956 (1970).

fused furano derivative. Unfortunately, an attempted alkylation of the tricyclic dienamine (**5**) with α-bromoacetone was unsuccessful and its hydrolysis product, 17β-hydroxy-des-A-estr-9(10)-en-5-one, was completely regenerated. However, preparation of the desirable 17β-acetoxy-3,5-seco-4-norestr-9(10)-ene-2,5-dione (**4a**) could be achived by a scheme involving propargylation of either the dienamine (**5**) or the phenylsulfonyl compound (**1**), the latter process giving the better yield of **4a**. Thus, treatment of the dienamine (**5**) with propargyl bromide in dimethylformamide (DMF) followed by acetylation gave a propargyl enone (**3**) in rather lower yield (27%) and the improved yield (50%) of **3** was obtained when the alkylation of **5** was carried out in dimethyl sulfoxide. The compound (**3**) in turn was converted in high yield to the above enedione (**4a**) by hydration with mercuric sulfate in methanol containing a trace of sulfuric acid.[5] The structure of **4a** thus obtained was suggested by the ultraviolet (UV) spectrum and by the indication in the proton magnetic resonance (PMR) spectrum of the presence of two sharp singlets for acetyl moieties and an AB-type quartet due to methylene protons in an acetonyl group. A modified hydration of **3** with mercuriated cation exchange resin[6] caused hydrolysis of the product partly accompaneid by cyclization affording a γ-diketone (**4b**) and a vinyl furan (**6b**) in yields of 44.6% and 23.8% respectively. Acetylation of **4b** gave an acetate identical with **4a** obtained from **5**. On the other hand, alkylation of the phenylsulfonyl compound (**1**) with propargyl bromide in the presence of α-methylsulfinyl carbanion[1] and subsequent acetylation of the product obtained afforded in 76% yield a propargyl compound (**2**), in which the α equatorial configuration of the introduced propargyl group was assumed from its PMR spectrum. The C_{11}-proton resonance at 5.89 ppm is not significantly deshielded compared to that observed at 6.49 ppm in the dienol acetate of **1** in which the sulfonyl group is apparently in proximity to the vinyl proton as discussed in the preceding paper.[1] Desulfurization reaction of compound (**2**) with zinc dust in acetic acid gave rise the concomitant hydration of the propargyl moiety in the molecule and there was obtained a mixture which consisted of 38% of the expected propargyl enone (**3**), 41% of its hydrated product (**4a**) and 2.7% of a vinyl furan derivative (**6a**), these compounds being separated by preparative thin-layer chromatography (TLC). The former two compounds were identified with the samples prepared through the dienamine (**5**) respectively, by mixed melting points, comparison of infrared (IR) spectra and TLC. Thus, when the phenylsulfonyl propargyl compound (**2**) was desulfurized with zinc dust in acetic acid and the product was hydrated without further purification, there was obtained a 79% yield of the acetonyl compound (**4a**) together with a 5.7% yield of the vinyl furan (**6a**). Compound (**6a**), whose structure can be readily assumed from the UV (λ_{max} 241.5 nm) and PMR spectrum (a broadened singlet due to aromatic methyl protons at 2.22 ppm), was also obtained in 53.7% yield by heating **4a** in benzene in the presence of *p*-toluenesulfonic acid. However, the reaction was accompanied by concomitant rearrangement and aromatization of the B-ring to give a vinyl furan (**7**) different from **6b** and a benzofuran derivative (**8**) in yields of 11% and 6% respectively, neither of which could be crystallized. The former exhibits quite similar UV and PMR spectral properties to those of **6b**, except that the 13-methyl signal was observed at a field 0.27 ppm lower than that of **6b**; hence the 8α-isomeric structure was tentatively assumed for **7**. Compound (**8**), whose UV spectrum shows an absorption maximum at 255 nm and an absorption band containing fine structures at about 280 nm, was assigned as the benzofuran derivative in accord with the PMR spectral evidence of signals due to two vicinal and one isolated vinyl protons. The acetonyl compound (**4a**) on hydrogenation over palladium on charcoal led to a saturated γ-diketone (**9**), which in turn was heated in boiling benzene in the presence of *p*-toluenesulfonic acid yielding the desired compound, 2-methyl-3-oxa-A-norestra-1,5-(10) dien-17β-ol acetate (**10b**). Though preparation of a 2-methylthienosteroid was attempted

5) D. Caine and F.N. Tuller, *J. Org. Chem.*, **34**, 222 (1969).
6) Z.G. Hajos, K.J. Doebel, and M.W. Goldberg, *J. Org. Chem.*, **29**, 2527 (1964).

by reaction of the acetonyl compound (**4a**) with phosphorous pentasulfide in boiling benzene, formation of the expected thienosteroid was not observed and instead the 2-methylfurano-steroid (**10b**) was obtained in high yield. The structure of **10b** and its hydrolysis product (**10a**) were supported by their UV, PMR and mass spectral data described in Experimental.

Since 5,5-ethylenedioxy-10β-methylsulfonyl-des-A-estr-9(11)-en-17-one (**11**) resists hydrolysis of the ketal moiety under the acidic conditions usually employed[1] and also contains a keto function convertible to a pregnane derivative, the transformation of **11** into a pregnane system through its cyanohydrin was first attempted, though this scheme was unfavorable for the following reasons. Whereas treatment of **11** with potassium cyanide in methanol and acetic acid[7] gave a cyanohydrin (**12**) in 58% yield, on transcyanohydrination of **11** with acetone cyanohydrin[8] an isomeric cyanohydrin (**13**) was deposited as crystals from the reaction mixture in high yield. Because it is known that there is a preference for α-attack of the C_{17}-carbonyl group by the CN ion[9,10] the cyanohydrin (**12**) was assigned as 17α-cyano-17β-ol and hence (**13**) as 17β-cyano-17α-ol. These assignments were also supported by the molecuar rotation difference shown in Table I and by the IR spectral data. The IR spectrum of **13**

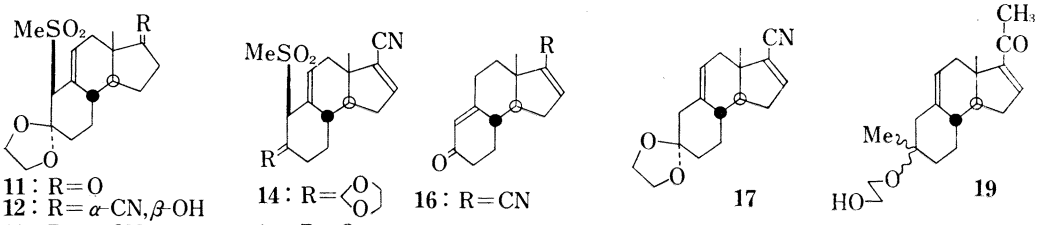
TABLE I. Molecular Rotation Difference between Cyanohydrins and the Parent Ketones

Parent ketone	M_D	α-CN, β-OH	β-CN, α-OH	Δ_1	Δ_2
3β-Acetoxy-5α-androstan-17-one[a]	+285	−82	+105	−367	−180
3β-Acetoxyandrost-5-en-17-one[a]	+14	−470	−198	−484	−212
5,5-Ethylenedioxy-10β-methylsulfonyl-des-A-estr-9(11)-en-17-one (**11**)	+380	−26	+59	−406	−321

a) Ref. 9

shows a more intense absorption band due to a CN group than that in the spectrum of **12**, this being in keeping with Nagata's observation that an equatorial cyano compound shows a higher CN band intensity than an axial epimer despite slight fluctuation of the absorption maximum in both epimers.[11] It was reasonably considered that the reaction of **11** with acetone cyanohydrin might proceed accompanied by an equilibrium and that precipitation of the less soluble cyanohydrin (**13**) with the CN group in the β configuration causes shifting the equilibrium in its favor. A similar predominant formation of 17β-cyano-17α-ol has been observed in the reaction of 3,3-ethylenedioxyestra-5(10),9(11)-dien-17-one with potassium cyanide.[12] Dehydration of the cyanohydrin (**13**) with phosphoryl chloride in pyridine[13] gave a dieneketal (**14**) in 90% yield, which in turn was hydrolized in high yield to a dienone (**15**) by treatment with perchloric acid in boiling acetone. Reduction of **15** with zinc dust in acetic acid afforded in moderate yield a desulfurized dienone (**16**), in which the keto function was protected by conversion to a ketal (**17**) with ethylene glycol. Grignard reaction of **17** with methyl magnesium bromide gave a complex mixture, from which the desired des-A-19-norpregna-9(10),16-diene-5,20-dione (**18**) could not be obtained. Column chromatography of the product over silica gel afforded a 20% yield of compound (**19**) as the only crystalline substance, the PMR spectrum of which shows three singlets assignable as methyl protons at 0.83, 1.09, and 2.25 ppm together with a multiplet due to an O–CH_2–CH_2–O group. These

7) K. Meyer, *Helv. Chim. Acta*, **29**, 1580 (1946).
8) A. Ercoli and P. de Ruggieri, *J. Am. Chem. Soc.*, **75**, 650 (1953).
9) H. Heusser, P. Th. Herzig, A. Fürst, and Pl. A. Plattner, *Helv. Chim. Acta*, **33**, 1093 (1950).
10) J.E. Baldwin, D.H.R. Barton, I. Dainis, and J.L.C. Pereira, *J. Chem. Soc., C*, **1968**, 2283; J.B. Jones, and J.D. Leman, *Can. J. Chem.*, **49**, 2420 (1971).
11) W. Nagata, M. Yoshioka, M. Narisada, and H. Watanabe, *Tetrahedron Letters*, **1964**, 3133.
12) J.C. Gasc and L. Nédeléc, *Tetrahedron Letters*, **1971**, 2005.
13) A. Butenandt and J. Schmidt-Thomé, *Chem. Ber.*, **71**, 1487 (1938); **72**, 182 (1939).

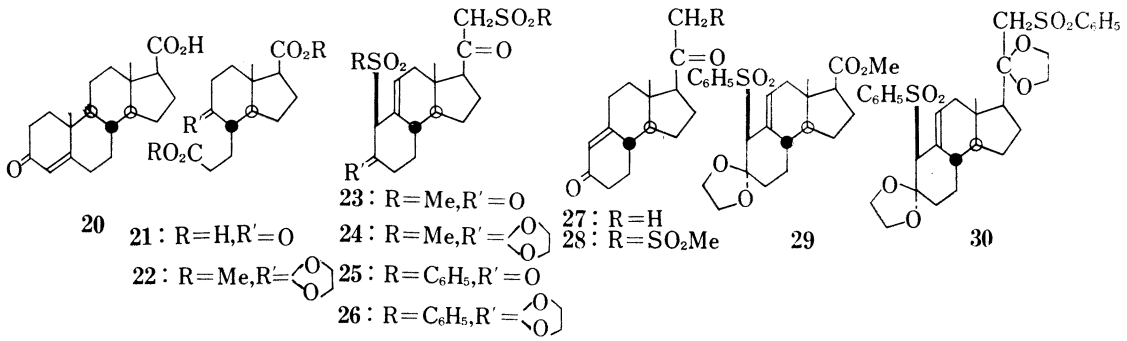


11 : R=O
12 : R=α-CN,β-OH
13 : R=β-CN, α-OH
14 : R=O,O
15 : R=O
16 : R=CN
18 : R=COCH3
17
19

Chart 2

coupled with an absorption band due to a hydroxyl group in the IR spectrum indicate that **19** arises from the formation of an acetyl side chain concurrently accompanied by cleavage of the ether linkage in the ketal moiety by the reagent.[14]

Successful condensation of dimethyl sulfone or phenyl methyl sulfone with methyl 1,1,5,5-bisethylenedioxy-7a-methyl-3aα,7aβ-hexahydroindan-4α-yl propionate as described previously[1] led us to investigate a scheme including the reaction of the reagents with methyl 1β-methoxycarbonyl-5-oxo-7a-methyl-3aα,7aβ-hexahydroindan-4α-yl propionate, the free acid (**21**) of which is readily obtainable by the microbiological oxidation of 3-oxoandrost-4-ene-17β-carboxylic acid (**20**) with Arthrobacter simplex.[15] When the dimethyl ester of **21** in which the keto function was protected by conversion to the ketal (**22**) by the usual ketalization was subjected to condensation with dimethyl sulfone, followed successively by treatment with acid then with alkali, there was obtained in 74% yield an expected bismethylsulfonyl compound (**23**) as an amorphous material, which was characterized by its spectral properties. Slow distillation of a solution of **23** in ethylene glycol in the presence of *p*-toluenesulfonic acid gave a high yield of a monoketal (**24**) as crystals. Unfortunately, desulfurization of **24** with sodium in liquid ammonia, followed by acid treatment and reoxidation with Jones reagent afforded only about 60% yield of a neutral fraction, from which 11.8% yield of the desired des-A-19-norpregn-9(10)-ene-5,20-dione (**27**) was obtained in addition to 33.8% yield of a compound containing a methylsulfonyl group. The latter compound was identified as 21-methylsulfonyl-des-A-19-norpregn-9(10)-ene-5,20-dione (**28**) by the UV spectrum



20
21 : R=H,R'=O
22 : R=Me,R'=O,O
23 : R=Me,R'=O
24 : R=Me,R'=O,O
25 : R=C6H5,R'=O
26 : R=C6H5,R'=O,O
27 : R=H
28 : R=SO2Me
29
30

Chart 3

14) A similar cleavage of the ether bond in a steroidal ethylene ketal with Grignard reagent has been observed. R.A. Mallory, S. Rovinski, and I. Scheer, *Proc. Chem. Soc.*, **1964**, 416; R. Zepter, *J. Prakt. Chem.*, **26**, 174 (1964); R.A. Mallory, S. Rovinsky, F. Kohen, and I. Scheer, *J. Org. Chem.*, **32**, 1417 (1967).

15) S. Hayakawa, Y. Kanematsu, and T. Fujiwara, *Nature*, **214**, 520 (1967); *idem*, *Biochem. J.*, **115**, 249 (1969) and to be published.

and by indication in the PMR spectrum of the presence of a methylsulfonyl group and of the lack of a methyl signal due to an acetyl moiety. The poor recovery of the neutral fraction in this reaction may suggest the occurrence of C–S bond fission of the methylsulfonyl moiety at C_{21} and loss of the β-ketosulfinic acid, or its reduced acid, either of which may be formed and dissolved into alkali during the post-treatment of the reaction. Moreover, reduction of the carbonyl group at C_{20} in **24** with sodium borohydride, followed by desulfurization with sodium or lithium in liquid ammonia, aicd treatment, and Jones oxidation afforded only the methylsulfonyl compound (**28**) in high yield. Therefore, it was considred that replacement of the methylsulfonyl group with a phenylsulfonyl counterpart may be suitable for preparation of **27**. This was demonstrated with the following successful result. Condensation of **22** with phenyl methyl sulfone, followed by treatment with acid and alkali, gave a bisphenylsulfonyl compound (**25**) as an oily substance, ketalization of which by the slow distillation method afforded a monoketal **26** as crystals in 69.9% overall yield based on the dicarboxylic acid **21**. In another run, employing the same sequence of the reactions except that the prolonged ketalization was performed, we obtained 11.1% yield of a bisketal (**30**) and 3.9% yield of a compound (**29**) containing an unreacted methyl carboxylate group besides 59.4% yield of the monoketal. Compound (**29**) was assigned as methyl 5,5-ethylenedioxy-10β-phenylsulfonyl-des-A-estr-9(11)-ene-17β-carboxylate from the PMR spectrum (in C_6D_6) showing a singlet due to methoxy methyl protons at 3.38 ppm and a broadened singlet owing to the 10α-proton at 3.84 ppm. Desulfurization of **26** with sodium in liquid ammonia, followed by acid treatment and reoxidation with Jones reagent gave the expected des-A-19-norpregn-9(10)-ene-5,20-dione (**27**) in 70% yield. The physical constants of the compound (**27**) so obtained are in good agreement with those described by Bucourt, *et al.*[16]

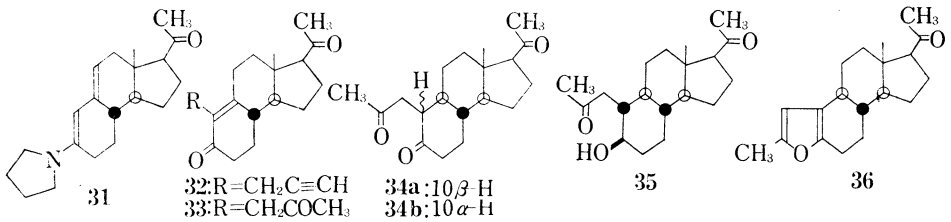


Chart 4

As described above, alkylation of the dienamine (**31**), readily prepared from **27** with propargyl bromide in hexamethylphosphoramide, gave a propargyl compound (**32**) in 53.1% yield, which in turn was hydrated quantitatively to an acetonyl compound (**33**) with mercuric sulfate. Hydrogenation of **33** over palladium on charcoal afforded 88.7% yield of 3,5-seco-4,19-bisnorpregnane-2,5,20-trione (**34a**) in addition to two minor products (**34b** and **35**) in yields of 5.1% and 1.3% respectively. Of these minor compounds, **35** was assigned as 5β-hydroxy-3,5-seco-4,19-bisnorpregnane-2,20-dione from the IR (ν_{OH} 3459 cm^{-1}) and PMR spectra. In the latter spectrum two acetyl methyl signals at 2.09 and 2.12 ppm besides one tertiary methyl signal at 0.63 ppm and a double triplet pattern at 3.26 ppm (J=4.5 and 14.5Hz) assignable as an axial proton geminal to a hydroxyl group were observed. Furthermore, this assignment was proved by the fact that Jones oxidation of **35** gave **34a**. Finally, heating both **34a** and **34b** in boiling benzene in the presence of *p*-toluenesulfonic acid afforded the desired 2-methyl-3-oxa-4,19-bisnorpregna-1,5(10)-dien-20-one (**36**) in high yield, the structure of which was confirmed by the spectral data including the mass spectrum. Hence, **34b** was assigned as an epimer of **34a**.

16) R. Bucourt, J. Tessier, and G. Nominé, *Bull. Soc. Chim. France*, **1963**, 1923.

Experimental[17]

10α-Propargyl-10β-phenylsulfonyl-17β-acetoxy-des-A-estr-9(11)-en-5-one (2)——To a stirred solution of α-methylsulfinyl carbanion generated from 270 mg of NaH washed with petroleum ether and 1.2 ml of DMSO in 5 ml of monoglyme, were added **1** (2.023 g) and 16 ml of monoglyme under nitrogen. The resulting mixture was warmed at 50° for 30 min then cooled to room temperature. To the mixture was added 0.6 ml of propargyl bromide. The stirred reaction mixture was allowed to stand for 22 hr at room temperature and then at 50° for 7 hr. The product extracted with CH_2Cl_2 was acetylated with 5 ml of Ac_2O in 10 ml of pyridine at room temperature overnight. After usual work-up, chromatography on 220 g of silica gel gave 1.922 g of **2**, which was recrystallized from acetone–hexane to afford 1.890 g (76.4%) of the pure sample, mp 180—182°. $[\alpha]_D^{22}$ +104.0±1.3° (c=1.082). IR ν_{max}cm^{-1}: 3272 (≡CH), 1718, 1259 (C=O, Ac), 1635 (Δ), 1586, 758, 716, 686 (C_6H_5) 1323, 1312, 1143 (SO_2). CD (in dioxane): $[\theta]_{335}$ −2588, $[\theta]_{324}$ −7490, $[\theta]_{312}$ −11010, $[\theta]_{302.5}$ −11730, $[\theta]_{251}$ +18720, $[\theta]_{245}$ +18720, $[\theta]_{222}$ +1100, $[\theta]_{210}$ +14210. PMR (δ): 1.00 (s, 3, Me), 1.81 (t, J=2.5 Hz, 1, ≡CH), 2.06 (s, 3, OAc), 2.55—3.22 (m, 2, CH_2), 4.78 (t, 1, 17α-H), 5.89 (m, 1, 11-H), 7.60 (m, 5, C_6H_5-H); (in C_6D_6) 1.04 (s, 3, Me), 1.62 (t, J=2.5 Hz, 1, ≡CH), 1.72 (s, 3, OAc), 2.78 & 3.19 (AB-type q, J_{AB}=15.5 Hz, 2, CH_2), 4.76 (t, 1, 17α-H), 5.93 (m, 1, 11-H). *Anal.* Calcd. for $C_{25}H_{28}O_5S$: C, 68.16; H, 6.41; S, 7.28. Found: C, 68.20; H, 6.41; S, 7.24.

Alkylation of Enamine 5 with Propargyl Bromide——A solution of **5** (6.489 g) in 32 ml of DMF was trated with 2.3 ml of propargyl bromide at room temperature for 65 hr then 15 ml of water was added. The mixture was warmed on a steam bath for 3 hr and extraction with CH_2Cl_2 gave a material which was acetylated with 12 ml of Ac_2O in 20 ml of pyridine. The product (*ca.* 5.8 g) was chromatographed on 150 g of Al_2O_3. The fraction eluted with petroleum ether–benzene (9:1—1:1) was recrystallized from ether-isopropyl ether giving 1.929 g (27.0%) of **3**, mp 128—129.5°. $[\alpha]_D^{27}$ −64.0±1.0° (c=1.093). IR ν_{max} cm^{-1}: 3311 (≡CH), 2111 (C≡C), 1738, 1248 (OAc), 1658, 1610 (C=C-C=O). UV λ_{max} nm (ε): 245.5 (15000). CD (in $CHCl_3$): $[\theta]_{348}$ −1451, $[\theta]_{338}$ −1274, $[\theta]_{312}$ +558, $[\theta]_{303}$ +599, $[\theta]_{280}$ +181. PMR (δ): 0.98 (s, 3, Me), 1.88 (t, J=2.5 Hz, 1, ≡CH), 2.05 (s, 3, OAc), 3.28 (br, s, $W_{h/2}$=5.5 Hz, 2, CH_2), 4.68 (t, 1, 17α-H). *Anal.* Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 76.09; H, 8.19. In another run, a solution of **5** (1.000 g) in 50 ml of DMSO was treated with propargyl bromide and worked up in the same way as described above. Chromatography of the acetylated product and recrystallization afforded 547 mg (49.7%) of **3**.

Desulfurization of 2——A mixture of **2** (135 mg) and zinc dust (1.0 g) in 10 ml of AcOH was stirred under reflux for 2.5 hr. The reacetylated product was separated by preparative TLC (cyclohexane: AcOEt= 2:1). In order of their decreasing mobility, the fractions afforded 2.5 mg (2.7%) of **6a**, 35 mg (38.0%) of **3**, and 40 mg (41.0%) of **4a**, mp 119—120°.

In another run, a mixture of **2** (711 mg) and zinc dust (5.5 g) in 35 ml of AcOH was refluxed for 30 min. The product was dissolved in 14 ml of MeOH and 1.75 ml of water. To the solution 27 mg of $HgSO_4$ and 0.14 ml of conc. H_2SO_4 were added under nitrogen. The resulting mixture was stirred for 1.5 hr at room temperature and poured into ice water. The product (571 mg) extracted with CH_2Cl_2 was reacetylated with 1.5 ml of Ac_2O in 3 ml of pyridine. Preparative TLC (cyclohexane:AcOEt=1:1) of the product gave 27 mg (5.7%) of **6a** and 406 mg (79.0%) of **4a**, mp 119—120°, which were identified with authentic samples by mixed mps and comparison of IR spectra, respectively.

Hydration Reaction of 3——a) A mixture of **3** (1.929 g), 102 mg of $HgSO_4$ and 0.51 ml of conc. H_2SO_4 in 57 ml of 90% MeOH was stirred under nitrogen at room temperature for 10 min and poured into ice water. The product (2.01 g) extracted with CH_2Cl_2 was reacetylated with 1 ml of Ac_2O in 4 ml of pyridine. After usual work-up, recrystallization of the acetate from acetone–hexane gave 2.050 g of **4a**, mp 119.5—120.5°. $[\alpha]_D^{25}$ −81.3±2.1° (c=0.588). IR ν_{max} cm^{-1}: 1725, 1255 (OAc & C=O), 1664, 1618, (C=C-C=O). UV λ_{max}nm (ε): 247.5 (13700). CD (in MeOH): $[\theta]_{337}$ −1137, $[\theta]_{298}$ +1271, $[\theta]_{242}$ −17390, $[\theta]_{210}$ +16320. PMR (δ): 0.95 (s, 3, Me), 2.04 (s, 3, OAc), 2.13 (s, 3, Ac), 3.36 & 3.64 (AB-type q, J_{AB}=16.5 Hz, 2, CH_2), 4.62 (t, 1, 17α-H). *Anal.* Calcd. for $C_{19}H_{26}O_4$: C, 71.67; H, 8.23. Found: C, 71.78; H, 8.30.

b) Mercuriated cation exchange resin was prepared from 100 mg of Anberlite IR-120, 4 mg of HgO and 0.2 ml of 6N H_2SO_4 according to Hajos, *et al.*[5] A mixture of this resin and **3** (300 mg) in 2.4 ml of 80% MeOH was refluxed under stirring for 65 hr. The product was separated by prparative TLC (cyclohexane: AcOEt=1:1). The more mobile fraction gave 41 mg of **6b** and the less mobile fraction afforded 82 mg of **4b**, which was recrystallized from hexane to yield the pure sample, mp 153—154°. $[\alpha]_D^{28}$ −69.5±2.1° (c= 0.521). IR ν_{max} cm^{-1}: 3516 (OH), 1716 (C=O), 1666, 1618 (C=C-C=O). UV λ_{max} nm (ε): 249 (13500). CD

17) All melting points were measured on a Kofler hot-stage apparatus and are uncorrected. Optical rotations were determined in 1% EtOH–$CHCl_3$ with a Perkin-Elmer Polarimeter, type 141. Unless otherwise stated, IR spectra were recorded in Nujol mulls with a Koken Infrared spectrophotometer, Model DS-201B, and UV spectra in 95% EtOH on a Hitachi EPS-2 spectrophotometer. All PMR spectra were taken on $CDCl_3$ solutions with a Varian A-60 spectrometer, tetramethylsilane serving as internal standard. Mass spectra were observed with a Hitachi RMU-6 mass spectrometer (70 eV). For preparative TLC silica gel GF (Merck Co.) was used as an adsorbent.

(in MeOH): $[\theta]_{336}$ −1000, $[\theta]_{299}$ +1435, $[\theta]_{240}$ −15020, $[\theta]_{210}$ +16690, $[\theta]_{200}$ +11680. PMR (δ): 0.91 (s, 3, Me), 2.15 (s, 3, Ac), 3.42 & 3.62 (AB-type q, J_{AB}=17.0 Hz, 2, CH_2), 3.72 (t, 1, 17α-H). *Anal.* Calcd. for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75. Found: C, 73.99; H, 8.78. This compound on acetylation afforded an acetate identical with **4a**.

2-Methyl-3-oxa-A-norestra-1,5(10),9(11)-trien-17β-ol (6b)——A mixture of **4a** (1.500 g) and 150 mg of *p*-TsOH·H_2O in 150 ml of benzene was refluxed for 25 min with azeotropic removal of the formed water. Usual work-up gave the product (1.38 g), which was crystallized from pentane to afford 577 mg (40.9%) of **6a**. Recrystallization from ether–petroleum ether yielded the pure sample, mp 133.5—134°. $[\alpha]_D^{26}$ +89.7± 1.5° (c=0.848). IR ν_{max} cm^{-1}: 1735, 1251, 1240, 1230 (OAc), 1652, 1580, 797 (furan). UV λ_{max} nm (ε): 241.5 (11050), 212.5 (15190). CD (in isooctane): $[\theta]_{238}$ +25590, $[\theta]_{220}$ +5477, $[\theta]_{215}$ +7911. PMR (δ): 0.83 (s, 3, Me), 2.05 (s, 3, OAc), 2.22 (s, 3, arom-Me), 5.56 (m, 1, 11-H), 6.00 (br s, $W_{h/2}$=2.8 Hz, 1, 1-H). *Anal.* Calcd. for $C_{19}H_{24}O_3$: C, 75.97; H, 8.05. Found: C, 76.01; H, 8.22.

The mother liquor (802 mg) was purified by preparative TLC (cyclohexane:AcOEt=9:1) using the double development method. The more polar fraction gave 82 mg of **8** as an oily substance, whose homogeneity was confirmed by TLC using several developing solvent systems. UV $\lambda_{max}^{isooctane}$ nm (ε): 209.5 (27800), 251inf (12390), 255 (13570), 261inf (9610), 278.5 (2040), 283.5 (1570), 289 (2044). PMR (δ): 0.99 (s, 3, Me), 2.07 (s, 3, OAc), 2.44 (s, $W_{h/2}$=2.1 Hz, 3, furan-Me), 4.99 (m, 1, 17α-H), 6.34 (s, 1, 1-H), 6.95 & 7.20 (AB type q, J_{AB}=8.5 Hz, 2, 6-H & 7-H). The less polar fraction (433 mg) was found by TLC to be a mixture and was reduced by treatment with 72 mg of LAH in 13 ml of dry ether. The product was subjected to preparative TLC (cyclohexane:AcOEt=5:1) using the triple development method. The less mobile fraction gave 156 mg (12.8%) of **6b**, which was recrystallized from acetone–hexane to yield the pure sample, mp 103—105° $[\alpha]_D^{26}$ +116.6±1.9° (c=0.815). IR ν_{max} cm^{-1}: 3418, 3360 (OH), 1653, 1581, 794 (furan). UV $\lambda_{max}^{isooctane}$ nm (ε): 241.5 (10350), 212 (11220). CD (in isooctane): $[\theta]_{238}$ +27410. PMR (δ): 0.78 (s, 3, Me), 2.23 (s, $W_{h/2}$=2.5 Hz, 3, furan-Me), 3.79 (t, 1, 17α-H), 5.59 (m, $W_{h/2}$=8.0 Hz, 1, 11-H), 6.00 (s, $W_{h/2}$=2.5 Hz, 1, 1-H). Mass Spectrum *m/e*: 258 (M^+, 100%). *Anal.* Calcd. for $C_{17}H_{22}O_2 \cdot 3/5C_3H_6O$: C, 77.01; H, 8.80. Found: C, 76.95; H, 8.85. This compound was also obtained in quantitative yield by reductive hydrolysis of **6a** with LAH in dry ether. The more mobile fraction afforded 140 mg (11.5%) of **7** as an oily substance. UV $\lambda_{max}^{isooctane}$ nm (ε): 240 (11610), 206.5 (28320). CD (in isooctane): $[\varepsilon]_{238}$ +27520. PMR (δ): 1.05 (s, 3, Me), 2.24 (s, 3, furan-Me), 3.75 (t, 1, 17α-H), 5.52 (m, 1, 11-H), 6 01 (s, $W_{h/2}$=2.5 Hz, 1, 1-H).

17β-Acetoxy-3,5-seco-4-norestrane-2,5-dione (9)——A solution of **4a** (832 mg) in 3 ml of AcOEt and 0.48 ml of Et_3N was hydrogenated over pre-reduced 10% Pd-C (200 mg). After usual work-up, recrystallization of the product from acetone–hexane gave 613 mg (73.3%) of **9**, mp 135.5—136.5°. $[\alpha]_D^{24}$ −25.0± 0.7° (c=0.876). IR ν_{max} cm^{-1}: 1739, 1256, 1090 (OAc), 1719, 1707 (C=O). CD (in $CHCl_3$): $[\theta]_{287}$ −8027, $[\theta]_{235}$ −241. *Anal.* Calcd. for $C_{19}H_{28}O_4$: C, 71.72; H, 8.81. Found: C, 71.70; H, 8.83.

2-Methyl-3-oxa-A-norestra-1,5(10)-dien-17β-ol (10a)——a) A mixture of **9** (558 mg) and 91 mg of *p*-TsOH·H_2O in 55 ml of dry benzene was refluxed for 10 min. Recrystallization of the product from aq. acetone gave 432 mg (83.0%) of **10b**, mp 122—123°. $[\alpha]_D^{22}$ +33.7±5.4° (c=0.802). IR ν_{max} cm^{-1}: 1747, 1732, 1253, 1240, 1050, 1037 (OAc), 1638, 1528, 785. UV λ_{max} nm (ε): 225.5 (7520). CD (in isooctane): $[\theta]_{233.5}$ −9161, $[\theta]_{217}$ +7048. PMR (δ): 0.82 (s, 3, Me), 2.03 (s, 3, OAc), 2.24 (s, $W_{h/2}$=2.5 Hz, 3, furan-Me), 4.71 (t, 1, 17α-H), 5.83 (s, $W_{h/2}$=2.8 Hz, 1, 1-H). *Anal.* Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.66; H, 8.69. Reduction of **10b** (331 mg) with 55 mg of LAH in 10 ml of dry ether at 0° for 35 min and recrystallization of the product from aq. acetone afforded 256 mg (89.8%) of **10a**, mp 124.5—126.5°. $[\alpha]_D^{23}$ +51.3±5.0° (c=0.907). IR ν_{max} cm^{-1}: 3542, 3340, 1055 (OH), 1632, 1577, 805, 786. UV λ_{max} nm (ε): 225.5 (7170). CD (in MeOH): $[\theta]_{235}$ −6845, $[\theta]_{217}$ +4212. PMR (δ): 0.77 (s, 3, Me), 1.47 (s, 1, OH), 2.24 (s, $W_{h/2}$= 2.3 Hz, 3, furan-Me), 3.72 (t, 1, 17α-H), 5.83 (s, $W_{h/2}$=2.8 Hz, 1, 1-H). Mass Spectrum *m/e*: 260 (M^+, 100%). *Anal.* Calcd. for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.56; H, 9.26.

b) A mixture of **9** (300 mg) and 320 mg of P_2S_5 in 15 ml of dry benzene was refluxed for 30 min. Work-up gave 275 mg of **10b**, which was identified with the compound obtained in a) by mixed mps and comparison of IR spectra. No formation of a thieno-compound was observed.

5,5-Ethylenedioxy-10β-methylsulfonyl-17α-cyano-des-A-estr-9(11)-en-17β-ol (12)——To a chilled and stirred mixture of **11** (200 mg) and 1.15 g of KCN in 9 ml of EtOH, 1.23 ml of AcOH was added dropwise during 40 min. After addition of *ca.* 80 ml of water, the precipitate formed was collected by filtration, washed with water and dried. Recrystallization from acetone–hexane yielded 124 mg (57.5%) of **12**, mp 198.5—200°. $[\alpha]_D^{22}$ −7.1±0.7° (c=0.690), $[\alpha]_{365}^{22}$ −46.4±1.3° (c=0.690). IR ν_{max} cm^{-1}: 3457 (OH), 2233 (CN), 1285, 1125 (SO_2), 1097 (ketal). PMR (δ): 0.96 (s, 3, Me), 3.08 (s, 3, SO_2Me), 3.58 (s, 1, 10α-H), 4.02 (m, $W_{h/2}$= 5.0 Hz, 4, ketal-CH_2), 5.78 (m, 1, 11-H). *Anal.* Calcd. for $C_{18}H_{25}O_5NS$: C, 58.83; H, 6.86; N, 3.81; S, 8.73. Found: C, 58.81; H, 6.90; N, 3.59; S, 8.99.

5,5-Ethylenedioxy-10β-methylsulfonyl-17β-cyano-des-A-estr-9(11)-en-17α-ol (13)——A mixture of **11** (2.50 g), 3.0 ml of freshly prepared acetone cyanohydrin and 3 drops of Et_3N was warmed at 50—60° for 10 min and allowed to stand for 2 hr at room temperature. The mixture, which contained deposited crystals, was poured into water. The precipitate was collected by filtration, washed with water, dried and used for the next reaction without further purification (Yield: 2.641 g, 97.8%). Recrystallization from CH_2Cl_2–

MeOH gave the pure sample of **13**, mp 237.5—239.5° (decomp.). $[\alpha]_D^{22}$ +16.1±0.6° (c=0.871). IR ν_{max} cm^{-1}: 3455 (OH), 2227 (CN), 1645 (C=C), 1294, 1117 (SO_2), 1094 (ketal). PMR (δ): 1.03 (s, 3, Me), 3.07 (s, 3, SO_2Me), 3.58 (s, 1, 10α-H), 4.02 (m, $W_{h/2}$=5.0 Hz, 4, ketal-CH_2), 5.80 (m, 1, 11-H). *Anal.* Calcd. for $C_{18}H_{25}O_5NS$: C, 58.83; H, 6.86; N, 3.81; S, 8.73. Found: C, 58.83; H, 6.95; N, 3.55; S, 8.90.

5,5-Ethylenedioxy-10β-methylsulfonyl-17-cyano-des-A-estra-9(11),16-diene (14)——To a stirred solution of **13** (3.387 g) in 20 ml of pyridine, 4.6 ml of $POCl_3$ was added dropwise under nitrogen. After refluxing for 2 hr, the mixture was cooled and poured into iced 5% HCl. The crystals which formed were collected by filtration, washed with water and dried. Recrystallization from acetone–hexane gave 2.881 g (89.6%) of **14**, mp 256.5—258.5° (decomp.). $[\alpha]_D^{22}$ −68.9±1.6° (c=0.688). IR ν_{max} cm^{-1}: 2212 (CN), 1597 (C=C), 1312 1294, 1117 (SO_2), 1097 (ketal). PMR (δ): 1.00 (s, 3, Me), 3.08 (s, 3, SO_2Me), 3.57 (br. s, $W_{h/2}$=4.0 Hz, 1, 10α-H), 4.03 (m, 4, ketal-CH_2), 5.78 (m, $W_{h/2}$=10.0 Hz, 1, 11-H), 6.63 (q, $J_{15\alpha:16}+J_{15\beta:16}$=4.8 Hz, 1, 16-H). *Anal.* Calcd. for $C_{18}H_{23}O_4NS$: C, 61.87; H, 6.63; N, 4.01; S, 9.18. Found: C, 62.09; H, 6.67; N, 3.80; S, 9.21.

10β-Methylsulfonyl-17-cyano-des-A-estra-9(11),16-dien-5-one (15)——A mixture of **14** (500 mg), 0.9 ml of 70% $HClO_4$ and 20 ml of 75% acetone aq. was refluxed for 30 hr. After the usual work-up, crystallization of the product form ether and recrystallization from acetone-hexane afforded 411 mg (94.1%) of **15**, mp 132—133.5°. $[\alpha]_D^{22}$ +210.4±2.6° (c=0.950). IR ν_{max} cm^{-1}: 2220 (CN), 1735, 1716 (C=O), 1596 (C=C), 1312, 1129, 1121 (SO_2), 959, 742. UV λ_{max}^{MeOH} nm (ε): 215 (10720), 300 (167). CD (in MeOH): $[\theta]_{300}$ −1710, $[\theta]_{227}$ +31300. PMR (δ): 1.05 (s, 3, Me), 2.95 (s, 3, SO_2Me), 4.27 (s, $W_{h/2}$=3.0 Hz, 1, 10α-H), 5.82 (m, $W_{h/2}$= 10.0 Hz, 1, 11-H), 6.66 (q, $J_{15\alpha:16}+J_{15\beta:16}$=5.2 Hz, 1, 16-H). *Anal.* Calcd. for $C_{16}H_{19}O_3NS$: C, 62.93; H, 6.27; N, 4.59; S, 10.50. Found: C, 62.81; H, 6.52; N, 4.46; S, 10.76.

17-Cyano-des-A-estra-9(10),16-dien-5-one (16)——A stirred mixture of **15** (304 mg) and 3 g of zinc dust in 10 ml of 70% AcOH aq. was refluxed for 2 hr and worked up in the usual way. The product was purified by preparative TLC (CH_2Cl_2:AcOEt=4:1) and recrystallization from acetone–hexane gave 152 mg (67.2%) of **16**, mp 111—111.5°. $[\alpha]_D^{22}$ +47.6±1.2° (c=0.741). IR ν_{max} cm^{-1}: 2216 (CN), 1672, 1615 (C=C-C=O), 1599 (C=C), 962, 892, 837. PMR (δ): 1.09 (s, 3, Me), 5.94 (br. s, $W_{h/2}$=4.5 Hz, 1, 10-H), 6.68 (t, $J_{15\alpha:16}+J_{15\beta:16}$= 5.0 Hz, 1, 16-H). *Anal.* Calcd. for $C_{15}H_{17}ON$: C, 79.26; H, 7.54; N, 6.16. Found: C, 79.20; H, 7.38; N, 6.41.

5,5-Ethylenedioxy-17-cyano-des-A-estra-9(11),16-diene (17)——A mixture of **16** (1.095 g), 2.9 ml of ethylene glycol and 35 mg of p-TsOH–H_2O was refluxed for 9 hr with azeotropic removal of the formed water. The usual work-up gave 1.361 g of an oily substance which was subjected to chromatography over 26 g of alumina (II). The fractions eluted with petroleum ether–benzene (4:1—1:1) afforded 1.149 g of a solid, which was recrystallized from hexane to yield 1.017 g (77.8%) of **17**, mp 103.5—105.5°. $[\alpha]_D^{22}$ +89.5±1.3° (c=1.009). IR ν_{max} cm^{-1}: 2207 (CN), 1647, 1592 (C=C), 1097 (ketal), 1090, 1072, 1057, 1016, 957. PMR (δ): 0.89 (s, 3, Me), 3.95 (s, 4, ketal-CH_2), 5.40 (m, 1, 11-H), 6.61 (q, $J_{15\alpha:16}+J_{15\beta:16}$=5.0 Hz, 1, 16-H). *Anal.* Calcd. for $C_{17}H_{21}O_2N$: C, 75.24; H, 7.80; N, 5.16. Found: C, 75.47; H, 7.68; N, 5.16.

The Grignard Reaction of 17 with MeMgBr——To a stirred MeMgBr solution prepared from 902 mg of Mg in 7 ml of ether and 9 ml of an ethereal solution of MeBr (5.17 M), a solution of **17** (1.002 g) in 20 ml of ether was added dropwise during 30 min and the resulting mixture was refluxed for 43 hr with continuous stirring. The excess of the reagent was destroyed by addition of iced NH_4Cl aq. and the mixture was worked up in the usual way. The oily product (1.1 g) dissolved into 50 ml of 60% AcOH aq. was heated under reflux for 3 hr and the hydrolyzed product was extracted with CH_2Cl_2 yielding ca. 1.0 g of an oily substance, which was further treated with 1 ml of 70% $HClO_4$ in 20 ml of 75% acetone aq. for 2 hr at room temperature. The product was subjected to chromatography over 100 g of SiO_2 by using a dry column method (CH_2Cl_2:AcOEt=3:1, each 12 g eluate). Fraction 22—31 gave 122 mg of an oily mixture, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1735, 1700, 1670, 1590. Fraction 32—44 yielded 88 mg of an oily mixture, IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1669, 1615, 1595, whose TLC showed at least two spots. Fraction 53—71 afforded 227 mg (20.2%) of **19**, which was recrystallized from aqueous acetone to give the pure sample, mp 111.5—112.5°. $[\alpha]_D^{23.5}$ +123.9±2.4° (c=0.696). IR ν_{max} cm^{-1}: 3373 (OH), 3075 (C=C), 1647, 1597 (C=C-C=O), 1236, 1125, 1068. PMR (δ): 0.83 (s, 3, Me), 1.09 (s, 3, -O-C-Me), 2.25 (s, 3, COMe), 3.58 (m, 4, OCH_2CH_2O), 5.35 (m, 1, 11-H), 6.70 (q, $J_{15\alpha:16}+J_{15\beta:16}$=5.0 Hz, 1, 16-H). *Anal.* Calcd. for $C_{19}H_{28}O_3\cdot 1/2C_3H_6O$: C, 73.84; H, 9.37. Found: C, 73.87; H, 9.67.

Methyl 7a-Methyl-5,5-ethylenedioxy-1-methoxycarbonyl-3aα,7aβ-hexahydroindan-4α-yl Propionate (22)——A suspension of **21** (2.0 g) in 10 ml of MeOH was treated with excess of an ethereal solution of CH_2N_2 to give the methyl ester. This compound (2.3 g) was dissolved in 50 ml of benzene and 3.1 ml of ethylene glycol and 50 mg of p-TsOH·H_2O were added. The resulting mixture was refluxed for 4.5 hr and worked up in the usual way to yield 2.54 g of **22** as an oily substance. IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740, 1195, 1163.

10β,21-Bismethylsulfonyl-des-A-19-norpregn-9(11)-ene-5,20-dion (23)——A stirred mixture of 1.5 g of NaH washed with petroleum ether, 6.27 ml of DMSO and 22 ml of monoglyme was warmed at 60° under nitrogen for 50 min. To the mixture was added 2.66 g of dimethyl sulfone portionwise and the mixture was warmed at the same temperature for 1.2 hr with continuous stirring. To the mixture cooled to room temperature was added a solution of **22** (2.44 g) in 16 ml of monoglyme. The resulting mixture was stirred for 15 hr at room temperature then warmed at 60° for 4 hr with stirring. The cooled mixture was acidified with aq. AcOH and extracted with CH_2Cl_2. The CH_2Cl_2 solution was washed with Na_2CO_3 aq., dried over Na_2SO_4 and concentrated *in vacuo*. The residue (2.658 g) was dissolved in a mixture of 17 ml of 90% acetone and 0.27 ml of 70% $HClO_4$. After being stirred for 6 hr at room temperature, the mixture was neutralized

with Na_2CO_3 aq., concentrated to a half its initial volume *in vacuo* and poured into ice water. Extraction with CH_2Cl_2 afforded 2.215 g of an oily substance, which was dissolved in 4 ml of MeOH and added to 3.3 ml of 2.5% KOH–MeOH. The mixture was stirred for 1.5 hr at room temperature and diluted with water. Extraction with CH_2Cl_2 gave 2.12 g (73.7% based on the acid (**21**)) of **23**, TLC of which indicated its homogeneity. $[\alpha]_D^{22}$ +133.4±1.8° (c=0.965). IR ν_{max} cm^{-1}: 1714 (C=O), 1314, 1292, 1113 (SO_2). UV $\lambda_{max}^{dioxane}$ nm nm (ε): 225 (2950), 300 (244). CD (in dioxane): $[\theta]_{348}$ O, $[\theta]_{341}$ −280, $[\theta]_{337}$ O, $[\theta]_{304}$, +9950, $[\theta]_{296.5}$ +9570, $[\theta]_{258}$ +1310, $[\theta]_{230}$ +13130, $[\theta]_{220^{sh}}$ +10040, $[\theta]_{213}$ O. PMR (δ): 0.82 (s, 3, Me), 2.95, 3.08 (each s, 3, SO_2Me), 4.04 (s, 2, 21-CH_2), 4.28 (s, $W_{h/2}$=3.0 Hz, 1, 10α-H), 5.80 (m, $W_{h/2}$=9.0 Hz, 1, 11-H). *Anal.* Calcd. for $C_{18}H_{26}O_6S_2$: C, 53.71; H, 6.51; S, 15.93. Found: C, 53.51; H, 6.63; S, 15.65.

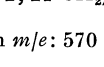
10β,21-Bismethylsulfonyl-5,5-ethylenedioxy-des-A-19-norpregn-9(11)-en-20-one (**24**)——A solution of **23** (2.12 g) and 120 mg of *p*-TsOH–H_2O in 120 ml of ethylene glycol was slowly distilled at 3—5 mmHg for 6 hr during which period 80 ml of distillate was removed. The remaining mixture was cooled, poured into iced Na_2CO_3 aq. and extracted with CH_2Cl_2. After removal of the solvent, the residue was recrystallized from acetone–hexane to afford 2.084 g (65.2% overall yield based on the acid (**21**)) of **24**, mp>250°. $[\alpha]_D^{22}$ +86.8±1.4° (c=0.906). IR ν_{max} cm^{-1}: 3034, 1652 (C=C), 1721 (C=O), 1294, 1132, 1125 (SO_2), 1103, 1077 (ketal). UV $\lambda_{max}^{CHCl_3}$ nm (ε): 298 (54). CD (in $CHCl_3$): $[\theta]_{300}$ +11790. PMR (δ): 0.75 (s, 3, Me), 3.06 (s, 6, SO_2Me), 3.56 (s, $W_{h/2}$=3.5 Hz, 1, 10α-H), 4.01 (m, 4, ketal-CH_2), 5.73 (m, 1, 11-H). *Anal.* Calcd. for $C_{20}H_{30}O_7S_2$: C, 53.79; H, 6.77; S, 14.37. Found: C, 53.69; H, 6.74; S, 14.17.

Desulfurization of 24——a) To a stirred solution of 1.25 g of Na in 100 ml of liquid ammonia a solution of **24** (900 mg) in 30 ml of dry THF was added dropwise during 30 min. The resulting mixture was stirred for 4 hr and allowed to stand for 18 hr at room temperature. After the excess of Na had been decomposed by addition of EtOH, the mixture was extracted with CH_2Cl_2. Work-up in the usual way gave 558 mg of an oily substance, which was dissolved into 17 ml of 70% acetone aq. and 0.56 ml of 70% $HClO_4$. The mixture was stirred for 2 hr at room temperature and poured into iced Na_2CO_3 aq. Extraction with CH_2Cl_2 gave 407 mg of an oily substance, the IR spectrum of which showed the absorption band due to a hydroxyl group. Oxidation of this substance with 0.15 ml of 8N Jones reagent in 4 ml of acetone afforded 390 mg of the product as an oil which exhibited at least 5 spots on TLC. Of these, the two major products were separated by means of preparative TLC (cyclohexane:AcOEt=1:1). The polar fraction gave 221 mg (33.8%) of **28**, which was recrystallized from acetone–hexane to yield the pure sample, mp 157—157.5°. $[\alpha]_D^{23}$ +108.4±1.9° (c=0.799). IR ν_{max} cm^{-1}: 1706 (C=O), 1656, 1607 (C=C-C=O), 1312, 1152 (SO_2), 1065, 962. UV λ_{max} nm (ε): 239 (17460), 300 (6770). PMR (δ): 0.86 (s, 3, Me), 3.08 (s, 3, SO_2Me), 4.05 (s, 2, 21-CH_2), 5.91 (s, $W_{h/2}$=4.0 Hz, 1, 10-H). *Anal.* Calcd. for $C_{17}H_{24}O_4S$: C, 62.93; H, 7.46; S, 9.88. Found: C, 63.10; H, 7.43; S, 9.99. The less polar fraction afforded 59 mg (11.8%) of **27**, which upon recrystallization from ether–petroleum ether yielded the pure sample, mp 80—81°. $[\alpha]_D^{22}$ +53.1±1.0° (c=0.941). IR ν_{max} cm^{-1}: 1707 (C=O), 1672, 1622 (C=C-C=O). UV λ_{max} nm (ε): 239 (16480). CD (in $CHCl_3$): $[\theta]_{292}$ +13850, $[\theta]_{237}$ −30240. PMR (δ): 0.81 (s, 3, Me), 2.13 (s, 3, $COCH_3$), 5.91 (br. s, $W_{h/2}$=4.0 Hz, 1, 10-H). *Anal.* Calcd. for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 77.80; H, 8.89. Reported[16] mp 80°; $[\alpha]_D$ +53°, UV λ_{max} nm (ε): 239 (16200).

b) To a suspension of **24** (392 mg) in 7 ml of MeOH was added 92 mg of $NaBH_4$ and the mixture was stirred for 30 min at room temperature. The resulting clear solution was poured into ice water and extracted with CH_2Cl_2 leaving 415 mg of a crystalline material. This substance dissolved in 6 ml of dry THF was treated with a solution of 250 mg of Li in ca. 70 ml of liquid ammonia for 3.5 hr. The product extracted with CH_2Cl_2 was treated with 0.28 ml of 70% $HClO_4$ in 3.6 ml of 70% acetone aq. for 2 hr at room temperature. Work-up in the usual way gave 246 mg of a solid, which was oxidized with Jones reagent in acetone affording 240 mg of the product. Crystallization from ether gave 228 mg (80.2%) of **28**, mp 157—157.5°, which was characterized by mixed mp and comparison of the IR spectrum.

c) In the same experiment as described above in b) except that Li was replaced with Na, a series of reactions starting with 360 mg of **24** gave 215 mg (86.3%) of **28** as crystals, mp 157—157.5°.

10β,21-Bisphenylsulfonyl-5,5-ethylenedioxy-des-A-19-norpregn-9(11)-en-20-one (**26**)——a) To a solution of methylsulfinyl carbanion generated from 1.46 g of NaH and 6 ml of DMSO in 23 ml of monoglyme was added 4.67 g of phenyl methyl sulfone and the mixture was warmed at 70° under nitrogen. To this a solution of **22** (2.540 g) in 27 ml of monoglyme was added dropwise during 35 min. The resulting mixture was stirred at room temperature for 1.5 hr and then at 70° for 2 hr. Work-up as described above gave 5.4 g of an oily material, which on treatment with 2 ml of 70% $HClO_4$ in 60 ml of 70% acetone aq. for 21 hr at room temperature, followed by treatment with 30 ml of 1% KOH–MeOH for 3 hr at the same temperature afforded 5.3 g of the product which was found to be a mixture of the desired **25** and the reagent, phenyl methyl sulfone. Purification of a part of this material (*ca.* 20 mg) by preparative TLC (cyclohexane: AcOEt=1: 1) gave 11 mg of pure **25**, which could not be crystallized from any solvent. A solution of the remainder of the material and 86 mg of *p*-TsOH–H_2O in 80 ml of ethylene glycol was slowly distilled at 3—5 mmHg for 5 hr during which period 50 ml of distillate was removed. Work-up as described above gave *ca.* 5 g of a material from which **26** was separated by dry column chromatography on 350 g of silica gel (CH_2Cl_2:AcOEt=1:1). Crystallization of the fraction corresponding to **26** from ether afforded 2.971 g (69.9%) of **26** as crystals, mp 180—182°; $[\alpha]_D^{23}$ +163.7±2.1° (c=0.957). IR ν_{max} cm^{-1}: 1710 (C=O), 1645

(C=C), 1586, 755, 686 (C_6H_5), 1300, 1152, 1139, 1104 (SO_2), 1072 (ketal). PMR (δ): 0.63 (s, 3, Me), 3.76 (m, 5, ketal-CH_2 & 10α-H), 4.13 (br s, 2, 21-CH_2), 5.61 (m, $W_{h/2}$=7.0 Hz, 1, 11-H), 7.56 (m, 6, C_6H_5-$H_{m,p}$), 7.87 (m, 4, C_6H_5-H_o). Mass Spectrum *m/e*: 570 (M^+, 1%), 99 ( , 100%). *Anal.* Calcd. for $C_{30}H_{31}O_7S_2$: C, 63.14; H, 6.01; S, 11.24. Found: C, 63.18; H, 6.06; S, 11.44.

b) In another run, a series of reactions of the acid **10** (4.901 g) with diazomethane, ethylene glycol, phenyl methyl sulfone, acid and then alkali gave *ca.* 15 g of a mixture of **25** and phenyl methyl sulfone. A solution of this mixture and 390 mg of *p*-TsOH·H_2O in 200 ml of ethylne glycol was distilled in the same way as described above except that the reaction time was prolonged to 9 hr. The product was subjected to dry column chromatography on 910 g of silica gel (CH_2Cl_2:AcOEt=5:4). In the order of elution with the solvent, the following products were obtained. 1) Phenyl methyl sulfone; 2) 314 mg (3.9%) of **29**, which was recrystallized from acetone–hexane to yield the pure sample, mp 201—203°. $[\alpha]_D^{24}$ +140.8±1.8° (c=1.004). IR ν_{max} cm^{-1}: 1733 (C=O), 1643 (C=C), 1585, 687 (C_6H_5), 1304, 1157, 1140 (SO_2), 1077 (ketal), 934. PMR (δ): 0.90 (s, 3, Me), 3.66 (s, 3, OMe), 3.73 (m, 5, ketal-CH_2 & 10α-H), 5.63 (m, $W_{h/2}$=8.5 Hz, 1, 11-H), 7.52 (m, 3, C_6H_5-H), 7.88 (m, 2, C_6H_5-H), (C_6D_6): 0.94 (s, 3, Me), 2.57—3.30 (m, 4, ketal-CH_2), 3.38 (s, 3, OMe), 3.84 (br s, $W_{h/2}$=4.0 Hz, 1, 10α-H), 5.71 (m, 1, 11-H), 7.07 (m, 3, C_6H_5-H), 7.90 (m, 2, C_6H_5-H). Mass Spectrum *m/e*: 446 (M^+, 2%), 305 (M^+-$SO_2C_6H_5$, 16%), 99 ( , 100%). *Anal.* Calcd. for $C_{24}H_{30}O_6S$: C, 64.55; H, 6.77; S, 7.18. Found: C, 64.68; H, 6.89; S, 7.28. 3) 7.67 g of a mixture of **26** and **30**, from which 5.364 g of pure **26** was crystallized by treatment with ether. The mother liquor was concentrated to dryness and the residue (2.068 g) was subjected to preparative TLC by using the four-times development method (cyclohexane:AcOEt=3:2). The more polar fraction (Rf=0.37) gave an additional 0.844 g of **26** and the combined yields were 6.208 g (59.4%). The less polar fraction (Rf=0.39) afforded 1.224 g (11.1%) of **30**, which was recrystallized from ether yielding the pure sample, mp 121—123°. $[\alpha]_D^{24}$ +79.4±1.4° (c=0.995). IR ν_{max} cm^{-1}: 3058, 1586, 687 (C_6H_5), 1305, 1153, 1142 (SO_2). 1080 (ketal). PMR (δ): 0.78 (s, 3, Me), 3.41 (s, 2, 21-CH_2), 3.83 (m, 9, ketal-CH_2 & 10α-H), 5.62 (m, $W_{h/2}$=8.5 Hz, 1, 11-H), 7.56 (m, 6, C_6H_5-H), 7.97 (m, 4, C_6H_5-H), (C_6D_6): 0.99 (s, 3, Me), 3.27 (m, 10, ketal-CH_2 & 21-CH_2), 3.84 (br. s, $W_{h/2}$=4 Hz, 1, 10α-H), 5.72 (m, 1, 11-H), 7.05 (m, 6, C_6H_5-H), 7.90 (m, 4, C_6H_5-H). Mass Spectrum *m/e*: 614 (M^+, 1%), 473 (M^+-$SO_2C_6H_5$, 44%), 332 (M^+−2×$SO_2C_6H_5$, 8%), 99 ( , 100%). *Anal.* Calcd. for $C_{32}H_{38}O_8S_2$: C, 62.52; H, 6.23; S, 10.43. Found: C, 62.50; H, 6.38; S, 10.32.

Desulfurization of 26——To a stirred solution of 1.724 g of Na in 500 ml of redistilled liquid ammonia a solution of **26** (5.338 g) in 110 ml of dry THF was added dropwise during 15 min. The mixture was stirred for 4 hr, allowed to stand overnight at room temperature, and treated as described above. The product (2.65 g) was further treated with 1.32 ml of 70% $HClO_4$ in 26.5 ml of 70% acetone aq. for 2.5 hr. Subsequent oxidation with Jones reagent in 22 ml of acetone gave 2.2 g of an oily material, which was purified by chromatography on 220 g of silica gel (CH_2Cl_2:AcOEt=3:1). Recrystallization from ether–petroleum ether yielded 1.605 g (70.0%) of **27**, mp 80—81°.

5-Pyrrolidyl-des-A-19-norpregna-5(10),9(11)-dien-20-one (31)——To a chilled solution of **27** (2.184 g) in 4.4 ml of MeOH was added 8.75 ml of pyrrolidine and the mixture was allowed to stand at room temperature for 25 min during which period crystals were deposited. To the mixture was added 1 ml of isopropyl ether and the crystals which formed were collected by filtration, washed with cold isopropyl ether and dried (2.393 g yield, 90.2%). This material was used for the following alkylation reaction without further purification. An analytical sample of **31** was prepared by recrystallization from isopropyl ether, mp 122—124° (decomp). $[\alpha]_D^{25}$ +244.1±4.7° (c=0.599). IR ν_{max} cm^{-1}: 1706 (C=O), 1661 (C=C), 1626, 1598, 1358 (enamine), 831. PMR (δ): 0.64 (s, 3, Me), 2.11 (s, 3, COMe), 5.02 (m, 2, 10-H & 11-H). CD (in CH_3CN): $[\theta]_{289}$ +27080. *Anal.* Calcd. for $C_{20}H_{29}ON\cdot 1/3H_2O$: C, 78.64; H, 9.79; N, 4.59. Found: C, 78.59; H, 9.60; N, 4.50. Reported[16] mp 142°; $[\alpha]_D$ +251°.

10-Propargyl-des-A-19-norpregn-9(10)-ene-5,20-dione (32)——A stirred mixture of **31** (2.188 g) and 0.61 ml of propargyl bromide in 32 ml of HMPA was allowed to stand in the dark for 25 hr then heated at 100—110° for 1.5 hr. After 26 ml of water had been added, the mixture was heated at 110° for 2 hr. After dilution with water, extraction with CH_2Cl_2 gave 2.2 g of an oily material, which was purified by preparative TLC (cyclohexane:AcOEt=1:1). The more polar fraction gave **161** mg (8.9%) of recovered **27**, mp 80—81°. **The** less polar fraction afforded 1.102 g (53.1%) of **32**, which was recrystallized from ether–petroleum ether to give the pure sample, mp 124—125°. $[\alpha]_D^{27}$ +29.3±0.3° (c=0.923). IR ν_{max} cm^{-1}: 3273 (≡CH), 2113 (C≡C), 1696 (C=O), 1665, 1606 (C=C-C=O), 1207. UV λ_{max} nm (ε): 246 (15110). PMR (δ): 0.81 (s, 3, Me), 2.13 (s, 3, COMe), 1.88 (t, J=2.6 Hz, 1, ≡CH), 3.27 (br, s, 2, ≡C-CH_2). *Anal.* Calcd. for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.03; H, 8.55.

3,5-Seco-4,19-bisnorpregn-9(10)-ene-2,5,20-trione (33)——To a chilled solution of **32** (875 mg) in 26 ml of 90% MeOH aq., 46 mg of $HgSO_4$ and 0.24 ml of conc. H_2SO_4 were added. The mixture was stirred for 20 min at room temperature. After removal of the precipitated solid by filtration, the filtrate was diluted

with 140 ml of ice water and extracted with CH_2Cl_2. The organic layer was washed with Na_2CO_3 aq. and dried over Na_2SO_4. Removal of the solvent *in vacuo* gave 939 mg of a crystalline residue, recrystallization of which from acetone–hexane yielded 910 mg (97.8%) of **33**, mp 110—111.5°. $[\alpha]_D^{25}$ +26.3±1.7° (c=0.391). IR ν_{max} cm^{-1}: 1717, 1700 (C=O), 1659, 1610 (C=C-C=O), 1199, 1153. UV λ_{max} nm (ε): 248 (14640). CD (in MeOH): $[\theta]_{337}$ −876, $[\theta]_{286.5}$ +14200, $[\theta]_{245}$ −31380, $[\theta]_{212}$ +14020. PMR (δ): 0.81 (s, 3, Me), 2.12 (s, 3, COMe), 2.17 (s, 3, COMe), 3.51 (s, $W_{h/2}$=3.4 Hz, 2, C-CH_2-C). *Anal.* Calcd. for $C_{19}H_{26}O_3$: C, 75.46; H, 8.67. Found: C, 75.74; H, 8.42.

Hydrogenation of 33——Compound (**33**) (866 mg) dissolved in 27 ml of AcOEt and 1.1 ml of Et_3N was hydrogenated over 200 mg of prereduced 10% Pd-C. After uptake of hydrogen ceased (*ca.* 96 ml of H_2), the mixture was worked up in the usual way. Recrystallization of the product from acetone–hexane gave 675 mg of **34a**, mp 127—128.5°. $[\alpha]_D^{25}$ +65.9±3.1° (c=0.340). IR ν_{max} cm^{-1}: 1721$_{sh}$, 1706 (C=O), 1205, 1194, 1173, 1149. CD (in $CHCl_3$): $[\theta]_{310^{sh}}$ +3130, $[\theta]_{301}$ +4290, $[\theta]_{292.5}$ +3790. PMR (δ): 0.71 (s, 3, Me), 2.10 (s, 3, COMe), 2.22 (s, 3, COMe). *Anal.* Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 75.21; H, 9.35. The mother liquor was concentrated to dryness *in vacuo*, and the residue (240 mg) was subjected to preparative TLC (cyclohexane:AcOEt=1:1). In order of their decreasing mobility, the fractions afforded 98 mg of **34a**; 58 mg (5.1%) of **34b**, which was recrystallized from acetone–hexane to yield the pure sample, mp 111—111.5°. $[\alpha]_D^{26}$ +61.6±3.8° (c=0.268). IR ν_{max} cm^{-1}: 1710, 1707 (C=O), 1230, 1196. CD (in $CHCl_3$): $[\theta]_{292}$ +8250. PMR (δ): 0.68 (s, 3, Me), 2.11 (s, 3, COMe), 2.16 (s, 3, COMe). *Anal.* Calcd. for $C_{19}H_{28}O_3$: C, 74.96; H, 9.27. Found: C, 74.72; H, 9.28; and 13 mg (1.3%) of **35**, which on recrystallization from acetone–hexane gave the pure sample, mp 119—121°. $[\alpha]_D^{25}$ +98.1±5.4° (c=0.256). IR ν_{max} cm^{-1}: 3459 (OH), 1707 sh, 1692 (C=O), 1196, 1154. CD (in $CHCl_3$): $[\theta]_{292}$ +12350. PMR (δ): 0.63 (s, 3, Me), 2.09 (s, 3, COMe), 2.12 (s, 3, COMe), 3.26 (dt, $J_{5\alpha:6\alpha}$=4.5 Hz, $J_{5\alpha:6\beta}$=$J_{5\alpha:10\beta}$=14.5 Hz, 1, 5α-H). *Anal.* Calcd. for $C_{19}H_{30}O_3$: C, 74.47; H, 9.87. Found: C, 74.74; H, 9.52. The combined yield of **34a** was 773 mg (88.7%). Jones oxidation of **35** (6.5 mg) in the usual way gave 6 mg of **34a**, which was identified with the sample prepared above by mixed mp, comparison of the IR spectrum and TLC.

2-Methyl-3-oxa-4,19-bisnorpregna-1,5(10)-dien-20-one (36)——A solution of **34a** (719 mg) and 85 mg of *p*-TsOH–H_2O in 72 ml of benzene was refluxed for 30 min with azeotropic removal of the formed water. The cooled mixture was poured into iced Na_2CO_3 aq. and extracted with CH_2Cl_2. Recrystallization of the product from aqueous acetone afforded 582 mg (86.0%) of **36**, mp 111—112°. $[\alpha]_D^{25}$ +125.9±4.7° (c=0.351). IR ν_{max} cm^{-1}: 1699 (C=O), 1658 ,1630, 1574, 949, 812 (furan). UV $\lambda_{max}^{isooctane}$ nm (ε): 226 (7760). CD (in isooctane): $[\theta]_{336}$ O, $[\theta]_{298}$ +9600, $[\theta]_{292}$ +9120, $[\theta]_{247.5}$ O, $[\theta]_{228}$ −12640, $[\theta]_{217.5}$ O, $[\theta]_{208}$ +9920, $[\theta]_{200}$ +6400. PMR (δ): 0.66 (s, 3, Me), 2.12 (s, 3, COMe), 2.24 (s, $W_{h/2}$=2.6 Hz, 3, furan-Me), 5.82 (s, $W_{h/2}$=2.3 Hz, 1, 1-H). Mass Spectrum m/e: 286 (M^+, 100%). *Anal.* Calcd. for $C_{19}H_{26}O_2$: C, 79.68; H, 9.15. Found: C, 79.75; H, 9.14. The same treatment of **34b** (20 mg) with acid as described above gave 17 mg of a compound identical with **36**.

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