Total Synthesis of Dinordrin and Analogues

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A total synthesis of optically active dinordrin (3c) is detailed, following a flexible and stereoselective route. A number of unexpected and potentially useful by-products have been identified. The preparation of the novel *A*-nor-steroid analogues (19), (20), and (21) is also reported. The *X*-ray crystallographic data of the 11β-hydroxylated tricyclic intermediate (13), the norestr-3(5)-ene-2,17-dione (16b), the alkylated dienedione (8b), and the diethynyldihydroxynorestr-3(5)-ene (21) are reported.

The *A*-nor-steroids form a class of non-natural compounds, with unusual chemical and biological properties. In 1962, Pincus reported the implantation inhibitor activity [1] exhibited by some *A*-norandrostanes, initially prepared by Jacques and co-workers.[2] These nor-steroids have seen a considerable revival of interest following recent publications by Ku Chih-ping and other Chinese investigators who reported that a significant antifertility activity is associated with 2,17α-diethynyl-*A*-nor-5α-androstane-2,17β-diyl dipropionate, as a mixture of isomers at position 2, called ' anordrin '.[3] Various clinical reports have described the use of anordrin administered postcoitally, and the Chinese scientists call it a ' vacation pill ' or ' pill no. 53 '.

In view of the potent fertility regulation properties reported for anordrin, the stereochemically pure 2β,17β-diol (1a) and its 2α-isomer (2a), the corresponding diacetates (1b) and (2b), as well as the dipropionates [anordrin-I, (1c)] and [anordrin-II, (2c)] were prepared by a classical route, and the interesting biological properties of anordrin-I (2α-ethynyl isomer) (1c) confirmed.[4] Since rather trivial chemical modifications of an active molecule can sometimes lead to substantial differences in the biological profile, it was decided to prepare the 19-nor counterpart of anordrin-I (1c) by chemical transformation of 19-nortestosterone, using known methodology.[4] The free diol (3a), the corresponding diacetate (3b), and the dipropionate (3c) were prepared.

The preparation of dinordrin-I (3c) and analogues from naturally occurring sapogenins and sterols is rather lengthy and low yielding, as more than 18 steps are involved in the chemical conversion of diosgenin (4) into dinordrin-I (3c), with a total yield not exceeding 4%.[5] Hence, a flexible and high yielding total synthetic route was desirable. In this report we describe a stereocontrolled preparation of dinordrin-I (3c) and some chemically related analogues that otherwise would be difficult to obtain.[6]

The initial steps of this approach are based on earlier work by Wiechert *et al.*[7] who reported a preparation of the optically active bicyclic indandione (5a), by aldol cyclization of an alkylated cyclopentanedione in the presence of (−)-(*S*)-proline. The indandione (5a) was dehydrated with acid to give the enedione (6a). The bicyclic sulphone (7a) was obtained by treatment of optically active (+)-7aβ-methyl-7,7a-dihydroindan-1,5(6*H*)-dione (6a) with paraformaldehyde and benzenesulphinic acid in triethanolamine. A survey of several reagents showed that the reaction led to a viscous oil in *ca.* 59% yield in triethanolamine, while, when performed in tetramethylethylenediamine, the reaction proceeded more smoothly and led to higher yields of the sulphone (7a) (69% after purification). Regardless of the nature of the base utilized in this condensation, and the use of either the sulphinic acid or the sodium salt, in all reactions 17—22% of the alkylated dienedione (8a) was isolated as a by-product.‡ Catalytic hydrogenation [8] of the enone (7a) in acidic medium, in the presence of palladium on charcoal, afforded the fairly labile crystalline sulphone (9a).

The sulphone (9a) was allowed to react with methyl-3,6-dioxoheptanoate ethylene 6-acetate (10) in anhydrous toluene in the presence of potassium hydride, to provide the bicyclic trioxoester (11a), possessing all the carbon atoms of the dinordrin steroid skeleton. The oxoester (10), a precursor for the construction of rings A and B, was prepared in two steps from acetonylacetone, by reaction with ethylene glycol, catalyzed with sulphuric acid in a two-phase system.[9] A mixture was obtained containing the starting diketone, the desired monoacetal and the diacetal (which could be recycled by acid treatment) in the ratio 28 : 56 : 16, respectively. These components were separated by fractional distillation *in vacuo*. The monoacetal was then condensed with dimethyl carbonate, previously treated with sodium hydride, in ether solution at reflux temperature, thus affording [9] the desired oxo ester (10) in 68% yield, after purification by distillation.

The condensation of the potassium salt of the enolate of the oxo ester (10) and the perhydroindandione (9a) was achieved in anhydrous toluene solution. This reaction seems to proceed, at least in part, *via* substitution of the sulphone group. The 4-methylene-5-oxoindan system, which would be the product of an initial elimination of sulphinic acid, has been used in a similar manner in another steroid total synthetic approach.[8] In the present case, however, if the elimination of benzenesulphinic acid is the predominant step, the Michael addition process does not seem to be favoured. Indeed, the best yield was obtained by slow addition of the sulphone (9a) to the enolate of compound (10). Conversely, addition of (10) to the sulphone (9a) gave lower yields. The crude product (11a) was directly subjected to the annelation reaction, by treatment with aqueous sodium hydroxide, followed by refluxing in toluene to provide the enedione (12a) in an overall yield >90%. Four steps are involved in this remarkable transformation of compound (11a) into (12a), namely ring formation (condensation) between positions 9 and 10, dehydration of the tertiary carbinol, hydrolysis of the ester group, and decarboxylation at position 6.

In the course of these reactions a by-product was generally present in the mixture, in amounts of up to 15%. Isolation of this crystalline material, followed by a careful study of its physical properties, allowed the assignment of the 11β-hydroxy structure (13). The *X*-ray crystallographic data (see Figure 1) support structure (13). No attempt was made to optimize the yield of formation of this compound (13). However, the consistent obtention of the 11β-hydroxylated inter-

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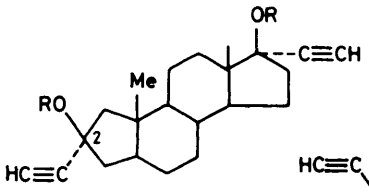
‡ A similar observation was made by Chinese scientists. We are grateful to Professor Huang Liang, Academia Medica, Beijing, for this information.



(1)
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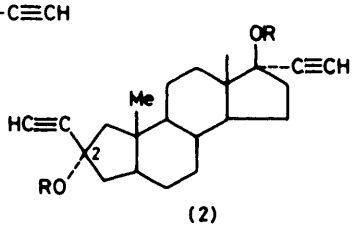
b; R = Ac
c; R = C(O)Et



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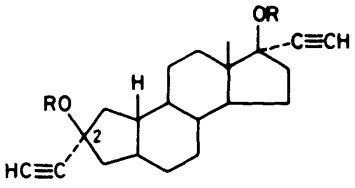

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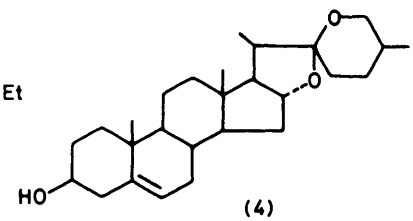
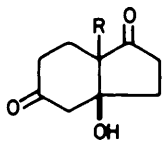


(4)



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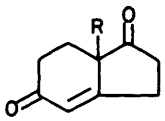

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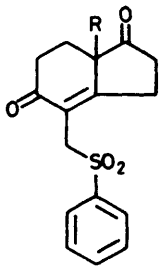

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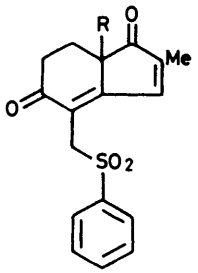

(8)
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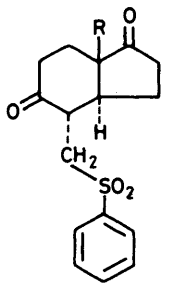

(9)
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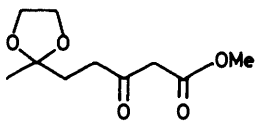
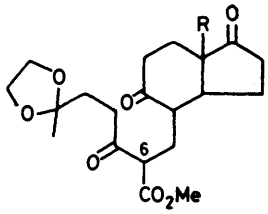


(10)



(11)
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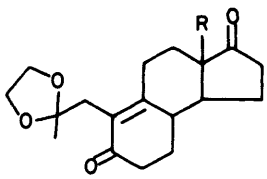

(12)
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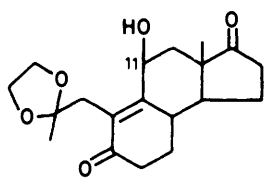
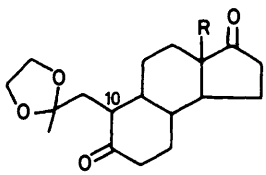
b; R = Et



(13)



(14)
a; R = Me
b; R = Et

mediate (13) is noteworthy and deserves further investigation. Indeed, this constitutes a potential avenue for the synthesis of 11- and 12-substituted estrane derivatives, and also a new route for the total synthesis of corticoid molecules.

Catalytic hydrogenation of the enone (12a) in ethanol solution and a trace of triethylamine, in the presence of 5% palladium on charcoal, yielded the saturated dione (14a). A brief exposure of the acetal (14a) to 1M-aqueous hydrochloric acid in acetone furnished the trione (15a), with the desired equatorial configuration for the chain at position 10, in 74% overall yield.

A variety of conditions were investigated for the intramolecular cyclization of the tricyclic ketone (15a). Treatment with methanolic potassium hydroxide gave a 2 : 1 mixture of the $\Delta^{1(10)}$- (16a) and $\Delta^{3(5)}$-enone (16b), in 75% yield, separated by t.l.c. and recrystallization. An examination of the enone (16b) by *X*-ray crystallography (see Figure 2) supports both the position of the double bond and the proposed stereochemistry. It was noted that the isomerization process of the $\Delta^{3(5)}$-enone (16b) to its $\Delta^{1(10)}$ counterpart (16a) was slowed down when potassium t-butoxide was used; thus up to 70% of the $\Delta^{3(5)}$-isomer (16b) could be obtained. In the latter experiment, however, a small amount (*ca.* 5%) of the β,γ-unsaturated ketone (16c) was identified. A drastically different result was obtained when the cyclization of (15a) was attempted in acidic medium. Treatment of the trione (15a) in refluxing benzene containing a trace of toluene-*p*-sulphonic acid produced the bridged steroid (17a) in 84% yield. Similar results were obtained in the 18-homo series (17b) (see below). These cyclization products are reminiscent of observations made initially by Johnson *et al.*[10]

Reduction with lithium in ammonia of the mixture of double bond isomers (16) in tetrahydrofuran (THF) solution provided the *A*-norestrane-2,17-dione (18a), shown to be identical with an authentic sample[4] by the usual criteria. Ethynylation at positions 2 and 17 of the diketone (18a) was achieved by addition of lithium acetylide–ethylenediamine complex, thus affording a mixture of isomeric 2-ethynyl derivatives separated by preparative t.l.c.[11] Esterification with

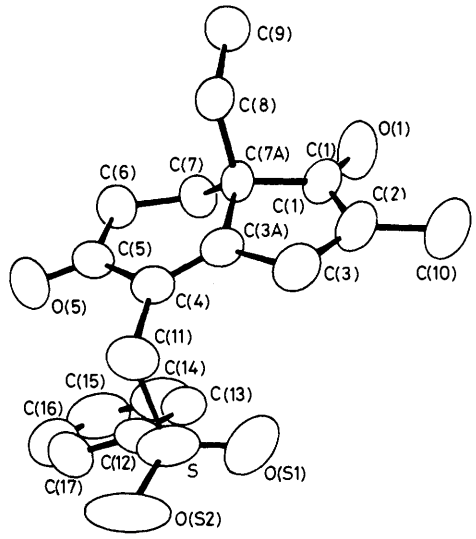


Figure 1. The molecular structure of the methylated dienedione (8b) showing the crystallographic numbering scheme

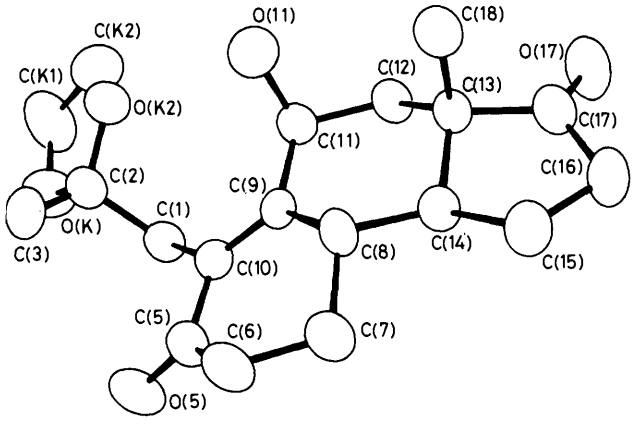
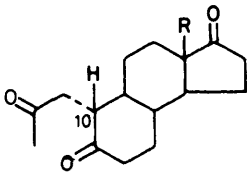


Figure 2. The molecular structure of the 4-nor-3,5-secoestr-9-ene-3,5,17-trione 3-acetal (13) showing the crystallographic numbering scheme

propionic anhydride of the alcohol (3a) then afforded dinordrin-I (3c) in the optically active form.

Parallel with our effort to construct the *A*-nor-steroid skeleton and to gain access to dinordrin, work was also carried out aimed at the synthesis of some analogues of dinordrin. Thus, the known 4-sulphonylmethyl-7aβ-ethyl-7,7a-dihydroindan-1,5(6*H*)-dione[7] (7b) was submitted to the above reaction sequence. The alkylated dienedione (8b) was again isolated as a by-product. Its structure and configuration were supported by *X*-ray crystallography (Figure 3). The tricyclic intermediate (12b) prepared by the above route was reduced catalytically (5% Pd–C) to generate the saturated dione (14b), which on treatment with dilute hydrochloric acid in acetone solution gave the corresponding trione (15b). Cyclization of ring A was accomplished in methanolic sodium hydroxide. The $\Delta^{3(5)}$-enone (16d) and its $\Delta^{1(10)}$-isomer (16e) were obtained in pure form after preparative t.l.c. and recrystallization from ethyl acetate–hexane. An examination of the physical properties of enone supports the position of the double bond. The isomeric mixture was reduced with lithium in liquid ammonia to afford the 18-homo-*A*-nor-dioxosteroid (18b). The diketone (18b) was then converted into 18-homodinordrin (19) by conventional techniques.[4]



(15)
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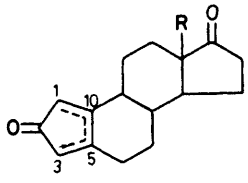
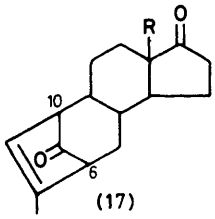
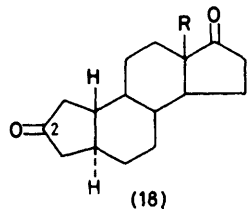
b; R = Et



(16)
a; $\Delta^{1(10)}$, R = Me
b; $\Delta^{3(5)}$, R = Me
c; $\Delta^{5(10)}$, R = Me
d; $\Delta^{3(5)}$, R = Et
e; $\Delta^{1(10)}$, R = Et



(17)
a; R = Me
b; R = Et



(18)
a; R = Me
b; R = Et

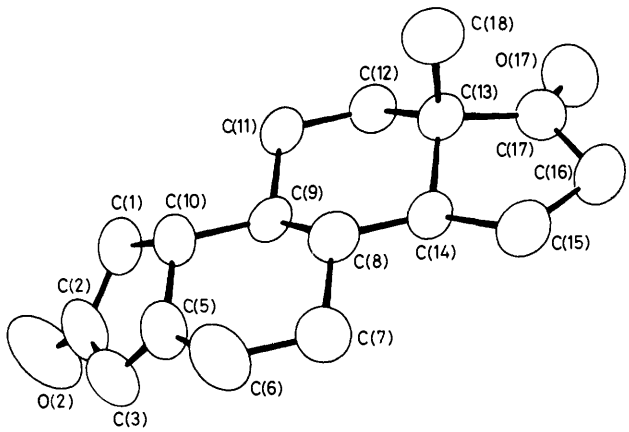
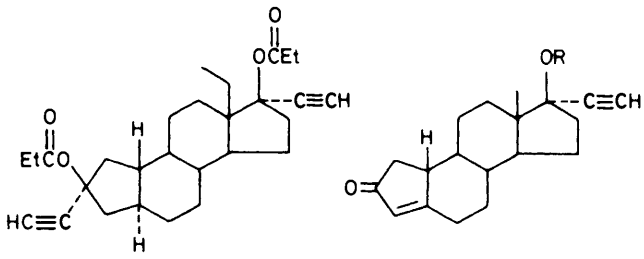


Figure 3. The molecular structure of the $\Delta^{3(5)}$-enone (16b) showing the crystallographic numbering scheme

Finally, an olefinic *A*-nor-steroid analogue was also prepared. Treatment of compound (16b) with sodium acetylide in THF at 0 °C gave the monoethynylated steroid (20a) in *ca.* 80% yield. Esterification of the tertiary alcohol grouping with a mixture of propionic acid and propionic anhydride catalyzed by toluene-*p*-sulphonic acid yielded the corresponding propionate (20b). Further treatment of compound (20a) with lithium acetylide in THF at −78 °C,[12] afforded the diethynylated product. T.l.c. separation followed by crystallization furnished a fairly labile substance to which structure (21) was assigned and confirmed by *X*-ray crystallography (see Figure 4).

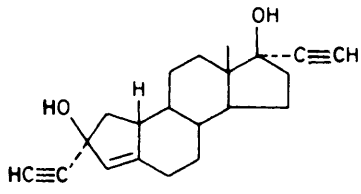
The above total synthetic procedure is short, flexible, and easy to perform, thus constituting a useful approach to this class of biologically important *A*-nor-steroids. It is noteworthy that the cyclization reaction of the intermediates (11), followed by catalytic reduction of enones (12), acid hydrolysis of the acetal, ring *A* closure, and Birch reduction of cyclopentenones of type (16) afforded the diones (18) with the correct stereochemistry at all asymmetric centres.

In clinical studies hyperestrogenic side effects have been



(19)

(20)
a; R = H
b; R = C(O)Et



(21)

reported for pure anordrin-I (1c). In the rodent, anordrin-I (1c) is uterotrophic, although significantly less so than ethynylestradiol. Dinordrin-I (3c) was *ca.* 20 times more active in this test than pure anordrin-I (1c), which means it is of the same uterotrophic potency as ethynylestradiol. Moreover, in the castrate female baboon, dinordrin-I (3c) exhibited *ca.* 1/150th the estrogenic potency of ethynylestradiol. Although these substances behaved more or less like impeded estrogens, the single-dose anti-implantation effect in rats of anordrin-I (1c), dinordrin-I (3c), dinordrin-II, and 18-homodinordrin (19) roughly paralleled their uterotrophic activity. In the assay systems, dinordrin-I (3c) was by far the most active compound.[4]

Experimental

M.p.s were determined with a Fisher–Johns apparatus and were corrected. I.r. spectra were obtained with a Beckman infrared spectrometer Model IR-10. U.v. spectra were taken with a Perkin-Elmer 576 ST spectrophotometer. Rotations were taken in chloroform solution (*c* 1.0), between 16 and 22 °C with a 1-dm tube at the sodium D-line, with a Carl-Zeiss 42017 polarimeter. ^{1}H N.m.r. spectra were recorded with a Varian EM-360 60 MHz spectrometer in deuteriochloroform containing tetramethylsilane as internal reference. Coupling constants are accurate to ±1 Hz. Low resolution mass spectra were recorded with a Dupont instrument, Model 21-490, ionizing energy 70 eV and high resolution spectra were obtained with a C.E.C. model 21-110 double focusing instrument.

X-Ray data were collected on an Enraf-Nonius CAD4 diffractometer and processed on a PDP 11-34 computer using the Enraf-Nonius SDP programmes.

Column chromatography was carried out using silica gel (Kieselgel 60, Art 9385, 230—400 mesh, Merck Darmstadt). T.l.c. was carried out with Camlab ' Polygram ' pre-coated silica plates, and Merck 2-mm thickness preparative plates were used for preparative t.l.c.

Microanalyses were performed by Galbraith Laboratories, Inc., Knoxville, Tennessee, U.S.A.

Ether refers to diethyl ether throughout.

Hexene-2,5-dione Ethylene Monoacetal.—A solution of hexane-2,5-dione (22.8 g, 0.2 mol) and ethylene glycol (50 g, 0.8 mol) in toluene (125 ml) was cooled to 0 °C. To this mixture conc. sulphuric acid (5 ml, 0.09 mol) was added. The mixture was vigorously stirred at 0 °C for 30 min. The lower layer was separated and extracted with toluene twice. A suspension of sodium hydrogencarbonate (25 g) in water (25 ml) was used to neutralize the main organic layer and to neutralize the toluene extracts. The combined organic solution was washed with brine and evaporated under reduced pressure (the toluene was distilled at 30 °C/32 mmHg). An oily residue was obtained containing the starting material, the desired monoacetal, and the diacetal in 28, 56, and 16% yield, respectively. The components of the crude product were separated by fractional distillation to give, after recovering the starting material, the desired monoacetal (15.4 g) as the second material distilled (97% pure), b.p. 99—101 °C/14 mmHg; $\nu_{max.}$ (neat) 1 718 cm^{-1}; δ 3.93 (s, 4 H, OC_2H_4O), 2.15 (s, 3 H, COMe), and 1.31 (s, 3 H, Me); *m/z* 158 (M^+), 143 (M^+ − Me), and 87 ($MeCOC_2H_4O^+$) (Found: C, 60.85; H, 8.65. Calc. for $C_8H_{14}O_3$: C, 60.72; H, 8.92%).

The diacetal was also obtained: b.p. >125 °C/14 mmHg, m.p. 58—59 °C (ether); δ 3.93 (s, OC_2H_4O) and 1.31 (s, 6 H, 2 Me) (Found: C, 59.6; H, 9.05. Calc. for $C_{10}H_{18}O_4$: C, 59.37; H, 9.87%).

The latter product could be easily reconverted into the starting material by treatment with aqueous mineral acid in acetone.

Methyl 3,6-Dioxoheptanoate Ethylene 6-Acetal (10).—Sodium hydride (10 g, 50% oil dispersion, 0.2 mol) was rinsed with hexane and then with anhydrous ether. Dimethyl carbonate (17 ml, 19 g, 0.2 mol) was added followed by anhydrous ether (25 ml). This suspension was stirred, and gently refluxed, and the hexanedione monoacetal (15.8 g, 0.1 mol) was added dropwise during 1.5 h (after *ca.* 45 min the evolution of hydrogen became vigorous). The reflux was continued for 45 min and then the mixture was stirred at room temperature for 5 h. The suspension was cooled to 0 °C and ethanol (5 ml) was added dropwise, with stirring. After 1 h the resulting gelatinous mixture was acidified by dropwise addition of a 30% aqueous acetic acid (50 ml), then the mixture was diluted with ethyl acetate (100 ml) and saturated with sodium chloride. The aqueous layer was separated and extracted twice with ethyl acetate. The organic layer was washed with 5% sodium hydrogencarbonate and water. The combined organic solution was evaporated under reduced pressure to give the β-oxo ester (10) (15 g, 68%; 98% pure), b.p. 102—104 °C/0.07 mmHg; $\nu_{max.}$ (neat) 1 710, 1 740, and 1 260 cm^{-1}; δ 3.91 (s, 4 H, OC_2H_4O), 3.71 (s, 3 H, CO_2Me), 3.47 (s, 2 H, CH_2), 1.8—2.8 (*m*, 4 H, 4- and 5-CH_2), and 1.31 (s, 3, Me); *m/z* 216 (M^+), 201 (M^+ − 15), and 87 (MeCO-

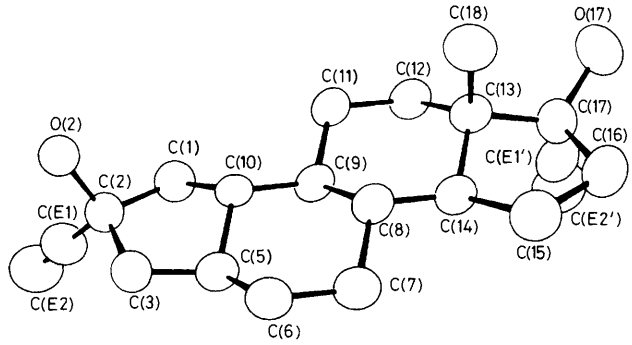


Figure 4. The molecular structure of 2α,17α-diethylnyl-2β,17β-dihydroxy-4-norestr-3(5)-ene (21) showing the crystallographic numbering scheme

Table 1. Crystal data, data collection, and refinement for compounds (8b), (13), (16b), and (21)

	(8b)	(13)	(16b)	(21)
Formula	$C_{19}H_{20}O_4S$	$C_{19}H_{25}O_5$	$C_{17}H_{22}O_2$	$C_{21}H_{30}O_2{\cdot}C_2H_5OH$
M	344.5	333.4	258.4	359.5
Crystal system	Monoclinic	Orthorhombic	Orthorhombic	Orthorhombic
Space group	$C2$	$P2_12_12_1$	$P2_12_12_1$	$P2_12_12_1$
a (Å)	25.350(3)	7.076(2)	6.831(2)	6.843(4)
b (Å)	6.295(2)	23.985(6)	8.004(2)	15.520(3)
c (Å)	11.607(2)	10.243(4)	26.553(6)	19.937(3)
α (°)	90	90	90	90
β (°)	108.35(2)	90	90	90
γ (°)	90	90	90	90
Z	4	4	4	4
Radiation	Mo-K_α (ν 0.7107 Å)	Mo-K_α	Mo-K_α	Mo-K_α
D_x (g/cm^3)	1.302(1)	1.274(1)	1.182(1)	1.128(1)
θ Range (°)	2—25	2—22.5	2—25	2—25
Max. count time/scan (s)	90	90	90	90
Scan width (θ°)	0.60 + 0.35tanθ	0.60 + 0.35tanθ	0.80 + 0.35tanθ	0.65 + 0.35tanθ
No. of reflections measured	1 768	2 729	1 751	2 603
No. of independent reflections with $F_o > 2\sigma(F_o)$ used	1 386	1 133	1 126	1 113
$R = \Sigma\|\|F_o\| - \|F_c\|\|/\Sigma F_o$	0.044	0.043	0.049	0.052
R_w	0.060	0.055	0.060	0.058
No. of parameters	216	217	238	235

Table 2. Bond distances (Å) for compound (8b) with e.s.d.s in parentheses

S–O(S1)	1.441(4)	C(2)–C(10)	1.502(5)	C(7A)–C(8)	1.559(5)
S–O(S2)	1.412(3)	C(3)–C(3A)	1.455(5)	C(8)–C(9)	1.521(5)
S–C(11)	1.780(4)	C(3A)–C(4)	1.336(4)	C(12)–C(13)	1.376(6)
S–C(12)	1.776(3)	C(3A)–C(7A)	1.490(4)	C(12)–C(17)	1.355(6)
O(1)–C(1)	1.207(4)	C(4)–C(5)	1.496(5)	C(13)–C(14)	1.389(6)
O(5)–C(5)	1.211(4)	C(4)–C(11)	1.501(4)	C(14)–C(15)	1.335(9)
C(1)–C(2)	1.461(5)	C(5)–C(6)	1.491(5)	C(15)–C(16)	1.362(10)
C(1)–C(7A)	1.523(5)	C(6)–C(7)	1.519(6)	C(16)–C(17)	1.365(7)
C(2)–C(3)	1.354(6)	C(7)–C(7A)	1.523(4)		

$C_2H_4)^+$) (Found: C, 55.6; H, 7.65. Calc. for $C_{10}H_{16}O_5$: C, 55.53; H, 7.46%).

(+)-(7aS)-7a-*Methyl*-4-*phenylsulphonylmethyl*-7,7a-*dihydroindan*-1,5(6H)-*dione* (7a).—A mixture of the bicyclic enedione (6a) (16.4 g, 100 mmol), paraformaldehyde (3.6 g, 120 mmol), and benzenesulphinic acid (18 g, 125 mmol) was dissolved in tetramethylethylenediamine (TMEDA) (50 ml) under nitrogen. To this solution, acetic acid (17 ml) was added slowly while stirring on an ice-bath. The ice-bath was removed and the solution was stirred at room temperature and under a closed nitrogen atmosphere for 3 days after which time the solution became a brown slushy solid. This material was diluted with more TMEDA (30 ml) and acetic acid (10 ml) and stirred under the same conditions for 2 additional days. The resulting crude mixture was diluted with methylene dichloride (500 ml) and washed with 10% hydrochloric acid, then with 5% sodium hydrogencarbonate and brine. All aqueous solutions were re-extracted with methylene dichloride and the combined organic layer was dried ($MgSO_4$) and evaporated to give a crude product. This material was chromatographed over silica gel to give the desired sulphone (7a) (21.9 g, 69%), m.p. 160—162 °C (lit.,[7] m.p. 140—146 °C); $[\alpha]_D$ +223°; $\nu_{max.}$ ($CHCl_3$) 1 745, 1 670, 1 650, 1 320, 1 305, and 1 140 cm^{-1}; $\lambda_{max.}$ (EtOH) 219 (ε 12 400) and 250 nm (ε 9 700); δ 1.32 (s, 3 H, Me), 4.40 and 4.08 (AB, J 13 Hz, CH_2SO_2), and 7.5—8.0 (m, 5 aromatic H); m/z 318 (M^+), 193, and 177.

The alkylated product (8a) was isolated from the mother-liquors as a component with a higher R_F value (5.6 g) (17%). It was recrystallized from ethyl acetate–ethanol to afford the pure sample, m.p. 130—132 °C; $[\alpha]_D$ +58°; $\nu_{max.}$ ($CHCl_3$) 1 710, 1 665, 1 630, 1 590, 1 325, 1 310, and 1 135 cm^{-1}; $\lambda_{max.}$ (EtOH) 216.5 (ε 11 700) and 302 nm (ε 17 200); δ 1.3 (s, 3 H, 7-Me), 2.04 (d, 3 H, J 2 Hz, vinylic Me), 4.29 (AB, J 2 Hz, CH_2SO_2), and 7.3—7.9 (m, 5 aromatic H, 1 vinylic H); m/z 330 (M^+), 189, and 161 (Found: C, 65.5; H, 5.65; S, 9.55. Calc. for $C_{18}H_{18}O_4S$: C, 65.40; H, 5.49; S, 9.70%).

(+)-(7aS)-7a-*Ethyl*-4-(*phenylsulphonylmethyl*)-7,7a-*dihydroindan*-1,5(6H)-*dione* (7b).—A suspension of the indandione (6b) (8.9 g, 50 mmol), paraformaldehyde (1.8 g, 60 mmol), and benzenesulphinic acid (8.5 g, 60 mmol) in triethanolamine (30 ml) and acetic acid (10 ml) was thoroughly mixed under nitrogen with a glass rod. The reaction vessel was then stoppered tightly and magnetically stirred at 50 °C for 50 h. After this time the resulting brownish material was diluted with chloroform and water (200 ml each), containing sodium hydrogen carbonate (5 g). The organic layer was separated and washed with 10% aqueous hydrochloric acid (200 ml) and the aqueous layer was re-extracted with additional chloroform. The organic extracts were dried ($MgSO_4$), filtered, and evaporated to give a crude product which after column chromatography and crystallization from ethyl acetate–ether afforded the pure sulphone (7b) (10.0 g, 61%), m.p. 126—127 °C (lit.,[7] 124—125 °C), $[\alpha]_D$ +192° (lit.,[7] +198°); $\nu_{max.}$ ($CHCl_3$) 1 740, 1 670, 1 645, 1 325, 1 310, and 1 145 cm^{-1}; $\lambda_{max.}$ (EtOH) 218 (ε 12 000) and 252 nm (9 600); δ 0.96 (t, J 7 Hz, 3 H, ethyl Me), 1.69 (J 7 Hz, 2 H, ethyl CH_2), 4.42 and 4.07 (AB, 2 H, J 13 Hz, CH_2SO_2), and 7.5—8.0 (m, 5 aromatic H); m/z 332 (M^+), 207, 191, 149, and 77.

Table 3. Bond angles (°) for compound (8b) with e.s.d.s in parentheses

O(S1)–S–O(S2)	118.6(3)	C(3)–C(3A)–C(7A)	108.1(3)	C(3A)–C(7A)–C(8)	109.7(3)
O(S1)–S–C(11)	108.7(2)	C(4)–C(3A)–C(7A)	123.4(3)	C(7)–C(7A)–C(8)	113.9(3)
O(S1)–S–C(12)	108.7(2)	C(3A)–C(4)–C(5)	119.1(3)	C(7A)–C(8)–C(9)	115.2(3)
O(S2)–S–C(11)	106.9(2)	C(3A)–C(4)–C(11)	124.5(3)	S–C(11)–C(4)	114.0(3)
O(S2)–S–C(12)	108.7(2)	C(5)–C(4)–C(11)	116.4(3)	S–C(12)–C(13)	117.2(3)
C(11)–S–C(12)	104.4(2)	O(5)–C(5)–C(4)	120.9(3)	S–C(12)–C(17)	121.2(4)
O(1)–C(1)–C(2)	126.3(3)	O(5)–C(5)–C(6)	121.5(3)	C(13)–C(12)–C(17)	121.6(4)
O(1)–C(1)–C(7A)	125.6(3)	C(4)–C(5)–C(6)	117.6(3)	C(12)–C(13)–C(14)	117.0(4)
C(2)–C(1)–C(7A)	108.1(3)	C(5)–C(6)–C(7)	115.6(3)	C(13)–C(14)–C(15)	121.8(5)
C(1)–C(2)–C(3)	108.4(3)	C(6)–C(7)–C(7A)	108.7(3)	C(14)–C(15)–C(16)	119.7(4)
C(1)–C(2)–C(10)	122.9(4)	C(1)–C(7A)–C(3A)	101.4(3)	C(15)–C(16)–C(17)	120.6(5)
C(3)–C(2)–C(10)	128.6(3)	C(1)–C(7A)–C(7)	115.6(3)	C(12)–C(17)–C(16)	119.2(5)
C(2)–C(3)–C(3A)	110.8(3)	C(1)–C(7A)–C(8)	106.1(3)		
C(3)–C(3A)–C(4)	128.3(3)	C(3A)–C(7A)–C(7)	109.4(2)		

A less polar component isolated by column chromatography was identified as compound (8b) (3.6 g, 22%). After recrystallization from ethyl acetate–ether, an analytical sample was obtained, m.p. 137—138 °C; $[\alpha]_D$ +30°; $\nu_{max.}$ ($CHCl_3$) 1 710, 1 665, 1 625, 1 590, 1 325, 1 310, and 1 135 cm^{-1}; $\lambda_{max.}$ (EtOH) 216.5 (ε 12 000) and 302 nm (19 000); δ 0.83 (t, *J* 7 Hz, 3 H, ethyl Me), 1.75 (*J* 7 Hz, 2 H, ethyl CH_2), 2.02 (d, 3 H, *J* 2 Hz, vinylic Me), 4.30 (br, 2 H, CH_2SO_2), and 7.4—7.9 (m, 5 aromatic H and 1 vinylic H); *m/z* 344 (M^+), 203, 175, and 161 (Found: C, 66.3; H, 5.9; S, 9.2. Calc. for $C_{19}H_{20}O_4S$: C, 66.26; H, 5.85; S, 9.31%).

Crystallographic details of *X*-ray intensity and refinement data collection for the four compounds (8b), (13), (16b), and (21) are given in Table 1. Pertinent bond distances and angles for (8b) are in Tables 2 and 3, and the fractional atomic co-ordinates are in Table 4. Tables of anisotropic thermal parameters, hydrogen-atom co-ordinates, and observed and calculated structure factors for all four structures have been deposited as a Supplementary Publication (SUP No. 23670, 40 pages).*

(+)-(7aS)-7a-*Methyl*-4-(*phenylsulphonylmethyl*)*perhydroindan*-1,5-*dione* (9a).[7]—A solution of the unsaturated sulphone (7a) (2.5 g) in glacial acetic acid (100 ml) containing 5% Pd–C (350 mg) was shaken under hydrogen (30 lb in^{-1}) for 4 h. The solution was filtered and evaporated to yield a gummy material. The pure reduced sulphone (9a) was isolated by chromatography of the crude product on a column of silica gel using gradient ethyl acetate–hexane as solvent. Recrystallization of the combined pure fractions from ethyl acetate–hexane gave an analytical sample of (9a) as prisms (1.63 g, 65%), m.p. 92—94 °C; $[\alpha]_D$ +115°; $\nu_{max.}$ ($CHCl_3$) 1 735, 1 710, 1 315, and 1 150 cm^{-1}; δ 1.22 (s, 3 H, Me), 4.03, 3.08, and 2.86 (m, 3 H, $CHCH_2SO_2$), and 7.4—8.0 (m, 5 aromatic H); *m/z* 320 (M^+), 179, and 161.

(+)-(7aS)-7a-*Ethyl*-4-(*phenylsulphonylmethyl*)*perhydroindan*-1,5-*dione* (9b).—Starting with the enone (7b) and following the same procedure as for reduction of compound (7a), the sulphone (9b) was obtained in *ca.* 70% yield, after recrystallization from ethyl acetate–hexane; m.p. 162—164 °C; $[\alpha]_D$ +84° (lit.,[7] m.p. 160—161 °C, $[\alpha]_D$ +82°); $\nu_{max.}$ ($CHCl_3$) 1 740, 1 710, 1 305, and 1 105 cm^{-1}; δ 0.86 (t, *J* 7 Hz, 3 H, ethyl Me), 1.72 (*J* 7 Hz, 2 H, ethyl CH_2), 4.04, 3.09, and 2.89 (m, 3 H, $CHCH_2SO_2$), and 7.5—8.1 (m, 5 aromatic H); *m/z* 334 (M^+), 193, 177, and 175.

* For details of the Supplementary Publications Scheme see Instructions to Authors (1983), *J. Chem. Soc., Perkin Trans. 1*, 1983, Issue 1.

Table 4. Fractional atomic co-ordinates for compound (8b) with e.s.d.s in parentheses

Atom	*x*	*y*	*z*	*B*(A2)
S	0.905 92(4)	1.377 2(3)	1.465 04(9)	5.99(3)
C(1)	0.900 8(1)	0.859 5(5)	0.983 5(3)	5.86(8)
C(5)	0.825 7(1)	1.713 0(5)	1.189 3(3)	6.00(8)
C(S1)	0.929 6(1)	1.170 0(7)	1.468 2(3)	8.2(1)
C(S2)	0.919 3(2)	1.498 3(9)	1.572 9(3)	9.3(1)
C(1)	0.917 3(1)	1.000	1.056 9(3)	3.94(8)
C(2)	0.966 3(1)	0.992 1(7)	1.164 7(4)	4.38(8)
C(3)	0.965 8(1)	1.164 9(8)	1.233 9(4)	4.45(9)
C(3A)	0.917 7(1)	1.297 8(6)	1.176 7(3)	3.49(8)
C(4)	0.896 6(1)	1.454 7(7)	1.226 2(3)	3.75(8)
C(5)	0.842 7(1)	1.553 9(7)	1.153 9(3)	4.05(8)
C(6)	0.810 5(1)	1.448 8(8)	1.037 9(3)	4.60(9)
C(7)	0.828 4(1)	1.223 9(7)	1.020 5(3)	3.94(8)
C(7A)	0.891 3(1)	1.219 8(6)	1.050 4(3)	3.17(7)
C(8)	0.913 2(1)	1.351 1(7)	0.960 9(3)	4.08(8)
C(9)	0.889 3(2)	1.287 7(8)	0.828 1(4)	5.6(1)
C(10)	1.007 2(2)	0.812 1(8)	1.190 2(4)	6.0(1)
C(11)	0.921 8(2)	1.534 0(8)	1.353 8(4)	5.0(1)
C(12)	0.831 6(2)	1.350 8(9)	1.409 0(3)	4.51(9)
C(13)	0.810 7(2)	1.170 7(8)	1.343 4(4)	5.1(1)
C(14)	0.753 2(2)	1.152(1)	1.298 4(4)	7.4(1)
C(15)	0.719 6(2)	1.306(1)	1.312 4(4)	8.4(2)
C(16)	0.741 6(2)	1.482(1)	1.378 5(4)	7.8(1)
C(17)	0.797 7(2)	1.504(1)	1.428 6(4)	6.2(1)

Anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $4/3[a^2\beta(1,1) + b^2\beta(2,2) + c^2\beta(3,3) + ab\beta(1,2)\cos\gamma + ac\beta(1,3)\cos\beta + bc\beta(2,3)\cos\alpha]$

(+)-4-*Nor*-3,5-*secoestr*-9-*ene*-2,5,17-*trione Ethylene* 2-*Acetal* (12a).—Potassium hydride (oil suspension) was rinsed with anhydrous pentane several times and dried under nitrogen. This freshly prepared potassium hydride (1.2 g, 30 mmol) was suspended in toluene (150 ml) and a solution of the β-oxo ester (10) (2.16 g, 10 mmol) in toluene (25 ml) was added dropwise (15 min) with stirring under nitrogen. After being stirred for 1 h at room temperature, a solution of the sulphone (9a) (2.9 g, 9 mmol) in toluene (25 ml) was added dropwise (30 min) and stirred for 7 h at room temperature. The mixture was then cooled in an ice-bath and treated with acetic acid (2 ml). The resulting solution was filtered, the solid was cautiously dissolved in ethanol (5 ml), diluted with water, and extracted with methylene dichloride. The extract was added to the filtered toluene solution and evaporated to dryness under reduced pressure to afford an oil, which was dissolved in methanol (200 ml), cooled to 0 °C and treated with 10% aqueous potassium hydroxide (40 ml). After being stirred at 0 °C for 2.5 h the solution was neutralized with acetic acid and evaporated under reduced pressure to give a gummy

Table 5. Bond distances (Å) for compound (13) with e.s.d.s in parentheses

C(1)–C(2)	1.546(5)	C(7)–C(8)	1.518(5)	C(13)–C(17)	1.508(4)
C(1)–C(10)	1.507(4)	C(8)–C(9)	1.522(4)	C(13)–C(18)	1.527(5)
C(2)–C(3)	1.495(5)	C(8)–C(14)	1.527(4)	C(14)–C(15)	1.518(5)
C(2)–O(K1)	1.424(4)	C(9)–C(10)	1.351(4)	C(15)–C(16)	1.539(5)
C(2)–O(K2)	1.423(4)	C(9)–C(11)	1.519(4)	C(16)–C(17)	1.500(5)
C(5)–O(5)	1.212(4)	C(11)–O(11)	1.426(5)	C(17)–O(17)	1.213(4)
C(5)–C(6)	1.492(5)	C(11)–C(12)	1.535(4)	C(K1)–C(K2)	1.451(6)
C(5)–C(10)	1.496(5)	C(12)–C(13)	1.515(4)	C(K1)–O(K1)	1.380(6)
C(6)–C(7)	1.513(5)	C(13)–C(14)	1.520(4)	C(K2)–O(K2)	1.406(5)

Table 6. Bond angles (°) for compound (13) with e.s.d.s in parentheses

C(2)–C(1)–C(10)	114.3(3)	C(8)–C(9)–C(10)	122.7(3)	C(17)–C(13)–C(18)	104.6(2)
C(1)–C(2)–C(3)	114.5(3)	C(8)–C(9)–C(11)	116.5(3)	C(8)–C(14)–C(13)	113.8(3)
C(1)–C(2)–O(K1)	106.7(3)	C(10)–C(9)–C(11)	120.7(3)	C(8)–C(14)–C(15)	119.7(3)
C(1)–C(2)–O(K2)	111.1(3)	C(1)–C(10)–C(5)	114.9(3)	C(13)–C(14)–C(15)	104.4(3)
C(3)–C(2)–O(K1)	109.9(3)	C(1)–C(10)–C(9)	125.0(3)	C(14)–C(15)–C(16)	102.3(3)
C(3)–C(2)–O(K2)	108.5(3)	C(5)–C(10)–C(9)	120.1(3)	C(15)–C(16)–C(17)	105.2(3)
O(K1)–C(2)–O(K2)	105.8(3)	C(9)–C(11)–O(11)	108.8(3)	C(13)–C(17)–C(16)	109.0(3)
O(5)–C(5)–C(6)	120.7(4)	C(9)–C(11)–C(12)	114.8(3)	C(13)–C(17)–O(17)	125.3(3)
O(5)–C(5)–C(10)	121.3(3)	O(11)–C(11)–C(12)	109.2(3)	C(16)–C(17)–O(17)	125.5(3)
C(6)–C(5)–C(10)	117.9(3)	C(11)–C(12)–C(13)	112.1(3)	C(K2)–C(K1)–O(K1)	107.4(4)
C(5)–C(6)–C(7)	110.5(3)	C(12)–C(13)–C(14)	108.3(2)	C(K1)–C(K2)–O(K2)	105.8(4)
C(6)–C(7)–C(8)	111.9(3)	C(12)–C(13)–C(17)	116.0(3)	C(2)–O(K1)–C(K1)	109.7(3)
C(7)–C(8)–C(9)	112.7(3)	C(12)–C(13)–C(18)	112.6(3)	C(2)–O(K2)–C(K2)	108.7(3)
C(7)–C(8)–C(14)	110.3(3)	C(14)–C(13)–C(17)	100.0(3)		
C(9)–C(8)–C(14)	108.7(2)	C(14)–C(13)–C(18)	114.9(3)		

material. This was dissolved in toluene (400 ml) and refluxed (Dean-Stark apparatus) for 2.5 h. The solution was then filtered and the solid was rinsed with ethyl acetate which was added to the toluene solution and washed with water. The aqueous layer was re-extracted with further ethyl acetate and the combined organic layer was dried ($MgSO_4$) and evaporated. The residue showing one major spot on t.l.c. was percolated through silica gel (10 g; eluted with 1 : 1 ethyl acetate–hexane) to give the cyclized product (12a) (2.7 g, 94%) as an oil; $[\alpha]_D$ +70°; $\nu_{max.}$ ($CHCl_3$) 1 738, 1 660, and 1 600 cm^{-1}; $\lambda_{max.}$ (EtOH) 248 nm (ε 13 000); δ 1.05 (s, 3 H, 18-Me), 1.26 (s, 3 H, 3-Me), 2.84 (s, 2 H, 1-CH_2), and 3.88 (s, 4 H, OCH_2CH_2O); *m/z* 318 (M^+), 303 (M^+ − Me), 258, and 87 ($MeCOC_2H_4O^+$).

As a by-product, (+)-11β-hydroxy-4-nor-3,5-secoestr-9-ene-3,5,17-trione (ethylene 3-acetal (13) was obtained in up to 15% yield.

After recrystallization from ethyl acetate–hexane an analytical sample of this hydroxylated compound (13) was obtained, m.p. 175—177 °C; $[\alpha]_D$ +77°; $\nu_{max.}$ ($CHCl_3$) 3 450, 1 735, and 1 670 cm^{-1}; $\lambda_{max.}$ (EtOH) 245 nm (ε 12 500); δ 1.2 (s, 3 H, 18-Me), 1.24 (s, 3 H, 3-Me), 3.93 (s, 4 H, OCH_2CH_2O), and 4.87 (m, 1 H, 11α-H); *m/z* 334 (M^+), 319 (M^+ − Me), 303, and 87 ($MeCOC_2H_4O^+$) (Found: C, 68.45; H, 8.05. Calc. for $C_{19}H_{25}O_5$: C, 68.24; H, 7.84%).

Pertinent bond distances and angles for (13) are listed in Tables 5 and 6, and the fractional atomic co-ordinates are in Table 7.

Table 7. Fractional atomic co-ordinates for compound (13) with e.s.d.s in parentheses

Atom	*x*	*y*	*z*	*B*(*A*2)
C(1)	0.871 4(6)	0.089 4(2)	0.618 2(3)	3.59(8)
C(2)	1.078 8(6)	0.104 9(2)	0.587 7(4)	4.24(9)
C(3)	1.107 4(7)	0.163 8(2)	0.544 3(5)	5.6(1)
C(5)	0.664 3(6)	0.175 3(2)	0.632 6(4)	3.82(9)
O(5)	0.649 5(5)	0.174 4(1)	0.514 8(3)	5.69(8)
C(6)	0.585 9(6)	0.222 6(2)	0.710 2(4)	4.30(9)
C(7)	0.507 4(6)	0.201 8(2)	0.838 7(4)	4.08(9)
C(8)	0.655 0(6)	0 170 7(1)	0.917 7(3)	3.04(8)
C(9)	0.766 8(5)	0.129 2(1)	0.836 0(3)	2.72(7)
C(10)	0.770 2(5)	0.130 7(1)	0.704 2(3)	2.85(7)
C(11)	0.887 2(5)	0.087 5(2)	0.910 4(4)	3.27(8)
O(11)	1.060 2(4)	0.113 7(1)	0.946 7(3)	5.78(8)
C(12)	0.793 2(6)	0.063 0(2)	1.032 8(4)	3.61(8)
C(13)	0.700 2(5)	0.107 5(1)	1.115 7(3)	2.89(7)
C(14)	0.561 8(6)	0.139 5(1)	1.030 6(3)	3.08(8)
C(15)	0.438 5(7)	0.171 0(2)	1.126 8(4)	4.30(9)
C(16)	0.408 3(6)	0.127 6(2)	1.235 5(4)	5.3(1)
C(17)	0.567 8(6)	0.086 9(2)	1.220 5(4)	3.85(8)
O(17)	0.585 7(4)	0.043 8(1)	1.281 5(3)	5.53(7)
C(18)	0.843 6(7)	0.143 6(2)	1.188 3(4)	4.39(9)
C(K1)	1.283(1)	0.034 0(2)	0.536 6(5)	7.4(1)
C(K2)	1.299 5(7)	0.045 0(2)	0.675 5(5)	6.0(1)
O(K1)	1.141 0(5)	0.067 6(1)	0.488 4(3)	6.12(8)
O(K2)	1.197 7(4)	0.094 7(1)	0.697 2(2)	4.82(6)

Anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $4/3[a^2\beta(1,1) + b^2\beta(2,2) + c^2\beta(3,3) + ab\beta(1,2)\cos\gamma + ac\beta(1,3)\cos\beta + bc\beta(2,3)\cos\alpha]$

(+)-18-*Homo*-4-*nor*-3,5-*secoestr*-9-*ene*-2,5,17-*trione Ethylene* 3-*Acetal* (12b).—In a manner similar to the procedure described above, the sulphone (9b) was added to the anion of the β-oxo ester (10) and the product obtained was directly processed for cyclization, hydrolysis, and decarboxylation to give the tricyclic enedione (12b) (81%). After recrystallization from ethyl acetate–hexane, a pure sample was obtained, m.p. 94—95 °C; $[\alpha]_D$ +30°; $\nu_{max.}$ ($CHCl_3$) 1 735, 1 665, and 1 600 cm^{-1}; $\lambda_{max.}$ (EtOH) 248 nm (ε 1 300); δ 0.86 (t, *J* 7 Hz, 3 H, ethyl-Me), 1.23 (s, 3 H, 3 Me), 1.69 (*J* 7 Hz, ethyl CH_2), 2.83 (s, 2 H, 1-CH_2), and 3.87 (s, 4 H, OCH_2CH_2O); *m/z* 332 (M^+), 317 (M^+ − Me), 272, and 87 ($MeCOC_2H_4O^+$) (Found: C, 72.35; H, 8.7. Calc. for $C_{20}H_{28}O_4$: C, 72.29; H, 8.43%).

(+)-4-*Nor*-3,5-*secoestrane*-2,5,17-*trione Ethylene* 2-*Acetal* (14a).—A solution of the enone (12a) (3.18 g, 10 mmol) in

Table 8. Bond distances (Å) for compound (16b) with e.s.d.s in parentheses

O(2)–C(2)	1.185(4)	C(6)–C(7)	1.544(5)	C(13)–C(14)	1.536(4)
O(17)–C(17)	1.221(4)	C(7)–C(8)	1.507(5)	C(13)–C(17)	1.526(4)
C(1)–C(2)	1.506(6)	C(8)–C(9)	1.534(4)	C(13)–C(18)	1.536(5)
C(1)–C(10)	1.534(5)	C(8)–C(14)	1.520(4)	C(14)–C(15)	1.532(5)
C(2)–C(3)	1.462(5)	C(9)–C(10)	1.528(4)	C(15)–C(16)	1.533(5)
C(3)–C(5)	1.313(5)	C(9)–C(11)	1.520(4)	C(16)–C(17)	1.507(5)
C(5)–C(6)	1.502(5)	C(11)–C(12)	1.517(4)		
C(5)–C(10)	1.503(5)	C(12)–C(13)	1.523(5)		

Table 9. Bond angles (°) for compound (16b) with e.s.d.s in parentheses

C(2)–C(1)–C(10)	106.2(3)	C(9)–C(8)–C(14)	108.0(2)	C(14)–C(13)–C(17)	100.3(3)
O(2)–C(2)–C(1)	125.8(4)	C(8)–C(9)–C(10)	111.4(2)	C(14)–C(13)–C(18)	114.5(3)
O(2)–C(2)–C(3)	127.0(4)	C(8)–C(9)–C(11)	113.0(3)	C(17)–C(13)–C(18)	104.8(3)
C(1)–C(2)–C(3)	107.2(3)	C(10)–C(9)–C(11)	112.5(3)	C(8)–C(14)–C(13)	112.7(3)
C(2)–C(3)–C(5)	109.9(4)	C(1)–C(10)–C(5)	102.2(3)	C(8)–C(14)–C(15)	120.9(3)
C(3)–C(5)–C(6)	127.9(4)	C(1)–C(10)–C(9)	116.6(3)	C(13)–C(14)–C(15)	104.0(3)
C(3)–C(5)–C(10)	114.4(3)	C(5)–C(10)–C(9)	110.9(3)	C(14)–C(15)–C(16)	102.6(3)
C(6)–C(5)–C(10)	117.6(4)	C(9)–C(11)–C(12)	113.4(3)	C(15)–C(16)–C(17)	106.9(3)
C(5)–C(6)–C(7)	108.1(3)	C(11)–C(12)–C(13)	111.1(3)	O(17)–C(17)–C(13)	126.0(3)
C(6)–C(7)–C(8)	111.9(3)	C(12)–C(13)–C(14)	109.4(3)	O(17)–C(17)–C(16)	126.7(3)
C(7)–C(8)–C(9)	111.9(3)	C(12)–C(13)–C(17)	117.4(3)	C(13)–C(17)–C(16)	107.3(3)
C(7)–C(8)–C(14)	112.4(3)	C(12)–C(13)–C(18)	110.3(3)		

95% ethanol (200 ml) containing triethylamine (2 ml) and 5% Pd–C (300 mg) was shaken under hydrogen (30 lb in^{-2}) in a Parr hydrogenation apparatus. After 7 h the solution was filtered, evaporated under reduced pressure and chromatographed on a column (silica gel, eluted by gradient ethyl acetate and hexane) to give the reduced product (14a) (2.6 g, 83%) as an oil, $[\alpha]_D$ +60°; $\nu_{max.}$ ($CHCl_3$) 1 735 and 1 710 cm^{-1}; δ 0.98 (s, 3 H, 18-Me), 1.27 (s, 3 H, 3-Me), and 3.88 (s, 4 H, OCH_2CH_2O); *m/z* 320 (M^+), 305 (M^+ – Me), 260, and 87 ($MeCOC_2H_4O^+$).

This material was used directly for the next step.

(+)-18-*Homo*-4-*nor*-3,5-*secoestrane*-2,5,17-*trione Ethylene* 2-*Acetal* (14b).—Hydrogenation of the enone (12b) under the conditions described above for slightly longer period of time gave the reduced product (14b) (80%) as an oil, $[\alpha]_D$ +13°; $\nu_{max.}$ ($CHCl_3$) 1 735 and 1 710 cm^{-1}; δ 0.81 (t, *J* 7 Hz, 3 H, ethyl Me), 1.26 (s, 3 H, 3-Me), and 3.93 (s, 4 H, OCH_2CH_2O); *m/z* 334 (M^+), 319 (M^+ – Me), and 305.

This material was used directly for the next step.

(+)-4-*Nor*-3,5-*secoestrane*-2,5,17-*trione* (15a).—A solution of the acetal (14a) (4.0 g, 12.5 mmol) dissolved in acetone (400 ml) was acidified with 1M-hydrochloric acid (20 ml) and stirred at room temperature for 2 h. The solution was neutralized with aqueous sodium hydrogencarbonate (1.5 g) and then evaporated to an aqueous suspension. This was extracted with methylene dichloride, dried ($MgSO_4$), and the organic layer evaporated under reduced pressure. Recrystallization from ethyl acetate–hexane gave pure triketone (15a) (3.2 g, 93%), m.p. 135—136 °C; $[\alpha]_D$ +65°; $\nu_{max.}$ ($CHCl_3$) 1 735 and 1 710 cm^{-1}; δ 0.96 (s, 3 H, 18-Me) and 2.22 (s, 3 H, MeCO); *m/z* 276 (M^+), 261 (M^+ – Me), 233 (M^+ – C_2H_3O), and 219 (M^+ – C_3H_5O) (Found: C, 74.1; H, 9.15. Calc. for $C_{17}H_{24}O_3$: C, 73.88; H, 8.75%).

(+)-18-*Homo*-4-*nor*-3,5-*secoestrane*-2,5,17-*trione* (15b).—Treatment of the acetal (14b) (1.5 g, 4.5 mmol) in acetone (150 ml) with dilute hydrochloric acid (7.5 ml) for 2 h at room temperature afforded the triketone (15b). The product was isolated, as above, in 96% yield (1.25 g). After recrystallization from ethyl acetate–hexane a pure sample of (15b) was obtained, m.p. 149—150 °C; $[\alpha]_D$ +16°; $\nu_{max.}$ ($CHCl_3$) 1 735, 1 720, and 1 305 cm^{-1}; δ 1.77 (t, *J* 7 Hz, 3 H, ethyl-Me) and 2.21 (s, 3 H, MeCO); *m/z* 290 (M^+), 261 (M^+ – Et), 247 (M^+ – C_2H_3O), and 233 (M^+ – C_3H_5O) (Found: C, 74.65; H, 9.3. Calc. for $C_{18}H_{28}O_3$: C, 74.45; H, 9.02%).

(+)-4-*Norestr*-5(10)-*ene*-2,17-*dione* (16c) *and* (+)-4-*Norestr*-3(5)-*ene*-2,17-*dione* (16b).—Under argon a solution of the triketone (15a) (50 mg, 0.18 mmol) in toluene (5 ml) was added to a cooled (ice-bath) suspension of potassium t-butoxide (30 mg, 27 mmol) in dry toluene (1 ml). The ice-bath was removed and the mixture was stirred at room temperature for 2.5 h, then quenched with saturated sodium phosphate (5 ml). The organic layer was separated, washed with brine solutions, and dried ($MgSO_4$). The aqueous layer was extracted with ethyl acetate, washed with brine and the organic extracts combined. Evaporation followed by preparative t.l.c. (1 : 1 ethyl acetate–hexane) gave the enone (16b) as the major product. It was crystallized in ethyl acetate–hexane (32 mg, 70%), m.p. 189—191 °C (lit.,[11] 188—189 °C); $[\alpha]_D$ +25° (lit.,[11] same); $\nu_{max.}$ ($CHCl_3$) 1 740, 1 690, and 1 615 cm^{-1}; $\lambda_{max.}$ (EtOH) 232 nm (ε 16 000); δ 0.96 (s, 3 H, 18-Me) and 5.85 (br s, 1 vinylic H); *m/z* 258 (M^+), 243 (M^+ – 15), 240 (M^+ – H_2O), 230 (M^+ – CO), 214, 212, 202, and 201.

Pertinent bond distances and angles for (16b) are in listed in Tables 8 and 9, and the fractional atomic co-ordinates are in Table 10.

(+)-4-Norestr-5(10)-ene-2,17-dione (16c), which has a higher R_F value than (16b), was isolated in *ca.* 5% yield. Recrystallization from ethyl acetate–hexane gave an analytical sample of the $\Delta^{5(10)}$-compound (16c), m.p. 129—130 °C, $[\alpha]_D$ +106°; $\nu_{max.}$ ($CHCl_3$) 1 740 cm^{-1}; δ 0.93 (s, 3 H, 18-Me) and 2.85 (br s, 4 H, 1- and 3-CH_2); *m/z* 258 (M^+), 230 (M^+ – CO), 202, and 201.

Treatment of (15a) in methanolic potassium hydroxide solution either at 0 °C or at room temperature gave mainly starting material, along with some 5-hydroxy intermediate. Attempts to cyclize (15a) with proline only led to recovered starting material.

Table 10. Fractional atomic co-ordinates for compound (16b) with e.s.d.s in parentheses

Atom	*x*	*y*	*z*	*B*(*A*2)
O(2)	1.042 8(5)	0.976 8(5)	0.316 7(1)	11.6(1)
O(17)	0.176 9(4)	0.350 1(4)	0.525 2(1)	6.65(7)
C(1)	0.726 7(7)	0.923 1(4)	0.352 6(2)	5.50(9)
C(2)	0.897 0(7)	0.896 7(5)	0.317 5(2)	6.5(1)
C(3)	0.846 7(7)	0.756 7(6)	0.284 6(1)	6.2(1)
C(5)	0.673 0(6)	0.698 5(5)	0.296 5(1)	5.08(9)
C(6)	0.570 4(7)	0.548 4(6)	0.275 1(1)	6.6(1)
C(7)	0.519 7(6)	0.429 9(5)	0.319 1(1)	5.52(9)
C(8)	0.404 8(5)	0.517 4(4)	0.359 7(1)	3.97(7)
C(9)	0.515 4(5)	0.668 8(4)	0.380 8(1)	3.64(7)
C(10)	0.574 5(5)	0.789 7(4)	0.339 0(1)	4.25(8)
C(11)	0.406 8(6)	0.755 3(4)	0.423 5(1)	4.33(8)
C(12)	0.344 2(6)	0.637 2(4)	0.365 2(1)	4.57(8)
C(13)	0.231 5(5)	0.488 8(4)	0.444 1(1)	3.82(7)
C(14)	0.355 1(5)	0.402 3(4)	0.403 4(1)	4.04(7)
C(15)	0.249 6(7)	0.236 1(5)	0.394 5(2)	5.81(9)
C(16)	0.184 6(6)	0.186 5(4)	0.447 6(2)	5.65(9)
C(17)	0.193 7(5)	0.342 1(4)	0.479 5(1)	4.91(8)
C(18)	0.027 4(6)	0.544 1(5)	0.426 5(2)	5.51(9)

Anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $4/3[a^2\beta(1,1) + b^2\beta(2,2) + c^2\beta(3,3) + ab\beta(1,2)\cos\gamma + ac\beta(1,3)\cos\beta + bc\beta(2,3)\cos\alpha]$

(−)-18-*Homo*-4-*norestr*-3(5)-*ene*-2,17-*dione* *and* (−)-18-*Homo*-4-*norestr*-1(10)-*ene*-2,17-*dione*.—To a solution of the trione (15b) (500 mg, 1.7 mmol) in methanol (200 ml), potassium hydroxide (1 g) was added. The solution was stirred at reflux temperature for 2 h, then cooled to 0 °C and neutralized with acetic acid. The residue obtained after evaporation of the methanol was diluted with water and extracted with methylene dichloride. The organic solution was dried ($MgSO_4$) and evaporated. The product was crystallized in ether–hexane to give a *ca.* 1 : 1 mixture of the $\Delta^{1(10)}$ and $\Delta^{3(5)}$-enones (445 mg, 95%). The two products were separated by mechanical means and recrystallized from ethyl acetate–hexane to give each component in pure form. The $\Delta^{3(5)}$-isomer (16d) had m.p 149—150 °C; $[\alpha]_D$ −11° (lit.,[11] m.p. 147—149°, $[\alpha]_D$ −10°); $\nu_{max.}$ ($CHCl_3$) 1 735, 1 695, and 1 610 cm^{-1}; $\lambda_{max.}$ (EtOH) 232 nm (ε 21 000); δ 0.78 (t, *J* 7 Hz; 3 H, ethyl-Me) and 5.85 (br s, 1 vinylic H); *m*/*z* 272 (M^+), 247 (M^+ − 15), 243, 228, 216, 215, and 200. The $\Delta^{1(10)}$-isomer (16e) had m.p. 156—158 °C, $[\alpha]_D$ −147°; $\nu_{max.}$ 1 735, 1 700, and 1 615 cm^{-1}; $\lambda_{max.}$ (EtOH) 232 nm (ε 24 000); δ 0.78 (t, *J* 7 Hz, 3 H, ethyl-Me) and 5.83 (br s, 1 vinylic H); *m*/*z* 272 (M^+), 247 (M^+ − 15), and 243 (M^+ − Et).

2,6α-*Cyclo*-4-*nor*-A-*secoestr*-1(2)-*ene*-5,17-*dione* (17a).—The triketone (15a) (100 mg) was dissolved in benzene (75 ml) containing a small amount of 4A molecular sieves. To this solution toluene-*p*-sulphonic acid (100 mg) was added and the mixture was stirred at 60 °C for 3 h. The solution was then cooled to room temperature, filtered and washed with 5% sodium hydrogencarbonate and brine. Evaporation of the solvent under reduced pressure followed by preparative t.l.c. afforded a solid which was crystallized in ether–hexane to give the bridged compound (17a) (79 mg, 84%), m.p. 115—117 °C; $[\alpha]_D$ +105°; $\nu_{max.}$ ($CHCl_3$) 1 735 and 1 580 cm^{-1}; $\lambda_{max.}$ (EtOH) 223 nm (ε 7 000); δ 0.9 (s, 3 H, 18-Me), 2.26 (s, vinylic Me), 5.82 (br s, 1 vinylic H); *m*/*z* 258 (M^+), 243 (M^+ − Me), 215 ($M^+ - C_2H_3O$), 201 ($M^+ - C_3H_5O$), 187, and 134 (Found: M^+ 258.161 46. Calc. for $C_{17}H_{22}O_2$: *M* 258.161 97).

2,6α-*Cyclo*-18-*homo*-4-*nor*-A-*secoestr*-1(2)-*ene*-5,17-*dione* (17b).—Cyclization of the triketone (15b) under acidic condition by the method described above gave the 18-homo bridged product (17b) (77%). The compound was recrystallized in ether–hexane to give an analytical sample, m.p. 107—108 °C; $[\alpha]_D$ +103°; $\nu_{max.}$ ($CHCl_3$) 1 730br and 1 570 cm^{-1}; $\lambda_{max.}$ (EtOH) 223 nm (ε 8 000); δ 0.77 (t, *J* 7 Hz, 3 H, ethyl-Me), 2.26 (s, vinylic Me), and 5.82 (br s, 1 vinylic H); *m*/*z* 272 (M^+), 243 (M^+ − Et), 215 ($M^+ - C_3H_5O$), 201, 187, and 134 (Found: M^+ 272.184 41. Calc. for $C_{18}H_{24}O_2$: *M* 272.177 62).

4-*Nor*-5α-*estrane*-2,17-*dione* (18a).—A mixture of the enediones (16a) and (16b) (1.23 g, 4 mmol) dissolved in anhydrous THF (25 ml) was added dropwise (3 min) to lithium (500 mg) in liquid ammonia (250 ml) with stirring. The stirring was continued for 5 min and ammonium chloride crystals were added. The ammonia was evaporated by warming to room temperature and the remaining material, diluted in water, was extracted with methylene dichloride several times. The organic solution was then dried ($MgSO_4$) and evaporated to give a crude product containing several components, as evidenced by t.l.c. Treatment of an acetone solution (150 ml) of the latter material with Jones reagent [13] (2 ml) for 30 min followed by cooling (ice-bath) and quenching with isopropyl alcohol (3 ml) resulted in one major product as shown by t.l.c. The solution was neutralized with 5% sodium hydrogencarbonate and the organic solvent evaporated under reduced pressure. The residue was diluted with water and extracted with methylene dichloride (thrice) and stored over anhydrous magnesium sulphate. Evaporation of the solvent followed by column chromatography and recrystallizations in ethyl acetate–hexane gave an analytical sample of dione (18a) (727 mg, 59%), shown to be identical with an authentic sample.[4] The diketone (18a) showed m.p. 162—165 °C (lit.,[4,11] m.p. 156—157 °C); $[\alpha]_D$ +285°; $\nu_{max.}$ ($CHCl_3$) 1 740 cm^{-1}; δ 2.89 (s, 3 H, 18-Me); *m*/*z* 260 (M^+), 245 (M^+ − Me), 242 ($M^+ - H_2O$), 216 ($M^+ - C_2H_4O$), 204, 203 ($M^+ - C_3H_5O$), and 201.

When this procedure was applied to the pure $\Delta^{3(5)}$-isomer (16b), the total yield of pure diketone (18a), after recrystallization, exceeded 67%.

18-*Homo*-4-*nor*-5α-*estrane*-2,17-*dione* (18b).—Following the procedure described above, a mixture of isomeric *A*-ring enones was reduced to give the desired 18-homo-*A*-norestradione (18b) (57%). Recrystallisation from ether–hexane gave an analytical sample of the diketone (18b), m.p. 108—110 °C; $[\alpha]_D$ +214° (lit.,[14] m.p. 102—104 °C; $[\alpha]_D$ +211°); $\nu_{max.}$ ($CHCl_3$) 1 740 cm^{-1}; δ 0.77 (t, *J* 7 Hz, 3 H, ethyl-Me); *m*/*z* 274 (M^+), 256 ($M^+ - H_2O$), 246 ($M^+ - C_2H_4$), 245 (M^+ − Et) 230 ($M^+ - C_2H_2O$), 227, 218, 217 ($M^+ - C_3H_5O$), 202, and 189.

(−)-17α-*Ethynyl*-17β-*hydroxy*-4-*norestr*-3(5)-*en*-2-*one* (20a).—A stream of acetylene gas (purified by being passed through sulphuric acid, a dry ice–acetone trap and a 20-cm column containing 4A molecular sieves, potassium hydroxide pellets and calcium sulphate) was blown, for 30 min, over the surface of a stirred suspension of potassium hydroxide powder (60% anhyd.; 1.5 g) in THF (anhyd.; 20 ml) at 0 to −5 °C, under argon. The enedione (16b) (90 mg, 0.35 mmol) was dissolved in THF (5 ml) containing a catalytic amount of acetone (*ca.* 5 drops) and was then added to the potassium hydroxide suspension. The reaction mixture was stirred for 30 min. Examination by t.l.c. showed one major product with a higher R_F value than the starting material. Water (2 ml) was added to dissolve the excess of potassium hydroxide; then the organic layer was separated and washed with brine. The aqueous layer was extracted several times with ethyl acetate and the extracts were washed with brine. The organic layers

Table 11. Bond distances (Å) for compound (21) with e.s.d.s in parentheses

O(2)–C(2)	1.427(6)	C(6)–C(7)	1.539(7)	C(13)–C(18)	1.529(7)
O(17)–C(17)	1.422(6)	C(7)–C(8)	1.525(7)	C(14)–C(15)	1.522(7)
O(ET)–C(ET1)	1.408(7)	C(8)–C(9)	1.524(7)	C(15)–C(16)	1.534(7)
C(1)–C(2)	1.548(7)	C(8)–C(14)	1.524(7)	C(16)–C(17)	1.559(7)
C(1)–C(10)	1.524(7)	C(9)–C(10)	1.518(6)	C(17)–C(E1′)	1.483(8)
C(2)–C(3)	1.559(7)	C(9)–C(11)	1.537(7)	C(E1′)–C(E2′)	1.155(7)
C(2)–C(E1)	1.474(8)	C(11)–C(12)	1.534(7)	C(E1)–C(E2)	1.151(7)
C(3)–C(5)	1.520(7)	C(12)–C(13)	1.536(7)	C(ET1)–C(ET2)	1.471(9)
C(5)–C(6)	1.516(7)	C(13)–C(14)	1.532(7)		
C(5)–C(10)	1.524(7)	C(13)–C(17)	1.543(7)		

Table 12. Bond angles (°) for compound (21) with e.s.d.s in parentheses

C(2)–C(1)–C(10)	104.6(4)	C(9)–C(8)–C(14)	108.9(4)	C(8)–C(14)–C(13)	113.3(4)
O(2)–C(2)–C(1)	111.5(4)	C(8)–C(9)–C(10)	108.7(4)	C(8)–C(14)–C(15)	119.8(4)
O(2)–C(2)–C(3)	110.9(4)	C(8)–C(9)–C(11)	112.8(4)	C(13)–C(14)–C(15)	103.9(4)
O(2)–C(2)–C(E1)	106.7(5)	C(10)–C(9)–C(11)	113.2(4)	C(14)–C(15)–C(16)	104.9(4)
C(1)–C(2)–C(3)	103.5(4)	C(1)–C(10)–C(5)	100.7(4)	C(15)–C(16)–C(17)	106.6(5)
C(1)–C(2)–C(E1)	110.7(5)	C(1)–C(10)–C(9)	119.1(4)	O(17)–C(17)–C(13)	115.0(4)
C(3)–C(2)–C(E1)	113.7(4)	C(5)–C(10)–C(9)	111.7(4)	O(17)–C(17)–C(16)	108.2(5)
C(2)–C(3)–C(5)	106.2(5)	C(9)–C(11)–C(12)	112.5(4)	O(17)–C(17)–C(E1′)	107.7(5)
C(3)–C(5)–C(6)	117.7(5)	C(11)–C(12)–C(13)	111.2(4)	C(13)–C(17)–C(16)	103.3(5)
C(3)–C(5)–C(10)	103.0(4)	C(12)–C(13)–C(14)	108.3(4)	C(13)–C(17)–C(E1′)	112.4(5)
C(6)–C(5)–C(10)	111.3(4)	C(12)–C(13)–C(17)	116.8(4)	C(16)–C(17)–C(E1′)	110.1(5)
C(5)–C(6)–C(7)	109.0(4)	C(12)–C(13)–C(18)	110.6(4)	C(17)–C(E1′)–C(E2′)	178.9(6)
C(6)–C(7)–C(8)	112.2(4)	C(14)–C(13)–C(17)	101.3(4)	C(2)–C(E1)–C(E2)	178.3(7)
C(7)–C(8)–C(9)	112.5(4)	C(14)–C(13)–C(18)	112.3(4)	O(ET)–C(ET1)–C(ET2)	111.2(5)
C(7)–C(8)–C(14)	112.8(4)	C(17)–C(13)–C(18)	107.4(4)		

were dried ($MgSO_4$), evaporated and the residue, after chromatography (t.l.c.), was recrystallized to give the ethynylated product (20a) (78 mg, 79%); m.p. 184—186 °C; $[\alpha]_D$ −90°; $\nu_{max.}$ ($CHCl_3$) 3 445, 3 280, 1 665, and 1 610 cm^{-1}; $\lambda_{max.}$ (EtOH) 232.5 nm (ε 15 000); δ 0.92 (s, 3 H, 18-Me), 2.55 (s, 1 H, C≡CH), and 5.83 (br s, vinylic H); *m/z* 284 (M^+), 269 (M^+ − Me), 266 ($M^+ - H_2O$), and 217 (Found: C, 80.0; H, 8.6. Calc. for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51%).

(−)-17α-*Ethynyl*-2-*oxo*-4-*norestr*-3-(5)-*en*-17β-*yl Propionate* (20b).—The 17β-hydroxy compound (20a) (100 mg, 0.35 mmol) was dissolved in propionic acid (6 ml) and propionic anhydride (4.5 ml). A few crystals of toluene-*p*-sulphonic acid were added and the solution was stirred at room temperature for 2 h. The reaction was monitored by t.l.c. and when completed the solution was added to a saturated aqueous solution of sodium hydrogencarbonate containing some ice. This mixture was stirred until the solution was hydrolysed. The product was then extracted with ethyl acetate, dried ($MgSO_4$), filtered and evaporated to dryness under reduced pressure. The residue was chromatographed and recrystallized to give a pure sample of the ester (20b) (89 mg, 74%), m.p. 159—160 °C; $[\alpha]_D$ −140°; $\nu_{max.}$ ($CHCl_3$) 3 290, 1 725, 1 675, and 1 615 cm^{-1}; $\lambda_{max.}$ (EtOH) 232.5 nm (ε 15 000); δ 0.94 (s, 3 H, 18-Me), 1.13 (t, *J* 7 Hz, 3 H, propionate Me), 2.35 (*J* 7 Hz, 2 H, propionate CH_2), 2.57 (s, 1 H, C≡CH), and 5.81 (br s, 1 vinylic H); *m/z* 340 (M^+), 325 (M^+ − Me), and 284 (Found: C, 77.55; H, 8.3. Calc. for $C_{22}H_{28}O_3$: C, 77.61; H, 8.29%).

2α,17α-*Diethynyl*-2β,17β-*dihydroxy*-4-*norestr*-3(5)-*ene* (21).—The 2-ketone (20a) (26 mg, 0.1 mmol) dissolved in anhydrous THF (1 ml) was added dropwise to a solution of lithium acetylide prepared by bubbling purified and dried acetylene through a solution of butyl-lithium (1 ml of a 2.2M-solution) in anhydrous THF (3 ml) at −78 °C and connected to a free flow of argon. The addition was performed during 3 min. Then, acetylene was added for 5 more min. The solution was stirred at − 78°C for 10 h. After that time it was allowed to warm to room temperature and the mixture was quenched by a slurry of potassium carbonate. The organic layer was separated and the aqueous layer was extracted with ethyl acetate

Table 13. Fractional atomic co-ordinates for compound (21) with e.s.d.s in parentheses

Atom	*x*	*y*	*z*	*B*(*A*2)
C(2)	0.191 4(7)	0.589 0(3)	0.059 0(2)	4.7(1)
O(17)	0.111 2(7)	0.087 7(3)	0.348 0(2)	5.2(1)
O(ET)	0.456 6(8)	0.157 3(3)	0.396 8(3)	6.5(1)
C(1)	0.302(1)	0.439 3(4)	0.072 7(3)	4.4(2)
C(2)	0.218(1)	0.508 8(4)	0.025 2(3)	4.2(2)
C(3)	0.017(1)	0.470 2(4)	0.003 2(3)	4.5(2)
C(5)	0.006(1)	0.381 0(4)	0.034 4(3)	4.0(2)
C(6)	−0.195(1)	0.344 2(4)	0.048 5(3)	4.3(2)
C(7)	−0.172(1)	0.257 8(5)	0.085 6(3)	4.4(2)
C(8)	−0.047(1)	0.266 2(4)	0.148 6(3)	3.6(2)
C(9)	0.153(1)	0.305 3(4)	0.134 2(3)	3.4(1)
C(10)	0.124(1)	0.391 0(4)	0.098 8(3)	3.4(1)
C(11)	0.281(1)	0.312 1(4)	0.197 2(3)	4.1(2)
C(12)	0.297(1)	0.226 3(4)	0.235 0(3)	4.0(2)
C(13)	0.094 1(9)	0.189 4(4)	0.250 9(3)	3.6(1)
C(14)	−0.019(1)	0.180 7(4)	0.185 0(3)	3.7(2)
C(15)	−0.197(1)	0.126 8(5)	0.203 9(4)	5.1(2)
C(16)	−0.124(1)	0.066 2(4)	0.259 3(3)	5.2(2)
C(17)	0.087(1)	0.096 1(4)	0.277 5(3)	4.3(2)
C(18)	−0.012(1)	0.246 3(5)	0.301 8(4)	5.1(2)
C(E1′)	0.233(1)	0.039 5(4)	0.244 6(4)	4.6(2)
C(E2′)	0.345(1)	−0.005 7(5)	0.219 4(4)	6.9(2)
C(E1)	0.352(1)	0.525 3(5)	−0.031 1(4)	5.6(2)
C(E2)	0.456(1)	0.536 2(6)	−0.075 7(4)	7.4(2)
C(ET1)	0.428(1)	0.228 6(6)	0.439 4(4)	6.9(2)
C(ET2)	0.545(2)	0.302 9(5)	0.417 4(4)	8.8(3)

Anisotropically refined atoms are given in the form of the isotropic equivalent thermal parameter defined as: $4/3[a^2\beta(1,1) + b^2\beta(2,2) + c^2\beta(3,3) + ab\beta(1,2)\cos\gamma + ac\beta(1,3)\cos\beta + bc\beta(2,3)\cos\alpha]$

and added to the organic portion. The organic fraction was dried ($MgSO_4$). Evaporation of the organic solvents at 30 °C under reduced pressure gave a crude product (29 mg). Preparative t.l.c. (1 : 1 ethyl acetate–hexane) gave a mixture from which the 2α-isomer (21) slowly crystallized. A sample of the pure isomer (21) had m.p. 115—119 °C; $[\alpha]_D$ −116°; $\nu_{max.}$ 3 400, 3 310, 2 250, and 2 120 cm^{-1}; δ 0.88 (s, 3 H, 18-Me), 2.57 and 2.60 (s, 2 H, C≡CH), and 5.34 (br, 1 vinylic H); *m/z* 310 (M^+) and 292 ($M^+ - H_2O$) (Found: C, 81.05; H, 8.2. Calc. for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44%).

Pertinent bond distances and angles for (21) are listed in Tables 11 and 12, and fractional atomic co-ordinates are in Table 13. The crystal structure includes one molecule of ethanol [C(ET1)–C(ET2)–O(ET)] per molecule.

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