Synthetic Approaches to the Ring System of Nicandra (Benzenoid Ring D) Steroids

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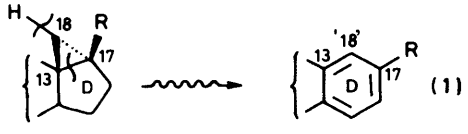
The androstenolone derivative (**5**) has been converted into the aromatic ring D steroid (**39**), with the C/D system of the novel natural steroid Nic-10. The route employs the seco-acid (**15**) which is cyclised to the D-enone (**16**). Selective D-aromatisation was ensured by regioselective 16α-phenylselenenylation [see (**37**)] and exclusive 1,2-addition of an acetyl anion equivalent gave (**38**). Oxidation and hydrolysis afforded the desired ketone (**39**), in which the former C/D angular methyl is incorporated into the new D-ring, as in the likely biosynthesis of *Nicandra* steroids.

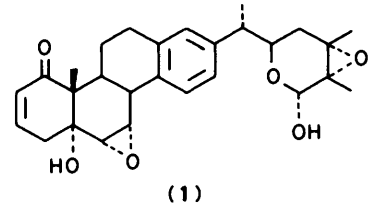
The withanolides[1] are a large group of 24-methyl plant steroids, found in members of the Solanaceae, and characterised by a high level of oxidative modification. In one particular subgroup[2] isolated from leaves of *Nicandra physaloides* (the 'shoo-fly' plant) the modifications include the unique feature of an aromatic ring D bearing a side chain displaced from its usual site adjacent to the C/D junction. The major extractive of *N.physaloides*, Nic-1(**1**)[2b] is almost certainly the chief constituent of 'nicandrenone' a crystalline material shown to exhibit marked insect antifeedant activity,[3] particularly towards the tobacco hornworm, which preferentially feeds on *Solanaceae*. Nicandrenone was also highly toxic when administered to houseflies. Three related compounds, Nic-10(**2a**), Nic-12(**2b**), and Nic-17(**2c**) were also isolated.[2b]

The biosynthesis of the D-ring in Nic-1 appears to involve C(13)–C(17) bond fission, and functionalisation of C-18 followed by its incorporation into a new ring D, with subsequent aromatisation, as summarised in Equation (1). Oxidative modifications are also required in rings A and B and the side chain: in relation to these the aromatisation sequence could be late, as suggested by the circumstantial co-occurrence of Nic-3[2a] (**3**) with Nic-1, or early, thus implicating intermediates such as (**4**).

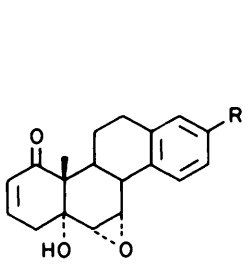


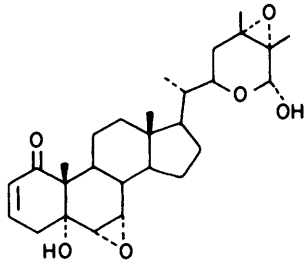
(1)

Steroids with a benzenoid ring-D have been prepared in several total syntheses. Three approaches have been described: the annelation of a substituted tetralone;[4] the intramolecular Diels–Alder construction of rings B/C, with aryl D arising from a benzocyclobutene;[5] and biomimetic A,B,C cyclisation[6] with cation termination by substitution into ring D. All these approaches incorporate the aromatic ring from the start. None is well suited to the synthesis of a Nic steroid, with the correct attachment of the side chain being a major obstacle. Partial synthesis appeared a more attractive prospect for the practical preparation of the Nic-1 ring system in hypothetical biosynthetic precursors such as (**4**) and compounds with potential insecticidal or antifeedant activities. We thus embarked on investigation of the transformation of the 'normal' steroid C/D constitution into the Nic-1 aryl-D structure incorporating the previous angular methyl (C-18). Such a route would complement synthetic work on withanolide side chains[7] and A/B functional arrangements[7a,7c,8] related to the Nic-1 structure. Two broad possibilities for effecting the change of Equation (1). in the laboratory can be seen; first, generation of a C-18 cation

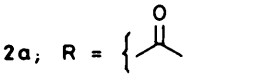


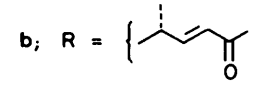
(1)

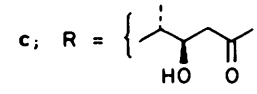


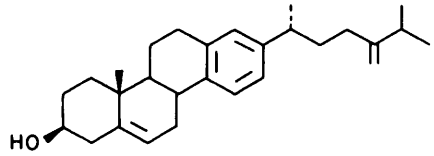


(3)





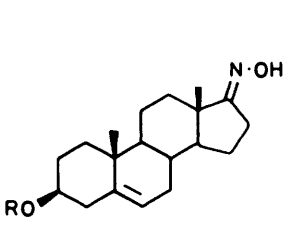




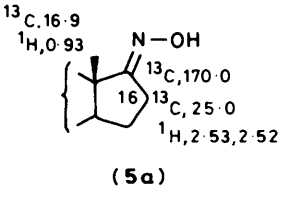
(4)

(*e.g.* following C-18 hydroxylation) and D expansion by ring bond migration. This is attractive biomimetically, but the most appropriate functional group assembly for this reaction is not readily predicted. Secondly, bond C(13)–C(17) could be cleaved, and C(17)–C(18) formed in a second step. We chose to examine this path as the most expeditious.

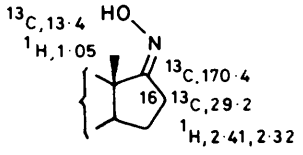
Cleavage of the C(13)–C(17) bond has been reported by Moffatt and co-workers[9] in the reaction of 3β-acetoxy-17-hydroxyiminoandrost-5-ene (**5**) with dimethyl sulphoxide–dicyclohexylcarbodi-imide–trifluoroacetic acid in which the nitrile (**6**) was obtained (61%). A cyclic fragmentation



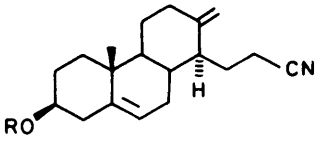
(5; R = Ac)
(9; R = Me)



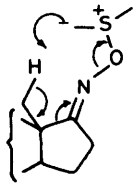
(5a)



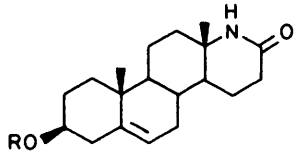
(5b)



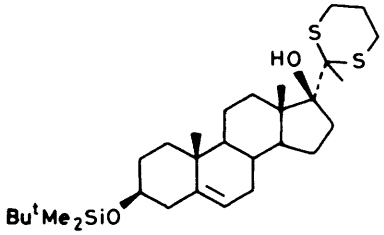
(6; R = Ac)
(10; R = Me)



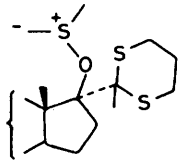
(7)



(8; R = Ac)
(11; R = Me)



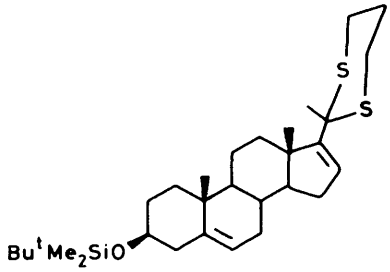
(12)



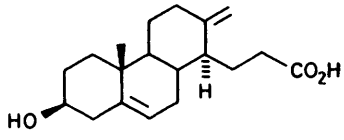
(13)

mechanism (7) was proposed to rationalise this result. In our hands not more than 35% nitrile (6) could be obtained under Moffatt's conditions, and lactam (8) was the major product: the 3β-methoxy series (9) gave similar yields of (10) and (11). In case this discrepancy was caused by variation in the stereoisomeric composition of the oxime (5) we separated the *E*-(5a) and *Z*-(5b) isomers. The stereochemistry followed from the ^{13}C and ^{1}H n.m.r. shifts shown. However the total oxime sample, prepared from the corresponding ketone according to the literature,[9] contained $<1\%$ *Z*-isomer.

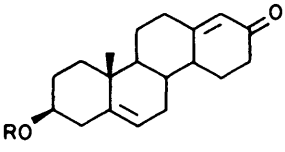
During the course of our work Pfenninger and Graf[10] reported attempts at fragmentation of several 17-hydroxyimino steroids by Moffatt's method, including both (5a) and (5b) [from (5a) by acid-catalysed isomerisation]. The nitrile (6) could be obtained from the oxime (5a) in 34% yield, but not from the oxime (5b), although models suggest that the cyclic mechanism (7) should be aided by *Z*-geometry. Oxime fragmentation to nitrile is well documented,[11] and we examined several recommended reagents with the *E*-oxime. The nitriles (6) and (10) were obtained in 29 and 30% yields with phosphorus pentachloride in benzene at 5 °C, rather similar to the 'activated' dimethyl sulphoxide method. Reasonably good yields of lactam from normal Beckmann rearrangement could be obtained, *e.g.* >60% isolated using thionyl chloride. It thus seems likely that a cyclic mechanism is not operating but that the *E*-oxime can adopt suitable geometry for a concerted fragmentation.[10] We also observed that treatment of the alcohol (12) with dimethyl sulphoxide–trifluoroacetic anhydride–benzene–pyridine to promote formation of the intermediate (13), led only to olefin (14) although (13) appears well set up for C(13)–C(17) fragmentation.



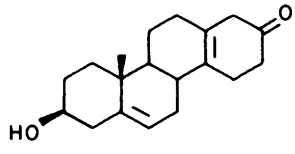
(14)



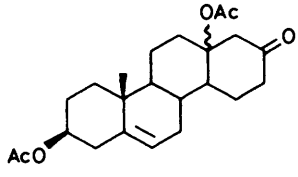
(15)



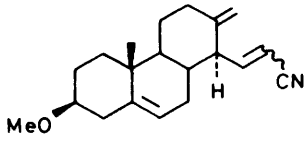
(16; R = H)
(19; R = Ac)
(21; R = Bu^tMe2Si)



(17)



(18)



(20)

The nitrile (6) was readily hydrolysed to the acid (15). The latter could also be made from the lactam (8) (30%) by way of opening to the amino acid, exhaustive *N*-methylation, and Hofmann elimination, following a literature procedure,[12] and thus partly compensating for the rather poor yield of nitrile. Formation of the C(13–C(18)* bond was achieved by treatment of acid (15) with trifluoroacetic anhydride.[13] The major (61%) product (16) was accompanied by a little of the unconjugated enone (17). Alternatively, the acid (15) formed the β-acetoxy ketone (18) on treatment with acetic anhydride–stannic chloride; elimination in base provided (16) 70%. The enone (16) has been previously described,[14] as the unexpected product, in low yield, of reaction of the acid chloride of (15) with dimethylcadmium. In another approach, the nitrile (10) was deprotonated with lithium di-isopropylamide (LDA) and phenylselenenylated; hydrogen peroxide oxidation then afforded the *E*- and *Z*-isomers of the unsaturated nitrile (20). The corresponding dienyl anion was then generated but neither

* When incorporated into ring D, C-18 becomes C-17a, using accepted D-homosteroid numbering.[15]

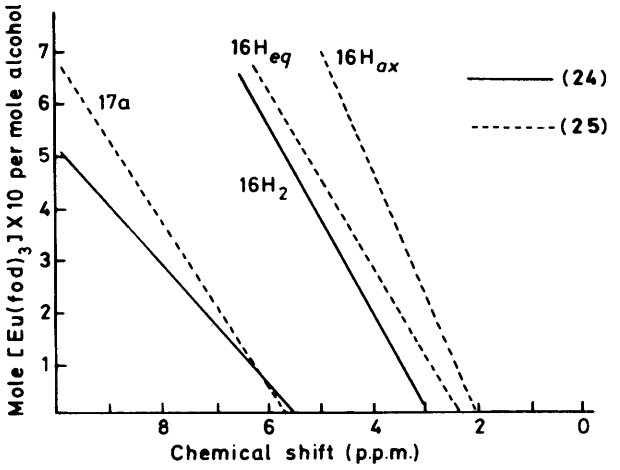


Figure 1. Eu(fod)$_3$ induced chemical shifts in the ^{1}H n.m.r. spectra of alcohols (**24**) and (**25**)

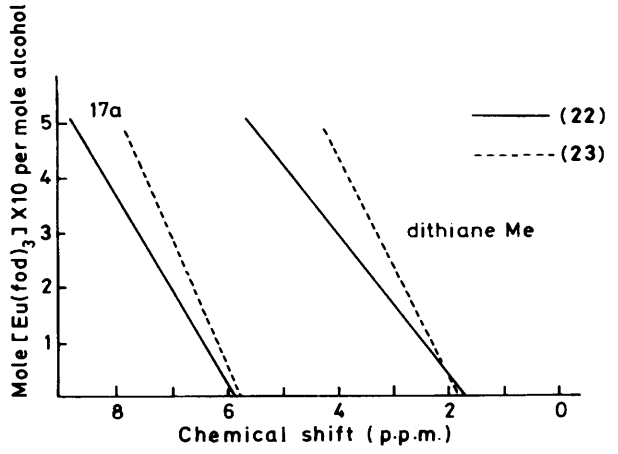
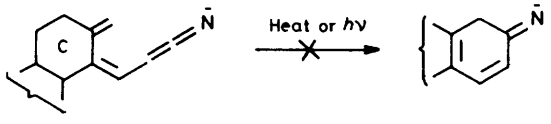


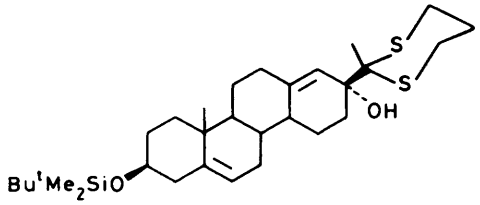
Figure 2. [Eu(fod)$_3$] induced chemical shifts in the ^{1}H n.m.r. spectra of alcohols (**22**) and (**23**)

thermal nor photochemical activation could induce the cyclisation [Equation (2)] to an aromatic amide anion.

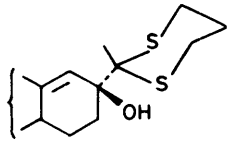


(2)

The attachment of a suitable side chain to C-17 was then required. Since Nic-10 contains a simple acetyl group, and extension of this to the more complex examples appears feasible, addition of acetyl anion equivalents to the *O*-protected enone (**21**) was investigated. The desired 1,2-addition was achieved with 2-lithio-2-methyl-1,3-dithiane, affording the epimers (**22**) and (**23**), (82%), and with lithium acetylide–ethylenediamine

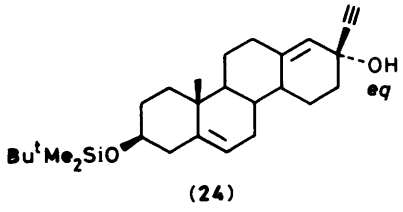


(**22**)

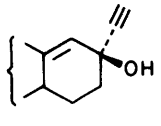


(**23**)

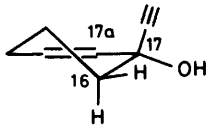
complex, giving the epimers (**24**) and (**25**) (74%). The relative stereochemistry of the two pairs of diastereoisomeric alcohols was determined by europium shift reagent [Eu(fod)$_3$] studies. Figure 1 shows the response to this reagent of 17a-H, 16-H$_{eq.}$, and 16-H$_{ax}$ for (**24**) and (**25**). The isomer showing identical shift behaviour by 16-H$_{ax.}$ and 16-H$_{eq.}$ is allocated the ψ-*eq.*(α) hydroxy orientation as in (**24**), see also (**24a**); the 17a-H is also more responsive in this isomer, not unexpectedly. Isomers (**22**) and (**23**) can also be distinguished by the relative shifts of 17a-H (Figure 2).



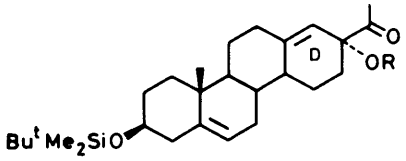
(**24**)



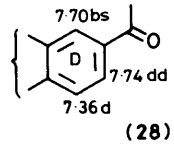
(**25**)



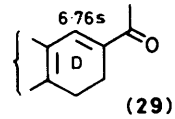
(**24a**)



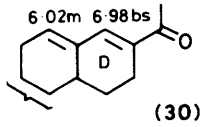
(**26**; R = Ac)
(**27**; R = H)



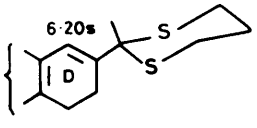
(**28**)



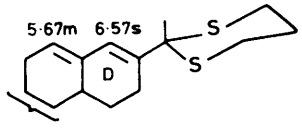
(**29**)



(**30**)



(**31**)

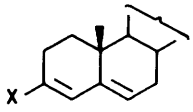


(**32**)

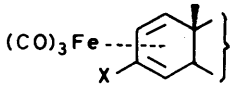
The ethynyl group in the alcohol (**24**) was readily hydrated with aqueous mercuric acetate to provide the α-acetoxy ketone (**26**); basic hydrolysis gave the corresponding alcohol (**27**). Dehydration and dehydrogenation of the alcohols (**22**)—(**25**),

or (27), might be expected to lead to the desired aromatic ring D compounds if no unfavourable double bond shifts occurred. In practice, treatment of the ketol (27) with dichlorodicyanoquinone and trifluoroacetic acid afforded a mixture whose ^{1}H n.m.r. spectrum suggested that it contained the aromatic ketone (28) together with the homo- and hetero-annular dienes (29) and (30). Acid-catalysed dehydration of the alcohols (22) and (23) gave a 1:1 mixture of the dienes (31) ($\lambda_{max.}$ 227 nm, log ε 4.0) and (32) ($\lambda_{max.}$ 248 nm, log ε 4.3). Some ^{1}H n.m.r. details are shown in the Figures. Alper and his colleagues[16] have shown that heteroannular dienes (33) in the cholestane series can be converted into the homoannular diene complexes (34). This appeared an attractive method for converting (32) into (31). However the dithiane (35), prepared from cholest-4-en-3-one proved stable on long exposure to pentacarbonyliron, nonacarbonyldi-iron, or benzylideneacetone(tricarbonyl)iron, perhaps because of steric factors.

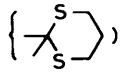
It thus became apparent that it was necessary to direct the aromatisation of ring D through controlled dehydrogenation. As a preliminary step, the enone (19) was deprotonated with LDA and the anion quenched with benzeneselenenyl chloride. Oxidation of the product then afforded the phenol (36). This procedure has recently been recommended for the synthesis of

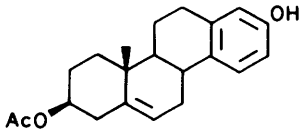


(33; X = H, Me, OR)

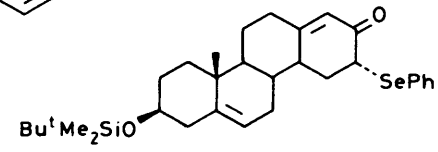


(34)

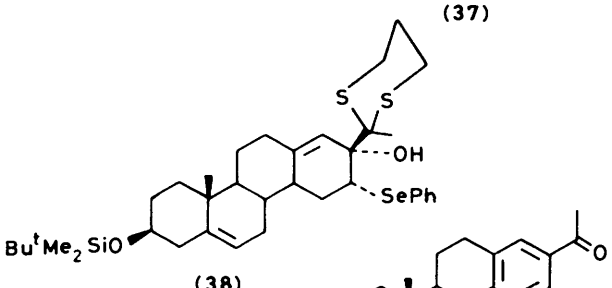
(35; X = )



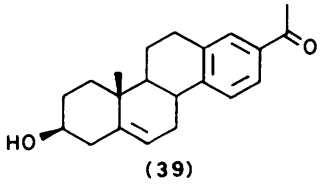
(36)



(37)

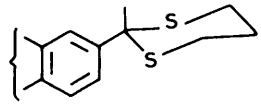


(38)

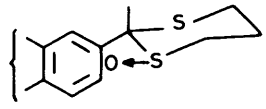


(39)

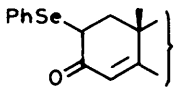
phenols from cyclohexanones.[17] The *O*-protected enone (21) was phenylselenenylated in the same way and the 16-α selenide (37) was isolated (66%); the quasi-equatorial orientation of 16-H was indicated by n.m.r. analysis. Kinetic deprotonation of (22) thus occurs specifically at C-16 rather than C-12 or C-14. 2-Lithio-2-methyl-1,3-dithiane addition then proceeded cleanly (54%) in a 1,2-fashion, despite the increased steric crowding of C-17, and stereospecifically from the β-face, to yield (38). Oxidation by hydrogen peroxide was followed by aqueous acid hydrolysis, at room temperature. This reaction proceeded slowly to yield the desired aromatic ketone (39). Two other products were isolated, the aromatised dithiane (40), and the corresponding *S*-oxide (41). Both these compounds could be hydrolysed to (39), giving a total yield of ketone of 70%, overall 16% in the five steps from the nitrile (6).



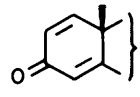
(40)



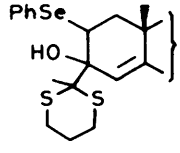
(41)



(42)



(43)



(44)

A model for the sequence (22) → (37) → (38) was examined before carrying out these reactions. Thus cholest-4-en-3-one was phenylselenenylated exclusively at C-2, *via* the anion, to yield the stereoisomers of (42), as demonstrated by elimination to cholesta-1,4-dien-3-one[18] (43). It was also ascertained that (42) would add to lithiomethyldithiane in 1,2-fashion, to give the diastereoisomers of (44).

Experimental

Unless otherwise stated, the following conditions apply. M.p.s are uncorrected. ^{1}H N.m.r. measurements were made at 90 MHz in deuteriochloroform with tetramethylsilane as internal standard; ^{13}C n.m.r. were also recorded in deuteriochloroform. I.r. and u.v. spectra were determined with chloroform and ethanol solutions, respectively. 'Chromatography' means column chromatography using Merck silica 60, 40—60 μm mesh, and with applied pressure *ca.* 1 atm. Solvents for chromatography were freshly distilled. Mass spectra were recorded using electron impact ionisation. Light petroleum refers to the fraction b.p. 40—60 °C.

(E)- *and* (Z)- 3β-*Acetoxy*-17-*hydroxyiminoandrost*-5-*ene* (**5a**) *and* (**5b**).—3β-Acetoxyandrost-5-en-17-one (10 g) was treated with hydroxylamine hydrochloride by the literature[9] method to yield the oximes (10.5 g), m.p. 159—160 °C. Column chromatography (ethyl acetate–light petroleum, 1:2) gave the *E*-oxime (**5a**), m.p. 177—179 °C (from hexane) (lit.,[9] 184 °C) (Found: C, 72.75; H, 9.3; N, 4.05. Calc. for $C_{21}H_{31}NO_3$: C, 73.05; H, 9.0; N, 4.05%); δ (^{13}C n.m.r., 47.5 MHz) 170.2 (s, C=O), 170.0 (s, C-17), 139.2 (s, C-5), 121.7 (d, C-6), 73.6 (d, C-3), 54.0 (d, C-14), 50.2 (d, C-9), 43.6 (s, C-13), 38.0 (t, C-4), 36.9 (t, C-1), 36.6 (s, C-10), 33.9 (t, C-12), 31.2 (C-7 and C-8), 27.2 (t, C-2), 25.0 (t, C-16), 23.3 (t, C-15), 21.3 (q, *Me*CO), 20.4, t, C-11), 19.3 (q, C-19), and 16.9 (q, C-18). Repeated chromatography of mother liquors from which the *E*-isomer had crystallised gave the *Z*-oxime (**5b**) (30 mg), m.p. 132—133 °C from hexane, no lit.[10] m.p. quoted (Found: C, 72.6; H, 9.05; N, 4.05%); δ (^{13}C n.m.r.; 62.9 MHz), 171.2 (s, C=O), 170.5 (s, C-17), 140.1 (s, C-5), 122.1 (d, C-6), 73.9 (d, C-3), 54.2 (d, C-14), 50.4 (d, C-9), 45.8 (s, C-13), 38.2 (t, C-4), 37.0 (t, C-1), 35.2 (s, C-10), 34.1 (t, C-12), 31.4 (C-7, C-8), 29.1 (t, C-16), 27.8 (t, C-2), 23.3 (t, C-15), 21.4 (q, C-*Me*CO), 20.6 (t, C-11), 19.4 (q, C-19), and 13.7 (q, C-18).

3β-*Acetoxy*-13,17-*secoandrosta*-5,13(18)*diene*-17-*carbonitrile* (**16**) *and* 3β-*Acetoxy*-17a-*aza*-D-*homoandrost*-5-*en*-17-*one* (**8**).—3β-Acetoxy-17-hydroxyiminoandrost-5-ene (10g, 28.9 mmol) in dry benzene (50 cm^3) and dry dimethyl sulphoxide (50 cm^3) was cooled in ice, and dicyclohexylcarbodi-imide (18.3 g, 89.7 mmol) was added under nitrogen. To the stirred solution was added trifluoroacetic acid (1.65 cm^3, 14.5 mmol), and the mixture was stirred overnight, the temperature being allowed to rise to ambient. Oxalic acid (8 g) was added, and the suspension was stirred for 30 min. The precipitated dicycohexylurea was filtered off, and the filtrate was washed with dilute hydrochloric acid (3 × 50 cm^3), 8% aqueous sodium hydrogen carbonate (3 × 50 cm^3), and brine (3 × 50 cm^3). The organic solution was then dried and evaporated to dryness and the residue chromatographed on silica using ethyl acetate–light petroleum (1:4), to yield the nitrile (**6**) (2.84 g, 30%), m.p. 104—105 °C (lit.,[9] 105—106 °C); δ 5.40 (1 H, d, *J* 4.5 Hz, 6-H), 4.84 (1 H, br s, 18-H_a), 4.52 (1 H, br s, 18-H_b), 4.58 (1 H, m, 3-H), 2.07 (3 H, s, COMe), and 0.94 (3 H, s, 19-H_3). Elution with chloroform–methanol (97:3) gave the lactam (**8**) (4.1 g, 41%), m.p. 294—296 °C (lit.,[19] 295—298 °C); δ 6.69 (1 H, NH), 5.35 (1 H, m, 6-H), 4.55 (1 H, m, 3-H), 2.02 (3 H, s, COMe), 1.01 (3 H, s, 18-H_3), and 0.93 (3 H, s, 19-H_3).

The lactam (**8**) could alternatively be prepared from 3β-acetoxy-17-hydroxyiminoandrost-5-ene (0.5 g) in dioxane (9 cm^3) at −15 °C with thionyl chloride (0.25 cm^3) in dioxane (5 cm^3) over 30 min. The reaction mixture was diluted with water, neutralised with aqueous ammonia, and extracted with dichloromethane. Evaporation of the dried extracts gave the lactam (0.31 g, 61%), m.p. 296 °C (from dichloromethane). Hydrolysis of this acetoxy lactam (**8**) with potassium carbonate in aqueous methanol at reflux for 2.5 h gave the corresponding hydroxy lactam, 3β-*hydroxy*-17a-*aza*-D-*homoandrost*-5-*en*-17-*one* (90%), m.p. 272—275 °C, (Found: C, 75.0; H, 9.95; N, 4.75. $C_{19}H_{29}NO_2$ requires C, 75.25; H, 9.55; N, 4.6%).

3β-*Hydroxy*-18-*nor*-D-*homoandrosta*-5,13(17a)-*dien*-17-*one* (**1b**).—(*a*) The seco nitrile (**6**), (5.08 g) was refluxed overnight with ethanol (60 cm^3) and aqeuous sodium hydroxide (25%; 390 cm^3). The cooled solution was acidified to yield crystals of 3β-hydroxy-13,17-secoandrosta-5,13(18)-dien-17-oic acid (**15**), m.p. 181.5—183.5 °C (lit.,[12] m.p. 184—185 °C). More acid was obtained from the filtrate by ethyl acetate extraction, to give a total of 4.54 g (96%). The acid had δ(CD_3OD) 5.37 (1 H, m, 6-H), 4.80 (1 H, br s, 18-H_a), 4.60 (1 H, s, 18-H_b), 3.48 (1 H, m, 3-H), and 0.93 (3 H, s, 19-H_3). The acid (**15**) (2.7 g) was suspended in dry dichloromethane (250 cm^3) and the stirred suspension was treated under nitrogen with trifluoroacetic anhydride (3.7 cm^3). After being stirred overnight a clear solution formed, from which the dichloromethane was evaporated. The residue was dissolved in methanol (200 cm^3) and stirred with sodium hydrogen carbonate for 1 h. Filtration and evaporation yielded an oil which was taken up in ethyl acetate and washed (dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and brine). Evaporation of the dried solution was followed by chromatography of the residue. Elution with ethyl acetate–light petroleum (1:2) gave the *title ketone* (**16**) (1.6 g, 62%), m.p. 209—210 °C (lit.,[14] 211—214 °C) (Found: C, 79.5; H, 9.1. $C_{19}H_{26}O_2$ requires C, 79.7; H, 9.1%); $\nu_{max.}$ 3 420, 1 675, and 1 620 cm^{-1}; $\lambda_{max.}$ 241 nm (16 000); δ 5.81 (1 H, br s, 17a-H), 5.40 (1 H, m, 6-H), 3.54 (1 H, m, 3-H), 1.70 (1 H, s, OH), and 0.92 (3 H, s, 19-H_3); δ (^{13}C n.m.r., 62.9 MHz), 200 (s, C-17), 166.4 (s, C-13), 140.4 (s, C-5), 123.8 (d, C-17a), 120.7 (d, C-6), 71.4 (d, C-3), 48.7 (d, C-9), 44.1 (d, C-14), 41.9 (t, C-4), 39.5 (d, C-8), 37.0 (t, C-1), 36.8 (s, C-10), 36.4 (t, C-16), 35.5 (t, C-12), 32.1 (t, C-7), 31.4 (t, C-2), 26.5 (t, C-11, C-15), and 19.2 (q, C-19). A faster-moving band afforded the isomeric 3β-*hydroxy*-18-*nor*-D-*homoandrosta*-5,13(14)-*dien*-17-*one* (**17**) (0.36 g, 14%), m.p. 139—141 °C (Found: M^+, 286.193. $C_{19}H_{26}O_2$ requires *M*, 286.193); $\nu_{max.}$ 3 470 and 1 695 cm^{-1}; δ 5.40 (1 H, m, 6-H), 3.50 (1 H, m, 3-H), 2.76 (2 H, br s, 17a-H_2), 2.40 (1 H, s, OH), and 1.00 (3 H, s, 19-H_3); δ (^{13}C n.m.r., 62.9 MHz), 211.3 (s, C-17), 141.5 (s, C-5), 131.6 and 126.8 (both s, C-13 and C-14), 121.3 (d, C-6), 71.7 (d, C-3), 48.9 (d, C-9), 44.6 (t, C-16), 42.0 (t, C-4), 38.9 (t, C-17a), 37.1 (t, C-1), 37.0 (s, C-10), 36.0 (d, C-8), 31.4 (t, C-2), 31.0 (t, C-7 and C-12), 27.4 (t, C-11), 22.1 (t, C-15), and 18.6 (q, C-19).

(*b*) 3β-Hydroxy-13,17-secoandrosta-5,13(18)-dien-17-oic acid (0.9 g) and acetic anhydride (15 cm^3) were refluxed for 45 min, and then cooled to ambient temperature. Stannic chloride (0.2 cm^3) was added, and the solution was maintained at 80 °C for 10 min before being poured into water (100 cm^3). The product was stirred for 20 min and was then extracted with chloroform. The dried extracts yielded on evaporation 3β,13-*diacetoxy*-18-*nor*-D-*homoandrost*-5-*en*-17-*one* (**18**) (0.86 g), m.p. 183—186 °C (from methanol) (Found; C, 70.9; H, 8.65. $C_{23}H_{32}O_5$ requires 71.1; H, 8.25%); $\nu_{max.}$ 1 740 and 1 715 cm^{-1}; δ 5.45 (1 H, m, 6-H), 2.03 (3 H, s, COMe), 1.98 (3 H, s, COMe), and 0.98 (3 H, s, 19-H_3). This product was refluxed in methanol (40 cm^3) with water (10 cm^3) and potassium carbonate (500 mg) for 15 min. After dilution with water the solution was extracted with chloroform. Evaporation of the dried extracts afforded the title compound (0.61 g, 72%), m.p. 139—141 °C, with u.v., i.r., and ^1H n.m.r. spectra indistinguishable from those of the above sample. This compound formed an acetate (**19**), m.p. 141 °C (from light petroleum), on acetylation in acetic anhydride (lit.,[14] 143 °C).

3β-*Acetoxy*-17-*hydroxy*-18-*nor*-D-*homoandrosta*-5,13,15,17-*tetraene* (**36**).—The acetoxyandrostadienone (**19**) (80 mg, 0.25 mmol) and benzeneselenenyl chloride (56 mg), 0.3 mmol) were dissolved in ethyl acetate (2.5 cm^3). After 45 min at room temperature, water (0.5 cm^3) was added to the stirred solution. The aqueous phase was then removed and the organic solution was treated with 4% hydrogen peroxide (0.07 cm^3) and THF (1 cm^3). After 1 h the solution was diluted with ethyl acetate, washed with water, dried, and evaporated. The residue, on recrystallisation from carbon tetrachloride, gave the *title compound* (**36**) (60 mg, 75%), m.p. 225—227 °C (Found: C, 77.15; H, 7.85; $C_{21}H_{26}O_3$ requires C, 77.30; H, 8.0%); $\nu_{max.}$(KBr) 3 470, 1 705, 1 590, 1 510, and 1 445 cm^{-1}; δ 7.9 (1 H, d, *J* 8 Hz, 15-H), 6.6 (1 H, d, *J* 8 Hz, 16-H), 6.55 (1 H, s, 17a-H), 5.5 (1 H, m, 6-H), 2.03 (3 H, s, COMe), and 1.04 (3 H, s, 19-H_3).

3β-(*Dimethyl-t-butylsiloxy*)-18-*nor*-D-*homoandrosta*-5,13(17a)-*dien*-17-*one* (**21**).—The hydroxy enone (**16**) (1.55 g), dimethyl-t-butylsilyl chloride (0.996 g), imidazole (0.973 g), and dry dimethylformamide (26 cm^3) were stirred together under nitrogen at room temperature overnight. The mixture was diluted with water and extracted with dichloromethane. The extracts were washed with dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and brine, before being dried and evaporated to afford the *title compound* (**21**), (1.89 g, 87%), m.p. 146—147.5 °C (Found: C, 75.15; H, 10.15. $C_{25}H_{40}O_2Si$ requires C, 75.0; H, 10.0%); $\nu_{max.}$(Nujol) 1 675, 1 625, 1 615, 1 250, 1 090, 833, and 770 cm^{-1}; δ 5.80 (1 H, s, 17a-H), 5.3 (1 H, 6-H), 3.60 (1 H, m, 3-H), and 0.93 (3 H, s, 19-H_3).

3β-(*Dimethyl-t-butylsiloxy*)-16α-*phenylseleno*-18-*nor*-D-*homoandrosta*-5,13(17a)-*dien*-17-*one* (**37**).—A solution of lithium di-isopropylamide (1.27 mmol) was prepared at 0 °C from di-isopropylamine (0.178 cm^3), butyl-lithium (1.47M; 0.86 cm^3), and THF (20 cm^3), and then cooled to −78 °C. Hexamethylphosphoramide (0.26 cm^3) was added, and after 60 min, a solution of the enone (**21**) (0.5 g, 1.25 mmol) in THF (5 cm^3) was added dropwise. After a further 60 min benzene-

selenenyl chloride (0.24 g) in THF (5 cm^3) was added in one portion, and the mixture was stirred for 15 min, before it was diluted with water and brine. The product was extracted with ethyl acetate, and the extracts were washed (dilute hydrochloric acid, aqueous sodium hydrogen carbonate, and brine) and dried. The residue from evaporation was chromatographed (ethyl acetate–light petroleum, 1:7) to yield the *title compound* (**37**), (460 mg, 66%), m.p. 114—114.5 °C (Found: C, 66.75; H, 8.25%; M^+ 556.217. $C_{31}H_{44}O_2SeSi$ requires C, 66.9; H, 7.9%; *M*, 556.228); $\nu_{max.}$(KBr) 1 660, 1 610, 1 575, 1 250, 1 090, 833, and 770 cm^{-1}; δ 7.67 (2 H, m, *o*-ArH), 7.36 (3 H, m, *m*, *p*-ArH), 5.90 (1 H, br s, 17a-H), 5.40 (1 H, m, 6-H), 4.00 (1 H, t, *J* 2 Hz, 16-H), 3.60 (1 H, m, 3-H), 1.00 (12 H, s, 19-H_3, Me_3C), and 0.10 (6 H, s, Me_2Si). Starting ketone (**22**) (100 mg) was also recovered.

3β-(*Dimethyl-t-butylsiloxy*)-17α-*hydroxy*-17-(2-*methyl*-1,3-*dithian*-2-*yl*)-16α-*phenylseleno*-18-*nor*-D-*homoandrosta*-5,13(17a)-*diene* (**38**).—Butyl-lithium (1.3M; 0.6 cm^3) was added to 2-methyl-1,3-dithiane (0.105 g) in dry THF (10 cm^3) under nitrogen at −40 °C. After 2 h at this temperature, the solution was transferred slowly to a stirred solution of the ketone (**37**) (216 mg) in THF (5 cm^3) at −40 °C. After the reaction mixture had been stirred for 2 h it was quenched with saturated aqueous ammonium chloride and extracted with ethyl acetate. The extracts were washed with aqueous sodium hydrogen carbonate, dried, and evaporated. The residual oil was chromatographed (ethyl acetate–light petroleum, 1:7) to yield starting ketone (99 mg), and the *title compound* (**38**) (145 mg, 54%), m.p. 131—133 °C (Found: M^+, 690.247. $C_{36}H_{54}O_2S_2SeSi$ requires *M*, 690.250); $\nu_{max.}$ 3 400 and 1 580 cm^{-1}; δ 7.63 (2 H, m, *o*-ArH), 7.48 (3 H, m, *m*, *p*-ArH), 5.56 (1 H, br s, 17a-H), 5.28 (1 H, m, 6-H), 4.57 (1 H, br t, *J* 2 Hz, 16-H), 3.49 (1 H, m, 3-H), 3.49 (1 H, s, OH), 2.95 (4 H, m, 2 × CH_2S), 1.80 (3 H, s, Me), 0.90 (3 H, s, 19-H_3), 0.89 (9 H, s, Me_3C), and 0.06 (6 H, s, Me_2Si).

17-*Acetyl*-3β-*hydroxy*-18-*nor*-D-*homoandrosta*-5,13,15,17-*tetraene*. (**39**).—The dithiane adduct (**38**) (144 mg) was stirred with a chloroform (2 cm^3), pyridine (0.2 cm^3), water (2 cm^3), and 30% hydrogen peroxide (0.8 cm^3) for 30 h at ambient temperature. The organic layer was combined with chloroform extracts of the aqueous layer, and the organic mixture washed with dilute hydrochloric acid, and aqueous sodium hydrogen carbonate. The dried solution was evaporated to a solid which was dissolved in THF (5 cm^3) and 2M hydrochloric acid (2 cm^3) with mercuric chloride (40 mg). The solution was stirred at room temperature, with t.l.c. monitoring. Three products were observed after 3 days, but on continued stirring only one eventually remained. This was isolated by chromatography using chloroform–methanol (97.5:2.5) to yield the *title compound* (**39**) (70%), m.p. 156—158 °C (Found: M^+, 310.194. $C_{21}H_{26}O_2$ requires *M*, 310.193); $\nu_{max.}$ 3 410, 1 665, 1 640, 1 600, and 1 580 cm^{-1}; $\lambda_{max.}$ 265 nm (18 000); δ 7.74 (1 H, dd, *J* 8.2 and 1.8 Hz, 16-H), 7.69 (1 H, br s, 17a-H), 7.36 (1 H, d, *J* 8.2, 15-H), 5.51 (1 H, 6-H), 3.59 (1 H, m, 3-H), 2.90 (3 H, m, 8-H, 12-H_2), 2.72 (1 H, dd, *J* 2.1, 16 Hz, 7-H), 2.63 (1 H, ddd, *J* 2.1, 5.5, 16 Hz, 7-H), 2.58 (3 H, s, COMe), 2.40 (1 H, dd, *J* 2.5, 12.5 Hz, 4-H), 2.30 (1 H, dd, *J* 2, 12.5 Hz, 4-H), and 1.06 (3 H, s, 19-H_3).

Chromatography of the mixture before completion of reaction gave two other products; 3β-*hydroxy*-17-(2-*methyl*-1,3-*dithian*-2-*yl*)-18-*nor*-D-*homoandrosta*-5,13,15,17-*tetraene* (**40**), m.p. 173—175 °C (Found: M^+, 400.186. $C_{24}H_{32}O\,S_2$ requires *M*, 400.189), $\nu_{max.}$(KBr) 3 400, 1 655, 1 600, 1 260, and 810 cm^{-1}; δ 7.33 (3 H, m, ArH), 5.49 (1 H, m, 6-H), 3.56 (1 H, m, 3-H), 2.80 (5 H, 2 × CH_2S, 8-H), 2.62 (4 H, 12-H_2, 7-H_2), 2.35 (2 H, m, 4-H_2), 2.05 (2 H, m, CH_2CH_2S), 1.92 (3 H, s, CH_3), and 1.05 (3 H, s, 19-H_3); and the corresponding S-oxide (**41**), m.p. 180—182 °C (Found: M^+, 416.182. $C_{24}H_{32}O_2S_2$ requires *M*, 416.184), $\nu_{max.}$ 3 650, 3 400, 1 655, 1 600, 1 260, 1 030, and 810 cm^{-1}; δ 7.40 (3 H, m, ArH), 5.49 (1 H, m, 6-H), 3.50 (1 H, m, 3-H), 3.16 (1 H, m, $CH_{ax.}SO$), 2.98 (2 H, m, $CH_{eq.}SO$, 8-H), 2.80 (4 H, CH_2S, 12-H_2), 2.35 (2 H, m, 4-H_2), 2.25 (2 H, m, CH_2CH_2S), 2.00 (3 H, s, CH_3), and 1.05 (3 H, s, 19-H_3).

3β-(*Dimethyl-t-butylsiloxy*)-17α-*hydroxy*-17β-(2-*methyl*-1,3-*dithian*-2-*yl*)-18-*nor*-D-*homoandrosta*-5,13(17a)-*diene* (**22**) *and* (**23**).—The enone (**21**) (0.61 g, 1.4 mmol) in THF (10 cm^3) was added to 2-lithio-2-methyl-1,3-dithiane (0.57 g, 4.1 mmol) in THF (100 cm^3) at −40 °C. After 30 min at −40 °C the solution was allowed to warm to ambient temperature over 1 h and then diluted with aqueous ammonium chloride. The mixture was extracted with chloroform. The dried extracts were evaporated and the residue chromatographed using ethyl acetate–light petroleum (1:4) to yield the 17α-*hydroxy stereoisomer* (**22**) (0.19 g), the 17β-*hydroxy stereoisomer* (**23**), (0.17 g), and a mixed fraction (0.3 g) (total yield 0.66 g, 82%). The 17α-hydroxy isomer, m.p. 130—132 °C (Found: M^+, 534.305. $C_{30}H_{50}O_2S_2Si$ requires *M*, 534.302), had $[\alpha]_D^{25}$ +24.8° ($CHCl_3$); $\nu_{max.}$(KBr) 3 300, 1 630, 1 250, 1 090, 833, and 770 cm^{-1}; δ 5.80 (1 H, s, 17a-H), 5.24 (1 H, m, 6-H), 3.42 (1 H, m, 3-H), 2.85 (4 H, 2 × CH_2S), 1.72 [3 H, s, $CH_3C(SR)_2$], 0.96 (12 H, s, Me_3C, 19-H_3), and 0.08 (6 H, s, Me_2Si). The 17β-hydroxy isomer, m.p. 126—127 °C (Found: M^+ 534.305), had $[\alpha]_D^{25}$ −134.8° ($CHCl_3$); $\nu_{max.}$(KBr) 3 300, 1 630, 1 250, 1 090, 833, and 770 cm^{-1}; δ 5.72 (1 H, s, 17a-H), 5.25 (1 H, m, 6-H), 3.42 (1 H, m, 3-H), 2.86 (4 H, 2 × CH_2S), 1.78 [3 H, s, $CH_3C(SR)_2$], 0.90 (12 H, s, Me_3C, 19-H_3), and 0.08 (6 H, s, Me_2Si).

3β-(*Dimethyl-t-butylsiloxy*)-17-*ethynyl*-17α-*hydroxy*-18-*nor*-D-*homoandrosta*-5,13(17a)-*diene* (**24**) *and* (**25**).—Lithium acetylide–ethylenediamine complex (0.27 g, 3.75 mmol) was added to the enone (**21**) (400 mg) in dry THF (50 cm^3), and the suspension was stirred under nitrogen for 3 h. After the addition of brine, the organic products were extracted into dichloromethane. The dried extracts were evaporated and the residue was chromatographed using ethyl acetate–light petroleum (1:2), to yield the 17α-*hydroxy isomer* (**24**), m.p. 150—152 °C, and the 17β-*hydroxy isomer* (**25**), m.p. 137—139 °C, total yield 317 mg (74%). The 17α-hydroxy compound (Found: C, 75.55; H 10.05. $C_{27}H_{42}O_2Si$ requires C, 76.05; H, 9.85%) had $[\alpha]_D^{24}$ −120.7° ($CHCl_3$); δ 5.45 (1 H, s, 17a-H), 5.35 (1 H, m, 6-H), 3.50 (1 H, m, 3-H), 2.51 (1 H, s, C≡CH), 2.20 (1 H, s, OH), 0.90 (12 H, s, Me_3C, 19-H_3), and 0.70 (6 H, s, Me_2Si). The 17β-*hydroxy isomer* (Found: C, 75.7; H, 10.0%) had $[\alpha]_D^{23}$ +34.0° ($CHCl_3$); δ 5.53 (1 H, s, 17a-H), 5.33 (1 H, m, 6-H), 3.48 (1 H, m, 3-H), 2.48 (1 H, s, C≡C–H), 2.16 (1 H, s, OH), 0.87 (12 H, s, Me_3C, 19-H_3), and 0.06 (6 H, s, Me_2Si).

17α-*Acetoxy*-17-*acetyl*-3β-(*dimethyl-t-butylsiloxy*)-18-*nor*-D-*homoandrosta*-5,13(17a)-*diene* (**26**).—The acetylene (**24**) (0.104 g) was stirred at room temperature for 16 h in a two-phase mixture of ethyl acetate (15 cm^3) and water (2 cm^3) containing mercuric acetate (0.57 g). After addition of water the mixture was extracted with ethyl acetate. The extracts were washed, dried, and evaporated to a solid. Purification by chromatography gave the *title compound* (**26**) (60 mg, 49%), m.p. 140—142 °C (Found: M^+, 486.319. $C_{29}H_{46}O_4Si$ requires *M*, 486.317); $\nu_{max.}$ 1 730, 1 720, 1 650, 1 250, 1 090, 835, and 772 cm^{-1}; δ 5.61 (1 H, s, 17a-H), 5.32 (1 H, m, 6-H), 3.48 (1 H, m, 3-H), 2.20 (3 H, s, MeCO), 2.18 (3 H, s, MeCO), 0.94 (12 H, s, Me_3C and 19-H_3), and 0.07 (6 H, s, Me_2Si).

17β-*Acetyl*-3β-(*dimethyl-t-butylsilyl*)-17α-*hydroxy*-18-*nor*-D-*homoandrosta*-5,13(17a)-*diene* (**27**).—The above acetate (**26**) (60 mg) was hydrolysed with ethanolic sodium hydroxide at ambient temperature, in the standard fashion, to yield the *title ketol* (**27**) (83%), m.p. 128—130 °C (Found: M^+, 444.306.

$C_{27}H_{44}O_3Si$ requires M, 444.305), $\nu_{max.}$(KBr) 3 450, 1 702, 1 350, 1 250, 1 090, 885, 865, 833, and 770 cm^{-1}; δ 5.36 (1 H, m, 6-H), 5.23 (1 H, s, 17a-H), 3.48 (1 H, m, 3-H), 3.40 (1 H, s, OH), 2.24 (3 H, s, MeCO), 0.95 (12 H, s, Me_3C, 19-H_3), and 0.08 (6 H, s, Me_2Si); δ (^{13}C n.m.r., 62.9 MHz) 211.1 (s, C=O), 147.8 (s, C-13), 141.2 (s, C-5), 120.5 (d, C-6), 118.5 (d, C-17a), 76.9 (s, C-17), 72.5 (d, C-3), 49.7 (d, C-9), 42.9 (d, C-14), 42.6 (t, C-4), 38.0 (t, C-1), 37.3 (t, C-16), 37.0 (s, C-10), 35.9 (t, C-15), 32.1 (t, C-2), 32.0 (t, C-7), 30.8, (t, C-12), 28.1 (q, C-21), 26.0 (q, *Me*$_3$C), 24.7 (d, C-8), 22.0 (t, C-11), 19.4 (q, C-19), 18.2 (s, Me_3C), and −4.5 (s, Me_2Si).

3β-*Methoxy*-13,17-*secoandrosta*-5,13(18)*diene*-17-*carbonitrile* (**10**) *and* 3β-*Methoxy*-17a-*aza*-D-*homoandrost*-5-*en*-17-*one* (**11**).—17-Hydroxyimino-3β-methoxyandrost-5-ene (0.5 g) in dry benzene (5 cm^3) and dry dimethyl sulphoxide (5 cm^3) at 0 °C was treated with dicyclohexylcarbodi-imide (0.78 g) and trifluoroacetic acid (0.15 cm^3). The mixture was set aside at ambient temperature for 24 h and then filtered. The filtrate, diluted with benzene, was washed with dilute hydrochloric acid and aqueous sodium hydrogen carbonate, dried, and evaporated. The residue was chromatographed, eluting with chloroform–acetone (3:1), to yield the *title nitrile* (**10**) (0.18 g, 37%), m.p. 102—103 °C (from light petroleum) (Found: C, 80.0; H, 9.8; N, 4.6. $C_{20}H_{29}NO$ requires C, 80.25; H, 9.7; N, 4.7%); $\nu_{max.}$ 2 260 and 1 650 cm^{-1}; δ 5.33 (1 H, m, 6-H), 4.78 (1 H, s, 18-H_a), 4.47 (1 H, s, 18-H_b), 3.36 (3 H, s, MeO), 3.00 (1 H, m, 3-H), and 0.90 (3 H, s, 19-H_3). Elution with chloroform–methanol (98:2) gave the *title lactam* (**11**) (0.24 g, 48%), m.p. 219—220 °C (Found: M^+, 317.233. $C_{20}H_{31}O_2N$ requires M, 317.235); $\nu_{max.}$(KBr) 3 450, 3 200, 3 100, 1 675, and 1 610 cm^{-1}; δ 6.90 (1 H, br s, NH), 5.40 (1 H, m, 6-H), 3.40 (3 H, s, MeO), 3.00 (1 H, m, 3-H), 1.20 (3 H, s, 18-H_3), and 1.02 (3 H, s, 19-H_3). The lactam could also be prepared in 60% yield from the oxime by treatment with thionyl chloride in dioxane.

3β-*Methoxy*-13,17-*secoandrosta*-5,13(18),15-*triene*-17-*carbonitrile* (**20**).—The seco nitrile (**10**) (2.44 g, 8.1 mmol) in THF (4 cm^3) at −78 °C was treated with lithium di-isopropylamide (*ca.* 1M solution in hexane–THF, 9.7 mmol) for 30 min. Diphenyl diselenide (3.25 g, 9.7 mmol) in THF (5 cm^3) was then added dropwise to the reaction mixture (at −78 °C), followed by aqueous ammonium chloride. The product was extracted into chloroform, and the extracts were washed (dilute hydrochloric acid and aqueous sodium hydrogen carbonate), dried, and evaporated. The intermediate phenylseleno nitrile (2.1 g) was isolated on a dry silica column using chloroform elution. Without further purification it was dissolved in ethyl acetate (25 cm^3) with THF (10 cm^3) and hydrogen peroxide (30%, 2.2 cm^3). The mixture was stirred at room temperature for 2 h, with initial cooling to keep the temperature below 35 °C; it was then washed with water and aqueous sodium sulphite, dried, and evaporated to give the title nitrile (**20**) (1.23 g) as an oil containing the 15*E*- and 15*Z*-isomers; δ 6.5 (1 H, dd, $J_{14.15}$ 11 Hz, $J_{15.16}$ 16 Hz, 15-H, *E*-isomer), 6.3 (1 H, dd, $J_{14.15} = J_{15.16}$ 10 Hz, 15-H, *Z* isomer), 5.6 (1 H, d, *J* 10 Hz, 16-H, *Z*), 5.4 (1 H, 6-H), 5.2 (1 H, d, *J* 16 Hz, 16-H, *E*), 4.75 (1 H, s, 18-Ha), 4.45 (1 H, s, 18-H_b), and 3.34 (3 H, s, MeO).

3β-(*Dimethyl-t-butylsiloxy*)*androst*-5-*en*-17-*one*.—A solution of 3β-hydroxyandrost-5-en-17-one (1.44 g), imidazole (0.85 g), and t-butyldimethylsilyl chloride (0.9 g) in dry dimethylformamide (10 cm^3) was kept under nitrogen overnight, then was poured into water. The *title compound* (1.9 g, 95%), m.p. 142—144 °C, was isolated by chloroform extraction (Found: C, 74.4; H, 10.55. $C_{25}H_{42}O_2Si$ requires C, 74.65; H, 10.45%).

3β-(*Dimethyl-t-butylsiloxy*)-17β-*hydroxy*-17α-(2-*methyl*-1,3-*dithian*-2-*yl*)*androst*-5-*ene*. (**12**).—3β-(Dimethyl-t-butylsiloxy)-androst-5-en-17-one (0.402 g, 1 mmol) in THF (5 cm^3) was added dropwise to 2-lithio-2-methyl-1,3-dithiane (1 mmol) in THF (25 cm^3) at −70 °C. After 60 min the solution was allowed to warm to −20 °C. After 2 h the temperature was raised to −5 °C and maintained there for a further 16 h. Aqueous ammonium chloride was added to the mixture and organic products were collected in ethyl acetate. The extracts were dried and evaporated and the residue chromatographed using ethyl acetate–light petroleum (1:4), to yield the starting ketone (0.3 g, 75%) and the *title alcohol* (**12**) (0.14 g, 25%) as an oil (Found: M^+, 536.319. $C_{30}H_{52}O_2S_2Si$ requires M, 536.318); $\nu_{max.}$ 3 650 and 1 625 cm^{-1}; δ 5.30 (1 H, m, 6-H), 3.4 (1 H, m, 3-H), 3.4 (1 H, s, OH), 2.9 (4 H, m, 2 × CH_2S), 2.58 (2 H, m, CH_2CH_2S), 1.95 [3 H, s, $MeC(SR)_2$], 0.98 (6 H, s, 18-H_3, 19-H_3), 0.88 (9 H, s, Me_3C), and 0.03 (6 H, s, Me_2Si).

3β-(*Dimethyl-t-butylsiloxy*)-17-(2-*methyl*-1,3-*dithian*-2-*yl*)*androsta*-5,16-*diene* (**14**).—The alcohol (**12**) (90 mg) in benzene (4 cm^3) and dimethyl sulphoxide (2 cm^3) with trifluoroacetic anhydride (0.55 cm^3) and pyridine (0.55 cm^3) was stirred under nitrogen for 16 h. The mixture was diluted with water and extracted with dichloromethane. The extracts were washed (dilute hydrochloric acid, water), and evaporated. The residue was purified by chromatography using ethyl acetate–light petroleum (1:3) to yield the *title compound* (**14**) (50 mg, 57%), m.p. 177—178 °C (Found: M^+, 518.306. $C_{30}H_{50}S_2Si$ requires M, 518.307); δ 5.80 (1 H, m, 16-H), 5.40 (1 H, m, 6-H), 3.50 (1 H, m, 3-H), 2.01 [3 H, s, $CH_3C(SR)_2$], 1.00 (6 H, s, 18-H_3 and 19-H_3), 0.92 (9 H, s, Me_3C), and 0.03 (6 H, s, Me_2Si).

3β-*Hydroxy*-3α-(2-*methyl*-1,3-*dithian*-2-*yl*)*cholest*-4-*ene*.—Cholest-4-en-3-one (0.384 g, 1 mmol) in THF (5 cm^3) was added, at −78 °C, to 2-lithio-2-methyl-1,3-dithiane (2 mmol) in THF (30 cm^3). The mixture was stirred at −60 °C for 2 h and at −10 °C for 14 h, when aqueous ammonium chloride was added. The mixture was extracted with ethyl acetate. The extracts were washed with brine, dried, and evaporated. Chromatography of the residue, with chloroform elution, gave the *title alcohol* (0.394 g, 77%), m.p. 149—150 °C (Found: C, 74.55; H, 10.3; S, 11.55. $C_{32}H_{54}OS_2$ requires C, 74.15; H, 10.4; S, 12.35%); $\nu_{max.}$ 3 575, 3 439, and 1 640 cm^{-1}; δ 5.68 (1 H, s, 4-H), 2.90 (4 H, 2 × CH_2SR), 1.82 [3 H, s, $CH_3C(SR)_2$], 0.98 (3 H, s, 19-H_3), 0.98, (6 H, d, 26-H_3, 27-H_3), 0.82 (3 H, s, 21-H_3), and 0.68 (3 H, s, 18-H_3).

3-(2-*Methyl*-1,3-*dithian*-2-*yl*)*cholesta*-3,5-*diene* (**35**).—The above alcohol (0.15 g), was dissolved in chloroform (20 cm^3) with trifluoroacetic acid (0.1 cm^3). After 20 min the solution was evaporated, and the residue redissolved in ethyl acetate. The solution was washed with aqueous sodium hydrogen carbonate, dried, and evaporated to give the *title diene* (**35**) (0.14 g, 97%), m.p. 131—133 °C (Found: M^+, 500.353. $C_{32}H_{52}S_2$ requires M, 500.351); $\nu_{max.}$ 1 650, 1 602, and 905 cm^{-1}; $\lambda_{max.}$ 240 (21 300), 247 (22 900), and 256inflnm (14 600); δ 6.52 (1 H, s, 4-H), 5.52 (1 H, m, 6-H), 2.72 (4 H, m, 2 × CH_2-S), 1.64 [3 H, s, $Me(SR)_2$], 0.97 (3 H, s, 19-H_3), 0.90 (6 H, 26-H_3, 27-H_3), 0.80 (3 H, 21-H_3), and 0.68 (3 H, s, 18-H_3). This diene was unchanged on being refluxed with pentacarbonyliron in dibutyl ether for 72 h, with nonacarbonyldi-iron in light petroleum (b.p. 40—60 °C) for 36 h, or with benzylideneacetone(tricarbonyl)iron in toluene for 42 h.

2-*Phenylselenocholest*-4-*en*-3-*one*.—Lithium di-isopropylamide (1.07 mmol) in THF (10 cm^3) was cooled to −78 °C. Hexamethylphosphoramide (0.19 ml) was added, followed, after 1 h, by a solution of cholest-4-en-3-one (0.4 g, 1.04 mmol) in

THF (5 cm^3). After 1 h benzeneselenenyl bromide (0.25 g, 1.04 mmol) was added and the reaction stirred for 15 min. Aqueous ammonium chloride was added and organic products collected in ethyl acetate. The extracts were washed, dried, and evaporated. The residue was chromatographed using chloroform–light petroleum (2:1) to give the title compound (**42**), (0.37 g, 66%) as a mixture of C-2 epimers. The 2*R* isomer had δ 7.7 (2 H, ArH), 7.4 (3 H, ArH), 5.85 (1 H, s, 4-H), 4.25 (1 H, dd, *J* 5, 12 Hz, 2β-H), 1.28 (3 H, s, 19-H_3), 0.90 (6 H, 26-H_3, 27-H_3), 0.83 (3 H, s, 21-H_3), and 0.71 (3 H, 18-H_3). The 2*S* isomer had δ 7.7 (2 H, ArH), 7.4 (3 H, ArH), 5.85 (1 H, s, 4-H), 4.00 (1 H, dd, *J* 5, 5 Hz, 2α-H), 1.10 (3 H, 19-H_3), 0.90 (6 H, 26-H_3, 27-H_3), 0.83 (3 H, 21-H_3), and 0.66 (3 H, 18-H_3).

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