Angular trifluoromethyl group. Part 6.[1] Studies in the series of 19,19,19-trifluoroandrostenedione† derivatives

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Efforts devoted to the preparation of 19,19,19-trifluoroandrost-4-ene-3,17-dione starting from 9,9,9-trifluoro-Wieland–Miescher ketone 1, as well as an improved synthesis of this latter compound are described.

Introduction

Following our initial work on the preparation of steroids angularly substituted by a trifluoromethyl group,[2] recent interest in this area focused mainly on 18,18,18-trifluoro derivatives of estrogenic hormones.[3]

On the other hand, the quest for new inhibitors of the human cytochrome *P*-450 enzyme aromatase, involved in estrogen biosynthesis, is a subject of constant research.[4] In the field of fluorinated steroids it has been shown that 19,19-difluoroandrostenedione may act as an irreversible inhibitor of this enzyme.[5] This interesting result encouraged us to embark on a programme directed towards the synthesis of 19,19,19-trifluoroandrostenedione.[6]

Results and discussion

The selected strategy for the preparation of the steroid nucleus was based on work by Daniewski on the non-fluorinated series,[7,8] starting from the Wieland–Miescher ketone. We have already published the preparation of the trifluoromethylated analogue **1** of this useful ketone[9] and a preliminary account was made on its transformation into a steroid framework.[10] Here we describe in full this latter work as well as major improvements, and emphasis is made on our efforts directed toward the preparation of 19,19,19-trifluoroandrostenedione.

Wieland–Miescher ketone is known to react selectively at the unconjugated carbonyl group with lithium acetylide in liquid ammonia,[11] the other carbonyl being presumed to be protected from nucleophilic attack by enolisation. When applied to its trifluoromethylated analogue **1**, this reaction led only to the formation of tars (an amorphous non-fluorinated black powder was isolated). Under less basic conditions, condensation of dione **1** with lithium trimethylsilylacetylide in diethyl ether[12] proved to be unselective, leading to a mixture of the mono **28** (36%) and the bis adduct **29** (28%). This result points to a higher reactivity of the conjugated ketone in **1** and thus to the necessity of its protection in order to achieve selective ethynylation. Unfortunately our first attempt to protect this group as an enol acetate led, under the employed conditions,[13] to the formation of the bis acetate **30** (76%).

Better results were obtained when enol ether **2** was formed in 82% yield upon silylation of dione **1** with *tert*-butyldimethylsilyl trifluoromethanesulfonate, using 2,6-dimethylpyridine (2,6-lutidine) as the base (Scheme 1). We earlier[10] assigned structure **31** to this compound on the basis of precedent evidence for the formation of a heteroannular enol under thermodynamic conditions.[14] However, compound **2** was also formed when the corresponding enolate was generated under kinetic conditions [lithium diisopropylamide (LDA), −78 °C] known to give the homoannular isomer.[15] Moreover, 2D NMR experiments on its derivative **3** (*vide infra*) are only reconcilable with a homoannular diene structure.

The conjugated carbonyl function having been protected, condensation of compound **2** with lithium trimethylsilylacetylide was straightforward, leading to the bis-silyl compound **3** (90%), whose homoannular diene structure was supported by NMR correlation experiments. Thus, one of the vinylic protons at δ 4.61 was correlated with the other (δ 5.54) and also with two nuclei at δ 3.25 and 2.67. These two latter protons are in an isolated site, because they did not show any additional correlation except between each other. This circumstance is only possible with a structure like **3** where the vinylic proton (δ 4.61) is at position 7 (^{1}H NMR numbering) and the two correlated nuclei are at position 8.

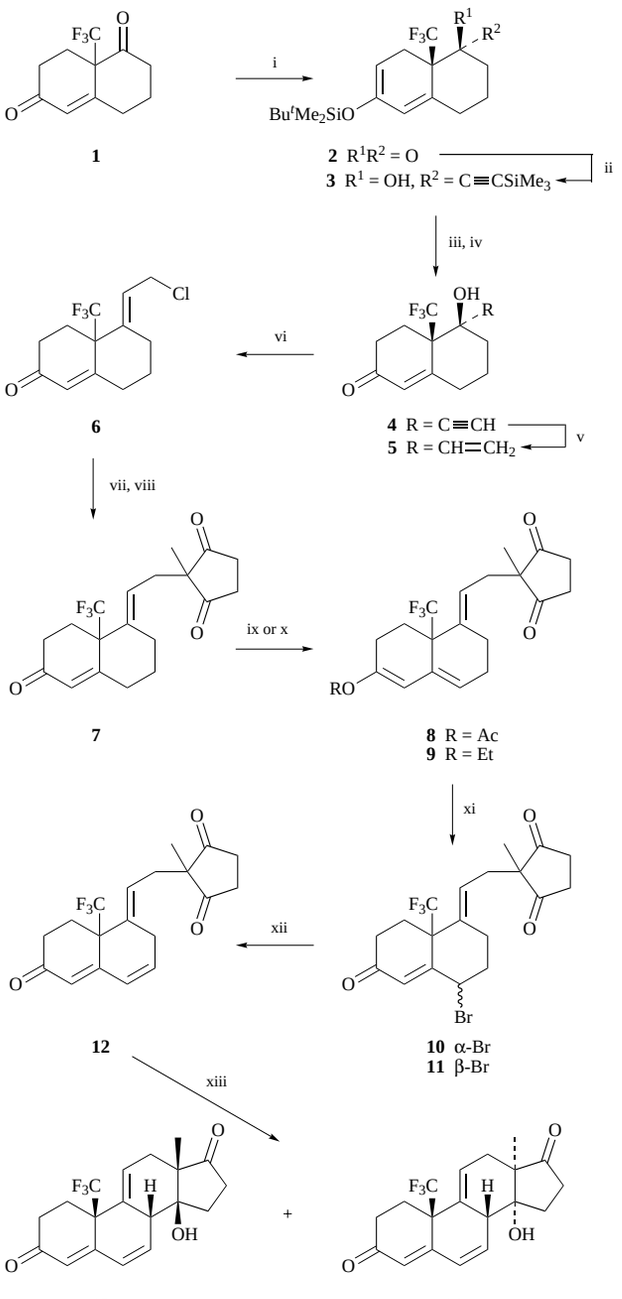
Attempted simultaneous deprotection of both silyl blocking groups in compound **3** with the usually used reagent tetrabutylammonium fluoride (TBAF) in tetrahydrofuran (THF), resulted in the destruction of the molecule with loss of the fluorine atoms. This behaviour was attributed to the sensitivity of the enone system to a retroaldol-type reaction in a basic medium (*vide infra* for a demonstrative example). Stepwise deprotection using first a weakly basic medium (K_2CO_3, MeOH) to remove the acetylenic trimethylsilyl group, then an acidic medium (1 mol dm^{-3} HCl) to cleave the enol silyl ether was more gratifying, the acetylenic alcohol **4** being isolated in 89% yield in the best case. Unfortunately this reaction was not very reproducible, affording variable amounts, from run to run (up to 40%) of the non-fluorinated furan by-product **15**. This compound is suspected to arise *via* initial opening of the bicyclic system (Scheme 2), followed by stepwise elimination of the fluorine atoms and final acid-induced cyclisation. This problem was solved later (*vide infra*) by the use of an alternative preparation for compound **4**.

Selective hydrogenation of the triple bond in alkyne **4**, using Lindlar catalyst in methanol, was straightforward, and afforded the vinylic alcohol **5** in 90% yield.

Under the original conditions described for the transformation of the non-fluorinated analogue of compound **5** to the analogue of the chloride **6** by means of thionyl dichloride,[7] we observed a very slow and incomplete reaction. However, by using a slightly modified protocol,[16] the somewhat unstable allylic chloride **6** was easily obtained in 91% yield.

Condensation of chloride **6** with the sodium salt of 2-methylcyclopentane-1,3-dione, after *in situ* exchange of the chlorine atom for a iodine atom, afforded the secosteroid **7** (78%) along

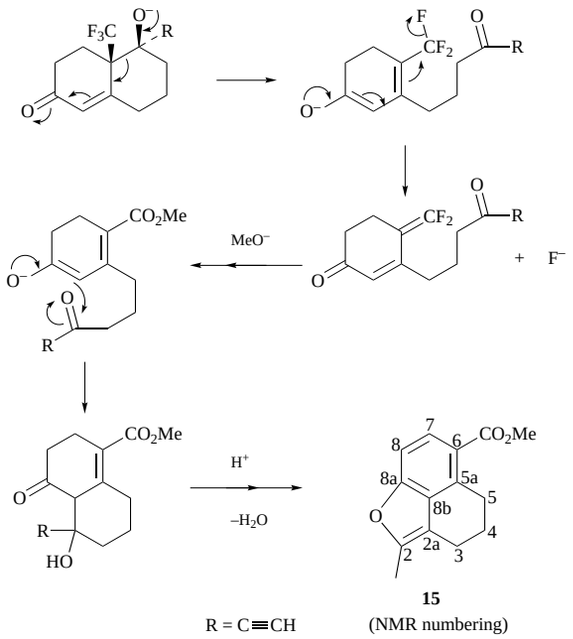
† The trivial name androstenedione refers to androst-4-ene-3,17-dione.



Scheme 1 *Reagents and conditions:* i, Bu^tMe_2SiOTf, 2,6-lutidine, CH_2Cl_2, 0 °C; ii, $LiC{\equiv}CSiMe_3$, Et_2O, 0 °C; iii, K_2CO_3, MeOH; iv, 1 mol dm^{-3} HCl; v, H_2, Lindlar catalyst, MeOH; vi, $SOCl_2$, pyridine, CH_2Cl_2, 0 °C; vii, NaI, DMF; 2-methylcyclopentane-1,3-dione sodium salt, MeOH; ix, Ac_2O, $HClO_4$, AcOEt; x, ethyl orthoformate, PTSA, 1,4-dioxane; xi, NBS, AcOH, NaOAc, aq. pyridine, 0 °C; xii, AgOTf, 2,6-Bu^t_2-4-Me-pyridine, CH_2Cl_2; xiii, MeONa, MeOH, 0 °C

with the O-alkylated product **33** (10%) and the diene **32** (6%). Analogous side-products were also observed during a similar condensation in the non-fluorinated series.[17]

At this stage, it was conceivable to achieve cyclisation of trione **7** to a steroid framework under acidic conditions.[17] However, even in a very acidic medium (trifluoroacetic acid), the trifluoromethylated trione **7** remained unchanged. We did not even observe migration of the exocyclic 9,11 (steroid numbering) double bond to the presumably more stable 8,9 endocyclic isomer. We thus envisaged the base-induced cyclisation of a dienolate anion[7,8] as a surrogate; this in turn involved the introduction of an additional 6,7 (steroid numbering) double bond conjugated to the C-3 carbonyl group. The use of 2,3-dichloro-5,6-dicyano-*p*-benzoquinone (DDQ) to achieve this purpose[18] proved to be very sluggish, leading mainly to unchanged starting material and a very low yield (5%) of a product **35** resulting from oxidation of the five-membered ring rather than that of the enone system.



Scheme 2

We next thought to introduce the requisite additional double bond by a bromination–dehydrobromination sequence.[18] Attempted direct radical bromination[19] of enone **7** was unselective. To achieve selective bromination, formation of an enol ether was planned. Formation of an enol acetate under perchloric acid catalysis[20] was not fully satisfactory, leading to a mixture of the wanted acetate **8** (70%) and the bis-acetate **34** (16%), subsequent again to the attack on the five-membered ring. Better results were obtained in the preparation of the ethyl enol ether,[21] when compound **9** was isolated in 74% yield after reaction with triethyl orthoformate for 6 h, the remainder of the crude material being unchanged starting molecule. This yield could not be improved by using a longer reaction time, compound **9** degrading slowly in the reaction medium.

Bromination[7] of either enol acetate **8** or enol ether **9** afforded, in a 4.5:1 ratio, the epimeric bromides **10** and **11** in the same combined yield (81%) irrespective of the nature of the starting material. Dehydrobromination of this mixture in a basic medium was again troublesome, the brominated molecules being destroyed with loss of the fluorine atoms under conditions [Li_2CO_3, pyridine, hexamethylphosphoramide (HMPA)] working well in the non-fluorinated series.[7] A comparable result was obtained with non-nucleophilic bases such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) and 1,5-diazabicyclo[4.3.0]non-5-ene (DBN).[22] Silver salts of poorly nucleophilic anions have been used for the elimination of tertiary chlorine atoms[23] and we independently found that silver triflate was a mild dehydrohalogenating agent.[24] We were pleased to find that the latter salt, in conjunction with 2,6-di-*tert*-butyl-4-methylpyridine, was in fact the reagent of choice for the dehydrobromination of compounds **10** and **11**, leading to the triene **12** in 90% yield. Use of silver trifluoroacetate was less satisfactory, compound **12** being isolated in only 69% yield accompanied by side-products. No substitute could be found for the hindered pyridine base used.

Base-induced cyclisation of trienone **12** was achieved in conditions (MeONa, MeOH; 0 °C) close to those described for its non-fluorinated analogue,[7] but contrary to the result observed in the non-fluorinated series, we were able to isolate, beside the expected 13β,14β cyclisation product **13** (65%), the 13α,14α isomer **14** (15%). Both structures were confirmed by X-ray analysis: the crystal structure for steroid **13** has already been

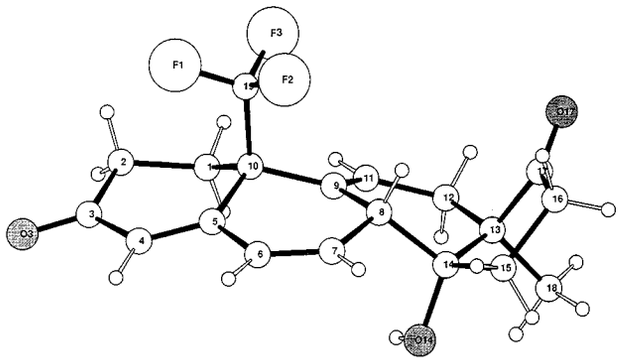
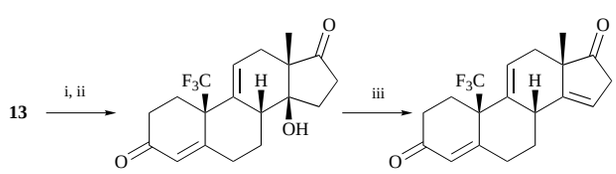


Fig. 1 Crystal structure of 19,19,19-trifluoro-14α-hydroxy-13α-androsta-4,6,9(11)-triene-3,17-dione **14**

described,[10] that for its isomer **14** is given in the Experimental section, and shown in Fig. 1. Global yield of both compounds depends on the reaction temperature (the reaction is very slow at −40 °C and the yield is lower at 20 °C) but not their ratio, which remains close to 4:1. We don't know if the non-fluorinated analogue of compound **14** is not formed at all[7] or if it was missed during the purification process (steroid **14** is by far more polar than its isomer **13**) and this fact precludes further discussion of the eventual influence of the trifluoromethyl group on the stereochemical outcome of this cyclisation.

At first, transformation of steroid **13** into 19,19,19-trifluoro-androstenedione involving only hydrogenation of the Δ^6 and 9,11 double bonds and reduction of the 14β hydroxy group to a 14α hydrogen seemed possible. The Δ^6 double bond of the non-fluorinated analogue of compound **13** had been reduced with molecular hydrogen using 2% palladium on strontium carbonate as catalyst.[7] However, under these conditions, compound **13** gave in 70% yield a 1:1 mixture of the expected enone **16** (Scheme 3) with its unconjugated isomer **36**, along with three



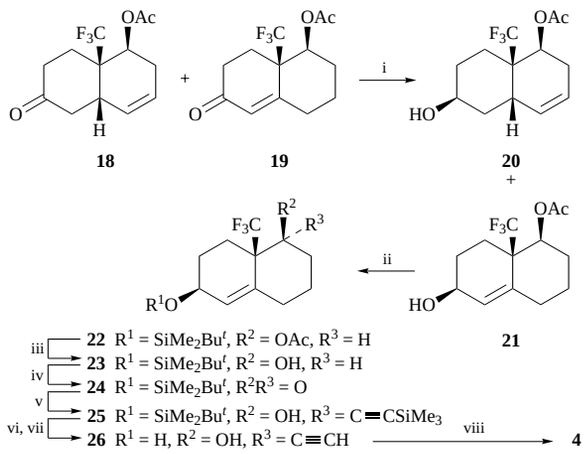
Scheme 3 *Reagents and conditions:* i, cyclohexene, 10% Pd–C, EtOH, reflux; ii, PTSA, benzene, reflux; iii, $SOCl_2$, pyridine, 0 °C

other, unidentified products (the structure of one of them, formed in ~8% yield, suggests a dehydrogenation reaction). No reaction was observed with Wilkinson's catalyst,[25] and attempted reduction with lithium in liquid ammonia[26] led mainly to a mixture of alcohols resulting from further reduction of the 17-carbonyl in **36**. However, we found that transfer hydrogenation,[27] using cyclohexene as a source of hydrogen, in refluxing ethanol gave better results, the enone **16** being isolated in 95% yield after reconjugation of the double bond of its isomer **36** formed only in a small amount (~10%).

Further elimination of the tertiary hydroxy group by using thionyl dichloride in pyridine[28] readily afforded triene **17** (86%). To date, all efforts to convert this compound into 19,19,19-trifluoroandrostenedione have failed. It was thus not possible to reduce the 9,11 double bond using various conditions. This failure could be due to the steric effect induced by the trifluoromethyl group. Nevertheless dione **17** was tested for biological activity, but unfortunately this compound does not inhibit human placental aromatase up to 10^{-6} M at a substrate concentration of 250 nM.

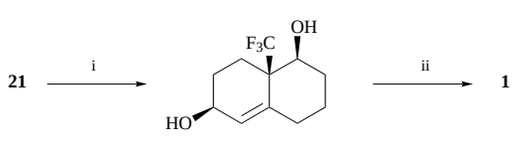
As explained in an earlier part of this text, conversion of ketone **1** into the acetylenic compound **4** was not fully satisfactory. Side-products were observed resulting from the lability, in a basic medium, of some intermediates induced by the presence of an α,β-unsaturated ketone acting as a leaving group. To prevent this drawback we thought to protect this functionality as an allylic alcohol.

Reduction of a 2:1 mixture of acetates **18** and **19**, as obtained in our earlier work,[9] with sodium borohydride in 10:1 THF–methanol (Scheme 4) afforded the easily separable alco-



Scheme 4 *Reagents and conditions:* i, $NaBH_4$, THF, MeOH, 0 °C; ii, Bu^tMe_2SiOTf, 2,6-lutidine, CH_2Cl_2, 0 °C; iii, K_2CO_3, MeOH; iv, PCC, CH_2Cl_2; v, $LiC{\equiv}CSiMe_3$, Et_2O, 0 °C; vi, TBAF, THF; vii, 1 mol dm^{-3} HCl; viii, Jones reagent, acetone

hols **21** (63%) and **20** (31%). Although we were not able to obtain satisfactory analytical data for compound **21** (in contrast to its isomer **20**), its transformation into alkyne **4** was straightforward. The allylic alcohol was first protected as its *tert*-butyldimethylsilyl ether **22** (95%); selective deprotection of the 1-acetate functionality could then be accomplished with potassium carbonate in methanol (94%) without side-reactions. The resulting alcohol **23** was oxidised with pyridinium chlorochromate (PCC) to the corresponding ketone **24** in 94% yield (use of the more acidic Jones reagent resulted in the removal of the protecting silyl group and simultaneous oxidation of both alcohol functions, leading ultimately to trifluoro-Wieland–Miescher ketone **1**). Silylacetylene **25** was obtained by condensation of ketone **24** with lithium trimethylsilylacetylide (93%). Simultaneous cleavage of both silyl protecting groups with TBAF then gave cleanly the alcohol **26** (92%), which upon Jones oxidation afforded ketone **4** in 94% yield, thus completing the synthesis. Incidentally, this scheme was adapted to an alternative preparation of ketone **1** (Scheme 5): Jones oxidation of

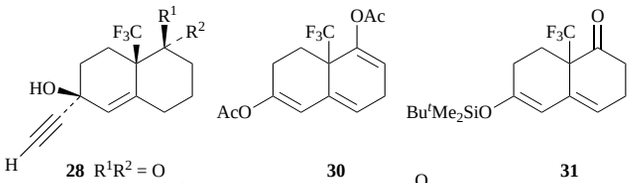


Scheme 5 *Reagents and conditions:* i, K_2CO_3, MeOH; ii, Jones reagent, acetone

the diol **27**, obtained by saponification of acetate **21** (96%), produced ketone **1** in 94% yield. This new route is more amenable to scaling up and must now be preferred over our older preparation[9] of the trifluoro analogue of Wieland–Miescher ketone, compound **1**.

Experimental

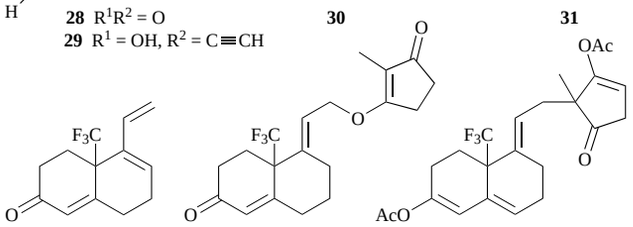
General information may be found in previous parts in this series.[1,9]



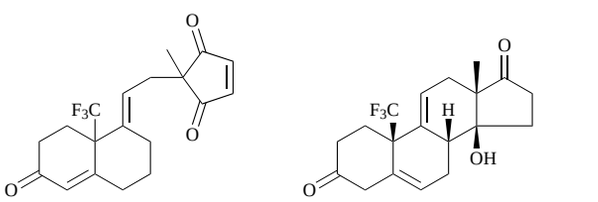
28 $R^1R^2 = O$
29 $R^1 = OH$, $R^2 = C{\equiv}CH$

30

31



32 **33** **34**



35 **36**

6-(*tert*-Butyldimethylsilyloxy)-3,4,8,8a-tetrahydro-8a-(trifluoromethyl)naphthalen-1(2*H*)-one 2

2,6-Lutidine (1.48 ml, 12.7 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (1.47 ml, 6.4 mmol) were added at 0 °C to a solution of ketone **1** (740 mg, 3.2 mmol) in dichloromethane (50 ml) kept under argon. The mixture was stirred for 4 h, the solvent was removed and the residue was taken up in pentane (50 ml). The precipitate was filtered off, and washed with additional pentane (50 ml). After removal of the solvent from the filtrate *in vacuo*, the residue was eluted on a column of silica gel (dichloromethane) to afford the *silyl ether* **2** (910 mg, 82%) as an oil (Found: M^+, 346.1573. $C_{17}H_{25}F_3O_2Si$ requires M, 346.1576); $\nu_{max}(CCl_4)/cm^{-1}$ 1715, 1655 and 1170; δ_H(200 MHz; $CDCl_3$) 5.73 (1 H, t, *J* 1.9, 5-H), 4.78–4.67 (1 H, m, 7-H), 2.62–1.40 (8 H, envelope), 0.80 (9 H, s, $SiBu^t$ and 0.00 (9 H, s, Me_3Si); δ_C(50 MHz; $CDCl_3$) 203.8 (C-1), 146.1 (C-6), 133.0 (C-5), 127.8 (C-4a), 125.8 (C-9, q, $^1J_{CF}$ 290), 99.9 (C-7), 55.0 (C-8a, q, $^2J_{CF}$ 23), 40.7 (C-2), 31.5 (C-4), 25.8 (C-8), 25.4 (*Me*$_3$CSi), 22.9 (C-3), 17.8 (Me_3*C*Si) and −4.8 (Me_2Si); δ_F(56 MHz; $CDCl_3$) −69.5; *m/z* 346 (M^+, 2%), 305 (17) and 75 (100).

6-(*tert*-Butyldimethylsilyloxy)-1,2,3,4,8,8aβ-hexahydro-8a-trifluoromethyl-1α-(trimethylsilylethynyl)naphthalen-1-ol 3

A solution of lithium trimethylsilylacetylide in diethyl ether was prepared by the addition of methyllithium (1.6 M in diethyl ether; 4.75 ml, 7.6 mmol) to a solution of trimethylsilylacetylene (1.07 ml, 7.6 mmol) in diethyl ether (60 ml) kept in an ice-bath under argon. After stirring of the mixture for 1 h at 0 °C, a solution of the ketone **2** (1.85 g, 5.3 mmol) in diethyl ether (20 ml) was added and the reaction mixture was allowed to warm to room temperature overnight. Saturated aq. ammonium chloride (30 ml) was added, the reaction medium was extracted with diethyl ether (3 × 50 ml), the extract was dried (Na_2SO_4) and the solvent was removed *in vacuo*. Silica gel column chromatography (dichloromethane) of the residue gave the acetylenic alcohol **3** (2.14 g, 90%) as an oil; $\nu_{max}(CCl_4)/cm^{-1}$ 2590 and 1650; δ_H(200 MHz; $CDCl_3$) 5.57–5.50 (1 H, m, 5-H), 4.67–4.55 (1 H, m, 7-H), 3.25 (1 H, d, $J_{8\alpha\text{-H},8\beta\text{-H}}$ 18.9, 8α- or 8β-H), 2.67 (1 H, dd, $J_{8\alpha\text{-H},8\beta\text{-H}}$ 18.9, $J_{7\text{-H},8\text{-H}}$ 5.8, 8β- or 8α-H), 2.45 (1 H, s, OH), 2.30–1.60 (6 H, envelope), 0.77 (9 H, s, Bu^tSi), 0.00 (9 H, s, Me_3Si) and −0.03 (6 H, s, Me_2Si); δ_C(50 MHz; $CDCl_3$) 144.9 (C-6), 133.2 (C-5), 127.0 (C-4a), 127.8 (C-9, q, $^1J_{CF}$ 288), 106.4 (*C*≡CSiMe_3), 99.5 (C-7), 94.7 (≡*C*SiMe_3), 76.4 (C-1), 51.1 (C-8a, q, $^2J_{CF}$ 21), 36.2 (C-2), 30.6 (C-4), 27.7 (C-8), 25.4 (*Me*$_3$CSi), 22.6 (C-3), 17.8 (Me_3*C*Si), −0.6 (Me_3Si) and −4.8 (Me_2Si); δ_F(56 MHz; $CDCl_3$) −64.0; *m/z* 429 ($M^+ - 15$, 19%), 337 (50) and 73 (100).

5α-Ethynyl-4,4aβ,5,6,7,8-hexahydro-5-hydroxy-4a-(trifluoromethyl)naphthalen-2(3*H*)-one 4

(*a*) From silylacetylene 3.—A mixture of potassium carbonate (1 g) and the silylacetylene **3** (500 mg, 1.13 mmol) in methanol (40 ml) was stirred for 2 h. The reaction mixture was diluted with dichloromethane (100 ml) and washed with 1 M aq. hydrochloric acid (30 ml). After drying of the organic phase ($MgSO_4$) and removal of the solvents *in vacuo*, the residue was eluted on a column of silica gel (20% diethyl ether–dichloromethane), to afford the *acetylenic ketone* **4** (260 mg, 89%), mp 115–116 °C (from diethyl ether) (Found: C, 60.6; H, 5.1. $C_{13}H_{13}F_3O_2$ requires C, 60.5; H, 5.1%); $\nu_{max}(CCl_4)/cm^{-1}$ 3590, 3290 and 1670; δ_H(200 MHz; $CDCl_3$) 6.03 (1 H, s, 1-H), 3.77 (1 H, s, OH), 2.92–2.74 (1 H, m), 2.64–2.26 (6 H, envelope), 2.59 (1 H, s, C≡CH), 2.01 (1 H, br d, *J* 13.1) and 1.90–1.70 (2 H, envelope); δ_C(50 MHz; $CDCl_3$) 196.5 (C-2), 156.2 (C-8a), 130.6 (C-1), 126.4 (C-9, q, $^1J_{CF}$ 288), 84.5 (*C*≡CH), 76.8 (C-5), 75.7 (C≡*C*H), 52.1 (C-4a, q, $^2J_{CF}$ 22), 36.5 (C-6), 33.5, 32.4 (C-3, -8), 26.0 (C-4) and 21.8 (C-7); δ_F(56 MHz; $CDCl_3$) −58.7; *m/z* 258 (M^+, 14%), 230 (41) and 53 (100). Further elution afforded *methyl* 4,5-*dihydro*-2-*methylnapththo*[1,8-bc]*furan* **15** (15 mg, 6%) (Found: M^+, 230.0943. $C_{14}H_{14}O_3$ requires M, 230.0943); $\nu_{max}(CCl_4)/cm^{-1}$ 1710, 1610 and 1360; δ_H(200 MHz; $CDCl_3$) 7.77 (1 H, d, *J* 8.5, 7- or 8-H), 7.07 (1 H, d, *J* 8.5, 8- or 7-H), 3.80 (3 H, s, CO_2Me), 3.17 (2 H, t, *J* 6.0, 5-H_2), 2.56 (2 H, t, *J* 6.0, 3-H_2), 2.28 (3 H, s, 2-Me) and 1.90 (2 H, quint., *J* 6.0, 4-H_2); δ_C(50 MHz; $CDCl_3$) 167.9 (*C*O_2Me), 154.5 (C-8a), 148.3 (C-2), 136.0 (C-5a), 129.6 (C-6), 126.6, 120.9 (C-7, -8), 112.4 (C-8b), 107.6 (C-2a), 51.5 (CO_2*Me*), 26.5, 23.7 (C-3, -5), 19.6 (C-4) and 12.2. (2-Me); *m/z* 230 (M^+, 100%), 199 (40), 171 (35) and 43 (40).

(*b*) By oxidation of diol 26.—Under standard conditions for the Jones oxidation, 3.10 g (12 mmol) of diol **26** gave 2.89 g (94%) of ketone **4**.

4,4aβ,5,6,7,8-Hexahydro-5β-hydroxy-4a-trifluoromethyl-5-vinylnaphthalen-2(3*H*)-one 5

The acetylenic alcohol **4** (1.16 g, 4.5 mmol) was hydrogenated over Lindlar catalyst in methanol (50 ml) for 4 h. After filtration over a pad of Celite and washing with diethyl ether (100 ml), the solution was concentrated *in vacuo* and the residue was recrystallised from diethyl ether to give the *vinylic alcohol* **5** (1.05 g, 90%), mp 86.5–87.5 °C (Found: C, 59.8; H, 5.8. $C_{13}H_{15}F_3O_2$ requires C, 60.0; H, 5.8%); $\nu_{max}(CCl_4)/cm^{-1}$ 3600, 1670 and 1140; δ_H(200 MHz; $CDCl_3$) 6.08 (1 H, d, *J* 1.7, 1-H), 6.00 (1 H, dd, *J* 16.9 and 10.7, C*H*=CH_2), 5.40 (1 H, dd, *J* 16.9 and 1.1, CH=CH_ZH), 5.15 (1 H, dd, *J* 10.7 and 1.1, CH=CHH_E), 2.54–2.15 (7 H, envelope), 1.90–1.79 (2 H, envelope) and 1.69–1.55 (2 H, envelope); δ_C(50 MHz; $CDCl_3$) 198.1 (C-2), 157.2 (C-8a), 140.5 (C-10), 130.5 (C-1), 126.7 (C-9, q, $^1J_{CF}$ 289), 113.5 (C-11), 77.7 (C-5), 51.7 (C-4a, q, $^2J_{CF}$ 21), 37.1 (C-6), 33.4, 32.6 (C-3, -8), 24.5 (C-4) and 21.2 (C-7); δ_F(56 MHz; $CDCl_3$) −59.0; *m/z* 260 (M^+, 2%), 190 (38) and 55 (100).

5-(2-Chloroethylidene)-4,4a,5,6,7,8-hexahydro-4a-(trifluoromethyl)naphthalen-2(3*H*)-one 6

Pyridine (450 μl, 5.6 mmol) and thionyl dichloride (410 μl, 5.6 mmol) were added to a stirred, cold (0 °C) solution of the vinylic alcohol **5** (980 mg, 3.8 mmol) in dichloromethane (50 ml) kept under argon. After 2 h, the reaction mixture was washed successively with water (10 ml) and saturated aq. $NaHCO_3$ (10 ml). The aqueous layer was back-extracted with dichloromethane (2 × 50 ml) and the pooled organic phases were dried ($MgSO_4$). After concentration *in vacuo*, the residue was eluted on a column of silica gel (10% diethyl ether–dichloromethane) to afford the chloride **6** as an unstable oil (960 mg, 91%) which had $\nu_{max}(CCl_4)/cm^{-1}$ 1670 and 1175; δ_H(200 MHz; $CDCl_3$) 6.00 (1 H,

d, *J* 1.2, 1-H), 5.83 (1 H, t, $J_{10\text{-}H,11\text{-}H}$ 7.3, 10-H), 4.18–3.99 (2 H, envelope, 11-H_2), 2.59–1.85 (9 H, envelope) and 1.53–1.29 (1 H, m); δ_C(50 MHz; $CDCl_3$) 196.5 (C-2), 156.3 (C-8a), 140.6 (C-5), 125.9 (C-9, q, $^1J_{CF}$ 288), 125.8 (C-10), 48.6 (C-4a, q, $^2J_{CF}$ 25), 39.2 (C-11), 33.7, 33.2 (C-8, -3), 29.1 (C-6), 25.8 (C-4) and 23.9 (C-7); δ_F(56 MHz; $CDCl_3$) −66.7.

Condensation of chloride 6 with 2-methylcyclopentane-1,3-dione

A solution of the chloride **6** (900 mg, 3.2 mmol) in anhydrous DMF (30 ml) containing dry sodium iodide (480 mg, 3.2 mmol) was stirred for 30 min under argon. A solution of the sodium salt of 2-methylcyclopentane-1,3-dione (550 mg) in anhydrous methanol (30 ml) was then added and the reaction mixture was stirred overnight. After removal of the solvents under high vacuum, the residue was taken up in dichloromethane (50 ml), filtered and washed well with the same solvent. Concentration of the filtrate, followed by silica gel column chromatography of the residue (diethyl ether gradient in dichloromethane) afforded in order of elution: 4,4a,7,8-*tetrahydro*-4a-*trifluoromethyl*-5-*vinylnaphthalen*-2(3H)-*one* **32** (50 mg, 6%) (Found: M^+, 242.0919. $C_{13}H_{13}F_3O$ requires M, 242.0918); $\nu_{max}(CCl_4)/cm^{-1}$ 1660 and 1160; δ_H(200 MHz; $CDCl_3$) 6.32 (1 H, dd, *J* 16.8 and 10.6, C*H*=CH_2), 6.16 (1 H, dd, *J* 5.0 and 2.1, 6-H), 6.06 (1 H, d, *J* 1.4, 1-H), 5.36 (1 H, dd, *J* 10.6 and 1.5, CH=CHH_E), 5.06 (1 H, dd, *J* 16.8 and 1.5, CH=CH_ZH) and 2.72–1.72 (8 H, envelope); δ_C(50 MHz; $CDCl_3$) 197.0 (C-2), 156.5 (C-8a), 135.0 (C-5), 133.9 (*C*H=CH_2), 128.9 (C-1), 127.9 (C-6), 127.9 (C-9, q, $^1J_{CF}$ 288), 116.5 (CH=*C*H_2), 46.7 (C-4a, q, $^2J_{CF}$ 22), 33.5 (C-3), 30.7 (C-8), 29.1 (C-7) and 26.0 (C-4); δ_F(56 MHz; $CDCl_3$) −65.0; 19,19,19-*trifluoro*-8,14-*secoandrosta*-4,9(11)-*diene*-3,14,17-*trione* **7** (890 mg, 78%), mp 80.5–81.5 °C (from diethyl ether) (Found: C, 64.3; H, 6.0. $C_{19}H_{21}F_3O_3$ requires C, 65.4; H, 6.0%); $\nu_{max}(CCl_4)/cm^{-1}$ 1720, 1670 and 1170; δ_H(200 MHz; $CDCl_3$) 5.95 (1 H, s, 4-H), 5.44 (1 H, t, $J_{11\text{-}H,12\text{-}H}$, 11-H), 2.83–1.84 (15 H, envelope), 1.46–1.26 (1 H, m) and 1.03 (3 H, s, Me); δ_C(50 MHz; $CDCl_3$) 215.8, 215.7 (C-14, -17), 196.6 (C-3), 156.7 (C-5), 138.8 (C-9), 129.6 (C-4), 126.0 (C-19, q, $^1J_{CF}$ 287), 123.4 (C-11), 55.9 (C-13), 48.6 (C-10, q, $^1J_{CF}$ 24), 34.9, 34.7 (C-15, -16), 33.7, 33.3, 33.2 (C-2, -6, -12), 29.2 (C-8), 25.7 (C-1), 24.0 (C-7) and 21.2 (C-18); δ_F(56 MHz; $CDCl_3$) −66.7; *m/z* 354 (M^+, 39%), 113 (30) and 59 (100); 4,4a,5,6,7,8-*hexahydro*-5-[2-(2-*methyl*-3-*oxocyclopent*-1-*enyloxy*)*ethylidene*]-4a-*trifluoromethylnaphthalen*-2(3H)-*one* **33** (120 mg, 10%) (Found: M^+, 354.1442. $C_{19}H_{21}F_3O_3$ requires M, 354.1443); $\nu_{max}(CCl_4)/cm^{-1}$ 1670, 1620 and 1170; δ_H(200 MHz; $CDCl_3$) 6.04 (1 H, d, *J* 1.4, 1-H), 5.79 (1 H, t, $J_{1'\text{-}H,2'\text{-}H}$ 5.4, 1′-H), 4.89–4.70 (2 H, envelope, 2′-H_2), 2.72–1.89 (13 H, envelope), 1.56 (3 H, s, Me) and 1.46–1.26 (1 H, m); δ_C(50 MHz; $CDCl_3$) 204.9 (C-3″), 196.8 (C-2), 183.1 (C-1″), 156.3 (C-8a), 139.4 (C-5), 130.0 (C-1), 125.9 (C-9, q, $^1J_{CF}$ 288), 125.2 (C-1′), 116.3 (C-2″), 65.6 (C-2′), 48.6 (C-4a, q, $^2J_{CF}$ 25), 33.9, 33.4 (C-3, -8, -4″), 29.4 (C-6), 27.0 (C-5″), 25.1 (C-4), 24.1 (C-7) and 5.9 (C-6″); δ_F(56 MHz; $CDCl_3$) −66.7; *m/z* 354 (M^+, 1%), 243 (95), 201 (65) and 84 (100).

Acylation of trione 7

The secosteroid **7** (810 mg, 2.29 mmol) was dissolved in 100 ml of an acylating solution composed of perchloric acid (0.04 ml, 72%), acetic anhydride (9.6 ml) and the rest ethyl acetate. After being stirred for 6 h, the solution was washed with saturated aq. $NaHCO_3$ (40 ml). The aqueous layer was back-extracted with ethyl acetate (4 × 50 ml) and the combined organic phases were dried ($MgSO_4$). After evaporation *in vacuo*, the residue was eluted on a silica gel column (5% diethyl ether–dichloromethane) to afford, in order of elution, 3-*acetoxytrifluoro*-8,14-*secoandrosta*-3,5,9(11)-*triene*-14,17-*dione* **8** (630 mg, 70%) (Found: M^+, 396.1548. $C_{21}H_{23}F_3O_4$ requires M, 396.1548); $\nu_{max}(CCl_4)/cm^{-1}$ 1750, 1720, 1600 and 1160; δ_H(200 MHz; $CDCl_3$) 5.96 (1 H, t, $J_{H\text{-}6,H\text{-}7}$ 4.9, 6-H), 5.83 (1 H, d, *J* 2.0, 4-H), 5.39 (1 H, t, $J_{11\text{-}H,12\text{-}H}$ 8.0, 11-H), 2.75–2.01 (13 H, envelope), 2.07 (3 H, s, OAc), 1.74–1.53 (1 H, m) and 1.07 (3 H, s, Me); δ_C(50 MHz; $CDCl_3$) 216.8, 216.5 (C-14, -17), 168.9 (O*C*OMe), 147.3 (C-3), 139.1 (C-9), 132.3 (C-5), 129.1 (C-6), 127.2 (C-19, q, $^1J_{CF}$ 288), 121.3 (C-11), 117.0 (C-4), 56.3 (C-13), 45.1 (C-10, q, $^2J_{CF}$ 25), 35.3, 35.0 (C-15, -16), 34.2 (C-12), 28.8 (C-8), 24.9 (C-1), 23.8 (C-2, -7), 20.9 (OCO*Me*) and 19.3 (C-18); δ_F(56 MHz; $CDCl_3$) −69.7; *m/z* 396 (M^+, 2%), 354 (33), 245 (15), 220 (37) and 205 (100); and 3,17-*diacetoxy*-19,19,19-*trifluoro*-8,14-*secoandrosta*-3,5,9(11),16-*tetraen*-14-*one* **34** (160 mg, 16%) (Found: M^+, 438.1656. $C_{23}H_{25}F_3O_5$ requires M, 438.1654) as a diastereoisomeric mixture which had $\nu_{max}(CCl_4)/cm^{-1}$ 1750, 1730 and 1130; δ_H(200 MHz; $CDCl_3$, signals indicated by * show further apparent splitting owing to the presence of two diastereoisomers) 5.97–5.89 (1 H, m, 6-H), 5.88–5.85 (1 H, m, 16-H), 5.83 (1 H, d, *J* 2.0, 4-H), 5.56–5.37 (1 H, m, 11-H), 2.95 (1 H, dd*, $J_{15\alpha\text{-}H,15\beta\text{-}H}$ 22.9, $J_{15\text{-}H,16\text{-}H}$ 2.5, 15α- or 15β-H), 2.76 (1 H, dd*, $J_{15\alpha\text{-}H,15\beta\text{-}H}$ 22.9, $J_{15\text{-}H,16\text{-}H}$ 6.9, 15β- or 15α-H), 2.60–2.15 (9 H, envelope), 2.15 (3 H, s*, 17-OAc), 2.07 (3 H, s, 3-OAc), 1.80–1.60 (1 H, m) and 1.08 (3 H, s, Me); δ_C(50 MHz; $CDCl_3$, * indicates the presence of diastereoisomers) 215.9 and 215.7 (C-14*), 168.8 (3-O*C*OMe), 167.95, 167.9 (17-O*C*OMe*), 151.8 and 151.0 (C-17*), 147.3 (C-3), 137.6 and 137.5 (C-9*), 132.15 and 132.0 (C-5*), 129.3 and 129.2 (C-6*), 127.2 (C-19, q, $^1J_{CF}$ 287), 122.3 (C-11), 117.0 (C-4), 108.6 and 108.1 (C-16*), 53.2 and 53.0 (C-13*), 45.0 (C-10, q, $^2J_{CF}$ 26), 41.1 and 40.8 (C-15*), 34.2 and 34.0 (C-12*), 28.7 (C-8), 24.9 (C-1), 23.9 and 23.8 (C-18*), 23.5 (C-2, -7), 21.0 and 20.8 (17-OCO*Me*) and 20.3 (3-OCO*Me*); δ_F(56 MHz; $CDCl_3$) −69.7; *m/z* 438 (M^+, 3%), 396 (30), 354 (17), 241 (22), 205 (58) and 149 (100).

3-Ethoxy-19,19,19-trifluoro-8,14-secoandrosta-3,5,9(11)-triene-14,17-dione 9

Ethyl orthoformate (10 ml) was added to a solution of the secosteroid **7** (1.26 g, 3.6 mmol) in 1,4-dioxane (40 ml) containing toluene-*p*-sulfonic acid (PTSA) (0.2 g). The solution was stirred for 6 h, then was diluted with dichloromethane (100 ml) and washed with saturated aq. $NaHCO_3$. After extraction with dichloromethane (2 × 50 ml) and drying of the organic phases ($MgSO_4$), the residue obtained upon evaporation of the mixture *in vacuo* was eluted on a silica gel column (5% diethyl ether–dichloromethane) affording the enol ether **9** (1.01 g, 74%) and 270 mg of starting material; compound **9** had $\nu_{max}(CCl_4)/cm^{-1}$ 1750, 1720, 1640 and 1170; δ_H(200 MHz; $CDCl_3$) 5.79–5.65 (1 H, m, 6-H), 5.37 (1 H, t, $J_{11\text{-}H,12\text{-}H}$ 7.8, 11-H), 5.20 (1 H, s, 4-H), 3.70 (2 H, q, *J* 7.0, OCH_2Me), 2.72–2.00 (13 H, envelope), 1.66–1.50 (1 H, m), 1.22 (3 H, t, *J* 7.0, OCH$_2$*Me*) and 1.06 (3 H, s, Me); δ_C(50 MHz; $CDCl_3$) 216.8, 216.5 (C-14, -17), 154.7 (C-3), 139.7 (C-9), 130.4 (C-5), 126.9 (C-19, q, $^1J_{CF}$ 288), 125.6 (C-6), 120.7 (C-11), 99.2 (C-4), 62.2 (O*C*H$_2$Me), 56.1 (C-13), 45.3 (C-10, q, $^2J_{CF}$ 24), 35.1, 34.9 (C-15, -16), 34.2 (C-12), 28.8 (C-8), 25.5 (C-1), 23.9, 23.4 (C-2, -7), 18.9 (C-18) and 14.1 (OCH$_2$*Me*); δ_F(56 MHz; $CDCl_3$) −69.3.

6α- and 6β-Bromo-19,19,19-trifluoro-8,14-secoandrosta-4,9(11)-diene-3,14,17-trione 10 and 11

Pyridine (410 μl), acetic acid (650 μl), sodium acetate (650 mg), water (7.5 ml) and *N*-bromosuccinimide (NBS) (280 mg, 1.6 mmol) were successively added to a stirred solution of the enol acetate **8** (620 mg, 1.6 mmol) in acetone (50 ml) cooled to 0 °C. After 1.5 h, the reaction mixture was diluted with dichloromethane (100 ml) and washed with saturated aq. $NaHCO_3$. After drying ($MgSO_4$) and removal of the solvent *in vacuo*, the residue was eluted through a column of silica gel (10% diethyl ether–dichloromethane) to give the 6α-*bromide* **10** (450 mg) and its 6β-isomer **11** (100 mg, combined yield 81%). An analytical sample of the *bromide* **10** was obtained by crystallisation from diethyl ether, mp 94.5–95.5 °C (Found: C, 52.6; H, 4.6. $C_{19}H_{20}BrF_3O_3$ requires C, 52.7; H, 4.65%); $\nu_{max}(CCl_4)/cm^{-1}$ 1720, 1680 and 1170; δ_H(200 MHz; $CDCl_3$) 6.68 (1 H, d, $J_{4\text{-}H,6\beta\text{-}H}$ 1.8, 4-H), 5.51 (1 H, t, $J_{11\text{-}H,12\text{-}H}$ 8.2, 11-H), 4.95 (1 H, ddd,

$J_{6\beta\text{-H},7\alpha\text{-H}}$ 11.0, $J_{6\beta\text{-H},7\beta\text{-H}}$ 4.7, $J_{\mathbf{4\text{-H},6\beta\text{-H}}}$ 1.8, 6β-H), 2.86–1.85 (14 H, envelope) and 1.08 (3 H, s, Me); $\delta_{\mathbf{C}}$(50 MHz; $CDCl_3$) 215.7, 215.6 (C-14, -17), 196.6 (C-3), 152.4 (C-5), 136.2 (C-9), 132.7 (C-4), 125.9 (C-19, q, $^1J_{\mathbf{CF}}$ 287), 124.8 (C-11), 56.3 (C-13), 50.2 (C-10, q, $^2J_{\mathbf{CF}}$ 25), 50.0 (C-6), 35.6 (C-7), 35.1, 34.9 (C-15, -16), 33.3, 33.1 (C-2, -12), 30.1 (C-8), 26.5 (C-1) and 19.8 (C-18); $\delta_{\mathbf{F}}$(188 MHz; $CDCl_3$) −66.3; *m/z* 321, 323 (15%), 241 (25) and 113 (100).

The isomeric 6β-bromide **11** had $\delta_{\mathbf{H}}$(200 MHz; $CDCl_3$) 6.26 (1 H, s, 4-H), 5.50 (1 H, t, $J_{\mathbf{11\text{-H},12\text{-H}}}$ 8.0, 11-H), 4.99 (1 H, t, $J_{6\alpha\text{-H},7\text{-H}}$ 5.2, 6α-H), 2.85–1.80 (14 H, envelope) and 1.09 (3 H, s, Me); $\delta_{\mathbf{F}}$(188 MHz; $CDCl_3$) −65.0.

19,19,19-Trifluoro-8,14-secoandrosta-4,6,9(11)-triene-3,14,17-trione 12

A solution of the mixture of preceding bromides **10** and **11** (500 mg, 1.15 mmol) in dichloromethane (35 ml), containing 2,6-di-*tert*-butyl-4-methylpyridine (360 mg, 1.75 mmol) and silver trifluoromethanesulfonate (450 mg, 1.75 mmol), and kept under argon, was stirred in the dark overnight. After filtration over a pad of Celite and removal of the solvent *in vacuo*, the residue was eluted through a column of silica gel (10% diethyl ether in dichloromethane) to afford the *triene* **12** (365 mg, 90%), mp 114–115 °C (from diethyl ether) (Found: C, 64.9; H, 5.4. $C_{19}H_{19}F_3O_3$ requires C, 64.8; H, 5.4%); $\nu_{\mathbf{max}}(CCl_4)/cm^{-1}$ 1730, 1660 and 1590; $\delta_{\mathbf{H}}$(200 MHz; $CDCl_3$) 6.33–6.15 (2 H, envelope, 6- and 7-H), 5.95 (1 H, s, 4-H), 5.53 (1 H, $J_{\mathbf{11\text{-H},12\text{-H}}}$ 6.9, 11-H), 3.25 and 2.95 (2 H, AB quartet, *J* 22.7, 8α- and 8β-H), 2.86–2.31 (9 H, envelope), 2.08–1.91 (1 H, m) and 1.09 (3 H, s, Me); $\delta_{\mathbf{C}}$(50 MHz; $CDCl_3$) 215.8, 215.7 (C-14, -17), 197.0 (C-3), 148.3 (C-5), 136.2 (C-9), 132.9, 128.3 (C-4, -7), 126.6 (C-6), 125.6 (C-19, q, $^1J_{\mathbf{CF}}$ 287), 124.9 (C-11), 55.8 (C-13), 46.1 (C-10, q, $^2J_{\mathbf{CF}}$ 25), 34.9, 34.7 (C-15, -16), 33.1, 32.8 (C-2, -12), 28.2 (C-8), 27.6 (C-1) and 19.3 (C-18); $\delta_{\mathbf{F}}$(188 MHz; $CDCl_3$) −70.7; *m/z* (CI, NH_3) 370 ($MH^+ + NH_3$, 20%), 353 (MH^+, 36) and 241 (100).

19,19,19-Trifluoro-14β-hydroxyandrosta-4,6,9(11)-triene-3,17-dione 13 and 19,19,19-trifluoro-14α-hydroxy-13α-androsta-4,6,9(11)-triene-3,17-dione 14

Dry, powdered sodium methoxide (200 mg, 3.7 mmol) was added to a stirred, cold (0 °C) solution of the secosteroid **12** (260 mg, 0.74 mmol) in anhydrous methanol (20 ml) kept under a stream of argon. After 2 h, the reaction mixture was neutralised by the addition of acetic acid. The solvent was removed *in vacuo* and the residue was taken up in ethyl acetate (50 ml) and washed with saturated aq. $NaHCO_3$ (10 ml). After drying (Na_2SO_4) and concentration, the residue was eluted through a column of silica gel (30% ethyl acetate–diethyl ether) to give the 14β-alcohol **13** (169 mg, 65%), mp 252–253 °C (from propan-2-ol) (Found: C, 64.6; H, 5.35. Calc. for $C_{19}H_{19}F_3O_3$: C, 64.8; H, 5.4%); $\nu_{\mathbf{max}}(CCl_4)/cm^{-1}$ 3600, 1740, 1670, 1620 and 1150; $\delta_{\mathbf{H}}$(200 MHz; $CDCl_3$) 6.50 (1 H, dd, $J_{\mathbf{6\text{-H},7\text{-H}}}$ 10.2, $J_{\mathbf{H,8\text{-H}}}$ 1.8, 6- or 7-H), 6.42 (1 H, dd, $J_{\mathbf{6\text{-H},7\text{-H}}}$ 10.2 and $J_{\mathbf{H,8\text{-H}}}$ 2.3, 7- or 6-H), 6.01 (1 H, s, 4-H), 5.84 (1 H, q, $J_{\mathbf{11\text{-H},12\text{-H}}}$, $J_{\mathbf{8\text{-H},11\text{-H}}}$ 3.2, 11-H), 3.22 (1 H, br s, 8-H), 2.73–2.05 (8 H, envelope), 1.83–1.55 (3 H, envelope) and 1.07 (3 H, s, Me); $\delta_{\mathbf{C}}$(50 MHz; $CDCl_3$) 217.3 (C-17), 197.3 (C-3), 148.5 (C-5), 135.8 (C-9), 130.1, 128.9 (C-4, -7), 128.9 (C-6), 126.0 (C-19, q, $^1J_{\mathbf{CF}}$ 286), 124.6 (C-11), 80.1 (C-14), 51.0 (C-13), 46.1 (C-10, q, $^2J_{\mathbf{CF}}$ 26), 42.7 (C-8), 33.8 (C-16), 33.3, 33.2 (C-2, -12), 27.8, 27.2 (C-1, -15) and 13.5 (C-18); $\delta_{\mathbf{F}}$(188 MHz; $CDCl_3$) −70.0; *m/z* 352 (M^+, 5%), 240 (100) and 171 (87). Further elution with the same eluent as before afforded the isomeric 14α-*alcohol* **14** (39 mg, 15%), which had mp 253–254 °C (from propan-2-ol) (Found: C, 64.6; H, 5.6%); $\nu_{\mathbf{max}}(CCl_4)/cm^{-1}$ 3600, 1740, 1670 and 1170; $\delta_{\mathbf{H}}$(200 MHz; $CDCl_3$) 6.49 (1 H, dd, $J_{\mathbf{6\text{-H},7\text{-H}}}$ 10.3, $J_{\mathbf{H,8\text{-H}}}$ 2.3, 6- or 7-H), 6.39 (1 H, dd, $J_{\mathbf{6\text{-H},7\text{-H}}}$ 10.3, $J_{\mathbf{H,8\text{-H}}}$ 2.1, 7- or 6-H), 5.98 (1 H, s, 4-H), 5.92 (1 H, q, $J_{\mathbf{11\text{-H},12\text{-H}}}$, $J_{\mathbf{8\text{-H},11\text{-H}}}$ 3.1, 11-H), 2.88 (1 H, br s, 8-H), 2.81–1.89 (11 H, envelope) and 1.07 (3 H, s, Me); $\delta_{\mathbf{C}}$(50 MHz; $CDCl_3$) 215.3 (C-17), 197.3 (C-3), 147.8 (C-5), 135.4 (C-9), 128.9 (C-4, -7), 127.7 (C-6), 127.4 (C-11), 77.7 (C-14), 51.1 (C-13), 46.0 (C-10, q, $^2J_{\mathbf{CF}}$ 26), 41.2 (C-8), 33.5 (C-16), 33.3 (C-2), 29.4, 29.2 (C-12, -15), 27.8 (C-1) and 13.5 (C-18). Carbon C-19 could not be located on the spectrum due to the poor solubility of the compound; $\delta_{\mathbf{F}}$(188 MHz; $CDCl_3$) −70.0; *m/z* 352 (M^+, 2%), 240 (100) and 171 (87).

Crystal data for 19,19,19-trifluoro-14α-hydroxy-13α-androsta-4,6,9(11)-triene-3,17-dione 14

A crystal was obtained as a prism from propan-2-ol with approximate dimensions 0.6 × 0.5 × 0.4 mm^3 and used for data collection. $C_{19}H_{19}F_3O_3$, M = 352.34, monoclinic, space group $P2_1/a$, with a = 22.373(9), b = 9.580(4), c = 7.604(4) Å, β = 97.11(2)°, V = 1617(1) $Å^3$, D_x = 1.447 g cm^{-3}, Z = 4, μ(Cu-Kα) = 1.021 mm^{-1}, $F(000)$ = 736.

Data collection and processing. —Intensities were measured on a Philips PW 1100 automatic four-circle diffractometer operating in the $\theta/2\theta$ mode using graphite-monochromated Cu-Kα radiation, λ = 1.5418 Å, T = 294(2) K, 4888 reflections measured ($5.0 \leqslant \theta \leqslant 62.0°$, $-25 \leqslant h \leqslant 25$, $-10 \leqslant k \leqslant 10$, $0 \leqslant l \leqslant 8$), 2534 unique reflections used ($R_{\mathbf{int}}$ = 0.0307). Lorentz and polarisation corrections were applied, none for absorption.

Structure analysis and refinement. —The structure was solved by direct methods using SHELXS86.[29] Refinement was carried out using intensities, F^2, in SHELXL-93.[30] All hydrogen atoms were located on difference-Fourier syntheses and refined. Full-matrix least-squares refinement of 302 parameters for 2294 independent reflections [$I \geqslant 2\sigma(I)$] gave final R_1- and wR_2-values of 0.047 and 0.108 (R_1 = 0.051 and wR_2 = 0.111 for all 2534 data). The atomic coordinates, thermal parameters, and bond lengths and angles are available from the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/115. Lists of observed and calculated structure factors and anisotropic thermal parameters are available from one of us (J. G.) The X-ray structure is presented in Fig. 1.

19,19,19-Trifluoro-14β-hydroxyandrosta-4,9(11)-diene-3,17-dione 16

A mixture containing the triene **13** (280 mg, 0.80 mmol), ethanol (20 ml), cyclohexene (1.2 ml) and the hydrogenation catalyst (10% Pd–C, 0.14 g) was refluxed for 2 h. After filtration over a pad of Celite and removal of the solvents *in vacuo*, the residue was dissolved in benzene (20 ml) containing a catalytic amount of PTSA and the solution was refluxed for 1 h. After evaporation of the benzene under reduced pressure the solid obtained was dissolved in dichloromethane and the solution was washed with saturated aq. $NaHCO_3$ (10 ml). After drying ($MgSO_4$) and removal of the solvent *in vacuo*, the crude product was purified by elution through a column of silica gel (diethyl ether) to give the *alcohol* **16** (268 mg, 95%), mp 175.5–176.5 °C (from diethyl ether) (Found: C, 64.4; H, 5.9. $C_{19}H_{21}F_3O_3$ requires C, 64.4; H, 6.0%); $\nu_{\mathbf{max}}(CCl_4)/cm^{-1}$ 3600, 1740, 1670 and 1140; $\delta_{\mathbf{H}}$(200 MHz; $CDCl_3$) 6.06 (1 H, s, 4-H), 5.96–5.68 (1 H, m, 11-H), 2.75–1.26 (16 H, envelope) and 1.10 (3 H, s, Me); $\delta_{\mathbf{C}}$(50 MHz; $CDCl_3$) 218.4 (C-17), 197.6 (C-3), 156.8 (C-5), 134.5 (C-9), 129.9 (C-4), 126.3 (C-19, q, $^1J_{\mathbf{CF}}$ 288), 124.3 (C-11), 80.5 (C-14), 51.3 (C-13), 48.1 (C-10, q, $^2J_{\mathbf{CF}}$ 25), 42.5 (C-8), 34.3 (C-16), 33.7, 32.5 (C-2, -12), 29.7 (C-6 and -15), 27.8 (C-1), 24.6 (C-7) and 12.8 (C-18); $\delta_{\mathbf{F}}$(56 MHz; $CDCl_3$) −68.0; *m/z* 354 (M^+, 2%), 243 (44) and 113 (100).

19,19,19-Trifluoroandrosta-4,9(11),14-triene-3,17-dione 17

Thionyl dichloride (105 μl, 1.44 mmol) was added to a stirred solution of alcohol **16** (250 mg, 0.71 mmol) in pyridine (2 ml) cooled to 0 °C. After 5 min, the reaction mixture was quenched with ice, followed by saturated aq. $NaHCO_3$ (10 ml). The aqueous layer was extracted with diethyl ether (3 × 50 ml), and

the organic phase was dried ($MgSO_4$). After removal of the solvents *in vacuo*, the residue was eluted on a column of silica gel (10% diethyl ether in dichloromethane) to give the *triene* **17** (205 mg, 86%), mp 173.5–174.5 °C (from diethyl ether) (Found: C, 67.7; H, 5.7. $C_{19}H_{19}F_3O_2$ requires C, 67.8; H, 5.7%); $\nu_{max}(CCl_4)/cm^{-1}$ 1740, 1730, 1670 and 1130; δ_H(200 MHz; $CDCl_3$) 6.06 (1 H, s, 4-H), 5.87 (1 H, dt, *J* 5.0 and 2.6, 11-H), 5.57 (1 H, q, $J_{15\text{-}H,16\text{-}H}$, $J_{8\text{-}H,15\text{-}H}$ 2.1, 15-H), 3.21 (1 H, br d, $J_{7\alpha\text{-}H,8\text{-}H}$10.8, 8-H), 3.07–2.75 (2 H, envelope, 16-H_2), 2.71–2.01 (9 H, envelope), 1.50–1.30 (1 H, m) and 1.11 (3 H, s, Me); δ_C(50 MHz; $CDCl_3$) 220.6 (C-17), 197.3 (C-3), 156.5 (C-5), 148.2 (C-14), 134.9 (C-9), 129.9 (C-4), 126.5 (C-11), 126.4 (C-19, q, $^1J_{CF}$ 288), 114.5 (C-15), 48.7 (C-13), 48.2 (C-10, q, $^2J_{CF}$ 25), 41.2 (C-8), 36.0 (C-16), 34.9, 33.8, 33.6 (C-2, -7, -12), 29.4 (C-6), 27.4 (C-1) and 20.2 (C-18); δ_F(56 MHz; $CDCl_3$) −67.7; *m/z* 336 (M^+, 43%), 308 (52), 239 (100) and 113 (60).

5β-Acetoxy-2,3,4,4a,5,6,7,8-octahydro-4a-(trifluoromethyl)-naphthalen-2β-ol 21

Sodium borohydride (540 mg, 14.3 mmol) was added to a stirred solution of a mixture of alkenes **18** and **19** (3.92 g, 14.2 mmol) in THF (50 ml)–methanol (5 ml) kept in an ice-bath. After stirring of the mixture for 2 h, brine (20 ml) was added and the aqueous phase was extracted with diethyl ether (3 × 50 ml). The residue obtained upon drying ($MgSO_4$) and removal of the solvents *in vacuo*, was eluted on a column of silica gel (10% diethyl ether–dichloromethane) to afford the alcohol **21** (2.49 g, 63%) as a solid. Mp ranged from 60 to 100 °C depending on the run; $\nu_{max}(CCl_4)/cm^{-1}$ 3580, 1720, 1650 and 1440; δ_H(200 MHz; $CDCl_3$) 5.78 (1 H, br s, 1-H), 4.73–4.55 (1 H, m, 5-H), 4.17–4.05 (1 H, m, 2-H), 2.38 (1 H, s, OH), 2.24–1.28 (10 H, envelope) and 2.02 (3 H, s, OAc); δ_C(50 MHz; $CDCl_3$) 170.2 (O*C*OMe), 135.6, 134.2 (C-8a, -1), 127.0 (C-9, q, $^1J_{CF}$ 288), 72.2 (C-5), 65.2 (C-2), 47.8 (C-4a, q, $^1J_{CF}$ 22), 31.8 (C-8), 27.6 (C-6), 26.9 (C-3, -4), 23.8 (C-7) and 20.5 (OCO*Me*); δ_F(56 MHz; $CDCl_3$) −60.3; *m/z* 234 (10%), 216 (20), 131 (70) and 43 (100). Further elution afforded the *isomeric alcohol* **20** (1.22 g, 31%), mp 101–102 °C (Found: C, 56.2; H, 6.2. $C_{13}H_{17}F_3O_3$ requires C, 56.1; H, 6.2%); $\nu_{max}(CCl_4)/cm^{-1}$ 3600, 1720 and 1370; δ_H(200 MHz; $CDCl_3$) 5.65–5.55 (2 H, envelope, 7-, 8-H), 5.50 (1 H, t, $J_{5\text{-}H,6\text{-}H}$ 7.7, 5-H), 3.72–3.63 (1 H, m, 2-H), 2.70–1.20 (10 H, envelope) and 2.10 (3 H, s, OAc); δ_C(50 MHz; $CDCl_3$) 170.3 (O*C*OMe), 128.6, 123.1 (C-7, -8), 128.0 (C-9, q, $^1J_{CF}$ 287), 68.2 (C-5), 65.3 (C-2), 43.9 (C-4a, q, $^2J_{CF}$ 22), 39.8 (C-8a), 35.8 (C-6), 29.3, 29.0 (C-1, -3), 23.7 (C-4) and 20.5 (OCO*Me*); δ_F(56 MHz; $CDCl_3$) −69.7; *m/z* 159 (15%), 131 (90) and 43 (100).

1β-Acetoxy-6β-(*tert*-butyldimethylsilyloxy)-1,2,3,4,4a,5,6,7,8,8aβ-octahydro-8a-(trifluoromethyl)naphthalene 22

2,6-Lutidine (5.07 ml, 43.5 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (5.0 ml, 21.8 mmol) were added at 0 °C to a solution of alcohol **21** (5.50 g, 19.8 mmol) in dichloromethane (100 ml) kept under argon. The mixture was stirred for 2 h, the solvent was removed *in vacuo*, and the residue was eluted on a column of silica gel (dichloromethane) to afford the *silyl ether* **22** (7.37 g, 95%) as an oil (Found: M^+, 392.1992. $C_{19}H_{31}F_3O_3Si$ requires M, 392.1994); $\nu_{max}(CCl_4)/cm^{-1}$ 1720 and 1170; δ_H(200 MHz; $CDCl_3$) 5.69 (1 H, s, 5-H), 4.87–4.71 (1 H, m, 1-H), 4.20–4.04 (1 H, m, 6-H), 2.25–1.20 (10 H, envelope), 1.99 (3 H, s, OAc), 0.82 (9 H, s, Bu^{t}Si) and 0.00 (6 H, s, Me_2Si); δ_C(50 MHz; $CDCl_3$) 170.0 (O*C*OMe), 133.9 (C-4a), 133.2 (C-5), 127.3 (C-9, q, $^1J_{CF}$ 288), 77.1 (C-1), 66.5 (C-6), 48.2 (C-8a, q, $^2J_{CF}$ 23), 32.1 (C-4), 27.8 (C-2), 27.2 (C-8), 26.9 (C-7), 25.8 (*Me*$_3$CSi), 24.2 (C-3), 20.7 (OCO*Me*), 18.1 (Me_3*C*Si) and −4.7 (Me_2Si); δ_F(56 MHz; $CDCl_3$) −61.0; *m/z* 392 (M^+, 2%), 335 (10), 275 (30), 201 (50) and 117 (100).

6β-(*tert*-Butyldimethylsilyloxy)-1,2,3,4,6,7,8,8aβ-octahydro-8a-(trifluoromethyl)naphthalen-1β-ol 23

Potassium carbonate (2 g) was added to a solution of acetate **22** (7.36 g, 18.8 mmol) in methanol (100 ml) and the mixture was stirred for 3 h. Methanol was removed *in vacuo* and the solid residue was taken up in water (30 ml), neutralised with 1 M aq. hydrochloric acid and extracted with diethyl ether (3 × 60 ml). Drying ($MgSO_4$), and removal of the solvent *in vacuo*, afforded the crude *alcohol* **23** (6.18 g, 94%) which was used without further purification for the next oxidation step. *Alcohol* **23** had mp 85–86 °C (from diethyl ether) (Found: M^+, 350.1890. $C_{17}H_{29}F_3O_2Si$ requires M, 350.1889); $\nu_{max}(CCl_4)/cm^{-1}$ 3600 and 1130; δ_H(200 MHz; $CDCl_3$) 5.62 (1 H, s, 5-H), 4.18–4.04 (1 H, m, 6-H), 3.44–3.26 (1 H, m, 1-H), 2.60–1.20 (11 H, envelope), 0.82 (9 H, s, Bu^{t}Si) and 0.00 (6 H, s, Me_2Si); δ_C(50 MHz; $CDCl_3$) 134.5 (C-4a), 133.7 (C-5), 127.8 (C-9, q, $^1J_{CF}$ 288), 78.0 (C-1), 66.8 (C-6), 49.0 (C-8a, q, $^2J_{CF}$ 21), 32.3 (C-4), 31.2 (C-2), 28.1, 27.5 (C-7, -8), 25.8 (*Me*$_3$CSi), 24.4 (C-3), 18.1 (Me_3*C*Si) and −4.7 (Me_2Si); δ_F(56 MHz; $CDCl_3$) −59.5; *m/z* 350 (M^+, 1%), 201 (20), 131 (60) and 75 (100).

6β-(*tert*-Butyldimethylsilyloxy)-3,4,6,7,8,8aβ-hexahydro-8a-(trifluoromethyl)naphthalen-1(2*H*)-one 24

A solution of alcohol **23** (6.0 g, 17.1 mmol) and PCC (7.39 g, 34.3 mmol) in dichloromethane (100 ml) was stirred for 8 h. The precipitate was removed by filtration over a pad of Celite and was washed with diethyl ether. Concentration of the filtrate *in vacuo*, followed by silica gel column chromatography (10% diethyl ether–dichloromethane), afforded the *ketone* **24** (5.61 g, 94%) as an oil (Found: M^+, 348.1733. $C_{17}H_{27}F_3O_2Si$ requires M, 348.1732); $\nu_{max}(CCl_4)/cm^{-1}$ 1710 and 1140; δ_H(200 MHz; $CDCl_3$) 5.75 (1 H, s, 5-H), 4.16–4.02 (1 H, m, 6-H), 2.70–1.20 (10 H, envelope), 0.83 (9 H, s, Bu^{t}Si) and 0.00 (6 H, s, Me_2Si); δ_C(50 MHz; $CDCl_3$) 203.7 (C-1), 134.7 (C-4a), 133.2 (C-5), 125.2 (C-9, q, $^1J_{CF}$ 287), 66.5 (C-6), 57.7 (C-8a, q, $^2J_{CF}$ 23), 40.3 (C-2), 31.9 (C-4), 28.4 (C-7), 25.7 (*Me*$_3$CSi), 24.7 (C-8), 23.7 (C-3), 18.0 (Me_3*C*Si) and −4.7 (Me_2Si); δ_F(56 MHz; $CDCl_3$) −64.7; *m/z* 348 (M^+, 1%) and 291 (100).

6β-(*tert*-Butyldimethylsilyloxy)-1,2,3,4,6,7,8,8aβ-octahydro-8a-trifluoromethyl-1α-(trimethylsilylethynyl)naphthalen-1-ol 25

A solution of lithium trimethylsilylacetylide in diethyl ether was prepared by the addition of methyllithium (1.6 M in diethyl ether; 13.2 ml, 21.1 mmol) to a solution of trimethylsilylacetylene (2.98 ml, 21.1 mmol) in diethyl ether (100 ml) kept in an ice-bath under argon. After stirring of the mixture for 2 h at 0 °C, a solution of the ketone **24** (4.90 g, 14 mmol) in diethyl ether (20 ml) was added and the reaction mixture was allowed to warm to room temperature overnight. After addition of saturated aq. ammonium chloride (30 ml) the reaction medium was extracted with diethyl ether (3 × 50 ml), the extract was dried (Na_2SO_4) and the solvent was removed *in vacuo*. Silica gel column chromatography (dichloromethane) of the residue, followed by recrystallisation from diethyl ether, gave the *acetylenic alcohol* **25** (5.87 g, 93%), mp 69.5–70.5 °C (Found: C, 59.2; H, 8.2. $C_{22}H_{37}F_3O_2Si_2$ requires C, 59.15; H, 8.3%); $\nu_{max}(CCl_4)/cm^{-1}$ 3580 and 1140; δ_H(200 MHz; $CDCl_3$) 5.60 (1 H, s, 5-H), 4.11–3.97 (1 H, m, 6-H), 2.39–1.42 (11 H, envelope), 0.74 (9 H, s, Bu^{t}Si), 0.00 (9 H, s, Me_3Si) and −0.08 (6 H, s, Me_2Si); δ_C(50 MHz; $CDCl_3$) 134.6 (C-4a), 132.9 (C-5), 27.4 (C-9, q, $^1J_{CF}$ 288), 107.1 (*C*≡C-SiMe$_3$), 91.6 (C≡*C*-SiMe$_3$), 76.7 (C-1), 67.4 (C-6), 51.5 (C-8a, q, $^2J_{CF}$ 21), 36.8 (C-2), 31.7 (C-4), 28.8 (C-7), 25.9 (*Me*$_3$CSi), 25.3 (C-8), 23.3 (C-3), 18.2 (Me_3*C*Si), −0.4 (Me_3Si) and −4.7 (Me_2Si); δ_F(56 MHz; $CDCl_3$) −58.3; *m/z* 446 (M^+, 2%), 295 (40), 155 (100) and 75 (90).

1α-Ethynyl-1,2,3,4,6,7,8,8aβ-octahydro-8a-(trifluoromethyl)-naphthalene-1β,6β-diol 26

A solution of TBAF (1.1 M; 35.5 ml, 39 mmol) in THF was added to a solution of the silyl ether **25** (5.80 g, 13 mmol) in the same solvent (100 ml), upon which the reaction mixture turned red. Stirring was continued for 30 h, aq. 1 M hydrochloric acid was then added until discoloration of the solution, followed by brine (30 ml). After extraction with diethyl ether (3 × 50 ml)

and drying (Na_2SO_4), the residue obtained after evaporation of the mixture *in vacuo* was eluted on a silica gel column (30% diethyl ether–dichloromethane), and recrystallisation from diethyl ether afforded the *diol* **26** (3.12 g, 92%), mp 131–132 °C (Found: C, 60.0; H, 5.8. $C_{13}H_{15}F_3O_2$ requires C, 60.0; H, 5.8%); $\nu_{max}(CCl_4)/cm^{-1}$ 3600, 3300 and 1140; δ_H(200 MHz; $CDCl_3$) 5.78 (1 H, s, 5-H), 4.22–4.04 (1 H, m, 6-H), 2.47 (1 H, s, C≡CH) and 2.49–1.52 (12 H, envelope); δ_C(50 MHz; $CDCl_3$) 134.1 (C-4a), 133.2 (C-5), 127.2 (C-9, q, $^1J_{CF}$ 288), 85.4 (*C*≡CH), 76.2 (C-1), 75.2 (C≡*C*H), 66.1 (C-6), 51.4 (C-8a, q, $^1J_{CF}$ 22), 37.2 (C-2), 31.7 (C-4), 28.5 (C-7), 25.0 (C-8) and 23.0 (C-3); δ_F(56 MHz; $CDCl_3$) −58.3; *m/z* 260 (M^+, 2%), 242 (20), 174 (100) and 70 (90).

1,2,3,4,6,7,8,8aβ-Octahydro-8a-(trifluoromethyl)naphthalene-1β,6β-diol 27

Potassium carbonate (0.6 g) was added to a solution of acetate **21** (1.2 g, 4.3 mmol) in methanol (50 ml) and the mixture was stirred for 3 h. Methanol was removed *in vacuo* and the solid residue was taken up in water (20 ml), neutralised with 1 M aq. hydrochloric acid and extracted with diethyl ether (3 × 50 ml). After drying (Na_2SO_4), and removal of the solvent *in vacuo*, crystallisation from diethyl ether afforded the *diol* **27** (0.98 g, 96%) which had mp 126.5–127.5 °C (Found: C, 56.05; H, 6.5. $C_{11}H_{15}F_3O_2$ requires C, 55.9; H, 6.4%); $\nu_{max}(CCl_4)/cm^{-1}$ 3600 and 2940; δ_H(200 MHz; $CDCl_3$) 5.76 (1 H, br s, 5-H), 4.23–4.03 (1 H, m, 6-H), 3.40–3.16 (1 H, m, 1-H) and 2.50–1.18 (12 H, envelope); δ_C(50 MHz; $CDCl_3$) 135.8 (C-4a), 131.3 (C-5), 127.6 (C-9, q, $^1J_{CF}$ 288), 77.7 (C-1), 65.8 (C-6), 48.9 (C-8a, q, $^2J_{CF}$ 21), 32.1 (C-4), 31.0 (C-2), 27.5, 27.3 (C-7, -8) and 24.4 (C-3); δ_F(56 MHz, $CDCl_3$) −60.0; *m/z* 236 (M^+, 4%), 218 (80), 200 (40), 174 (100) and 57 (100).

Condensation of lithium trimethylsilylacetylide with dione 1

A solution of lithium trimethylsilylacetylide in diethyl ether was prepared by the addition of methyllithium (1.6 M in diethyl ether; 205 μl, 0.33 mmol) to a solution of trimethylsilylacetylene (47 μl, 0.33 mmol) in the same solvent (10 ml) kept in an ice-bath under argon. After stirring of the mixture for 1 h at 0 °C, a solution of the ketone **1** (70 mg, 0.30 mmol) in diethyl ether (2 ml) was added and the reaction mixture was allowed to warm to room temperature overnight. After addition of saturated aq. ammonium chloride (10 ml), the reaction medium was extracted with diethyl ether (3 × 20 ml), and the extract was dried (Na_2SO_4) and the solvent was removed *in vacuo*. The residue was dissolved in THF (10 ml) and a solution of TBAF in THF (1.1 M; 1 ml) was added. After being stirred for 8 h, the solution was neutralised by addition of 1 M hydrochloric acid followed by brine (10 ml) and extracted with diethyl ether (3 × 20 ml). Drying of the organic phase ($MgSO_4$) and evaporation of the mixture *in vacuo* left a residue which was eluted on a silica gel column (20% diethyl ether–dichloromethane), to afford the *acetylenic alcohol* **28** (28 mg, 36%) (Found: M^+, 2588.0868. $C_{13}H_{13}F_3O_2$ requires M, 258.0868); $\nu_{max}(CCl_4)/cm^{-1}$ 3500, 3280, 1715 and 1595; δ_H(200 MHz; $CDCl_3$) 5.84 (1 H, s, 5-H), 2.75–2.56 (2 H, envelope), 2.44 (1 H, s, C≡CH), 2.38–1.97 (7 H, envelope) and 1.68–1.40 (2 H, envelope); δ_C(50 MHz; $CDCl_3$) 203.6 (C-1), 134.3 (C-4a), 132.8 (C-5), 125.5 (C-9, q, $^1J_{CF}$ 287), 85.8 (*C*≡CH), 72.7 (C≡*C*H), 65.2 (C-6), 58.3 (C-8a, q, $^2J_{CF}$ 23), 40.2 (C-2), 33.8 (C-7), 31.6 (C-4), 23.9 (C-8) and 23.2 (C-3); δ_F(56 MHz; $CDCl_3$) −65.0; *m/z* 258 (M^+, 3%), 189 (100) and 55 (62); further elution gave the diol **29** (24 mg, 28%); $\nu_{max}(CCl_4)/cm^{-1}$ 3590, 3290 and 1590; δ_H(200 MHz; $CDCl_3$) 5.78 (1 H, s, 5-H), 2.52 (1 H, s, C≡CH), 2.45 (1 H, s, C≡CH) and 2.41–1.66 (12 H, envelope); δ_C(50 MHz; $CDCl_3$) 134.5 (C-4a), 132.2 (C-5), 127.0 (C-9, q, $^1J_{CF}$ 288), 86.6 (*C*≡CH), 84.9 (*C*≡CH), 75.9 (C≡*C*H), 75.8 (C-1), 72.4 (C≡*C*H), 65.4 (C-6), 51.7 (C-8a, q, $^2J_{CF}$ 22), 37.2 (C-2), 34.2 (C-7), 31.6 (C-4), 24.4 (C-8) and 22.7 (C-3); δ_F(56 MHz; $CDCl_3$) −59.3.

3,8-Diacetoxy-1,2,6,8a-tetrahydro-8a-(trifluoromethyl)-naphthalene 30

Dione **1** (50 mg, 0.22 mmol) was dissolved in an acylating solution (100 ml) composed of perchloric acid (0.04 ml, 72%), acetic anhydride (5.96 ml) and ethyl acetate (94 ml), and the resulting solution was stirred for 6 h. The mixture was diluted with dichloromethane (200 ml), washed successively with saturated aq. $NaHCO_3$ (40 ml) and brine (20 ml), and dried ($MgSO_4$). The residue obtained after evaporation of the mixture *in vacuo* was eluted on a silica gel column (5% diethyl ether–dichloromethane) affording the *bis-acetate* **30** (52 mg, 76%) (Found: M^+, 316.0923. $C_{15}H_{15}F_3O_4$ requires M, 316.0922); $\nu_{max}(CCl_4)/cm^{-1}$ 1750 and 1160; δ_H(200 MHz; $CDCl_3$) 5.94 (1 H, d, *J* 1.9, 4-H), 5.85–5.83 (1 H, m, 5- or 7-H), 5.78–5.76 (1 H, m, 7- or 5-H), 3.02 (1 H, br d, $J_{6\alpha\text{-H},6\beta\text{-H}}$ 23.6, 6α- or 6β-H), 2.82 (1 H, dt, $J_{6\alpha\text{-H},6\beta\text{-H}}$ 23.6, $J_{5\text{-H},6\text{-H}}$ 5.1, $J_{6\text{-H},7\text{-H}}$ 5.1, 6β- or 6α-H), 2.62–2.15 (3 H, envelope), 2.12 (3 H, s, OAc), 2.08 (3 H, s, OAc) and 1.98–1.78 (1 H, m); δ_C(50 MHz; $CDCl_3$) 168.9 (O*C*OMe), 168.7 (O*C*OMe), 148.2 (C-3), 142.5 (C-8), 128.8 (C-4a), 127.4 (C-5), 126.8 (C-9, q, $^1J_{CF}$ 288), 118.7, 116.0 (C-7, -4), 45.6 (C-8a, q, $^2J_{CF}$ 26), 27.0 (C-6), 24.4 (C-1, -2), 21.0 (OCO*Me*) and 20.9 (OCO*Me*); δ_F(56 MHz; $CDCl_3$) −72.0; *m/z* 316 (M^+, 10%), 274 (50), 232 (70) and 43 (100).

19,19,19-Trifluoro-8,14-secoandrosta-4,9(11)-triene-3,14,17-trione 35

A solution of 1% dry hydrogen chloride in anhydrous 1,4-dioxane (10 ml) was added under argon to a solution of the secosteroid **7** (80 mg, 0.23 mmol) in anhydrous 1,4-dioxane. The solution was stirred for 10 min, and subsequently a solution of DDQ (56 mg) in 1,4-dioxane (5 ml) was added dropwise over a period of 1 h. After being stirred for 12 h, the mixture was filtered and the resulting solution was washed with saturated aq. $NaHCO_3$. After extraction with diethyl ether (3 × 30 ml) and drying ($MgSO_4$), the residue obtained upon evaporation of the mixture *in vacuo* was eluted on a silica gel column (10% diethyl ether–dichloromethane) and afforded starting material **7** (72 mg, 90% recovery) and *triene* **35** (4 mg, 5%) which had δ_H(200 MHz; $CDCl_3$) 7.18 (2 H, s, 15- and 16-H), 5.98 (1 H, s, 4-H), 5.31 (1 H, t, $J_{11\text{-H},12\text{-H}}$ 8.4, 11-H), 2.64–1.79 (13 H, envelope), 1.42–1.21 (1 H, m) and 1.12 (3 H, s, Me); δ_F(56 MHz; $CDCl_3$) −66.7.

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