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Elemental fluorine
Part 22. Fluorination of 3β-acetoxy-5α-androstan-17-one using fluorine and Selectfluor®

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ABSTRACT

Reactions of 3β-acetoxy-5α-androstan-17-one with elemental fluorine and Selectfluor® are reported and give contrasting results. Fluorine gives a mixture of mono-fluorinated steroids in which fluorine atoms are attached to tertiary carbon sites whereas Selectfluor® gives fluoro-steroid systems arising from electrophilic aliphatic substitution of the most sterically accessible secondary saturated positions. The identities of the fluoro-steroid products were determined by NMR analysis and X-ray crystallography.

1. Introduction

The sometimes-considerable enhancement of biological activity of steroids by the introduction [1] of a single fluorine atom into the structure was first reported by Fried and Sabo [2] when they compared glucocorticoid activities of 9α-halogeno derivatives of hydrocortisone acetate [3] (Scheme 1). This important early milestone in bio-organic fluorine chemistry prompted not only the synthesis of many fluorinated steroids [4] but numerous fluorinated bioactive compounds which, in turn, led to the launch of an increasing number of commercially very successful pharmaceuticals [5].

Consequently, the regio- and stereo-selective introduction of fluorine atoms into structurally sophisticated biologically active systems remains an important challenge in fluorine chemistry [6] and numerous fluorinating agents are now available [5,7,8] that meet some of the demands of synthetic chemists involved in the synthesis of selectively fluorinated systems.

The most direct method for introducing fluorine atoms into an organic molecule is the replacement of hydrogen atoms by fluorine using an electrophilic fluorinating agent, in aliphatic electrophilic substitution processes at saturated sites. Rozen and co-workers [9–11] demonstrated that tertiary carbon–hydrogen bonds could be transformed to carbon–fluorine bonds upon fluorination using fluorine in $CFCl_3/CHCl_3$ media at low temperature (−78 °C). The use of ozone-depleting solvents at low temperature is, however, not necessary because, subsequently, the Durham group reported that selective direct fluorination could be achieved in acetonitrile at ambient temperature [12,13]. We found that acetonitrile was an especially effective solvent for direct fluorination reactions and proposed that a transient 'N–F' species, formed by interaction of acetonitrile with fluorine, was a beneficial, contributing factor. For example, reaction of *trans*-decalin gives a single product arising from stereo selective replacement of hydrogen by fluorine at the most nucleophilic tertiary carbon–hydrogen bond, consistent with an electrophilic aliphatic substitution process (Scheme 2). In the context of the direct fluorination of steroids, Rozen [4,9] also demonstrated that tertiary saturated sites could be transformed to carbon–fluorine bonds and, by using electron withdrawing substituents at appropriate positions, was able to selectively fluorinate the most electron rich tertiary site in $CFCl_3/CHCl_3$ media at very low temperature.

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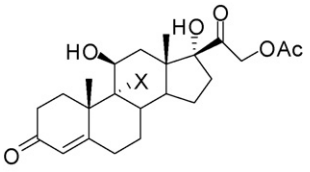


X	Relativebioactivity
H	1
F	11
Cl	4
Br	0.28
I	0.1

Scheme 1. Glucocorticoid activities of 9α-halogeno derivatives of hydrocortisone acetate.

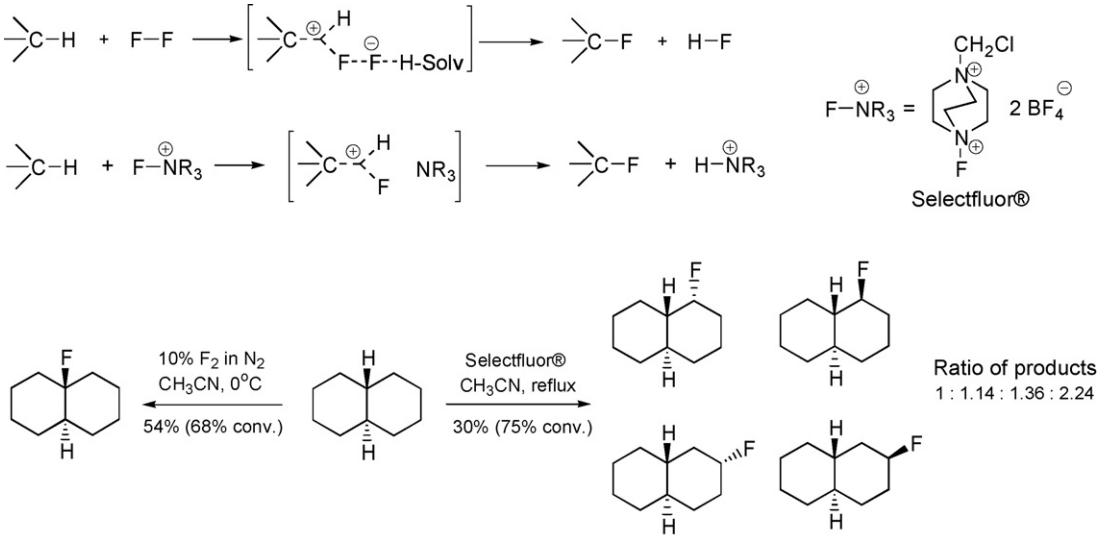
In related studies, we also demonstrated that a reagent of the N–F class [14], Selectfluor®, could be used for electrophilic fluorination at saturated sites [12,13] although, in these reactions, the most sterically accessible sites are fluorinated due to the larger steric requirement of the fluorinating agent. For example, reaction of *trans*-decalin using Selectfluor® gave a mixture of four mono-fluorinated products arising from substitution at the secondary sites only, with no fluorination at the most electron rich tertiary sites observed (Scheme 2).

In this paper, we show that fluorine and Selectfluor® can be used for the fluorination of carbon–hydrogen bonds in an androsterone derivative by electrophilic substitution processes. Reactions of Selectfluor® at saturated sites in steroids have not been reported previously.

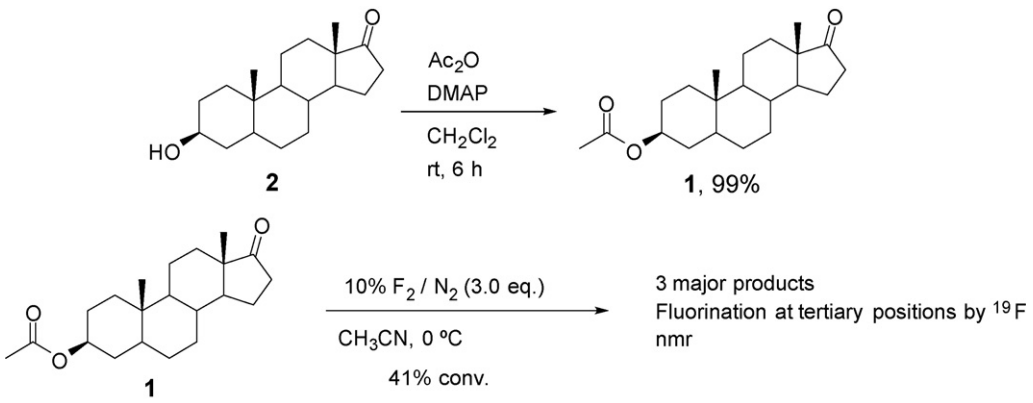
2. Results and discussion

Readily accessible 3β-acetoxy-5α-androstan-17-one **1** was chosen as a model substrate for fluorination reactions and was prepared quantitatively from commercially available epiandrosterone **2** by acetylation using acetic anhydride in dichloromethane in the presence of 4-dimethylaminopyridine [15] (Scheme 3). The acetylated steroid **1** was chosen as the substrate for fluorination studies because oxidation of the hydroxyl group in **2** by fluorine would be a competing process.

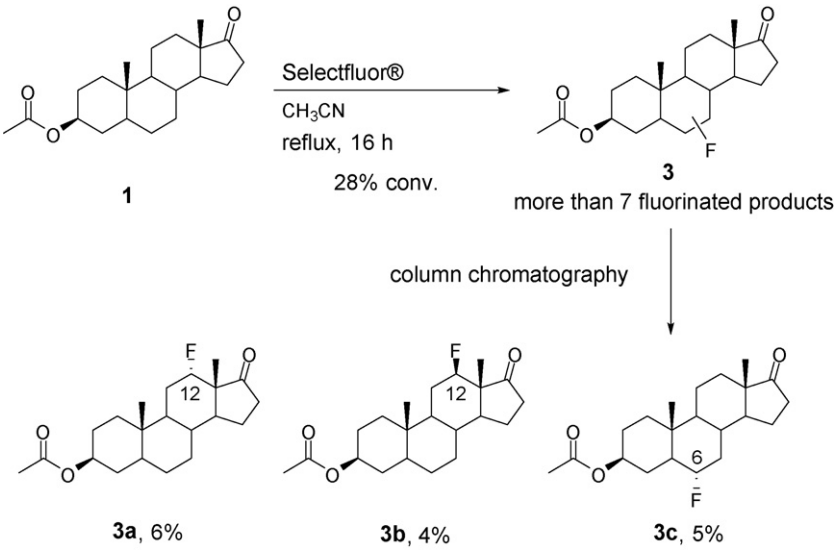
Direct fluorination of **1** using fluorine in acetonitrile at 0 °C gave three major mono-fluorinated products in the ratio of 1.4:1:1 arising from replacement of hydrogen at tertiary sites (Scheme 3). Purification of the crude product by column chromatography, recrystallisation or HPLC proved unsuccessful and the identities of the steroids could not be precisely determined by ^{19}F NMR spectroscopy. However, the chemical shifts of the resonance of the major products located at δ_F −162.39, −164.09 and −179.70 ppm, indicate fluorination predominantly at the tertiary positions. For other fluorinated steroid systems, fluorine attached to tertiary carbon is observed between −160 and −180 ppm whilst fluorine at secondary sites in steroids appear at chemical shifts between −180 and −190 ppm. These results are consistent with our earlier observations concerning reactions of fluorine at tertiary sites in



Scheme 2. Electrophilic aliphatic fluorination of saturated sites using fluorine or Selectfluor®.



Scheme 3. Synthesis and direct fluorination of 3β-acetoxy-5α-androstan-17-one **1**.



Scheme 4. Reaction of 3β-acetoxy-5α-androstan-17-one **1** with Selectfluor®.

decalin derivatives in acetonitrile and with results of fluorination reactions carried out in different media reported by Rozen [9].

Fluorination of 3β-acetoxy-5α-androstan-17-one **1** using one equivalent of Selectfluor® was carried out in acetonitrile under reflux conditions for 16 h (Scheme 4). The reaction proceeded in 28% conversion, and gave more than seven fluorinated products but the crude product could be purified by silica gel column chromatography to give enriched samples of the three major mono-fluorinated products **3a**, **3b** and **3c**.

These products were analyzed by ^{1}H and ^{13}C NMR, 2D NMR experiments (COSY, HSQC) and DEPT to determine the position of the fluorine atom and we found that ^{13}C NMR was the most effective characterisation technique, as used by Rozen for the characterisation of the fluorinated steroids [16].

In ^{13}C NMR, the replacement of a hydrogen atom by a fluorine atom influences the chemical shifts at the corresponding α, β and γ positions because, of course, the high electronegativity of a fluorine atom introduces a considerable change in the electronic environment. C–F coupling is also observed at the α and β positions with typical values for $^{1}J_{CF}$ and $^{2}J_{CF}$ of about 170 and 20 Hz, respectively, in the case of saturated cyclic hydrocarbons. Table 1 shows the chemical shifts and coupling constants of the isolated fluorinated products.

All α- and β-carbons are deshielded by the presence of a fluorine atom. The differences in the chemical shifts compared to the parent compound ($\Delta\delta$) were observed to be *ca.* 60 ppm for carbon atoms with fluorine attached (α carbon) and *ca.* 4–8 ppm for adjacent carbon atoms (β carbons), respectively. The γ-

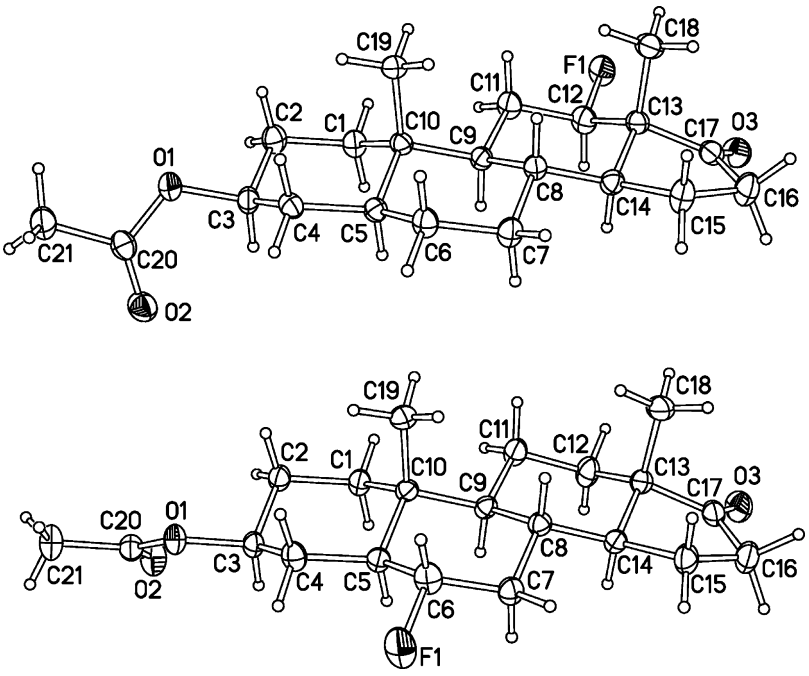


Fig. 1. X-ray molecular structures of **3b** (top) and **3c**, showing 50% probability thermal ellipsoids and omitting minor positions of disordered fluorine atoms.

Table 1
^{13}C NMR chemical shifts (ppm) and coupling constants (Hz) of fluorinated steroids

Compound	Position of the carbon relative to the fluorine atom[a]											
	α		β		γ *gauche*				γ *antiperiplanar*			
3a	C-12		C-11		C-13		C-9		C-14		C-18	
δ		90.4		26.4		51.4		48.4		43.8		13.3
$\Delta\delta$[b]		+59.0		+6.0		+3.7		−5.7		−7.4		−0.4
J_{CF}		173.7		22.0		20.1		–		–		7.2
3b	C-12		C-11		C-13		C-18				C-9	C-14
δ		92.0		27.6		51.4		8.2			52.1	48.6
$\Delta\delta$		+60.6		+7.6		+3.7		−5.5			−2.0	−2.6
J_{CF}		183.3		19.2		16.1		4.2			9.2	5.0
3c	C-6		C-5		C-7		C-4				C-8	C-10
δ		91.2		49.6		37.0		27.9			33.6	36.6
$\Delta\delta$		+63.0		+5.1		+6.3		−5.9			−1.3	+1.1
J_{CF}		172.9		14.9		18.4		4.2			11.5	8.0

[a] The carbons further away from the fluorine atom do not differ by more than 0.3 ppm from the corresponding carbons in the parent compound (3β-acetoxy-5α-androstan-17-one 1).
[b] $\Delta\delta$ is defined as the difference between the chemical shift of the relevant carbon atoms in the corresponding unfluorinated and fluorinated steroids; (+) represents a deshielding effect and (−) a shielding effect, both induced by the fluorine atom.

carbons, however, are divided into two groups. The carbons *gauche* to the fluorine atom are all shielded by 5.5–5.9 ppm, whereas the γ-carbons *anti* to the fluorine are shielded to a lesser extent (−1.1 to 2.6 ppm). Moreover, the γ-carbons *gauche* to the fluorine have a relatively small coupling constant (0–4.2 Hz), whilst the *anti* γ-carbons are coupled to the fluorine by 5.0–11.5 Hz. Consequently, identification of quaternary C, CH and CH_2 resonances by ^{13}C DEPT and a consideration of observed chemical shift and coupling constants relative to the non-fluorinated starting material, allows the structures of the fluorinated products to be deduced. Subsequently, the structures of **3b** and **3c** were confirmed by X-ray crystallography (Fig. 1).

Attempts to increase the yields of the fluorinated steroids by prolonging the reaction time was hampered by, the strongly acidic reaction medium that is formed upon substitution of hydrogen by fluorine when Selectfluor® is used as the fluorinating reagent leading to fluoride loss from the initial fluorinated product [13].

As deduced above, fluorination of steroid **1** using Selectfluor® proceeded exclusively at CH_2 sites indicating that the C–H bonds at the 12- and 6β-positions are the least sterically hindered sites among all the CH_2 sites in compound **1**. Consequently, fluorination of steroids at saturated CH sites is possible using either fluorine in acetonitrile at 0 °C or Selectfluor® in refluxing acetonitrile solution. In both reactions, however, several fluorinated products are formed with the major products arising from fluorination at the tertiary carbon when fluorine is the fluorinating agent and, in contrast, at CH_2 groups when Selectfluor® is used. These results are consistent with our earlier studies involving the fluorination of decalin and related hydrocarbon systems in acetonitrile [12,13]. This methodology, therefore, does provide limited quantities of fluorinated steroids but very difficult separation procedures are required to purify the individual products.

3. Experimental

3.1. General

All starting materials were obtained commercially. All solvents were dried using literature procedures. NMR spectra were recorded in deuteriochloroform, unless otherwise stated, on a spectrometer operating at 500 MHz (^1H NMR), 376 MHz (^{19}F NMR) and 100 MHz (^{13}C NMR) with tetramethylsilane and trichlorofluoromethane as internal standards. Mass spectra were recorded on a VG 7070E spectrometer coupled with a Hewlett Packard 5890 series II gas chromatograph. Elemental analyses were obtained on an Exeter Analytical CE-440 elemental analyser. Melting points and boiling points were recorded at atmospheric pressure unless otherwise stated and are uncorrected. The progress of reactions was monitored by ^{19}F NMR and column chromatography was carried out on silica gel.

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3.2. Preparation of 3β-acetoxy-5α-androstan-17-one 1

A mixture of epiandrosterone **2** (0.60 g, 2.07 mmol), acetic anhydride (0.42 g, 4.11 mmol), 4-dimethylaminopyridine (84 mg, 0.69 mmol) and dichloromethane (50 mL) was stirred at room temperature for 6 h. The reaction mixture was poured into water, neutralized by $NaHCO_3$, and extracted with dichloromethane (3× 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and evaporated to give a crude product (1.20 g). The crude mixture was chromatographed over silica gel (silica gel: 10 g, eluent: hexane/ethyl acetate (4:1)) to give *3β-acetoxy-5α-androstan-17-one* **1** (681 mg, 99%) as white crystals; mp 104–105 °C (lit. 103–104 °C [15]) (found: C, 75.88; H, 9.75. $C_{21}H_{32}O_3$ requires C, 75.86; H, 9.70%); δ_H 0.68 (1H, m, 9-H), 0.82 (6 H, 2 × s, 18-H and 19-H), 0.9–1.0 (2H, m, one of 1-H, one of 7-H), 1.1–1.4 (7H, m, one of 4-H, 5-H, 6-H, one of 11-H, one of 12-H, 14-H), 1.4–1.5 (3H, m, one of 2-H, 8-H, one of 15-H), 1.5–1.6 (2H, m, one of 4-H, one of 11-H), 1.7–1.8 (4H, m, one of 1-H, one of 2-H, one of 7-H, one of 12-H), 1.90 (1H, m, one of 15-H), 1.99 (3H, s, 21-H), 2.03 (1H, m, one of 16-H), 2.40 (1H, dd, *J* 9.0, *J* 19.5, one of 16-H), 4.65 (1H, m, 3-H); δ_C 12.1 (s, 19-C), 13.7 (s, 18-C), 20.4 (s, 11-C), 21.4 (s, 21-C), 21.7 (s, 15-C), 27.3 (s, 2-C), 28.2 (s, 6-C), 30.7 (s, 7-C), 31.4 (s, 12-C), 33.8 (s, 4-C), 34.9 (s, 8-C), 35.5 (s, 10-C), 35.7 (s, 16-C), 36.6 (s, 1-C), 44.5 (s, 5-C), 47.7 (s, 13-C), 51.2 (s, 14-C), 54.2 (s, 9-C), 73.4 (s, 3-C), 170.6 (s, 20-C), 221.1 (s, 17-C); IR (KBr) 2920, 2855, 1735 (C=O), 1241, 1020 cm^{-1}.

3.3. Reaction of 3β-acetoxy-5α-androstan-17-one 1 with fluorine

Elemental fluorine (27 mmol), as a 10% (v/v) mixture with nitrogen, was passed at a rate of *ca.* 50 mL min^{-1} through a stirred, cooled (0 °C) mixture which consisted of 3β-acetoxy-5α-androstan-17-one **1** (3.0 g, 9 mmol) and acetonitrile (140 mL). After addition of the fluorine, the reaction mixture was poured into water (100 mL), neutralized ($NaHCO_3$) and extracted with dichloromethane (3× 40 mL). The combined, dried ($MgSO_4$), organic extracts were evaporated to give a pale yellow solid (3.1 g, 41% conv.). ^{19}F NMR analysis of the crude product showed the presence of three major mono-fluorinated products; δ_F −162.39 (t, $^3J_{HF}$ 38.9, 5α-F), −164.09 (ddd, $^3J_{HF}$ 31.0, $^3J_{HF}$ 45.1, 9α-F), −179.70 (ddd, $^3J_{HF}$ 41.6, $^3J_{HF}$ 27.8, $^3J_{HF}$ 11.1, 14α-F); *m/z* (EI^+) 350 ($[M]^+$, 11%), 330 ($[M-HF]^+$, 21). Attempted purification of the individual isomers was unsuccessful.

3.4. Reaction of 3β-acetoxy-5α-androstan-17-one with Selectfluor®

A mixture consisting of 3β-acetoxy-5α-androstan-17-one **1** (300 mg, 0.905 mmol) and freshly distilled anhydrous acetonitrile (20 mL) was placed in the round-bottomed flask. Selectfluor® (321 mg, 0.906 mmol) was added to the mixture which was refluxed with stirring for 16 h. The mixture was poured into water (30 mL), neutralized by $NaHCO_3$ and extracted with dichloromethane (3× 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and evaporated to give a crude product (341 mg) which contained 3β-acetoxy-5α-androstan-17-one (71.6%); *m/z* (EI^+) 332 ($[M]^+$, 13%), 272 ($[M-C_2H_4O_2]^+$, 100), 3β-acetoxy-12α-fluoro-5α-androstan-17-one **3a** (11.1%); *m/z* (EI^+) 350 ($[M]^+$, 3%), 290 ($[M-C_2H_4O_2]^+$, 72), 3β-acetoxy-12β-fluoro-5α-androstan-17-one **3b** (5.0%); *m/z* (EI^+) 350 ($[M]^+$, 5%), 290 ($[M-C_2H_4O_2]^+$, 75), 3β-acetoxy-6α-fluoro-5α-androstan-17-one **3c** (4.7%); *m/z* (EI^+) 350 ($[M]^+$, 8%), 290 ($[M-C_2H_4O_2]^+$, 60), other isomers of mono-fluorinated acetoxyandrostanone (3 peaks, 6.8%); *m/z* (EI^+) 350 ($[M]^+$) and unidentified products (0.8 area %).

The crude mixture was chromatographed over silica gel [eluent: hexane/ethyl acetate (6:1)] to give *3β-acetoxy-12α-fluoro-5α-androstan-17-one* **3a** (19 mg, 6%); δ_H 0.81 (3H, s, 18-H), 0.83 (3H, s, 19-H), 1.0–2.0 (18H, m, 1-H, 2-H, 4-H, 5-H, 6-H, 7-H, 8-H, 9-H, 11-H, 14-H, 15-H), 2.01 (3H, s, 21-H), 2.12 (1H, dd, *J* 9.5, *J* 19.5, one of 16-H), 2.41 (1H, dd, *J* = 8.0, *J* 19.5, one of 16-H), 4.68 (1H, m, 3-H), 4.90 (1H, d, $^2J_{HF}$ 49.5, 12-H); δ_C 11.9 (s, 19-C), 13.3 (d, $^3J_{CF}$ 7.0, 18-C), 21.0 (s, 15-C), 21.4 (s, 21-C), 26.4 (d, $^2J_{CF}$ 22.0, 11-C), 27.2 (s, 2-C), 28.1 (s, 6-C), 30.5 (s, 7-C), 33.8 (s, 4-C), 34.4 (s, 8-C), 35.2 (s, 10-C), 36.3 (s, 1-C or 16-C), 36.3 (s, 1-C or 16-C), 43.8 (s, 14-C), 44.5 (s, 5-C), 48.4 (s, 9-C), 51.4 (d, $^2J_{CF}$ 20.0, 13-C), 73.3 (s, 3-C), 90.4 (d, $^1J_{CF}$ 173.5, 12-C), 170.6 (s, 20-C), 216.7 (s, 17-C); δ_F −187.0 (t, $^2J_{HF}$ 49.5); *m/z* (EI^+) 350 ($[M]^+$, 3%), 290 ($[M-C_2H_4O_2]^+$, 97); *3β-acetoxy-12β-fluoro-5α-androstan-17-one* **3b** (13 mg, 4%); δ_H 0.8–2.2 (19H, m, 1-

H, 2-H, 4-H, 5-H, 6-H, 7-H, 8-H, 9-H, 11-H, 14-H, 15-H, one of 16-H), 0.86 (3H, s, 19-H), 0.99 (3H, d, $^4J_{HF}$ 1.0, 18-H), 2.02 (3H, s, 21-H), 2.47 (1H, m, one of 16-H), 4.57 (1H, ddd, $^2J_{HF}$ 50.0, $^3J_{HH}$ 11.0, $^3J_{HH}$ 5.0, 12-H), 4.68 (1H, m, 3-H); δ_C 8.2 (d, $^3J_{CF}$ 4.0, 18-C), 12.0 (s, 19-C), 21.2 (d, $^4J_{CF}$ 2.0, 15-C), 21.4 (s, 21-C), 27.2 (s, 2-C), 27.6 (d, $^2J_{CF}$ 19.0, 11-C), 28.0 (s, 6-C), 29.7 (s, 7-C), 33.7 (s, 4-C and 8-C), 35.4 (s, 16-C), 35.5 (s, 10-C), 36.6 (s, 1-C), 44.4 (s, 5-C), 48.6 (d, $^3J_{CF}$ 5.0, 14-C), 51.4 (d, $^2J_{CF}$ 16.0, 13-C), 52.1 (d, $^3J_{CF}$ 9.0, 9-C), 73.2 (s, 3-C), 92.0 (d, $^1J_{CF}$ 183.0, 12-C), 170.7 (s, 20-C), 217.5 (s, 17-C); δ_F −183.5 (d, $^2J_{HF}$ 50.0); *m*/*z* (EI$^+$) 350 ([M]$^+$, 8%), 290 ([M–$C_2H_4O_2$]$^+$, 100); and, *3β-acetoxy-6α-fluoro-5α-androstan-17-one* **3c** (15 mg, 5%); δ_H 0.7–0.8 (1H, m, 9-H), 0.86 (3H, s, 18-H or 19-H), 0.86 (3H, s, 18-H or 19-H), 1.0–2.3 (18H, m, 1-H, 2-H, 4-H, 5-H, 7-H, 8-H, 9-H, 11-H, 12-H, 14-H, 15-H, one of 16-H), 2.03 (3H, s, 21-H), 2.44 (1H, m, one of 16-H), 4.31 (1H, m, $^2J_{HF}$ 50.0, 6-H), 4.68 (1H, m, 3-H); δ_C 13.2 (s, 18-C or 19-C), 13.8 (s, 18-C or 19-C), 20.2 (s, 11-C), 21.4 (s, 21-C), 21.7 (s, 15-C), 27.0 (s, 2-C), 27.9 (d, $^3J_{CF}$ 4.0, 4-C), 31.2 (s, 12-C), 33.6 (d, $^3J_{CF}$ 11.5, 8-C), 35.7 (s, 16-C), 36.6 (d, $^3J_{CF}$ 8.0, 10-C), 36.9 (s, 1-C), 37.0 (d, $^2J_{CF}$ 18.5, 7-C), 47.7 (s, 13-C), 49.6 (d, $^2J_{CF}$ 15.0, 5-C), 51.0 (s, 14-C), 53.5 (d, $^4J_{CF}$ 1.5, 9-C), 72.7 (s, 3-C), 91.2 (d, $^1J_{CF}$ 173.0, 6-C), 170.5 (s, 20-C), 220.4 (s, 17-C); δ_F −181.4 (d, $^2J_{HF}$ 49.5); *m*/*z* (EI$^+$) 350 ([M]$^+$, 16%), 290 ([M–$C_2H_4O_2$]$^+$, 100).

3.5. X-ray crystallography

X-ray diffraction experiments were carried out on Bruker 3-circle diffractometers with SMART 6K (**3b**) or SMART 1K (**3c**) CCD area detectors, using graphite-monochromated Mo Kα radiation ($\bar{\lambda}$ = 0.71073 Å) and a Cryostream (Oxford Cryosystems) open-flow N_2 cryostat. The structures were solved by direct methods and refined by full-matrix least squares against F^2 of all reflections, using SHELXTL software (version 6.14, Bruker AXS, Madison WI, USA, 2003). Both samples were in fact solid solutions of differently fluorinated products, *viz.* **3c** co-crystallised with **3a** in a 9:1 ratio, whereas the crystal of **3b** contained *ca.* 80% of this isomer, alongside small amounts of **3a**, **3c** and other fluorinated derivatives. The asymmetric unit of the latter structure comprised two independent molecules; both molecular sites were shared by alternative isomers in similar proportions. Absolute configurations could not be determined for the lack of anomalously scattering atoms and were inferred from those of the precursors. *Crystal data for* **3b**/**3c**[1]: $C_{21}H_{31}FO_3$, M = 350.46, T = 120 K, monoclinic, space group $P2_1$ (No. 4), a = 14.5966(5)/10.000(2), b = 7.5825(4)/8.078(2), c = 17.6469(9)/11.778(2) Å, β = 95.93(1)/90.60(3)°, U = 1869.4(2)/951.3(3) Å^3, Z = 2, D_x = 1.245/1.223 g cm^{-3}, μ = 0.09 mm^{-1}, 23,374/11,702 reflections, of which 5704/2692 unique and 4389/2313 Friedels, R_{int} = 0.069/0.023, w$R(F^2)$ = 0.120/0.091 on all data, $R(F)$ = 0.044/0.032 on 4959/2594 data with $I \geq 2\sigma(I)$.

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References

[1] For Part 21, see R.D. Chambers, G. Sandford, J. Trmcic, T. Okazoe, Org. Proc. Res. Dev. 12 (2008) 339–344.
[2] J. Fried, E.F. Sabo, J. Am. Chem. Soc. 76 (1954) 1455–1456.
[3] J. Fried, E.F. Sabo, J. Am. Chem. Soc. 75 (1953) 2273–2274.
[4] D. Alker, D.H.R. Barton, R.H. Hesse, J. Lister-James, R.E. Markwell, M.M. Pechet, S. Rozen, T. Takashita, H.T. Toh, Nouv. J. Chem. 4 (1980) 239–258.
[5] R.E. Banks, B.E. Smart, J.C. Tatlow, Organofluorine Chemistry. Principles and Commercial Applications, Plenum, New York, 1994.
[6] J.A. Wilkinson, Chem. Rev. 92 (1992) 505–519.
[7] B. Baasner, H. Hagemann, J.C. Tatlow, Houben-Weyl Organofluorine Compounds, vol. E10a, Thieme, Stuttgart, 2000.
[8] R.D. Chambers, Fluorine in Organic Chemistry, Blackwell, Oxford, 2004.
[9] S. Rozen, G. Ben-Scushan, J. Org. Chem. 51 (1986) 3522–3527.
[10] S. Rozen, C. Gal, J. Org. Chem. 52 (1987) 2769–2779.
[11] S. Rozen, C. Gal, J. Org. Chem. 52 (1987) 4928–4933.
[12] R.D. Chambers, M. Parsons, G. Sandford, R. Bowden, Chem. Commun. (2000) 959–960.
[13] R.D. Chambers, M. Parsons, G. Sandford, J.S. Moilliet, J. Chem. Soc., Perkin Trans 1 (2002) 2190–2197.
[14] G.S. Lal, G.P. Pez, R.G. Syvret, Chem. Rev. 96 (1996) 1737–1756.
[15] H.M.E. Cardwell, J.W. Cornforth, S.R. Duff, H. Holtermann, R. Robinson, J. Chem. Soc. (1953) 361–365.
[16] S. Rozen, G. Ben-Shushan, Magn. Reson. Chem. 23 (1985) 116–118.

[1] CCDC 683733 and 683734 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk).