PREPARATION OF STEROID OLEFINS FROM HEPTAFLUOROBUTYRATES*

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Steroids with hydroxyl group in positions 2, 3, 6, 7, 17 and 20 were esterified with heptafluorobutyric anhydride. The obtained esters on treatment with lithium bromide in *N*,*N*-dimethylacetamide in the presence of pyridinium tosylate afforded the corresponding olefins in high yields.
Key words: Steroids; Heptafluorobutyrates; Elimination; Olefins; NMR spectroscopy; Solvolysis.

Within the framework of our structure–activity studies[2,3] on brassinosteroids we needed to prepare compounds bearing a heptafluorobutyryloxy group in the position 20. During our synthetic studies we realized the great synthetic potential of this group.

Heptafluorobutyrates can be prepared in high yields by esterification of the corresponding hydroxy derivatives with heptafluorobutyric anhydride in pyridine at room temperature. In this manner we prepared a series of steroid esters containing the heptafluorobutyroxy group in various positions of the skeleton, in the presence as well as in the absence of other functional groups. We prepared the following esters: cholest-5-en-3β-yl heptafluorobutyrate (**1**), 5α-cholestan-2α-yl heptafluorobutyrate (**3**), 5α-cholestan-2β-yl heptafluorobutyrate (**4**), 5α-cholestan-6β-yl heptafluorobutyrate (**6**), 5α-cholestane-3β,7α-diyl 3-acetate 7-heptafluorobutyrate (**8**), 5α-cholestane-3β,7β-diyl 3-acetate 7-heptafluorobutyrate (**9**), 7-oxoandrost-5-ene-3β,17β-diyl 3-acetate 17-heptafluorobutyrate (**11**), 7a-homo-5α-cholestane-3β,7α-diyl 3-acetate 7-heptafluorobutyrate (**13**), and (20*R*)-6-oxo-3α,5-cyclo-5α-pregnan-20-yl heptafluorobutyrate (**15**).

All these heptafluorobutyrates were treated with lithium bromide in *N*,*N*-dimethylacetamide in the presence of a catalytic amount of pyridinium 4-toluenesulfonate at 160 °C for several hours. In all cases we isolated the corresponding olefins in high yields (see Table I). In the case of the 3α,5-cyclo derivative **15** the reaction proceeded with simultaneous cleavage of the cyclopropane ring under formation of 5α-pregna-2,17-dien-6-one (**16**).

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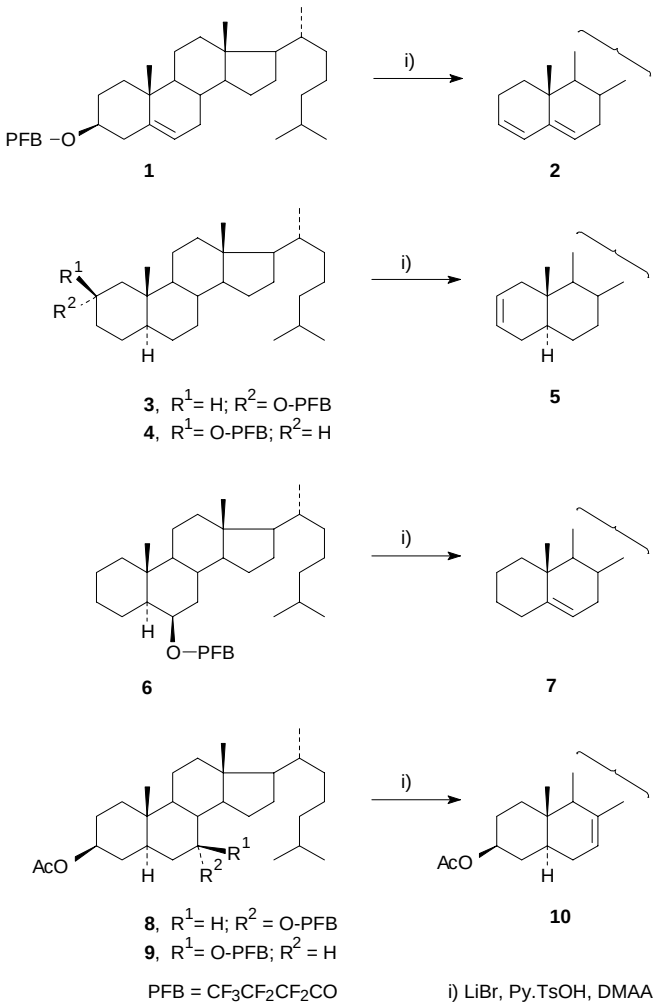
Heptafluorobutyrates can be easily handled: they melt without decomposition, can be chromatographed without problems on neutral silica gel and are stable at room temperature for several months. They proved to be suitable precursors for the preparation of the corresponding olefins. Whereas elimination of tosylates leads usually to mixtures of olefins[4] (*e.g.*, 3β-tosylates afford both the 2-olefin and the 3-olefin), we observed formation of mostly one isomer (Table I). In cases where both isomers were formed (compounds **3**, **4** and **13**), one of them largely predominated.



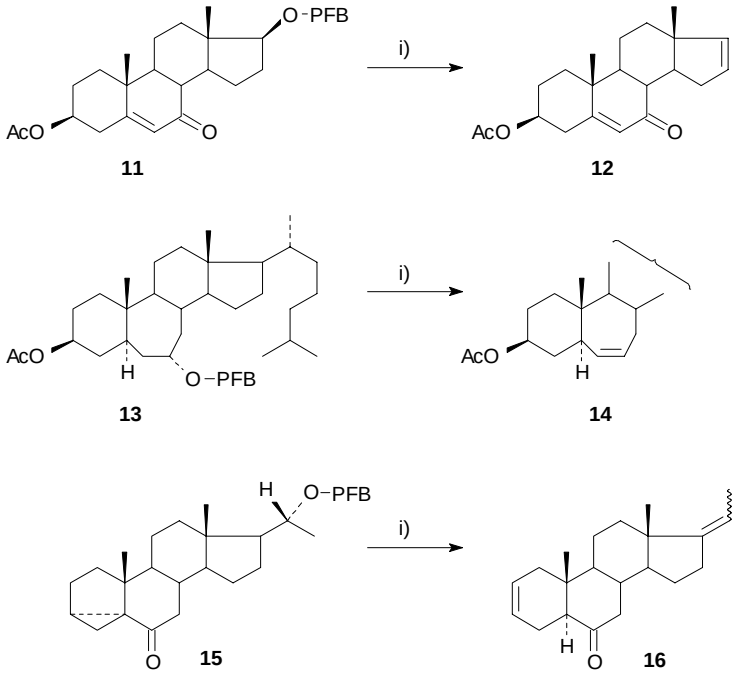


TABLE I
Reaction times and yields of olefins

Heptafluorobutyrate	Olefine	Time	Yield of olefine
1	2	2 h	94
3	5	2.5 h	90[a]
4	5	2.5 h	86[a]
6	7	2 h	84
8	10	2 h	84
9	10	2 h	88
11	12	50 min	89
13	14	4 h	58[b]
15	16	2 h	58

[a] Traces of the 1(2)-isomer detected. [b] Traces of the 7(7a)-isomer detected.

EXPERIMENTAL

The melting points were determined on a micro melting point apparatus Electrothermal (U.S.A.). Infrared spectra were recorded on a Bruker IFS 88 spectrometer in tetrachloromethane, wavenumbers are given in cm^{-1}. ^1H NMR spectra were taken on a Varian XL-200 instrument (FT mode, 200 MHz) at 23 °C in deuteriochloroform with tetramethylsilane as internal reference, unless stated otherwise. Chemical shifts are given in ppm (δ-scale), coupling constants (*J*) and multiplet half-widths ($W_{1/2}$) in Hz. Mass spectra were obtained with a ZAB-EQ spectrometer (EI at 70 eV). The identity of the prepared samples was checked by mixed melting points, thin-layer chromatography (TLC) on silica gel G (ICN Biochemicals; detection by spraying with sulfuric acid and heating), IR and ^1H NMR spectra. Preparative TLC was carried out on 200 × 200 mm plates coated with 0.7 mm thick layer of silica gel Woelm DC. Column chromatography was carried out on neutral silica gel 60–120 μm (Service Laboratories of the Institute). "Usual work-up" of a solution denotes washing with water, 5% aqueous potassium hydrogen carbonate, water, drying over anhydrous sodium sulfate, filtration and evaporation of the solvent to dryness *in vacuo*. Light petroleum was a fraction boiling at 40–62 °C.

Cholest-5-en-3β-yl Heptafluorobutyrate (**1**)

Heptafluorobutyric anhydride (3.00 g, 7.32 mmol) was added to a solution of cholesterol (1.00 g, 2.59 mmol) in pyridine (5 ml). After standing for 6 days, the mixture was poured into water, the product was extracted with ether and the organic layer was worked up in the usual manner. The residue was purified by chromatography on silica gel (60 g) in light petroleum–ether (49 : 1). Yield 904 mg of product **1** (60%). An analytical sample was obtained by crystallization from acetone. M.p. 114–115 °C. ^1H NMR spectrum: 0.68 s, 3 H (3 × H-18); 0.861 d, 3 H, J = 6.7 and 0.868 d, 3 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.92 d, 3 H, J = 6.4 (3 × H-21); 1.04 s, 3 H (3 × H-19); 4.86 m, 1 H, $W_{1/2}$ = 20 (H-3α); 5.44 d, 1 H, J = 5 (H-6). IR spectrum: 3 033 (=C–H); 1 777, 1 300, 1 268, 1 216, 1 191, 1 149, 1 124, 1 082, 969 (ester). For $C_{31}H_{45}F_7O_2$ (582.7) calculated: 63.90% C, 7.81% H, 22.82% F; found: 64.31% C, 8.03% H, 22.71% F.

Cholesta-3,5-diene (**2**)

Lithium bromide (210 mg, 2.4 mmol) and pyridinium 4-toluenesulfonate (18.5 mg, 0.07 mmol) were added to a solution of heptafluorobutyrate **1** (198 mg, 0.34 mmol) in *N*,*N*-dimethylacetamide (95 mg) and the mixture was heated at 160 °C for 2 h. After cooling, the reaction mixture was poured into water and extracted with ether. The ethereal extract was worked up in the usual manner. Yield 119 mg (94%) of diene **2** which, on recrystallization from acetone, melted at 77–80 °C (in accord with the literature data[5]).

5α-Cholestan-2α-yl Heptafluorobutyrate (**3**)

Heptafluorobutyric anhydride (0.30 g, 0.74 mmol) was added to a solution of 5α-cholestan-2α-ol[5] (120 mg, 0.32 mmol) in pyridine (2 ml). After standing for 48 h, the reaction mixture was worked up as described for the preparation of compound **1**. Yield 137 mg (72 %) of heptafluorobutyrate **3**, m.p. 61.7–62.2 °C (methanol). ^1H NMR spectrum: 0.65 s, 3 H (3 × H-18); 0.85 s, 3 H (3 × H-19); 0.865 d, 6 H, J = 6.1 (3 × H-26 and 3 × H-27); 0.90 d, 3 H, J = 6.7 (3 × H-21); 5.13 m, 1 H, $W_{1/2}$ = 22 (H-2β). IR spectrum: 1 776, 1 302, 1 268, 1 236, 1 216, 1 191, 1 146, 1 124, 1 084, 971, 942, 535 (ester). For $C_{31}H_{47}F_7O_2$ (584.7) calculated: 63.68% C, 8.10% H, 22.74% F; found: 63.75% C, 8.11% H, 22.81% F.

5α-Cholestan-2β-yl Heptafluorobutyrate (**4**)

Reaction of 5α-cholestan-2β-ol[6] (0.70 g, 1.9 mmol) and heptafluorobutyric anhydride (1.40 g, 3.42 mmol) in pyridine (7 ml) was carried out similarly as described for the preparation of compound **3** and afforded 800 mg (73%) of heptafluorobutyrate **4** which on crystallization from ethanol gave 613 mg of needles, m.p. 94.3–95 °C. ^{1}H NMR spectrum: 0.65 s, 3 H (3 × H-18); 0.86 d, 6 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.89 d, 3 H, J = 6.5 (3 × H-21); 0.91 s, 3 H (3 × H-19); 5.36 m, 1 H, $W_{1/2}$ = 8.0 (H-2α). IR spectrum: 1 776, 1 304, 1 269, 1 236, 1 216, 1 191, 1 144, 1 123, 1 084, 969, 941, 535 (ester). For $C_{31}H_{47}F_7O_2$ (584.7) calculated: 63.68% C, 8.10% H, 22.74% F, found: 63.71% C, 8.01% H, 22.71% F.

5α-Cholest-2-ene (**5**)

A) From 5α-cholestan-2α-yl heptafluorobutyrate (**3**): Lithium bromide (65 mg, 0.75 mmol) and pyridinium 4-toluenesulfonate (5.5 mg, 0.028 mmol) were added to heptafluorobutyrate **3** (60 mg, 0.10 mmol) in *N*,*N*-dimethylacetamide (2 ml) and the mixture was heated at 160 °C for 2.5 h. After cooling, the reaction mixture was poured into water and extracted with ether. The ethereal extract was worked up in the usual manner to give 32 mg (90%) of olefin **5**, which was crystallized from ethanol; m.p. 74–75 °C (in accord with the literature data[7]). ^{1}H NMR spectrum: 0.68 s, 3 H (3 × H-18); 0.75 s, 3 H (3 × H-19); 0.906 and 0.910, 2 d, 2 × 3 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.93 d, 3 H, J = 6.7 (3 × H-21); 5.59 m, 2 H (H-2 and H-3). MS spectrum, *m/z*: 370 (M^+), 355 (M – CH_3), 316 (M – CH_2=CH–CH=CH_2), 257 (M – side chain).

B) From 5α-cholestan-2β-yl heptafluorobutyrate (**4**): Lithium bromide (475 mg, 5.47 mmol) and pyridinium 4-toluenesulfonate (42 mg, 0.21 mmol) were added to heptafluorobutyrate **4** (450 mg, 0.77 mmol) in *N*,*N*-dimethylacetamide (4.5 ml) and the mixture was heated at 160 °C for 2.5 h. The reaction mixture was worked up as described in the preceding experiment to give 360 mg of a residue which was purified by chromatography on a column of silica gel (20 g), elution with heptane. The product fractions afforded 246 mg of pure olefin **5** (86%) which, on crystallization from acetone–ethanol (1 : 1), melted at 74.5–75 °C and was identical in all respects with the olefin obtained by procedure *A*. Only traces of the isomeric 5α-cholest-1-ene were detected (TLC and ^{1}H NMR) in the mother liquors.

5α-Cholestan-6β-yl Heptafluorobutyrate (**6**)

A mixture of 5α-cholestan-6β-ol[8] (1.95 g, 5.02 mmol), pyridine (10 ml) and heptafluorobutyric anhydride (6.00 g, 14.6 mmol) was allowed to stand at room temperature for 4 days. Extraction with ether and similar work-up as described for the preparation of compound **3** afforded 3.3 g of a residue which was chromatographed on a column of silica gel (100 g, elution with light petroleum–ether 9 : 1). Yield 1.63 g (83%) of an oil which did not crystallize. ^{1}H NMR spectrum: 0.66 s, 3 H (3 × H-18); 0.86 d, 6 H, J = 6.5 (3 × H-26 and 3 × H-27); 0.89 d, 3 H, J = 6.6 (3 × H-21); 0.95 s, 3 H (3 × H-19); 5.18 m, 1 H, $W_{1/2}$ = 6.0 (H-6). IR spectrum: 1 776, 1 301, 1 268, 1 237, 1 216, 1 185, 1 145, 1 122, 1 084, 971, 943, 536 (ester). For $C_{31}H_{47}F_7O_2$ (584.7) calculated: 63.68% C, 8.10% H, 22.74% F; found: 64.03% C, 8.25% H, 22.09% F.

Cholest-5-ene (**7**)

Lithium bromide (465 mg, 5.35 mmol) and pyridinium 4-toluenesulfonate (205 mg, 0.82 mmol) were added to heptafluorobutyrate **6** (2.20 g, 3.76 mmol) in *N*,*N*-dimethylacetamide (22 ml) and the mixture was heated at 160 °C for 2 h. After cooling, the reaction mixture was poured into water and extracted with ether. The ethereal layer was worked up in the usual manner. Yield 1.67 g (84%) of olefin **7** which was twice crystallized from propan-2-ol; m.p. 91–104 °C (reported[7] m.p. 85–94 °C).

^{1}H NMR spectrum: 0.69 s, 3 H (3 × H-18); 0.88 d, 6 H, J = 6.7 (3 × H-26 and 3 × H-27); 0.93 d, 3 H, J = 6.4 (3 × H-21); 1.01 s, 3 H (3 × H-19); 5.28 dm, 1 H, J = 5, $W_{1/2}$ = 10 (H-6). IR spectrum: 3 031 (=C–H); 1 667 (C=C).

5α-Cholestane-3β,7α-diyl 3-Acetate 7-Heptafluorobutyrate (**8**)

A mixture of 5α-cholestane-3β,7α-diol 3-acetate[9] (220 mg, 0.49 mmol), pyridine (2 ml) and heptafluorobutyric anhydride (0.30 g, 0.74 mmol) was allowed to stand at room temperature overnight. The reaction mixture was poured into water, the product was taken up in ether and worked up in the usual manner to give 260 mg of an oil which was purified by chromatography on a column of silica gel (20 g, elution with light petroleum–ether 4 : 1). Yield 240 mg (76%) of oily heptafluorobutyrate **8**. ^{1}H NMR spectrum: 0.66 s, 3 H (3 × H-18); 0.87 s, 3 H (3 × H-19); 0.87 d, 6 H, J = 6.7 (3 × H-26 and 3 × H-27); 0.93 d, 3 H, J = 6.1 (3 × H-21); 4.70 m, 1 H, $W_{1/2}$ = 21 (H-3α); 5.18 m, 1 H, $W_{1/2}$ = 6 (H-7β). IR spectrum: 1 774 (C=O heptafluorobutyrate); 1 735, 1 237, 1 029 (acetate). For $C_{33}H_{49}F_7O_4$ (642.7) calculated: 61.67% C, 7.68% H, 20.69% F; found: 61.60% C, 7.54% H, 20.11% F.

5α-Cholestane-3β,7β-diyl 3-Acetate 7-Heptafluorobutyrate (**9**)

A mixture of 5α-cholestane-3β,7β-diol 3-acetate[9] (115 mg, 0.26 mmol), pyridine (1 ml) and heptafluorobutyric anhydride (0.15 mg, 0.37 mmol) was set aside at room temperature for 26 h. The work-up was the same as in the preceding experiment and afforded 140 mg of an oily product which was purified on a column of silica gel (15 g, elution with light petroleum–ether 4 : 1). Yield 120 mg (73%) of oily heptafluorobutyrate **9**. ^{1}H NMR spectrum: 0.70 s, 3 H (3 × H-18); 0.90 s, 3 H (3 × H-19); 0.87 d, 6 H, J = 6.2 (3 × H-26 and 3 × H-27); 0.93 d, 3 H, J = 6.2 (3 × H-21); 4.70–4.90 m, 2 H (H-3α and H-7α). IR spectrum: 1 774 (C=O heptafluorobutyrate); 1 735, 1 236, 1 028 (acetate). For $C_{33}H_{49}F_7O_4$ (642.7) calculated: 61.67% C, 7.68% H, 20.69% F; found: 61.11% C, 7.58% H, 20.53% F.

5α-Cholest-7-en-3β-yl Acetate (**10**)

A) From heptafluorobutyrate **8**: Lithium bromide (200 mg, 2.30 mmol) and pyridinium 4-toluenesulfonate (20 mg, 0.10 mmol) were added to heptafluorobutyrate **8** (0.20 g, 0.31 mmol) in *N*,*N*-dimethylacetamide (2 ml) and the mixture was heated at 160 °C for 2 h. After cooling, the reaction mixture was poured into water, extracted with ether and the ethereal extract was worked up in the usual manner. The obtained oil (160 ml) was purified by chromatorgraphy on a small column of silica gel (20 g, elution with light petroleum–benzene 1 : 1). The pertinent fractions afforded 111 mg (84%) of olefin **10**; m.p. 113–116 °C (ethanol), in accord with the literature data[10] (m.p. 104–109 °C). ^{1}H NMR spectrum: 0.53 s, 3 H (3 × H-18); 0.81 s, 3 H (3 × H-19); 0.86 d, 3 H, J = 6.7 and 0.87 d, 3 H, J = 6.4 (3 × H-26 and 3 × H-27); 0.89 d, 3 H, J = 6.4 (3 × H-21); 2.03 s, 3 H (acetate); 4.72 m, 1 H, $W_{1/2}$ = 22 (H-3α); 5.14 m, 1 H, $W_{1/2}$ = 9 (H-7). IR spectrum: 3 040 (=C–H); 3 017, 1 664 (C=C); 1 732, 1 243, 1 031 (acetate).

B) From heptafluorobutyrate **9**: Heptafluorobutyrate **9** (52 g, 0.08 mmol) in *N*,*N*-dimethylacetamide (2 ml) was treated with lithium bromide (2.5 mg, 0.03 mmol) and pyridinium 4-toluenesulfonate (10 mg, 0.05 mmol) as described in the preceding experiment and the obtained residue (48 mg) was purified by preparative chromatography on two plates of silica gel in light petroleum–ether (9 : 1). Yield 31 mg (88%) of olefin **10**, m.p. 112–116 °C (ethanol), in all respects identical with olefin **10** obtained in the preceding experiment.

7-Oxoandrost-5-ene-3β,17β-diyl 3-Acetate 17-Heptafluorobutyrate (**11**)

Solid lithium tri-*tert*-butoxyaluminium hydride (1.40 g, 5.69 mmol) was added at room temperature to a solution of 7,17-dioxoandrost-5-en-3-yl acetate[11] (1.40 g, 4.06 mmol) in tetrahydrofuran (28 ml). After standing at room temperature for 7 min, the reaction mixture was carefully poured into water and the product was extracted in ether. The ethereal phase was washed with 10% hydrochloric acid and worked up in the usual manner. The reaction gave 17β-hydroxy-7-oxoandrost-5-en-3β-yl acetate as practically the sole product which was used in the next reaction without further purification.

17β-Hydroxy-7-oxoandrost-5-en-3β-yl acetate (0.50 g, 1.44 mmol) was dissolved in pyridine (2.5 ml), heptafluorobutyric anhydride (1.20 g, 2.93 mmol) was added and the mixture was set aside for 3 days. The reaction mixture was poured into a mixture of ice and water, the product was taken up in ether and the ethereal phase was worked up in the usual manner. The crude product was purified by chromatography on silica gel (70 g, elution with light petroleum containing 20% ether). Yield 0.52 g (85%) of heptafluorobutyrate **11**, m.p. 112–114 °C (acetone–water 4 : 1). ^{1}H NMR spectrum ($CDCl_3$ + CD_3OD, 1 : 1): 0.87 s, 3 H (3 × H-18); 1.23 s, 3 H (3 × H-19); 2.06 s, 3 H (acetate); 4.74 m, 1 H, $W_{1/2}$ = 20 (H-3α); 4.84 m, 1 H, $W_{1/2}$ = 16 (H-17α); 5.74 s, 1 H (H-6). IR spectrum: 3 033 (=C–H); 1 633 (C=C); 1 779, 1 302, 1 267, 1 237, 1 216, 1 187, 1 145, 1 123, 1 086, 1 036 (heptafluorobutyrate); 1 738, 1237 (acetate). For $C_{25}H_{29}F_7O_5$ (542.5) calculated: 55.35% C, 5.39 % H, 24.51% F; found: 55.11% C, 5.42% H, 23.93% F.

7-Oxo-androsta-5,16-dien-3β-yl 3-Acetate (**12**)

Lithium bromide (20 mg, 0.23 mmol) and pyridinium 4-toluenesulfonate (8.4 mg, 0.04 mmol) were added to heptafluorobutyrate **11** (45 mg, 0.08 mmol) in *N*,*N*-dimethylacetamide (2 ml) and the mixture was heated at 160 °C for 50 min. After cooling, the reaction mixture was poured into water, extracted with ether and the ethereal extract was worked up in the usual manner. The obtained oil (32 mg) was purified by preparative chromatography on two plates of silica gel in light petroleum–ether (4 : 1) to afford 19 mg (58 %) of crystalline product **12**, m.p. 74–79 °C (methanol). ^{1}H NMR spectrum: 0.89 s, 3 H (3 × H-18); 1.14 s, 3 H (3 × H-19); 2.03 s, 3 H (acetate); 4.85 m, 1 H, $W_{1/2}$ = 24 (H-3α); 5.63 s, 1 H (H-6); 6.07–6.28 m, 2 H (H-16 and H-17). IR spectrum: 3 035 (=C–H); 1 640, 1 633 (C=C); 1 738, 1 238, 1 031 (acetate). For $C_{21}H_{28}O_3$ (328.5) calculated: 76.79% C, 8.59% H; found: 76.71% C, 8.41% H.

7a-Homo-5α-cholestane-3β,7α-diyl 3-Acetate 7-Heptafluorobutyrate (**13**)

Heptafluorobutyric anhydride (0.50 g, 1.2 mmol) was added to a solution of 7α-hydroxy-7a-homo-5α-cholestan-3β-yl acetate[12] (167 mg, 0.36 mmol) in pyridine (8 ml). After standing at 30 °C overnight, the reaction mixture was poured into water, the product was taken up in ether and the ethereal layer was worked up in the usual manner. The crude product was purified by chromatography on silica gel (20 g, elution with light petroleum containing 30% ether). Yield 191 mg (81%) of oily heptafluorobutyrate **13**. ^{1}H NMR spectrum: 0.65 s, 3 H (3 × H-18); 0.87 s, 3 H (3 × H-19); 0.859 d, 3 H, *J* = 6.7 and 0.864 d, 3 H, *J* = 6.4 (3 × H-26 and 3 × H-27); 0.89 d, 3 H, *J* = 6.4 (3 × H-21); 2.02 s, 3 H (acetate); 4.64 m, 1 H, $W_{1/2}$ = 22 (H-3α); 5.16 m, 1 H, $W_{1/2}$ = 20 (H-7β). IR spectrum: 1 775, 1 303, 1 149, 1 085 (heptafluorobutyrate); 1 736, 1 030 (acetate). For $C_{34}H_{51}F_7O_4$ (656.8) calculated: 62.12% C, 7.83% H, 20.25% F; found: 62.11% C, 7.65% H, 20.01% F.

7a-Homo-5α-cholest-6-en-3β-yl 3-Acetate (**14**)

Lithium bromide (35.8 mg, 0.42 mmol) and pyridinium 4-toluenesulfonate (15.9 mg, 0.086 mmol) were added to heptafluorobutyrate **13** (170 mg, 0.26 mmol) in *N*,*N*-dimethylacetamide (1.7 ml) and

the mixture was heated at 160 °C for 4 h. After cooling, the reaction mixture was poured into water, extracted with ether and the ethereal extract was worked up in the usual manner to give 114 mg of an oil which on crystallization from aqueous methanol afforded 86 mg (73%) of olefin **14**, melting at 76–77 °C (on recrystallization from methanol), in accord with the literature data[12]. ^{1}H NMR spectrum: 0.64 s, 3 H (3 × H-18); 0.98 s, 3 H (3 × H-19); 0.86 d, 6 H, J = 6.7 (3 × H-26 and 3 × H-27); 0.90 d, 3 H, J = 6.4 (3 × H-21); 0.98 s, 3 H (3 × H-19); 2.02 s, 3 H (acetate); 4.62 m, 1 H, $W_{1/2}$ = 22 (H-3α); 5.41 m, 1 H, $W_{1/2}$ = 18 (H-6); 5.75 m, 1 H, $W_{1/2}$ = 24, (H-7). IR spectrum: 3 040 (=C–H); 1 672 (C=C); 1 735, 1 245 (acetate). The mother liquors contained traces (TLC) of the more polar $\Delta^{7(7a)}$-isomer.

5α-Pregna-2,17-dien-6-one (**16**)

Lithium bromide (580 mg, 6.68 mmol) and pyridinium 4-toluenesulfonate (265 mg, 1.33 mmol) were added to (20*R*)-6-oxo-3α,5-cyclo-5α-pregnan-20-yl heptafluorobutyrate[3] **15** (2.60 g, 4.92 mmol) in *N*,*N*-dimethylacetamide (54 ml) and the mixture was heated at 160 °C for 2 h. After cooling, the reaction mixture was poured into water, extracted with ether and the ethereal phase was washed thrice with water and dried over sodium sulfate. Evaporation of the solvent afforded 1.7 g of an oil which was chromatographed on silica gel (400 g, elution with light petroleum–ether 9 : 1). The obtained oil was crystallized from aqueous ethanol to give 0.85 g (58%) of diene **16**, m.p. 117.5–119.5 °C. ^{1}H NMR spectrum: 0.73 s, 3 H (3 × H-18); 0.80 s, 3 H (3 × H-19); 1.54 d, 3 H, J = 6.4 (3 × H-21); 5.11 m, 1 H, $W_{1/2}$ = 16 (H-20); 5.63 m, 2 H, $W_{1/2}$ = 9 (H-2 and H-3). Mass spectrum, *m/z*: 298 (M^+). IR spectrum: 3 030 (=C–H), 1 649, 673 (C=C); 1 719 (C=O). For $C_{21}H_{30}O$ (298.45) calculated: 84.51% C, 10.13% H; found: 84.40% C, 10.30% H.

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