Hydroboration of Tricarbonylironergosteryl Benzoate. Synthesis of (22*R*)- and (22*S*)-3β-Benzoyloxyergosta-5,7-dien-22-ol and (23*R*)-3β-Benzoyloxyergosta-5,7-dien-23-ol

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Hydration of tricarbonylironergosteryl benzoate *via* hydroboration and subsequent decomplexing affords a mixture of (22*R*)- and (22*S*)-3β-benzoyloxyergosta-5,7-dien-22-ol and (23*R*)-3β-benzoyloxyergosta-5,7-dien-23-ol. Oxidation gives 3β-benzoyloxyergosta-5,7-dien-22- and -23-one. On reduction these ketones yield (23*S*)-3β-benzoyloxyergosta-5,7-dien-23-ol in addition to the above three dienols. Stereochemical assignments are on the basis of molecular rotations.

PROTECTION of the 5,7-diene of ergosterol (1) as the tricarbonyliron derivative permits oxidation of the 3β-hydroxy function or selective hydrogenation of the 22(23)-double bond.[1] Such manipulation should also allow electrophilic functionalisation of the 22(23)-double bond with subsequent regeneration of the 5,7-diene. Hydration should provide 22- and 23-hydroxy-3β-benzoyloxyergosta-5,7-diene derivatives which are useful intermediates in the preparation of potential antirachitic calciferol (3) analogues [2] and also of interest in the biosynthesis of the 22(23)-double bond in ergosterol.[3] During our investigations of the chemistry of sterol tricarbonyliron complexes we found that tricarbonylironergosteryl benzoate (4) undergoes ready hydroboration with diborane and we herein report the utilisation of this reaction in the hydration of the 22(23)-double bond in ergosteryl benzoate (2) to produce the title compounds.

Reaction of tricarbonylironergosteryl benzoate (4) with diborane in tetrahydrofuran (THF) and subsequent oxidation with alkaline peroxide [4] furnished a mixture of iron complexes as a yellow foam which resisted crystallisation. However, the spectral data indicated it to be the anticipated isomeric mixture of 3β-benzoyloxy-22- and -23-hydroxytricarbonylironergosta-5,7-dienes. Acetylation of the mixture afforded the isomeric 22- and 23-acetates and trimethylsilylation gave the corresponding silyl ethers (6) and (7). The mass spectrum of the latter mixture showed *m/e* 730 (M^+) and a strong peak at *m/e* 187 [see (6)] which indicated the mixture to constitute mainly the 22-trimethylsilyloxy complexes.[5]

Decomplexing of the tricarbonyliron complexes was attempted with several oxidising agents out of which iron(III) chloride and trimethylamine *N*-oxide gave good yields of the parent diene. Removal of the $Fe(CO)_3$ moiety in 3β-benzoyloxy-22- and -23-hydroxytricarbonylironergosta-5,7-dienes with iron(III) chloride in ethanol and benzene gave two major and one minor diol monobenzoates which were isolated by p.l.c. (see Experimental section). All three compounds contained the intact 3β-benzoate and 5,7-diene functions. Microanalysis and spectral data indicated the compounds to be the expected 3β-benzoyloxy-22- and -23-hydroxyegosta-5,7-dienes.

The minor product was the least polar alcohol, m.p. 154—157°, $[\alpha]_D$ −34°. Oxidation of this with *N*-chlorosuccinimide, dimethyl sulphide, and triethylamine [6] gave the 23-ketone (13). The mass spectrum with *m/e* 445, 417, 99, and 71 (all from α-cleavage) and 402 (McLafferty cleavage) supported this formulation. Reduction of this ketone with sodium borohydride gave a mixture of (23*S*)- and (23*R*)-alcohols (10) and (11). Molecular rotation data (see below) suggested the hydroboration product to be the 23*R*-epimer (11).

The less polar of the two major alcohols was obtained in 34% yield, m.p. 167—168°, $[\alpha]_D$ −47°. The position of the hydroxy function in the side chain was established as C-22 from the mass spectral fragmentation of the trimethylsilyl ether which showed a strong peak at *m/e* 187 (see above). The more polar of the two major products, obtained in 39% yield with m.p. 185—188°, $[\alpha]_D$ −77°, was also shown to be a C-22 alcohol from the mass spectral fragmentation of the trimethylsilyl ether. The two major products gave the same ketone on oxidation.[6] In the mass spectrum both the M^+ and the (M^+ — benzoic acid) ion gave fragments from α-cleavage (*m/e* 431, 403, 309, 281, 113, and 85) of the ketone. The loss of isopentene by McLafferty fragmentation leading to an ion at *m/e* 446 further indicated the product to be the 22-ketone (12).

Sodium borohydride reduction of the 22-ketone (12) gave a mixture of (22*S*)- and (22*R*)-alcohols (8) and (9) in the ratio 10 : 3, identical with the two major products obtained above. The stereoselectivity of reduction of 22-ketones is known to be '*anti*-Cram'.[7] On this basis and from molecular-rotation data (see below) the less polar epimer was assigned as (22*R*)-3β-benzoyloxyergosta-5,7-dien-22-ol (9) and the more polar product as the (22*S*)-epimer (8). Saponification of these diol monobenzoates (8) and (9) gave the corresponding diols (14) and (15). Although the m.p.s of these were lower than the literature values [8] the optical rotations were in agreement. Both compounds gave satisfactory analyses.

Whilst this work was in progress the hydroboration and osmium tetraoxide oxidation of tricarbonylironergosteryl acetate (5) was reported.[9] However, the

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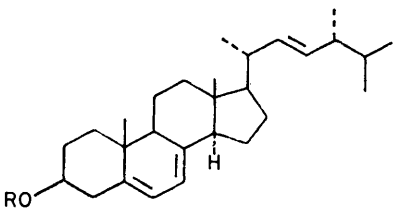
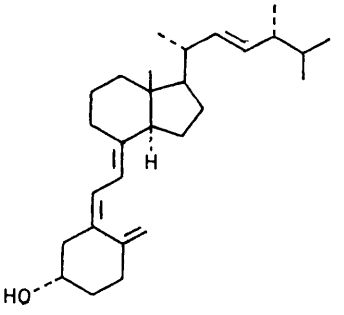
authors failed to separate the non-crystalline product from the hydroboration into its components.

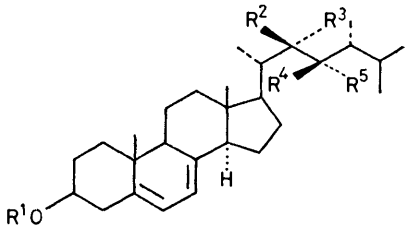
The configurations of the above obtained 22- and 23-alcohols were determined with the aid of their molecular rotations.[7] The molecular rotation data for 22- and 23-alcohols and ketones are given in the Table. Both epimers of the 22-alcohol (8) and (9) have molecular rotations in good agreement with data previously reported.[7] Data for the 23-alcohols (10) and (11) however, were in disagreement with the expected molecular rotations. Thus we were prompted to repeat the preparation [7] of (23*R*)- and (23*S*)-hydroxy-3α,5α-cycloergost-7-en-6-one (16) and (17), respectively. The molecular rotation for the (23*S*)-epimer (17) was found to be +237° in agreement with that reported. The (23*R*)-epimer (16) was however, found to have M_D +358°.* Since the assignment of stereochemistry of these two 23-alcohols was supported by *X*-ray data,[10] (23*R*)-epimers must have higher molecular rotations than their (23*S*)-analogues.



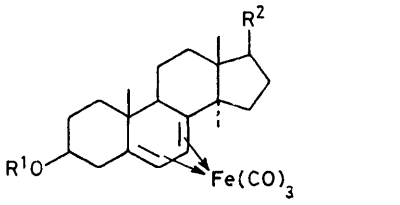
(1) R = H
(2) R = Bz



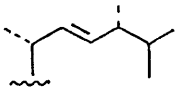
(3)



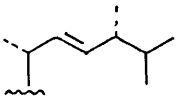
(8) R^1 = Bz, R^2 = OH, R^3 = R^4 = R^5 = H
(9) R^1 = Bz, R^3 = OH, R^2 = R^4 = R^5 = H
(10) R^1 = Bz, R^4 = OH, R^2 = R^3 = R^5 = H
(11) R^1 = Bz, R^5 = OH, R^2 = R^3 = R^4 = H
(12) R^1 = Bz, R^2,R^3 = O, R^4 = R^5 = H
(13) R^1 = Bz, R^4,R^5 = O, R^2 = R^3 = H
(14) R^2 = OH, R^1 = R^3 = R^4 = R^5 = H
(15) R^3 = OH, R^1 = R^2 = R^4 = R^5 = H



(4) R^1 = Bz, R^2 =

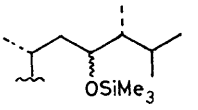


(5) R^1 = Ac, R^2 =

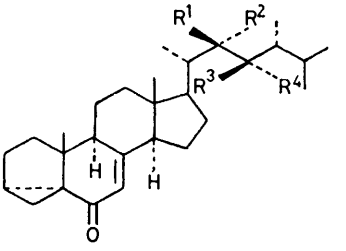


(6) R^1 = Bz, R^2 =

m/e 187



(7) R^1 = Bz, R^2 =



(16) R^4 = OH, R^1 = R^2 = R^3 = H
(17) R^3 = OH, R^1 = R^2 = R^4 = H
(18) R^2 = OH, R^1 = R^3 = R^4 = H
(19) R^1 = OH, R^2 = R^3 = R^4 = H

* Independently confirmed by Dr. G. Johnson of this Department.

EXPERIMENTAL

Unless otherwise stated, m.p.s were determined on a Kofler hot stage apparatus and are uncorrected, optical rotations were determined in AnalaR chloroform, u.v. spectra in ethanol, and n.m.r. spectra in deuteriochloroform at 60 and 220 MHz. Mass spectra were run on an A.E.I. MS 9 or Perkin-Elmer 270 mass spectrometer. All solvents were purified according to standard procedures. Light

petroleum refers to the fraction of boiling range 40—60°. Organic extracts were dried over $MgSO_4$. T.l.c. was carried out on silica gel GF 254 plates. For preparative work these were 1 mm thick; the developing solvent is given in parentheses.

TABLE

Molecular rotation data † for 22- and 23-hydroxysteroids

Steroid	M_D (°)	Δ(OH) [a] (°)	Δ(S−R) (°)
(8)	−401	−104	−154
(9)	−247	+50	
(10)	−295	+2	−114
(11)	−181	+116	
(19) [b]	+198	−99	−148
(18) [b]	+346	+49	
(17)	+237	−60	−121
(16)	+358	+61	
(23*S*)-Cholest-5-ene-3β,23α-diol [c]	−121	+33	−33
(23*R*)-Cholest-5-ene-3β,23β-diol [c]	−88	+66	

† $\Delta(OH) = M_D(\overset{*}{C}\text{–OH}) - M_D(\overset{*}{C}\text{–H})$.

[a] 22,23-Dihydroergosteryl benzoate, M_D −297°; 3α,5α-cycloergost-7-en-6-one, M_D +297°; cholest-5-en-3β-ol, M_D −154°. [b] Ref. 7. [c] J. E. van Lier and L. L. Smith, *J. Pharm. Sci.*, 1970, **59**, 719.

3β-*Benzoyloxy*-22- *and* -23-*hydroxytricarbonylironergosta*-5,7-*dienes*.—Diborane (1M) in THF (30 ml) was added to a solution of tricarbonylironergosteryl benzoate (4) [1] (1.28 g) in anhydrous THF (40 ml) at 0° and under nitrogen. The solution was stirred overnight at room temperature, cooled to 0°, and excess of water was added to destroy unchanged diborane. Aqueous sodium hydroxide (3M; 6 ml), and hydrogen peroxide (30% w/v; 6 ml) were added in sequence. After 0.5 h at room temperature, the mixture was extracted with ether and the extract washed with brine until neutral, dried, and evaporated to yield an isomeric mixture of 3β-benzoyloxy-22- and -23-hydroxytricarbonylironergosta-5,7-dienes as a yellow foam which resisted crystallisation (1.31 g, 100%), $\nu_{max.}$ 3 400 (OH), 2 040 and 1 970 (Fe–C≡O), 1 720 (COOR), and 1 600 cm^{-1}; τ(60 MHz) 1.80—2.10 (2 H, m, ArH), 2.40—2.67 (3 H, m, ArH), 4.90 (2 H, ABq J_{AB} 4 Hz, 6- and 7-H), 5.07br (1 H, m, 3α-H), 6.27br (1 H, m, 22- or 23-H), 7.40—9.00 (CH_2 envelope), and 9.03, 9.10br, and 9.27 (CH_3), *m/e* 630 (M^+ − CO), 614, 612, 602, 586, 584, 574, 559, 557, 541, 518, 396 (100%), and 380.

The above mixture (10 mg) was silylated with hexamethyldisilazane (10 mg) and chlorotrimethylsilane (1 drop) in pyridine (0.5 ml) to obtain a mixture of 22- and 23-*trimethylsilyloxy-complexes* (6) and (7) as a yellow oil (8 mg), *m/e* 730 (M^+), 702, 674, 646 (100%), 630, 590, 468, 452, and 187.

The isomeric mixture of 22- and 23-hydroxy-complexes (100 mg) was acetylated with acetic anhydride (0.2 ml) in pyridine (0.5 ml) to yield the corresponding mixture of *acetates* as a yellow foam (82 mg, 80%). Attempted crystallisation of this failed, $\nu_{max.}$ 2 040 and 1 965 (Fe–C≡O), 1 725 (COOR), and 1 600 cm^{-1}, τ(60 MHz) 1.90—2.17 (2 H, m, ArH), 2.47—2.77 (3 H, m, ArH), 4.93 (2 H, ABq J_{AB} 4 Hz, 6- and 7-H), 5.03br (2 H, m, 3α-H and 22- or 23-H), 7.40—9.00 (CH_2 envelope), 7.97 (3 H, s, $OCOCH_3$), and 9.03, 9.13(br), and 9.30 (CH_3), *m/e* 672 (M^+ − CO) and other fragments.

Oxidative Cleavage of the $Fe(CO)_3$ *Group*.—(a) *With iron*(III) *chloride hexahydrate in THF–ethanol–water*.[11] Tricarbonylironergosteryl benzoate (4) (128 mg) in THF (8 ml), ethanol (5 ml), and water (1 ml) was refluxed for 1.5 h with iron(III) chloride hexahydrate (500 mg). The mixture was cooled to room temperature and extracted with ether and the organic extract washed with brine and saturated EDTA solution, dried, and evaporated to yield ergosteryl benzoate (2) (60 mg, 60%).

(b) *With iron*(III) *chloride hexahydrate in ethanol–benzene*. A mixture of 22- and 23-hydroxy complexes (2.7 g) and iron(III) chloride hexahydrate (4.5 g) in ethanol (15 ml) and benzene (15 ml) were stirred for 48 h at room temperature. After dilution with benzene the mixture was washed several times with water, dried, and evaporated to obtain a mixture of 3β-benzoyloxy-22- and -23-hydroxy-ergosta-5,7-dienes (2.0 g, 100%).

(*c*) *With trimethylamine N-oxide*.[12] Tricarbonylironergosteryl benzoate (60 mg) and trimethylamine *N*-oxide (111 mg) in benzene (5 ml) was refluxed for 1 h (t.l.c. control). The mixture was cooled, filtered through alumina, and evaporated to give ergosteryl benzoate (2) (35 mg, 76%).

(23R)-3β-*Benzoyloxyergosta*-5,7-*dien*-23-*ol* (11), (22R)- (9), *and* (22S)-3β-*benzoyloxyergosta*-5,7-*dien*-22-*ol* (8).—The mixture of 3β-benzoyloxy-22- and -23-hydroxyergosta-5,7-dienes (2.0 g) obtained above [method (b)] was separated by p.l.c. [light petroleum–ether (17 : 3), four developments] to give (in order of increasing polarity) (23R)-3β-*benzoyloxyergosta*-5,7-*dien*-23-*ol* (11) (160 mg, 8%), m.p. 154—157° (from EtOAc–CH_3OH), $[\alpha]_D^{21}$ −34° (*c* 0.48), $\lambda_{max.}$ 229 (ε 10 100), 264 (6 800), 272 (9 200), 282 (9 400), and 294 nm (5 000), τ(220 MHz) 4.38, 4.59 (2 H, m, 6- and 7-H), 5.03 (1 H, m, 3α-H), 6.29 (1 H, m, 23-H), 9.00 (3 H, s, 10-CH_3), 9.00 (3 H, d, *J* 6.5 Hz, 24-CH_3), 9.06 (3 H, d, *J* 6.5 Hz, 20-CH_3), 9.13 and 9.16 [6 H, 2d, *J* 6.5 Hz, 25-$(CH_3)_2$], and 9.33 (3 H, s, 13-CH_3), *m/e* 518(M^+), 397, 396, 378, 253, 212, 199, 158, 145, 143, 141, 122, 105, 97, 95, 91, and 77 (Found: C, 80.85; H, 9.65. $C_{35}H_{50}O_3$ requires C, 81.05; H, 9.7%); (22R)-3β-*benzoyloxyergosta*-5,7-*dien*-22-*ol* (9) (685 mg, 34%), m.p. 167—168° (from EtOAc–CH_3OH), $[\alpha]_D^{20}$ −47° (*c* 0.73), $\lambda_{max.}$ 229 (ε 10 900), 264 (8 300), 272 (11 000), 282 (11 000), and 294 nm (6 100), τ(220 MHz) 4.39, 4.59 (2 H, m, 6- and 7-H), 5.04 (1 H, m, 3α-H), 6.23 (1 H, m, 22-H), 9.00 (3 H, s, 10-CH_3), 9.04 (3 H, d, *J* 6.5 Hz, 20-CH_3), 9.09 (3 H, d, *J* 6.5 Hz, 24-CH_3), 9.15 and 9.22 [6 H, 2d, *J* 6.5 Hz, 25-$(CH_3)_2$], and 9.35 (3 H, s, 13-CH_3), *m/e* 518(M^+), 398, 397, 396, 378, 253, 212, 199, 158, 157, 145, 143, 141, 105, 81, and 77 (Found: C, 80.8; H, 9.5%); and (22S)-3β-*benzoyloxyergosta*-5,7-*dien*-22-*ol* (8) (772 mg, 39%), m.p. 184—187° (from EtOAc–CH_3OH), $[\alpha]_D^{21}$ −77° (*c* 0.37), $\lambda_{max.}$ 229 (ε 13 900), 264 (10 500), 272 (13 900), 282 (14 200), and 294 nm (7 900), τ(220 MHz) 4.37, 4.58 (2 H, m, 6- and 7-H), 5.03 (1 H, m, 3α-H), 6.22 (1 H, m, 22-H), 9.00 (3 H, s, 10-CH_3), 9.05 (3 H, d, *J* 6.5 Hz, 20-CH_3), 9.12 (3 H, d, *J* 6.5 Hz, 24-CH_3), 9.17 [6 H, 2d, *J* 6.5 Hz, 25-$(CH_3)_2$], and 9.35 (3 H, s, 13-CH_3), *m/e* 518 (M^+), 397, 396, 378, 253, 212, 199, 159, 158, 157, 145, 143, 141, 122, 105, 97, 95, 81, and 77 (Found: C, 81.1; H, 9.55%).

A small portion of the (22*R*)-alcohol (9) was silylated in the usual manner (see above) to obtain the corresponding trimethylsilyl ether, *m/e* 468 (M^+ − benzoic acid), 396, 378, 363, and 187 (100%).

(22R)- *and* (22S)-*Ergosta-5,7-diene-3β,22-diol* (15) *and* (14).—Saponification of benzoates (9) and (8) with methanolic potassium hydroxide gave respectively, (22*R*)-ergosta-5,7-diene-3β,22-diol (15), m.p. 138—140° (from CH_3OH), $[\alpha]_D^{21}$ −112° (*c* 0.61) (lit.,[7] m.p. 162—165°, $[\alpha]_D$ −117°) (Found: C, 80.8; H, 10.9. $C_{28}H_{46}O_2$ requires: C, 81.1; H, 11.1%), and (22*S*)-ergosta-5,7-diene-3β,22-diol (14), m.p. 180—182° (from CH_3OH), $[\alpha]_D^{21}$ −144° (*c* 0.61) (lit.,[7] m.p. 204—206°, $[\alpha]_D$ −152°) (Found: C, 81.0; H, 11.1%).

3β-*Benzoyloxygerosta-5,7-dien-22-one* (12).—Methyl sulphide (0.1 ml) and (22*R*)-3β-benzoyloxergosta-5,7-dien-22-ol (9) (100 mg) in toluene (3 ml) were added with stirring in sequence at 0 and −25° to *N*-chlorosuccinimide (128 mg) in toluene (4 ml). After 2 h at −25°, triethylamine (202 mg) in toluene (0.4 ml) was added dropwise and the mixture was warmed to room temperature. Ether was added and the organic phase washed with 1% aqueous HCl and water, dried, and evaporated to give 3β-*benzoyloxyergosta-5,7-dien-22-one* (12) (80 mg, 80%), m.p. 156—159° (from EtOAc–CH_3OH), $[\alpha]_D^{21}$ −64° (*c* 0.40), $\nu_{max.}$ 1 720 and 1 700 cm^{-1}, $\lambda_{max.}$ 227 (ε 11 200), 262 (7 400), 271 (10 100), 281 (10 300), and 293 nm (5 700), τ(220 MHz) 4.42, 4.63 (2 H, m, 6- and 7-H), 5.08 (1 H, m, 3α-H), 8.90 (3 H, d, *J* 6.5 Hz, 20-CH_3), 9.00 (3 H, s, 10-CH_3), 9.14 (3 H, d, *J* 6.5 Hz, 24-CH_3), 9.17 and 9.20 [6 H, 2d, *J* 6.5 Hz, 25-$(CH_3)_2$], and 9.36 (3 H, s, 13-CH_3), *m/e* 516 (M^+), 446 (McLafferty cleavage), 431, 403, 394, 309, 281, 141, 113, 95, and 85 (α-cleavage) (Found: C, 81.1; H, 9.35. $C_{35}H_{48}O_3$ requires C, 81.35; H, 9.35%).

Oxidation of (22*S*)-3β-benzoyloxyergosta-5,7-dien-22-ol (8) (100 mg) by the same method gave 22-ketone (12) (75 mg, 75%), m.p. 156—159°, $[\alpha]_D^{21}$ −64° (*c* 0.43) (Found: C, 81.3; H, 9.2%). Identity with the ketone derived from the (22*R*)-alcohol (9) followed from all spectra data.

3β-*Benzoyloxyergosta-5,7-dien-23-one* (13).—Oxidation [5] of (23*R*)-3β-benzoyloxyergosta-5,7-dien-23-ol (11) (83 mg) gave 3β-*benzoyloxyergosta-5,7-dien-23-one* (13) (74 mg, 89%), m.p. 155—158° (from EtOAc–CH_3OH), $[\alpha]_D^{21}$ −56° (*c* 0.40), $\nu_{max.}$ 1 720 and 1 700 cm^{-1}, τ(220 MHz) 4.50, 4.71 (2 H, m, 6- and 7-H), 5.17 (1 H, m, 3α-H), 9.03 (3 H, s, 10-CH_3), 9.04 (3 H, d, *J* 6.5 Hz, 24-CH_3), 9.07 (3 H, d, *J* 6.5 Hz, 20-CH_3), 9.11 and 9.17 [6 H, 2d, *J* 6.5 Hz, 25-$(CH_3)_2$], and 9.34 (3 H, s, 13-CH_3), *m/e* 516 (M^+), 445, 417, 402 (McLafferty cleavage), 394, 323, 296, 141, 99, and 71 (α-cleavage) (Found: C, 81.1; H, 9.4%).

Reduction of 3β-*Benzoyloxyergosta-5,7-dien-23-one* (13).—Sodium borohydride (57 mg) and the ketone (13) (50 mg) in THF (4 ml), propan-2-ol (2 ml), and water (5 drops) were stirred for 3 h at room temperature. Water and ether were added and the organic layer was dried and evaporated to give a mixture of epimeric 23-alcohols (46 mg, 92%) in the ratio of 1 : 1. Purification by p.l.c. [light petroleum–ether (17 : 3), four developments] gave (23*R*)-3β-benzoyloxyergosta-5,7-dien-23-ol (11), m.p. 160—161°, $[\alpha]_D^{21}$ −35° (*c* 0.42), identical with that prepared previously, and (23S)-3β-*benzoyloxyergosta-5,7-dien-23-ol* (10), m.p. 123—126° (from EtOAc–CH_3OH), $[\alpha]_D^{21}$ −57° (*c* 0.38), $\nu_{max.}$ 3 400, 1 700, and 1 100 cm^{-1}, *m/e* 518 (M^+), 502, 487, 397, 396, 394, 378, 253, 158, 143, 122, and 105 (Found: C, 80.75; H, 9.45. $C_{35}H_{50}O_3$ requires C, 81.05; H, 9.7%).

Reduction of 3β-*Benzoyloxyergosta-5,7-dien-22-one* (12).—Sodium borohydride reduction of the ketone (12) as above gave (22*S*)- and (22*R*)-alcohols (8) and (9) in the ratio 10 : 3, whose identity were confirmed by comparison with samples from the hydroboration.

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REFERENCES

[1] D. H. R. Barton, A. A. L. Gunatilaka, T. Nakanishi, H. Patin, D. A. Widdowson, and B. R. Worth, *J.C.S. Perkin I*, 1976, 821; D. H. R. Barton and H. Patin, *ibid.*, p. 829.

[2] See *e.g.* T. Suda, H. F. De Luca, H. K. Schnoes, Y. Tanaka, and M. F. Halick, *Biochemistry*, 1970, **9**, 4776; D. E. M. Lawson, P. W. Wilson, and E. Kodicek, *Biochem. J.*, 1969, **115**, 269; D. E. M. Lawson, D. R. Fraser, E. Kodicek, H. R. Morris, and D. H. Williams, *Nature*, 1971, 230.

[3] J. D. Weete, *Phytochemistry*, 1973, **12**, 1843; L. W. Parks, F. T. Bond, E. D. Thompson, and P. R. Starr, *J. Lipid Res.*, 1972, **13**, 311.

[4] G. Zweifel and H. C. Brown, ' Organic Reactions ', Wiley, London, vol. 13, 1963.

[5] D. R. Crump, D. H. Williams, and B. Pelc, *J.C.S. Perkin I*, 1973, 2731.

[6] E. J. Corey and C. U. Kim, *J. Amer. Chem. Soc.*, 1972, **94**, 7586.

[7] D. H. R. Barton, J. P. Poyser, and P. G. Sammes, *J.C.S. Perkin I*, 1972, 53.

[8] J. Brynjolffssen, D. Hands, J. M. Midgley, and W. B. Whalley, *J.C.S. Perkin I*, 1976, 826.

[9] G. Evans, B. F. G. Johnson, and J. Lewis, *J. Organometallic Chem.*, 1975, **102**, 507.

[10] M. B. Hursthouse and S. Neidley, *J.C.S. Perkin II*, 1973, 781.

[11] G. F. Emerson and R. Pettit, *J. Org. Chem.*, 1964, **29**, 3620.

[12] Y. Shvo and E. Hazum, *J.C.S. Chem. Comm.*, 1974, 336.