Addition of Dichlorocarbene to Steroidal Olefins. Preparation of a Stereoisomer of Demethylgorgosterol, a Cyclopropane-containing Marine Sterol

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Dichlorocarbene generated by pyrolysis of sodium trichloroacetate added to the 24,28-double bond of 5α-stigmast-24(28)-ene [$\Delta^{24(28)}$-fucostene] (6) but failed to add to either the 5,6- or 22,23-double bond of ergosta-5,22-dien-3β-ol (brassicasterol) (19). However, dichlorocarbene generated by reaction of sodium hydroxide with chloroform in the presence of benzyltriethylammonium bromide added from the β side to the 5,6-double bond of cholesteryl (9), stigmasteryl (12), and brassicasteryl (18) acetates, to the 7,8-double bond (from the α side) of cholest-7-en-3β-yl (10) and 5α-ergosta-7, 22-dien-3β-yl (17) acetates, and to the 22,23-double bond of 5α-ergost-22-en-6β-yl (11) and brassicasteryl (18) acetates.

In connection with our work on steroids and terpenoids from marine sources and in view of the biogenetic significance of the unusual cyclopropane-containing marine sterols gorgosterol [1,2] (1), demethylgorgosterol [3] (2), acanthasterol [4] (3), and 9-oxo-9,11-secogorgost-5-ene-3β,11-diol [5] (4), we have been engaged in synthetic studies of such sterols for some years. Since *X*-ray diffraction analysis [2,5] of (1), (2), and (4) had already established the presence of a *transoid* cyclopropane ring (the configuration at carbon atoms 22, 23, and 24 is *R*), we decided to employ the side chain of Δ^{22}-olefinic steroids and introduce the additional methyl and methylene groups after appropriate protection of the Δ^5-3β-hydroxy-system. The recent report by Ikan *et al.*,[6] prompts us to report our results since these differ somewhat from those of the Israeli authors.

[1] R. L. Hale, J. Leclercq, B. Tursch, C. Djerassi, R. A. Gross, jun., A. J. Weinheimer, K. Gupta, and P. J. Scheuer, *J. Amer. Chem. Soc.*, 1970, **92**, 2179.

[2] N. C. Ling, R. L. Hale, and C. Djerassi, *J. Amer. Chem. Soc.*, 1970, **92**, 5281.

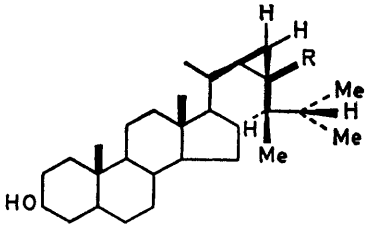
[3] F. J. Schmitz and T. Pattabhiraman, *J. Amer. Chem. Soc.*, 1970, **92**, 6073.

[4] K. C. Gupta and P. J. Scheuer, *Tetrahedron*, 1967, **24**, 5831; Y. M. Sheikh, C. Djerassi, and B. M. Tursch, *Chem. Comm.*, 1971, 217, 600.

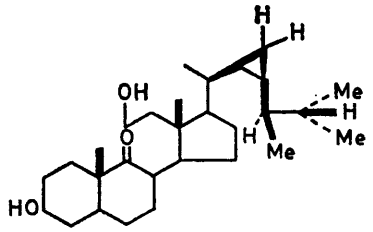
[5] E. L. Enwell, D. V. Der Helm, I. H. Hsu, T. Pattabhiraman, F. J. Schmitz, R. L. Spraggins, and A. J. Weinheimer, *J.C.S. Chem. Comm.*, 1972, 215.

[6] R. Ikan, A. Markus, and Z. Goldschmidt, *J.C.S. Perkin I*, 1972, 2423.

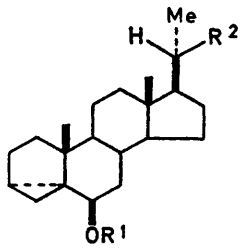
Carbenoid addition to a *trans* Δ^{22}-steroidal double bond appeared attractive. Although both stereoisomers were expected, it was hoped that a suitable separation procedure could be worked out. However, our limited attempts to methylenate the 22,23-double bond of brassicasterol (19) under a variety of Simmons–Smith [7] conditions with or without protection of the Δ^5-3β-hydroxy-system as a 3,5-cyclo-6-ether [8] or 6-acetate resulted in recovery of starting material.



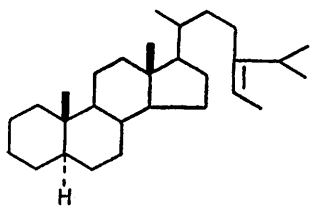
(1) R = Me, Δ^5, (22*R*,23*R*,24*R*)
(2) R = H, Δ^5, (22*R*,23*R*,24*R*)
(3) R = Me, Δ^7, 5α (22*R*,23*R*,24*R*)



(4) (22*R*,23*R*,24*R*)



(5) R^1 = Ac, R^2 = CH:CH·CH(Me)·CHMe$_2$ (*R*)



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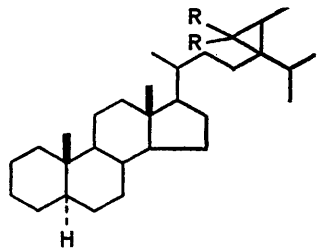


(7) R = Cl
(8) R = H

Methylene addition to $\Delta^{24(28)}$-fucostene (6) *via* Simmons–Smith [7a] reaction proceeded in poor yield (10%) but dichlorocarbene generated by pyrolysis of sodium trichloroacetate [9,10] added readily (69% yield) to furnish the dichloro-adduct (7) which on subsequent dechlorination with lithium in ammonium gave the hydrocarbon (8). However, dichlorocarbene generated by the foregoing method did not add to the 22,23-double bond of brassicasterol (19).

As an alternative source of a more reactive dichlorocarbene, we examined a procedure recently developed by Dehmlow *et al.*[11] Assuming that 5,6- and 22,23-steroidal double bonds are equally sterically accessible, that benzyltriethylammonium bromide is a true micelle,[12] and that the carbenoid addition takes place at the interface, then it is expected that the more polar group (acetate in the present case) will be oriented towards the charge heads while the steroidal side chain should be hidden in the lipophilic portion of the micelle. Since the frequency of exposure to carbenoid addition of various double bonds should decrease with increasing distance from the charge heads, the addition should take place preferentially at the nuclear unsaturation in the presence of the 22,23-double bond in steroids with nuclear and side chain unsaturations. Indeed, dichlorocarbene generated by the foregoing procedure readily added to cholesteryl acetate (9) from the β-side to furnish the adduct (20) and to cholest-7-en-3β-yl acetate (10) from the α-side to provide the adduct (28). These observations are apparently different from the previous observations [13,14] wherein both dichloro- and dibromo-carbenes were inert [15] to Δ^5-steroids bearing a 10β-methyl group although α attack did occur with a 5,7-diene [13] and β attack with a 3,5-diene.[14] The structure and stereochemistry of our adducts (20) and (28) was established by sodium–ammonia dechlorination

[7] (*a*) 24,25-Methylenelanost-8-en-3β-ol has recently been prepared, C. R. Toubiana and E. Lederer, *Bull. Soc. chim. France*, 1963, 2563, by Simmons–Smith reaction; (*b*) R. D. Smith and H. E. Simmons, *Org. Synth.*, 1961, **41**, 72; R. Ginsig and A. D Cross, *J. Amer. Chem. Soc.*, 1965, **87**, 4629; R. J. Rawson and I. T. Harrison, *J. Org. Chem.*, 1970, **35**, 2057.

[8] E. Fernholz and W. L. Ruigh, *J. Amer. Chem. Soc.*, 1940, **62**, 3346; J. A. Steele and E. Mosettig, *J. Org. Chem.*, 1963, **28**, 571.

[9] S. W. Toby and R. West, *Tetrahedron Letters*, 1963, 1179; S. W. Toby and R. West, *J. Amer. Chem. Soc.*, 1966, **88**, 2481; W. R. Moore, S. E. Krikorian, and J. E. La Prade, *J. Org. Chem.*, 1963, **28**, 1404.

[10] In our experiment dichlorocarbene generated by phenyl(trihalogenomethyl)mercury (W. E. Parham and R. J. Sperley, *J. Org. Chem.*, 1967, **32**, 926) failed to add to brassicasterol (19), T. Powers, unpublished results.

[11] M. Makosza and W. Wawryniewicz, *Tetrahedron Letters*, 1969, 4659; E. V. Dehmlow and J. Schonfeld, *Annalen*, 1971, **744**, 42; E. V. Dehmlow, *Tetrahedron*, 1971, **27**, 4071; 1972, **28**, 175; G. C. Joshi, N. Singh, and L. M. Pande, *Tetrahedron Letters*, 1972, 1461.

[12] E. H. Cordes and C. Gitler, 'Reaction Kinetics in the Presence of Micelle-forming Surfactants,' in 'Progress in Bio-Organic Chemistry,' vol. 1, eds. E. J. Kaiser and F. J. Kezdy, Wiley-Interscience, New York, 1973, pp. 1—53.

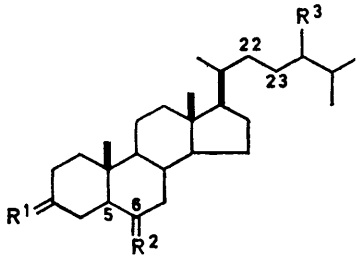
[13] M. Z. Nazer, *J. Org. Chem.*, 1965, **30**, 1737.

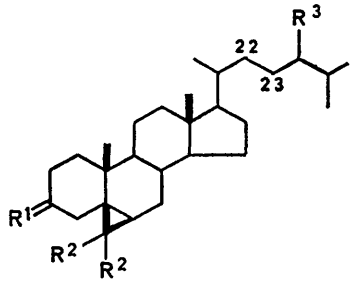
[14] L. H. Knox, E. Velarde, S. Berger, D. Guadriello, P. W. Landis, and A. D. Cross, *J. Amer. Chem. Soc.*, 1963, **85**, 1851.

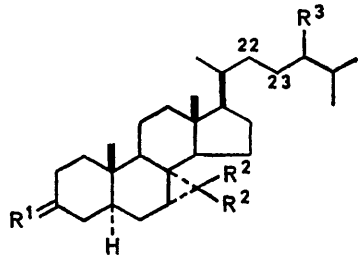
[15] Dichlorocarbene prepared by pyrolysis of $PhHgCCl_3$ has recently been added to the more nucleophilic 6-methylcholest-5-en-3β-yl benzoate (F. T. Bond and R. H. Cornelia, *Chem. Comm.*, 1968, 1189).

to the cyclopropane steroids (21) [16] and (29) and their subsequent Jones oxidation to the corresponding ketones (23) [16] and (30), which displayed the expected [16] Cotton effects.

sodium–ammonia reduction furnished (25). Its mass spectrum had peaks at *m/e* 287 and 285 corresponding to loss of the side chain with or without transfer of two hydrogens [17] and at *m/e* 245 representing the typical







(9) R^1 = 3β-OAc, $R^2 = R^3 = H$, Δ^5

(10) R^1 = 3β-OAc, $R^2 = H_2$, $R^3 = H$, $\Delta^{7,5\alpha}$

(11) $R^1 = H_2$, R^2 = 3β-OAc, R^3 = β-Me, Δ^{22}

(12) R^1 = 3β-OAc, $R^2 = H$, R^3 = α-Et, $\Delta^{5,22}$

(13) R^1 = 3β-OH, $R^2 = H$, R^3 = α-Et, $\Delta^{5,22}$

(14) $R^1 = O$, $R^2 = H_2$, R^3 = α-Et, $\Delta^{4,22}$

(15) $R^1 = O$, $R^2 = H_2$, R^3 = α-Et,4-Me, $\Delta^{4,22}$

(16) $R^1 = R^2 = H_2$, R^3 = α-Et, Δ^{22}

(17) R^1 = 3β-OAc, $R^2 = H_2$, R^3 = β-Me, $\Delta^{7,22}$

(18) R^1 = 3β-OAc, $R^2 = H$, R^3 = β-Me, $\Delta^{5,22}$

(19) R^1 = 3β-OH, $R^2 = H$, R^3 = β-Me, $\Delta^{5,22}$

(20) R^1 = 3β-OAc, R^2 = Cl, $R^3 = H$

(21) R^1 = 3β-OH, $R^2 = R^3 = H$

(22) R^1 = 3β-OAc, $R^2 = R^3 = H$

(23) $R^1 = O$, $R^2 = R^3 = H$

(24) R^1 = 3β-OAc, R^2 = Cl, R^3 = α-Et, Δ^{22}

(25) R^1 = 3β-OH, $R^2 = H$, R^3 = α-Et, Δ^{22}

(26) $R^1 = O$, $R^2 = H$, R^3 = α-Et, Δ^{22}

(27) R^1 = 3β-OH, $R^2 = H$, R^3 = β-Me, Δ^{22}

(28) R^1 = 3β-OAc, R^2 = Cl, $R^3 = H$

(29) R^1 = 3β-OH, $R^2 = R^3 = H$

(30) $R^1 = O$, $R^2 = R^3 = H$

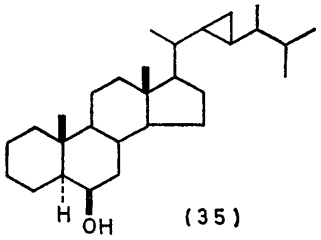
(31) R^1 = 3β-OAc, R^2 = Cl, R^3 = β-Me, Δ^{22}

(32) R^1 = 3β-OAc, $R^2 = H$, R^3 = β-Me, Δ^{22}

(33) R^1 = 3β-OH, $R^2 = H$, R^3 = β-Me, Δ^{22}

(34) $R^1 = O$, $R^2 = H$, R^3 = β-Me, Δ^{22}

Contrary to the behaviour with Δ^5- and Δ^7-sterols, dichlorocarbene addition to 5α-ergost-22-en-6β-yl acetate (11) proceeded slowly and resulted in a complex mixture which on subsequent dechlorination and preparative g.l.c. furnished one pure compound (<10%) which was assigned tentatively structure (35) on the basis of its retention time and mass spectrum.



(35)

Dichlorocarbene addition to stigmasteryl acetate (12) provided only one adduct (24) which on subsequent ring D [18] cleavage of steroids. The mass spectrum of (25) in conjunction with its n.m.r. spectrum indicating the presence of only three cyclopropane protons (δ −0·03 to 0·65) and two olefinic protons (δ 5·06) and the C-19 methyl signal [16] at δ 0·90 firmly established the structure and stereochemistry of (25). Jones oxidation of (25) led to the ketone (26) which displayed no u.v. absorption in the 240 nm region in both basic and neutral medium and gave a positive Cotton effect [16] as expected.

The mass spectra of (25) and (26) also contained peaks at *m/e* 314 and 312, respectively, corresponding to cleavage of the C-20–C-23 bond with concomitant transfer of one hydrogen and do not represent formal cleavage of a cyclopropane [19] between positions 22 and 23. Apparently this C-20–C-22 bond fission is a common feature of steroids [*e.g.* *m/e* 300 in (13)] of the stigmastane

[16] L. Kohout and J. Fajkos, *Coll. Czech. Chem. Comm.*, 1972, 3490.

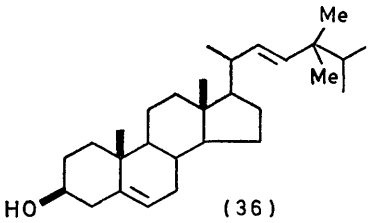
[17] S. G. Wyllie and C. Djerassi, *J. Org. Chem.*, 1968, **33**, 305.

[18] L. Tökés, G. Jones, and C. Djerassi, *J. Amer. Chem. Soc.*, 1968, **90**, 5465.

[19] J. R. Dias and C. Djerassi, *Org. Mass Spectrometry*, 1973, **7**, 753.

series carrying 20,22-unsaturation, *e.g.* (13) [*m/e* 314 (5%) and 300 (17)], (14) [*m/e* 312 (8) and 298 (34)], (15) [*m/e* 326 (20) and 312 (54)], and (16) [*m/e* 300 (6) and 286 (42)]. The peaks at *m/e* 314, 312, 326, and 300 in compounds (13), (14), (15), and (16) respectively possibly are generated by movement of the 22,23-double bond after ionization to C-23 followed by cleavage of the C-22–C-23 bond with transfer of one hydrogen.

A similar reaction sequence with 5α-ergosta-7,22-dien-3β-yl acetate (17) furnished compounds (31)—(34) whose structures were consistent with their spectral



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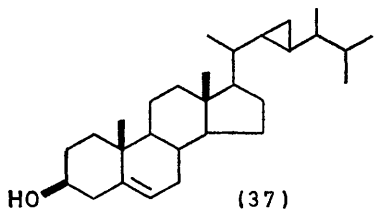

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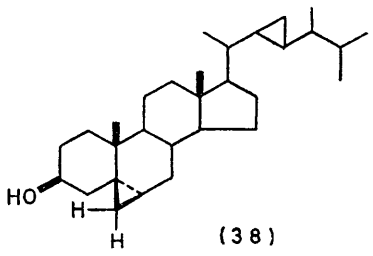

(38)

characteristics. However, a similar reaction sequence with brassicasteryl acetate (18) proceeded without any selectivity and furnished 5β,6β-methylene-ergost-22-en-3β-ol (27), 24,24-dimethylcholesta-5,22-dien-3β-ol (36), 5β,6β:22,23-dimethylene-ergostan-3β-ol (38), and (37). The mass spectrum of (36) had an intense peak at *m/e* 369 (70 eV, 85%; 15 eV 100%) corresponding to a loss of C_3H_7 presumably due to highly favoured fission of the C-24–C-25 bond and at *m/e* 271 representing the loss of the side chain and two hydrogens.[17] In addition the n.m.r. spectrum of (36) contained a singlet at δ 0·87 (6H)(24,24-dimethyl) consistent with the proposed structure. There is precedent for this type of carbene reaction.[15]

The n.m.r. and mass spectra of (37) were identical with those of natural demethylgorgosterol (2).[3] However there were substantial differences in optical rotation and gas chromatographic retention time thus showing that the natural (2) and synthetic (37) products must differ in the stereochemistry at position 22 and 23.

EXPERIMENTAL

M.p.s were determined with a Kofler hot stage apparatus. U.v. spectra were recorded in 95% ethanol with a Cary model 14 spectrometer; i.r. spectra were obtained for solutions in chloroform or as potassium bromide pellets with a Perkin-Elmer 421 spectrometer. N.m.r. spectra were obtained with [^{2}H]chloroform as solvent and tetramethylsilane or chloroform as internal reference on a Varian HA-100 spectrometer. Optical rotations were recorded with a Perkin-Elmer model 141 spectropolarimeter for solutions in chloroform; o.r.d. and c.d. curves were determined for solution in dioxan by Mrs. R. Records with a JASCO o.r.d./u.v. 5 spectrometer with c.d. attachment Low resolution mass spectra were obtained by Messrs. R. G. Ross and R. Conover with an A.E.I. MS9 and Atlas CH4 spectrometers operating at 70 eV using a direct inlet system. High resolution measurements were obtained with the MS9 instrument on line to the ACME computer facility of the Stanford University Medical Centre.

Oppenauer Oxidation of Fucosterol.—A mixture of fucosterol (2 g) in dry toluene (100 ml), distilled cyclohexanone (20 ml), and aluminium isopropoxide (2·5 g) was refluxed for 30 min. Removal of solvent under vacuum followed by p.l.c. over silica gel furnished fucostenone, m.p. 95·5—96·5° (lit.,[20] 95—98°).

$\Delta^{24(28)}$-Fucostene (6).—A solution of fucostenone [20] (800 mg) in dry ether (100 ml) was added to a stirred solution of liquid ammonia (100 ml) and lithium [21] (300 mg). After 40 min the mixture was quenched with t-butyl alcohol–ether followed by ethanol (10 ml) until the blue colour disappeared. The residue after evaporation of ammonia was partitioned between ether and water. The ether layer was washed with water and subjected to Jones oxidation for 5 min. Chromatography of the resulting product furnished pure $\Delta^{24(28)}$-fucosten-3-one (235 mg), m.p. 137—138·5°. Wolff–Kishner reduction of $\Delta^{24(28)}$-fucosten-3-one furnished $\Delta^{24(28)}$-fucostene [5α-stigmast-24(28)-ene] (6), m.p. 74—75° (40% yield), δ 0·68 (s, 18-H_3), 0·75 (s, 19-H_3), 1·55 (d, 29-H_3), and 5·22 (m, 28-H), *m/e* 398 (M^+), 383 ($M - CH_3$), 300 ($M - C_7H_{14}$, 100%), 285, 257 (*M*-side chain + 2H), 244, 231, 217, 218, and 203.

Carbene Additions to $\Delta^{24(28)}$-Fucostene.—To a solution of $\Delta^{24(28)}$-fucostene (6) (146 mg) in dry tetrachloroethylene (3 ml) and diethylene glycol dimethyl ether (0·75 ml) was added sodium trichloroacetate (500 mg). The mixture was heated under reflux for 1 h; two 200 mg portions of sodium trichloroacetate were added and after further refluxing for 30 and 45 min, the mixture was poured into water and extracted with chloroform. The chloroform extract after chromatography over silica gel furnished the dichlorocarbene adduct, 24,28-dichloromethylene-5α-stigmastane (7) (122 mg), m.p. 112·5—114° (from MeOH), δ 0·65 (3H, s, 18-H_3), 0·78 (s, 19-H_3), and 1·17 (d, *J* 6 Hz, 26- and 27-H_3), *m/e* 480—482 (M^+), 444—446 (M —HCl), 370 ($M - CH_3CH{=}CCl_2$), 300 ($M - C_8H_{14}Cl_2$), 285 (300 — CH_3), 257 (M — side chain + 2H), and 217 (ring D cleavage + 1H).

A solution of the dichloro-adduct (7) (120 mg) in dry ether (20 ml) was added to a solution of lithium (100 mg) in liquid ammonia (50 ml). The mixture was stirred for 1 h and quenched with ethanol (10 ml) and ether (20 ml). After evaporation of ammonia, the residue was partitioned between ether and water. The residue from the ether layer on repeated crystallization from methanol–ether furnished the cyclopropane adduct, 24,28-methylene-5α-

[20] E. R. H. Jones, P. A. Wilkinson, and R. H. Kerlogue, *J. Chem. Soc.*, 1942, 391.

[21] D. H. R. Barton, D. A. J. Ives, and B. R. Thomas, *J. Chem. Soc.*, 1954, 903.

stigmastane (8), m.p. 80—82°, $[\alpha]_D^{21}$ +19° (*c* 0·55), δ 0·25—0·45 (cyclopropane H), 0·65 (s, 18-H_3), 0·76 (s, 19-H_3), and 0·79 (d, *J* 6 Hz, 26- and 27-H_3), *m/e* 412 (M^+, 55%), 397 ($M - CH_3$), 385 ($M - C_3H_7$), 355, 300, 285 ($300 - CH_3$), and 217 (ring D cleavage + 1H).

A solution of $\Delta^{24(28)}$-fucostene (6) (185 mg) in ether (10 ml) was added to the organozinc prepared from a Zn–Cu couple (135 g) and di-iodomethane (5 g) in ether (50 ml) and the mixture was refluxed for 100 h. Work-up in the usual fashion followed by p.l.c. furnished starting material (163 mg) and the cyclopropane steroid (8) (20 mg).

Simmons–Smith Reaction with Brassicasterol (19).—Zinc (45 mg) and copper(I) chloride (120 mg) were refluxed under N_2 in ether (3·5 ml) for 15 min. Brassicasterol (ergosta-5,22-dien-3β-ol) (20 mg) was then added followed by CH_2I_2 (10 μl) and the mixture refluxed for 48 h under N_2. Only starting material was recovered after the usual work-up.

A solution of *i*-brassicasterol acetate (3α,5-cyclo-5α-ergost-22-en-5β-yl acetate) (5a) (500 mg) in ether (15 ml) and di-iodomethane (2·0 ml) was added to a suspension (refluxed prior to addition for 30 min) of zinc (2·8 g) and copper(I) chloride (0·4 g) in ether (10 ml). The mixture was worked up after 48 h and consisted essentially only of staring material (analytical g.l.c.).

5β,6β-*Dichloromethylenecholestan*-3β-*yl Acetate* (20).—To a solution of cholesteryl acetate (9) (2·0 g) benzyltriethylammonium bromide (0·2 g) in chloroform (30 ml) was added dropwise with vigorous stirring 50% sodium hydroxide (20 ml). The mixture was stirred for 96 h at room temperature, poured into water, and extracted with chloroform. The extract after washing with water was dried over sodium sulphate and evaporated to furnish a pale gum. Column chromatography over Florisil using benzene–hexane as eluant furnished the pure dichloro-adduct (20) (60%), as an oil, *m/e* 510—512 (M^+), $[\alpha]_D^{21}$ −40·6° (*c* 0·62), δ 0·63 (s, 18-H_3), 0·84 (d, *J* 6 Hz), 1·25 (s, 19-H_3), 2·05 (s, Ac), and 5·00br (1H, C*H*·OAc). Benzyltriethylammonium bromide was prepared by reaction of equimolar amounts of triethylamine and benzyl bromide in acetone. The yield of dichloro-adduct (20) was insensitive to the amounts of the catalyst (0·2—0·4 g) and chloroform (30—60 ml).

5β,6β-*Methylenecholestan*-3β-*ol* (21).—To a solution of sodium (1·2 g) in liquid ammonia (125 ml) was added the dichloro-adduct (20) (800 mg) in ether (60 ml). The mixture was stirred for 3 h and quenched with solid ammonium chloride. After evaporation of ammonia, the residue was partitioned in ether–water. The dried (Na_2SO_4) ether layer was evaporated and acetylated with acetic anhydride–pyridine and the resulting acetate chromatographed over alumina (grade II). Elution with hexane–benzene (3 : 7) furnished pure 5β,6β-methylenecholestan-3β-yl acetate (22) which on subsequent saponification furnished 5β,6β-methylenecholestan-3β-ol (21) in 60% yield, m.p. 98—100; $[\alpha]_D^{21}$ −5·0 ± 1° (lit.,[16] m.p. 101—102°, $[\alpha]_D^{20}$ −3·0°). Jones oxidation of (21) followed by crystallization from methanol–acetone–water furnished the corresponding ketone (23), M^+ 398, m.p. 72—73° (lit.,[19] 75—77°).

7α,8α-*Dichloromethylene*-5α-*cholestan*-3β-*yl Acetate* (28).—The *adduct* (28) was obtained in 80% yield and purified as described for (20); m.p. 129—130° (needles from methanol), $[\alpha]_D^{21}$ −46·4° (*c* 0, 112), M^+ 510, 512, δ 0·82 (s, 18-H_3), 0·86 (d, *J* 6 Hz, 26- and 27-H_3), 0·89 (s, 19-H_3), 2·00 (s, Ac), and 4·65br (1H, C*H*·OAc) (Found: C, 70·0; H, 9·4; Cl, 13·7. $C_{30}H_{50}Cl_2O_2$ requires C, 70·1; H, 9·7; Cl, 13·8%).

7α,8α-*Methyl*-5α-*cholestan*-3β-*ol* (29).—The dichloro-adduct (28) was dechlorinated with Na–NH_3 as described for (21) to furnish 7α,8α-methylene-5α-cholestan-3β-ol (29) in 70% yield, as a low melting solid, δ −0·07 (t, *J* 4·0 Hz), 0·25 (d, *J* 4·0 and 8·5 Hz), 0·75 (s, 18-H_3), 0·81 (d, *J* 6 Hz, 26- and 27-H_3), 0·86 (s, 19-H_3), and 3·43br (1H, C*H*·OH), *m/e* 400 (M^+), 385 ($M - CH_3$), 382 ($M - H_2O$), 367 ($385 - H_2O$), and 287 (M — side chain). Jones oxidation of (29) furnished the corresponding ketone (30), m.p. 148—149° (needles from MeOH), *m/e* 398 (M^+), 383 ($M - CH_3$), 285 (M — side chain), 247, 244 (ring D cleavage), 243 (ring D cleavage + 1H), 163, 149, 135, 107, 95, 93, 81, 69, 55, and 43, o.r.d. (*c* 0·35, dioxan) $[\phi]_{315}$ +2375, $[\phi]_{310}$ + 2093sh, $[\phi]_{306}$ 2024, and $[\phi]_{275}$ −864, c.d. (*c* 0·35, dioxan) $[\theta]_{294}$ +2388.

22,23-*Methylene*-5α-*ergostan*-6β-*ol* (35).—Dichlorocarbene addition to ergost-22-en-6β-ol (11) as described for (20) resulted in a poor yield 8—10%) of adducts which after partial enrichment by column chromatography over Florisil were directly dechlorinated with Na–NH_3 to furnish a mixture of four compounds, only one of which could be isolated in pure state by preparative g.l.c. over OV 3 (3%) and is tentatively assigned structure (35), m.p. 129—131, *m/e* 396 ($M - H_2O$), 381 ($396 - CH_3$), 298 ($396 - C_7H_{14}$ cleavage of cyclopropane), 283 ($298 - CH_3$), and 255 (M — side chain $+H_2O$).

5β,6β-*Dichloromethylenestigmast*-22-*en*-3β-*yl Acetate* (24).—Stigmasteryl acetate (12) under analogous conditions to that for (20) furnished only one dichlorocarbene adduct (24) (yield 40—60%), which on subsequent dechlorination with Na–NH_3 furnished 5β,6β-*methylenestigmast*-22-*en*-3β-*ol* (25), m.p. 118—120°, $[\alpha]_D^{21}$ −16·9° (*c* 0·195), δ −0·08 (1H, dd 4·5 and 8·5 Hz), 0·32 (t, *J* 4·5 Hz), 0·64 (3H, s, 18-H_3), 0·85 (d, *J* 6 Hz, 26- and 27-H_3), 0·88 (s, 19-H_3), 3·86br (1H, C*H*·OH), and 5·06 (2H, m), *m/e* 426 (M^+), 408 ($M - H_2O$), 328, 314, 287 (M — side chain), 285 (M — side chain + 2H), 269 ($287 - H_2O$), 245 (ring D cleavage + 1H), 149, 139, 125, 121, 107, 97, 95, 83, 69, and 55 (Found: M^+, 426·38690. $C_{30}H_{50}O$ requires M, 426·38615). Jones oxidation of (25) furnished 5β,6β-methylenestigmast-22-en-3-one (26), transparent in u.v. in both basic and neutral medium, m.p. 116—118°, *m/e* 424 (M^+), 381 ($M - C_3H_7$), 326, 312, 285 (M — side chain), 283 (M — side chain + 2H), 199, 123, 97, 95, 83, 69, and 55, o.r.d. (*c* 0·19, dioxan) $[\phi]_{329}$ +5584, $[\phi]_{310}$ +5584, $[\phi]_{294}$ +2856sh, and $[\phi]_{277}$ −4284, c.d. (*c* 0·19, dioxan) $[\theta]_{312.5}$ +3660sh, $[\theta]_{303}$ +6873, $[\theta]_{300}$ +6750 (min), and $[\theta]_{294}$ +7051.

7α,8α-*Dichloromethylene*-5α-*ergost*-22-*en*-3β-*yl Acetate* (31).—Dichlorocarbene addition to 5α-ergosta-7,22-dien-3β-yl acetate (17) in an analogous manner to (20) furnished the adduct (31) (80%), $[\alpha]_D^{21}$ −66·5° (*c* 0·305), M^+ 468—470, which on subsequent dechlorination with Na–NH_3 followed by acetylation and multiple crystallization from methanol furnished 7α,8α-*methylene*-5α-*ergost*-22-*en*-5β-*yl acetate* (32), m.p. 141—143, M^+ 454, *m/e* 394 ($M - CH_3CO_2H$), $[\alpha]_D^{21}$ +2·6° (*c* 0·84) (Found: C, 80·2; H, 10·9. $C_{31}H_{50}O_2$,0·5-CH_3OH requires C, 80·3; H, 11·10). Saponification of (32) gave 7α,8α-*methylene*-5α-*ergost*-22-*en*-3β-*ol* (33), m.p. 137—139°, $[\alpha]_D^{21}$ +16·3° (*c* 0·222), δ 0·00 (1H, t, *J* 5 Hz), 0·28 (1H, dd, *J* 5·0 and 9·0 Hz), 0·84 (s, 18-H_3), 0·87 (d, *J* 6 Hz, 26- and 27-H_3), 0·90 (s, 19-H_3), 3·55 (1H, m, C*H*·OH), and 5·20 (2H, m, 22- and 23-H), *m/e* 412 (M^+), 397 (M —

CH_3), 315, 285 (M — side chain + 2H), 269 (287 — H_2O), 135, 125, 122, 109, 107, 97, 83, and 69 (Found: C, 83·1; H, 11·5. $C_{29}H_{48}O$,0·5CH_3OH requires C, 82·7; H, 11·7%) (Found: M^+, 412·37050. $C_{29}H_{48}O$ requires M, 412·37050). Jones oxidation of (33) furnished 7α,8α-*methylene-5α-ergost*-22-*en*-3-*one* (34), m.p. 162—164° (needles from MeOH), M^+ 410, o.r.d. (*c* 0·51, dioxan) $[\phi]_{316}$ +2091, $[\phi]_{310}$ +1865sh, $[\phi]_{308}$ +1833sh, $[\phi]_{300}$ +804sh, and $[\phi]_{270}$ −1126, c.d. (*c* 0·51, dioxan) $[\theta]_{294}$ +2361] (Found: M^+, 410·3530. $C_{29}H_{46}O$ requires M, 410·35485).

Dichlorocarbene Addition to Brassicasteryl Acetate (18).—Brassicasteryl acetate (18) was prepared from ergosterol according to Thomson *et al.*,[22] except that tosylation was carried out at 0°, solvolysis of the tosylate was effected at reflux for 5 min in buffered acetone, and excess of acetone was removed under vacuum. The crude *i*-alcohol was directly oxidized and the resulting 3α,5α-cyclo-Δ⁷-6-ketone was purified by repeated crystallization. Lithium–ammonia reduction of 3α,5α-cycloergosta-7,22-dien-6-one for 30 min furnished 5α-ergost-22-en-6β-ol, m.p. 120—122°, M^+ 400, δ 0·69 (s, 18-H_3), 0·81 (d, *J* 6 Hz, 26- and 27-H_3), 1·01 (s, 19-H_3), 3·80 ($W_{\frac{1}{2}}$ 7 Hz, C*H*·OH), and 5·25 (2H, m, 22- and 23-H), which on acetylation furnished the oily acetate (11).

Addition of dichlorocarbene to brassicasteryl acetate (18) in the manner described for (20) furnished a complex mixture of adducts which after enrichment by column chromatography over Florisil was directly dechlorinated with Na–NH_3. The crude mixture was acetylated and the corresponding acetate fractionally crystallized to furnish a three-component crystalline mixture [(18) (50%), (36) (21%), and (37) (18%) acetates] and a supernatant composed of two major components [(27) (50%) and (38) (20%) acetates]. Final separation was effected by preparative g.l.c. over OV 3 (3%) on Gas Chrom Q. 5β,6β-Methylene-ergosten-22-en-3β-ol (27) had m.p. 144—146° (needles from MeOH), δ −0·06 (dd, *J* 5·0 and 8·0 Hz), 0·32 (t, *J* 5·0 Hz), 0·64 (s, 18-H_3), 0·85 (d, *J* 6 Hz, 26- and 27-H_3), 0·89 (s, 19-Hs), 3·85br (1H, C*H*·OH), and 5·14 (2H, m, 22- and 23-H), *m/e* 412 (M^+), 397 (M — CH_3), 394 (M — H_2O), 379 (394 — CH_3), 369 (M — C_3H_7), 351 (369 — H_2O 328, 314, 287 (M — side chain), 285 (M — side chain + 2H), 269 (287 — H_2O). 24,24-Dimethylcholesta-5,22-dien-3β-ol (36) had m.p. 156—157°, $[\alpha]_D^{21}$ −44·1° (*c* 0·102), δ 0·67 (3H, s, 18-H_3), 0·84 (d, *J* 6 Hz, 26- and 27-H_3), 0·87 (s, 24-H_3), 0·99 (3H, s, 19-H_3), 3·50br (1H, C*H*·OH), 5·15 (2H, m, 22- and 23-H), and 5·33 (1H, m, 6-H), *m/e* 412 (M^+), 394 (M — H_2O), 369 (M — C_3H_7, 86%), 351 (369 — H_2O), 309, 300, 273 (M — side chain), 271, 255 (273 — H_2O), 213, 159, 145, 133, 97, 81, 69, and 55. 22,23-Di-*epi*-23-demethylgorgosterol (37) had m.p. 163—165°, $[\alpha]_D^{21}$ −64·4° (*c* 0·09), δ 0·18 (m, cyclopropane H), 0·61 (s, 18-H_3), 0·80 and 0·99 (each d, *J* Hz, 21- and 24-H_3), 0·87 (d, *J* 6·5 Hz, 26- and 27-H_3), 1·00 (s, 19-H_3), 3·53 (m, C*H*·OH), and 5·35 (m, 6-H), *m/e* 412 (M^+), 394 (M — H_2O), 379 (394 — CH_3), 328, 314 (100%), 299 (314 — CH_3), 281 (299 — H_2O), 271 (M — side chain + 2H), 83, 69, and 55 [mass spectrum identical with that of natural [3] (isolated from *P. porosa*) demethylgorgosterol]. 5β,6β:22,23-Dimethylene-ergostan-3β-ol (38) had m.p. 165—167° (coarse needles from MeOH), *m/e* 426 (M^+), 411 (M — CH_3), 408 (M^+ — H_2O), 328 (cleavage of 22,23-cyclopropane [19]), 295, 285, 107, 95, 83, 81, 69, 55, and 43, δ −0·09 (dd, *J* 5 Hz), 0·38 (m), 0·56 (s, 18-H_3), 0·79 (d, *J* 5·5 H_2, 24-H_3), 0·88 (s, 19-H_3 and d, *J* 6·5 Hz, 26- and 27-H_3), 0·97 (d, *J* 5·5 Hz, 21-H_3), and 3·84 (m, C*H*·OH).

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[22] M. J. Thomson, C. F. Cohen, and S. M. Lancaster, *Steroids*, 1965, **5**, 745.