Conformational Studies. Part 3.[1] Synthesis of Some Alicyclic Dienes

By **Michael H. Barnes** and **W. Basil Whalley*** The School of Pharmacy, The University, London WC1N 1AX

(+)-*trans*-1,2,3,4,4a,8a-Hexahydro-4a-methylnaphthalene, cholesta-1,3-diene, and cholesta-1,3,7-triene have been synthesised by standard methods. These chiral, *cisoid*, homoannular dienes exhibit o.r.d. curves of sign in agreement with the predictions of the Chiral Diene Rule.

THE Diene Chirality Rule predicts [2] that the long-wavelength (lowest energy) Cotton effect of a non-planar conjugated diene will be primarily dependent (particularly as regards sign) upon the inherent dissymmetry, or helicity of the chromophore. On this basis a right-handed helix should exhibit positive o.r.d. and c.d. curves, whereas the opposite should obtain for a left-handed helix. This concept has satisfactorily accommodated many appropriate (especially *cisoid*) dienes, and has rationalised several apparent exceptions, *e.g.* laevopimaric acid.[3] Very recent work [4] has produced a number of authentic exceptions to the Rule as expressed in its initial form. In the early stages of its development we and Dr. U. Weiss and his colleagues synthesised various, simple dienes to test the validity of the Diene Rule. This paper describes some of our initial work.

Since the bicyclic system (1) had been investigated [5] it seemed of interest to synthesise the related 1,3-diene (2) and the more rigid, steroid analogues (3) and (4) in order to elucidate the effect, if any, of a 7,8-double bond (steroid numbering) on the chiroptical properties of the *cisoid* diene. We now report the synthesis of these three *cisoid* dienes.

For our initial objective (+)-(2) the commencing point was (+)-*trans*-1,4,4a,5,8,8a-hexahydro-2-methoxy-4a-methyl-4-oxo-1-naphthyl camphorsulphonate [6] (5; R = (+)-camphorsulphonyloxy). This was converted [6] by zinc and acetic acid into (−)-*trans*-4a,5,8,8a-tetrahydro-3-methoxy-8a-methylnaphthalen-1(4*H*)-one (5; R = H). Hydrogenation of (5; R = H) gave (−)-*trans*-4a,5,6,7,8,8a-hexahydro-3-methoxy-8a-methylnaphthalen-1(4*H*)-one (6). Reduction of (6) with lithium aluminium hydride, followed by acidic hydrolysis of the enol ether and dehydration afforded (+)-*trans*-4a,5,6,7,8,8a-hexahydro-8a-methylnaphthalen-2(1*H*)-one (7; R = O). Reduction of this αβ-unsaturated ketone with lithium aluminium hydride yielded the alcohol (7; R = H, α-OH); the configuration at C-3 was assigned on general principles and by analogy with the exclusive reduction [7] of cholest-1-en-3-one to the 3β-ol. Slow distillation of the 3,5-dinitrobenzoate [7; R = H, α-3,5-$(NO_2)_2C_6H_3{\cdot}CO_2$] gave (+)-*trans*-1,2,3,4,4a,8a-hexahydro-4a-methylnaphthalene (2), $\lambda_{max.}$ 261 nm (ε 3 700), τ 4.03—4.60 (4 H, m, H-5—8), 8.50 (8 H, envelope, 4 CH_2), and 9.13 (3 H, s, Me). Although this diene did not form an adduct with maleic anhydride it reacted readily with tetracyanoethylene. In accord with the Chirality Rule,[2] the diene exhibited a positive o.r.d. curve, similar to that of the triene (1) (Table).

Cholesta-1,3-diene (4) has been available [8] previously in very small quantities. It is now readily accessible by

[1] Part 2, J. M. Midgley, W. B. Whalley, P. A. Dodson, G. F. Katekar, and B. A. Lodge, preceding paper.

[2] (*a*) A. Moscowitz, E. Charney, U. Weiss, and H. Ziffer, *J. Amer. Chem. Soc.*, 1961, **83**, 4661; (*b*) H. J. C. Jacons and E. Havinger, *Rec. Trav. chim.*, 1965, **84**, 932; (*c*) U. Weiss, H. Ziffer, and E. Charney, *Tetrahedron*, 1965, **21**, 3105; (*d*) E. Charney, *ibid.*, p. 2126.

[3] U. Weiss, W. B. Whalley, and I. L. Karle, *J.C.S. Chem. Comm.*, 1972, 16.

[4] *E.g.* H. Paaren, R. M. Moriarty, and J. Flippen, *J.C.S. Chem. Comm.*, 1976, 114; R. Ahmad, J. M. Midgley, and W. B. Whalley, unpublished observations; personal communication from Professor A. W. Burgstahler.

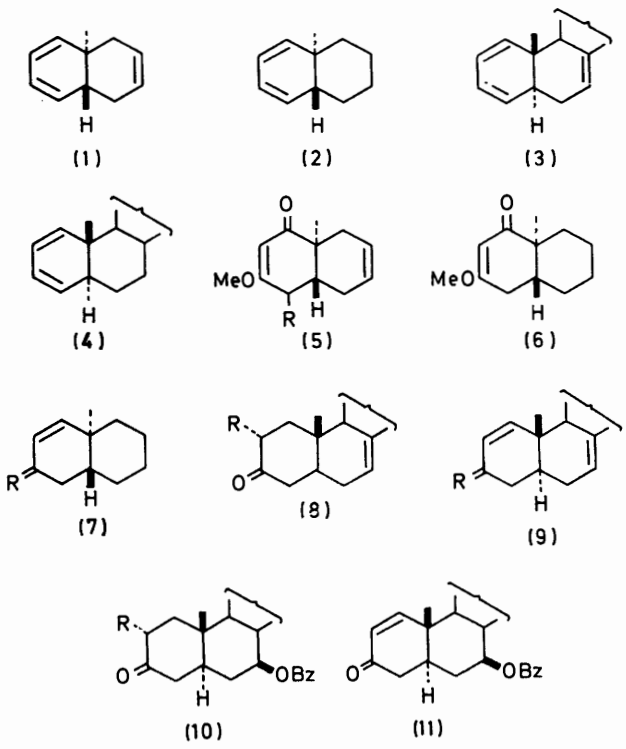
[5] H. Ziffer and U. Weiss, *J. Org. Chem.*, 1962, **27**, 2694.

[6] A. J. Speziale, J. A. Stephens, and Q. E. Thompson, *J. Amer. Chem. Soc.*, 1954, **76**, 5011.

[7] W. Bergmann, M. Kita, and D. J. Giancola, *J. Amer. Chem. Soc.*, 1954, **76**, 4974.

[8] Ch. Tamm and R. Albrecht, *Helv. Chim. Acta*, 1959, **42**, 2177.

dehydrochlorination of 3β-chlorocholest-1-ene; the n.m.r. spectrum of the product (4) exhibited signals at



τ 4.05—4.50 (4 H, m, H-1—4) and the o.r.d. curve was negative as required (Table).

O.r.d. data

Compound	$\lambda_{max.}$/nm	$\varepsilon_{max.}$	Molecular amplitude (°)
(1) *	261	3 450	+350
(2)	261	3 700	+272
(3)	262	2 900	−135
(4)	263	3 700	−107

* Data from ref. 5.

Cholesta-1,3,7-triene (3) was obtained by two processes. In the first, cholest-7-en-3-one (8; R = H) was brominated to yield the 2α-bromide (8; R = Br). The α-configuration of the halogen, in accord with an equatorial location (in a chair), was assigned on the basis of the $\nu_{max.}$ value [1 728 in contrast to 1 707 cm^{-1} for the ring A carbonyl group in (8; R = H)]. Additionally, since dehydrobromination of (8; R = Br) gave cholesta-1,7-dien-3-one, τ 2.98 (1 H, d, $J_{1.2}$ 10 Hz, H-1), 4.10 (1 H, d, $J_{1.2}$ 10 Hz, H-2), and 4.73 (1 H, m, H-7), the halogen atom must be located at C-2. Since various processes for the dehydrohalogenation of (8; R = Br) furnished only low yields of cholest-1,7-dien-3-one, the alternative route [9] in which (8; R = Br) was treated with semicarbazide hydrochloride to yield the semicarbazone (9; R = N·NH·CO·NH_2), which was then converted into the ketone (9; R = O) with *p*-hydroxybenzaldehyde, was explored. Reduction of the ketone (9; R = O) with lithium aluminium hydride gave cholesta-1,7-dien-3β-ol (9; R = H, β-OH), the orientation of the hydroxy-group being assigned by analogy [7] with the established reduction of cholest-1-en-3-one to the 3β-ol. Treatment of the 3β-ol (9; R = H, β-OH) with thionyl chloride gave 3β-chlorocholesta-1,7-diene (9; R = H, β-Cl), the orientation being well established by previous work.[10] Dehydrohalogenation of the chloride (9; R = H, β-Cl) with pyridine–dimethylformamide gave cholesta-1,3,7-triene (3) τ 4.08—4.40 (4 H, m, H-1—4) and 4.40 (1 H, m, H-7). The o.r.d. curve was negative, in accord with the simple Diene Rule. Collateral evidence for the structure (3) was provided by its hydrogenation to cholest-7-ene, identical with an authentic specimen.

Since the overall yields of the triene (3) obtained by this process were low, an alternative approach was investigated. 7β-Benzoyloxycholestan-3-one [11] (10; R = H) was readily brominated to form the 2α-bromide (10; R = Br). Dehydrobromination with collidine or by the semicarbazide process [9] gave 7β-benzoyloxy-cholest-1-en-3-one (11), τ 3.00 (1 H, d, $J_{1.2}$ 9.5 Hz, H-1) and 4.15 (1 H, d, $J_{1.2}$ 9.5 Hz, H-2). Pyrolysis of (11) gave cholesta-1,7-dien-3-one in low yield, identical with that obtained by the alternative process.

The chiroptical data for compounds (1)—(4) (Table) (*a*) are in accord with the predictions [2] of the Diene Chirality Rule and (*b*) imply that the non-conjugated double bond, in these substances, does not significantly modify the angle of skew in the *cisoid* diene chromophores.

The preparation of cholesta-1,6-dien-3-one and several derivatives is recorded in the Experimental section.

EXPERIMENTAL

Unless indicated to the contrary, light petroleum signifies the fraction of b.p. 60—80 °C; rotations were determined for solutions in ethanol, unless otherwise stated.

(+)-trans-1,2,3,4,4a,8a-*Hexahydro*-4a-*methylnaphthalene* (2).—A solution of (−)-*trans*-4a,5,8,8a-tetrahydro-3-methoxy-8a-methylnaphthalene-1(4*H*)-one [5] (5; R = H) (1 g) in ethanol (110 ml) containing prehydrogenated 10% palladium–charcoal (0.15 g) was shaken in hydrogen [uptake 132 ml (1.05 mol equiv.) in 30 min]. Addition of water to the concentrated filtrate gave (−)-trans-4a,5,6,7,8,8a-*hexahydro*-3-*methoxy*-8a-*methylnaphthalene*-1(4H)-*one* (6) (0.9 g), which formed needles, m.p. 93° (from aqueous methanol), $[\alpha]_D^{22}$ −92° (*c* 3.25), $\lambda_{max.}$ 249 nm (log ε 4.17), $\nu_{max.}$ 1 600 and 1 650 cm^{-1} (αβ-unsaturated ketone) [Found: C, 74.6; H, 9.4; OMe, 15.4. $C_{11}H_{15}O(OMe)$ requires C, 74.2; H, 9.3; OMe, 16.0%].

A solution of this ketone (2.7 g) in ether (20 ml) was added slowly to a suspension of lithium aluminium hydride (0.5 g) in ether (15 ml). After isolation in the usual manner a solution of the oily product (2.4 g) in methanol (10 ml) and 25% sulphuric acid (5 ml) was refluxed for 1 h to give (+)-*trans*-4a,5,6,7,8,8a-hexahydro-8a-methylnaphthalen-2-(1*H*)-one as an oil (1.2 g), b.p. 27° at 5 mmHg, $[\alpha]_D^{22}$ +51° (*c* 2.4), $\lambda_{max.}$ 230 nm (log ε 3.96) [lit.,[12] $\lambda_{max.}$ 229 nm (log ε 3.98) for a specimen prepared by an alternative method]. The 2,4-dinitrophenylhydrazone separated from ethanol in red plates, m.p. 191° (Found: C, 58.7; H, 6.0; N, 16.2. Calc.

[9] C. Djerassi, *J. Amer. Chem. Soc.*, 1949, **71**, 1003.
[10] H. B. Henbest and R. A. Wilson, *J. Chem. Soc.*, 1956, 3289.
[11] H. Heymann and L. F. Fieser, *Helv. Chim. Acta*, 1952, **35**, 631.

for $C_{17}H_{20}N_4O_4$: C, 59.3; H, 5.9; N, 16.3%) (lit.,[12] m.p. 191—192°).

Reduction of this ketone (1.15 g) in ether (25 ml) containing lithium aluminium hydride (0.3 g) occurred at room temperature during 3 h to yield *trans*-1,2,4a,5,6,7,8,8a-octahydro-8aα-methylnaphthalen-2α-ol (0.95 g) as an oil, after purification from benzene on silica [elution with benzene–ether (2 : 3)], $[\alpha]_D^{20}$ −4° (*c* 3.8). The *3,5-dinitrobenzoate* separated from light petroleum in pale yellow needles, m.p. 118° (Found: C, 59.5; H, 5.9; N, 8.1. $C_{18}H_{20}N_2O_6$ requires C, 60.0; H, 5.6; N, 7.8%).

Slow distillation of this ester (0.35 g) at *ca.* 155° and 0.2 mmHg gave (+)-trans-1,2,3,4,4a,8a-*hexahydro*-4a-*methylnaphthalene* (2) (0.25 g) as an oil which was purified by distillation, $[\alpha]_D^{20}$ +50° (*c* 3.02 in cyclohexane) (Found: C, 88.8; H, 11.0. $C_{11}H_{16}$ requires C, 89.1; H, 10.9%). When subjected to g.l.c. (1 m column containing 25% silicone oil; argon as carrier gas) this hydrocarbon formed one peak with retention time 40 min; o.r.d. $[\phi]_{278}$ +9 550°, $[\phi]_{232}$ +17 600°, *a* + 272° (*c* 0.003 92 in hexane).

Prepared by the interaction of tetracyanoethylene (0.1 g) and the diene (2) (0.1 g) in tetrahydrofuran (1 ml) during 6 days the *adduct* formed needles (0.1 g), m.p. 115° (from light petroleum) (Found: C, 73.9; H, 5.9; N, 20.5. $C_{17}H_{16}N_4$ requires C, 73.9; H, 5.8; N, 20.3%).

(+)-trans-1,4,4a,5,6,7,8,8a-*Octahydro*-2-*methoxy*-4a-*methyl*-4-*oxo*-1-*naphthyl Camphorsulphonate*.—Absorption of hydrogen (35 ml, 1.1 mol. equiv.) occurred during 80 min when a solution of *trans*-1,4,4a,5,8,8a-hexahydro-2-methoxy-4a-methyl-4-oxo-1-naphthyl camphorsulphonate[6] (0.45 g) in ethanol (110 ml) containing 5% palladium–charcoal (0.05 g) was shaken in hydrogen. The resultant *octahydro-derivative* formed plates (0.33 g), m.p. 140° (from ethanol), $[\alpha]_D^{20}$ +60° (*c* 0.60), $\lambda_{max.}$ 247 nm (log ε 4.24), $\nu_{max.}$ 1 750 (sulphonic ester) and 1 650 and 1 620 cm^{-1} (αβ-unsaturated ketone) (Found: C, 61.9; H, 7.5; S, 7.5. $C_{21}H_{30}O_6S$ requires C, 61.5; H, 7.3; S, 7.8%).

2α-*Bromocholest*-7-*en*-3-*one* (8; R = Br).—A stirred solution of cholest-7-en-3-one (1 g) in ether (40 ml) was treated dropwise during 3 min, with bromine (0.16 ml) dissolved in acetic acid (0.84 ml). The colour of the bromine was rapidly discharged after each addition. After 10 min the mixture was poured into an excess of N-sodium hydrogen carbonate and the product isolated with ether. Purification by chromatography from light petroleum (b.p. 40—60 °C) on silica [elution with benzene–light petroleum (b.p. 40—60 °C)] gave 2α-*bromocholest*-7-*en*-3-*one* (0.7 g) in needles, m.p. 153—155° (from aqueous acetone), $[\alpha]_D^{21}$ +3° (*c* 5.28 in $CHCl_3$) (Found: C, 69.8; H, 9.4; Br, 17.4. $C_{27}H_{43}BrO$ requires C, 69.9; H, 9.3; Br, 17.2%).

Cholesta-1,7-*dien*-3-*one*.—(*a*) A solution of 2α-bromocholest-7-en-3-one (0.4 g) in collidine (7 ml) was refluxed for 7 h, cooled, and poured into an excess of 2N-sulphuric acid. After isolation with ether the product was chromatographed from light petroleum (b.p. 40—60 °C) on alumina [elution with benzene–light petroleum (1 : 1)]. The impure diene was then purified by t.l.c. on silica [benzene–light petroleum (b.p. 40—60 °C) (17 : 3)] to yield *cholesta*-1,7-*dien*-3-*one* (80 mg) as needles, m.p. 109° (from methanol), $[\alpha]_D^{19}$ −6° (*c* 5.97 in $CHCl_3$), $\lambda_{max.}$ 229 nm (log ε 4.02) (Found: C, 84.7; H, 11.3. $C_{27}H_{42}O$ requires C, 84.8; H, 11.1%).

(*b*) A solution of 2α-bromocholest-7-en-3-one (2 g) in t-butyl alcohol (100 ml) and chloroform (60 ml) containing semicarbazide (0.6 g) was shaken vigorously in nitrogen for 5 h. The solvent was removed under reduced pressure, ethanol (20 ml) and water (30 ml) were added, and the solid residue was collected and purified from ethanol–chloroform to yield the *semicarbazone* (1.4 g) of cholesta-1,7-dien-3-one in needles, m.p. 231—233°, $\lambda_{max.}$ ($CHCl_3$) 268 nm (log ε 4.47) (Found: C, 75.9; H, 10.4; N, 9.6. $C_{28}H_{45}N_3O$ requires C, 76.5; H, 10.3; N, 9.6%). Alternatively the same semicarbazone was formed, but in lower yield, when a solution of 2α-bromocholest-7-en-3-one (0.25 g) and semicarbazide hydrochloride (50 mg) in acetic acid (5 ml) was heated on a steam-bath for 2 h, with or without the addition of sodium acetate (0.1 g).

A solution of this semicarbazone (0.1 g) and *p*-hydroxybenzaldehyde (0.4 g) in acetic acid (20 ml) and water (4 ml) was maintained at room temperature. The crude product was purified as in (*a*) to yield cholesta-1,7-dien-3-one (0.04 g), m.p. 98°, identical with that prepared by method (*a*). Use of pyruvic acid in place of *p*-hydroxy-benzaldehyde gave a lower yield of the same ketone.

(*c*) 2α-Bromocholest-7-en-3-one (2.15 g) was added during 2 min to boiling dimethylacetamide (22 ml) containing calcium carbonate (2 g). The mixture was refluxed for a further 15 min; then the product was isolated and purified as in (*b*) to yield cholesta-1,7-diene-3-one (0.5 g), m.p. 98°.

A mixture of 2α-bromocholest-7-en-3-one (0.1 g) and 2,4-dinitrophenylhydrazine (0.05 g) in acetic acid (4.5 ml) was refluxed (in nitrogen) for 5 min. On cooling the clear solution deposited a crystalline solid which was purified from ethanol to yield the 2,4-*dinitrophenylhydrazone* of cholesta-1,7-dien-3-one in red-brown needles (0.05 g), m.p. 191°, $\nu_{max.}$ ($CHCl_3$) 260 and 368 nm (log ε 4.22 and 4.43) (Found: C, 70.4; H, 8.4; N, 10.0. $C_{33}H_{46}N_4O_4$ requires C, 70.4; H, 8.2; N, 10.0%). The same derivative (m.p. and mixed m.p.) was obtained directly from cholesta-1,7-dien-3-one.

(*d*) To a solution of 7β-benzoyloxycholestan-3-one (1.25 g) in acetic acid (50 ml) containing one drop of 48% hydrobromic acid was added dropwise during 7 min (with stirring) a reagent (5.2 ml) prepared from bromine (0.5 ml), sodium acetate (0.8 g), and acetic acid (19.5 ml). After 3 min the mixture was diluted with water and the precipitate collected, washed, and dried. Purified by chromatography from light petroleum on silica [elution with benzene–light petroleum (3 : 1)] 7β-*benzoyloxy*-2α-*bromocholestan*-3-*one* formed needles (1 g), m.p. 194—195° (from light petroleum), $[\alpha]_D^{19}$ +66° (*c* 2.02 in $CHCl_3$) (Found: C, 69.5; H, 8.4; Br, 13.6. $C_{34}H_{49}BrO_3$ requires C, 69.7; H, 8.4; Br, 13.6%).

A solution of this ketone (0.25 g) in collidine (5 ml) was refluxed for 1 h, and the product isolated in the usual manner. Purified by chromatography from light petroleum on neutral alumina [elution with benzene–light petroleum (3 : 1)] 7β-*benzoyloxycholest*-1-*en*-3-*one* formed needles (60 mg), m.p. 165—167° [from light petroleum (b.p. 40—60 °C)], $[\alpha]_D^{20}$ +131° (*c* 2.12 in $CHCl_3$), $\lambda_{max.}$ 230 nm (log ε 4.40), $\nu_{max.}$ 1 710 (benzoate ester) and 1 680 cm^{-1} (αβ-unsaturated ketone) (Found: C, 80.5; H, 9.5. $C_{34}H_{48}O_3$ requires C, 80.9; H, 9.6%). The same unsaturated ketone was prepared by way of the semicarbazone. Thus, interaction of 7β-benzoyloxy-2α-bromocholestan-3-one (0.5 g) and semicarbazide hydrochloride (0.1 g) in acetic acid (14 ml) on a steam-bath during 20 min gave the *semicarbazone* (460 mg) of 7β-benzoyloxycholest-1-en-3-one, which formed feathery needles, m.p. 225—227° (from light petroleum–chloroform), $\lambda_{max.}$ 232 and 265 nm (log ε 4.40 and 4.49) (Found: C, 74.8; H, 9.2; N, 7.4. $C_{35}H_{51}N_3O_3$ requires C, 74.8; H, 9.2;

[12] C. Djerassi and D. Marshall, *J. Amer. Chem. Soc.*, 1958, **80**, 3986.

N, 7.5%). Interaction of this semicarbazone (420 mg) with *p*-hydroxybenzaldehyde (1.6 g) in acetic acid (30 ml) and water (6 ml) during 95 h gave, after chromatography, 7β-benzoyloxycholest-1-en-3-one (140 mg), identical (m.p., mixed m.p., and i.r. spectrum) with the previously prepared specimen.

When a solution of 7β-benzoyloxy-2α-bromocholestan-3-one and 2,4-dinitrophenylhydrazine in acetic acid was heated on a steam bath the *2,4-dinitrophenylhydrazone* of 7β-benzoyloxycholest-1-en-3-one formed during 20 min and was purified from ethanol–chloroform to give orange needles, m.p. 253° (decomp.), $\lambda_{max.}$ 370 nm (log ε 4.51) (Found: C, 70.4; H, 7.8; N. 8.2. $C_{40}H_{52}N_4O_6$ requires C, 70.2; H, 7.7; N, 8.2%). The same derivative (m.p. and mixed m.p.) was obtained directly from 7β-benzoyloxycholest-1-en-3-one.

7β-Benzoyloxycholest-1-en-3-one (120 mg) was slowly distilled at *ca.* 300 °C at 10 mmHg during 50 min. A solution of the distillate in chloroform was washed with 2N-sodium hydrogen carbonate (to remove benzoic acid) and water, dried, and evaporated. Chromatography from light petroleum on alumina [elution with benzene–light petroleum (1 : 3)] furnished cholesta-1,7-dien-3-one, forming needles (32 mg) from methanol, identical (m.p., mixed m.p., and i.r. spectrum) with specimens prepared by the previous methods.

Cholesta-1,3,7-triene.—Reduction of cholesta-1,7-dien-3-one (0.1 g) in ether (10 ml) with lithium aluminium hydride (0.02 g) during 5 min gave *cholesta-1,7-dien-3β-ol* (0.085 g), which was purified by t.l.c. on silica [benzene–ethyl acetate (5 : 1) as eluant] followed by crystallisation from aqueous methanol to yield needles, m.p. 150°, $[\alpha]_D$ −7° (*c* 9.64 in $CHCl_3$) (Found: C, 84.6; H, 11.5. $C_{27}H_{44}O$ requires C, 84.3; H, 11.5%). Oxidation of this alcohol with Jones reagent regenerated almost quantitatively cholesta-1,7-dien-3-one (m.p., mixed m.p., and i.r. spectrum).

A solution of cholesta-1,7-dien-3β-ol (14 mg) in benzene (2 ml) was treated with a reagent (2.3 ml) prepared from thionyl chloride (1.5 ml) and benzene (18 ml). After 75 min the mixture was diluted with water, and the product isolated with ether. Purification from acetone gave *3β-chlorocholesta-1,7-diene* (60 mg) in needles, m.p. 86—88°, $[\alpha]_D^{21}$ +9° (*c* 5.20 in $CHCl_3$) (Found: C, 80.8; H, 11.0; Cl, 8.9. $C_{27}H_{43}Cl$ requires C, 80.5; H, 10.8; Cl, 8.8%).

A solution of this chloro-compound (45 mg) in dimethylformamide (1.8 ml) and pyridine (0.2 ml) was refluxed for 16 h. After isolation with ether the brown crystalline product was decolourised by filtration of a solution in light petroleum through a column of neutral alumina. Purification of the product from acetone gave *cholesta-1,3,7-triene* (25 mg) in needles, m.p. 69—70°, $[\alpha]_D^{20}$ −31° (*c* 5.45 in $CHCl_3$), $\lambda_{max.}$ 262 nm (log ε 3.46), o.r.d. (*c* 0.429 in cyclohexane) $[\phi]_{400}$ −340°, $[\phi]_{278}$ −6 700°, $[\phi]_{239}$ +6 000°, *a* −135° (Found: C, 88.7; H, 11.4. $C_{27}H_{42}$ requires C, 88.5; H, 11.6%). Hydrogenation of this triene (63 mg) in dioxan (20 ml) containing Raney nickel (0.2 g) during 5 h gave cholest-7-ene (50 mg), m.p. 87—88°, in needles (from acetone), identical (m.p., mixed m.p., and i.r. spectrum) with an authentic specimen [13] prepared by Wolff–Kishner reduction of cholest-7-en-3-one.

Cholesta-1,3-diene.—A solution of 3β-chlorocholest-1-ene (0.1 g) in dimethylformamide (3.5 ml) and pyridine (0.4 ml) was refluxed during 20 h. After isolation in the usual manner, cholesta-1,3-diene separated from acetone in needles (70 mg), m.p. 62°, $[\alpha]_D^{20}$ +79° (*c* 1.63 in $CHCl_3$), $\lambda_{max.}$ 263 nm (log ε 3.57) (lit.,[8] m.p. 67—68°, $[\alpha]_D$ +73°) (Found: C, 87.9; H, 11.9. Calc. for $C_{27}H_{44}$: C, 88.0; H, 12.0%), o.r.d. (*c* 0.009 05 in cyclohexane) $[\phi]_{400}$ +340°, $[\phi]_{274}$ −2 410°, $[\phi]_{234}$ +8 300°, *a* −107°.

Cholesta-1,6-dien-3-one.—Oxidation of 7α-benzoyloxycholestan-3β-ol (0.5 g) with Jones reagent gave 7α-benzoyloxycholestan-3-one (430 mg) as a solid, which was not crystallised although it gave only one spot on t.l.c. with silica [benzene–ethyl acetate (9 : 1) as solvent]; $\nu_{max.}$ 1 715br cm^{-1} (C=O and ester).

A solution of this ketone (285 mg) in acetic acid (10 ml) containing 1 drop of hydrobromic acid was brominated during 3 min with bromine (90 mg) in acetic acid (5 ml) containing sodium acetate (0.2 g). After chromatography from light petroleum on silica [elution with light petroleum–benzene (1 : 9)], *7α-benzoyloxy-2α-bromocholestan-3-one* formed a solid (250 mg), m.p. 87°, $\nu_{max.}$ 1 715—1 730 cm^{-1} (Found: C, 69.6; H, 8.6; Br, 13.0. $C_{34}H_{49}BrO_3$ requires C, 69.7; H, 8.4; Br, 13.7%).

Dehydrobromination of this bromo-ketone (1 g) in boiling collidine (20 ml) occurred during 1.5 h to yield 7α-benzoyloxycholest-1-en-3-one as an oil (420 mg), showing one spot on t.l.c., $\lambda_{max.}$ 230 nm (log ε 4.23), $\nu_{max.}$ 1 720 and 1 680 cm^{-1} (αβ-unsaturated ketone).

Distillation of this ester (3.2 g) at 300 °C and 8—12 mmHg during 50 min, followed by isolation of the product in the usual way and chromatography on silica from benzene–light petroleum (elution with the same solvent mixture) gave (i) a semi-crystalline solid (1.5 g) and (ii) starting material (1.3 g), identified by i.r. spectrum and t.l.c. Further purification of the crystalline fraction by chromatography (same system) gave *cholesta-1,6-dien-3-one*, which separated from methanol in needles (585 mg), m.p. 95—97°, τ 2.75 (1 H, d, $J_{1,2}$ 9 Hz, H-1), 4.09 (1 H, d, $J_{1,2}$ 9 Hz, H-2), 4.46 (1 H, d, $J_{6,7}$ 2 H), and 4.58 (1 H, d, $J_{6,7}$ 2 Hz), $[\alpha]_D^{19}$ −61° (*c* 1.05 in $CHCl_3$), $\nu_{max.}$ 1 675 and 1 600 cm^{-1} (αβ-unsaturated ketone), $\lambda_{max.}$ 232 nm (log ε 4.01) (Found: C, 84.6; H, 11.1. $C_{27}H_{42}O$ requires C, 84.8; H, 11.1%).

Reduction of this ketone (0.1 g) with lithium aluminium hydride (20 mg) in ether (10 ml) during 10 min gave *cholesta-1,6-dien-3β(?)-ol*, which formed needles (90 mg), m.p. 128—129°, $[\alpha]_D^{20}$ −22° (*c* 0.61 in $CHCl_3$) (from methanol, after preliminary purification by t.l.c. as described for cholesta-1,7-dien-3β-ol) (Found: C, 84.0; H, 11.2. $C_{27}H_{44}O$ requires C, 84.3; H, 11.5%).

6,7-Dibromocholestan-3-one.—A solution of bromine (95 mg, 1.1 mol. equiv.) in acetic acid (5 ml) was added dropwise to cholest-6-en-3β-ol (420 mg) dissolved in ether (5 ml). The resultant *6ξ,7ξ-dibromocholestan-3β-ol* (0.5 g) formed needles, m.p. 120—123° (from light petroleum–ether) $[\alpha]_D^{20}$ −15° (*c* 0.75 in $CHCl_3$) (Found: C, 59.4; H, 8.5; Br, 28.9. $C_{27}H_{46}Br_2O$ requires C, 59.3; H, 8.5; Br, 29.3%). Oxidation of this alcohol (140 mg) with an excess of Jones reagent in acetone (7 ml) gave *6ξ,7ξ-dibromocholestan-3-one* (120 mg) in needles, m.p. 157° (from light petroleum), $[\alpha]_D^{19}$ −20° (*c* 1.69 in $CHCl_3$), $\nu_{max.}$ 1 720 cm^{-1} (C=O) (Found: C, 59.6; H, 8.3; Br, 30.5. $C_{27}H_{44}Br_2O$ requires C, 59.6; H, 8.1; Br, 29.4%).

Bromination of this ketone (85 mg) in acetic acid (5 ml) containing one drop of hydrobromic acid occurred rapidly when bromine (30 mg, 1 mol. equiv.) and sodium acetate (50 mg) in acetic acid (5 ml) were added slowly. Chromatography on silica from light petroleum–benzene (3 : 1) (elution with the same solvent) gave a small quantity of a

[13] R. B. Turner, W. R. Meador, and R. E. Winkler, *J. Amer. Chem. Soc.*, 1957, **79** 4122.

high melting solid. Continued elution with light petroleum–benzene (3 : 2) gave 2α,6,7-*tribromocholestan*-3-*one* (55 mg) in needles, m.p. 149—150° (from light petroleum), $[\alpha]_D^{19}$ −24° (*c* 2.88 in $CHCl_3$), $\nu_{max.}$ 1 740 cm^{-1} (C=O) (Found: C, 51.8; H, 6.9; Br, 39.7. $C_{27}H_{43}Br_3O$ requires C, 52.0; H, 6.9; Br, 38.5%).

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