J. Chem. Soc. (C), 1969

## Aromatic Steroids. Part III.<sup>1</sup> Chromium Trioxide Oxidation of Some 19-Norcholesta-1,3,5(10)-trienes

By R. C. Cambie,\* Valerie F. Carlisle, and T. D. R. Manning, Department of Chemistry, University of Auckland, New Zealand

Chromium trioxide oxidation of ring-A-substituted 19-norcholesta-1,3,5(10)-trienes gives results similar to those obtained for analogous oestra-1,3,5(10)-trienes. 3-Methoxy-19-norcholesta-1,3,5(10)-triene yields the 9βhydroxy-11-oxo-derivative as the major product but introduction of a methyl group in the C-1 position blocks oxidation in the C-11 position. Oxidation of compounds with substituents in positions other than C-3 yields the 6-oxoderivatives as the major products.

A possible pathway to the 9-hydroxy-11-oxo-derivatives is considered.

IN Part II<sup>1</sup> we reported that chromium trioxide oxidation of oestra-1,3,5(10)-trienes possessing a C-3 methoxy-group gave the 98-hydroxy-11-oxo-derivative in addition to the 6-oxo-derivative as a minor product. In contrast oxidation of oestra-1,3,5(10)-trienes possessing a weak electron-donating substituent (e.g. acetoxy) in the C-3 position afforded 6-oxo-derivatives as the major product as did also 2- and 4-methyl and 1-methoxyoestra-1,3,5(10)-trienes. In order to test the generality of these observations the chromium trioxideoxidation products of some ring-A-substituted 19-norcholesta-1,3,5(10)-trienes were also examined.

Oxidation of 3-methoxy-19-norcholesta-1,3,5(10)-triene (I;  $R^1 = R^2 = R^4 = H$ ,  $R^3 = OMe$ ) gave similar products to those from 3-methoxyoestra-1,3,5(10)-tri-

enes and in comparable yields. The neutral fraction, after chromatography on silica gel, afforded the 6-oxoderivative (II;  $R^1 = R^2 = R^4 = H$ ,  $R^3 = OMe$ ) (5%), the 9 $\beta$ -hydroxy-11-oxo-derivative (III;  $R^1 = \beta OH, R^2 =$ H<sub>2</sub>) (32%) and impure 9 $\beta$ -hydroxy-dione (III; R<sup>1</sup> =  $\beta$ OH, R<sup>2</sup> = O) (3%). Also isolated was a small fraction (0.6%) whose i.r. spectrum and analysis indicated that it was 9a-hydroxy-3-methoxy-19-norcholesta-1,3,5(10)triene-6,11-dione (III;  $R^1 = \alpha OH$ ,  $R^2 = O$ ). The C-11 carbonyl peak (v<sub>max.</sub> 1730 cm.<sup>-1</sup>) was at a position expected for a ring-A-aromatic 9a-hydroxy-11-oxosteroid <sup>2,3</sup> while the broad hydroxy-absorption ( $\nu_{max}$ . 3520-3300 cm.<sup>-1</sup>) indicated intermolecular hydrogenbonding. In all oxidations carried out in both the oestratriene <sup>1,4</sup> and 19-norcholestatriene series this was the only case in which a ketol with a C-9a-hydroxy-

<sup>3</sup> K. Igarashi, Chem. and Pharm. Bull. (Japan), 1961, 9, 729. <sup>4</sup> R. C. Cambie and T. D. R. Manning, J. Chem. Soc. (C), 1968, 2603

<sup>&</sup>lt;sup>1</sup> Part II, R. C. Cambie, Valerie F. Carlisle, C. J. Le Quesne, and T. D. R. Manning, preceding paper. <sup>2</sup> H. Hasegawa and K. Tsuda, Chem. and Pharm. Bull.

<sup>(</sup>Japan), 1964, 12, 473.

group was isolated, reflecting the greater stability of ring-A-aromatic 11-oxo-steroids with *cis* B/C-ring junctions than with trans B/C-ring junctions.<sup>3,5,6</sup>



of 3-methoxy-1-methyl-19-norcholesta-Oxidation 1,3,5(10)-triene (I;  $R^1 = Me$ ,  $R^2 = R^4 = H$ ,  $R^3 =$ OMe) gave a neutral oil which was shown by t.l.c. to contain at least eight compounds, the major one of which was the 6-oxo-derivative (II;  $R^1 = Me$ ,  $R^2 =$  $R^4 = H$ ,  $R^3 = OMe$ ). Its yield was so small however that it could not be obtained pure. The i.r. spectrum of the remaining oil showed a carbonyl peak at 1705 cm.-1 but no hydroxy-bands and thus the oil did not appear to contain a compound with a ketol-group. Dreiding models indicate that like a C-1 methoxygroup,<sup>1</sup> a C-1 methyl group blocks the C-11 position, apparently to such an extent that oxidation at this position cannot occur.

In the oestratriene series the oxidation of some 1-methoxy-4-methyloestra-1,3,5(10)-trienes was investigated in order to see if a methoxy-group in the C-1 position activated the C-9 position to oxidation as did a C-3 methoxy-group. No evidence for the formation of a C-9,11 ketol was obtained but the results were subject to reservation since, in most cases, products were not isolated in sufficient quantity or purity to be positively identified. In the present work oxidation of 1-methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene (I;  $R^1 = OMe$ ,  $R^2 = R^3 = H$ ,  $R^4 = Me$ ) also gave a neutral fraction containing a large number of products, from which only the 6-oxo-derivative was isolated in a pure state by preparative t.l.c. Again, no evidence was obtained for the formation of any ketol but chromatography of the acid fraction on silica gel gave 1-methoxy-19-norcholesta-1,3,5(10)-triene-4-carboxylic acid (I;  $R^1 = OMe$ ,  $R^2 = R^3 = H$ ,  $R^4 = CO_2H$ ) which was isolated as its methyl ester. That a C-1 methoxygroup was necessary for ready oxidation of the C-4 methyl group to a carboxy-group was shown by the oxidation of 4-methyl-19-norcholesta-1,3,5(10)-triene (I;  $R^1 = R^2 = R^3 = H$ ,  $R^4 = Me$ ), the reaction proceeding at a much slower rate than for any other steroid studied. The neutral fraction again contained a number of products, the major ones of which were starting material (30%) and the 6-oxo-derivative (II;  $R^1 = R^2 = R^3 =$ H,  $R^4 = Me$ ) (21%). The acid fraction, however, was negligible. The 6-oxo-derivatives (II;  $R^1 = OAc$ ,  $R^2 = R^3 = H$ ,  $R^4 = Me$ ) and (II;  $R^1 = OBz$ ,  $R^2 =$  $R^3 = H$ ,  $R^4 = Me$ ) were the only products isolated from oxidations of 4-methyl-19-norcholesta-1,3,5(10trien-l-yl acetate (I;  $R^1 = OAc$ ,  $R^2 = R^3 = H$ ,  $R^4 =$ Me) and 4-methyl-19-norcholesta-1.3.5(10)-trien-1-vl benzoate (I;  $R^1 = OBz$ ,  $R^2 = R^3 = H$ ,  $R^4 = Me$ ).

As expected, oxidation of 2-methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene (I;  $R^1 = R^3 = H, R^2 =$ OMe,  $R^4 = Me$ ) afforded the 6-oxo-derivative in high vield (80%) as a result of the activating effect of the para-methoxy-group on the C-6 benzylic position. Also isolated from this reaction was a crystalline compound (9%) whose u.v. and i.r. spectra were similar to those of 3-acetoxy-7-oxa-oestra-1,3,5(10),8-tetraen-6-one (IV;  $R^1 = R^3 = H$ ,  $R^2 = OAc$ ,  $R^4 = H_2$ )<sup>1</sup> and which was therefore assigned the structure (IV;  $R^1 = OMe$ ,  $R^2 =$ H,  $R^3 = Me$ ,  $R^4 = C_8 H_{17}$ , · · · H).

The formation of 9-hydroxy-11-oxo-derivatives as major oxidation products of ring-A-aromatic steroids appears to be restricted to those compounds which possess a strong electron-donating group such as a methoxy-group in the C-3 position. The activating effect of a 3-methoxy-group on the para-benzylic position in ring-A-aromatic steroids has been observed previously by Tsuda and his co-workers 7 who found that bromination of 3-acetoxyoestra-1,3,5(10),9(11)-tetraene gave the expected 9,11-dibromo-addition product but the corresponding C-3 methoxy-compound gave equilenin methyl ether under the same conditions. Moreover, Wiberg and Evans<sup>8</sup> have observed that p-methoxydiphenylmethanes are oxidised by chromic acid at a much faster rate than diphenylmethanes with other substituents, and have pointed out that a p-methoxygroup is particularly well suited for stabilizing an electron deficiency. The initial product of chromic acid oxidation of a tertiary benzylic carbon atom is the corresponding tertiary alcohol<sup>9</sup> and it seems probable therefore that the 9-hydroxy-11-oxo-steroid derivatives are formed by initial hydroxylation at the C-9 position. Dehydration would then afford the  $\Delta^{9(11)}$ -unsaturated steroid which would be expected to be in equilibrium By analogy with the known with the  $\Delta^8$ -isomer. relative stabilities of 3-methoxyoestra-1,3,5(10),9(11)tetraen-17-one and 3-methoxyoestra-1,3,5(10),8-tetraen-17-one,<sup>10</sup> however, the former would be expected to predeterminate at equilibrium. It is suggested that the

7 K. Tsuda, S. Nozoe, and Y. Okada, Chem. and Pharm. Bull. (Japan), 1963, **11**, 1022.

<sup>8</sup> K. B. Wiberg and R. J. Evans, Tetrahedron, 1960, 8, 313. <sup>9</sup> K. B. Wiberg in 'Oxidation in Organic Chemistry,' Academic

Press, New York, 1965, Part A, p. 87.
<sup>10</sup> G. H. Douglas, J. M. H. Graves, D. Hartley, G. A. Hughes, B. J. McLoughlin, J. Siddal, and H. Smith, J. Chem. Soc., 1963, 5072.

<sup>&</sup>lt;sup>5</sup> E. J. Bailey, J. Elks, J. F. Oughton, and L. Stephenson, J. Chem. Soc., 1961, 4535; J. Elks, J. F. Oughton, and L. Stephenson, Proc. Chem. Soc., 1959, 6. <sup>6</sup> H. Hasegawa, S. Nozoe, and K. Tsuda, Chem. and Pharm.

Bull. (Japan), 1963, 11, 1037.

 $\Delta^{9(11)}$ -derivative is then converted into the ketol by further oxidation, possibly via a pathway involving epoxidation, similar to one proposed by Tsuda and his co-workers <sup>2</sup> for the peracid oxidation of  $\Delta^{9(11)}$ -oestra-1,3,5(10) trienes to ketols.

## EXPERIMENTAL

For general experimental conditions and for the general oxidation procedure see Parts I<sup>4</sup> and II,<sup>1</sup> respectively.

19-Norcholesta-1,3,5(10)-trien-3-yl Acetate (I;  $R^1 = R^2 =$  $R^4 = H$ ,  $R^3 = OAc$ ).—A solution of biphenyl (1.2 g.) and lithium (60 mg.) in freshly distilled tetrahydrofuran (5 ml.) was stirred and heated under reflux in an atmosphere of nitrogen for 1 hr. The dark green solution was cooled to 35° and a solution of cholesta-1,4-dien-3-one (0.75 g.), diphenylmethane (0.45 g.), and tetrahydrofuran (5 ml.) was added. The mixture was stirred under reflux for 30 min. and then diluted with 2N-hydrochloric acid. The solution was extracted with ether and the extract was washed, dried, and concentrated to yield a yellow oil which was chromatographed on silica gel. Fractions eluted with benzene contained 19-norcholesta-1,3,5(10)-trien-3-ol which was acetylated with acetic anhydride-pyridine to give 19-norcholesta-1,3,5(10)-trien-3-yl acetate (85%) as needles, m.p. 76-77° (unchanged after recrystallisation from a number of solvents),  $[\alpha]_{\rm p} + 67^{\circ}$  (c 0.65 in cyclohexane) (lit.,<sup>11</sup> 93.5—95°,  $[\alpha]_{\rm p} + 62^{\circ}$  in CHCl<sub>3</sub>) (Found: C, 82.3; H, 10.4. Calc. for  $C_{23}\tilde{H}_{42}O_2$ : C, 81.9; H, 10.3%),  $\lambda_{max}$  (cyclohexane) 210 (\$ 10,100), 217 (\$ 8950), 270 (\$ 620), and 277 mµ (\$ 560),  $\nu_{\rm max}$  1765 (3-OAc), 1610, 1582, 1482, and 1195 cm.<sup>-1</sup> (OAc), 8 (CCl<sub>4</sub>) 0.70 (s, 18-ang. Me), 2.17 (s, 3-OAc), 2.84 (m. 6-benzylic H), 6.69 (d,  $J_{2.4}$  2 c./sec., 4-ArH), 6.75 (2d,  $J_{2,4}$  2,  $J_{1,2}$  8.1 c./sec., 2-ArH), and 7.17 p.p.m. (d,  $J_{1,2}$ 8.1 c./sec., 1-ArH)

Attempted preparation of 19-norcholesta-1,3,5(10)-trien-3-ol by using the conditions of Afonso et al.<sup>12</sup> in the above reaction gave a nonphenolic intractable oil. The reaction was very sensitive to moisture and very dry reagents and a dry atmosphere of nitrogen were essential for its success. Development of a red colour in the biphenyl-lithium solution prior to the addition of cholesta-1,4-dien-3-one indicated either that moisture had entered the system or that metallation of the solvent had occurred.13

19-Norcholesta-1,3,5(10)-trien-3-ol (I;  $R^1 = R^2 = R^4 =$ H,  $R^3 = OH$ ).—A solution of the trienyl-acetate (2.3 g.) was saponified with 5%-methanolic potassium hydroxide and the product was crystallised from hexane to yield 19-norcholesta-1,3,5(10)-trien-3-ol (2.0 g., 90%) as needles, m.p. 113—115°,  $[\alpha]_{D} + 82.5^{\circ}$  (c 0.43 in EtOH) (lit.,<sup>11</sup> 113— 114°,  $[\alpha]_{\rm D}$  +74.9° in CHCl<sub>3</sub>),  $\lambda_{\rm max}$  210 ( $\epsilon$  7660), 221sh ( $\epsilon$  6630), and 282 m $\mu$  ( $\epsilon$  1680),  $\nu_{\rm max}$  3595 (phenolic OH), 3330br (H-bonded OH), 1609, 1590, 1502 (Ph), and 1180 cm.<sup>-1</sup> (phenolic OH),  $\delta$  (CCl<sub>4</sub>) 0.70 (s, 18-ang. Me), 2.73 (m, C-6 benzylic H), 4.85-5.32 br (s, OH), 6.42 (s, 4-ArH), 6.48 (d,  $J_{1,2}$  8.2 c./sec., 2-ArH), and 7.03 p.p.m. (d,  $J_{1,2}$ 8.2 c./sec., 1-ArH).

3-Methoxy-19-norcholesta-1,3,5(10)-triene (I;  $R^1 = R^2 =$  $R^4 = H, R^3 = OMe$ ).—Methyl iodide (12.0 g.) was added to a mixture of 19-norcholesta-1,3,5(10)-trien-3-ol (1.5 g.), potassium (1.3 g.), and dry benzene (400 ml.) which had been previously heated under reflux for 3 hr. The mixture

<sup>11</sup> J. Romo, G. Rosenkranz, and C. Djerassi, J. Org. Chem., 1950, 15, 1289.

## J. Chem. Soc. (C), 1969

was heated under reflux for a further 3 hr., and the cooled solution was filtered and concentrated. Chromatography of the residue on silica gel gave 3-methoxy-19-norcholesta-1,3,5(10)-triene (1.5 g., 97%) as a viscous oil (Found: C, 84.6; H, 11.3; O, 4.6. C27H42O requires C, 84.8; H, 11.1; O, 4.2%),  $\lambda_{max}$  (cyclohexane) 210 ( $\varepsilon$  11,300), 222 ( $\varepsilon$  8800), 280 ( $\varepsilon$  8800), and 288 m $\mu$  ( $\varepsilon$  8200),  $\nu_{max}$  2860 (OMe), 1610, 1580, 1500 (Ph), 1255 and 1040 cm.<sup>-1</sup> (OMe),  $\delta$  (CCl<sub>4</sub>) 0.70 (s, 18-ang. Me), 2.78 (m, 6-benzylic H), 3.70 (s, 3-OMe), 6·47 (d,  $J_{2,4}$  2 c./sec., 4-ArH), 6·55 (2d,  $J_{2,4}$  2,  $J_{1,2}$  8·3 c./sec., 2-ArH), and 7.05 p.p.m. (d,  $J_{1.2}$  8.3 c./sec., 1-ArH), o.r.d. (c 0.445 in cyclohexane)  $[\phi]_{589} + 368^{\circ}$ ,  $[\phi]_{500} + 488^{\circ}$ ,  $[\phi]_{400}$  $+695^{\circ}$ , and  $[\phi]_{300}$   $+1380^{\circ}$  (pk).

Oxidation of 3-Methoxy-19-norcholesta-1,3,5(10)-triene.---A solution of 3-methoxy-19-norcholesta-1,3,5(10)-triene (1.48 g.) in acetone (140 ml.) was treated dropwise with 4n-chromium trioxide-sulphuric acid (21 ml.) to yield a yellow neutral oil (1.03 g.) and a brown acidic oil (200 mg.).

The neutral oil was chromatographed on deactivated alumina (60 ml.). Elution of the column with light petroleum yielded starting material (120 mg., 9%) while initial benzene-light petroleum (1:5) eluates gave 3-methoxy-19-norcholesta-1,3,5(10)-trien-6-one (70 mg.) which crystallised from acetone as plates, m.p. 118-120° (Found: C, 81.7; H, 10.3.  $C_{27}H_{40}O_2$  requires C, 81.8; H, 10.2%),  $\lambda_{max}$  (cyclohexane) 220 ( $\epsilon$  23,840), 250 ( $\epsilon$  9100), 257sh ( $\epsilon$ 7920), and 320 mµ ( $\epsilon$  3125),  $\nu_{max}$  1675 (6-CO), 1610, 1570, 1495 (Ph), and 1290 cm.<sup>-1</sup> (CO),  $\delta$  0.72 (s, 18-ang. Me), 3.87 (s, 3-OMe), 7.12 (2d,  $J_{1,2}$  8.8,  $J_{2,4}$  3 c./sec., C-2 ArH), 7.39 (d,  $J_{1,2}$  8.8 c./sec., 1-ArH), and 7.61 p.p.m. (d,  $J_{2,4}$ **3** c./sec., 4-ArH), o.r.d. ( $c \ 0.230$ )  $[\phi]_{589} + 38^{\circ}$ ,  $[\phi]_{500} + 120^{\circ}$ ,  $[\phi]_{400} + 1085^{\circ}$ ,  $[\phi]_{355} + 7260^{\circ}$  (pk), and  $[\phi]_{340} + 5360^{\circ}$ .

Later benzene-light petroleum (1:5) eluates gave  $9\beta$ -hydroxy-3-methoxy-19-norcholesta-1,3,5(10)-trien-11-one (450 mg.) as a pale yellow viscous oil (Found: C, 78.4; H, 9.8; O, 11.5.  $C_{27}H_{40}O_3$  requires C, 78.6; H, 9.8; O, 11.6%),  $\lambda_{\text{max}}$  218 ( $\epsilon$  9940), 277 ( $\epsilon$  2060), and 283 m $\mu$  ( $\epsilon$  1945),  $v_{\text{max}}$  3460 (intramol. bonded OH), 1703 (11-CO), 1610, 1575, 1500 (Ph), and 1110 cm.<sup>-1</sup> (OH), δ 0.71 (s,  $W_{\frac{1}{2}}$  2 c./sec., 18-ang. Me), 2.20 (d, J 12.8 c./sec., 12 $\beta$ -H showing further fine splitting due to coupling with 18-Me), 2.71 (d, J 12.8 c./sec., 12a-H), 2.71 (m, 6-H), 3.75 (s, 3-OMe), 4.18 (s, OH), and 6.65 p.p.m. (s, 1-, 2-, and 3-ArH), o.r.d. (c 0.415)  $[\phi]_{589}$  +471°,  $[\phi]_{500}$  +725°,  $[\phi]_{400}$  +1427°,  $[\phi]_{303} + 14,800^{\circ} \text{ (pk), and } [\phi]_{205} + 12,650^{\circ}.$ 

Elution of the column with benzene-light petroleum (1:1) gave impure 9β-hydroxy-3-methoxy-19-norcholesta-1,3,5(10)-trien-6,11-dione (54 mg.) as an oil,  $\nu_{max}$ , 3465 (OH), 1706 (11-CO), and 1695 cm.<sup>-1</sup> (6-CO).

Elution of the column with benzene-ether (4:1) gave 9a-hydroxy-3-methoxy-19-norcholesta-1,3,5(10)-triene-6,11dione (10 mg.) which crystallised from ether as needles, m.p. 168-170° (Found: C, 76.0; H, 9.1. C27H38O4 requires C, 76.0; H, 9.0%),  $\lambda_{max}$  211 ( $\varepsilon$  10,220), 228 ( $\varepsilon$  8950), and 283 m $\mu$  ( $\varepsilon$  12,350),  $\nu_{max}$  3520—3300br (intermol. bonded OH), 1730 (11-CO), 1695 (6-CO), 1605, 1575, 1500 (Ph), and 1100 cm.<sup>-1</sup> (OH),  $\delta$  0.82 (s, 18-ang. Me), 3.90 (s, 3-OMe), and 6.5-7.05 p.p.m. (m, 1-, 2-, and 3-ArH), o.r.d. (c 0.04)  $[\phi]_{589} + 630^{\circ}, \ [\phi]_{500} + 955^{\circ}, \ [\phi]_{400} \ 1915^{\circ}, \ [\phi]_{303} + 6600^{\circ} \ (\mathrm{pk}),$ and  $[\phi]_{280} + 5750^{\circ}$ .

1-Methyl-19-norcholesta-1,3,5(10)-trien-3-yl Acetate (I;  $R^1 = Me$ ,  $R^2 = R^4 = H$ ,  $R^3 = OAc$ ).—Cholest-4-en-3-one

12 A. Afonso, H. L. Herzog, C. Federbush, and W. Charney, Steroids, 1966, 7, 429. <sup>13</sup> J. J. Eisch, J. Org. Chem., 1963, 28, 707.

(3.0 g.) was brominated by Inhoffen's procedure <sup>14</sup> and the product was chromatographed on silica gel. Elution with light petroleum-benzene (1:1) gave  $2\alpha,6\beta$ -dibromocholest-4-en-3-one <sup>15</sup> (1.48 g., 35%), needles (from acetone), m.p. 159—162.5° (lit.,<sup>14</sup> 162—163°) (Found: C, 59.9; H, 7.8; Br, 29.6. Calc. for C<sub>27</sub>H<sub>42</sub>Br<sub>2</sub>O: C, 59.8; H, 7.8; Br, 29.5%) while later fractions eluted with the same solvent gave 6\beta-bromocholest-4-en-3-one (530 mg., 15%), needles (from acetone), m.p. 128—130°,  $[\alpha]_{\rm D}$  +11° (lit.,<sup>16</sup> 131°,  $[\alpha]_{\rm D}$  +7°), undepressed by a sample prepared from  $5\alpha,6\beta$ -dibromocholestan-3-one by the method of Dane *et al.*<sup>17</sup> (Found: C, 70.1; H, 9.4; Br, 17.3. Calc. for C<sub>27</sub>H<sub>43</sub>BrO: C, 69.9; H, 9.4; Br, 17.3%). 6β-Bromocholest-4-en-3-one has not been previously isolated from this reaction although its intermediacy has hitherto been postulated.<sup>14, 15, 18</sup>

Dehydrohalogenation of  $2\alpha$ ,  $2\beta$ -dibromocholest-4-en-3-one with collidine hydrobromide for 5 hr.19 gave cholesta-1,4,6trien-3-one in 53% yield (cf. ref. 15). Treatment of the latter with acetic anhydride and toluene-p-sulphonic acid according to the method of Romo et al.20 gave 1-methyl-**19-norcholesta-1,3,5(10),6-tetraen-3-yl** acetate (86%).Hydrogenation of the acetate (610 mg.) in ethyl acetate (100 ml.) over platinum oxide at 20° and atmos. press. gave 1-methyl-19-norcholesta-1,3,5(10)-trien-3-yl acetate (590 mg., 98%) which crystallised from methanol as needles, m.p. 67-69 (Found: C, 82.2; H, 10.4; O, 7.6. C29H44O2 requires C, 82.0; H, 10.4; O, 7.5%),  $\lambda_{max}$  216 ( $\epsilon$  8500) and 273 mµ ( $\epsilon$  440),  $\nu_{max}$  1755 (3-OAc), 1600 (Ph), and 1210 cm.<sup>-1</sup> (OAc),  $\delta$  (CCl<sub>4</sub>) 0.75 (s, 18-ang. Me), 2.15 (s, 3-OAc), 2.30 (s, 1-Me), 2.76 (m, 6-benzylic H), and 6.63 p.p.m. (s,  $W_{\frac{1}{2}}$  3 c./sec., 2- and 4-ArH), o.r.d. (c 0.220 in MeOH)  $[\phi]_{589} + 500^{\circ}$ ,  $[\phi]_{500} + 708^{\circ}$ ,  $[\phi]_{400} + 1135^{\circ}$ ,  $[\phi]_{300} + 2390^{\circ}$ , and  $[\phi]_{250} + 5240^{\circ}$ .

Saponification of the trienyl-acetate (400 mg.) with 5% methanolic potassium hydroxide (40 ml.) under reflux for 2 hr. followed by chromatography on silica gel gave 1-methyl-19-norcholesta-1,3,5(10)-trien-3-ol (370 mg., 90%), needles (from methanol), m.p. 127–128°,  $[\alpha]_{\rm p}$  +146° (*c* 0·12 in MeOH), lit.,<sup>20</sup> 126·5–128°,  $[\alpha]_{\rm p}$  +135·6° in CHCl<sub>3</sub>),  $\lambda_{\rm max}$  220 ( $\varepsilon$  5770), 282 ( $\varepsilon$  1390), and 287 mµ ( $\varepsilon$  1410),  $v_{\rm max}$ . (CCl<sub>4</sub>) 3600 (phenolic OH), 3360 (H-bonded OH), 1605, 1593, 1480 (Ph), and 1150 cm.<sup>-1</sup> (phenolic OH),  $\delta$  0·80 (s, 18-ang. Me), 2·30 (s, 1-Me), 2·70 (m, 6-benzylic H), 5·08 (s, OH), and 6·48 p.p.m. (s,  $W_{\frac{1}{2}}$  4·1 c./sec., 2- and 4-ArH).

3-Methoxy-1-methyl-19-norcholesta-1,3,5(10)-triene (I;  $R^1 = Me$ ,  $R^2 = R^4 = H$ ,  $R^3 = OMe$ ).—The above hydroxy-triene (300 mg.) was methylated with dimethyl sulphate-sodium hydroxide to yield a brown gum which was percolated as a light petroleum solution through silica gel. Removal of solvent gave 3-methoxy-1-methyl-19-norcholesta-1,3,5(10)-triene (200 mg.) as an oil,  $[\alpha]_D + 114^\circ$  (c 0.75 in cyclohexane) (lit.,<sup>21</sup>  $[\alpha]_D + 113^\circ$  in CHCl<sub>3</sub>) (Found: C, 85·1; H, 11·1; O, 3·8.  $C_{28}H_{44}O$  requires C, 84·8; H, 11·2; O, 4·0%),  $\lambda_{max}$  (cyclohexane) 212 ( $\varepsilon$  13,850), 225sh ( $\varepsilon$  9300), 281 ( $\varepsilon$  1530), and 288 m $\mu$  ( $\varepsilon$  1595),  $\nu_{max}$  2880 (3-OMe), 1605, 1580, 1480 (Ph), and 860 cm.<sup>-1</sup> (isolated ArH),  $\delta$ 

<sup>14</sup> H. H. Inhoffen, Ber., 1936, 69, 2141.

 <sup>15</sup> C. Djerassi, G. Rosenkranz, J. Romo, St. Kaufmann, and J. Pataki, J. Amer. Chem. Soc., 1950, 72, 4534.
 <sup>16</sup> C. W. Bird, R. C. Cookson, and S. H. Dandegaonker, J.

<sup>16</sup> C. W. Bird, R. C. Cookson, and S. H. Dandegaonker, *J. Chem. Soc.*, 1956, 3675.

<sup>17</sup> E. Dane, Y. Wang, and W. Schulte, Z. Physiol. Chem., 1936, **245**, 80; Chem. Abs., 1937, **31**, 2606.

<sup>18</sup> L. Ruzicka, W. Bosshard, W. H. Fischer, and H. Wirz, *Helv. Chim. Acta*, 1936, **19**, 1147; H. Reich and A. Lardon, *Helv. Chim. Acta*, 1946, **29**, 671; H. Martens, *Annalen*, 1949, **563**, 131. 0.75 (d, 18-ang. Me), 2.32 (s, 1-Me), 2.76 (m, 6-benzylic H), 3.76 (s, 3-OMe), and 6.56 p.p.m. (s,  $W_{\frac{1}{2}}$  5 c./sec., 2- and 4-ArH).

Oxidation of 3-methoxy-1-methyl-19-norcholesta-1,3,5(10)-triene (80 mg.) in acetone (15 ml.) with 4N-chromium trioxide-sulphuric acid (1·1 ml.) gave a neutral oil (50 mg.),  $\nu_{max}$  1710 and 1685 cm.<sup>-1</sup>, t.l.c. of which showed the presence of eight compounds. Preparative t.l.c. gave the 6-oxo-derivative as an oil,  $\nu_{max}$  1685 cm.<sup>-1</sup> (6-CO), which could not be obtained pure from further preparative t.l.c.

4-Methyl-19-norcholesta-1,3,5(10)-trien-1-yl Acetate (I: $R^1 = OAc$ ,  $R^2 = R^3 = H$ ,  $R^4 = Me$ ).—A solution of cholesta-1,4-dien-3-one (5.0 g.) in acetic anhydride (185 ml.) and a 5% solution of anhydrous fused zinc chloride in glacial acetic acid (520 mg. in 7.5 ml.) was kept at 20° under an atmosphere of nitrogen for 24 hr. The solution was diluted with ether (2 l.) and extracted with an icecold 10% sodium hydroxide solution until all the acetic anhydride had been decomposed and the acids removed. The solvent was removed and the yellow gum (6.1 g) was chromatographed on silica gel, the column being eluted with light petroleum. Initial fractions, after rechromatography from hexane to remove a persistent trace of hydrocarbon, afforded 4-methyl-19-norcholesta-1,3,5(10)-trien-1-yl acetate (4.71 g.) as a clear gum,  $[\alpha]_{\rm D}$  +140° (c, 1.3 in cyclohexane) which emulsified with polar solvents such as ethanol and acetone but which was freely soluble in ether, chloroform, benzene, and light petroleum (Found: C, 82.1; H, 10.0.  $\rm C_{29}H_{44}O_2$  requires C, 82.0; H, 10.4%),  $\lambda_{max}$  (cyclohexane) 229 (z 4600) and 265 mµ (z 1600),  $\nu_{max}$  (CS<sub>2</sub>) 1765 (1-OAc), 1595 (Ph), 1206, 1194, (OAc), and 892, and 806 cm.<sup>-1</sup> (2 adj. ArH), 8 0.74 (s, 18-ang. Me), 0.86 (d, 21-Me), 0.90 (d, 25-gem-Me<sub>2</sub>), 2.18 (s, coincident 4-Me and 1-OAc), 2.59 (m, 6- and 9-benzylic H), 6.62 (d,  $J_{\rm 2,3}$  8.2 c./sec., 3-ArH) and 6.92 p.p.m. (d,  $J_{2,3}$  8.2 c./sec., 2-ArH).

Chromatography of the acetate on alumina resulted in partial hydrolysis and from one column which was left standing for 5 days before elution, 4-methyl-19-norcholesta-1,3,5(10)-trien-1-ol was obtained in a quantitative yield from benzene eluates. Crystallisation from light petroleum gave needles, m.p. 145·5—146°,  $[\alpha]_{\rm D}$  +177° (c, 0.95 in cyclohexane) (lit.,<sup>22</sup> 145·5—146°,  $[\alpha]_{\rm D}$  +161° in CHCl<sub>3</sub>),  $\lambda_{\rm max}$ . (cyclohexane) 221 ( $\varepsilon$  12,000) and 283 m $\mu$  ( $\varepsilon$  1400),  $v_{\rm max}$ . (CS<sub>2</sub>) 3600 (1-OH), 1380, 1180 (phenolic OH), and 800 cm.<sup>-1</sup> (2 adj. ArH),  $\delta$  0.75 (s, 18-ang. Me), 0.86 (d, 21-Me), 0.90 (d, 25-gem-Me\_2), 2.11 (s, 4-Me), 2.55 (m, 6-benzy-lic H), 2.95 (d,  $J_{8,9}$  10 c./sec., 9-benzylic H), 4.47 (s, 1-OH), 6.27 (d,  $J_{2,3}$  8 c./sec., 3-ArH), and 6.71 p.p.m. (d,  $J_{2,3}$  8 c./sec., 2-ArH), o.r.d. (c 0.23)  $[\phi]_{589}$  +678°,  $[\phi]_{294}$  +4600° (pk),  $[\phi]_{257}$  -2594° (tr),  $[\phi]_{222}$  +3000° (pk.), and  $[\phi]_{200}$  -1096° (tr).

The phenol was also isolated (80%) by hydrolysis of the acetate with 2n-methanolic potassium hydroxide for 1 hr.

Oxidation of 4-Methyl-19-norcholesta-1,3,5(10)-trien-1-yl Acetate.—A solution of chromium trioxide (5.02 g.) in the minimum amount of water, was diluted with glacial acetic

<sup>&</sup>lt;sup>19</sup> M. Fieser, M. A. Romero, and L. F. Fieser, *J. Amer. Chem. Soc.*, 1955, 77, 3305.

<sup>&</sup>lt;sup>20</sup> J. Romo, C. Djerassi, and G. Rosenkranz, *J. Org. Chem.*, 1950, **15**, 896.

<sup>&</sup>lt;sup>21</sup> J. Elkes, J. F. Oughton, and L. Stephenson, J. Chem. Soc., 1961, 4531.

<sup>&</sup>lt;sup>22</sup> A. L. Wilds and C. Djerassi, J. Amer. Chem. Soc., 1946, **68**, 1712.

J. Chem. Soc. (C), 1969

acid (21 ml.) and added to a solution of 4-methyl-19-norcholesta-1,3,5(10)-trien-1-yl acetate (6.42 g.) in glacial acetic acid (42 ml.). The mixture was kept at  $20^{\circ}$  for 22 hr. and worked up to yield a neutral fraction (5.4 g.) which was chromatographed from light petroleum on silica gel. Fractions eluted with benzene afforded 4-methyl-6-oxo-19-norcholesta-1,3,5(10)-trien-1-yl acetate as a gum (Found: C, 79.45; H, 9.5; O, 11.0. C<sub>29</sub>H<sub>42</sub>O<sub>3</sub> requires C, 79.4; H, 9.65; O, 10.9%),  $\lambda_{max.}$  (cyclohexane) 210 ( $\epsilon$  25,120), 245 ( $\epsilon$  7940), and 299 mµ ( $\epsilon$  2000),  $\nu_{max}$  1765 (1-OAc), 1690 (6-CO), and 1200 cm.<sup>-1</sup> (OAc),  $\delta$  0.74 (s, 18-ang. Me), 0.84 (d, 21-Me), 0.88 (d, 25-gem-Me<sub>2</sub>), 2.21 (1-OAc), 2.53(s, 4-Me), 6.88 (d,  $J_{2.3}$  9 c./sec., 3-ArH), and 6.99 p.p.m. (d,  $J_{2,3}$  9 c./sec., 2-ArH), o.r.d. (c 0.33 in cyclohexane)  $[\phi]_{589} + 486^{\circ}, \ [\phi]_{387} + 1240^{\circ} \ (\mathrm{br,pk}), \ [\phi]_{356} + 108^{\circ} \ (\mathrm{tr}),$ and  $[\phi]_{364} + 3510^{\circ}$  (pk).

4-Methyl-6-oxo-19-norcholesta-1,3,5(10)-trien-1-ol (II;  $R^1 = OH$ ,  $R^2 = R^3 = H$ ,  $R^4 = Me$ ).—The above acetate (5.0 g.) was heated under reflux with aqueous methanolic potassium hydroxide [700 mg. in the minimum amount of water and diluted with methanol (30 ml.)] in a stream of nitrogen. Repeated chromatography of the neutral fraction, obtained by saponification, on alumina gave (from chloroform eluates) 4-methyl-6-oxo-19-norcholesta-1,3,5(10)trien-1-ol (3.3 g.) which crystallised from benzene as fine needles, m.p. 241-242° (with decomp. from 238°) (Found: C, 81.3; H, 10.2. C<sub>27</sub>H<sub>40</sub>O<sub>2</sub> requires C, 81.8; H, 10.2%),  $\lambda_{\rm max}$  228 ( $\epsilon$  16,980), 259 ( $\epsilon$  8510), and 330 mm ( $\epsilon$  3980),  $\nu_{\rm max}$ (Nujol) 3230 (1-OH), 1660 (6-CO), 1280, 1260, 1230 (phenolic OH), and 830 cm.<sup>-1</sup> (2 adj. ArH),  $\delta$  (pyridine) 0.70 (s, 18-ang. Me), 0.87 (d, 21-Me), 0.91 (d, 25-gem-Me<sub>2</sub>), 2.46 (d,  $J_{8,9}$  10 c./sec., 9-benzylic H), 2.51 (s, 4-Me),  $\delta$  (CDCl<sub>3</sub>)  $f_{8,9}$  10 c./sec., 2-ArH), o.r.d. (c 0.37) [ $\phi$ ]<sub>589</sub> +150°, [ $\phi$ ]<sub>379</sub> +642° (pk),  $[\phi]_{353} - 150^{\circ}$  (tr),  $[\phi]_{275} + 1498^{\circ}$  (pk), and  $[\phi]_{245}$  $+169^{\circ}$  (tr).

Oxidation of 4-Methyl-19-norcholesta-1,3,5(10)-trien-1-yl Benzoate (I;  $R^1 = OBz$ ,  $R^2 = R^3 = H$ ,  $R^4 = Me$ ). Benzoylation of 4-methyl-19-norcholesta-1,3,5(10)-trien-1-ol (560 mg.) with pyridine (5 ml.) and benzoyl chloride (3 ml.) under reflux for 3 hr. afforded the trienyl benzoate as a clear gum (490 mg.) after chromatography on alumina,  $\nu_{max}$  (CCl<sub>4</sub>) 1720 (1-OBz), 1610, 1595, 1455, (Ph), 1125 (OBz), and 940, 712, and 685 cm.<sup>-1</sup> (ArH). The benzoate (720 mg.) was oxidised with chromium trioxide (490 mg.) dissolved in the minimum amount of water and then diluted with glacial acetic acid (10 ml.). Chromatography of the neutral fraction and elution with benzene-ether (1:1)4-methyl-6-oxo-19-norcholesta-1,3,5(10)-trien-1-yl afforded benzoate (550 mg.) as a clear gum (Found: C, 81.6; H, 9.1; O, 9.85. C34H44O3 requires C, 81.6; H, 8.9; O, 9.6%),  $\lambda_{\rm max.}$  (cyclohexane) 275 ( $\epsilon$  19,950), 283 ( $\epsilon$  18,200), and 300 mµ ( $\varepsilon$  13,180),  $\nu_{max}$  1730 (1-OBz) 1700 (6-CO), 1605, 1580 (Ph), and 1455, 1375, 1260 cm.<sup>-1</sup> (aryl ester),  $\delta$  0.82 (s, 18-ang. Me), 0.92-1.28 (m, 21-Me and 25-gem-Me2), 2.65 (s, 4-Me), 7.1-8.4 p.p.m. (m, 2-, 3-, and benzoyl ArH), o.r.d. (c, 0.417 in cyclohexane)  $[\phi]_{589} + 312^{\circ}$ ,  $[\phi]_{380}$  $+1150^{\circ}$ ,  $[\phi]_{374}$   $+1308^{\circ}$  (pk),  $[\phi]_{345}$   $+1055^{\circ}$  (br, tr), and  $[\phi]_{318} + 2200^{\circ}.$ 

Oxidation of 1-Methoxy-4-methyl-19-norcholesta-1,3,5(10)triene (I;  $R^1 = OMe$ ,  $R^2 = R^3 = H$ ,  $R^4 = Me$ ).—Methylation of 4-methyl-19-norcholesta-1,3,5(10)-trien-1-ol (1.0 g.)

<sup>24</sup> J. Schmitt, J. J. Panouse, P.-J. Cornu, A. Hallot, H. Pluchet, and P. Comoy, Bull. Soc. Chim. France, 1965, 1934.

with potassium-methyl iodide gave a yellow oil which after chromatography on alumina afforded 1-methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene (950 mg., 95%). Crystallisation from methanol-ether gave needles, m.p. 104—105°,  $[\alpha]_{\rm D}$  +174° (c, 0.83 in cyclohexane) (lit.,<sup>23</sup> 104—105°,<sup>22</sup>  $[\alpha]_{\rm D}$  +165° in CHCl<sub>3</sub>),  $\lambda_{\rm max}$ , 210 ( $\varepsilon$  41,000), 222sh ( $\varepsilon$  29,800), and 281 m $\mu$  ( $\varepsilon$  5830),  $\delta$  0.72 (s, 18-ang. Me), 2.16 (s, 4-Me), 3.76 (s, 1-OMe), 6.67 (d,  $J_{2,3}$  8.2 c./sec., 3-ArH) and 6.97 (d,  $J_{2,3}$  8.2 c./sec., 2-ArH).

The methoxy-triene (820 mg.) in acetone (120 ml.) was oxidised with 4N-chromium trioxide-sulphuric acid (11·2 ml.) to yield a neutral fraction (380 mg.) and an acid fraction (400 mg.).

Preparative t.l.c. of the neutral fraction, which contained at least ten compounds (t.l.c.), yielded starting material (16 mg., 2%) and the major component, 1-methoxy-4-methyl-19-norcholesta-1,3,5(10)-trien-6-one (40 mg., 5%) which crystallised from methanol-ether as needles, m.p. 80-82° (Found: C, 82·1; H, 10·2; O, 7·9. C<sub>28</sub>H<sub>42</sub>O<sub>2</sub> requires C, 81·9; H, 10·3; O, 7·8%),  $\lambda_{max}$  (cyclohexane) 219 ( $\varepsilon$  22,220), 248 ( $\varepsilon$  6890), 254 ( $\varepsilon$  6770), and 320 m $\mu$  ( $\varepsilon$  3450),  $\nu_{max}$  1675 (6-CO), 1570, 1555 (Ph) and 1275 cm.<sup>-1</sup> (6-CO),  $\delta$  0·73 (s, 18-ang. Me), 2·56 (s, 4-Me), 3·82 (s, 1-OMe), 6·97 (d,  $J_{2.3}$  8·4 c./sec., 3-ArH), and 7·08 p.p.m. (d,  $J_{2.3}$  8·4 c./sec., 2-ArH), o.r.d. (c 0·477) [ $\phi$ ]<sub>589</sub> +542°, [ $\phi$ ]<sub>500</sub> +722°, [ $\phi$ ]<sub>400</sub> +1188°, [ $\phi$ ]<sub>376</sub> +1470° (pk), and [ $\phi$ ]<sub>355</sub> +850° (tr.).

No other compound was isolated in sufficient quantity or purity for identification.

The acid fraction from oxidation was chromatographed on silica gel, methylated with diazomethane, and rechromatographed to yield methyl 1-methoxy-19-norcholesta-1,3,5(10)-triene-4-carboxylate (170 mg.) as a viscous oil (Found: C, 79·3; H, 10·3.  $C_{29}H_{24}O_3$  requires C, 79·0; H, 10·1%),  $\lambda_{max}$ . (cyclohexane) 215 ( $\epsilon$  26,200), 223 ( $\epsilon$ 24,050), and 258 mµ ( $\epsilon$  11,100),  $\nu_{max}$ . (CCl<sub>4</sub>) 1720 (4-CO<sub>2</sub>Me), 1588, 1578 (Ph), and 1212 cm.<sup>-1</sup> (CO<sub>2</sub>Me),  $\delta$  0·74 (s, 18-ang. Me), 3·00 (m, 6-benzylic H), 3·78 (s, 1-OMe), 3·81 (s, 4-CO<sub>2</sub>Me), 6·59 (d,  $J_{2,3}$  9 c./sec., 2-ArH), and 7·71 p.p.m. (d,  $J_{2,3}$  9 c./sec., 3-ArH), o.r.d. (c, 0·550 in cyclohexane) [ $\phi$ ]<sub>589</sub> +1070°, [ $\phi$ ]<sub>500</sub> +1490°, [ $\phi$ ]<sub>400</sub> +2140°, [ $\phi$ ]<sub>300</sub> +7950°, and [ $\phi$ ]<sub>288</sub> +9550° (pk).

4-Methyl-19-norcholesta-1,3,5(10)-triene (I;  $R^1 = R^2 = R^3 = H$ ,  $R^4 = Me$ ).—Cholest-4-en-3-one was treated with acetyl bromide and  $\alpha$ -bromopropionic acid by the method of Schmitt *et al.*<sup>24</sup> Chromatography of the product on alumina and elution with light petroleum gave 4-methyl-19-norcholesta-1,3,5(10)-triene as a gum (97%). The same product was also formed by treatment of cholesta-1,4-dien-3-one with lithium aluminium hydride.<sup>25</sup> The gum slowly crystallised on storage as needles, m.p. 49—51° (lit.,<sup>25</sup> 49°),  $\lambda_{max}$ . (EtOH) 263 m $\mu$  ( $\varepsilon$  250),  $\nu_{max}$ . 1170, 1090, 1030, 970 (aromatic in-plane def.), and 780, 740 cm.<sup>-1</sup> (aromatic out-of-plane def.),  $\delta$  0.72 (18-ang. Me), 0.84 (d, 21-Me), 0.90 (d, 25-gem-Me<sub>2</sub>), 2.15 (s, 4-Me), 2.65 (m, 6-benzylic H), and 6.90 p.p.m. (m, 1-, 2-, and 3-ArH).

Oxidation of 4-Methyl-19-norcholesta-1,3,5(10)-triene.—A solution of 4-methyl-19-norcholesta-1,3,5(10)-triene (1.45 g.) in acetone (220 ml.) was treated dropwise with 4N-chromium trioxide-sulphuric acid (19 ml.) to yield a neutral oil (1.37 g.) which contained nine products (t.l.c.). Chromatography on silica gel and elution with light petroleum

<sup>25</sup> H. Dannenberg and H.-G. Neumann, Annalen, 1961, 646, 148.

<sup>23</sup> H. H. Inhoffen and G. Zühlsdorff, Ber., 1941, 74, 604.

2-Methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene (I;  $R^1 = R^3 = H$ ,  $R^2 = OMe$ ,  $R^4 = Me$ ).—2 $\alpha$ ,  $5\alpha$ -Epidioxycholest-3-ene (7.03 g., 77%), prepared from cholesta-2,4-diene 26 by irradiation with two 250-w lamps in the presence of eosin and oxygen,26 was isomerised in quantitative yield to 5a-hydroxycholest-3-en-2-one, m.p. 171-173° (lit., 27 173°), by absorption on activated alumina for 4 hr.<sup>28</sup> and then eluting with ether-methanol (1:1). The product (5.4 g.) in methanol (760 ml.) was heated under reflux with sulphuric acid (7.6 ml.) for 50 min. Chromatography of the product (isolated by ether-extraction) on alumina and elution with light petroleum-benzene yielded 2-methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene (5.3 g., 98%) which crystallised from acetone as needles, m.p. 52-53°,  $[\alpha]_{\rm D}$  +90° (c, 0.7 in cyclohexane) (lit.,<sup>29</sup> 51.5-52.5°  $[\alpha]_{\rm p}$  +76.6° in CHCl<sub>3</sub>),  $\nu_{\rm max}$  2830, 1240, 1060 (OMe), 1610 and 1580 cm.<sup>-1</sup> (Ph),  $\delta$  (CCl<sub>4</sub>) 0.68 (s, 18-ang. Me), 2·13 (s, 4-Me), 2.59 (m, 6-benzylic H), 3.69 (s, 2-OMe), 6.46 (s, 1-ArH), and 6.57 (s, 3-ArH).

<sup>26</sup> H. E. Stavely and W. Bergmann, J. Org. Chem., 1936, 1, 575; E. L. Skau and W. Bergmann, J. Org. Chem., 1938, 3, 166.
 <sup>27</sup> W. Bergmann, F. Hirschmann, and E. L. Skau, J. Org. Chem., 1939, 4, 29.

Oxidation of 2-Methoxy-4-methyl-19-norcholesta-1,3,5(10)triene.---A solution of 2-methoxy-4-methyl-19-norcholesta-1,3,5(10)-triene (2.0 g.) in acetone (230 ml.) was oxidised with 4N-chromium trioxide-sulphuric acid (27 ml.) to yield a neutral fraction (1.85 g.) as a yellow solid. Chromatography on deactivated alumina and elution with light petroleum-benzene (1:1) gave 2-methoxy-4-methyl-19-norcholesta-1,3,5(10)-trien-6-one (1.62 g., 80%) which crystallised from methanol as needles, m.p. 103-104° (Found: C, 82·1; H, 10·5. C<sub>28</sub>H<sub>42</sub>O<sub>2</sub> requires C, 81·9; H, 10·3%),  $\lambda_{\rm max}$  (cyclohexane) 207 (z 17,700), 223 (z 18,350), 229 (z 17,880), and 270 m $\mu$  ( $\epsilon$  15,650),  $\nu_{max.}$  2860 (2-OMe), 1660 (6-CO), 1590, 1560, 1480 (Ph), 1240 (6-CO), and 868 cm.<sup>-1</sup> (isolated ArH), 8 0.70 (s, 18-ang. Me), 2.57 (s, 4-Me), 3.80 (s, 2-OMe), 6.53 (s, 1-ArH), and 6.67 (s, 3-ArH), o.r.d. (c 0.68 in cyclohexane)  $[\phi]_{589} + 55^{\circ}$ ,  $[\phi]_{400} + 1122^{\circ}$ ,  $[\phi]_{564} + 3080^{\circ}$  (pk),  $[\phi]_{318} 0^{\circ}$ , and  $[\phi]_{278} - 2800^{\circ}$  (tr).

Elution of the column with ether-benzene (1:5) yielded 2-methoxy-4-methyl-7-oxa-19-norcholesta-1,3,5(10),8-tetraen-6-one (0·17 g., 9%) which crystallised from methanol as plates, m.p. 178—179° (Found: C, 78·8; H, 9·8; O, 11·3. C<sub>27</sub>H<sub>40</sub>O<sub>2</sub> requires C, 79·0; H, 9·3; O, 11·7%),  $\lambda_{max}$  206 ( $\epsilon$  16,790), 226 ( $\epsilon$  16,100), and 277 m $\mu$  ( $\epsilon$  15,400),  $\nu_{max}$  206 ( $\epsilon$  16,790), 226 ( $\epsilon$  16,100), and 277 m $\mu$  ( $\epsilon$  15,400),  $\nu_{max}$  206 ( $\epsilon$  0(2-OMe), 1670 (6-CO), 1600, 1570 (Ph), and 1255 cm.<sup>-1</sup> (6-CO),  $\delta$  0·71 (s, 18-ang. Me), 2·58 (s, 4-Me), 3·84 (s, 2-OMe), 6·69 (d,  $J_{1,3}$  2·5 c./sec., 3-ArH), and 6·95 (d,  $J_{1,3}$  2·5 c./sec., 1-ArH), o.r.d. (c 0·493 in EtOH) [ $\phi$ ]<sub>589</sub> +82°, [ $\phi$ ]<sub>400</sub> +776°, [ $\phi$ ]<sub>348</sub> +4050° (pk), and [ $\phi$ ]<sub>320</sub> +425°.

## [8/1795 Received, December 6th, 1968]

<sup>28</sup> B. R. Davis and T. G. Halsall, J. Chem. Soc., 1962, 1833.
 <sup>29</sup> R. J. Conca and W. Bergmann, J. Org. Chem., 1953, 18, 1104.