Functionalisation of Saturated Hydrocarbons. Part 6.[1] Selective Oxidation of Steroids and Related Compounds

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The oxidation of a series of steroids by the Gif system gives, almost without exception, the 20-ketone as major isolated product. The side-chain cleavage is made more selective by modification of rings A or B. The oxidation of oleana-1,12-diene-3,11-dione has also been studied and the two principal products have been identified.

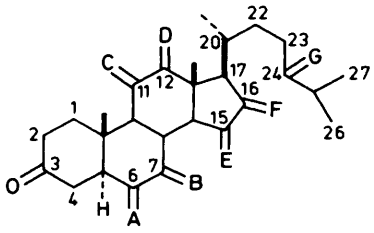
The Gif system (iron catalyst–O_2-pyridine–acetic acid–zinc) for the oxidation of saturated hydrocarbons gives, selectively, attack on secondary positions with formation of ketones. In simple hydrocarbons C–C bond cleavage has never been seen, although looked for with diligence. However, the oxidation of 3β,5α,6β-triacetoxycholestane affords as major isolated product the corresponding 20-ketone (12%) with cleavage of the 20,22-C–C bond.[2] This paper is concerned with the effect of substituents in the steroid nucleus on the yield of 20-ketone. This process is of potential industrial importance.

Apart from the 20-ketone, all the other major isolated products were ketones, the 15-, 16-, and 24-keto-derivatives of the starting compound being the next most abundant.[2] In addition smaller amounts of ketones at almost every secondary position in the molecule were found. In our more detailed study [2b] the reaction products were very thoroughly fractionated (during one year) by h.p.l.c. techniques and finally *ca.* 45% of the oxidation products were isolated pure. Clearly, the present study on the systematic variation of substrate did not justify the same effort in fractionation. With one exception we have only sought to isolate the major products pure. Even here the yields obtained do not reflect what could be obtained by thorough fractionation. The yields can, however, be compared with each other since the effort of separation was the same for each experiment.

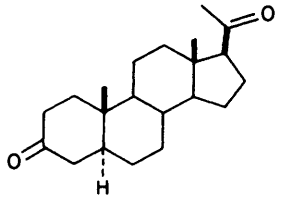
We began our studies by investigating carefully, in collaboration with Dr. A. K. Göktürk, the major oxidation products of 5α-cholestan-3-one (**1**). The major products isolated were the 20-ketone (**9**), followed by the ring oxidised products at the 6-(**2**), 7-(**3**), 15- (**6**), and 16-positions (**7**). In addition, the 24-ketone (**8**) was present in comparable amounts. The 11- (**4**) and 12-ketones (**5**) were also isolated, albeit as minor components.

The evidence for the structures of all the oxidised products is predominantly based on 400 MHz ^{1}H n.m.r. data, (Tables 1 and 2) which give the characteristic shifts of the C-18 and C-19 methyl singlets. The chemical shifts are diagnostic of the substitution pattern and may be calculated from the corresponding shifts of the parent steroid.[2,3] A comparison of the observed and calculated values for cholestanone (**1**) is presented in Table 1. In addition, molecular rotation difference studies [4,5] (Table 3), mass spectral and i.r. data (particularly characteristic for the 15- and 16-ketones) are all in excellent agreement with the proposed structures.[6]

We then turned our attention to cholest-4-en-3-one (**10**) and discovered a dramatic effect in the selectivity of oxidation. In the case of cholestan-3-one the major ring oxidation products were the 6- and 7-ketones. In contrast, the major ring isolated oxidation products of cholest-4-en-3-one were the 15- and 16-ketones (**12**) and (**13**). Furthermore no 6- or 7-oxo products were



(**1**) A,B,C,D,E,F,G = H_2
(**2**) A = O,B,C, D,E,F,G = H_2
(**3**) B = O,A,C, D,E,F,G = H_2
(**4**) C = O,A,B, D,E,F,G = H_2
(**5**) D = O,A,B,C,E,F,G = H_2
(**6**) E = O,A,B,C,D,F,G = H_2
(**7**) F = O,A,B,C,D,E,G = H_2
(**8**) G = O,A,B,C,D,E,F = H_2



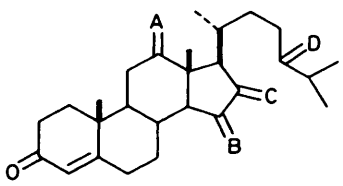
(**9**)

isolated. The 20-ketone (**15**) (7.6% based on starting material consumed), was again found to be the major product together with a lesser quantity of the 24-ketone (**14**) and a minor amount of the 12-ketone (**11**). Thus, the inclusion of the double bond to give a conjugated enone appears to deactivate not only the A ring but also the B ring to oxidation by the Gif system. Intrigued by this result we prepared the corresponding cholesta-1,4-dien-3-one (**16**) by dehydrogenation of cholestanone (**1**) with benzeneseleninic anhydride [7] and subjected this to an oxidation. Whilst the yield of 20-ketone (**19**) (9.4% based on starting material consumed) was more than was obtained with cholestenone (**10**), the yields of the other ketones showed a slight decrease and only the 15- and 24-ketones (**17**) and (**18**) were isolated as other major products.

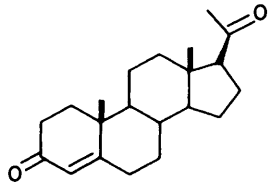
This change in selectivity could be due to an extension of the electron-withdrawing effect of the carbonyl moiety *via* the double bond, or it could be a long range conformational transmission effect.[8]

Table 1. Chemical shifts of C-18 and C-19 methyl protons for 3-oxo steroidal oxidation products

		Cholestanone (1)		Cholestenone (10)		Cholestadienone (16)	
		C-18	C-19)	C-18	C-19	C-18	C-19
6-Ketone	Calc:	0.70	0.96	0.75	1.14	0.75	1.18
	Found:	0.69	0.96				
7-Ketone	Calc:	0.69	1.29	0.74	1.47	0.74	1.51
	Found:	0.68	1.28				
11-Ketone	Calc:	0.65	1.23	0.70	1.41	0.70	1.45
	Found:	0.68	1.16				
12-Ketone	Calc:	1.06	1.11	1.11	1.29	1.11	1.33
	Found:	1.06	1.11	1.10	1.28		
15-Ketone	Calc:	0.76	1.02	0.80	1.20	0.82	1.24
	Found:	0.76	1.01	0.80	1.20	0.84	1.24
16-Ketone	Calc:	0.85	1.05	0.89	1.23	0.90	1.27
	Found:	0.84	1.05	0.87	1.22		
20-Ketone	Calc:	0.63	1.01	0.68	1.19	0.70	1.23
	Found:	0.63	1.01	0.67	1.19	0.70	1.23
24-Ketone	Calc:	0.68	1.01	0.72	1.19	0.73	1.23
	Found:	0.68	1.01	0.71	1.18	0.74	1.23



(10) A,B,C,D = H_2
(11) A = O, B,C,D = H_2
(12) B = O, A,C,D = H_2
(13) C = O, A,B,D = H_2
(14) D = O, A,B,C = H_2



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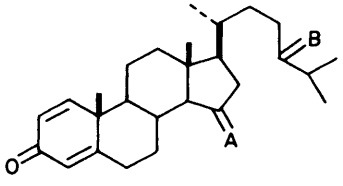
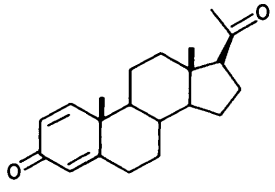
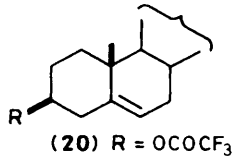


(16) A , B = H_2
(17) A = O, B = H_2
(18) B = O, A = H_2



(19)



(20) R = $OCOCF_3$

Further examination of the effect of substitution at C-3 was undertaken by oxidation of the 3β-trifluoroacetate of cholesterol (**20**). However, a direct comparison with the corresponding acetate (**28**) proved impossible, owing to the lability of the trifluoroacetyl group under the reaction conditions. Interestingly the 3β-toluene-*p*-sulphonate derivative of cholestanol (**21**) gave comparable results to those obtained with cholestanone and 3β-cholestanyl acetate.[2] Again the 20-ketone (**27**) was found to be the most abundant product, but the 6- and 7-ketones (**22**) and (**23**) were found to be the major steroid ring oxidised products.

A further interesting property of the Gif system is that it has been shown not to form epoxides with a simple olefinic hydrocarbons, *e.g.* cyclohexene.[9] Cholesteryl acetate (**28**) was chosen as a suitable substrate to investigate the effect of an isolated double bond in a more complex system. The major oxidation products were the 20-ketone (**33**) and the 7-ketone (**29**) (5.1% and 5.9%, respectively, based on starting material consumed). The other oxidation products isolated were the 15-, 16-, and 24-ketones (**30**), (**31**), and (**32**), but no epoxidation products were observed as determined by a h.p.l.c. co-injection with a mixture of the authentic α- and β-epoxides.[10] The authentic epoxides were shown to be stable both to the reaction and work-up conditions, thus establishing that no epoxide formation occurred during the reaction. However, the formation of the 7-oxo product (**29**) illustrates the susceptibility of a secondary allylic position of an isolated double bond towards oxidation under the reaction conditions. The preference for the 7-oxo product, rather than the 4-oxo product presumably arises from a deactivation of the A-ring by the acetate group. The steroid results are summarised in Table 4.

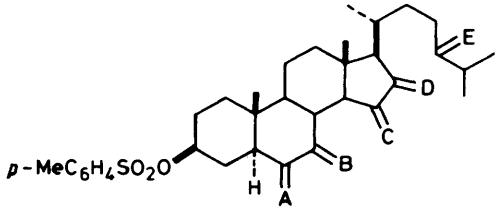
Further support for the increased reactivity of an allylic position in the Gif system was obtained by the oxidation of the oleanenone (**34**), which afforded the 11-ketone (**35**) as the single major product in 4.2% yield.

By analogy to the deactivation of rings A and B and partial deactivation of the C ring in cholestenone (**10**), we envisaged that a substrate such as the triterpenoid (**36**) would be selectively oxidised in the E ring to give the 21- and 22-ketones as the major products. Both the B and D rings should be relatively inert to oxidation owing to the presence of the enone systems in rings A and C, and the 19-position was thought to be too sterically hindered to afford a good yield of the corresponding oxidised product.

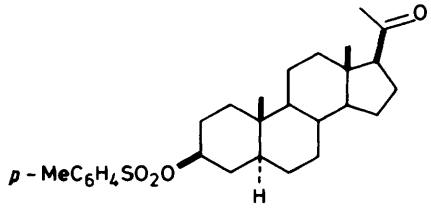
The diene-dione (**36**) was synthesized from 3β-acetoxyoleanene (**39**) by a chromium trioxide oxidation to afford the 11-oxo derivative (**40**).[11] The acetate group was hydrolysed with aqueous sodium hydroxide in methanol to give the corresponding alcohol (**41**), which was treated with Jones' reagent at 0 °C to afford the desired ketone (**35**) in an overall yield of 55% from (**39**). The final dehydrogenation step was achieved with benzeneseleninic acid at 95 °C in chlorobenzene to yield 71% of the required substrate (**36**). Oxidation, according to the Gif procedure, of (**36**) proceeded smoothly to afford two major products, one of which, as predicted, was the 21-ketone (**38**). The other was the corresponding 16-ketone (**37**). The structural assignments were based primarily on the chemical shifts of the eight quaternary methyl singlets in the ^1H n.m.r. spectrum;

Table 2. Chemical shifts of C-18 and C-19 methyl protons for 3β-substituted steroidal oxidation products

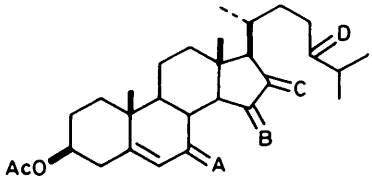
		Cholestanyl toluene-*p*-sulphonate (**21**)		Cholesteryl acetate (**28**)		7-Oxocholesteryl acetate (**29**)	
6-Ketone	Calc:	0.65	0.72	0.70	0.92	0.70	1.16
	Found:	0.64	0.72				
7-Ketone	Calc:	0.64	1.05	0.69	1.23	0.69	1.49
	Found:	0.63	1.05	0.68	1.21		
15-Ketone	Calc:	0.71	0.78	0.76	1.03	0.65	1.43
	Found:	0.72	0.78	0.77	1.02		
16-Ketone	Calc:	0.80	0.81	0.85	1.07	1.33	1.31
	Found:	0.79	0.81	0.84	1.06		
20-Ketone	Calc:	0.60	0.78	0.65	1.03	0.65	1.21
	Found:	0.58	0.78	0.63	1.02	0.66	1.22
24-Ketone	Calc:	0.63	0.77	0.68	1.03	0.68	1.21
	Found:	0.63	0.77	0.68	1.02	0.68	1.21



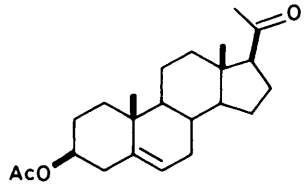
(**21**) A,B,C,D,E = H_2
(**22**) A = O, B,C,D,E = H_2
(**23**) B = O, A,C,D,E = H_2
(**24**) C = O, A,B,D,E = H_2
(**25**) D = O, A,B,C,E = H_2
(**26**) E = O, A,B,C,D = H_2



(**27**)



(**28**) A,B,C,D = H_2
(**29**) A = O, B,C,D = H_2
(**30**) B = O, A,C,D = H_2
(**31**) C = O, A,B,D = H_2
(**32**) D = O, A,B,C = H_2



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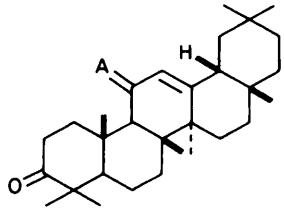


(**34**) A = H_2
(**35**) A = O

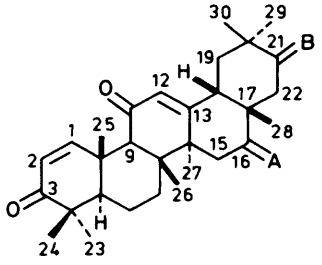
Table 5 shows the close agreement between the calculated and the experimentally observed values.

In a second example of our efforts directed towards the successful prediction and control of regioselectivity, we selected the 7-ketone of cholesteryl acetate (**29**) as a suitable substrate. We reasoned that the presence of the enone system in the B ring could deactivate all the steroidal rings, resulting in oxidation occurring solely in the side chain. It was thus gratifying to discover that the two major oxidation products were the 20- and 24-ketones (**42**) and (**43**).

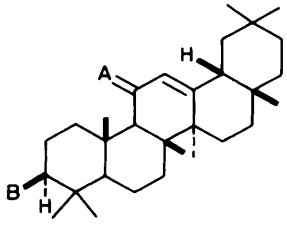
In conclusion, the Gif system selectively oxidised steroidal methylenes, which are devoid of proximal carbonyl function-

Table 3. Molecular rotation relationship of the steroidal oxidation products.[2]

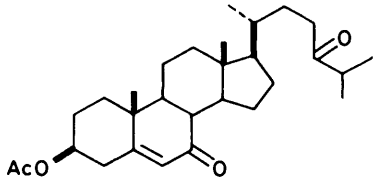
		(1)		(10)		(16)		(21)		(28)		(29)	
Compd.	$\Delta_{calc.}$	M_D/°	Δ	M_D/°	Δ	M_D/°	Δ	M_D/°	Δ	M_D/°	Δ	M_D/°	Δ
6-Ketone	−113	+16	−142					−39	−77				
7-Ketone	−233	−68	−226					−167	−205	−425	−241		
11-Ketone	+79	+232	+74										
12-Ketone	+270	+256	+98	+466	+123								
15-Ketone	+106	+288	+130	+263	−80	+194	+87	+133	+95	−84	+100		
16-Ketone	−507	−584	−742	−204	−547			−395	−433	−327	−143		
20-Ketone	+197	+436	+278	+543	+200	+374	+267	+274	+236	+75	+259	−242	+183
24-Ketone	−10	+152	−6	+321	−22	+83	−24	+45	+7	−177	+7	−424	+1



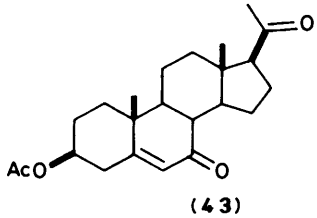
(**36**) A,B = H_2
(**37**) A = O, B = H_2
(**38**) B = O, A = H_2



(**39**) A = H_2, B = OAc
(**40**) A = O, B = OAc
(**41**) A = O, B = OH



(**42**)



(**43**)

Table 4. Yields (%) of oxidised products, based on consumed starting material

Steroid	(1)	(10)	(16)	(21)	(28)	(29)
6-Ketone	4.1			2.9		
7-Ketone	3.8			2.3	5.9	
11-Ketone	1.1					
12-Ketone	1.0	1.3				
15-Ketone	3.3	2.2	1.0	2.0	2.8	
16-Ketone	2.1	1.3		1.4	0.9	
20-Ketone	4.6	7.6	9.4	4.2	5.1	4.8
24-Ketone	2.9	3.4	1.6	1.8	2.0	1.7

Table 5. Chemical shifts of C-23 to C-30 methyl protons for the oxidation products of oleana-1,12-diene-3,11-dione (**36**)

Position	C-23	C-24	C-25	C-26	C-27	C-28	C-29,	C-30
(**36**)	1.12	1.17	1.20	1.39	1.42	0.90	0.91,	0.92
16-Ketone								
Calc:[a]	1.12	1.15	1.22	1.46	1.42	1.28	0.91,	0.92
Found:	1.12	1.17	1.20	1.47	1.43	1.29	0.91,	0.91
21-Ketone								
Calc:[a]	1.09	1.17	1.20	1.38	1.40		1.05,	1.25
Found:	1.12	1.17	1.20	1.37	1.43	1.02	1.05,	1.24
19-Ketone								
Calc:[c]	1.12	1.17	1.23	1.41	1.28		1.08,	1.17
22-Ketone								
Calc.:[d]	1.16	1.16	1.20	1.26	1.42		0.95,	0.96

[a] Calculated using the differences between olean-12-ene and the corresponding 16-oxo derivative (T. Kikuchi, M. Takayama, T. Toyoda, M. Arimoto, and M. Niwa, *Chem. Pharm. Bull.*, 1973, **21**, 2243). [b] Calculated using the differences between 3-oxo-olean-12-en-28-oic acid and 3,21-dioxo-olean-12-en-28-oic acid (M. Takai, S. Amagaya, and Y. Ogihara, *J. Chem. Soc., Perkin Trans. 1*, 1977, 1801). [c] B. Tursch, R. Savoir, R. Ottinger, and G. Chiurdoglu, *Tetrahedron Lett.*, 1967, 539. [d] Calculated using the differences between diphenylmethyl 3-oxo-olean-12-en-28-oate and the corresponding 22-oxo derivative (P. J. Beeby, *Aust. J. Chem.*, 1978, **31**, 1313).

ality. We are, therefore, in a position to be able to predict and control, to a significant extent, the sites of oxidation by modification of the functionality in the A and B rings. We have also demonstrated that the oxidation is compatible with several functional groups: ketones, esters, sulphonate esters, enones, and double bonds (although the allylic position is susceptible to oxidation to ketone). Even the cholesta-1,4-dien-3-one system has been shown to be stable to the reaction conditions by the appropriate control experiments.

At the present time the prediction of selectivity is rather more simple than the explanation! However, it appears that the inclusion of electron-withdrawing substituents in the A ring deactivate the ring towards oxidation. An extension of this effect, as exemplified by cholestenone, further deactivates the B and C rings, although a conformational transmission effect may also have a role to play.

Experimental

M.p.s were determined with a Kofler hot-stage apparatus and are uncorrected. ^{1}H N.m.r. spectra were obtained for solutions

in deuteriochloroform and a 400 MHz Bruker WM 400 instrument was generally used. Optical rotations were measured with a Perkin-Elmer 141 polarimeter in chloroform solutions. I.r. spectra were recorded with a Perkin-Elmer 297 infrared spectrophotometer and u.v. spectra with a Perkin-Elmer Lambda 5 u.v./vis. spectrophotometer. Mass spectra were performed with a Riber R 1010 machine and accurate mass measurements were carried out with a V. G. 70-7OE spectrometer in the dynamic mode. H.p.l.c. was performed with a Waters Associates Liquid Chromatograph equipped with a Lambda-max 480 LC spectrophotometer variable u.v. detector and a R401 Differential Refractometer Unit. Preparative normal phase Ultrasphere-SiO_2 and reverse phase Ultrasphere ODS, 5μM, 10 mm × 25 cm columns and SDS Purex grade solvents were used in h.p.l.c. work.

T.l.c. was carried out on T.L.C.-Ready-foils F1500/LS 254 and column chromatography with Merck Silica Gel 60.

Oxidation of Steroids: General Procedure.—In a typical reaction, steroid (3 mmol), zinc (1.96 g, 10 equiv.), iron cluster[12] (10—15 mg), pyridine (45 ml), water (3 ml) and acetic acid (3.45 ml, 20 equiv.) in a conical flask (150 ml) were stirred under the static pressure of an oxygen-filled balloon at room temperature for 5 h. After the completion of the reaction as judged by consumption of Zn, the mixture was cooled in an ice-bath and carefully acidified with an ice-cooled solution of 25% sulphuric acid and then extracted with ether (4 × 250 ml). The combined ethereal extracts were washed with water, 5% aqueous sodium carbonate, brine, and water, dried ($MgSO_4$), and evaporated under reduced pressure to yield the crude oxidation mixture. Yields of oxidation products are based on starting material consumed.

Oxidation of 5α-Cholestan-3-one (**1**).—(In collaboration with Dr. A. K. Göktürk.) The crude oxidation mixture, obtained as described above, was chromatographed on silica gel and eluted with hexane–ether (25%) to give first unchanged starting material (695 mg, 60%). Further elution afforded the crude oxidation mixture which was further purified by h.p.l.c. {normal phase, hexane–ethyl acetate 85:15 (v/v), 3 ml/min and reverse phase, acetonitrile–water [95:5 to 90:10 (v/v)], 4 ml/min} to give: the 6-ketone (**2**) (19.8 mg, 4.1%), m.p. 172—173 °C (from MeOH) (lit.,[13] 172 °C); $[\alpha]_D^{25}$ +4° (*c* 1.6, $CHCl_3$) (lit.,[13] $[\alpha]_D$ +4°); $\nu_{max.}$($CHCl_3$) 1 705 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.69 (3 H, s, 18-H), 0.86 (6 H, d, *J* 6 Hz, 26- and 27-H), 0.92 (3 H, d, *J* 6 Hz, 21-H), and 0.96 (3 H, s, 19-H); *m/z* 400 (M^+), 385, 244; the 7-ketone (**3**) (18.1 mg, 3.8%), m.p. 188—189 °C (from MeOH) (lit.,[13] 190 °C); $[\alpha]_D^{25}$ −17° (*c* 1.3, $CHCl_3$) (lit.,[13] $[\alpha]_D$ −19°); $\nu_{max.}$($CHCl_3$) 1 705 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.68 (3 H, s, 18-H), 0.86 (6 H, d, *J* 6 Hz, 26- and 27-H), 0.92 (3 H, d, *J* 6 Hz, 21-H), 1.28 (3 H, s, 19-H); *m/z* 400 (M^+); the 11-ketone (**4**) (5.1 mg, 1.1%), m.p. 132—135 °C (from MeOH) (lit.,[14] 135.5—137 °C); $[\alpha]_D^{25}$ +58° (*c* 0.2, $CHCl_3$); $\nu_{max.}$($CHCl_3$) 1 705 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.68 (3 H, s, 18-H), 0.86 (6 H, d, *J* 6 Hz, 26- and 27-H), 0.90 (3 H, d, *J* 6 Hz, 21-H), and 1.16 (3 H, s, 19-H); *m/z* 400 (M^+); the 12-ketone (**5**) (4.9 mg, 1.0%), m.p. 185—187 °C (from MeOH) (lit.,[15] 187—188 °C); $[\alpha]_D^{25}$ +64° (*c* 0.6, $CHCl_3$); $\nu_{max.}$ 1 705 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.85 (3 H, d, *J* 6 Hz, 21-H), 0.87 (6 H, d, *J* 6 Hz, 26- and 27-H), 1.06 (3 H, s, 18-H) and 2.64 (2 H, t, *J* 15 Hz, 11-H); *m/z* 400 (M^+); the 15-ketone (**6**) (15.8 mg, 3.3%), m.p. 152—154 °C (from acetone–MeOH); $[\alpha]_D^{25}$ +72° (*c* 1.9, $CHCl_3$); $\nu_{max.}$ 1 705 (ketone) and 1 730 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.76 (3 H, s, 18-H), 0.86 (6 H, d, *J* 6 Hz, 26- and 27-H), 1.00 (3 H, d, *J* 6 Hz, 21-H), 1.01 (3 H, s, 19-H), and 2.71 (1 H, m, 14-H); *m/z* 400 (M^+), 385, 232; the 16-ketone (**7**) (10.3 mg, 2.1%), m.p. 129—132 °C (from MeOH); $[\alpha]_D^{25}$ −146° (*c* 0.1, $CHCl_3$); $\nu_{max.}$($CHCl_3$) 1 705 (ketone) and 1 730 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.84 (3 H, s, 18-H), 0.86 (6 H, d, *J* 6 Hz, 26- and 27-H), 0.97 (3 H, d, *J* 6 Hz, 26- and 27-H), 0.97 (3 H, d, *J* 6 Hz, 21-H), and 1.05 (3 H, s, 19-H); *m/z* 400 (M^+), 385; 20-ketone (**9**) (17.3 mg, 4.6%), m.p. and mixed m.p. 200—201 °C (from MeOH) (lit.,[16] 200.5 °C); $[\alpha]_D^{25}$ +119° (*c* 1.2, $CHCl_3$) (lit.,[16] $[\alpha]_D$ +121°); $\nu_{max.}$($CHCl_3$) 1 705 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.63 (3 H, s, 18-H), 1.01 (3 H, s, 19-H), 2.12 (3 H, s, 21-H), and 2.53 (1 H, t, *J* 9 Hz, 17-H); the 24-*ketone* (**8**) (13.8 mg, 2.9%), m.p. 124—127 °C (from MeOH); $[\alpha]_D^{25}$ +38° (*c* 1.6, $CHCl_3$); $\nu_{max.}$($CHCl_3$) 1 705 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.68 (3 H, s, 18-H), 0.91 (3 H, d, *J* 7 Hz, 21-H), 1.01 (3 H, s, 19-H), 1.10 (6 H, d, *J* 7 Hz, 26- and 27-H), and 2.61 (1 H, heptet, *J* 7 Hz, 25-H); *m/z* 400 (M^+), 385 (Found: C, 81.15; H, 10.88. $C_{27}H_{44}O_2$ requires C, 80.94; H, 11.07%).

Oxidation of Cholest-4-en-3-one (**10**).—The crude oxidation mixture obtained (as described above) was chromatographed on silica gel and eluted with hexane–ether (7:3, v/v) to give first unchanged starting material (750 mg, 65%). Further elution afforded an impure mixture of ketones which were subjected to further purification by h.p.l.c. as follows: normal phase, hexane–ethyl acetate (8:2, v/v), 3 ml/min. and reverse phase, acetonitrile–water up to 95:5 (v/v), 4 ml/min. The major products thus isolated were the 12-ketone (**11**) (4.9 mg, 1.3%), m.p. 113—116 °C (lit.,[17] 117—118 °C); $[\alpha]_D^{24}$ +117° (*c* 0.4, $CHCl_3$) (lit.,[17] $[\alpha]_D^{23}$ +119°); $\lambda_{max.}$(EtOH) 240 nm (ε 15 900); $\nu_{max.}$(CH_2Cl_2) 1 620 (C=C), 1 660 (unsaturated ketone) and 1 695 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.86 (9 H, m, 21-H, 26-, and 27-H), 1.10 (3 H, s, 18-H), 1.28 (3 H, s, 19-H), 2.66 (2 H, t, *J* 13 Hz, 11-H) and 5.77 (1 H, s, 4-H); *m/z* 398 (M^+), 383, 275, and 245 (Found: *m/z*, 398.3194. $C_{27}H_{42}O_2$ (M^+) requires 398.3185); the 15-ketone (**12**) (9.5 mg, 2.2%), m.p. 109—111 °C (from acetone); $[\alpha]_D^{24}$ +66° (*c* 0.9, $CHCl_3$); $\lambda_{max.}$(EtOH) 242 nm (ε 12 300); $\nu_{max.}$(Ch_2Cl_2) 1 615 (C=C), 1 660 (unsaturated ketone), and 1 725 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$), 0.80 (3 H, s, 18-H), 0.87 (6 H, d, *J* 6 Hz, 26-H and 27-H), 0.99 (3 H, d, *J* 6 Hz, 21-H), 1.20 (3 H, s, 19-H), 2.83 (1 H, m, 14-H), and 5.73 (1 H, s, 4-H); *m/z* 398 (M^+), 383, 356 [Found: *m/z* 398.3196. $C_{27}H_{42}O_2$ (M^+) requires 398.3185]; the 16-ketone (**13**) (5.1 mg, 1.3%), m.p. 92—96 °C; $[\alpha]_D^{24}$ −51° (*c* 0.5, $CHCl_3$); $\lambda_{max.}$(EtOH) 242 nm (ε 10 700); $\nu_{max.}$(CH_2Cl_2) 1 620 (C=C), 1 660 (unsaturated ketone) and 1 725 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.87 (9 H, m, 18-, 26-, and 27-H), 0.98 (3 H, d, *J* 6 Hz, 21-H), 1.22 (3 H, s, 19-H), and 5.75 (1 H, s, 4-H); *m/z* 398 (M^+), 383, and 356 [Found: *m/z* 398.3156. $C_{27}H_{42}O_2$ (M^+) requires 398.3185]; progesterone (**15**) (26 mg, 7.6%), m.p. and mixed m.p. 128—130 °C (from methanol) (lit.,[18] 129.5—130.5 °C); $[\alpha]_D^{24}$ +193° (*c* 0.9, $CHCl_3$) (lit.,[19] $[\alpha]_D^{20}$ +196°); the 24-ketone (**14**) (14 mg, 3.4%), m.p. 116—118 °C (from hexane) (lit.,[20] 118—119 °C); $[\alpha]_D^{24}$ +81° (*c* 0.4, $CHCl_3$) (lit.,[20] $[\alpha]_D$ +83.5°); $\lambda_{max.}$(EtOH) 243 nm (ε 14 450); $\nu_{max.}$(CH_2Cl_2) 1 615 (C=C), 1 660 (unsaturated ketone), and 1 700 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.71 (3 H, s, 18-H), 0.91 (3 H, d, *J* 6 Hz, 21-H), 1.10 (6 H, d, *J* 7 Hz, 26- and 27-H), 1.18 (3 H, s, 19-H), 2.60 (1 H, heptet, *J* 7 Hz, 25-H) and 5.72 (1 H, s, 4-H); *m/z* 398 (M^+), 383, 354, and 312 [Found: *m/z*, 398.3184. $C_{24}H_{42}O_2$ (M^+) requires 398.3185].

Oxidation of Cholesta-1,4-dien-3-one (**16**).—The crude oxidation mixture obtained (as described above) was chromatographed on silica gel and eluted with hexane–ether (7:3, v/v) to give first unchanged starting material (710 mg, 62%). Further elution afforded an impure mixture of ketones which was subjected to further purification as follows: (a) by normal phase h.p.l.c., hexane–ethyl acetate (8:2, v/v), 3 ml/min, and (b) by reverse phase h.p.l.c., acetonitrile–water up to (95:5, v/v), 3 ml/min. The major products thus isolated were: the 15-ketone (**17**) (4.6 mg, 1.0%), m.p. 168—173 °C; $[\alpha]_D^{23}$ +49° (*c* 0.4, $CHCl_3$); $\lambda_{max.}$(EtOH) 242 nm (ε 13 800); $\nu_{max.}$(CH_2Cl_2) 1 620

(C=C), 1 660 (unsaturated ketone), and 1 730 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.84 (3 H, s, 18-H), 0.87 (6 H, 2 d, *J* 6 Hz, 26- and 27-H), 0.99 (3 H, d, *J* 6 Hz, 21-H), 1.24 (3 H, s, 19-H), 2.94 (1 H, m, 14-H), 6.08 (1 H, s, 4-H), 6.24 (1 H, d, *J* 11 Hz, 2-H), and 7.03 (1 H, d, *J* 11 Hz, 1-H); *m/z* 396 (M^+), 381, 311, 283, 275, and 261 [Found: *m/z*, 396.3025. $C_{27}H_{40}O_2$ (M^+) requires 396.3028]; the 20-ketone (**19**) (32 mg, 9.4%), m.p. and mixed m.p. 148—150 °C (from methanol) (lit.,[21] 152—153 °C); $[\alpha]_D^{23}$ +120° (*c* 1.0, $CHCl_3$) (lit.,[21] +120°); $\lambda_{max.}$(EtOH) 244 nm (ε 14 700); $\nu_{max.}(CH_2Cl_2)$ 1 625 (C=C), 1 660 (unsaturated ketone) and 1 700 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.70 (3 H, s, 18-H), 1.23 (3 H, s, 19-H), 2.12 (3 H, s, 21-H), 6.08 (1 H, s, 4-H), 6.24 (1 H, d, *J* 11 Hz, 2-H), and 7.06 (1 H, d, *J* 11 Hz, 1-H); *m/z* 312 (M^+), 297; the 24-ketone (**18**) (6.9 mg, 1.6%), m.p. 140—142 °C (from ethanol) (lit.,[22] 142—144 °C); $[\alpha]_D^{23}$ +21° (*c* 0.5, $CHCl_3$); $\lambda_{max.}$(EtOH) 243 nm (ε 14 100); $\nu_{max.}(CH_2Cl_2)$ 1 620 (C=C), 1 660 (unsaturated ketone) and 1 695 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.74 (3 H, s, 18-H), 0.91 (3 H, d, *J* 6 Hz, 21-H), 1.09 (6 H, d, *J* 7 Hz, 26- and 27-H), 1.23 (3 H, s, 19-H), 2.61 (1 H, heptet, *J* 7 Hz, 25-H), 6.07 (1 H, s, 4-H), 6.23 (1 H, d, *J* 11 Hz, 2-H), and 7.05 (1 H, d, *J* 11 Hz, 1-H); *m/z* 396 (M^+), 381, 310, 275, and 261 [Found: *m/z*, 396.3030. $C_{27}H_{40}O_2$ (M^+) requires 396.3028].

Oxidation of Cholestan-3β-yl Toluene-p-sulphonate (**21**).—The crude reaction mixture (obtained as described above) was chromatographed on silica gel and eluted with hexane–ether (95:5, v/v) to give first unchanged starting material (1.08 g, 66%). Further elution afforded a mixture of ketone which was subjected to further purification by h.p.l.c. [normal phase, hexane–ethyl acetate (95:5, v/v), 3 ml/min and reverse phase, acetonitrile–water (95:5, v/v), 4 ml/min]. The major products thus isolated were: the 6-ketone (**22**) (16.2 mg, 2.9%), m.p. 189—190 °C (from MeOH) (lit.,[23] 169—179 °C); $[\alpha]_D^{25}$ −7° (*c* 1.5, $CHCl_3$) (lit.,[23] $[\alpha]_D^{21}$ −5.5°); $\lambda_{max.}$(EtOH) 220 nm (ε 13 900); $\nu_{max.}(CH_2Cl_2)$ 1 600 (aromatic) and 1 705 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.64 (3 H, s, 18-H), 0.72 (3 H, s, 19-H), 0.86 (6 H, d, *J* 7 Hz, 26- and 27-H), 0.90 (3 H, d, *J* 6 Hz, 21-H), 2.44 (3 H, s, $CH_3C_6H_4$), 4.40 (1 H, m, 3α-H), 7.32 (2 H, d, *J* 8 Hz), 7.78 (2 H, d, *J* 8 Hz); *m/z* 556 (M^+), 384 and 369; the 7-*ketone* (**23**) (12.5 mg, 2.3%), m.p. 131—133 °C (from acetone–water); $[\alpha]_D^{25}$ −30° (*c* 1.2, $CHCl_3$); $\lambda_{max.}$(EtOH) 220 nm (ε 13 700); $\nu_{max.}(CH_2Cl_2)$ 1 600 (aromatic) and 1 705 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.63 (3 H, s, 18-H), 0.86 (6 H, d, *J* 7 Hz, 26- and 27-H), 0.89 (3 H, d, *J* 6 Hz, 21-H), 1.06 -3 H, s, 19-H), 2.46 (3 H, s, $CH_3C_6H_4$), 4.33 (1 H, m, 3α-H), 7.32 (2 H, d, *J* 8 Hz), and 7.78 (2 H, d, *J* 8 Hz); *m/z* 556 (M^+), 541, 384, 369, and 348 [Found: *m/z* 556.3602. $C_{34}H_{52}SO_4$ (M^+) requires 556.3586] (Found: C, 73.25; H, 9.7. $C_{34}H_{52}SO_4$ requires C, 73.04; H, 9.74%); the 15-*ketone* (**24**) (11.3 mg, 2.0%), m.p. 153—154 °C (from MeOH); $[\alpha]_D^{25}$ +24° (*c* 1.0, $CHCl_3$); $\lambda_{max.}$(EtOH) 220 nm (ε 14 000); $\nu_{max.}(CH_2Cl_2)$ 1 600 (aromatic) and 1 735 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.72 (3 H, s, 18-H), 0.78 (3 H, s, 19-H), 0.86 (6 H, d, *J* 7 Hz, 26- and 27-H), 0.97 (3 H, d, *J* 6 Hz, 21-H), 2.45 (3 H, s, $CH_3C_6H_4$), 3.10 (1 H, m, 14-H), 4.42 (1 H, m, 3α-H), 7.33 (2 H, d, *J* 8 Hz), and 7.79 (2 H, d, *J* 8 Hz); *m/z* 556 (M^+), 541, 384, and 369 (Found: C, 72.95; H, 9.5. $C_{34}H_{52}O_4S$ requires C, 73.07; H, 9.74%); the 16-*ketone* (**25**) (7.8 mg, 1.4%), m.p. 126—128 °C (from MeOH); $[\alpha]_D^{25}$ −71° (*c* 0.7, $CHCl_3$); $\lambda_{max.}$(EtOH) 220 nm (ε 13 700); $\nu_{max.}(CH_2Cl_2)$ 1 600 (aromatic) and 1 730 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.79 (3 H, s, 18-H), 0.81 (3 H, s, 19-H), 0.86 (6 H, d, *J* 7 Hz, 26- and 27-H), 0.95 (3 H, d, *J* 6 Hz, 21-H), 2.45 (3 H, s, $CH_3C_6H_4$), 4.44 (1 H, m, 3α-H), 7.33 (2 H, d, *J* 8 Hz), and 7.79 (2 H, d, *J* 8 Hz); *m/z* 556 (M^+), 541, 384, and 369 (Found: C, 73.0; H, 9.5. $C_{34}H_{52}O_4S$ requires C, 73.07; H, 9.74%); the 20-ketone (**27**) (19.5 mg, 4.2%), m.p. 131—132 °C (from MeOH) (lit.,[24] 132—133 °C); $[\alpha]_D^{24}$ +58° (*c* 1.5, $CHCl_3$ (lit.,[24] $[\alpha]_D$ +56°); $\lambda_{max.}$(EtOH) 220 nm (ε 14 100); $\nu_{max.}(CH_2Cl_2)$ 1 600 (aromatic) and 1 700 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.58 (3 H, s, 18-H), 0.78 (3 H, s, 19-H), 2.10 (3 H, s, 21-H), 2.45 (3 H, s, $CH_3C_6H_4$), 2.50 (1 H, t, *J* 9 Hz, 17-H), 4.42 (1 H, m, 3α-H), 7.33 (2 H, d, *J* 8 Hz), and 7.79 (2 H, d, *J* 8 Hz); *m/z* 472 (M^+), 300 and 285; the 24-*ketone* (**26**) (10.0 mg, 1.8%); m.p. 107—110 °C (from MeOH); $[\alpha]_D^{25}$ +8° (*c* 0.9, $CHCl_3$); $\lambda_{max.}$(EtOH) 220 nm (ε 13 850); $\nu_{max.}(CH_2Cl_2)$ 1 600 (aromatic) and 1 700 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.63 (3 H, s, 18-H), 0.77 (3 H, s, 19-H), 0.89 (3 H, d, *J* 6 Hz, 21-H), 1.10 (6 H, d, *J* 7 Hz, 26- and 27-H), 2.45 (3 H, s, $CH_3C_6H_4$), 2.61 (heptet, *J* 7 Hz, 25-H), 4.41 (1 H, m, 3α-H), 7.32 (2 H, d, *J* 8 Hz), 7.78 (2 H, d, *J* 8 Hz); *m/z* 556 (M^+), 384 and 369 (Found: C, 72.95; H, 9.5. $C_{34}H_{52}O_4S$ requires C, 73.07; H, 9.74%).

Oxidation of Cholesteryl Acetate (**28**).—The crude oxidation mixture (obtained as described above) was chromatographed on silica gel and eluted with hexane–ether (9:1, v/v) to give first the unchanged starting material (846 mg, 68%). Further elution afforded an impure mixture of ketones which was subjected to further purification by normal phase h.p.l.c., hexane–5% ethyl acetate, 3 ml/min, and reverse phase h.p.l.c., acetonitrile–water up to 9:1 (v/v), 4 ml/min. The major products thus isolated were: 7-ketone (**29**) (24 mg, 5.9%), m.p. 156—158 °C (from acetone) (lit.,[25] 156—158 °C); $[\alpha]_D^{24}$ −96° (*c* 1.0, $CHCl_3$) (lit.,[26]; $[\alpha]_D^{25}$ −97°), $\lambda_{max.}$(EtOH) 240 nm (ε 12 000); $\nu_{max.}(CH_2Cl_2)$ 1 630 (C=C), 1 670 (unsaturated ketone) and 1 725 cm^{-1} (acetate); δ (400 MHz, $CDCl_3$) 0.68 (3 H, s, 18-H), 0.86 (6 H, d, *J* 6 Hz, 26- and 27-H), 0.9 (3 H, d, *J* 6 Hz, 21-H), 1.21 (3 H, s, 19-H), 2.05 (3 H, s, CH_3CO_2). 4.61 (1 H, m, 3-H), and 5.38 (1 H, m, 6-H); *m/z* 442 (M^+), 382 (100%), 367, 297, 269, and 174 [Found: *m/z* 382.3237. $C_{27}H_{42}O$ (M^+ − HOAc) requires 382.3235]; the 15-*ketone* (**30**) (11.1 mg, 2.8%), m.p. 163.5—164.5 °C (from hexane); $[\alpha]_D^{24}$ −19° (*c* 1.0, $CHCl_3$); $\nu_{max.}(CH_2Cl_2)$ 1 730 cm^{-1} (br, acetate and ketone); δ (400 MHz, $CDCl_3$) 0.77 (3 H, s, 18-H), 0.87 (6 H, 2d, *J* 6 Hz, 26- and 27-H), 1.00 (3 H, d, *J* 6 Hz, 21-H), 1.02 (3 H, s, 19-H), 2.04 (3 H, s, CH_3CO_2), 2.85 (1 H, m, 14-H), 4.61 (1 H, m, 3-H), and 5.38 (1 H, m, 6-H); *m/z* 442 (M^+), 382 (100%), 367 [Found: *m/z* 382.3251. $C_{27}H_{42}O$ (M^+ − HOAc) requires 382.3235] (Found: C, 78.6; H, 10.55. $C_{29}H_{46}O_3$ requires C, 78.68; H, 10.47%); the 16-ketone (**31**) (3.6 mg, 0.9%) m.p. 130—135 °C (lit.,[27]); $[\alpha]_D^{24}$ −74° (*c* 0.2, $CHCl_3$); $\nu_{max.}(CH_2Cl_2)$ 1 730 cm^{-1} (br, acetate, and ketone); δ (400 MHz, $CDCl_3$) 0.84 (3 H, s, 18-H), 0.87 (6 H, 2d, *J* 6 Hz, 26- and 27-H), 0.98 (3 H, d, *J* 6 Hz, 21-H), 1.06 (3 H, s, 19-H), 2.05 (3 H, s, CH_3CO_2), 4.61 (1 H, m, 3-H), and 5.38 (1 H, m, 6-H); *m/z* 442 (M^+), 382 (100%), 367.297 [Found: *m/z* 382.3253. $C_{27}H_{42}O$ (M^+ − HOAc) requires 382.3235]; the 20-ketone (**33**) (17.2 mg, 5.1%), m.p. and mixed m.p. 147—148 °C (from acetone) (lit.,[28] 146—147 °C); $[\alpha]_D^{24}$ +21° (*c* 1.0, EtOH) (lit.,[28] $[\alpha]_D$ +19.9°); $\nu_{max.}(CH_2Cl_2)$ 1 695 (ketone) and 1 725 cm^{-1} (acetate); δ (400 MHz, $CDCl_3$) 0.63 (3 H, s, 18-H), 1.02 (3 H, 19-H), 2.04 (3 H, s, CH_3CO_2), 2.13 (3 H, s, 21-H), 2.55 (1 H, t, *J* 9 Hz, 17-H), 4.61 (1 H, m, 3-H), and 5.38 (1 H, m, 6-H); *m/z* 358 (M^+), 298 (100%) [Found: *m/z* 298.2303. $C_{21}H_{30}O$ (M^+ − HOAc) requires 298.2297]; the 24-ketone (**32**) (7.7 mg, 2.0%), m.p. 122—125 °C (lit.,[29,30] 127—128 °C); $[\alpha]_D^{24}$ −40° (*c* 0.3, $CHCl_3$) (lit.,[29] $[\alpha]_D^{15}$ −43°, lit.,[31] ($[\alpha]_D^{26}$ −41°), $\nu_{max.}(CH_2Cl_2)$ 1 705 (ketone) and 1 725 cm^{-1} (acetate); δ (400 MHz, $CDCl_3$) 0.68 (3 H, s, 18-H), 0.92 (3 H, d, *J* 6 Hz, 21-H), 1.02 (3 H, s, 19-H), 1.10 (6 H, d, *J* 7 Hz, 26- and 27-H), 2.04 (3 H, s, CH_3CO_2), 2.62 (1 H, heptet, *J* 7 Hz, 25-H), 4.61 (1 H, m, 3-H), and 5.38 (1 H, m, 6-H); *m/z* 442 (M^+) and 382 (100%) [Found: *m/z*, 382.3228. $C_{27}H_{42}O$ M^+ − HOAc) requires 382.3235].

Oxidation of Olean-12-en-3-one (**34**).—The crude oxidation mixture (obtained as described above) was purified by chromatography on silica gel and eluted with hexane–ether

(8:2, v/v) to give first unchanged starting material (590 mg, 69%). Further elution gave the crude u.v. active product which was further purified by h.p.l.c. [normal phase: hexane–ethyl acetate (75:25, v/v), 3 ml/min] to give the 11-ketone (**35**) (35.7 mg, 13.8%), m.p. 236—237 °C (from MeOH) (lit.,[31] 237 °C); $[\alpha]_D^{25}$ +140° (*c* 0.5, $CHCl_3$) (lit.,[31] $[\alpha]_D^{20}$ +143°); $\nu_{max.}(CH_2Cl_2)$ 1 620 (olefin), 1 655 (unsaturated ketone) and 1 700 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.88 (3 H, s, 28-H), 0.90 (6 H, 2s, 29- and 30-H), 1.07 (3 H, s, 24-H), 1.11 (3 H, s, 23-H), 1.18 (3 H, s, 25-H), 1.27 (3 H, s, 26-H), 1.37 (3 H, s, 27-H), and 5.64 (1 H, s, 12-H); *m/z* 438 (M^+).

3β-*Acetoxyolean*-12-*en*-11-*one* (**40**).—3β-Acetoxyolean-12-ene (**39**) (3.00 g, 6.41 mmol) and chromium trioxide (2.00 g, 19.6 mmol) were heated to reflux in acetic acid (120 ml) for 15 min. The cooled solution was poured into water (200 ml) and filtered. The crude product was purified by flash chromatography [hexane–ether, 8:2 (v/v)] to afford the 11-ketone (**40**) (2.04 g, 66%), m.p. 288—290 °C (from MeOH) (lit.,[11] 291—292 °C); $[\alpha]_D^{25}$ +69° (*c* 0.3, $CHCl_3$); $\nu_{max.}(CH_2Cl_2)$ 1 650 (unsaturated ketone) and 1 720 cm^{-1} (acetate); *m/z* (C.I.) 483 (MH^+) and 423 (MH^+ − HOAc).

Olean-12-*ene*-3,11-*dione*.—To a stirred solution of the acetate (**40**) (1.70 g, 3.51 mmol) in ethanol (50 ml) was added a 40% aqueous sodium hydroxide (5 ml). The solution was stirred at room temperature for 4 h, until all starting material had been consumed, as judged by t.l.c. The reaction mixture was poured into iced dilute HCl (200 ml), the solid collected by filtration, washed with water, and dissolved in acetone. Jone's reagent was slowly added to the stirred cooled (0 °C) solution until all alcohol had been consumed (*ca.* 2 h). The product was extracted into dichloromethane (3 × 100 ml) and the combined organic extracts were washed with 5% aqueous $NaHCO_3$ and water, dried ($MgSO_4$), and evaporated under reduced pressure to afford virtually pure diketone, which was subjected to flash chromatography [hexane–ether, 75:25 (v/v)] to give the title compound (1.28 g, 83%), m.p. 236—237 °C (from MeOH) (lit.,[11] 237 °C); $[\alpha]_D^{25}$ +140° (*c* 0.8, $CHCl_3$) (lit.,[11] $[\alpha]_D^{20}$ + 143°); $\nu_{max.}(CH_2Cl_2)$ 1 620 (double bond), 1 655 (unsaturated ketone), and 1 700 cm^{-1} (ketone); *m/z* 438 (M^+).

Oleana-1,12-*diene*-3,11-*dione* (**36**).—To a stirred solution of the ketone (**35**) (1.25 g, 2.85 mmol) in chlorobenzene (10 ml) was added benzeneseleninic acid (590 mg, 3.14 mmol). The resulting solution was heated to 95 °C until all starting material had been consumed as judged by t.l.c. (*ca.* 30 min). The reaction mixture was concentrated under reduced pressure and purified by flash chromatography [hexane–ether 75:25 (v/v)] to give the *diene-dione* (**36**) (884 mg, 71%), m.p. 196—198 °C; $[\alpha]_D^{24}$ +189° (*c* 0.35, $CHCl_3$); $\lambda_{max.}$(EtOH) 245 nm (ε 13 800); $\nu_{max.}(CH_2Cl_2)$ 1 615 (olefin) and 1 655 cm^{-1} (unsaturated ketone); δ (400 MHz, $CDCl_3$) 0.90 (3 H, s, 28-H), 0.91 (3 H, s, 29-H), 0.92 (3 H, s, 30-H), 1.12 (3 H, s, 23-H), 1.17 (3 H, s, 24-H), 1.20 (3 H, s, 25-H), 1.39 (3 H, s, 26-H), 1.42 (3 H, s, 27-H), 2.67 (1 H, s, 9-H), 5.69 (1 H, s, 12-H), 5.81 (1 H, d, *J* 10 Hz, 2-H), 7.75 (1 H, d, *J* 10 Hz, 1-H); *m/z* 436 (M^+ (Found: C, 82.45; H, 10.0. $C_{30}H_{44}O_2$ requires C, 82.52; H, 10.16%).

Gif Oxidation of Oleana-1,12-*diene*-3,11-*dione* (**36**).—The crude oxidation mixture was chromatographed on silica gel and eluted with hexane–ether (8:2, v/v) to give first unchanged starting material (880 mg, 67%) and then the product mixture, which was further purified by h.p.l.c. [normal phase, hexane–30% ethyl acetate, 3 ml/min and reverse phase, acetonitrile–water 9:1 (v/v), 3 ml/min]. The major products thus isolated were the 16-ketone (**37**) (16.6 mg, 3.8%), m.p. 238—241 °C (from MeOH); $[\alpha]_D^{24}$ +107° (*c* 0.5, $CHCl_3$); $\lambda_{max.}$(EtOH) 245 nm (ε 14 500); $\nu_{max.}(CH_2Cl_2)$ 1 620 (olefin), 1 665 (unsaturated ketone) and 1 705 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 0.91 (6 H, 2 s, 29- and 30-H), 1.12 (3 H, s, 23-H), 1.17 (3 H, s, 24-H), 1.20 (3 H, s, 25-H), 1.29 (3 H. s, 28-H), 1.43 (3 H, s, 27-H), 1.47 (3 H, s, 26-H), 2.15 (1 H, m, 18-H), 2.66 (1 H, s, 9-H), 2.72 (1 H, dd, *J* 14 and 4 Hz, 15β-H), 2.83 (1 H, d, *J* 16 Hz, 15α-H), 5.84 (1 H, d, *J* 10 Hz, 2-H), 5.90 (1 H, s, 12-H), and 7.72 (1 H, d, *J* 10 Hz, 1-H); *m/z* 450 (M^+) and 435 (Found: *m/z* 450.3140. $C_{30}H_{42}O_3$ requires 450.3134) and then the 21-ketone (**38**) (10.6 mg, 2.4%), m.p. 245—249 °C (from MeOH); $[\alpha]_D^{24}$ +77° (*c* 0.3, $CHCl_3$); $\lambda_{max.}$(EtOH) 245 nm (ε 14 900); $\nu_{max.}(CH_2Cl_2)$ 1 620 (olefin), 1 665 (unsaturated ketone), and 1 705 cm^{-1} (ketone); δ (400 MHz, $CDCl_3$) 1.02 (3 H, s, 28-H), 1.05 (3 H, s, 30-H), 1.12 (3 H, s, 23-H), 1.17 (3 H, s, 24-H), 1.20 (3 H, s, 25-H), 1.24 (3 H, s, 29-H), 1.37 (3 H, s, 26-H), 1.43 (3 H, s, 27-H), 2.56 (2 H, m, 22-H), 2.69 (1 H, s, 9-H), 5.80 (1 H, s, 12-H), 5.82 (1 H, d, *J* 10 Hz, 2-H), and 7.72 (1 H, d, *J* 10 Hz, 1-H); *m/z* 450 (M^+ and 435 (Found: *m/z* 450.3120. $C_{30}H_{42}O_3$ requires 450.3134).

Oxidation of 7-*Oxocholesterol Acetate* (**29**).—The crude oxidation mixture was chromatographed on silica gel and eluted with hexane–ether (7:3, v/v) to give first the unchanged starting material (861 mg, 65%) and then a mixture of ketones which was further purified by h.p.l.c. [normal phase, hexane–ethyl acetate 7:3 (v/v), 3 ml/min and reverse phase, acetonitrile–water up to 95:5 (v/v), 4 ml/min] to give the 20-ketone (**43**) (19 mg, 4.8%), m.p. 152—153 °C (from MeOH) (lit.,[32] 153—153.5 °C); $[\alpha]_D^{23}$ −65° (*c* 0.8, $CHCl_3$) (lit.,[32] $[\alpha]_D$ −68°); $\lambda_{max.}$ 232 nm (ε 14 500); $\nu_{max.}(CHCl_3)$ 1 650 (olefin), 1 670 (unsaturated ketone), 1 700 (ketone), and 1 730 cm^{-1} (acetate); δ (400 MHz, $CDCl_3$) 0.66 (3 H, s, 18-H), 1.22 (3 H, s, 19-(H), 2.06 (3 H, s, CH_3CO_2), 2.14 (3 H, s, 21-H), 4.73 (1 H, m, 3α-H), and 5.72 (1 H, s, 6-H); *m/z* 312 (M^+ − HOAc); the 24-ketone (**42**) (8.2 mg, 1.7%), m.p. 160—164 °C (from MeOH); $[\alpha]_D^{24}$ −93° (*c* 0.4, $CHCl_3$); $\lambda_{max.}$(EtOH) 232 nm (ε 14 000); $\nu_{max.}(CH_2Cl_2)$ 1 630 (olefin), 1 670 (unsaturated ketone), 1 700 (ketone), and 1 730 cm^{-1} (acetate); δ (400 MHz, $CDCl_3$) 0.68 (3 H, s, 18-H), 0.92 (3 H, d, *J* 7 Hz, 21-H), 1.10 (6 H, d, *J* 7 Hz, 26- and 27-H), 1.21 (3 H, s, 19-H), 2.05 (3 H, s, CH_3CO_2), 2.61 (1 H, heptet, *J* 7 Hz, 25-H), 4.72 (1 H, m, 3α-H), and 5.72 (1 H, s, 6-H); *m/z* 396 (M^+ − HOAc).

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References

1 Part 5, D. H. R. Barton, J. Boivin, W. B. Motherwell, N. Ozbalik, K. M. Schwartzentruber, and K. Jankowski, *Nouv. J. Chim.*, in press.
2 (*a*) D. H. R. Barton, A. K. Göktürk, J. W. Morzycki, and W. B. Motherwell, *J. Chem. Soc., Perkin Trans. 1*, 1985, 583 and references there cited; (*b*) D. H. R. Barton, A. K. Göktürk, and K. Jankowski, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2109.
3 R. E. Zürcher, *Helv. Chim. Acta*, 1963, 2054.
4 J. E. Bridgeman, P. C. Cherny, A. S. Clegg, J. M. Evans, E. R. H. Jones, A. Kasal, V. Kumar, G. D. Meakins, Y. Morisawa, E. E. Richards, and P. D. Woodgate, *J. Chem. Soc. C*, 1970, 250.
5 D. H. R. Barton and E. R. H. Jones, *J. Chem. Soc.*, 1944, 659; D. H. R. Barton, *ibid.*, 1945, 813.
6 C. Beard, J. M. Wilson, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, 1964, **86**, 269.
7 D. H. R. Barton, C. R. A. Godfrey, J. W. Morzycki, W. B. Motherwell, and S. V. Ley, *J. Chem. Soc., Perkin Trans. 1*, 1982, 1947.
8 D. H. R. Barton, F. McCapra, P. J. May, and F. Thudium, *J. Chem. Soc.*, 1960, 1297, and references there cited.

9 D. H. R. Barton, J. Boivin, M. J. Gastiger, J. Morzycki, R. S. Hay-Motherwell, W. B. Motherwell, N. Ozbalik, and K. M. Schwartzentruber, *J. Chem. Soc., Perkin Trans. 1*, 1986, 947.
10 T. Westphalen, *Chem. Ber.*, 1915, **48**, 1064.
11 F. S. Spring, *J. Chem. Soc.*, 1933, 1345.
12 D. H. R. Barton, M. J. Gastiger, and W. B. Motherwell, *J. Chem. Soc., Chem. Commun.*, 1983, 731.
13 D. H. R. Barton and J. D. Cox, *J. Chem. Soc.*, 1948, 783.
14 D. G. Patterson and C. Djerassi, *J. Org. Chem.*, 1979, **44**, 1866.
15 R. Beslow, S. Baldwin, T. Flechtner, P. Kalicky, S. Lin, and W. Washburn, *J. Am. Chem. Soc.*, 1973, **95**, 3251.
16 A. Butenandt and L. Mamoli, *Chem. Ber.*, 1935, **68**, 1847.
17 D. N. Kirk and V. Petrow, *J. Chem. Soc.*, 1959, 1691.
18 R. V. Oppenauer, *Rec. Trav. Chim.*, 1937, **56**, 137.
19 H. Bretschneider, *Chem. Ber.*, 1941, **74**, 1360.
20 A. Ercoli and P. de Ruggieri, *J. Am. Chem. Soc.*, 1953, **75**, 3284.
21 F. Sondheimer, M. Velasco, and G. Rosenkranz, *J. Am. Chem. Soc.*, 1955, **77**, 5673.
22 K. Ochi, I. Matzunaga, M. Shindo, and K. Kaneko, *Chem. Pharm. Bull.*, 1978, **26**, 2386.
23 R. M. Dodson and B. Riegel, *J. Org. Chem.*, 1948, **13**, 424.
24 J. Schmidt, J. J. Panouse, P. Cornoy, A. Hallot, P-J. Cornu, and H. Pluchet, *Bull. Soc. Chim. Fr.*, 1962, 455.
25 Z. Cohen and Y. Mazur, *J. Org. Chem.*, 1979, **44**, 2318.
26 S. Bergström and O. Wintersteiner, *J. Biol. Chem.*, 1941, **141**, 597.
27 See: J. Passons, S. J. Wony, and W. T. Beher, *Henry Ford. Hosp. Med. Bull.*, 1965, **13**, 303—316.
28 A. Butenandt and G. Fleischer, *Chem. Ber.*, 1937, **70**, 96.
29 D. H. Hey, J. Honeyman, and W. J. Peal, *J. Chem. Soc.*, 1950, 2881.
30 B. Riegel and I. A. Kaye, *J. Am. Chem. Soc.*, 1944, **66**, 723.
31 F. S. Spring and T. Vickerstaff, *J. Chem. Soc.*, 1934, 650.
32 C. W. Marshall, R. E. Ray, I. Laos, and B. Riegel, *J. Am. Chem. Soc.*, 1957, **79**, 6308.

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