Tetrahedron Vol 39, No 4, pp 649 to 655, 1983
Printed in Great Britain

0040-4020/83/040649-07$03.00/0
Pergamon Press Ltd.

OXIDATIVE TRANSFORMATIONS OF TRITERPENOIDS OF THE URSANE AND OLEANANE SKELETA WITH HYDROGEN PEROXIDE. INTRODUCTION OF 11,12-DOUBLE BOND AND 13(28)OXIDE MOIETY IN THE URSANE SYSTEM†

P. L. MAJUMDER* and A. BAGCHI
Department of Chemistry, University College of Science, Calcutta-700009, India

(*Received in the UK 8 October 1981*)

Abstract—Treatment of oleanolic acid acetate (**1b**) with H_2O_2 in boiling HOAc gave the epoxy-γ-lactone **2b** and the 12-hydroxy-γ-lactone **3b**. The total absence of the 12-ketodihydro acid **4b** among the oxidation products of **1b** has been rationalised. The results of this reaction with several isomeric pairs of triterpenoids of the ursane and oleanane skeleta bearing functional groups at C-17 other than a carboxyl group show that for any appreciable oxidation involving the intermediacy of a 12β,13β-epoxide **6a** or **6b**, the 17-carboxyl group is an essential requirement. An intramolecular epoxidation of 12,13-double bond of **1a** and **1b** by 17-percarboxy acid formed *in situ* has been envisaged. The reactions aiming at introducing 11,12-double bond and 13(28)-oxide moiety in the ursane system are described. The desired compound **2c** was obtained by treatment of the triol **1p** with TsOH. With H_2O_2/TsOH, **1p**, however, gave besides **2c**, the rearranged product **8a**. The difference in the chemical behaviour of **1p** and **1q** has been explained.Treatment of **2e** with H_2O_2 in boiling HOAc gave the epoxide **2f**. The mechanism of formation of **2a** and **2b** is discussed in the light of this observation.

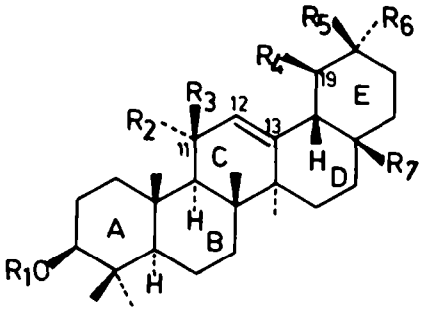
In continuation of our earlier work[1] on the reinvestigation of the action of H_2O_2 on ursolic acid acetate (**1a**), we report in this communication the results of further investigations of this reaction on several isomeric pairs of ursane and oleanane derivatives. The paper also deals with reactions leading to the generation of a 11,12-double bond and a 13(28)-oxide moiety in the ursane skeleton.

The characterisation[1] of the products **2a**, **3a** and **4a** obtained[1,2] from **1a** by the action of H_2O_2 in boiling HOAc prompted us to apply this reaction to oleanolic acid acetate (**1b**), particularly in view of the report of **3b** by Barton *et al.*[3] as the sole oxidation product of **1b** in a similar reaction. Using the condition of Jeger *et al.*,[2] we could not only reisolate **3b**, but also obtain a second compound (O–I), $C_{32}H_{48}O_5$ (M^+ 512), m.p. 295°, $[\alpha]_D$ +42° ($CHCl_3$), which from its spectral data [δ_{ppm} 3.0, 2H, s (–CH$\overset{O}{\diagdown\!\diagup}$CH–); ν_{max} 1765 cm^{-1} (γ-lactone)] and by chemical correlation with **3b** was shown to have the structure **2b**, a compound obtained earlier by Kitagawa *et al.*[4a,b] in course of photochemical irradiation of oleanolic acid. Treatment of O–I with 6N ethanolic H_2SO_4 afforded the hydroxy keto-derivative **3c** which on acetylation gave **3d**, identical in all respects with the product of chromic acid oxidation of **3b**.

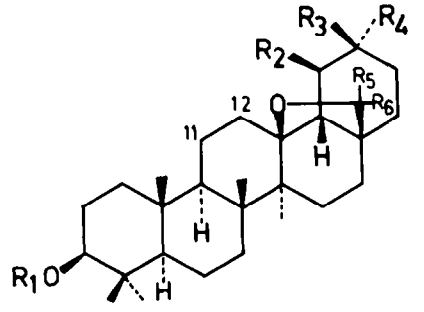
It is interesting to note that while oxidation of **1a** afforded, besides **2a** and **3a**, the keto-dihydro derivative **4a**, the corresponding oleanane analogue **4b** is totally absent in identical oxidation of **1b**, although **1a** and **1b** differ only in the alkyl substitution pattern in their E ring. This may be attributed to the additional steric effect of the 19-methyl group in **1a**, as evident from the conformational expressions **5a** and **5b** (Scheme 1) for **1a** and **1b**, respectively. Based on the mechanism we have proposed[1] earlier, the formation of a keto-dihydro derivative **4a** or **4b** requires the intermediacy of a 12β,13β-epoxide **6a** or **6b**, which would rearrange presumably through hydride shift (Scheme 1, path "a"); the formation of **3a** and **3b** may involve the alternative paths "b" and "c". In the ursane series (as in **1a**) both these processes would be expected to involve a high activation energy due to steric interference of the 19-methyl group either to the nucleophile (H_2O; path "b") or to the peracid (path "c") approaching from the α-side. This makes the reaction leading to **4a** a significantly competitive process. In the absence of such additional steric effect of the 19-methyl group in the oleanane system (as in **1b**), the reaction leading to **3b** as well as **2b** becomes considerably less energetic and so proceeds well before the path "a" becoming a competing process to give **4b**. The steric effect of the 19-methyl group in modifying the chemical properties of the ursane derivatives as indicated above finds strong analogy in our earlier[1] observation of the remarkable stability of the epoxide **2a** towards acids, and the ease with which **3e** forms the enolacetate with Ac_2O/Py compared to the normal behaviour of the oleanane analogues **2b** and **3d**. The formation of **2a** and **2b** has been assumed to take place by the alternative routes "d" or "e", of which the latter process is discouraged in view of the low availability of the triplet oxygen under the reaction condition, and the path "d" is more favoured in the light of our present investigation (vide infra).

Based on the assumption that a 17-hydroxymethyl group in the ursane and oleanane systems might undergo nucleophilic participation like a 17-carboxyl function in these systems, both uvaol (**1c**) and erythrodiol (**1d**) were subjected to this reaction which afforded three products

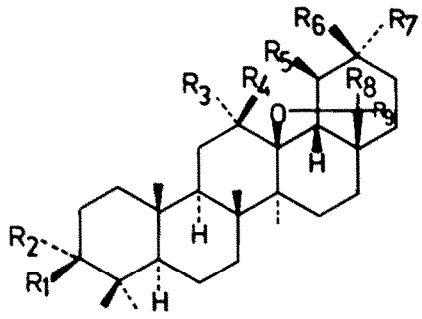
†Preliminary accounts of this work were presented at the Annual Convention of Chemists, 1978, Waltair, India, *Abstracts*, Org. 111, p. 47; Annual Convention of Chemists, 1979, Kurukshetra, India, *Abstracts*, Org. 133, p. 51, Annual Convention of Chemists, 1980, IIT, Powai, India, *Abstracts*, Org. 11, p. 5.



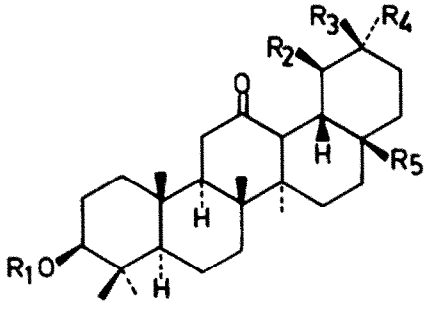
1a : R_1=Ac, R_2=R_3=R_5 =H, R_4=R_6 = Me, R_7 =CO_2H
1b : R_1=Ac, R_2=R_3=R_4 =H, R_5=R_6 =Me, R_7 =CO_2H
1c : R_1=R_2=R_3=R_5 =H, R_4=R_6=Me, R_7=CH_2OH
1d : R_1=R_2=R_3=R_4 =H, R_5=R_6=Me, R_7=CH_2OH
1e : R_1=R_2=R_3=R_5 =H, R_4=R_6 =Me, R_7=CH_2OAc
1f : R_1=Ac, R_2=R_3 =R_5 =H, R_4 =R_6= Me, R_7=CH_2OH
1g : R_1=Ac, R_2=R_3 =R_5 = H, R_4 = R_6 =Me, R_7=CH_2OAc
1h : R_1=Ac, R_2=R_3 =R_4 =H, R_5 =R_6 =Me, R_7=CH_2OH
1i : R_1=R_2 =R_3 =R_4=H, R_5 =R_6 =Me, R_7 =CH_2OAc
1j : R_1=Ac, R_2 =R_3 = R_4 = H, R_5 = R_6 = Me, R_7=CH_2OAc
1k : R_1=Ac, R_2 =R_3 =R_5 = H, R_4=R_6 = R_7=Me
1l : R_1=Ac, R_2 =R_3 =R_5 = H, R_4 =R_6 = Me, R_7=CO_2Me
1m: R_1=Ac, R_2 = R_3 = R_4 = H, R_5 = R_6 = Me, R_7 =CO_2Me
1n : R_1=Ac, R_2 = R_3 =R_5 =H, R_4 =R_6 =Me, R_7 =COCl
1o : R_1=Ac, R_2 = R_3 = O, R_4 = R_6 = Me, R_5 = H, R_7 = CO_2Me
1p : R_1 = R_3 = R_5 = H, R_2 = OH, R_4 = R_6 = Me, R_7 = CH_2OH
1q : R_1 = R_3 = R_4 = H, R_2 = OH, R_5 = R_6 = Me, R_7 = CH_2OH



2a : R_1=Ac, R_2=R_4=Me, R_3=H, R_5,R_6=O, 11α,12α-epoxy
2b : R_1=Ac, R_2=H, R_3=R_4=Me, R_5,R_6=O, 11α,12α-epoxy
2c : R_1=R_3=R_5=R_6=H, R_2=R_4=Me, $\Delta^{11,12}$
2d : R_1=R_2=R_5=R_6=H, R_3=R_4=Me, $\Delta^{11,12}$
2e : R_1=Ac, R_2=R_4=Me, R_3=R_5=R_6=H, $\Delta^{11,12}$
2f : R_1=Ac, R_2=R_4=Me, R_3=R_5=R_6=H, 11α,12α-epoxy



3a: R_1=OAc, R_2=R_4=R_6=H, R_3=OH, R_5=R_7=Me, R_8,R_9=O
3b: R_1=OAc, R_2=R_4=R_5=H, R_3=OH, R_6=R_7=Me, R_8,R_9=O
3c: R_1=OH, R_2=R_5=H, R_3,R_4=O, R_6=R_7=Me, R_8,R_9=O
3d: R_1=OAc, R_2=R_5=H, R_3,R_4=O, R_6=R_7=Me, R_8,R_9=O
3e: R_1=OAc, R_2=R_6=H, R_3,R_4=O, R_5=R_7=Me, R_8,R_9=O
3f: R_1=OH, R_2=R_4=R_6=R_8=R_9=H, R_3=Br, R_5=R_7=Me
3g: R_1,R_2=O, R_3=Br, R_4=R_6=R_8=R_9=H, R_5=R_7=Me



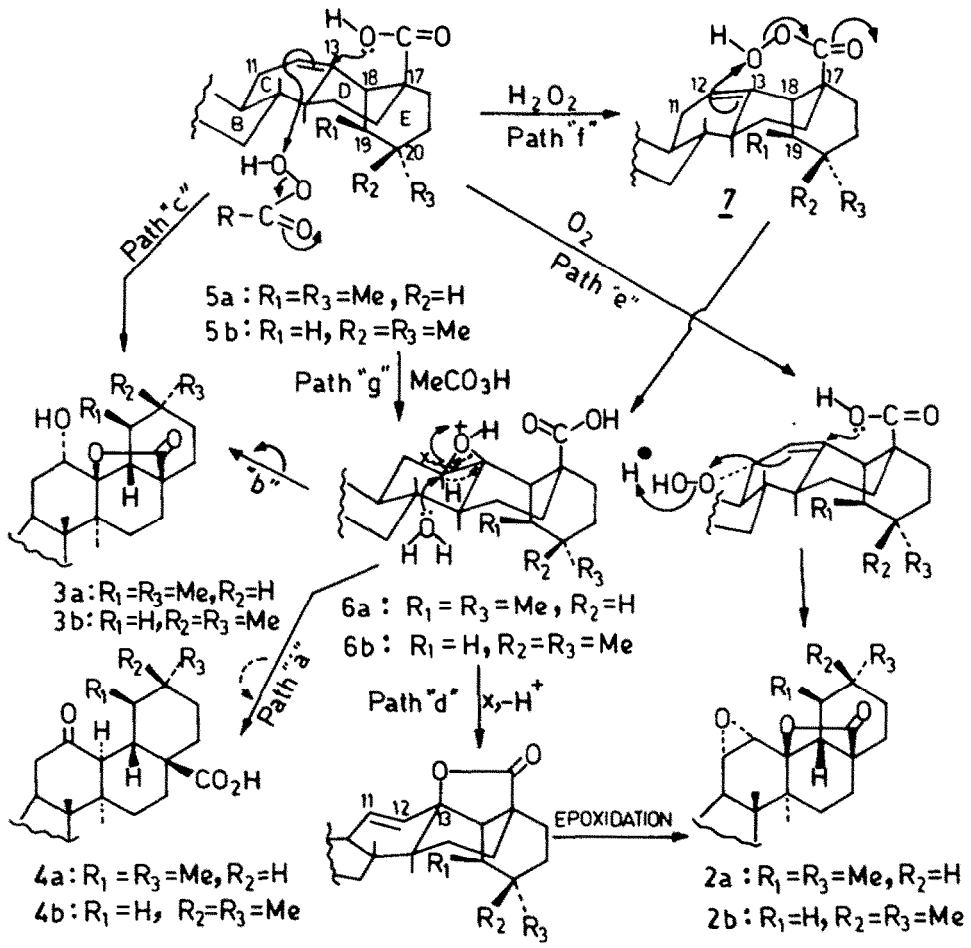
4a: R_1=Ac, R_3=H, R_2=R_4=Me, R_5=CO_2H
4b: R_1=Ac, R_2=H, R_3=R_4=Me, R_5=CO_2H
4c: R_1=Ac, R_2=R_4=Me, R_3=H, R_5=CO_2Me
4d: R_1=Ac, R_2=H, R_3=R_4=Me, R_5=CO_2Me

in each case. With **1c**, the three compounds, $C_{32}H_{52}O_3$ (M^+ 484), m.p. 159°; $C_{32}H_{52}O_3$ (M^+ 484), m.p. 242° and $C_{34}H_{54}O_4$ (M^+ 526), m.p. 151°, were shown to be 28-O-acetyl uvaol (**1e**), 3-O-acetyl uvaol (**1f**) and 3,28-O,O-diacetyl uvaol (**1g**), respectively, from their various spectral data and by chemical correlation with **1c**. Similarly, with **1d**, the three products were found to be the corresponding isomeric 28-O-acetyl erythrodiol (**1i**), 3-O-acetyl erythrodiol (**1h**) and 3,28-O,O-diacetyl erythrodiol (**1j**). The above reaction with **1g** and **1j** resulted only in partial deacetylation to give **1e** (~33%) and **1f** (~10%) and **1i** (~40%) and **1h** (~10%) respectively. Surprisingly enough, in any of these reactions not a trace of any oxidation product could be detected. In fact, **1e**, **1f** and **1g** were obtained from **1c** and **1h**, **1i** and **1j** from **1d** by simply heating **1c** and **1d** with 80% HOAc. The total absence of any oxidation product in the reactions of **1c** and **1d** with H_2O_2/HOAc established the significant role played by the C-17 carboxyl group in initiating oxidative transformations of **1a** and **1b**. This was further supported by the results of similar oxidation of the following triterpenoids of the α- and β-amyrin skeleta bearing at C-17 functional groups other than a carboxyl group. Thus when α-amyrin acetate (**1k**) and acetyl methyl ursolate (**1l**) were subjected to the above reaction, the former was only partially hydrolysed to form a trace of its deacetyl derivative (~10%), while the latter was oxidised only in trace to the corresponding 12-ketodihydro derivative **4c** (~4%), m.p. 272° [ν_{max} 1235 and 1735 (OAc and CO_2Me), 1700 (>CO) cm^{-1}]. Similar oxidation of acetyl methyl oleanolate (**1m**) gave also a very small amount of the 12-ketodihydro derivative **4d** (~6%), m.p. 177° [ν_{max} 1240 and 1725 (OAc and CO_2Me), 1700 (>CO) cm^{-1}], although in a slightly better yield than its ursane analogue **4c**.

The above observations indicate that for any appreciable oxidation with H_2O_2 to be initiated by the 12,13-double bond in ursane and oleanane skeleta, the presence of a 17-carboxyl group is an essential requirement. It further advocates the possibility that the 17-carboxyl group in **1a** or **1b** is first converted *in situ* to a percarboxylic acid function which is sterically well-poised to epoxidise the 12,13-double bond intramolecularly (Scheme 1, path "f"). Due to excessive steric crowding the alternative intermolecular epoxidation (path "g") of the 12,13-double bond by peracetic acid formed *in situ* is less facile, though not excluded completely.

Attempt to prepare the percarboxy acid **7** corresponding to **1a** by the action of alkaline H_2O_2 on the acid chloride **1n**, however, failed due to remarkable stability of **1n** towards S_N2 reactions on steric ground. **1n** [m.p. 295°, ν_{max} 1800 cm^{-1} (COCl)] is one of the most stable acid chlorides, hitherto known, which remains unchanged under ordinary hydrolytic conditions and can be crystallised and chromatographed.

The participation of the percarboxy acid **7** in the oxidation of **1a** or **1b** was, however, indicated by the results of oxidation of the former (**1a**) and its methyl ester (**1l**) in H_2O_2 in absence of HOAc, thereby excluding the possibility of the formation of peractic acid. Thus treatment of **1a** with H_2O_2 in boiling benzene gave the



Scheme 1.

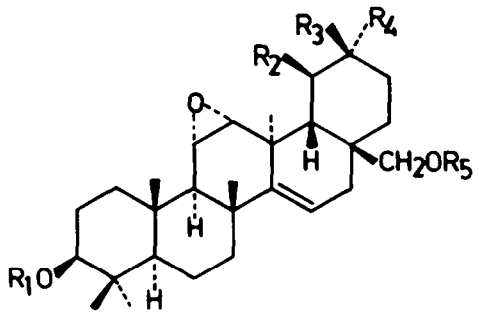
12-ketodihydro acid **4a** (characterised as its methyl ester), albeit in poor yield. The thin-layer chromatogram of the total reaction product, however, indicated the formation, in traces, of two more compounds which were different from **2a** and **3a**. Under identical reaction condition, **1l**, on the other hand, remained unchanged. This therefore demands the generation of **7** for the formation of the 12β,13β-epoxide **6a** acting as the obligatory intermediate for **4a**.

The report by Kitagawa *et al.*[4b] of the formation of **2d** which was considered to be a precursor of a number of physiologically active saikogenins, prompted us to prepare its ursane counterpart **2c**, as it would also serve to establish the validity of the mechanistic path "d" for the formation of **2a** and **2b**. In one of the methods, uvaol was treated with NBS[5] in aqueous dioxan in presence of light. This has yielded two compounds, A, $C_{30}H_{49}O_2Br$ (M^+ 521), m.p. 189° and B, $C_{30}H_{47}O_2Br$ (M^+ 519), m.p. 204°, which were shown to have the structures **3f** and **3g**, respectively from their spectral data. Reduction of **3g** with $NaBH_4$ afforded **3f** confirming their interrelationship.

Attempted dehydrobromination of **3f** with collidine[6] at 140°, however, regenerated uvaol. Collidine being a bulky base fails to abstract the axial hydrogen at C-11 due to severe 1,3-diaxial interactions in the transition state, and instead, eliminates the bromine at C-12 as a bromonium ion. Treatment of **3f** with LiF[7] in DMF providing a base like F^- of considerably smaller volume also failed to bring about the desired dehydrobromination.

In an alternative method, acetyl methyl ursolate (**1l**) was treated with NBS[5] to give a compound, $C_{33}H_{50}O_5$ (M^+ 526), m.p. 235°, which shows UV absorption, λ_{max} 250 nm (log ϵ 4.06), characteristic of an enone. This and its other spectral data are consistent with the structure **1o**. Reduction of **1o** with LAH afforded the triol **1p** [ν_{max} 3340–3380 cm^{-1} (OH)] which appears to be fairly stable compared to its reported[4b] oleanane isomer **1q**. Treatment of **1p** with TsOH gave the compound C, $C_{30}H_{48}O_2$ (M^+ 440), m.p. 210°. It shows the IR band at 3340 cm^{-1} for hydroxyl group and formed a monoacetyl derivative, $C_{32}H_{50}O_3$ (M^+ 482), m.p. 220°. Compound C was shown to have the structure **2c** on the basis of the PMR and mass spectral data of the compound and its monoacetyl derivative. Its formation can be explained by the cyclisation of the 17-hydroxymethyl group of **1p** to form the 13(28)-oxide ring with concomitant acid catalysed elimination of the 11-hydroxyl group and migration of the 12,13-double bond to 11,12-position.

Treatment of **1p** with H_2O_2/TsOH in a manner similar to that used by Kitagawa *et al.*[4b] with **1q**, on the other hand, gave besides **2c**, a second compound D, $C_{30}H_{48}O_3$ (M^+ 456), m.p. 235°, the latter being the major compound. Compound D shows IR band at 3520–3400 cm^{-1} for hydroxyl group. It formed a diacetyl derivative,



8a: $R_1=R_3=R_5=H$, $R_2=R_4=Me$

8b: $R_1=R_2=R_5=H$, $R_3=R_4=Me$

8c: $R_1=R_5=Ac$, $R_3=H$, $R_2=R_4=Me$

$C_{34}H_{52}O_5$ ($M^{+\cdot}$ 540), m.p. 185°. The PMR spectra of compound D and its diacetate coupled with their typical taraxerene type of mass spectral fragmentations[8] establish the structure **8a** for compound D.

The formation of **8a** from **1p** by the action of H_2O_2/TsOH may be assumed to be initiated by the generation of an 11-hydroperoxy function,[4b] followed by acid-catalysed rearrangement involving migration of 14-methyl to C-13. The alternative route involving nucleophilic participation of the 17-hydroxymethyl group to give the 11,12-epoxide of **2c** does not work at all with **1p**, whereas under identical reaction condition **1q** is reported[4b] to give both **8b** and the 11,12-epoxide of **2d**, the latter being the major product. Such difference in the chemical behaviour of **1p** and **1q** may again be assumed to be due to the steric effect of the 19-methyl group in the former. The severe nonbonded interaction between 14- and 19-methyl groups in the 11-hydroperoxy intermediate derived from **1p** forces the reaction exclusively towards the thermodynamically less stable[9] product **8a** totally suppressing the alternative course to give the 11,12-epoxide of **2c**. In absence of any such steric interaction the results with **1q** are those to be expected.

It would be interesting to note that **2c** is a compound very close to the one conceived as an intermediate (path "d", Scheme 1) for the formation of **2a** and **2b**. Although m-chloroperbenzoic acid at ambient temperature failed to epoxidise **2e**, the latter on treatment with H_2O_2 in boiling HOAc afforded a compound, $C_{32}H_{50}O_4$ ($M^{+\cdot}$ 498), m.p. 170°, which from its various spectral data was shown to be the desired epoxide **2f**. This therefore speaks strongly in favour of the mechanistic path "d" for the formation of **2a** and **2b**.

EXPERIMENTAL

M.ps were determined in a Kofler block and were uncorrected. IR spectra were run in KBr disc in Beckman Infrared Spectrophotometer (Model 20). PMR spectra were recorded in a 80 MHz Varian CFT-20 instrument in $CDCl_3$ using TMS as the internal standard. Mass spectra were run in an AEI MS9 instrument equipped with a direct inlet system and operating at 70 eV. *m/e* values of only the most characteristic peaks are given and the figures in the first brackets attached to *m/e* values indicate relative abundance. Silica gel (60–100 mesh) was used for column chromatography and silica gel G for TLC performed at room temperature. All analytical samples were routinely dried over P_2O_5 at 55–138° depending on the m.ps of the compounds for 24 h *in vacuo*. Anhydrous Na_2SO_4 was used for drying organic solvents and petrol used had b.p. 60–80°.

Formation of **2b** *and* **3b**. Oleanolic acid acetate (0.45 g), m.p. 263°, in glacial HOAc (5.5 ml) was stired and treated with 3.9 ml of a mixture of 30% H_2O_2 (2.8 ml) and glacial HOAc (2.8 ml) uniformly during 15 min at 100–105° and the reaction was left. After 2 h the remaining soln was added during 10 min and the reaction was left for a further 1 h. The mixture was diluted (75 ml) and was extracted with ether, washed, dried and the solvent evaporated. The residue was methylated with diazomethane in the usual manner and then chromatographed. The petrol–EtOAc (50:1) eluate on evaporation gave the methyl ester of **1b** (0.4 g), m.p. 210°. The early fractions of the petrol–EtOAc (10:1) gave **2b** (0.025 g), crystallised from $CHCl_3$–MeOH (1:2), m.p. 295°, $[\alpha]_D$ +42° ($CHCl_3$); R_f 0.30 in petrol–EtOAc (4:1); ν_{max} 1765 (γ-lactone), 1720 and 1240 (OAc), 870 (epoxide) cm^{-1}; δ_{ppm} 4.4, 1H, m (–CHOAc), 3.0, 2H, s, Wh/2 3 Hz (–CH–CH–), 2.04, 3H, s (–OCOCH$_3$) and 0.8–1.24 (7 Me); *m/e* 512 ($M^{+\cdot}$, 30), 497(20), 468(7), 452(9), 277(57), 263(57), 249(17), 235(13), 234(17), 218(17), 217(54), 205(41), 204(98), 203(89), 189(100), 175(54) and 133(54).

Later fractions of petrol–EtOAc (5:1) gave **3b** (0.01 g), crystallised in fine needles from petrol–EtOAc, m.p. 277°, $[\alpha]_D$ +58.8° ($CHCl_3$); R_f 0.5 in petrol–EtOAc (2:1); ν_{max} 3540 (OH), 1770 (γ-lactone), 1730 and 1240 (OAc); δ_{ppm} 4.4, 1H, m (>CHOAc), 3.80, 1H, m, Wh/2 7 Hz (>CHOH), 1.97, 3H, s (OCOCH$_3$) and 0.79–1.23 (7 Me); *m/e* 514 ($M^{+\cdot}$, 21), 499(42), 496(12), 454(23), 453(40), 300(16), 264(30), 250(28), 249(28), 246(23), 234(16), 218(44), 205(65), 204(42), 203(30), 189(100), 177(53) and 175(39).

Acid-catalysed hydrolysis of **2b** *and formation of* **3c** *and* **3d**. **2b** (0.015 g) in 6N H_2SO_4 (2.5 ml) and abs EtOH (3 ml) was refluxed for 40 min according to the method of Kitagawa *et al.*[4b] The product was chromatographed and the petrol–EtOAc (5:1) eluate gave **3c** (0.012 g) which on acetylation with Ac_2O/Py gave **3d** (0.01 g), crystallised from petrol–EtOAc, m.p. 272°. It was identical in all respects with the compound obtained by chromic acid oxidation of **3b** following the method of Kitagawa *et al.*[4b]

Treatment of uvaol (**1c**) *and erythrodiol* (**1d**) *with* H_2O_2/HOAc *and formation of* **1e**, **1f**, **1g** *and* **1h**, **1i** *and* **1j**. Uvaol (0.5 g) and erythrodiol (0.25 g) were treated separately with 30% H_2O_2 in HOAc in the same manner as in **1b**. The products in each case after usual workup were chromatographed. From the products of **1c**, the petrol–EtOAc (50:1) eluate gave **1g** (0.043 g), crystallised from $CHCl_3$–MeOH (1:9), m.p. 151°; ν_{max} 1245 and 1735 cm^{-1} (OAc); δ_{ppm} 5.16, 1H, m (>C=CH–CH$_2$–), 4.53, 1H, m (>CHOAc), 3.83, 2H, AB q, J 10 Hz (–C–CH$_2$–OAc), 2.03, 6H, s (–OCOCH$_3$) and 0.86–1.23 (7 Me). The early fractions of the petrol–EtOAc (20:1) yielded **1f** (0.015 g), crystallised from $CHCl_3$–MeOH (1:9), m.p. 242°. (Found: C, 79.5; H, 10.7. $C_{32}H_{52}O_3$ requires: C, 79.3; H, 10.8%.) ν_{max} 3560 (OH), 1720 and 1265 (OAc) cm^{-1}; δ_{ppm} 5.1, 1H, m (>C=CH–CH$_2$–), 4.4, 1H, m (>CHOAc), 3.35, 2H, AB q, J 10 Hz (–C–CH$_2$OH), 2.05, 3H, s (–OCOCH$_3$) and 0.86–1.24 (7 Me). The later fractions of the petrol–EtOAc (20:1) afforded **1e** (0.345 g), crystallised from $CHCl_3$–MeOH, m.p. 159°. (Found: C, 79.2; H, 10.9. $C_{32}H_{52}O_3$ requires: C, 79.3; H, 10.8%.) ν_{max} 3620 (OH), 1725 and 1230 (OAc) cm^{-1}; δ_{ppm} 5.19, 1H, m (>C=CH–CH$_2$–), 3.77, 2H, AB q, J 10 Hz (–C–CH$_2$OAc), 3.28, 1H, m (>CHOH), 1.99 3H, s (–OCOCH$_3$) and 0.76–1.20 (7 Me).

The products from **1d** on similar chromatography gave **1j** (0.023 g), crystallised from $CHCl_3$–MeOH (1:9), m.p. 182°; δ_{ppm}

5.1, 1H, m (>C=CH–CH$_2$–), 4.42, 1H, m (>CHOAc), 3.88, 2H, AB q, J 10 Hz (–C(–)–CH$_2$OAc), 1.95, 6H, s (–OCOCH$_3$) and 0.8–1.2 (7 Me). **1h** (0.008 g), m.p. 155° and **1i** (0.10 g), m.p. 181°, both crystallised from CHCl$_3$–MeOH (1:9). (For **1h** Found: C, 79.4; H, 10.7. $C_{32}H_{52}O_3$ requires: C, 79.3; H, 10.8%. For **1i** Found: C, 79.2; H, 10.9. $C_{32}H_{52}O_3$ requires. C, 79.3; H, 10.8%.) **1i**: ν_{max} 3480 (OH), 1260 and 1710 (OAc) cm^{-1}; δ_{ppm} 5.1, 1H, m (>C=CH–CH$_2$–), 3.75, 2H, AB q, J 10 Hz (–C(–)–CH$_2$OAc), 3.15, 1H, m (>CHOH), 1.98, 3H, s (–OCOCH$_3$) and 0.87–1.26 (7 Me). **1h**: δ_{ppm} 5.1, 1H, m (>C=CH–CH$_2$–), 4.5, 1H, m (>CHOAc), 3.35, 2H, AB q, J 10 Hz (–C(–)–CH$_2$OH), 2.0, 3H, s (–OCOCH$_3$) and 0.85–1.2 (7 Me). Both **1e** and **1f** gave **1g**, and both **1h** and **1i** gave **1j** on acetylation.

Attempted formation of perursolic acid acetate (**7**). **1a** (0.3 g) in benzene (10 ml) was kept overnight under anhyd condition with oxalyl chloride (1 ml) in the cold. Benzene was removed under reduced pressure. The residue in toluene (15 ml) was stirred with 30% H_2O_2 (0.5 ml) and 1(N) NaOH (0.3 ml) at room temperature for 3 h. The product on neutralisation and usual workup did not liberate iodine from an acidified solution of KI. It was chromatographed and the petrol–EtOAc (50:1) eluate furnished **1n** (0.08 g), crystallised from CHCl$_3$–MeOH, m.p. 295°, ν_{max} 1800 (–COCl), 1240 and 1730 (OAc) cm^{-1}. Stirring **1n** with Na_2O_2 in a mixture of toluene and DMSO for 3 h also did not bring about a change.

Reaction of uvaol (**1c**) *with NBS*. **1c** (0.5 g) in dioxan (15 ml) exposed to light from a 500 Watt electric lamp was stirred[5] for 1 h at room temperature with freshly crystallised NBS (0.3 g) in presence of finely powdered $CaCO_3$ (0.11 g). It was filtered and the filtrate was diluted with water, extracted with ether, dried and the solvent removed. The residue was chromatographed. The petrol–EtOAc (80:1) eluate gave **3g** (0.04 g), crystallised from CHCl$_3$–MeOH (1:9), m.p. 204°. (Found: C, 69.1; H, 8.9. $C_{30}H_{47}O_2Br$ requires: C, 69.4; H, 9.0%.) ν_{max} 1698 (>C=O) cm^{-1}; δ_{ppm} 4.17, 1H, m; Wh/2 3 Hz (–CH$_2$–CH(Br)–C(–)–), 3.45, 2H, AB q, J 7 Hz (–C(–)–O–CH$_2$–C(–)–), 2.55, 2H, m (–CO–CH$_2$–) and 0.84–1.26 (7 Me). *m/e* 519 (M$^+$, 2), 439(40), 431(17), 301(13), 299(15), 245(11), 234(21), 233(100), 231(36), 219(38), 215(28), 207(13), 205(43), 203(51), 201(24), 191(42) and 163(17).

The petrol–EtOAc (50:1) furnished **3f** (0.06 g) crystallised from CHCl$_3$–MeOH, m.p. 189°. (Found: C, 69.2; H, 9.2. $C_{30}H_{49}O_2Br$ requires: C, 69.09; H, 9.42%.) ν_{max} 3400 cm^{-1} (OH); δ_{ppm} 4.2, 1H, m, Wh/2 3 Hz (–CH$_2$–CH(Br)–C(–)–), 3.45, 2H, AB q, J 7 Hz (–C(–)–O–CH$_2$–C(–)–), 3.16, 1H, m (>CH–OH) and 0.8–1.26 (7 Me).

NaBH$_4$ *reduction of* **3g**. **3g** (0.015 g) in MeOH was treated with NaBH$_4$ (0.006 g) in portions and the soln was kept overnight. The product after usual workup gave **3f** (0.013 g).

Attempted dehydrobromination of **3f** *with collidine and* LiF. (a) **3f** (0.05 g) in collidine (5 ml) was heated at 140° for 2 h in an atmosphere of nitrogen. The product was acidified with 6(N) HCl, extracted with ether dried and the solvent removed. The residue was chromatographed. The petrol–EtOAc (10:1) eluate, on evaporation, gave **1c** (0.045 g).

(b) **3f** (0.02 g) in dry DMF (10 ml) was refluxed with LiF (0.155 g) for 2.5 h. The product was then diluted with water, acidified with conc HCl and extracted with ether. The residue on removal of solvent was chromatographed to give **3f** (0.005 g) in petrol–EtOAc (50:1) eluate. Petrol–EtOAc (10:1) eluate afforded an uncharacterised compound (0.012 g), crystallised from CHCl$_3$–MeOH (1:9), m.p. > 300°, δ_{ppm} 4.85 (1H, s), 3.24 (1H, s), 3.12 (2H, AB q, J 7 Hz) and 0.76–0.97 (7 Me).

NBS oxidation of **1l** *and formation of* **1o**. **1l** (1 g) in dioxan (30 ml) was stirred at room temperature with freshly crystallised NBS (0.6 g) in presence of finely divided $CaCO_3$ (0.226 g) as in **1c**. The product, worked up in the usual manner, was chromatographed. The petrol–EtOAc (10:1) eluate gave **1o**, m.p. 235°, ν_{max} 1732 (CO$_2$Me), 1235 and 1720 (OAc), 1620 and 1658 (>C=C–C=O) cm^{-1}; *m/e* 526 (M$^+$, 65), 511(9), 467(16), 466(16), 317(100), 276(99), 261(19), 257(63), 249(12), 248(17), 217(56), 189(99) and 175(99).

LAH reduction of **1o**. **1o** (0.3 g) in THF (15 ml) was reduced by a slurry of LAH (0.5 g) in THF (10 ml) in the usual manner. The product after usual workup was repeatedly crystallised from petrol–EtOAc to give pure **1p** (0.25 g), m.p. 213°. (Found: C, 78.9; H, 10.9. $C_{30}H_{50}O_3$ requires: C, 78.6; H, 11.0%); *m/e* 458 (M$^+$, 2), 441(28), 440(81), 271(11), 234(37), 216(11), 207(31), 203(100) and 189(18).

Formation of **2c** *from* **1p**. A soln of **1p** (0.12 g) in a mixture of CH_2Cl_2 (10 ml) and ^{t}BuOH (2 ml) was stirred with TsOH (0.035 g) at room temperature for 27 h. The product after removal of solvent under reduced pressure was worked[4b] up to give a residue which was chromatographed. The petrol–EtOAc (10:1) eluate gave **2c** (0.105 g), crystallised from CHCl$_3$–MeOH (1:9), m.p. 210°. (Found: C, 81.6; H, 11.0. $C_{30}H_{48}O_2$ requires: C, 81.8; H, 10.9%.) δ_{ppm} 5.67, 1H, d, J 10 Hz (–C(–)–CH=CH–), 5.37, 1H, dd, J_1 10 Hz, J_2 3 Hz (–C(–)–CH=CH–CH–), 3.34, 2H, AB q, J 6 Hz (–C(–)–O–CH$_2$–C(–)–), 3.20, 1H, m (>CHOH) and 0.72–1.02 (7 Me); *m/e* 440 (M$^+$, 42), 409(9), 290(26), 257(35), 206(10), 203(35), 189(19), 175(21), 173(23), 161(60), 135(63), 95(89) and 81(100). Acetyl derivative (**2e**), crystallised from CHCl$_3$–MeOH (1:9), m.p. 220°; ν_{max} 1250 and 1730 cm^{-1} (OAc); δ_{ppm} 5.67, 1H, d, J 10 Hz (H-12), 5.35, 1H, dd, J_1 10 Hz J_2 3 Hz (H-11), 4.45, 1H, m (H-3), 3.32, 2H, AB, q, J 6 Hz (H$_2$-28), 1.95, 3H, s (OCOCH$_3$) and 0.8–1.0 (7 Me).

Treatment of **1p** *with* H_2O_2/TsOH *and formation of* **2c** *and* **8a**. A soln of **1p** (0.2 g) in a mixture of CH_2Cl_2 (6 ml) and ^{t}BuOH (2 ml) was stirred with 30% H_2O_2 (0.5 ml) and TsOH (0.06 g) at room temperature for 42 h. The product was worked up as before and chromatographed. The petrol–EtOAc (10:1) eluate gave **2c** (0.07 g), and petrol–EtOAc (5:1) eluate yielded **1p** (0.02 g). Further elution of the column with petrol–EtOAc (1:1) gave **8a** (0.1 g), crystallised from petrol–EtOAc, m.p. 235°. (Found: C, 78.7; H, 10.6. $C_{30}H_{48}O_3$ requires: C, 78.9; H, 10.5%.) ν_{max} 3400–3520 (OH), 880 (–CH(O)–CH–) cm^{-1}; δ_{ppm} 5.47, 1H, m (–H$_2$C–CH=C(–)–), 3.25, 1H, m (>CHOH), 3.12; 2H, s (–CH$_2$OH), 3.05, 1H, t, J 5 Hz and 2.87, 1H, d, J 5 Hz (–CH–CH(O)–CH–C(–)–) and 0.75–1.1 (7 Me); *m/e* 456 (M$^+$, 11), 425(25), 407(47), 391(33), 317(67), 301(68), 287(49), 271(59), 267(72), 253(100), 241(99), 237(93), 227(99), 217(99), 205(99), 203(98), 191(97), 189(91) and 175(92). Diacetate (**8c**) crystallised from CHCl$_3$–MeOH, m.p. 185°, ν_{max} 1250 and 1740 (OAc), 880 (–CH(O)–CH–) cm^{-1}. δ_{ppm} 5.48, 1H, m (–CH$_2$–CH=C–), 4.48, 1H, m (>CHOAc), 3.68, 2H, s (–CH$_2$OAc), 3.05, 1H, t, J 5 Hz and 2.87, 1H, d, J 5 Hz, (–CH(O)–CH–C(–)–), 2.04, 6H, s (OCOCH$_3$), 0.88–1.24 (7 Me), *m/e* 540 (M$^+$, 30), 481(78), 480(45), 465(51), 420(28), 389(18), 344(25), 293(11), 279(29), 262(10), 229(33), 202(57), 189(76), 175(71) and 135(100).

Treatment of **2e** *with m-chloroperbenzoic acid and* H_2O_2/HOAc. (a) **2e** (0.3 g) in CH_2Cl_2 was stirred with m-chloroperbenzoic acid (0.2 g) at room temperature for 22 h. The product

was worked up in the usual manner. The PMR spectrum of the product did not show any signal for epoxide proton.

(b) **2e** (0.3 g) was refluxed with 30% H_2O_2 in glacial HOAc in a manner similar to that used for **1b**. Usual workup of the product followed by chromatography gave **2f** (0.03 g), crystallised from petrol–EtOAc, m.p. 170°. (Found: C, 77.0; H, 10.1. $C_{32}H_{50}O_4$ requires: C, 77.1; H, 10.0%.) ν_{max} 1242, 1742 (OAc), 870 (epoxide) cm^{-1}; δ_{ppm} 4.54, 1H, m (–CHOAc), 3.49, 2H, AB q, J 7 Hz (–CH_2–O–C–), 3.02, 1H, br. signal, Wh/2 4 Hz (H-11), 2.82, 1H, d, J 4 Hz (H-12), 2.02, 3H, s (–OCOCH_3) and 0.8–1.21 (7 Me); *m/e* 498 (M^+, 5), 291(5), 277(8), 249(6), 217(11), 205(9), 204(8), 203(21), 202(11), 201(14), 189(27) and 175(22).

Acknowledgements—We thank Dr. B. C. Das, C.N.R.S., Gif-Sur-Yvette, France and Dr. G. F. Smith, Department of Chemistry, The University of Manchester, U.K. for the mass spectra. AB is thankful to UGC for financial assistance.

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