REACTION OF 3-KETO AND 2-KETOTRITERPENOIDS WITH 3-CHLOROPEROXYBENZOIC ACID IN ALIPHATIC ALCOHOLS. A NEW METHOD OF PREPARATION OF α-HYDROXY KETONES*

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19β,28-Epoxy-18α-oleanan-3-one (*I*), 19β,28-epoxy-24-nor-18α-oleanan-3-one (*XIV*) and 3-lupanone (*XVII*) are hydroxylated with 3-chloroperoxybenzoic acid in the presence of methanol or ethanol and 0·01—0·1% of sulfuric acid in position 2α. Hydroxy ketones *VII*, *XV*, and *XVI* are formed, respectively. The reaction is sensitive to the concentration of sulfuric acid; beyond this concentration range predominantly various 3,4-seco derivatives are formed (for example *VI*, *IX*, *X*, *XVIII*). 2-Oxo derivative *IV* is hydroxylated in a similar manner, giving rise to 3α-hydroxy--2-ketone *VIII*, while 1-oxo derivative *XIII* does not react. A reaction path is proposed for the hydroxylation, comprising the enol form or the enol ether as an intermediate.

It is known that triterpenoid and 4,4-dimethylsteroid 3-oxo derivatives react with peroxy acids (*cf.* refs[1,2] and the references therein) under cleavage of the $C_{(3)}$—$C_{(4)}$ bond, leading to seven-membered lactones (for example *V*). The reaction is usually carried out in dichloromethane, chloroform, acetic or formic acid. In the presence of sulfuric acid or boron trifluoride etherate the formation of various 3,4-seco-3-acids and a seven-membered lactone[1-3] with a single methyl group on $C_{(4)}$ was observed. In this paper the reaction of triterpenoids containing a keto group in ring A with 3-chloroperoxybenzoic acid in the presence of methanol or ethanol, under catalysis with sulfuric acid, was investigated. Preliminary experiments with 19β,28-epoxy-18α--oleanan-3-one (*I*) and methanol indicated that the concentration of sulfuric acid has a decisive effect on the composition of the products. In following text the concentration is given in weight percents, referred to the total volume of the solution.

The reaction of ketone *I* with 3-chloroperoxybenzoic acid in a mixture of methanol and dichloromethane and without acid catalysis proceeds very slowly: after 4 weeks the reaction mixture contains in addition to the starting ketone *I* a complex mixture of products which could not be separated or identified. If the reaction medium contained about 0·005% of sulfuric acid, the known[1] methyl ester of 4-hydroxy-3,4-seco acid *VI* is formed after 11 days as the sole product. If the concentration of sulfuric acid is increased 2α-hydroxy-3-oxo-derivative *VII* appears in the reaction mixture,

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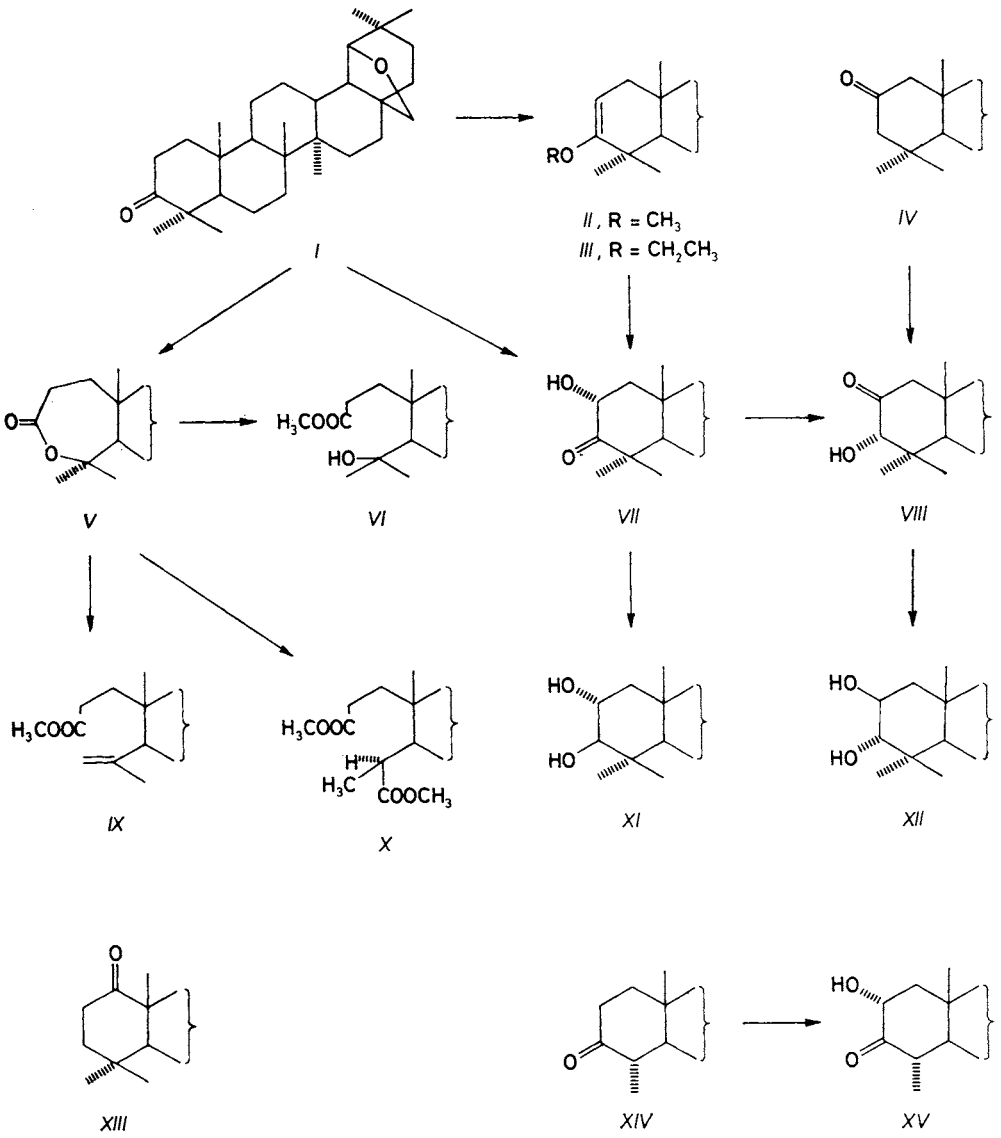
and at concentrations 0·01%–0·1% and reaction times of tens of hours hydroxy ketone *VII* is the main product of the oxidation and the 3,4-seco derivatives are formed in negligible amounts only. For example, at a 0·05% concentration of sulfuric acid hydroxy ketone *VII* was obtained in about 80% yield by mere crystallization. A further increase of sulfuric acid concentration led first to the appearance of 3α-hydroxy-2-oxo derivative *VIII* in the reaction mixture, formed by isomerization of hydroxy ketone



VII. Moreover, the part of methyl esters of various 3,4-seco acids also increases. These seco derivatives again become the main reaction products at high concentrations of sulfuric acid. For example, if the concentration is 10%, the reaction mixture contains, after 1 h, predominantly the unsaturated methyl ester[1] *IX*, which is further oxidized with 3-chloroperoxybenzoic acid if the reaction time is prolonged. A mixture of seco derivatives is formed from which the most abundant (about 50%) was isolated and identified as dimethyl ester *X*. The same dimethyl ester is formed as the main product if the sulfuric acid concentration is increased to 40%.

The structures of hydroxy ketones *VII* and *VIII* follow from the infrared, mass, and ^{1}H NMR spectra. In the ^{1}H NMR spectrum of 2α-hydroxy-3-ketone *VII* the signals of protons are evident in positions 1β (δ 2·52 dd) and 2β (δ 4·55 dd), with the coupling constants ($J_{1\alpha,1\beta}$ = 13·0 Hz, $J_{1\alpha,2\beta}$ = 12·8 Hz and $J_{1\beta,2\beta}$ = 6·8 Hz) characteristic[4] of 2α-substituted 3-ketones. In the spectrum of 3α-hydroxy-2-ketone *VIII* an AB system of protons is evident on $C_{(1)}$ (δ 2·14 d and 2·47 d, J = 17·9 Hz) and a proton singlet on $C_{(3)}$ (δ 4·33). The configurations of the hydroxyl groups of both hydroxy ketones *VII* and *VIII* were confirmed by reduction with sodium borohydride to known diols[5]: from hydroxy ketone *VII* 2α,3β-diol *XI* was obtained as the main product, and from hydroxy ketone *VIII* 2β,3α-diol *XII*. The structure of dimethyl ester *X* was also confirmed by spectral methods. From the ^{1}H NMR spectrum it further follows that dimethyl ester *X* (m.p. 152–154°C, $[\alpha]_D$ +64°) is only one of the possible $C_{(4)}$-isomeric dimethyl esters. In ref.[6] the mixture of both isomers is described, with m.p. 130–134°C and $[\alpha]_D$ +53°. On the basis of optical rotation values of the similar 3,4-seco methyl esters[6,7] with a cyano group instead of a methoxycarbonyl group on $C_{(2)}$ (4*R*-isomer: +23°, 4*S*-isomer: +64°) it is possible to propose 4*S* configuration for the dimethyl ester *X*.

The formation of the esters of 3,4-seco acids (*VI*, *IX*, and *X*) can be explained by Baeyer–Villiger oxidation of ketone *I* and subsequent reactions of lactone *V* with 3-chloroperoxybenzoic acid and methanol in acid medium. According to literature[1] lactone *V* is only transesterified at low concentration of sulfuric acid, giving rise to hydroxy ester *VI*, while at higher concentrations it affords the unsaturated ester *IX*. Lactone *V* gave hydroxy ester *VI* as the sole product even in the presence of 3-chloroperoxybenzoic acid, methanol and 0·05% sulfuric acid, *i.e.* under the conditions which in the case of ketone *I* lead to hydroxylation. At a 40% concentration of sulfuric acid 3-chloroperoxybenzoic acid reacts with lactone *V* under formation of a similar mixture of 3,4-seco esters as formed from ketone *I*. From it again the most abundant dimethyl ester *X* was isolated. This dimethyl ester is formed undoubtedly by epoxidation of the double bond in ester *IX*, rearrangement of the epoxide to aldehyde, oxidation of the aldehyde group with 3-chloroperoxybenzoic acid to the carboxyl group (*cf.* also refs[6,7]) and esterification with methanol.

From these results it follows that two concurrent reactions take place under the effect of 3-chloroperoxybenzoic acid on ketone *I* in the presence of methanol and

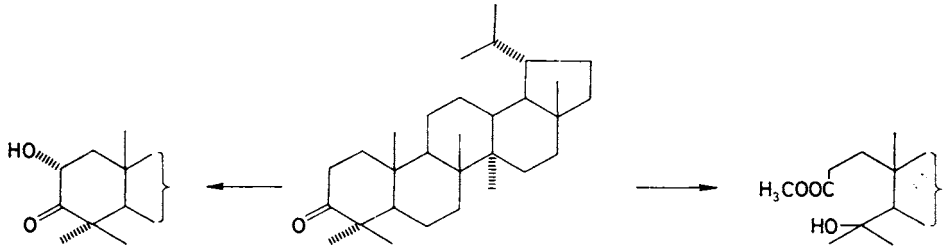
sulfuric acid. The first one – Baeyer–Villiger oxidation – prevails at low or high sulfuric acid concentrations and leads to esters of 3,4-seco acids, *via* lactone *V*. The second – hydroxylation of ketone in α-position – proceeds optimally at sulfuric acid concentrations of about 0·05%.

The formation of hydroxy ketone *VII* by reaction of ketone *I* with peroxy acid is interesting and unexpected. Hydroxy ketone *VII* is also formed when ethanol is substituted for methanol and chloroform for dichloromethane; hydroxylation takes place even in methanol alone. According to the ^{1}H NMR spectrum of the crude product no methyl ester of 3-chlorobenzoic acid or no methoxy ketones either are formed during hydroxylation. Instead of 3-chloroperoxybenzoic acid, peroxybenzoic acid prepared according to ref.[8] may also be used for hydroxylation, but it must be carefully freed of methyl benzoate (the remainders of methyl benzoate do not affect the hydroxylation course, it is true, but they prevent the isolation and the purification of hydroxy ketone *VII* by crystallization). If methanol is replaced by acetic acid or acetonitrile, hydroxylation does not take place. Hydroxylation is not affected by the presence of inhibitors of radical reactions (for example quinol).

The hydroxylation with 3-chloroperoxybenzoic acid in the presence of methanol and 0·05% sulfuric acid was also checked with other ketones. 2-Oxo derivative *IV* afforded, after 2 days, 3α-hydroxy-2-ketone *VIII* in almost quantitative yield. On the contrary, 1-oxo derivative *XIII* was recovered unchanged under the same conditions after 18 days. The Baeyer–Villiger oxidation observed[1] when dichloromethane was used (without methanol and sulfuric acid) as solvent did not take place either. 24-Nor-3-ketone *XIV*, which contains a single methyl group on $C_{(4)}$, is hydroxylated in position 2, giving 2α-hydroxy ketone *XV*. It is known that 2-oxo and 3-oxotriterpenoids and 4,4-dimethylsteroids easily enolize under formation of a double bond in position 2 (3), while 1-ketones enolize very reluctantly[9,10]. Some reactions of 24-nor-3-ketone *XIV* (bromination, enol-acetylation)[11] show that the enol form with a 2(3)-double bond is formed easily. If the above mentioned results of the reactions of ketones *I*, *IV*, *XIII*, and *XIV* are taken into consideration, it seems probable that the enol form (or enol ether, since the presence of alcohol is indispensable for hydroxylation) plays an important role in the hydroxylation of ketones with peroxy acid. The α-configuration of the hydroxy groups in hydroxy ketones *VII*, *VIII*, and *XV* is in agreement with the intermediate with the 2(3)-double bond. It is known that this double bond (*cf.* ref.[5] and references therein) is attacked exclusively from the α side. Therefore the reactivity of enol ethers as possible intermediates was investigated.

Enol ether *III* was prepared on reaction of ketone *I* with ethyl orthoformate in ethanol and benzene. When ethanol was replaced by methanol, enol ether *II* was obtained. Both enol ethers react with 3-chloroperoxybenzoic acid in dichloromethane or in a mixture of dichloromethane, methanol and sulfuric acid (0·05%) at −18°C within a few minutes and only hydroxy ketone *VII* is formed. At room temperature a strong exothermic reaction takes place and a mixture of hydroxy ketone *VII* and

ketone *I* is formed within a few seconds. If the hydroxylation with 3-chloroperoxybenzoic acid is carried out with a 2,2-dideuterio derivative of ketone *I* (prepared according to ref.[4]), the deuterium in the position 2β of the hydroxy ketone *VII* is predominantly retained (84%, determined by mass spectrometry). This shows that if the enol form or the enol ether is an intermediate, the rate of the attack with the peroxy acid is higher than of the back formation of ketone *I*. The attack of the peroxy acid on the intermediate with the 2(3)-double bond probably causes the formation of the unstable 2α,3α-epoxy-3β-hydroxy (or alkoxy) derivative which then affords 2α-hydroxy ketone *VII*. A similar reaction course may be also proposed for the hydroxylation of 2-oxo derivative *IV*. The dependence of the course of the reaction of ketone *I* with 3-chloroperoxybenzoic acid on sulfuric acid concentration and the existence of the optimum concentration for hydroxylation (see above) is interesting. It is evidently caused by the fact that sulfuric acid affects the relative rates of the reactions involved in different ways, *i.e.* the Baeyer–Villiger oxidation, enolization and epoxidation of the enol form (or enol ether).



XVI *XVII* *XVIII*

Hydroxylation of 2-keto- and 3-ketotriterpenoids with peroxy acids in the presence of aliphatic alcohol represents a new advantageous method of preparation of 2α--hydroxy-3-ketones and 3α-hydroxy-2-ketones. In the case of hydroxy ketone *VII* the reaction of ketone *I* with 3-chloroperoxybenzoic acid in a small volume of methanol and a slightly higher concentration of sulfuric acid (0·15%) than above was found the most suitable one from the preparative point of view. Hydroxy ketone *VII* crystallizes during the reaction directly from the reaction mixture in about 80% yield. 3-Lupanone (*XVII*) reacts similarly as ketone *I*: under the effect of 3-chloroperoxybenzoic acid in a mixture of methanol and dichloromethane with 0·05% sulfuric acid it gives 2α-hydroxy ketone *XVI*, while at a 0·005% concentration of sulfuric acid methyl ester *XVIII* is formed.

EXPERIMENTAL

The melting points were determined on a Kofler block and they are not corrected. Optical rotations were measured on an automatic polarimeter ETL-NPL (Bendix–Ericsson) in chloroform solution

(c = 0·5—1·0), with a ±2° accuracy. The infrared spectra were measured on a PE 684 (Perkin–Elmer) instrument, in chloroform. The ^{1}H NMR spectra were measured on a Tesla BS 487 A instrument at 80 MHz, in deuteriochloroform, using hexamethyldisiloxane as internal reference. The chemical shifts were calculated for tetramethylsilane as standard (δ_{HMDS} = 0·06) and they are given in ppm (δ-scale). The ^{1}H NMR spectrum of hydroxy ketone *XV* was measured on a Varian XL 200 instrument at 200 MHz, in deuteriochloroform with tetramethylsilane as internal reference. The mass spectra were measured on a Varian MAT 311 spectrometer at 70 eV ionizing electrons energy and a 95—135°C temperature of the direct inlet system. The identity of the samples prepared by various procedures was tested by thin-layer chromatography, infrared and ^{1}H NMR spectra. Thin-layer chromatography was carried out on silica gel G (Merck) using 10% sulfuric acid and heating for detection, or on Silufol sheets (Kavalier, Votice) using detection with a 5% phosphomolybdic acid in ethanol and heating. For preparative chromatography on thin layers silica gel G (Merck) was used and the plates were detected by spraying with morin solution in methanol (0·2%) and inspection in UV light of 254 nm wavelength. For column chromatography silica gel Silpearl (Kavalier, Votice) was used. Analytical samples were dried under reduced pressure at 100°C, over phosphorus pentoxide.

3-Chloroperoxybenzoic acid was a product of Koch and Light (Great Britain). The solvents used for the reactions with peracids were allowed to stand over solid sodium hydrogen carbonate for several days and then distilled. The preparation of ketone *I* is described in ref.[12], *IV* in ref.[13], *XIII* in ref.[5], *XIV* in ref.[11], *XVII* in ref.[14] and lactone *V* in ref.[1].

Reaction of 19β,28-Epoxy-18α-oleanan-3-one (*I*)

A solution of sulfuric acid in methanol was added to a solution of ketone *I* in dichloromethane, and 3-chloroperoxybenzoic acid was then added to the mixture. The solution was allowed to stand in darkness at room temperature; the reaction course was monitored by thin-layer chromatography. After the indicated time the mixture was diluted with ether, the organic layer was washed gradually with water, 5% potassium iodide solution, water, 5% sodium sulfite solution, saturated sodium hydrogen carbonate solution and water. After drying over sodium sulfate the solvents were evaporated. In preliminary experiments the composition of the mixtures of products was determined by thin-layer chromatography and by ^{1}H NMR spectra; methyl esters of 3,4-seco-3--acids were identified, independently of structure, on the basis of the $COOCH_3$ group signal at $\delta \sim$ 3·65, 2α-hydroxy-3-ketone *VII* on the basis of the doublet of doublets of 2β-H at δ 4·55 and 3α-hydroxy-2-ketone *VIII* on the basis of the singlet of 3β-H at δ 4·33.

From the experiments carried out on a preparative scale only some synthetically advantageous experiments are mentioned below. Unless stated otherwise they were carried out in the above described manner. The concentration of sulfuric acid is given in weight percentage referred to the total volume of the solution.

a) *With 0·005% sulfuric acid*: Reaction of ketone *I* (150 mg) with 3-chloroperoxybenzoic acid (200 mg) in dichloromethane (5 ml) and methanol (5 ml) for 11 days gave, after crystallization of the product from methanol, 120 mg (72%) of methyl 19β,28-epoxy-4-hydroxy-3,4-seco-18α--oleanan-3-oate (*VI*), identical with an authentic sample[1]. M.p. 192—194°C, ref.[1] gives m.p. 193—196°C.

b) *With 0·05% sulfuric acid*: Ketone *I* (200 mg) reacted with 3-chloroperoxybenzoic acid (200 mg) in dichloromethane (5 ml) and methanol (10 ml) for 24 h. On crystallization from a mixture of acetone and heptane 155 mg (75%) of 19β,28-epoxy-2α-hydroxy-18α-oleanan-3-one (*VII*) were obtained, m.p. 225—230°C, $[\alpha]_D$ +46°. Infrared spectrum: 3 500 (OH), 1 716 (C=O), 1 038 (C—O—C) cm^{-1}. ^{1}H NMR spectrum: 0·80 s, 0·90 s, 0·93 s, 1·03 s, 1·09 s, 1·15 s, 1·19 s

(7 × CH_3), 2·52 dd (1β-H), 4·55 dd (2β-H), $J_{1\alpha,1\beta}$ = 13·0 Hz, $J_{1\alpha,2\beta}$ = 12·8 Hz, $J_{1\beta,2\beta}$ = 6·8 Hz, 3·51 s (19α-H), 3·44 d and 3·76 d (J = 8 Hz, 28-H_2). Mass spectrum: m/z (%): 456 (M^+, 49), 454 (5), 438 (24), 385 (45), 383 (23), 369 (12), 245 (18), 81 (100). For $C_{30}H_{48}O_3$ (456·7) calculated: 78·90% C, 10·59% H; found: 78·91% C, 10·50% H.

If the reaction is carried out under the same conditions but in a mixture of chloroform and ethanol, hydroxy ketone *VII* is again formed as the main product according to thin-layer chromatography, which was then isolated by crystallization in 60% yield. If peroxybenzoic acid in a mixture of dichloromethane and methanol is used for the reaction, the yield of hydroxy ketone *VII* after crystallization is 85%.

c) *With 0·15% sulfuric acid*: A suspension of ketone *I* (1·8 g) in a solution of 3-chloroperoxybenzoic acid (1·4 g) in 30 ml of methanol containing 0·15% of sulfuric acid was stirred for 3 h until complete dissolution, and then allowed to stand overnight. The separated crystals were filtered off under suction and washed with methanol. Yield, 1·6 g (86%) of hydroxy ketone *VII*.

d) *With 10% sulfuric acid*: On reaction with 3-chloroperoxybenzoic acid (250 mg) in dichloromethane (2 ml) and methanol (8 ml) ketone *I* (340 mg) afforded a mixture of products after 1 h reaction time. Chromatography on a thin layer of silica gel (27 g, development with light petroleum–ether mixture 4 : 1) gave 150 mg (41%) of methyl 19β,28-epoxy-3,4-seco-18α-olean-4(23)-en-3-oate (*IX*), identical with an authentic sample[1]. On prolongation of the reaction time to 1 month the same mixture was obtained as under *e*), from which dimethyl ester *X* was isolated as under *e*) in a 52% yield.

e) *With 40% sulfuric acid*: Ketone *I* (250 mg) and 3-chloroperoxybenzoic acid (600 mg) in a mixture of dichloromethane (5 ml) and methanol (10 ml) was allowed to react for 2 days. A mixture of esters of 3,4-seco acids was formed from which chromatography on a silica gel column (15 g; elution with a light petroleum–ether mixture 8 : 1) gave dimethyl ester of (4*S*)-19β,28-epoxy-3,4-seco-18α-oleanane-3,23-dioic acid (*X*). Yield, 130 mg (44%), m.p. 152–154°C (chloroform–methanol), $[\alpha]_D$ +64°. Infrared spectrum: 1 740 (C=O), 1 038 (C–O–C) cm^{-1}. ^1H NMR spectrum: 0·79 s, 0·84 s, 0·91 s, 0·93 s, 0·98 s and 1·08 d (J = 7·1 Hz), (6 × CH_3), 3·65 s (2 × OCH_3), 3·52 s (19α-H), 3·43 d and 3·77 d (J = 8 Hz, 28-H_2). Mass spectrum: m/z (%): 516 (M^+, 18), 486 (16), 445 (20), 430 (52), 429 (59), 411 (16), 399 (15), 397 (18), 343 (32), 273 (10), 81 (100). For $C_{32}H_{52}O_5$ (516·8) calculated: 74·38% C, 10·14% H; found: 74·60% C, 10·21% H. Ref.[6] gives m.p. 130–134°C and $[\alpha]_D$ +53° for a mixture of (4*R*)- and (4*S*)-isomers. If sulfuric acid is replaced by 10% boron trifluoride etherate a mixture is formed after two days, from which 52% of dimethyl ester *X* were obtained.

Reaction of Lactone *V*

The reactions with lactone *V* were carried out under the same conditions as in the case of ketone *I*, under corresponding headings. When the reaction was carried out as under *a*) and *b*) methyl ester *VI* was obtained as the main product, which was isolated by crystallization from a mixture of chloroform and methanol, in 85% and 55% yields, respectively. In the reaction of lactone *V* under the conditions given under *e*) a mixture of methyl esters of 3,4-seco acids was obtained, from which dimethyl ester *X* was obtained as the major product by column chromatography in a 20% yield.

Reaction of 19β,28-Epoxy-18α-oleanan-2-one (*IV*)

The reaction was carried out in the same manner as in the case of ketone *I*, under *b*). Crystallization from a mixture of chloroform and methanol gave 85% of 19β,28-epoxy-3α-hydroxy-18α-

oleanan-2-one (*VIII*), m.p. 228–232°C, $[\alpha]_D$ +114°. Infrared spectrum: 3 525 (OH), 1 712 (C=O), 1 033 (C—O—C) cm^{-1}. ^1H NMR spectrum: 0·80 s, 0·82 s, 0·90 s, 0·93 s, 1·01 s, 1·12 s and 1·20 s (7 × CH_3), 2·14 d and 2·47 d (AB system, J = 17·9 Hz, 1-H_2), 3·51 s (19α-H), 3·49 d and 3·78 d (J = 8 Hz, 28-H_2), 4·33 s (3β-H). Mass spectrum: m/z (%): 456 (M^+, 36), 454 (9), 438 (10), 385 (26), 383 (18), 369 (10), 245 (14), 95 (100). For $C_{30}H_{48}O_3$ (456·7) calculated: 78·90% C, 10·59% H; found: 78·75% C, 10·53% H.

Reaction of 19β,28-Epoxy-24-nor-18α-oleanan-3-one (*XI*)

The reaction was carried out in the same manner as in the case of ketone *I* under *b*). Crystallization from methanol gave 68% of 19β,28-epoxy-2α-hydroxy-24-nor-18α-oleanan-3-one (*XV*), with m.p. 255–259°C (sublimates at 220°C), $[\alpha]_D$ +83°. Infrared spectrum: 3 486 (OH), 1 712 (C=O), 1 033 (C—O—C) cm^{-1}. ^1H NMR spectrum (200 MHz): 0·80 s, 0·89 s, 0·93 s, 1·03 s, 1·06 d (J = 6·4 Hz) and 1·14 s (6 × CH_3), 2·46 ddq (4β-H), 2·60 dd (1β-H), 3·56 d (OH) and 4·26 m (2β-H). $J_{1\alpha,1\beta}$ = 12·6 Hz, $J_{1\alpha,2\beta}$ = 11·8 Hz, $J_{1\beta,2\beta}$ = 7·4 Hz, $J_{2\beta,OH}$ = 3·5 Hz, $J_{2\beta,4\beta}$ = 1·3 Hz, $J_{4\beta,5\alpha}$ = 12·6 Hz, $J_{4\beta,23}$ = 6·4 Hz, 3·53 s (19α-H), 3·45 d and 3·77 d (J = 7·8 Hz, 28-H_2). Mass spectrum: m/z (%): 442 (M^+, 100), 440 (17), 427 (9), 424 (20), 412 (22), 411 (24), 371 (87), 220 (37), 191 (60), 177 (32). For $C_{29}H_{46}O_3$ (442·7) calculated: 78·68% C, 10·47% H; found: 78·59% C, 10·33% H.

Reactions of 3-Lupanone (*XVII*)

The reactions were carried out under the same conditions as in the case of ketone *I*. When the reaction was carried out as under *a*) the reaction mixture contained according to thin-layer chromatography methyl 4-hydroxy-3,4-secolupan-3-oate (*XVIII*) as the main product, which was obtained by double crystallization from methanol in a 45% yield. M.p. 208–210°C, $[\alpha]_D$ −5°. Infrared spectrum: 3 605 and 3 516 (OH), 1 730 (C=O), 1 156 (C—O) cm^{-1}. ^1H NMR spectrum: 0·75 s, 0·80 s, 0·96 s, 1·05 s, 1·27 s, 1·27 s, 0·76 d (J = 7 Hz) and 0·91 d (J = 7 Hz) (8 × CH_3), 2·3–2·5 m, 3·63 s (OCH_3). For $C_{31}H_{54}O_3$ (474·8) calculated: 78·43% C, 11·46% H; found: 78·39% C, 11·29% H.

When the reaction was carried out as under *b*), crystallization from acetone gave 67% of 2α-hydroxy-3-lupanone (*XVI*), m.p. 228–232°C, $[\alpha]_D$ −22°. Infrared spectrum: 3 490 (OH), 1 716 (C=O) cm^{-1}. ^1H NMR spectrum: 0·77 s, 0·90 s, 1·10 s, 1·10 s, 1·15 s, 1·19 s, 0·76 d (J = = 7 Hz) and 0·84 d (J = 7 Hz) (8 × CH_3), 2·50 dd (1β-H), 4·54 dd (2β-H), $J_{1\alpha,1\beta}$ = 13·0 Hz, $J_{1\alpha,2\beta}$ = 12·8 Hz, $J_{1\beta,2\beta}$ = 6·9 Hz. For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·22% C, 11·39% H.

19β,28-Epoxy-3-methoxy-18α-olean-2-ene (*II*) and 19β,28-Epoxy-3-ethoxy-18α-olean-2-ene (*III*)

A suspension of ketone *I* (1·2 g) in a mixture of ethyl orthoformate (1 ml), 2% sulfuric acid in methanol (5 ml) and benzene (1 ml) was stirred until dissolution (10 min) and then allowed to stand at room temperature for 2 h. The separated crystals were filtered off under suction and crystallized from a mixture of chloroform and methanol containing a trace of pyridine. Yield, 1·1 g (90%) of *II*, sublimating at 240°C, m.p. 256–259°C, $[\alpha]_D$ +78°. Infrared spectrum: 1 667 (C=C), 1 032 and 1 026 (C—O—C) cm^{-1}. ^1H NMR spectrum: 0·80 s, 0·88 d, 0·92 s, 0·93 s, 0·94 s, 1·00 s, 1·05 s (7 × CH_3), 1·64 bd (1α-H), 2·08 dd (1β-H), 4·38 dd (2-H), $J_{1\alpha,1\beta}$ = 16·0 Hz, $J_{1\alpha,2}$ = 1·8 Hz, $J_{1\beta,2}$ = 6·8 Hz, 3·43 s (OCH_3), 3·54 s (19α-H), 3·42 d and 3·79 d (J = 8 Hz, 28-H_2). For $C_{31}H_{50}O_2$ (454·7) calculated: 81·88% C, 11·08% H; found: 81·59% C, 10·92% H. Using the same procedure and substituting ethanol for methanol in the reaction and crystallization,

III was obtained in 83% yield, m.p. 255–257°C (at 240°C the needles were converted to platelets), $[\alpha]_D$ +78°. Infrared spectrum: 1 668 (C=C), 1 031 (C—O—C) cm^{-1}. ^1H NMR spectrum: 0·80 s, 0·89 s, 0·92 s, 0·93 s, 0·95 s, 1·00 s, 1·05 s (7 × CH_3), 1·24 t and 3·64 q (J = 7·0 Hz, CH_3CH_2O), 1·62 bd (1α-H), 2·05 dd (1β-H), 4·36 dd (2-H), $J_{1\alpha,1\beta}$ = 16·0 Hz, $J_{1\alpha,2}$ = 2 Hz, $J_{1\beta,2}$ = 6·5 Hz, 3·54 s (19α-H), 3·44 d and 3·80 d (J = 8 Hz, 28-H_2). For $C_{32}H_{52}O_2$ (468·8) calculated: 81·99% C, 11·18% H; found: 81·75% C, 11·03% H.

Reactions of Enol Ethers *II* and *III*

a) A solution of 3-chloroperoxybenzoic acid (50 mg) in dichloromethane (1 ml) was added dropwise at −18°C to a solution of enol ether *II* (0·1 g) in dichloromethane (5 ml). The mixture was allowed to stand at this temperature for 20 min (according to thin-layer chromatography the reaction is already terminated after 5 min), then diluted with ether and further worked up as in the case of the reaction of ketone *I* with 3-chloroperoxybenzoic acid. Crystallization of the residue from methanol gave 80 mg (78%) of hydroxy ketone *VII*. If — under the same conditions — a solution of enol ether *II* is mixed with a solution of 3-chloroperoxybenzoic acid at room temperature, a strongly exothermic reaction takes place and the reaction mixture contains according to thin-layer chromatography ketone *I* and hydroxy ketone *VII* in an approximately 1 : 1 ratio. The same products were obtained in the reactions of enol ether *III*.

b) A solution of 3-chloroperoxybenzoic acid (50 mg) in methanol (1 ml) was added dropwise at −18°C to a solution of enol ether *II* (0·1 g) in a mixture of dichloromethane (3 ml) and 0·1% solution of sulfuric acid in methanol (4 ml) and the mixture was allowed to stand at this temperature for 10 min. It was then worked up as under *a*). Crystallization from methanol gave 88 mg (85%) of hydroxy ketone *VII*. If this reaction was carried out at room temperature the reaction mixture contained after 5 min a mixture of compounds *I* and *VII*, which is after a further 18 h converted to hydroxy ketone *VII* which was obtained by crystallization from methanol in a 65% yield. Enol ether *III* reacted in the same way.

Reduction of Hydroxy Ketones *VII* and *VIII*

A suspension of sodium borohydride (50 mg) in methanol (2 ml) was added to a solution of hydroxy ketone *VII* (150 mg) in benzene (5 ml) and the mixture was allowed to stand at room temperature for 18 h under occasional shaking. It was diluted with ether, the solution washed with water, dilute hydrochloric acid and water, dried over sodium sulfate and the solvents evaporated. According to thin-layer chromatography two products were formed in a 3 : 1 ratio. The more polar, predominant 19β,28-epoxy-18α-oleanane-2α,3β-diol (*XI*) was obtained by double crystallization from a mixture of chloroform and methanol in 43% yield (65 mg). M.p. 257 to 259°C (sublimates at 240°C), $[\alpha]_D$ +42°. Ref.[5] gives m.p. 255–257°C, $[\alpha]_D$ +45°. The diol *XI* was identical with an authentic sample[5].

Using the same procedure hydroxy ketone *VIII* was reduced to give 19β,28-epoxy-18α-oleanane-2β,3α-diol (*XII*) as the sole product (according to thin-layer chromatography). After crystallization from ethanol the yield was 78%. M.p. 264–266°C (sublimates at 210°C), $[\alpha]_D$ +91°. Ref.[5] gives m.p. 264–267°C, $[\alpha]_D$ +94°. The diol *XII* was identical with an authentic sample[5].

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