TRITERPENOID 2,3-KETOLS, DIOLS AND THEIR ACETATES: PREPARATION AND CONFORMATION OF THE RING A*

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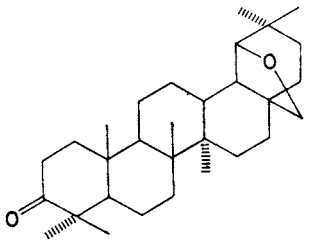
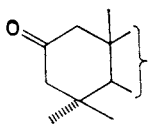
19β,28-Epoxy-18α-oleanane derivatives *I*—*III* were converted into hydroxy ketones *IV*, *VIII* and *X*, acetoxy ketones *V*, *VII*, *IX* and *XI*, diols and their mono- and diacetates *XII*—*XXV*. Seven of the eight possible isomeric 2,3-diol monoacetates were obtained. Conformation of the ring A in these compounds has been derived from the ^{1}H NMR and IR spectra. In 2β-acetoxy-3-ketone *VII*, 3α-hydroxy- and 3α-acetoxy-2-ketones *VIII* and *IX*, and in 2β,3α-diol monoacetates *XVIII* and *XIX* the ring A exists predominantly in a boat conformation.

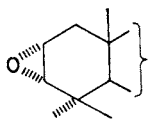
As a continuation of our studies on conformation of the ring A in 2,3-disubstituted pentacyclic triterpenoids (see refs[1-3] and references therein), this paper concerns the preparation and stereochemistry of isomeric hydroxy and acetoxy ketones, diols and their monoacetates derived from 19β,28-epoxy-18α-oleanane. The known[4,5] ketones *I* and *II* and the epoxide *III* were used as the starting compounds.



I



II



III

The 2α-hydroxy-3-ketone *IV* was prepared according to ref.[6] by hydroxylation of ketone *I* with 3-chloroperoxybenzoic acid in a mixture of dichloromethane and methanol, containing small amount of sulfuric acid. The same hydroxylation of 2-ketone *II* led[6] to 3α-hydroxy-2-ketone *VIII*. The structures of *IV* and *VIII* had been confirmed already previously[6] by reduction to the diols *XVII* and *XXI*. Both *IV* and *VIII* were isomerized by treatment with sulfuric acid or alumina to give

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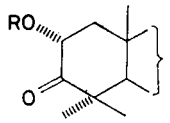
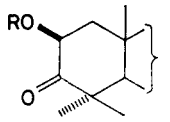
3β-hydroxy-2-ketone *X* in almost quantitative yield. Similar isomerizations were observed with analogous 4,4-dimethylsteroid and triterpenoid acetoxy ketones[7-9]. When *IV* and *VIII* were isomerized with a very low concentration of sulfuric acid (0·08% (v/v)) in a mixture of dichloromethane and methanol, an equilibrium was slowly established only between these two ketols. After two or three days the equilibrium mixture contained (according to optical rotation and ^{1}H NMR spectrum) 60–70% of *IV* and 30–40% of *VIII*. When the reaction time was prolonged or the concentration of sulfuric acid was increased, 3β-hydroxy-2-ketone *X* appeared in the reaction mixture. With still higher concentration of the acid (about 2%) the ketols *IV* and *VIII* disappeared completely, the ketol *X* being the only product. These facts show that the isomerizations involve both the mechanisms suggested[10] for acid-catalyzed isomerizations of α-ketols. The equilibrium between the two less stable ketols *IV* and *VIII*, in which the α-configuration of the hydroxyl remains intact, can be established by a mechanism involving protonation of the carbonyl group followed by intramolecular 1,2-hydride shift (H-2β ⇄ H-3β). This process is relatively fast and can be observed only at low concentrations of the acid. The second mechanism consists in enolization of the carbonyl group and formation of 2,3-enediol intermediate. This reaction is slower and leads to the thermodynamically most stable isomer, 3β-hydroxy-2-ketone *X*.

Acetylation of ketols *IV*, *VIII* and *X* with acetic anhydride in pyridine afforded acetoxy ketones *V*, *IX* and *XI*. The fourth isomer (2β-acetoxy-3-ketone *VII*) was obtained from 2α,3α-epoxide *III* via 2β,3α-diol 2-acetate *XVIII*. Since refluxing epoxide *III* in acetic acid, as well as the sulfuric acid-catalysed reaction with acetic acid at room temperature, led to the known[2] diacetate *XX*, the epoxide was opened with acetic acid containing sodium acetate. After 12 days at room temperature, a 1 : 1 mixture of monoacetates *XVIII* and *XIX* was obtained. Obviously, the 2α,3α-epoxide ring is diaxially opened[2] to give primarily 2-acetate *XVIII* which is then transformed into the isomeric 3-acetate *XIX* by migration of the acetyl group under the reaction conditions (vide infra). The 3-acetate *XIX* was also prepared by reduction of 3α-acetoxy-2-ketone *IX* with sodium borohydride. Acetylation of both monoacetates led to the same diacetate *XX*. Oxidation of *XVIII* with pyridinium chlorochromate afforded 2β-acetoxy-3-ketone *VII*.

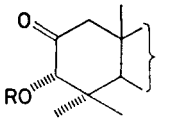
Attempts to prepare 2β-hydroxy-3-ketone *VI* by hydrolysis of acetoxy ketone *VII* failed even under very mild conditions (potassium hydrogen carbonate in aqueous methanol at room temperature). In the absence of air oxygen, the reaction gave the isomeric ketol *X* whereas in the presence of air oxidation to the known[11] 2,3-diketone *XXVI* took place. The same diketone was obtained by oxidation of *IV* with air oxygen in an alkaline medium. As shown by ^{1}H NMR spectrum (δ 6·48 s, H-1 and 5·91 s, OH) and infrared spectrum (3 450 cm^{-1}, OH; 1 666 and 1 644 cm^{-1}, C=C—C=O), in chloroform solution the diketone exists practically entirely in the enol form *XXVII*.



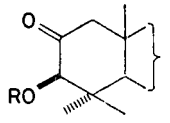
IV, R = H
V, R = Ac



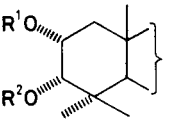
VI, R = H
VII, R = Ac



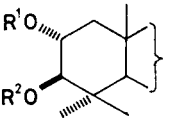
VIII, R = H
IX, R = Ac



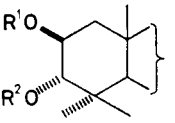
X, R = H
XI, R = Ac



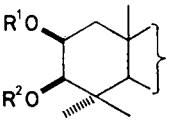
XII, R^1 = Ac ; R^2 = H
XIII, R^1 = R^2 = H



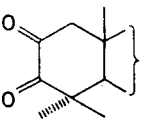
XIV, R^1 = Ac ; R^2 = H
XV, R^1 = H ; R^2 = Ac
XVI, R^1 = R^2 = Ac
XVII, R^1 = R^2 = H



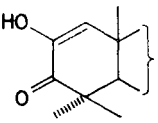
XVIII, R^1 = Ac ; R^2 = H
XIX, R^1 = H ; R^2 = Ac
XX, R^1 = R^2 = Ac
XXI, R^1 = R^2 = H



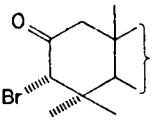
XXII, R^1 = Ac ; R^2 = H
XXIII, R^1 = H ; R^2 = Ac
XXIV, R^1 = R^2 = Ac
XXV, R^1 = R^2 = H



XXVI



XXVII



XXVIII

Ac = $COCH_3$

Another series of compounds was prepared by reduction of acetoxy ketones *V* and *XI* with sodium borohydride. Compound *V* afforded 2α,3β-diol 2-acetate *XIV* (60%), 2α,3α-diol 2-acetate *XII* (13%) and 2α,3β-diol 3-acetate *XV* (4%). Apparently, the latter acetate arose from *XIV* by acetyl migration either during the reduction or in the work-up step. Acetates *XIV* and *XV* afforded the same diacetate *XVI*, identical with the compound prepared[2] from 2α,3β-diol *XVII*. Alkaline hydrolysis of acetate *XII* led to 2α,3α-diol *XIII*. Reduction of 3β-acetoxy-2-ketone *XI* with an equivalent of hydride at room temperature gave a mixture of 2β,3β-diol monoacetates *XXII* and *XXIII* in which the latter slightly predominated. Reaction with excess hydride at the same temperature led to 2β,3β-diol *XXV* which was also obtained by reduction of hydroxy ketone *X*. When the reduction of *XI* was performed at −18°C with equimolar amount of hydride, 3-acetate *XXIII* with only minor amount of the isomeric acetate *XXII* was obtained. Compounds *XXII*, *XXIII* and *XXV* were acetylated to furnish 2β,3β-diol diacetate *XXIV*. The described procedures afforded seven of the eight possible 2,3-diol monoacetates.

The acetyl migration in diol monoacetates *XIV*, *XV*, *XVIII*, *XIX*, *XXII* and *XXIII* was verified under conditions used in the reaction of epoxide *III* with acetic acid. As shown by TLC, the isomerizations in acetic acid, containing sodium acetate, took place within several hours at room temperature. In ether, which had been shaken with dilute hydrochloric acid, the monoacetates were isomerized during several minutes. The composition of equilibrium mixtures of monoacetates, obtained in this way but after several times longer reaction times, was 1 : 1 for 2α,3β-compounds *XIV* and *XV*, as well as for 2β,3α-isomers *XVIII* and *XIX*. In the case of 2β,3β-monoacetates, 3-acetate *XXIII* predominated over 2-acetate *XXII*, their ratio being 3 : 2. The equilibrium mixtures contained no diols or diacetates: the transfer of the acetyl group proceeds obviously via a cyclic transition state. For 2β,3α-diol monoacetates *XVIII* and *XIX* the cyclic transition state can be realized only in the boat form of the ring A because in the chair form the axial groups in positions 2β and 3α are too far from each other.

The position and configuration of the functional groups on the ring A in the synthesized compounds follow from the above-described reactions, from the known stereochemistry of opening 2α,3α-epoxides, from the stereoselectivity of reduction of 2-oxo and 3-oxo groups and from analogies in the steroid and triterpenoid field[2,6–9,12]. Moreover, they are confirmed by ^{1}H NMR spectra (Tables I and II). In the case of the diol monoacetates, the chemical shifts of protons in positions 2 and 3, together with signal multiplicities, clearly show the position of the acetate and hydroxyl groups.

The conformation of the ring A in the hydroxy ketones follows from the infrared spectra in the O—H stretching vibration region (Table III). According to the literature[13,14], spectra of equatorial α-hydroxy ketones exhibit only a band of hydroxyl, bonded intramolecularly to *n*-electrons of the carbonyl group. This hydrogen bond is characterized by a large shift $\Delta\nu$(OH) (about 120–140 cm^{-1}). On the other hand, axial hydroxy ketones exhibit a typical free hydroxyl band and a band at about 3 600 cm^{-1} due to a weak hydrogen bonding to the carbonyl π-electrons. The $\Delta\nu$(OH) values for hydroxy ketones *IV* and *X* agree with an equatorial hydroxyl in the chair form of the ring A. However, in the spectrum of 3α-hydroxy-2-ketone *VIII* (which should have an axial hydroxyl in the chair form) the bands characteristic of an axial hydroxyl are very weak whereas the band at 3 493 cm^{-1} (corresponding to an equatorial hydroxyl) is very strong. This means that the ring A exists predominantly in a boat conformation in which the C—O and C=O bonds are almost coplanar. The same conclusion follows from the ^{1}H NMR spectra (Table I): for 2-oxo compounds *II*, *X* and *XXVIII* with chair conformation of the ring A (for conformation of *XXVIII* see ref.[15]) the coupling constant J(1α, 1β) is typically 12–13 Hz. The high value (17·9 Hz) found for hydroxy ketone *VIII* corresponds[16] to a boat conformation close to a classical boat with C(3) and C(10) in the stem-stern positions in which the C=O bond approximately bisects the H—C(1)—H angle

(in Newman projection). For 3α-acetoxy ketone *IX* the value of $J(1\alpha, 1\beta)$ (15 Hz) lies between the mentioned values; this may indicate that both the boat and chair conformations are comparably populated. In accord with the presence of boat form, compounds *VIII* and *IX* exhibit no long-range coupling between H-1β and H-3β which occurs in 2-oxo compounds existing in the chair form (see *II* and *XXVIII* where $J(1\beta, 3\beta) \sim 1{\cdot}5$ Hz).

For 2α-hydroxy- and 2α-acetoxy-3-ketones *IV* and *V* the vicinal coupling constants $J(1\alpha, 2)$ and $J(1\beta, 2)$ agree with the chair conformation of the ring A whereas the values for 2β-acetoxy-3-ketone *VII* correspond to those found for the boat form in other 2β-substituted 3-oxotriterpenoids[1,17].

As concerns the conformation of the ring A, the CD spectra afford no significant information: 3-ketones *IV* and *V* show a weak Cotton effect and all the 2-ketones (*VIII*–*XI*) exhibit a positive Cotton effect ($\Delta\varepsilon$ + 1·5 to +2·4) not very different from that of the unsubstituted 2-ketone *II* ($\Delta\varepsilon$ +2·2, ref.[15]). The values for compounds *V*, *IX*–*XI* are close to those published[7–9,17] for 4,4-dimethylsteroid and triterpenoid analogues.

TABLE I

Chemical shifts (δ, ppm) and coupling constants (J, Hz) of A-ring protons in ^{1}H NMR spectra of ketones

Compound[a]	Substituent in position		H-3	H-2	H-1α	H-1β	$J(1\alpha,2)$	$J(1\beta,2)$	$-J(1\alpha,1\beta)$
	2	3							
IV[b]	α-OH	=O	—	4·55	<1·7	2·52	12·8	6·8	13·0
V[c]	α-OAc	=O	—	5·62	<1·7	2·32	13·6	6·4	12·6
VII[c]	β-OAc	=O	—	5·64	[d]	[d]	11·4	8·6	[d]
VIII[b]	=O	α-OH	4·33	—	2·14	2·47	—	—	17·9
IX[c]	=O	α-OAc	5·03	—	2·17	2·42	—	—	15·0
XXVIII[e]	=O	α-Br	3·97	—	2·95	2·28	—	—	13·3
X[f]	=O	β-OH	3·87	—	2·02	2·56	—	—	12·2
XI[f,g]	=O	β-OAc	4·94	—	1·96	2·51	—	—	12·4
II[h]	=O	—	2·26(α) 2·17(β)	—	1·93	2·42	—	—	12·6

[a] For compounds *IV*–*VI* the parameters were obtained by first order analysis, for other compounds the system H-1α and H-1β was analysed as an AB system. The assignment of protons on C(1) is based on the long-range coupling between H-1α and 10β-CH_3, observed as broadening of the H-1α signal; [b] see ref.[6]; [c] other signal at 2·13 s (CH_3COO); [d] value not determined; [e] for preparation see ref.[2], $J(1\beta,3\beta) \sim 1{\cdot}3$; [f] $J(1\alpha,3\alpha) \sim 0{\cdot}8$; [g] other signal at 2·17 s (CH_3COO); [h] taken from ref.[5], $J(1\beta,3\beta) \sim 1{\cdot}5$.

TABLE II

Chemical shifts (δ, ppm) and coupling constants (J, Hz) of A-ring protons in ^{1}H NMR spectra of diols and their acetates

Compound[a]	Substituent in position		H-2[b]	H-3[c]	CH_3COO[d]	$J(2, 3)$	$\Sigma J(1, 2)$	$J(1\alpha, 2)$	$J(1\beta, 2)$
	2	3							
XII	α-OAc	α-OH	5·24	3·49	2·07	2·6	16·8	12·0	4·8
XIII	α-OH	α-OH	~3·97	~3·40	—	~3	~17	[e]	[e]
XIV	α-OAc	β-OH	4·97	3·17	2·07	10·4	16·0	11·6	4·4
XV	α-OH	β-OAc	3·80	4·51	2·12	10·1	15·8	11·1	4·7
XVIII	β-OAc	α-OH	4·92	3·73	2·06	9·5	14·6	~7	~7
XIX	β-OH	α-OAc	3·86	4·97	2·10	9·1	14·0	~7	~7
XXII	β-OAc	β-OH	5·20	3·29	2·06	~4	~7·5	~4	~4
XXIII	β-OH	β-OAc	4·12	4·63	2·14	3·6	6·5	~3	~3
XXIV	β-OAc	β-OAc	5·34	4·62	2·02 2·03	4·0	~7·5	~4	~4
XXV	β-OH	β-OH	4·12	3·21	—	4·1	~7	~3	~3

[a] Parameters obtained by first order analysis, accuracy: $\delta \pm 0{\cdot}01$, $J \pm 0{\cdot}3$ Hz, lower accuracy due to line overlap denoted ~; [b] doublet; [c] multiplet; [d] singlet; [e] value not determined.

TABLE III

Wavenumbers and intensities of the OH-stretching vibration bands in IR spectra of hydroxy ketones measured on Unicam SP 700 spectrometer in tetrachloromethane (c 1·7 to 2·5 . 10^{-3} mol. $.l^{-1}$), $B = (\pi/2)\,\Delta\nu_{1/2}\varepsilon$, $\Delta\tilde{\nu}$ refer to the corresponding alcohols without the keto group (see ref.[3]), f free, b bonded, sh shoulder

Ketone[a]		$\tilde{\nu}$ cm^{-1}	$\Delta\tilde{\nu}$ cm^{-1}	$\Delta\tilde{\nu}_{1/2}$ cm^{-1}	ε $l\,mol^{-1}\,cm^{-1}$	$B . 10^{-3}$ $l\,mol^{-1}\,cm^{-2}$
IV	b	3 488	132	60	47	4·4
VIII	f	3 621	17	17	6	0·2
	b	~3 605 sh	~33			
	b	3 493	145	52	56	4·6
X	b	3 491	142	44	55	3·8

[a] All the ketones have a very weak carbonyl overtone band at 3 390—3 405 cm^{-1} (ε 2—4).

The conformation of the ring A in the diols and their acetyl derivatives was derived from the vicinal coupling constants in the same manner as described in ref.[3]. For the compounds listed in Table II, a complete analysis of the four-spin systems of protons on the ring A (H-1α, H-1β, H-2 and H-3) was not possible because the H-1α and H-1β signals were obscured by other signals and could not be identified. Therefore, Table II contains first order constants which represent only approximate values and which can differ significantly from the real coupling constants. However, the constant $J(2, 3)$ and the sum of constants $J(1\alpha, 2)$ and $J(1\beta, 2)$ ($\sum J(1, 2)$) are sufficiently accurate within the experimental error limits (for a more detailed discussion see ref.[3]). In all the compounds the found values of J and $\sum J(1, 2)$ are very similar to those published[3,8] for analogous diols and diacetates of corresponding configurations; this means that also the conformation of the ring A is similar. In compounds of the 2α,3α- (*XII* and *XIII*), 2α,3β- (*XIV* and *XV*) and 2β,3β-configuration (*XXII* to *XXV*) these values are consistent with the chair conformation, in the case of 2β,3α--diol monoacetates *XVIII* and *XIX* the high values of $J(2, 3)$ and $\sum J(1, 2)$ indicate high population of the boat form. As described in ref.[3], the percentage of the boat form was estimated from $J(2, 3)$ and $\sum J(1, 2)$ using $J(2, 3) = 3$ Hz, $\sum J(1, 2) = 7$ Hz

TABLE IV

Wavenumbers and intensities of OH-stretching vibration bands in IR spectra of diols and their monoacetates. Spectra were measured on PE-684 spectrometer in tetrachloromethane (c 1·4 to 2·3 . 10^{-3} mol l^{-1}), ε were calculated without band separation, f free, b bonded

Compound[a]	Substituents in position		$\tilde{\nu}$, cm^{-1} (ε, l mol^{-1} cm^{-1})			
	2	3	f	f or b	b	b
XII	α-OAc	α-OH	~3 640 (13) sh	3 615 (65)	—	3 530 (2)
XIII	α-OH	α-OH	3 645 (45)	3 626 (48)	3 583 (56)	—
XIV	α-OAc	β-OH	—	3 624 (47)	3 570 (19)	—
XV	α-OH	β-OAc	~3 640 (8)sh	3 605 (38)	~3 590 (33)sh	~3 540 (13)sh
XVII[b]	α-OH	β-OH	3 633 (46)	—	3 596 (76)	—
XVIII	β-OAc	α-OH	—	3 621 (53)	3 580 (16)	—
XIX	β-OH	α-OAc	—	3 616 (52)	3 583 (20)	—
XXI[b]	β-OH	α-OH	3 634 (52)	—	3 594 (52)	—
XXII	β-OAc	β-OH	~3 635 (8)sh	3 608 (41)	~3 580 (15)	~3 540 (11)sh
XXIII	β-OH	β-OAc	—	3 610 (70)	~3 570 (4)	—
XXV	β-OH	β-OH	3 635 (62)	—	3 583 (46)	

[a] All the monoacetates show a very weak broad band in the region 3 450—3 480 cm^{-1} (ε 3—6) due to overlap of carbonyl overtone with intermolecularly bonded OH band; [b] taken from ref.[3].

and $J(2, 3) = 12$ Hz, $\sum J(1, 2) = 18{\cdot}2$ Hz, as characteristic values for the chair and boat form, respectively (see method *D* in ref.[3]). Thus, the found population of the boat form in compound *XVIII* is 72% (from $J(2, 3)$) and 68% (from $\sum J(1, 2)$); for acetate *XIX* the respective numbers are 68% and 63%. Similar populations (about 60%) have been reported[3] for 2β,3α-diol *XXI* (in pyridine where the boat is not stabilized by the hydrogen bonding) and its diacetate *XX*.

The infrared spectra in the OH stretching region of the isomeric 2,3-diols and their monoacetates are compared in Table IV. For diols *XIII*, *XVII*, *XXI* and *XXV* both the positions and intensities of the free ($3\,626-3\,645$ cm^{-1}) and intramolecularly bonded ($3\,583-3\,596$ cm^{-1}) hydroxyl bands agree well with those published for analogous diols[8]. The presence of a bonded hydroxyl band in the spectrum of 2β,3α- diol *XXI* indicates a boat conformation of the ring A (see also ref.[3]). A more complex situation exists in the monoacetates because in their molecules the hydroxyl can be hydrogen-bonded to *n*-electrons of the ether or carbonyl oxygen or to π-electrons; moreover, various rotamers of the C—O bonds in the hydroxyl as well as the ester group may exist. Spectra of some monoacetates (*XV*, *XXII*) exhibit up to four bands in the ν(OH) region. The weak absorptions at about $3\,640$ cm^{-1} are probably due to a suitable rotamer of the free OH group. The broad bands at about $3\,540$ and $3\,580$ cm^{-1} can be safely ascribed to bonded hydroxyl whereas the narrow bands at $3\,605-3\,624$ cm^{-1} may be due to either free hydroxyl or a hydroxyl engaged in a weak hydrogen bond[18]. The mentioned broad bands are strong in monoacetates *XIV*, *XV* and *XXII* with equatorial hydroxyl, whereas in compounds with axial hydroxyl (*XII*, *XXIII*) they are very weak. In the chair form of 2β,3α-diol monoacetates *XVIII* and *XIX* an intramolecular hydrogen bond is not possible and therefore the band at about $3\,580$ cm^{-1} confirms the presence of a boat form, in accord with the ^{1}H NMR results.

EXPERIMENTAL

The melting points were determined on a Kofler block and are uncorrected. Optical rotations were measured in chloroform (*c* 0·4—0·9) on an automatic polarimeter ETL-NPL (Bendix–Ericsson); accuracy ±2°. IR spectra were recorded in chloroform on a PE 684 (Perkin–Elmer) spectrometer; wavenumbers are given in cm^{-1}. CD spectra were taken in dioxane on a Dichrographe II (Roussel–Jouan) instrument, ^{1}H NMR spectra were obtained with a Tesla BS 487A (80 MHz, CW-mode) spectrometer in deuteriochloroform with hexamethyldisiloxane (HMDS) as internal standard; chemical shifts are referenced to tetramethylsilane as standard (δ(HMDS) = 0·06). The chemical shifts and coupling constants were obtained from expanded spectra (1 Hz/cm). All the studied compounds exhibited signals due to H-19 (δ 3·50—3·54, s), H-28 (*exo*) (δ 3·42 to 3·46, d), H-28 (*endo*) (δ 3·75—3·80, bd) and seven singlets of methyl protons in the region 0·6—1·25. The other signals are given in Tables I and II. Mass spectra were measured on a Varian MAT 311 instrument (electron energy 70 eV, direct inlet at 120—240°C). Column chromatography was performed on silica gel Silpearl (Kavalier, Votice), the reactions were monitored and the purity checked by thin-layer chromatography (TLC) on silica gel G (Merck; detection

by spraying with 10% sulfuric acid and heating) or on Silufol sheets (Kavalier, Votice; detection by spraying with 10% ethanolic phosphomolybdic acid and heating). Preparative TLC was carried out on silica gel G (Merck; detection by UV light after spraying with 0·2% solution of morin in methanol). Analytical samples were dried at 100°C over phosphorus pentoxide in vacuo (about 25 Pa).

Acetylation was performed by treatment with a mixture of acetic anhydride–pyridine (1 : 10) at room temperature for 20—48 h, decomposition with ice and the usual work-up. „The usual work-up procedure" denotes the following procedure: the reaction mixture was diluted with water, the products were extracted with ether, the ethereal solution was washed with dilute (1 : 4) hydrochloric acid or a solution of sodium hydrogen carbonate (as required), with water, dried over sodium sulfate and the ether was distilled off.

Isomerization of 19β,28-Epoxy-2α-hydroxy-18α-oleanan-3-one (*IV*) and 19β,28-Epoxy-3α-hydroxy-18α-oleanan-2-one (*VIII*)

The hydroxy ketones *IV* (m.p. 226—230°C, $[\alpha]_D$ +46°; CD spectrum: $\Delta\varepsilon$ +0·48 (294 nm)) and *VIII* (m.p. 229—232°C, $[\alpha]_D$ +114°, CD spectrum: $\Delta\varepsilon$ +1·53 (290 nm)) were prepared as described[6]. A solution of *IV* (50 mg) in a mixture of methanol (2 ml) and dichloromethane (1 ml) containing 0·08% (v/v) of sulfuric acid was set aside for 2 days at room temperature and then processed in the usual manner. According to TLC and ^{1}H NMR spectra, the mixture contained only the hydroxy ketones *IV* and *VIII*. The optical rotation ($[\alpha]_D$ +72°) corresponded to 62% of *IV*; the ^{1}H NMR spectrum (ratio of integrated intensities of H-2β in *IV* and H-3β in *VIII*) showed 70% of *IV*. The equilibrium mixture obtained in the same manner from the hydroxy ketone *VIII* had $[\alpha]_D$ +71° (63% of *IV*), according to ^{1}H NMR spectrum the content of *IV* was 68%. Six crystallizations of the equilibrium mixtures from chloroform–heptane afforded *VIII* (yield 10—15%). When the isomerization time was prolonged (14 days) the reaction mixtures contained hydroxy ketone *X* (TLC).

19β,28-Epoxy-3β-hydroxy-18α-oleanan-2-one (*X*)

A) A solution of hydroxy ketone *IV* (250 mg) in a mixture of methanol (10 ml) and dichloromethane (5 ml), containing 1% (v/v) of sulfuric acid, was set aside at room temperature for 2 days. The usual work-up procedure, followed by crystallization from methanol, afforded hydroxy ketone *X* (220 mg; 88%), m.p. 234—238°C, $[\alpha]_D$ +40°. IR spectrum: 3 490 (OH); 1 708 (C=O); 1 033 (C—O—C). CD spectrum: $\Delta\varepsilon$ +2·40 (289 nm). Mass spectrum, *m/z* (%): 456 (M^+, 80), 385 (40), 383 (40), 369 (16), 323 (9), 313 (7), 245 (18), 81 (100). For $C_{30}H_{48}O_3$ (456·7) calculated: 78·90% C, 10·59% H; found: 78·99% C, 10·61% H. The hydroxy ketone *X* was prepared in the same manner also from the isomer *VIII* in 84% yield.

B) A solution of hydroxy ketone *IV* (70 mg) in acetone (5 ml), containing 2% (v/v) of sulfuric acid, was refluxed for 10 min. The reaction mixture was diluted with water, the product was collected and crystallized from methanol. The obtained product *X* (55 mg; 79%) was identical with the substance obtained under *A*).

C) Hydroxy ketone *IV* (110 mg) in benzene (2 ml) was adsorbed on neutral alumina (Reanal, activity II; 3 g). After 2 days the hydroxy ketone *X* (95 mg, 86%, after crystallization from acetone) was eluted with ether. Compound *X* was obtained in the same manner also from the isomer *VIII*.

D) A mixture of acetoxy ketone *VII* (30 mg), methanol (15 ml) and 10% aqueous potassium hydrogen carbonate solution (1 ml) was allowed to stand at room temperature for 3 days under nitrogen. The usual work-up and crystallization from acetone gave 20 mg (73%) of *X*, identical with the sample obtained under *A*).

2α-Acetoxy-19β,28-epoxy-18α-oleanan-3-one (*V*)

The title ketone *V* was obtained by acetylation of hydroxy ketone *IV* in 89% yield; m.p. 231 to 234°C (chloroform–methanol); $[\alpha]_D$ +47°. IR spectrum: 1 750 and 1 255 ($OCOCH_3$); 1 731 (C=O); 1 036 (C—O—C). CD spectrum: $\Delta\varepsilon$ +0·12 (314 nm), 0 (300 nm), −0·23 (280 nm). Mass spectrum, *m/z* (%): 498 (M^+, 15), 483 (2), 456 (4), 438 (10), 427 (22), 367 (4), 245 (7), 43 (100). For $C_{32}H_{50}O_4$ (498·8) calculated: 77·06% C, 10·10% H; found: 77·38% C, 10·22% H.

2β-Acetoxy-19β,28-epoxy-18α-oleanan-3-one (*VII*)

Pyridinium chlorochromate (30 mg) was added to a solution of *XVIII* (85 mg) in dichloromethane (2 ml). After standing for 2 days at room temperature, the mixture was poured on a column of silica gel (3 g) and the product was eluted with ether. Crystallization from acetone afforded *VII* (60 mg; 71%), m.p. 266–272°C; $[\alpha]_D$ + 120°. IR spectrum: 1 740, 1 250 ($OCOCH_3$); 1 724 (C=O); 1 032, 1 023 (C—O—C). For $C_{32}H_{50}O_4$ (498·8) calculated: 77·06% C, 10·10% H; found: 77·21% C, 10·19% H.

3α-Acetoxy-19β,28-epoxy-18α-oleanan-2-one (*IX*)

The title ketone *IX* was obtained by acetylation of hydroxy ketone *VIII* in 82% yield; m.p. 285 to 290°C (chloroform–methanol); $[\alpha]_D$ +68°. IR spectrum: 1 743, 1 253 ($OCOCH_3$); 1 724 (C=O); 1 033 (C—O—C). CD spectrum: $\Delta\varepsilon$ +1·47 (291 nm). Mass spectrum, *m/z* (%): 498 (M^+, 17), 483 (1), 480 (2), 456 (6), 438 (17), 427 (30), 367 (5), 245 (9), 202 (85), 43 (100). For $C_{32}H_{50}O_4$ (498·8) calculated: 77·06% C, 10·10% H; found: 77·10% C, 10·39% H.

3β-Acetoxy-19β,28-epoxy-18α-oleanan-2-one (*XI*)

The acetate *XI* was prepared by acetylation of *X* in 92% yield; m.p. 288–291°C (chloroform–methanol), $[\alpha]_D$ +98°. IR spectrum: 1 744, 1 250 ($OCOCH_3$); 1 726 (C=O); 1 048, 1 030 (C—O—C). CD spectrum: $\Delta\varepsilon$ +2·30 (302 nm). Mass spectrum, *m/z* (%): 498 (M^+, 32), 483 (9), 480 (4), 456 (11), 438 (68), 427 (79), 423 (37), 245 (11), 203 (87), 149 (93), 95 (100). For $C_{32}H_{50}O_4$ (498·8) calculated: 77·06% C, 10·10% H; found: 77·03% C, 10·28% H.

19β,28-Epoxy-18α-oleanane-2,3-dione (*XXVI*)

A) A mixture of *VII* (30 mg), methanol (10 ml) and 10% aqueous potassium hydrogen carbonate solution (1 ml) was stirred in the presence of air for 6 h. After standing overnight at room temperature the mixture was processed as usual and the product was crystallized from ether to give 25 mg (91%) of diketone *XXVI*, m.p. 226–227°C; $[\alpha]_D$ +99° (reported[11] m.p. 223–225°C, $[\alpha]_D$ +97°). IR spectrum: 3 450 (OH), 1 666, 1 644 (O=C—C=C); 1 059, 1 031 (C—O—C).

B) A stream of air was introduced for 6 h into a solution of *IV* (650 mg) and sodium hydroxide (12 g) in ethanol (250 ml). The mixture was concentrated to 50 ml under diminished pressure, diluted with water, and the separated product was collected and purified by chromatography on silica gel (15 g) in light petroleum–ether (6 : 1). Crystallization from acetone afforded diketone *XXVI* (520 mg; 78%), m.p. 224–227°C, identical with the sample prepared under *A*).

Reaction of 2α,3α;19β,28-Diepoxy-18α-oleanane (*III*) with Acetic Acid

A) A mixture of epoxide *III* (ref.[4]; 250 mg) and 5% solution of sodium acetate in acetic acid (20 ml) was stirred to dissolution (4 h) and then set aside at room temperature for 12 days. After

the usual work-up the products were separated by chromatography on silica gel (20 g) in light petroleum–ether (8 : 1). Two products were obtained. 19β,28-Epoxy-18α-oleanane-2β,3α-diol 2-acetate (*XVIII*; 86 mg, 30%), m.p. 249–252°C (chloroform–methanol), $[\alpha]_D$ +91°. IR spectrum: 3 607, 3 443 (OH); 1 728, 1 254 ($OCOCH_3$); 1 030 (C—O—C). For $C_{32}H_{52}O_4$ (500·8) calculated: 76·75% C, 10·47% H; found: 76·58% C, 10·38% H. 19β,28-Epoxy-18α-oleanane-2β, 3α-diol 3-acetate (*XIX*; 92 mg, 32%), m.p. 246–249°C (ether), $[\alpha]_D$ +75°. IR spectrum: 3 625 (OH); 1 737, 1 255 ($OCOCH_3$); 1 037 (C—O—C). For $C_{32}H_{52}O_4$ (500·8) calculated: 76·75% C, 10·47% H; found: 76·58% C, 10·39% H.

B) A solution of epoxide *III* (130 mg) in acetic acid (3 ml) was refluxed for 6 h and then processed in the usual manner. Crystallization from methanol afforded diacetate *XX* (115 mg; 74%), m.p. 202–203°C, identical with the compound described in ref.[2] (reported[2] m.p. 202 to 204°C). The diacetate *XX* was also obtained by treatment of *III* with 1% solution of sulfuric acid in acetic acid at room temperature for 2 days and acetylation of acetates *XVIII* and *XIX*.

Reduction of 2α-Acetoxy-19β,28-epoxy-18α-oleanan-3-one (*V*)

Sodium borohydride (200 mg) in methanol (5 ml) was added to a solution of *V* (350 mg) in benzene (5 ml). After standing at room temperature overnight the mixture was worked up as usual and the residue was chromatographed on a column of silica gel (40 g). Elution with light petroleum–ether (6 : 1) afforded in succession three products. 19β,28-Epoxy-18α-oleanane-2α,3α-diol 2-acetate (*XII*, 45 mg, 13%), m.p. 223–226°C (methanol), $[\alpha]_D$ +13°. IR spectrum: 3 610 to 3 500 (OH); 1 721, 1 249 ($OCOCH_3$); 1 030 (C—O—C). For $C_{32}H_{52}O_4$ (500·8) calculated: 76·75% C, 10·47% H; found: 76·63% C, 10·49% H. 19β,28-Epoxy-18α-oleanane-2α,3β-diol 2-acetate (*XIV*, 210 mg, 60%), m.p. 256–259°C (chloroform–methanol), $[\alpha]_D$ +8°. IR spectrum: 3 623, 3 580–3 550 (OH); 1 729, 1 253 ($OCOCH_3$); 1 032 (C—O—C). For $C_{32}H_{52}O_4$ (500·8) calculated: 76·75% C, 10·47% H; found: 76·67% C, 10·37% H. 19β,28-Epoxy-18α-oleanane-2α, 3β-diol 3-acetate (*XV*, 15 mg, 4%), m.p. 234–236°C (methanol), $[\alpha]_D$ +35°. IR spectrum: 3 610–3 595 (OH); 1 730, 1 255 ($OCOCH_3$); 1 031 (C—O—C). For $C_{32}H_{52}O_4$ (500·8) calculated: 76·75% C, 10·47% H; found: 76·61% C, 10·33% H.

Acetates *XIV* and *XV* were acetylated to give diacetate *XVI*, identical with the sample prepared in ref.[2]; m.p. 245–248°C (chloroform–ethanol); $[\alpha]_D$ +20° (reported[2] m.p. 247–249°C, $[\alpha]_D$ +18°).

Reduction of 3α-Acetoxy-19β,28-epoxy-18α-oleanan-2-one (*IX*)

Acetoxy ketone *IX* (64 mg) was treated analogously as described for the reduction of *V*. Preparative TLC on silica gel in light petroleum–ether (3 : 1) followed by crystallization from ether gave 2β,3α-diol 3-acetate *XIX* (42 mg; 65%), identical with the sample prepared from *III*.

Reduction of 3β-Acetoxy-19β,28-epoxy-18α-oleanan-2-one (*XI*)

A) Sodium borohydride (120 mg) was added portionwise at −18°C to a solution of *XI* (1·6 g) in a mixture of benzene (60 ml) and methanol (20 ml). After standing at −18°C for 12 h, boric acid (80 mg) was added and the mixture was poured on ice and extracted three times with ether precooled to 0°C. The ethereal layer was washed with water, dried over sodium sulfate and the solvent was evaporated under diminished pressure. Crystallization of the residue from ether–methanol afforded 1·4 g (87%) of 19β,28-epoxy-18α-oleanane-2β,3β-diol 3-acetate (*XXIII*), m.p. 248–250°C; $[\alpha]_D$ +64°. IR spectrum: 3 598, 3 500–3 400 (OH); 1 728, 1 248 ($OCOCH_3$); 1 031 (C—O—C). For $C_{32}H_{52}O_4$ (500·8) calculated: 76·75% C, 10·47% H; found: 76·96% C, 10·41% H.

B) Acetoxy ketone *XI* was reduced as described under *A*), except that the reaction and the work-up were carried out at room temperature. The product mixture was separated by chromatography on a silica gel column. Elution with light petroleum–ether (6 : 1) afforded 47% of acetate *XXIII*, identical with the product obtained under *A*), and 37% of 19β,28-epoxy-18α-oleanane-2β,3β-diol 2-acetate (*XXII*), m.p. 296–299°C (methanol); $[\alpha]_D$ +57°. IR spectrum: 3 599 (OH); 1 731, 1 249 ($OCOCH_3$); 1 032 (C—O—C). For $C_{32}H_{52}O_4$ (500·8) calculated: 76·75% C, 10·47% H; found: 76·49% C, 10·64% H.

C) Acetoxy ketone *XI* (200 mg) was reduced as described under *B*) except that an excess of the hydride (150 mg) was used. Crystallization from chloroform–methanol gave 160 mg (67%) of 19β,28-epoxy-18α-oleanane-2β,3β-diol (*XXV*), m.p. 302–304°C, $[\alpha]_D$ +59°. IR spectrum: 3 625, 3 600–3 550 (OH); 1 053, 1 031 (C—O—C). For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·49% C, 10·93% H. The diol *XXV* was obtained in the same manner also from hydroxy ketone *X* in 90% yield.

19β,28-Epoxy-18α-oleanane-2α,3α-diol (*XIII*)

Methanolic sodium hydroxide (2%, 2 ml) was added to a solution of acetate *XII* (30 mg) in benzene (1 ml). After reflux for 2 h the mixture was concentrated to 1 ml and cooled. The separated product was filtered and crystallized from methanol; yield 20 mg (73%) of *XIII*, m.p. 287–289°C $[\alpha]_D$ +46°. IR spectrum: 3 640–3 550 (OH); 1 030 (C—O—C). For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·42% C, 11·12% H.

19β,28-Epoxy-18α-oleanane-2β,3β-diol Diacetate (*XXIV*)

The title compound was prepared by acetylation of monoacetates *XXII* and *XXIII* or diol *XXV*; m.p. 206–208°C (ethanol); $[\alpha]_D$ +56°, IR spectrum: 1 739, 1 255 ($OCOCH_3$); 1 032 (C—O—C). For $C_{34}H_{54}O_5$ (542·8) calculated: 75·23% C, 10·03% H; found: 75·40% C, 9·84% H.

Isomerization of Diol Monoacetates *XIV*, *XV*, *XVIII*, *XIX*, *XXII* and *XXIII*

The isomerization was performed with both isomers of the same configuration using the following two procedures:

A) The monoacetate (30 mg) was dissolved in 2% solution of sodium acetate in acetic acid (1 ml). After standing at room temperature for 2 days the mixture was worked up in the usual manner.

B) The monoacetate (30 mg) was dissolved in ether (10 ml) which had been shaken with dilute (1 : 4) hydrochloric acid. After standing at room temperature for 6 h the mixture was processed as usual. The ratio of the monoacetates in the equilibrium mixtures was estimated from TLC. According to TLC, the mixtures contained no diols or diacetates. The equilibrium mixtures of isomeric monoacetates of the same configuration were combined and both monoacetates were separated by preparative TLC on silica gel (10 g) in light petroleum–ether (1 : 1).

The mixtures of 2α,3β-diol monoacetates *XIV* and *XV* (*XIV* : *XV* = 1 : 1) afforded 35% of *XIV* and 38% of *XV*; mixtures of 2β,3α-diol monoacetates *XVIII* and *XIX* (1 : 1) gave 39% of *XVIII* and 37% of *XIX*; mixtures of 2β,3β-diol monoacetates *XXII* and *XXIII* (2 : 3) furnished 32% of *XXII* and 52% of *XXIII*.

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