CONFORMATION OF RING A OF 2,3-DISUBSTITUTED TRITERPENES WITH CHLORINE OR ALKOXY GROUP IN THE POSITION 2*

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Chloro, methoxy and ethoxy derivatives of 19β,28-epoxy-18α-oleanane *II*—*VII*, *IX*—*XV* were prepared by stereospecific procedures from epoxides *I* and *VIII* and olefin *XVII*. The conformation of ring A in these derivatives has been derived on the basis of infrared, ultraviolet and ^{1}H-NMR spectra and circular dichroism. In 3-oxo derivatives *V*—*VII* the ring A is practically entirely in boat form. In chlorohydrins and alkoxy alcohols of 2β,3α-configuration the boat form prevails highly; if chlorine is present in the position 2β, the content of the chair form is negligibly low, if an oxygen function is present in this position about 15% of the chair form is present at conformational equilibrium. In acid catalysed equilibrium mixture of isomeric 2-chloro-3-oxo derivatives *V* and *XII* and 2-methoxy-3-oxo derivatives *VI* and *XIII* the 2α-isomer prevails slightly (~57%), similarly as in 2-bromo-3-oxo derivatives.

In steroid and triterpenoid derivatives containing two methyl groups in the position 4 and a further substituent in the position 2β it was found that the boat form of the ring A may be more stable than the chair form. This phenomenon was observed predominantly in bromoketones and bromohydrins and in some instances also in fluoroketones, acetoxy ketones, dibromo derivatives, diols, and their acetates (ref.[1-10] and the references therein). The position of the equilibrium of the boat and the chair form of the ring A depends mainly on the magnitude of 1,3-*syn*-axial interactions between the 2β substituent and the 4β and 10β methyl groups, and on the possibility of stabilization of the boat form by an intramolecular hydrogen bond[5,6,8-10]. In this paper we discuss the effect of chlorine, methoxy and ethoxy group in the position 2 on the conformation of the ring A in 3-oxo derivatives and 3-hydroxy derivatives of 19β,28-epoxy-18α-oleanane. Analogous 2-methoxy-3-oxo derivatives, isomeric at $C_{(2)}$, were prepared in the 4,4-dimethyl-5α-cholestane series by Sigg and Tamm[11] by substitution reaction with sodium methoxide from 2α-bromo-3-oxo derivative; on the basis of infrared spectra these authors inferred that in the 2β-isomer the ring A is predominantly in the boat form.

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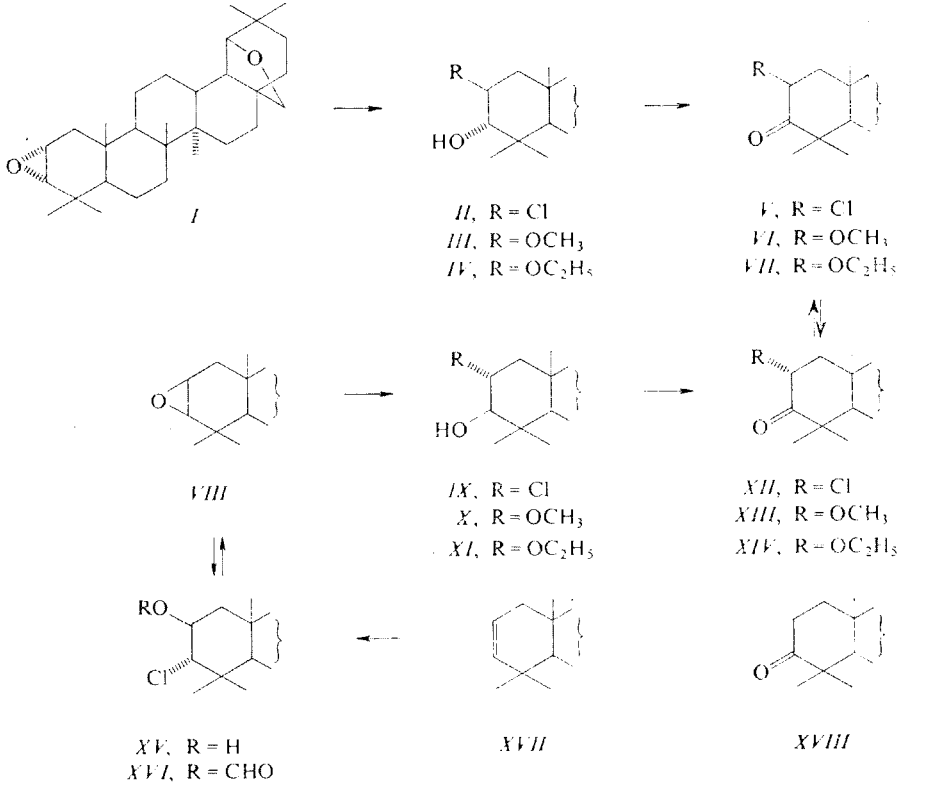
For the preparation of chlorohydrins and alkoxy alcohols *II*–*IV*, *IX*–*XI* we made use of the known course of opening of triterpenic 2,3-epoxides: the 2α,3α-epoxide *I* opens according to the Fürst–Plattner rule, affording 2β,3α-derivatives exclusively, while the 2β,3β-epoxide *VIII* reacts to 90% anomalously, giving rise to diequatorial 2α,3β-derivatives[7]. The corresponding ketones were prepared by oxidation with sodium dichromate in a buffered medium (acetic acid, sodium acetate), in order to prevent isomerizations in the position 2 during oxidation (*cf.*[5,7]). On reaction of α-epoxide *I* with hydrochloric acid 2β-chloro-3α-hydroxy derivative *II* was formed as the sole product which regenerated epoxide *I* under the effect of potassium hydroxide. Its oxidation gave 2β-chloro ketone *V* which on reduction with zinc afforded the known[12] ketone *XVIII*. From the β-epoxide *VIII* 2α-chloro-3β-hydroxy derivative *IX* was obtained under the effect of hydrochloric acid as the main product in addition to a small amount of 2β-hydroxy-3α-chloro derivative *XV*. The second product was also prepared by a procedure elaborated earlier[13] for the preparation of an analogous bromohydrin: on reaction of olefin *XVII* with chlorine in dimethylformamide in the presence of silver perchlorate a mixture of chlorohydrin *XV* and 2β-formyloxy-



-3α-chloro derivative *XVII* was obtained. Both chlorohydrins *IX* and *XV* and formate *XVI* give rise to β-epoxide *VIII* under the effect of hydroxides. Oxidation of chlorohydrin *IX* gave 2α-chloro ketone *XII* which was converted to ketone *VIII* with zinc. All these reactions have their counterparts in corresponding bromo derivatives[3,5-7] and they confirm the structure and the configuration of the prepared derivatives. Methoxy alcohols *III* and *X* and ethoxy alcohols *IV* and *XI* were prepared from epoxides *I* and *VIII* under the effect of methanol or ethanol and catalysis with sulfuric acid. 2-Alkoxy-3-oxo derivatives *VI*, *VII*, *XIII* and *XIV*, obtained by their oxidation, are instable and melt within a broad temperature range under decomposition. Only thin-layer chromatography could be used as a criterion of their sterical purity, and in the case of methoxy ketones *VI* and *XIII* ^{1}H-NMR spectra were also used: as the singlet of the methoxy group appears in the 2β-isomer *VI* at 3·37 p.p.m., while in isomer *XIII* it is at 3·40 p.p.m., it was possible to check the admixture of one isomer in the other on the basis of spectral data.

In our recent studies[7,12] we have demonstrated that the thermodynamical stabilities of triterpenic 2α-bromo-3-oxo and 2β-bromo-3-oxo derivatives are approximately equal: for the content of 2β-bromo ketone in the equilibrium mixture obtained by acid catalysed isomerization of derivatives of 19β,28-epoxy-18α-oleanane we found the value 42 ± 3%, for derivatives of 20β,28-epoxy-18α,19β*H*-ursane it was 40 ± 3%. Therefore, it was interesting to determine the position of the equilibrium for ketones *V*–*VII* and *XII*–*XIV*, containing a chlorine atom or an alkoxy group in the position 2. Both chloro ketones *V* and *XII* were isomerized (using hydrochloric acid) to a mixture which according to optical rotation contained 43 ± 5% of 2β-chloro-ketone *V*. In the case of methoxy ketones *VI* and *XIII* the determination of the equilibrium was complicated by the fact that their decomposition took place both in acid and in alkaline medium. Therefore, the isomerization course was followed chromatographically on silica gel thin layers and the isomerization was interrupted before the equilibrium was attained, during the formation of the first traces of the decomposition products. From the optical rotation values of the mixtures formed the content of the 2β-isomer *XIII* at equilibrium has been evaluated, 43 ± 10%. In the case of ethoxy ketones *VII* and *XIV* the position of the equilibrium could not be determined, due to their rapid decomposition. All the data mentioned above are in good agreement within the experimental errors; a similar agreement was also observed by Levisalles and Rudler–Chauvin[10] when comparing the composition of the equilibrium mixtures of isomeric 2-fluoro and 2-bromo derivatives of 4,4-dimethyl-5α-cholestan-3-one. From this it follows that the differences in character of polar substituents (such as F, Cl, Br, OCH_3) have no, or only a negligible, effect on the position of equilibrium in 4,4-dimethyl-3-ketones substituted on $C_{(2)}$.

In Tables I and II spectral data of ketones *V*–*VII* and *XII*–*XIV* are summarized, from which the following conclusions may be drawn concerning the conformation of the ring A. It is known[14,15] that the equatorial halogen shifts the stretching vibration

TABLE I

Characteristic Spectral Parameters of 3-Oxo Derivatives

Compound	Substituent in the position 2	Infrared spectra[a]		Circular dichroism[b]		
		ν(CO) cm^{-1}	$\Delta\nu$(CO) cm^{-1}	λ nm	$\Delta\varepsilon$	Γ nm
V	β-Cl	1 737	+29	288[c]	+2·8	36
VI	β-OCH_3	1 728	+20	300[c]	+2·0	37
VII	β-OC_2H_5	1 727	+19	298[c]	+2·9	37
XII	α-Cl	1 731[d]	+23	310	+0·23	23
				~275	−0·12	~30
XIII	α-OCH_3	1 721[d]	+13	316[c]	+0·52	35
XIV	α-OC_2H_5	1 721[d]	+13	~316	+0·45	~37
XVIII	—	1 708	—	330[e]	−0·024	7
				293[e]	+0·71	35

[a] Measured in 0·5% tetrachloromethane solutions in cells 1 mm thick, on a UR-20 spectrophotometer calibrated in the carbonyl region with atmospheric water vapour; accuracy ±1 cm^{-1}; [b] measured in dioxan on a Roussel–Jouan 185 Dichrographe; [c] the band displays a vibrational structure; [d] a further weak band or a shoulder at about 1 710–1 713 cm^{-1}, similarly as in the analogous bromo ketone[12]; [e] taken from literature[19].

of the carbonyl group to higher frequencies, while the axial halogen affects it only negligibly. Similar shifts, but slightly less distinct, were also observed in equatorial and axial methoxy ketones[16–18]. The shifts of the carbonyl frequencies (ν(CO)) in chloro, methoxy and ethoxy ketones *V*–*VII* and *XII*–*XIV*, when compared with unsubstituted ketone *XVIII*, correspond to the situation when the substituent in the position 2 is equatorial in all these derivatives. This means that the 2α-isomers *XII* to *XIV* have their A ring in chair form, while the 2β-isomers *V*–*VII* have them in boat form. As no further band in the region about 1 710 cm^{-1} has been observed in 2β-isomers *V*–*VII*, which would indicate the presence of the form with an axial substituent, the content of the chair form in the conformational equilibrium must be very low. The C—O—C vibrations in alkoxy ketones *VI*, *VII*, *XIII* and *XIV* also correspond according to ref.[16] to an equatorial conformation of alkoxy groups (~1 120 cm^{-1}); in axial methoxy ketones these vibrations are shifted[16] to the region about 1 080 cm^{-1}. In methoxy ketones *VI* and *XIII* these conclusions were also corroborated by ultraviolet spectra. Both isomers *VI* and *XIII* have their $n \rightarrow \pi^*$ transition band of the carbonyl group at 291 nm (ε = 37 or 40, resp.)*, *i.e.*, they display a small hypso-

* The centre of the absorption band is given; in both methoxy ketones the bands have a distinct vibrational structure (in cyclohexane).

chromic shift only, relatively to ketone *XVIII* (294 nm, $\varepsilon = 36$). The axial methoxyketones are characterized by a large bathochromic shift[17,18]. The circular dichroism of ketones *V*–*VII* and *XII*–*XIV* is similar as in analogous 2-bromo-3-oxo derivatives[4,5]: for 2α-isomers with the ring A in chair form a weakly positive Cotton effect

TABLE II

Coupling Constants and Chemical Shifts of Protons in Ring A in 3-Oxo Derivatives

Measured at 100 MHz on a Varian HA-100 instrument in deuteriochloroform, using tetramethylsilane as internal standard; analysed as an ABX system; the coupling constants in Hz, accuracy ±0·3 Hz; chemical shifts in p.p.m. (δ-scale).

Compound	Substituent in the position 2	$J_{1\alpha,2}$	$J_{1\beta,2}$	$-J_{1\alpha,1\beta}$	δ_{2H}	$\delta_{1\alpha H}$	$\delta_{1\beta H}$
V	β-Cl	10·9	9·2	13·4	4·96	2·44	1·87
VI	β-OCH_3	10·8	8·0	~14	4·23	2·19	<1·70
XII	α-Cl	13·2	6·1	12·7	4·92	1·60	2·57
XIII	α-OCH_3	11·2	6·2	12·5	4·04	<1·70	2·36

TABLE III

Frequencies and Intensities of the OH Stretching Vibrations

Measured in $5-8 \cdot 10^{-3}$M solutions in tetrachloromethane, using a grating Unicam SP 700 spectrophotometer; accuracy ±2 cm^{-1}; f free, b bonded; $B = \pi/2 \cdot \varepsilon^{(a)} \cdot \Delta\nu_{1/2}^{(a)}$; $\Delta\nu$(OH) are taken with reference to the corresponding unsubstituted alcohols (see[8]).

Compound	Substituent in position 2	Substituent in position 3	ν(OH) cm^{-1}	Δν(OH) cm^{-1}	$\varepsilon^{(a)}$ $l \cdot mol^{-1} \cdot cm^{-1}$	$\Delta\nu_{1/2}^{(a)}$ cm^{-1}	$B \cdot 10^{-3}$ $l \cdot mol^{-1} \cdot cm^{-2}$
II	β-Cl	α-OH	b 3 595	43	64	24	2·4
III	β-OCH_3	α-OH[a]	f 3 638	0	13	20	0·4
			b 3 586	52	50	34	2·7
IV	β-OC_2H_5	α-OH[a]	f 3 638	0	11	17	0·3
			b 3 583	55	46	32	2·3
IX	α-Cl	β-OH	b 3 597	36	68	23	2·5
X	α-OCH_3	β-OH	b 3 594	39	67	31	3·3
XI	α-OC_2H_5	β-OH	b 3 592	41	56	30	2·6
XV	β-OH	α-Cl[a]	f 3 622	0	14	15	0·33
			b 3 584	38	64	20	2·0

[a] After graphical separation.

is characteristic, for 2β-isomers in boat form, a strongly positive Cotton effect is observed; however, the values $\Delta\varepsilon$ are in 2β-chloro and 2β-alkoxy ketones *V*–*VII* slightly lower than in 2β-bromo ketones[5]. The vicinal coupling constants $J_{1\beta,2}$ and $J_{1\alpha,2}$ (Table II) of chloroketones *V* and *XII* and methoxy ketones *VI* and *XIII* correspond to the values found for triterpenic 2-bromo-3-oxo derivatives and 2-acetoxy--3-oxo derivatives[4]. In the case of the 2β-isomers *V* and *VI* these coupling constants exclude the existence of the ring A in chair form and indicate that the geometry of the boat form is very similar to the geometry in 2β-bromo and 2β-acetoxy derivatives[4]. These results, together with the results published for bromo ketones[3-5,12], fluoro ketones[10] and acetoxy ketones[4] lead to the conclusion that in triterpenoid and 4,4-dimethylsteroid 3-oxo derivatives the 1,3-*syn*-axial interactions of any of the mentioned 2β-substituents (F, Cl, Br, OCH_3, OC_2H_5, $OCOCH_3$) with 4β and 10β-methyl groups destabilize the chair form of the ring A to such an extent that the conformational equilibrium is shifted practically totally to the boat form side.

For the determination of the ring A conformation in chlorohydrins and alkoxy alcohols the frequencies and intensities of the OH stretching vibrations in the infrared spectra were used (Table III), similarly as in the case of 2,3-bromohydrins and diols[8]. The shifts of the bonded hydroxyl bands ($\Delta\nu$(OH)) are comparable with those found for bromohydrins and diols[8]; the values of apparent integrated intensities B are approximately equal in chlorohydrins as in bromohydrins, while in ethoxy alcohols and especially in methoxy alcohols they are distinctly higher. In the case of diequatorial 2α,3β-isomers *IX*–*XI* with the ring A in chair form the spectrum contains a band of a bonded hydroxyl only. 2β-Chloro-3α-hydroxy derivative *II* also contains the bonded hydroxyl band only, so that its A ring must be practically only in the boat form, similarly as in the analogous bromohydrin[8]. In the spectra of 2β-hydroxy-3α-chloro derivative *XV* and 2β-alkoxy-3α-hydroxy derivatives *III* and *IV*, in addition to the strong band of the bonded hydroxyl, due to the boat form, a weak free hydroxyl band is also present, which we consider to be due to the chair form (see also[8]). Under the reasonable assumption that the intrinsic integrated intensities[20] of the bonded hydroxyl (in boat form) and the free hydroxyl (in chair form) are approximately equal, similarly as in bromohydrins[8], the contents of the boat form in chlorohydrin *XV* was found to be 85%, as calculated from the ratio of the integrated intensities of the free and the bonded hydroxyl (B_f/B_b). The same procedure when applied to 2β-methoxy derivative *III* led to the value 87% and in the case of 2β-ethoxy derivative *IV* to the value 88%; however, for alkoxy alcohols it is not evident whether the mentioned assumption is justified (in diols we found[8] that $B_b \cong 2 \,.\, B_f$). The content of the boat form was therefore also determined from the value B_b under the assumption that the intrinsic integrated intensity of the bonded hydroxyl in boat form of 2β,3α--isomer *III* or *IV* is equal as in corresponding diequatorial 2α,3β-isomer *X* or *XI*; the values found for derivatives *III* and *IV* (82% and 88%, resp.) agree within the experimental errors (approx. ±5%) with the values mentioned above. In 2β-hydroxy-

-3α-bromo derivative we found[8] from the infrared spectrum 85% and from its NMR spectrum 88% of the boat form. In derivatives which have in position 2β an oxygen-containing function the boat form is therefore less populated (independently on the 3α-substituent), than in derivatives containing 2β-chlorine or bromine. On the basis of the comparison of bromohydrins, diols, and their acetates of various configuration, we came in paper[8] to the conclusion that this effect is caused by the differences in 1,3-*syn*-axial interaction of the 2β-substituent, and that the 1,3-*syn*-axial interaction CH_3/Br is at least 0·5 kcal mol^{-1} higher than the interactions CH_3/OH and $CH_3/OCOCH_3$. This conclusion may be now generalized at least qualitatively in the following manner: 1,3-*syn*-axial interaction between the methyl group and chlorine or bromine is larger than between the methyl group and the oxygen-containing functional group (OH, OCH_3, OC_2H_5, $OCOCH_3$).

EXPERIMENTAL

The melting points were determined on a Kofler block. Optical rotations were measured in chloroform (*c* 0·5—1·0) on an automatic polarimeter ETL-NPL (Bendix-Ericsson) with a ±1—3° error. The infrared spectra were measured in chloroform on a UR-20 (Zeiss, Jena) spectrophotometer, the ultraviolet spectra in cyclohexane on a Unicam SP 700 spectrophotometer. The purity of the samples was checked by thin-layer chromatography on silica gel (5—30 μm) containing 6% of gypsum. The working up of the reaction mixtures was carried out as follows: The mixture was diluted with water, extracted with ether or chloroform and the extract washed with water, 5% sodium hydrogen carbonate solution (if the reaction was carried out in acid medium), and again with water. After drying the extract over sodium sulfate the solvent was distilled off under reduced pressure and the residue crystallized. The identity of the compounds was confirmed by infrared spectra, thin-layer chromatography and mixed melting points. Samples for analysis were dried over phosphorus pentoxide at 100°C and 0·1—1 Torr for 8—20 hours. The preparation of starting epoxides *I* and *VIII* and olefin *XIV* has been described in refs[12,13,21].

2β-Chloro-19β,28-epoxy-18α-oleanan-3α-ol (*II*)

36% hydrochloric acid (75 ml) was added to a solution of α-epoxide *I* (2·50 g) in chloroform (150 ml) and the mixture stirred for 2 hours. After working up and crystallization from chloroform–methanol chlorohydrin *II* (2·50 g) was obtained, m.p. 215—217°C, $[\alpha]_D$ + 90°. IR spectrum: 3600 (OH), 1035 (C—O—C) cm^{-1}. For $C_{30}H_{49}ClO_2$ (477·1) calculated: 75·51% C, 10·35% H; found: 75·60% C, 10·40% H. Crystallization from chloroform–cyclohexane gave another modification of m.p. 227—229°C.

A solution of chlorohydrin *II* (34 mg) and potassium hydroxide (200 mg) in ethanol (15 ml) was refluxed for 3 hours. After working up epoxide *I* (26 mg) was obtained which was identical with an authentic specimen. M.p. 255—257°C, $[\alpha]_D$ + 43°.

2β-Methoxy-19β,28-epoxy-18α-oleanan-3α-ol (*III*) and 2β-Ethoxy-19β,28-epoxy-18α-oleanan-3α-ol (*IV*)

Sulfuric acid (1 ml) was added to a solution of epoxide *I* (440 mg) in a mixture of benzene (50 ml) and methanol (25 ml) and the mixture was stirred for 1·5 hours. After working up (extraction

with benzene) the product was chromatographed on silica gel (20 g). Elution with chloroform (50 ml) gave methoxy alcohol *III* (368 mg), m.p. 203–204°C (chloroform–methanol), $[\alpha]_D$ + 110°. IR spectrum: 3575 (OH), 1098, 1036 (COC) cm^{-1}. For $C_{31}H_{52}O_3$ (472·7) calculated: 78·76% C, 11·09% H; found: 78·94% C, 10·79% H.

When ethanol was used instead of methanol ethoxy alcohol *IV* was prepared in the same manner as above, m.p. 260–261°C (chloroform–methanol), $[\alpha]_D$ + 107°. IR spectrum: 3585 (OH), 1100, 1036 (C–O–C) cm^{-1}. For $C_{32}H_{54}O_3$ (486·8) calculated: 78·96% C, 11·18% H; found: 79·18% C, 11·19% H.

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

A solution of sodium dichromate dihydrate (200 mg) in acetic acid (8 ml) was added to a solution of chlorohydrin *II* (112 mg) and anhydrous sodium acetate (80 mg) in acetic acid (22 ml) and the mixture allowed to stand at room temperature for 22 hours. After working up chloroketone *V* (80 mg) was obtained, m.p. 221–223°C (chloroform–methanol or chloroform–hexane), $[\alpha]_D$ + + 130°. IR spectrum: 1732 (CO), 1035 (C–O–C) cm^{-1}. For $C_{30}H_{47}ClO_2$ (475·1) calculated: 75·83% C, 9·97% H; found 75·80% C, 9·98% H. The same preparation ($[\alpha]_D$ + 131°) was obtained when the oxidation was carried out with chromium trioxide in acetic acid.

A mixture of chloro ketone *V* (25 mg), zinc dust (160 mg), and acetic acid (5 ml) was refluxed for 4 hours. After working up ketone *XVIII* (20 mg) was obtained, which was identical with an authentic specimen[12]. M.p. 230–232°C (chloroform–methanol), $[\alpha]_D$ + 82°.

2β-Methoxy-19β,28-epoxy-18α-oleanan-3-one (*VI*) and 2β-Ethoxy-19β,28-epoxy-18α-oleanan-3-one (*VII*)

On oxidation of methoxy alcohol *III* (carried out in the same manner as in the preparation of chloroketone *V*) methoxy ketone *VI* was obtained, after crystallization from a mixture of chloroform and methanol, with m.p. 175–185°C (decomposition), $[\alpha]_D$ + 107°. When the reaction was repeated a preparation was obtained with $[\alpha]_D$ + 105°. IR spectrum: 1725 (CO), 1131, 1037 (C–O–C) cm^{-1}. For $C_{31}H_{50}O_3$ (470·7) calculated: 79·10% C, 10·71% H; found: 79·16% C, 10·71% H.

In a similar manner ethoxyketone *VII* was prepared from ethoxy alcohol *IV*. It was purified by preparative thin-layer chromatography on silica gel (benzene–ether 8 : 1) and crystallized from a benzene–ether–heptane mixture, m.p. 202–214°C (decomp.), $[\alpha]_D$ + 101°. IR spectrum: 1725 (CO), 1125, 1032 (C–O–C) cm^{-1}. For $C_{32}H_{52}O_3$ (484·7) calculated: 79·28% C, 10·81% H; 79·45% C, 10·70% H.

2α-Chloro-19β,28-epoxy-18α-oleanan-3β-ol (*IX*)

Hydrochloric acid (36%; 15 ml) was added to a solution of epoxide *VIII* (500 mg) in chloroform (50 ml) and the mixture stirred for 3 hours. After working up the reaction product was chromatographed on silica gel (30 g, elution with benzene). Chlorohydrin *IX* (314 mg) was obtained, melting at 251–252°C (chloroform–methanol or chloroform–cyclohexane) and with $[\alpha]_D$ + 34°. IR spectrum: 3600 (OH), 1035 (C–O–C) cm^{-1}. For $C_{30}H_{49}ClO_2$ (477·1) calculated: 75·51% C, 10·35% H; found: 75·52% C, 10·34% H. Further chlorohydrin *XV* (19 mg) was eluted, identical with the sample mentioned below. Reaction of chlorohydrin *IX* (39 mg) with potassium hydroxide (similarly as in the case of derivative *II*) gave epoxide *VIII* (28 mg).

2α-Methoxy-19β,28-epoxy-18α-oleanan-3β-ol (*X*) and 2α-Ethoxy-19β,28-epoxy-18α-oleanan-3β-ol (*XI*)

On reaction of epoxide *VIII* (440 mg) with methanol (carried out in a similar manner as in the preparation of derivative *III*) methoxy alcohol *X* (226 mg) was obtained after chromatography and crystallization from a chloroform–methanol mixture, m.p. 198–199°C, $[\alpha]_D$ + 4°. IR spectrum: 3575 (OH), 1097, 1035 (C—O—C) cm^{-1}. For $C_{31}H_{52}O_3$ (472·7) calculated: 78·76% C, 11·09% H; found: 78·61% C, 10·95% H.

In the same manner when ethanol was used, ethoxy alcohol *XI* was obtained, m.p. 198–199°C (chloroform–methanol), $[\alpha]_D$ + 2°. IR spectrum: 3600 (OH), 1096, 1037 (C—O—C) cm^{-1}. For $C_{32}H_{54}O_3$ (486·8) calculated: 78·96% C, 11·18% H; found: 78·96% C, 11·04% H.

2α-Chloro-19β,28-epoxy-18α-oleanan-3-one (*XII*)

On oxidation of chlorohydrin *IX* (56 mg), in the same manner as in the preparation of chloro ketone *V*, chloro ketone *XII* (33 mg) was obtained, m.p. 234–236°C (chloroform–methanol), $[\alpha]_D$ + 38°. When the reaction was repeated the preparations with $[\alpha]_D$ + 40° and +41° were obtained. IR spectrum: 1728 (CO), 1036 (C—O—C) cm^{-1}. For $C_{30}H_{47}ClO_2$ (475·1) calculated: 75·83% C, 9·97% H; found: 75·58% C, 9·67% H.

2α-Methoxy-19β,28-epoxy-18α-oleanan-3-one (*XIII*) and 2α-Ethoxy-19β,28-epoxy-18α-oleanan-3-one (*XIV*)

From methoxy alcohol *X* methoxy ketone *XIII*, m.p. 162–168°C (decomp.; chloroform–methanol), $[\alpha]_D$ + 67°, was prepared in the same manner as that used in the preparation of chloro ketone *V*. Samples obtained in repeated reactions had $[\alpha]_D$ + 66·5° and +67°. IR spectrum: 1719 (CO), 1126, 1036 (C—O—C) cm^{-1}. For $C_{31}H_{50}O_3$ (470·7) calculated: 79·10% C, 10·71% H; found: 78·90% C, 10·50% H.

In a similar manner ethoxy ketone *XIV* was prepared from ethoxy alcohol *XI*. It was purified by thin-layer chromatography in benzene–ether 8 : 1 and crystallized from a mixture of benzene, ether and heptane. M.p. 160–168°C (decomp.), $[\alpha]_D$ + 67°. IR spectrum: 1720 (CO), 1123, 1115, 1032 (C—O—C) cm^{-1}. For $C_{32}H_{52}O_3$ (484·7) calculated: 79·28% C, 10·81% H; found: 79·05% C, 10·88% H.

3α-Chloro-19β,28-epoxy-18α-oleanan-2β-ol (*XV*)

To a solution of olefin *XVII* (500 mg) in chloroform (25 ml) a solution of freshly prepared silver perchlorate monohydrate (400 mg) in dimethylformamide (20 ml) was added, followed by dropwise addition over 30 minutes and under stirring of a solution of chlorine (84 mg) in dimethylformamide (10 ml). The mixture was stirred for 10 minutes, then filtered and worked up. The residue was chromatographed on silica gel (50 g). Benzene eluted 3α-chloro-2β-formyloxy-19β,28-epoxy-18α-oleanane (*XVI*, 30 mg), m.p. 262–266°C (chloroform–light petroleum). IR spectrum: 1725, 1182 (OCHO), 1036 (C—O—C) cm^{-1}. Elution with chloroform gave chlorohydrin *XV* (198 mg), m.p. 227–230°C (chloroform–light petroleum), $[\alpha]_D$ + 100°. IR spectrum: 3575 (OH), 1035 (C—O—C) cm^{-1}. For $C_{30}H_{49}ClO_2$ (477·1) calculated: 75·51% C, 10·35% H; found: 75·45% C, 10·45% H. When silver perchlorate was used which had been dried over phosphorus pentoxide for two months formate *XVI* was formed as the main product. On reaction of chlorohydrin *XV* (38 mg) with potassium hydroxide (similarly as in the case of chlorohydrin *II*) epoxide *VIII* (25 mg) was obtained; using the same procedure epoxide *VIII* (28 mg) was obtained from formate *XVI* (40 mg).

Isomerization of Ketones *V*, *VI*, *XII* and *XIII*

To a solution of chloro ketone *V* or *XII* (20—30 mg) in chloroform (2 ml) 36% hydrochloric acid (0·03 ml) was added and the mixture shaken. After standing at room temperature for 17 hours and working up the residue was induced to crystallize by the addition of several drops of methanol, and then dried at 100°C. Using thin-layer chromatography a check was made that no side-reaction had taken place. In all equilibrium mixtures of chloro ketones *V* and *XII* obtained by this procedure (or also by isomerization with dry hydrogen chloride in chloroform) $[\alpha]_D$ were within the 78·5 $\pm$ 2° limits. Isomerization of methoxy ketones *VI* and *XIII* were carried out in the same manner; after 8 hours a mixture having $[\alpha]_D$ + 88° was obtained from isomer *VI*, and $[\alpha]_D$ + 80° from isomer *XIII*.

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