PREPARATION AND STEREOCHEMISTRY OF 1,2 AND 2,3-BROMOHYDRINS, BROMO KETONES, EPOXIDES AND DIOLS OF TRITERPENES*

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The series of 1,2 and 2,3-disubstituted derivatives of 19β,28-epoxy-18α-oleanane and 20β, 28--epoxy-18α,19β*H*-ursane was prepared from derivatives *IV*, *XV*, *XXIII*, *XXXVI* and *XXXIX* according to the Schemes 1—3. The structure of the substances prepared and the configuration of the substituents was demonstrated by chemical reactions. The effect of the bromine atom configuration in the position 2 on the stereochemistry of the reduction of the 1-oxo group with sodium borohydride is discussed, as well as the contraction of ring A in the reaction of 1α-hydroxy--2α-bromo derivative *XIX* with alkaline hydroxide, further the stereochemistry of the opening of β-epoxide *XIV* and *XXXVI* with hydrobromic acid, and isomerization equilibria of 2-bromo--1-oxo derivatives *XII* and *XVIII* and 2-bromo-3-oxo derivatives *XXVI*, *XXXVIII*, *XLII*, and *XLIII*. Differences have been observed between 1,2 and 2,3-disubstituted derivatives which show that the boat form of the ring A is less favoured in 1,2-disubstituted derivatives than in analogous 2,3-disubstituted derivatives. The presence of 8β-methyl group is evident during the opening of 2β,3β-epoxides and in the positions of the equilibrium of 2-bromo-3-oxo derivatives by the fact that the boat form of the ring A is more favoured.

During the study of the conformation of ring A in 4,4-dimethyl steroids and triterpenes*** it was observed that in derivatives containing an additional substituent in the position 2β, for example a bromine atom, the ring A exists completely or partly in the boat conformation (see ref.[1-13] and the references therein). It was further observed[4] that differences exist in the position of the equilibrium of isomeric 2-bromo-3-oxo derivatives between 4,4-dimethylsteroids and triterpenes, which indicate a considerable effect of the 8β-methyl group in triterpenes on the conformation of ring A. The majority of the studies mentioned was devoted to derivatives that contain two polar functions in the positions 2 and 3. Less is so far known about the stereochemistry of analogous 1,2-disubstituted derivatives. In the 4,4-dimethylcholestane

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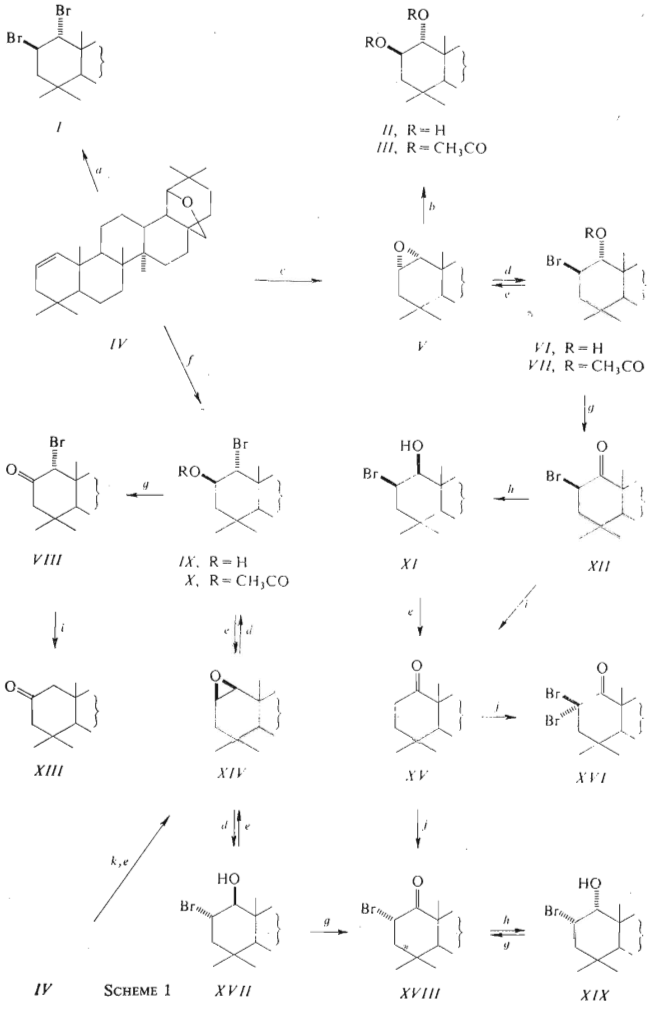
*** Under the concept "triterpenes" those triterpenes are meant that have an unrearranged skeleton and contain 4α, 4β, 8β and 10β methyl groups.


Br
Br
I
RO
RO
II, R = H
III, R = CH3CO
a
O
IV
c
b
O
V
d
e
RO
Br
VI, R = H
VII, R = CH3CO
f
g
Br
O
VIII
g
Br
RO
IX, R = H
X, R = CH3CO
HO
Br
XI
h
O
Br
XII
i
e
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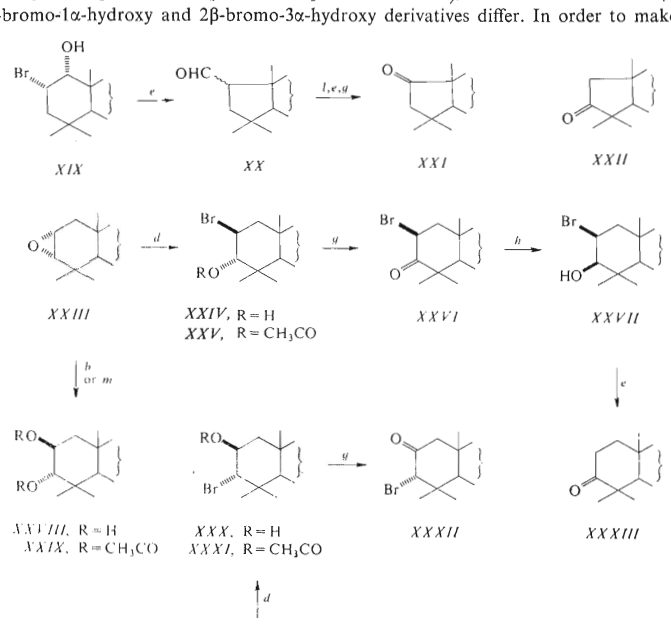
e
d
O
XIII
O
XIV
O
XV
j
O
Br
Br
XVI
d
e
j
k, e
HO
Br
XVII
g
O
Br
XVIII
h
g
HO
Br
XIX

IV SCHEME 1

series Levisalles and coworkers[8] prepared some 1,2-disubstituted derivatives, and also pointed out the fact that while the positions of equilibria of isomeric 2-bromo-1-oxo and 2-bromo-3-oxo derivatives agree (which would indicate a certain pseudosymmetry of ring A with respect to the positions 2 and 5), the conformations of 2β--bromo-1α-hydroxy and 2β-bromo-3α-hydroxy derivatives differ. In order to make



SCHEME 2

a Bromine, *b* perchloric acid, *c* peroxybenzoic acid, *d* hydrobromic acid, *e* potassium hydroxide, *f* N-bromosuccinimide, dimethyl sulfoxide, *g* sodium dichromate, sodium acetate, acetic acid, *h* sodium borohydride, *i* zinc, *j* pyridinium bromide perbromide, *k* bromine, silver perchlorate, dimethylformamide, *l* 3-chloroperoxybenzoic acid, *m* alumina.

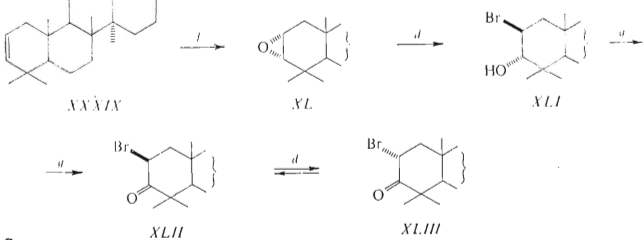
the study of the effect of various substituents on the conformation of ring A possible and also to check the effect of 8β-methyl group and to determine whether 1,2 and 2,3-disubstituted triterpenes satisfy the idea of pseudosymmetry of ring A, we prepared in this study a series of disubstituted derivatives (bromo hydrins, bromo ketones and diols derived from 19β,28-epoxy-18α-oleanane and 20β,28-epoxy-18α,19β*H*--ursane) with the functional groups in the positions 1,2 and 2,3.

The preparation of disubstituted derivatives was carried out by conventional methods based predominantly on the *trans*-opening of epoxides and on reductions of bromo ketones with sodium borohydride, which have many analogies in the chemistry of steroids and triterpenes[3–14]. For this reason these methods are not further discussed in detail and they are only summarized in the Schemes 1–3. 1,2-Disubstituted derivatives of 19β,28-epoxy-18α-oleanane were prepared from the known[15] unsaturated derivative *IV* and from 1-oxo derivative *XV* (see[16]) according to Scheme 1. The preparation of 2,3-disubstituted derivatives of the same skeleton started from the described[4,14] epoxides *XXIII* and *XXXVI* and it is shown in Scheme 2. Derivatives *XXIV*–*XXVI*, *XXX*, *XXXVII* and *XXXVIII* and their possible further reactions or preparation by other routes were already described in our earlier papers[4,14]. For the sake of comparison 2,3-disubstituted derivatives of 20β,28-epoxy-18α,19β*H*--ursane *XL*–*XLII* were prepared from the olefin *XXXIX* (see[17]) according to Scheme 3. The configuration of the functional groups of all derivatives prepared follows from the method of preparation, from analogies[3–14], and from the reactions shown in Schemes 1–3 or other reactions which were already published[4,14,15]. In the text below only those reactions will be discussed which are interesting from the point of view of comparison of 1,2 and 2,3-disubstituted derivatives or which enable a checking of the effect of the 8β-methyl group in comparison with 4,4-dimethyl steroids.

During the reduction of bromo ketones *XII* and *XVIII* with sodium borohydride the presence of bromine in the position 2 and its configuration are manifested distinctly by the stereochemistry of the reduction of 1-oxo group. While on reduction of unsubstituted 1-oxo derivative with hydrides a mixture of both epimeric alcohols is formed in which the axial 1α-hydroxy derivative prevails in an approximately 3 : 1 ratio[8,16], reduction of 2α-bromo ketone *XVIII* gave only 2α-bromo-1α-hydroxy derivative *XIX* with the axial hydroxy group. In contrast to this, from 2β-bromo ketone *XII* 2β-bromo-1β-hydroxy derivative *XI* was formed as the sole product. Hence, in both cases the formation of *cis*-bromo hydrin is prefered and the change in configuration of the bromine atom has a total change of the stereochemistry of the reduction as a consequence. Although it is known (see[18] and the references therein) that the presence of α-halogen "may cause anomalies" during the reduction of ketones, in none of the several cases described in the steroid series are the differences so distinct as in bromo ketones *XII* and *XVIII*. Similarly as in the case of bromo ketone *XII* the reduction of 2β-bromo-3-oxo derivative *XXVI* is also stereospecific

and the sole product is *cis*-bromohydrin *XXVII*. The course of the reduction of 2α-bromo-3-oxo derivative *XXXVIII* differs, however, from that of 2α-bromo-1-oxo derivative *XVIII* and *trans*-bromohydrin *XXXVII* is formed as the main product[4] similarly as in 4,4-dimethylsteroids[5,7].

In contrast to *cis*-bromohydrins *XI* and *XXVII* which give corresponding ketones *XV* and *XXXIII* under the effect of potassium hydroxide, the reaction of 1α-hydroxy--2α-bromo derivative *XIX* under the same conditions did not afford ketone *XV* but a mixture of aldehydes *XX* with a five-membered ring *A* (Scheme 2). For the confirmation of the structure this mixture was submitted to Baeyer-Villiger oxidation and then converted by subsequent hydrolysis to a mixture of hydroxy derivatives the oxidation of which gave a derivative with a carbonyl group in a five-membered cycle (1732 cm^{-1}). This ketone is not identical with the known[19] 2-oxo-A-norderivative *XXII* and therefore its structure is evidently *XXI*. It is known that similar contractions of rings take place in halogenohydrins, for example under the effect of silver compounds[20,21], but with alkali hydroxides *cis*-halogenohydrins generally give ketones[3,22-24]. In the series of 4,4-dimethylsteroids and triterpenes all isomeric 2,3-*cis*-bromohydrins also give ketones[3,5-7] only, so that the behaviour of bromohydrin *XIX* is quite exceptional. The comparison of the course of the reaction of *cis*-bromohydrins that differ by the position of the hydroxyl group is interesting: in the case of 1α-hydroxy-2α-bromo derivative *XIX* a rearrangement takes place while 2α-bromo-3α-hydroxy derivative gives a ketone[5]. Under the supposition[22] that the formation of ketone in these isomers takes place *via* a boat-like transition state in which the requirement of the antiperiplanarity of the C—Br and C—H bonds[23] is fulfilled, it may be judged that in 1,2-disubtituted derivative *XIX* the boat-like transition state is disadvantageous in comparison with the 2,3-isomer.



XXXIX *XL* *XLI*

XLII *XLIII*

SCHEME 3

The reaction then takes place in the chair form by migration of the substituent in the antiperiplanar position with respect to the C—Br bond, *i.e.* of the carbon atom in the position 1.

A further reaction in which the differences between the positions 1,2 and 2,3 are manifest is the opening of the epoxides with hydrobromic acid. Both α-epoxides *V* and *XXIII* open uniformly under formation of "normal" products (*VI*, *XXIV*) which correspond to a diaxial opening of epoxides according to Fürst-Plattner rule. From β-epoxides *XIV* and *XXXVI* a mixture of "normal" products (*IX*, *XXX*) and "anomalous" diequatorial bromohydrins *XVII* and *XXXVII* are formed; their mutual ratio differs in both epoxides (Table I). As isomerizations of bromohydrins in acid medium are known[25], it was further checked that all four bromohydrins (*IX*, *XXX*, *XVII*, *XXXVII*) are stable under the conditions used during the reaction of epoxides with hydrobromic acid, so that they represent kinetically determined products. In the series of 4,4-dimethylsteroids and triterpenes anomalous opening of 2β,3β--epoxides was already observed[3,5,7,9]; in the case of 1β,2β-epoxides it is still unknown (in the case of reductions of steroidal 1β,2β-epoxides the formation of normal products[26,27] has been described). Anomalous opening of 2β,3β-epoxides was explained[3,5] by the fact that the reaction takes place *via* the boat transition state and the attack of the nucleophile takes place on $C_{(2)}$ in an antiperiplanar position to the 3β-hydroxy group formed, while the normal opening takes place in the chair form by an attack on $C_{(3)}$. According to Francois and Levisalles[9] two factors play their role in the competition of both transition states, which act against a normal opening: the first factor is the prevention of the attack on the neopentyl carbon $C_{(3)}$, the second consists in unfavourable diaxial interactions between the substituents on the β-side (4β and 10β methyl groups) and the 2β-hydroxy group formed; these interactions increase the energy of the chair-like transition state. From the values given in Table I it follows that a less amount of anomalous product is formed from 1β,2β-epoxide *XIV*, which means that the boat transition state is less pronounced in it than in the 2,3-isomer *XXXVI*. This difference is probably not caused by the first factor, because both $C_{(1)}$ and $C_{(3)}$ are neopentyl type and their accessibility from the α-side is approximately the same. The sole difference between the positions 1 and 3 consists in the presence of the methylene group in the position 11; the steric hindrance caused by this group (if it plays a role) would cause an effect opposite to that observed. The second factor cannot have a decisive effect either, because the diaxial interactions between the groups on the β-side in the chair-like transition state are similar in both epoxides. Hence, we consider that the differences observed between the positions 1,2 and 2,3 are caused by energy relationships in the boat transition state. The differences between these positions were further investigated using acid catalyzed isomerization of 2α- and 2β-bromo ketones with the carbonyl group in the position 1 (*XII*, *XVIII*) and in the position 3 (*XXVI*, *XXXVIII* and *XLII*, *XLIII*). The results are shown in Table II. It was proved[3–5,7,8,28] that the ring A of 2α-bromo derivatives

in the 1-oxo and 3-oxo series exists in solution in the chair form practically exclusively, while in 2β-bromo derivatives it is in boat form. Hence, it can be expected that the energy differences between the chair and boat form of the ring A will be manifest also

TABLE I

The Composition of Mixtures of Bromohydrins after Reaction of β-Epoxide with Hydrobromic Acid and the Differences of Activation Free Energies

Skeleton	2β,3β-Epoxide	$\Delta G^{\neq a}$	1β,2β-Epoxide	$\Delta G^{\neq a}$
	% of anomalous product	kcal . mol^{-1}	% of anomalous product	kcal . mol^{-1}
19β,28-Epoxy--18α-oleanane	90 ± 2[b]	−1·3 ± 0·2	47 ± 5[c]	0·1 ± 0·1
4,4-Dimethyl-cholestane	81[d]	−0·8	—	—
8-Lanostene	79[e]	−0·8	—	—

[a] $\Delta G^{\neq} = \Delta G^{\neq}_{boat} - \Delta G^{\neq}_{chair}$, calculated for 22°C from the ratio of the anomalous and normal products; [b] calculated from optical rotation of the mixture of bromohydrins *XXX* and *XXXVII*, from the yields after chromatographic separation 92 ± 3%; [c] calculated from the optical rotation of the mixture of bromo ketone *VIII* and *XVIII*, obtained on oxidation of the crude mixture of bromohydrins *IX* and *XVII*; [d] lit.[5]; [e] lit.[7].

TABLE II

Composition of the Equilibrium Mixtures of Isomeric 2-Bromo Ketones and the Differences of Free Energies

Skeleton	3-Oxo series	$\Delta G°$	1-Oxo series	$\Delta G°$
	% of β-isomer	kcal . mol^{-1}	% of β-isomer	kcal . mol^{-1}
19β,28-Epoxy--18α-oleanane	42 ± 3[a,b]	0·2 ± 0·1	9 ± 2[a,c]	1·4 ± 0·2
20β,28-Epoxy--18α,19β*H*-ursane	40 ± 3[a]	0·2 ± 0·1	—	—
4,4-Dimethyl-cholestane	17 ± 5[d,e]	0·9 ± 0·3	16 ± 3[d,f]	1·0 ± 0·2
8-Lanostene	22 ± 5[d,g]	0·7 ± 0·2	—	—

[a] In chloroform at 22 ± 2°C; [b] the same value was measured in acetic acid, see[4]; [c] 7% from the circular dichroism measurement, 8% in acetic acid; [d] in acetic acid; [e] lit.[5]; [f] lit.[8]; [g] lit.[7].

in the position of the isomerization equilibrium of 2-bromo ketones. From the values given in Table II for 1-oxo and 3-oxo derivatives of 19β,28-epoxy-18α-oleanane it may be seen that in 2-bromo-1-oxo derivatives the 2β-epimer is less abundant in equilibrium than in 2-bromo-3-oxo derivatives; from this it follows that the boat form is less advantageous in 1-oxo derivatives than in 3-oxo derivatives in comparison with the chair form.

The isomerizations were carried out under the effect of hydrogen bromide in chloroform and the composition of the equilibrium mixtures was determined from optical rotation of the mixture of bromo ketones after their isolation from the reaction mixture. It should be noted that the elimination of hydrogen bromide before the measurement of the rotation is indispensable because the measurement in the presence of hydrogen bromide may lead to erroneous values (for example in 1-oxo derivatives *XII* and *XVIII*, see Experimental). As it is known that bromo ketones undergo isomerization easily already during their preparation or isolation from the reaction mixture[5], special care was given to their steric purity. Although some of them were already obtained earlier by unspecific reactions (*XII*, *XVIII*, see[29]) or under conditions which do not exclude a partial isomerization (*XXVI*, *XXXVIII*, see[4]), we prepared them in this study again by oxidation of bromohydrins with sodium dichromate in a buffered medium (acetic acid, sodium acetate) under conditions that according to[5] do not lead to isomerizations. The isolation from the reaction mixture was carried out in several ways and the measurement of optical rotation was used to follow whether these derivatives are changed during their isolation or crystallisation. Another criterion of the purity of bromo ketones *XII*, *XVIII* and *XXVI* was the reduction with sodium borohydride during which the formation of bromohydrins of opposite configuration of bromine was not observed even in traces. The reduction was carried out in the presence of boric acid[5], because — as was found for 2β-bromo-1-oxo derivative *XII* — partial isomerization takes place under the usual conditions of reduction to 2α-bromo derivative *XVIII*, which then gives rise to bromohydrin *XIX*. 2α-Bromo-3-oxo derivative *XLIII* was already prepared by a stereospecific procedure earlier[4].

From all the examples mentioned here it is evident that appreciable differences exist in triterpenes between 1,2 and 2,3-disubstituted derivatives. These differences are in disagreement with the pseudosymmetry of the ring A. Both during the reaction course (rearrangement of bromohydrin *XIX*, opening of β-epoxides *XIV* and *XXXVI*) and in the equilibrium position of bromo ketones the same effect is observed, *i.e.* that the boat form (or the boat transition state) is less advantageous in 1,2-disubstituted derivatives than in 2,3-isomers. The data given in Tables I and II also enable a quantitative estimation of this effect. In the case of the opening of epoxides the difference of activation free energies of the boat and chair transition state ($\Delta G^{\neq} = \Delta G^{\neq}_{\text{boat}} - \Delta G^{\neq}_{\text{chair}}$) can be made use of, calculated from the ratio of the anomalous and normal product of reaction of β-epoxides with hydrobromic acid. The change of $\Delta G^{\neq}$ going from 2β,3β-epoxide to 1β, 2β-epoxide equals 1·4 kcal . mol^{-1}. In the case of the isomerization equilibria of 2-bromo ketones, ΔG° (Table II) may be considered as the difference of free energies between the chair form of 2α-bromo ketone and the boat form of 2β-bromo ketone, under the supposition that the content of the remaining two forms in the conformation equilibria of each bromo ketone — *i.e.* the boat form of the 2α-isomer and the chair form of the 2β-isomer — is negligibly

low (the errors caused by neglecting up to 15% of these forms in conformational equilibria would be lower than the experimental errors given in Table II). From the comparison of the values ΔG° for 2-bromo-1-oxo and 2-bromo-3-oxo derivatives of 19β,28-epoxy-18α-oleanane the difference of 1·2 kcal . mol^{-1} can be calculated between both series of derivatives, which agrees, within the experimental errors, with the above given value from ΔG^+.

In a similar manner it is possible to check the effect of the 8β-methyl group by comparing the course of the opening of epoxides and the positions of the equilibria of bromo ketones derived from 19β,28-epoxy-18α-oleanane and 20β,28-epoxy--18α,19β*H*-ursane with the data published[5,7,8] for analogous derivatives of 4,4-dimethylcholestane and 8-lanostene which do not contain the 8β-methyl group. The values listed in Table II confirm an earlier conclusion[4] that in the series of 2-bromo-3-oxo derivatives the presence of the 8β-methyl group manifests itself by the shift of the equilibrium to the boat form ($\Delta\Delta G^\circ$ = 0·7 or 0·5 kcal . mol^{-1}, resp.). The same effect is also observed during the opening of 2β,3β-epoxides (Table I): in derivative *XXXVI* the boat transition state is more pronounced than in derivatives of 4,4-dimethyl-cholestane and 8-lanostene. The $\Delta\Delta G^+$ value (0·5 kcal . mol^{-1}) again agrees with the $\Delta\Delta G^\circ$ value from the isomerization of bromo ketones. The agreement of these values, obtained from such different processes, is in the case of both effects evidently not accidental and it indicates that general steric effects are under play, that become manifest in the same manner both in the transition states and in the equilibrium systems.

It is interesting that the position of the equilibrium of 2-bromo derivatives of 4,4-dimethyl-cholestan-1-one (Table II) does not agree with the above-mentioned effects: on one hand, on comparison with 3-oxo derivatives the difference between the positions 1,2 and 2,3 does not become evident, and on the other hand, on comparison with triterpenes an opposite effect of the 8β-methyl group appears. It is possible that some new effect plays its role here, for example, that the geometry — and also the energy — of the boat form of 2β-bromo-1-oxo derivatives differs in triterpenes and 4,4-dimethylsteroids. Another possibility is that during the long period of isomerization in acetic acid (see Experimental in ref.[8]) other changes in the molecule have taken place.

EXPERIMENTAL

The melting points were determined on a Kofler block. Optical rotations were measured in chloroform (*c* 0·5—1·5) on an automatic polarimeter Bendix-Ericsson with a ±1—2° accuracy. The infrared spectra were measured in chloroform on a UR-20 (Zeiss, Jena, GDR) instrument and on a model of the Institute of Apparatus Technology, Czechoslovak Academy of Sciences (Brno), For column chromatography neutral alumina (Reanal, activity II) and silica gel CH (70—200μm) were used. The course of the reactions and the purity of the samples were followed by thin-layer chromatography on alumina, silica gel according to Stahl (type 60) and silica gel with 10% of silver nitrate. Unless otherwise stated the working up of the reaction mixtures was carried out in the following manner: the mixture was poured into an excess of water, then extracted with ether or chloroform, the extract was washed with water, saturated sodium hydrogen carbonate and

water, and dried over sodium sulfate. The solvent was disttiled off under reduced pressure. The acetyl derivatives were prepared by reaction with a mixture of pyridine and acetic anhydride (2 : 1) at room temperature for 18—24 hours. The reaction mixture was poured into a mixture of water and ice and worked up as above, with the difference that extract was washed with dilute hydrochloric acid (1 : 4). The identity of compounds was confirmed by infrared spectra, thin-layer chromatography, and mixture melting point. Samples for analysis were dried over phosphorus pentoxide at 100°C and 0·1—1 Torr for 8-20 hours.

1α,2β-Dibromo-19β,28-epoxy-18α-oleanane (*I*)

Bromine (57 mg) in chloroform (0·8 ml) was added to a solution of olefin *IV* (125 mg, see[15]) in chloroform (5 ml) dropwise under stirring over 5 minutes and the mixture allowed to stand for 10 minutes. After working up the product was crystallized from ether to afford 70 mg of dibromo derivative *I*, m.p. 210—215°C (decomp.), $[\alpha]_D$ +53°. IR spectrum: 1035 cm^{-1} (COC). For $C_{30}H_{48}Br_2O$ (584·5) calculated: 61·64% C, 8·28% H; found: 61·42% C, 8·48% H.

19β,28-Epoxy-18α-oleanane-1α,2β-diol (*II*)

Perchloric acid (80%; 0·2 ml) was added to a solution of epoxide *V* (0·7 g) in a mixture of dioxan (50 ml) and water (2 ml) and the mixture allowed to stand at room temperature for 2 hours and worked up. The crude product was dissolved in ether and chromatographed on alumina (80 g). Elution with ether gave diol *II* (0·5 g) of m.p. 250—251°C (chloroform–cyclohexane), $[\alpha]_D$ +74°. IR spectrum: 3620, 3450 (OH), 1033 (COC) cm^{-1}. For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·55% C, 10·86% H. Diacetate *III*: m.p. 207—208°C (chloroform–methanol) $[\alpha]_D$ +44°. IR spectrum: 1740, 1255 (CH_3COO), 1032 (COC) cm^{-1}. For $C_{34}H_{54}O_5$ (542·8) calculated: 75·23% C, 10·03% H; found: 75·25% C, 10·05% H.

1α,2α;19β,28-Diepoxy-18α-oleanane (*V*)

A) A solution of olefin *IV* (305 mg) and peroxybenzoic acid (152 mg) in chloroform (10 ml) was allowed to stand at 0°C for 30 hours. After working up and crystallization from n-heptane and from chloroform–methanol mixture epoxide *V* was obtained (265 mg), m.p. 265—267°C, $[\alpha]_D$ +57°. Lit.[15] gives m.p. 258—260°C, $[\alpha]_D$ +56°.

B) A mixture of bromohydrin *VI* (40 mg), potassium hydroxide (300 mg) and ethanol (20 ml) was refluxed for 1 hour. After working up crude epoxide *V* was obtained (30 mg), m.p.258—262°, $[\alpha]_D$ +55°, identical with the sample described under *A*).

2β-Bromo-19β,28-epoxy-18α-oleanan-1α-ol (*VI*)

Hydrobromic acid (48%; 21 ml) was added to a solution of epoxide *V* (0·7 g) in chloroform (8 ml) and the mixture was shaken for 3 hours. After working up and crystallization from chloroform–cyclohexane bromohydrin *VI* was obtained (0·45 g) which decomposes between 220—250°C (on slow heating of the sample; if the heating was rapid decomposition took place at 270—273°C). $[\alpha]_D$ +67°. IR spectrum: 3600 (OH), 1030 (COC) cm^{-1}. For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·08% C, 9·47% H; found: 68·93% C, 9·43% H. Acetate *VII*: m.p. 198—202°C (decomposition; chloroform-methanol), $[\alpha]_D$ +48°. IR spectrum: 1745, 1244 (CH_3COO), 1030 (COC) cm^{-1}. For $C_{32}H_{51}BrO_3$ (563·6) calculated: 68·19% C, 9·12% H; found: 68·20% C, 9·05% H.

1α-Bromo-19β,28-epoxy-18α-oleanan-2-one (*VIII*)

A solution of bromohydrin *IX* (150 mg), anhydrous sodium acetate (200 mg), and sodium dichromate dihydrate (270 mg) in acetic acid (40 ml) was allowed to stand at room temperature for 2 hours. After working up the product was dissolved in benzene and chromatographed on silica gel (9 g). Elution with a cyclohexane–benzene–ether mixture (6 : 2 : 1) gave bromo ketone *VIII* (110 mg), m.p. 263–264°C (cyclohexane), $[\alpha]_D$ +3°. IR spectrum: 1717, 1425 (CO—CH_2), 1033 (COC), cm^{-1}. For $C_{30}H_{47}BrO_2$ (519·6) calculated: 69·36% C, 9·12% H; found: 69·45% C, 9·26% H. In an attempt at isomerization with a 3·5% solution of hydrogen bromide in chloroform at room temperature for 4 days bromoketone *VIII* was recovered, $[\alpha]_D$ +4°.

1α-Bromo-19β,28-epoxy-18α-oleanan-2β-ol (*IX*)

N-Bromosuccinimide (180 mg) was added to a solution of olefin *IV* (220 mg) in a mixture of chloroform (18 ml) and dimethyl sulfoxide (7 ml) and water (0·25 ml) and the mixture allowed to stand in darkness at room temperature for 22 hours. After working up and crystallization from a mixture of chloroform and cyclohexane bromohydrin *IX* (120 mg) was obtained, m.p. 208 to 213°C (decomp.), $[\alpha]_D$ +74°. IR spectrum: 3620, 3400 (OH), 1030 (COC) cm^{-1}. For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·08% C, 9·47% H; found: 69·36% C, 9·48% H. Acetate *X*: m.p. 230–235°C (chloroform–methanol), $[\alpha]_D$ +45°. IR spectrum: 1747, 1250 (CH_3COO), 1027 (COC) cm^{-1}. For $C_{32}H_{51}BrO_3$ (563·6) calculated: 68·19% C, 9·12% H; found: 68·50% C, 9·36% H.

2β-Bromo-19β,28-epoxy-18α-oleanan-1β-ol (*XI*)

A solution of boric acid (1·5 g) in ethanol (100 ml) was added to bromoketone *XII* (240 mg) in benzene (20 ml), and a solution of sodium borohydride (300 mg) in ethanol (50 ml) was added to the mixture over 2·5 hours. The mixture was allowed to stand for another 3·5 hours at room temperature, then diluted with water, acidified with hydrochloric acid and extracted with ether. The extract was washed with water and dried over sodium sulfate. The crude product was pure according to thin-layer chromatography and did not contain isomeric bromohydrins *VI* and *XIX*. On crystallization from a mixture of chloroform and methanol and chloroform–hexane bromohydrin *XI* (170 mg) was obtained, m.p. 199–202°C and after solidification 277–278°C (if the sample was heated rapidly or if it was put into the melting point apparatus at 190°C). According to thin-layer chromatography the bromohydrin changes during the melting at 200°C quantitatively to ketone *XV*. If the sample is heated slowly, this reaction takes place without an observable melting and the sample then has m.p. 277–278°C. $[\alpha]_D$ +85°. IR spectrum: 3565 (OH), 1035 (COC) cm^{-1}. The sample for analysis was dried at room temperature for 5 days. For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·08% C, 9·47% H; found: 69·33% C, 9·67% H. When the reaction was carried out in the absence of boric acid the crude product also contained bromohydrin *XIX*. In an attempt at acetylation of bromohydrin *XI* (70 hours) the unreacted material was recovered, when the temperature was increased to 45°C the decomposition to ketone *XV* already took place.

2β-Bromo-19β,28-epoxy-18α-oleanan-1-one (*XII*)

A suspension of bromohydrin *VI* (350 mg) in acetic acid (75 ml) which contained anhydrous sodium acetate (220 mg) and sodium dichromate dihydrate (600 mg) was allowed to stand at room temperature under occasional shaking for 3 days and then it was worked up. Crystallization from a chloroform–methanol mixture gave bromo ketone *XII* (260 mg), m.p. 228–232°C, $[\alpha]_D$ −7°. The analytical sample, obtained by double crystallization from the same mixture of solvents

had m.p. 232–233°C, $[\alpha]_D$ −8°. IR spectrum: 1724 (CO), 1033 (COC) cm^{-1}. For $C_{30}H_{47}BrO_2$ (519·6) calculated: 69·36% C, 9·12% H; found: 69·51% C, 9·21% H. Lit.[29] gives m.p. 214 to 215/252–253°C. When the oxidation was repeated the crude bromo ketone *XII* obtained by wetting the residue with ether and also the samples after crystallization had their $[\alpha]_D$ within the $-7\pm1°$ range.

19β,28-Epoxy-18α-oleanan-2-one (*XIII*)

Zinc dust (200 mg) was added in several portions over 2 hours to a boiling solution of bromo ketone *VIII* (30 mg) in acetic acid (20 ml). Ketone *XIII* (15 mg) was obtained, m.p. 242–244°C (chloroform–methanol), $[\alpha]_D$ +73°, identical with an authentic specimen[14].

1β,2β; 19β,28-Diepoxy-18α-oleanane (*XIV*)

A) From bromohydrin *IX* (140 mg) epoxide *XIV* (100 mg) of m.p. 214–215°C (chloroform–methanol) and $[\alpha]_D$ +60° was obtained under the effect of potassium hydroxide, in the same manner as epoxide *V*. IR spectrum: 1037 (COC) cm^{-1}. For $C_{30}H_{48}O_2$ (440·7) calculated: 81·76% C, 10·98% H; found: 82·01% C, 10·69% H. An identical preparation was obtained in the same manner from bromohydrin *XVII*.

B) To a solution of olefin *IV* (1·2 g) in chloroform (60 ml) a solution of silver perchlorate monohydrate (1·2 g) in dimethylformamide (50 ml) was added and a solution of bromine (650 mg) in dimethyl formamide (3·8 ml) was added dropwise to the mixture over 20 minutes. The mixture was stirred for 5 minutes, the separated silver bromide was filtered off and the filtrate worked up. Reaction of the product with potassium hydroxide (as under *A*) gave epoxide *XIV* (750 mg), m.p. 208–209°C (chloroform–methanol), $[\alpha]_D$ +60°, identical with the preparation described under *A*).

19β,28-Epoxy-18α-oleanan-1-one (*XV*)

A) Reaction of bromo ketone *XII* (50 mg) with zinc as in the preparation of ketone *XIII* gave ketone *XV* (30 mg), m.p. 274–276°C (chloroform–methanol), $[\alpha]_D$ +95°, identical with an authentic sample prepared according to[16]. Lit.[16] gives m.p. 275–276°C, $[\alpha]_D$ +93°.

B) Bromohydrin *XI* (40 mg) when reacted with potassium hydroxide as in the preparation of epoxide *V* gave ketone *XV* (25 mg), m.p. 278–279°C (chloroform–methanol), identical with the sample prepared under *A*).

2α-Bromo-19β,28-epoxy-18α-oleanan-1β-ol (*XVII*)

A solution of epoxide *XIV* (100 mg) in chloroform (10 ml) was shaken with 48% hydrobromic acid (10 ml) for 4 hours. After working up a mixture of bromohydrins *IX* and *XVII* (110 mg) was obtained. This mixture (80 mg) was separated by preparative thin-layer chromatography on silica gel (elution with cyclohexane–benzene–ether 3 : 1 : 1). Bromohydrin *IX* (40 mg) of m.p. 205–208°C (decomp.) was obtained, $[\alpha]_D$ +73°, which was identical with the preparation mentioned above. Further, bromohydrin *XVII* (30 mg) was obtained, m.p. 238–241°C (chloroform–methanol), $[\alpha]_D$ +55°. IR spectrum: 3560 (OH), 1030 (COC) cm^{-1}. For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·08% C, 9·47% H; found: 69·19% C, 9·40% H. During an attempt at the separation of the mixture by column chromatography on silica gel bromohydrin *XVII* and a polar, bromine-free substance were obtained only. After oxidation of a crude mixture of bromohydrins *IX* and *XVII* under conditions mentioned during the preparation of bromo ketone *VIII* a mixture of bromo ketones *VIII* and *XVIII* was obtained, $[\alpha]_D$ +40°. Bromohydrins *IX* and *XVII* were isolated unchanged from the experiment aiming at the isomerization with hydrobromic acid under conditions given above, for 72 hours.

2α-Bromo-19β,28-epoxy-18α-oleanan-1-one (*XVIII*)

A) A solution of bromohydrin *XVII* (240 mg), anhydrous sodium acetate (200 mg), and sodium dichromate dihydrate (500 mg) in acetic acid (25 ml) was allowed to stand at room temperature for 24 hours and the mixture was worked up. After crystallization from a mixture of chloroform and cyclohexane and chloroform–methanol bromo ketone *XVIII* (170 mg) was obtained, m.p. 268–270°C, $[\alpha]_D$ +80°. IR spectrum: 1730 (CO), 1037 (COC) cm^{-1}. Lit.[29] gives m.p. 265 to 266°C, $[\alpha]_D$ +85°. For $C_{30}H_{47}BrO_2$ (519·6) calculated: 69·36% C, 9·12% H; found: 69·44% C, 9·26% H. When the oxidation was repeated the crude product and the samples after crystallization had their $[\alpha]_D$ within the +81° ±1° range.

B) From bromohydrin *XIX* (120 mg) bromo ketone *XVIII* (115 mg) of m.p. 265–267°C (ether) and $[\alpha]_D$ +81°, identical with the preparation described under *A*), was obtained in the same manner as under *A*).

C) To a solution of ketone *XV* (950 mg) in acetic acid (120 ml) 0·3% solution of hydrogen bromide in acetic acid (1·5 ml) and pyridinium bromide perbromide (0·9 g) was added and the mixture allowed to stand at room temperature for 17 hours. After working up 1 g of a mixture of ketones *XV*, *XVI* and *XVIII* of $[\alpha]_D$ +68° was obtained. This mixture (300 mg) was dissolved in n-hexane and chromatographed on silica gel (65 g) with benzene–hexane (5 : 1) which eluted dibromo ketone *XVI* (50 mg), m.p. 240°C (decomp.), $[\alpha]_D$ +44°. IR spectrum: 1734 (CO), 1032 (COC) cm^{-1}. Lit.[29] gives 237–238°C (decomp.), $[\alpha]_D$ +25°. Elution with benzene gave bromo ketone *XVIII* (160 mg), m.p. 269–270°C (chloroform–methanol), $[\alpha]_D$ +81°. On further elution a mixture of ketones *XV* and *XVIII* was obtained. The best method of obtaining pure bromo ketone *XVIII* from the mixture after bromination consists in the reduction with sodium borohydride (see preparation of bromohydrin *XIX*), chromatographic separation of bromohydrin *XIX* on silica gel, and oxidation as under *B*).

2α-Bromo-19β,28-epoxy-18α-oleanan-1α-ol (*XIX*)

Bromo ketone *XVIII* (90 mg) was reduced with sodium borohydride in the same manner as in the preparation of bromohydrin *XI*. In the crude product no isomeric bromohydrins *XI* and *XVII* were found. Bromohydrin *XIX* (81 mg) was obtained which had m.p. 254–256°C (chloroform–methanol), $[\alpha]_D$ +23°. IR spectrum: 3580 (OH), 1035 (COC) cm^{-1}. For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·08% C, 9·47% H; found: 69·03% C, 9·71% H.

19β,28-Epoxy-18α-A-noroleanan-1-one (*XXI*)

A mixture of bromohydrin *XIX* (200 mg), potassium hydroxide (500 mg) and ethanol (50 ml) was refluxed for 2·5 hours, diluted with water, and the precipitated material filtered off under suction and washed with water. A mixture of isomeric aldehydes *XX* (170 mg) was thus obtained, m.p. 140–145°C, IR spectrum: 2840, 2745, 1716 (CHO), 1036 (COC) cm^{-1}. A mixture of aldehydes *XX* (160 mg) was allowed to react with 3-chloroperoxybenzoic acid (200 mg) in chloroform (10 ml) at room temperature for 3 days. After working up the product was hydrolysed with potassium hydroxide (300 mg) in methanol (10 ml) by 3 hours' boiling. The mixture of hydroxy derivatives obtained was oxidized with sodium dichromate in the same manner as in the preparation of bromo ketone *VIII* for 24 hours. After working up the crude product was dissolved in benzene and chromatographed on alumina (20 g). Benzene eluted norketone *XXI* (80 mg), m.p. 233 to 235°C (methanol), $[\alpha]_D$ +84°. IR spectrum: 1732, 1413 ($COCH_2$), 1036 (COC) cm^{-1}. For $C_{29}H_{46}O_2$ (426·7) calculated: 81·63% C, 10·87% H; found: 81·64% C, 10·75% H.

2β-Bromo-19β,28-epoxy-18α-oleanan-3α-ol (*XXIV*)

On reaction of epoxide *XXIII* (850 mg) with hydrobromic acid, similarly as in the preparation of bromohydrin *VI*, bromohydrin *XXIV* was obtained (970 mg) which according to thin-layer chromatography was free of other isomers; m.p. 215—219°C (cyclohexane). Lit.[4] gives m.p. 215—217°C. Attempts to obtain 2α-hydroxy (or acetoxy)-3β-bromo derivative in the same manner as in the case of analogous cholestane derivatives[30,31] were unsuccesfull: heating of bromohydrin *XXIV* or acetate *XXV* (see[4]) to melting point led to the elimination of hydrogen bromide, while the isomerization of bromohydrin *XXIV* with 1·7% hydrogen bromide in chloroform (3 days at room temperature) or perchloric acid in heptane[25] (2 hours' boiling) did not take place. In an attempt at isomerization of acetate *XXV* in boiling nitromethane for 21 hours, according to ref.[31], the starting acetate *XXV* was recovered unchanged.

2β-Bromo-19β,28-epoxy-18α-oleanan-3-one (*XXVI*)

A solution of bromohydrin *XXIV* (330 mg), anhydrous sodium acetate (300 mg), and sodium dichromate dihydrate (700 mg) in acetic acid (50 ml) was allowed to stand at room temperature for 5 hours. After working up and concentration of the ethereal solution bromo ketone *XXVI* crystallized out (220 mg), m.p. 205—214°C, $[\alpha]_D \pm 127°$. After working up by pouring the mixture into water, filtering off the precipitate and washing with water and drying at 100°C the same product was obtained, $[\alpha]_D$ +127°. After crystallization from chloroform–methanol bromo ketone *XXVI* had m.p. 216—218°C, $[\alpha]_D$ +129°, in agreement with lit.[4]. When the oxidation was repeated the samples of bromo ketone *XXVI* had $[\alpha]_D$ within the $+128° \pm 1°$ limits.

2β-Bromo-19β,28-epoxy-18α-oleanan-3β-ol (*XXVII*)

Bromo ketone *XXVI* (100 mg) was dissolved in warm ethanol (50 ml); after cooling, a solution of boric acid (600 mg) was added, dissolved in ethanol (25 ml), followed by gradual addition of sodium borohydride (150 mg) in ethanol (25 ml) over 1 hour. The mixture was allowed to stand for 1 hour, then diluted with water, the separated precipitate was filtered off under suction, washed with water and dried at room temperature. According to thin layer chromatography the crude product did not contain isomeric bromohydrins *XXIV* and *XXXVII*, but it contained traces of ketone *XXXIII* and of 3β-hydroxy derivative, which were eliminated by a rapid filtration of a benzene solution of the product through silica gel (4 g). Crystallization from cyclohexane gave bromohydrin *XXVII* (90 mg), m.p. 196—197°C and, after solidification, 234—236°C (if the sample was introduced at 195°C). At about 195°C hydrogen bromide is eliminated and ketone *XXXIII* is formed. On slow heating of the sample the formation of ketone takes place without an observable melting and the sample then has m.p. 236—237°C, $[\alpha]_D$ +62°. IR spectrum: 3590, 3565 (OH), 1036 (COC) cm^{-1}. The sample for analysis was dried at room temperature for three days. For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·08% C, 9·47% H; found: 69·27% C, 9·61% H. Bromohydrin *XXVII* is unstable and gives ketone *XXXIII* even on crystallization from methanol, or on standing in a mixture of benzene and ethanol, and also during the common working up of the reaction mixture after reduction.

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

A) Epoxide *XXIII* (355 mg) was dissolved in a mixture of benzene and light petroleum (1 : 1, 8 ml) and adsorbed on alumina (40 g, act. I—II). After two days diol *XXVIII* (350 mg) was eluted with chloroform and crystallized from cyclohexane or benzene in two modifications: plates of m.p. 263—266°C and prisms of m.p. 246—248°C and 260—263°C after solidification

(if the sample was heated rapidly or introduced at 230—240°C; at slow heating the change of modification takes place without melting about 240°C and the sample melts at 264—267°C). $[\alpha]_D$ +94°. For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·80% C, 11·11% H. Diacetate *XXIX* crystallized from a mixture of chloroform–hexane in needles of m.p. 178—181°C, and from chloroform–methanol in prisms of m.p. 202—204°C, $[\alpha]_D$ +77°. IR spectrum: 1737, 1265, 1040, 1030 (CH_3COO and COC) cm^{-1}. For $C_{34}H_{54}O_5$ (542·8) calculated: 75·23% C, 10·03% H; found: 75·06% C, 10·08% H.

B) A solution of epoxide *XXIII* (100 mg) in a mixture of dioxan (25 ml), water (3 ml) and 80% perchloric acid (1 ml) was allowed to stand at room temperature for 5 days. After working up and chromatography on silica gel (5 g, elution with ether) diol *XXVIII* (100 mg) was obtained in the form of plates of m.p. 260—263°C (cyclohexane), identical with the preparation described under *A*). $[\alpha]_D$ +95°.

3α-Bromo-19β,28-epoxy-18α-oleanan-2-one (*XXXII*)

When oxidized as in the preparation of bromo ketone *XXVI* (2 hours) bromohydrin *XXX* (320 mg, see[14]) gave after crystallization from chloroform–cyclohexane bromo ketone *XXXII* (220 mg) in the form of prisms of m.p. 237—239°C (decomposition). From chloroform–methanol the substance crystallized in the form of plates of m.p. 243—244·5°C, $[\alpha]_D$ +166°. IR spectrum: 1716 (CO), 1036 (COC) cm^{-1}. For $C_{30}H_{47}BrO_2$ (519·6) calculated: 69·36% C, 9·12% H; found: 69·17% C, 9·33% H.

19β,28-Epoxy-18α-oleanan-3-one (*XXXIII*)

On reaction of bromohydrin *XXVII* (60 mg) with potassium hydroxide, as in the case of the preparation of epoxide *V*, ketone *XXXIII* (50 mg) was obtained, m.p. 233—235°C (chloroform–methanol), identical with an authentic specimen[4].

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

Epoxide *XXXVI* (3·15 g) was dissolved in benzene and chromatographed on alumina (100 g, act. I—II). Benzene eluted epoxide *XXXVI* (1·27 g), methanol eluted diol *XXXIV* (1·70 g), m.p. 247—250°C. An analytical sample obtained by crystallization from chloroform–methanol and chloroform–ethyl acetate and benzene had m.p. 255—257°C, $[\alpha]_D$ +45°. For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·38% C, 10·92% H. Diacetate *XXXV*: m.p. 247—249°C (chloroform–ethyl acetate), $[\alpha]_D$ +18°. IR spectrum: 1738, 1264, 1032 (CH_3COO and COC) cm^{-1}. For $C_{34}H_{54}O_5$ (542·8) calculated: 75·23% C, 10·03% H; found: 75·37% C, 9·82% H.

2α-Bromo-19β,28-epoxy-18α-oleanan-3β-ol (*XXXVII*) and
3α-Bromo-19β,28-epoxy-18α-oleanan-2β-ol (*XXX*)

A solution of epoxide *XXXVI* (920 mg) in chloroform (15 ml) was shaken with 48% hydrobromic acid (10 ml) for 4 hours. The crude product contained according to thin-layer chromatography bromohydrins *XXX* and *XXXVII* only. The product was dissolved in benzene and chromatographed on silica gel (70 g). A mixture of benzene and ether (19 : 1) eluted bromohydrin *XXXVII* (870 mg) of m.p. 239—241°C (chloroform–methanol), identical with an authentic sample[4]. Further elution with the same mixture gave bromohydrin *XXX* (80 mg), identical with an authentic specimen[14]. M.p. 212—215°C (cyclohexane). Acetate *XXXI* crystallized from n-hexane either in the form of plates of m.p. 192·5—194°C or in the form of needles of m.p. 115—120°C/192 to

193°C (on slow heating a change in crystal modification takes place without melting). From methanol it crystallized in needles, m.p. 178—180°C, or plates, m.p. 193—195°C, $[\alpha]_D$ +102°C. IR spectrum: 1731, 1251 (CH_3COO), 1037 (COC) cm^{-1}. For $C_{32}H_{51}BrO_3$ (563·6) calculated: 68·19% C, 9·12% H; found: 68·06% C, 9·24% H. Bromohydrins *XXX* and *XXXVII* were isolated unchanged after an attempt at their isomerization with hydrobromic acid for 70 hours, under the conditions mentioned above. For the calculation of the composition of the mixture of bromohydrins $[\alpha]_D$ values were used, obtained as a mean of 4—7 independent measurements on various preparations: bromohydrin *XXX*: +103 ± 1°, bromohydrin *XXXVII*: +31·5 ± 1°, crude product after reaction: +38·9 ± 0·5°.

2α-Bromo-19β,28-epoxy-18α-oleanan-3-one (*XXXVIII*)

Oxidation of bromohydrin *XXXVII* (230 mg) was carried out in the same manner as bromo ketone *XXVI*, the product was precipitated with water, filtered off under suction and dried at 100°C. The crude bromo ketone *XXXVIII* (230 mg) had $[\alpha]_D$ +35°C, while after crystallization from chloroform–methanol its $[\alpha]_D$ was +34·5°, m.p. 234—236°C, in agreement with literature[4]. When the oxidation was repeated and the mixture worked up in the conventional manner preparations of $[\alpha]_D$ +35 ± 0·5° were obtained.

2α,3α; 20β,28-Diepoxy-18α,19β*H*-ursane (*XL*)

A solution of olefin *XXXIX* (570 mg, see[17]) and 3-chloroperoxybenzoic acid (300 mg) in chloroform (20 ml) was allowed to stand at 0°C for 26 hours. Epoxide *XL* (360 mg) of m.p. 257—259°C (chloroform–hexane), $[\alpha]_D$ +30°, was obtained. IR spectrum: 1060, 829 (COC) cm^{-1}. For $C_{30}H_{48}O_2$ (440·7) calculated: 81·76% C, 10·98% H; found: 81·53% C, 11·12% H.

2β-Bromo-20β,28-epoxy-18α,19βH-ursan-3α-ol (*XLI*)

Similarly as in the preparation of bromohydrin *VI* epoxide *XL* (430 mg) gave on reaction with hydrobromic acid and crystallization from chloroform–cyclohexane bromohydrin *XLI* (205 mg), m.p. 232—234°C, $[\alpha]_D$ +80°. IR spectrum: 3580 (OH), 1062 (COC) cm^{-1}. For $C_{30}H_{49}BrO_2$ (521·6) calculated: 69·08% C, 9·47% H; found: 69·01% C, 9·47% H.

2β-Bromo-20β,28-epoxy-18α,19β*H*-ursan-3-one (*XLII*)

Oxidation of bromohydrin *XLI* (340 mg) by a procedure identical with that applied in the preparation of bromo ketone *XXVI*, and crystallization of the product from chloroform–hexane gave bromo ketone *XLII* (160 mg), m.p. 254—256°C (decomposition), $[\alpha]_D$ +121°. IR spectrum: 1734 (CO), 1062 (COC) cm^{-1}. For $C_{30}H_{47}BrO_2$ calculated: 69·36% C, 9·12% H; found: 69·09% C, 9·02% H.

Isomerization of Bromo Ketones

A solution of 2-bromo-1-oxo derivative *XII* or *XVIII* (30—40 mg) in chloroform (10 ml), containing 3·5% of hydrogen bromide, was allowed to stand at 22 ± 2°C for 7 days; after working up the crystalline residue was dried at 100°C. Thin-layer chromatography and infrared spectra indicated that no side-reactions took place. The mixtures of bromo ketones *XII* and *XVIII* obtained had $[\alpha]_D$ +73 ± 1° (when rotation was measured in the presence of hydrogen bromide $[\alpha]_D$ was +91°). When the isomerization was carried out in acetic acid containing 4% of hydrogen bromide

after 2 days standing a mixture was obtained of $[\alpha]_D +74 \pm 1°$. Isomerization of 2-bromo-3-oxo derivatives was carried out with 1·1% hydrogen bromide in chloroform for 17 hours, as above. For the equilibrium mixtures of derivatives *XXVI* and *XXXVIII* the value $[\alpha]_D +74 \pm 2°$, and for the mixtures of derivatives *XLII* and *XLIII* (see[4]) the value $[\alpha]_D +66·5 \pm 1°$ was found.

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