ELIMINATION REACTIONS ON ANGULAR HYDROXYMETHYL GROUP OF THE LUPANE SKELETON*

A.VYSTRČIL[a], V.KŘEČEK[a] and M.BUDĚŠÍNSKÝ[b]

[a] *Department of Organic Chemistry, Charles University, 12840 Prague 2,*
[b] *Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6*

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It was shown that on dehydration of 28-lupanol derivatives *I*, *V*, or solvolysis of 28-tosyl derivatives *III*, *VI* and *VII* identical "anhydro derivatives" *VIII*, *X* and *XI* are formed as the main products. Their structure with the expanded ring E and with the 17(22)-double bond was proposed on the basis of IR and PMR spectra of these anhydro compounds, their dihydro derivatives *XII*–*XV*, derivatives with the functionalised ring E, *XVI*–*XXIV*, *XXVII*, *XXVIII*, and the mass spectrum of the thioketal *XXV*. Equilibration of ketones *XVII* and *XXVIII* demonstrated that ketone *XVII* with *cis*-annelated rings D/E is distinctly more stable ($-\Delta G = 1{\cdot}2$ kcal/mol) than the isomeric ketone *XXVIII* with *trans*-annelated rings D/E.

In previous papers[1,2] we discussed the consequences of steric interactions of the side chain of the lupane skeleton. In order to determine the dependence of these interactions on the ring E size it was necessary to solve the possibility of the preparation of 19α-isopropyl-29,30-dinor-(or 28,29,30-trinor)-18α-oleanane derivatives. Among several possibilities expansion of ring E in 28-lupanol derivatives during the elimination of the 28-hydroxy group seemed most viable. These reactions were already described, either using Vesterberg's procedure[3], *i.e.* by direct elimination of the hydroxyl group under the effect of phosphorus pentachloride in light petroleum, or according to Ruzicka[4] by reaction of 28-methanesulfonate with sodium iodide in acetone. The products formed – at that time called "anhydrobetulin and derivatives" – were not further investigated and their structure has not yet been determined. Therefore we first investigated these reactions more thoroughly on simpler 28-lupanol derivatives, aiming at the optimisation of the reaction conditions as well as the determination of the structure of the products formed.

After preliminary studies[5–7] it became evident that the original Vesterberg's procedure was satisfactory, while Ruzicka's method had to be modified[8] to the solvolysis of 28-O-tosyl derivatives in dimethylaniline. It was observed that on reaction of 3β-acetoxy-28-lupanol (*V*) or its 28-O-tosyl derivative *VI* under these conditions

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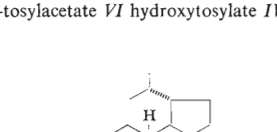
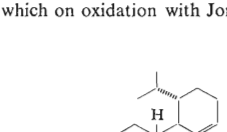
the main reaction product was in both instances identical but that the solvolytic procedure was better reproducible. In order to be able to identify safely the angular 8β- and 14α-methyl group signals during the interpretation of the PMR spectra it was necessary to prepare a series of these anhydro derivatives differing by substitution at the position $C_{(3)}$ (refs[9–12]). In order to prove that undesirable changes do not take place in any reaction step we carried out these preparations in three variants. In the case of the first procedure anhydro acetate *X* was converted by base catalysed hydrolysis to hydroxy derivative *IX* the oxidation of which with chromium trioxide in pyridine gave 3-oxo derivative *XI*. Further, on reduction of 3-oxo derivative *XI* according to Huang and Minlon 3-deoxy derivative *VIII* was prepared. For an alternative preparation of oxo derivative *XI* and deoxy derivative *VIII* we made use of the relative stability of the 28-*p*-toluenesulfonyloxy group: on hydrolysis of 28--O-tosylacetate *VI* hydroxytosylate *IV* was prepared which on oxidation with Jones



I; $R^1 = R^2 = R^3 = H$
II; $R^1 = R^2 = H$, $R^3 = Ac$
III; $R^1 = R^2 = H$, $R^3 = Ts$
IV; $R^1 = OH$, $R^2 = H$, $R^3 = Ts$
V; $R^1 = OAc$, $R^2 = R^3 = H$
VI; $R^1 = OAc$, $R^2 = H$, $R^3 = Ts$
VII; $R^1 + R^2 = O$, $R^3 = Ts$

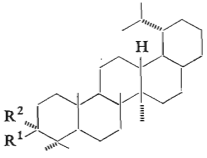


VIII; $R^1 = R^2 = H$
IX; $R^1 = OH$, $R^2 = H$
X; $R^1 = OAc$, $R^2 = H$
XI; $R^1 + R^2 = O$

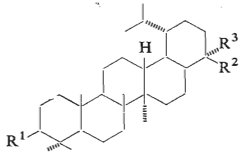
reagent was rapidly converted – without side reactions – to oxo derivative *VII*; subsequent solvolysis again afforded anhydro derivative *XI*. In the last reaction variant elimination of the 28-*p*-toluenesulfonyloxy group was carried out at the last step. From the known[13] methyl ester of 3-deoxydihydrobetulinic acid 28-lupanol (*I*) was prepared by reduction with lithium aluminum hydride and then transformed to acetate *II* for further characterisation. Tosylate *III* obtained on tosylation of hydroxy derivative *I* was again submitted to solvolysis in dimethylaniline affording thus anhydro derivative *VIII* in good yield, identical with the preparation prepared by the above mentioned procedures.

General characterisation of anhydro derivatives *VIII*–*XI*. Elimination of the 28-OR group is in all instances connected with formation of a new double bond (IR: 1672–1675 cm^{-1}) which is according to PMR spectra trisubstituted, *i.e.* it ap-

pears as a one-proton multiplet (δ = 5·335 to 5·29 p.p.m., $W_{1/2}$ = 9·2 to 10 Hz). The isopropyl chain of anhydro derivatives *VIII*–*XI* appears in the spectrum as a six-proton doublet (δ = 0·87 p.p.m., J = 6 Hz), the chemical shift of which, when compared with saturated derivatives *XII*–*XV*, shows that the isopropyl chain is not in the closest proximity of the double bond. The signals of the 8β- and 14α-methyl groups are shifted by this double bond downfield ($\Delta\delta$ = +0·01 to +0·035 p.p.m. and +0·01 to 0·045 p.p.m., resp.). These partial findings fit best with the assumption of the presence of the double bond in anhydro derivatives *VIII*–*XI* in the position 16 (17) or 17 (22.) In order to decide between these alternatives we considered it useful to convert a suitable anhydro derivative (*VIII* or *X*) to an oxo derivative the oxo group of which would be in the place of the original disubstituted double-bonded carbon



XII; $R^1 = R^2 = H$
XIII; $R^1 = OH$, $R^2 = H$
XIV; $R^1 = OAc$, $R^2 = H$
XV; $R^1 + R^2 = O$



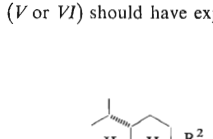
XVI; $R^1 = R^2 = H$, $R^3 = OH$
XVII; $R^1 = H$, $R^2 + R^3 = 0$
XVIII; $R^1 = R^3 = OH$, $R^2 = H$
XIX; $R^1 = OAc$, $R^2 = H$, $R^3 = OH$
XX; $R^1 = OAc$, $R^2 = OH$, $R^3 = H$
XXI; $R^1 = R^3 = OAc$, $R^2 = H$
XXII; $R^1 = R^2 = OAc$, $R^3 = H$
XXIII; $R^1 = OAc$, $R^2 + R^3 = O$
XXIV; $R^1 = OAc$, $R^2 + R^3 = NOH$
XXV; $R^1 = OAc$, $R^2 + R^3 = SCH_2CH_2S$

atom. The first step in this direction was the reaction of anhydro derivatives with diborane, giving rise to saturated secondary hydroxy derivatives. From models it is evident that the *cis*-addition of diborane[14] to the double bond of anhydro derivatives *VIII*–*XI* from both the α and β side is connected with the formation of an equatorial hydroxy group, while in the case of α-side addition the D/E rings become *cis*-annelated, and in the case of β-side addition they are *trans*-annelated. These two alternatives should be discriminated on the basis of the Cotton effect of oxo derivative derived from the corresponding hydroxy compound.

By this procedure hydroxy acetate *XIX* was formed from the easily accessible acetate *X*, accompanied by a small amount of diol; as this diol was identical with the product (*XVIII*) of the base catalysed hydrolysis of acetate *XIX*, it must have arisen

by hydrolysis of 3-O-acetyl group during the oxidation of the alkyl borane adduct in alkaline medium. The main product of this reaction was characterised as diacetate *XXI*. The considered reaction course is in agreement with the spectroscopic properties of the products: in the PMR spectrum of acetate *XIX* a multiplet at 3·865 p.p.m. is indicative, the half-width of which ($W_{1/2}$ = 27 Hz) clearly indicates that it is due to an axial hydrogen. The same conclusion follows from the spectrum of diacetate *XXI* (multiplet at 5·15 p.p.m., $W_{1/2}$ = 22 Hz). On oxidation of hydroxy derivative *XIX* with chromium trioxide in pyridine ketone *XXIII* was prepared which was also characterised as oxime *XXIV*. The carbonyl group of ketone *XXIII* is in a six-membered (or larger) cycle (IR: 1713, 1432 cm^{-1}). In its PMR spectrum both a complex two-proton multiplet at 2·20–2·00 p.p.m., and a one-proton multiplet at 2·50 p.p.m. are significant. By this it is proved that *a*) a 16 (17) double bond cannot be present in the starting anhydro derivative *X*, because the α-methylene group of the oxo derivative *XXIII* should then be on $C_{(15)}$ and should appear as an AB-quartet, and *b*) the ring E of the starting lupane derivative (*V* or *VI*) should have expanded during the formation of anhydro derivative *X*.

XXVI



XXVII; R^1 = OH, R^2 = H
XXVIII; $R^1 + R^2$ = 0

We came to the same conclusion by two other independent proofs: the first is the mass spectrum of thioketal *XXV* which was prepared in the conventional manner[15] from ketone *XXIII*. The fragment *m/e* 131 due to ion *XXVI* could not be formed if the oxo group in ketone *XXIII* was on $C_{(16)}$. The second, independent, proof concerning the position of the original trisubstituted double bond of anhydro derivative *X* was brought about by the reduction of ketone *XXIII* with sodium borohydride; a mixture of epimeric hydroxy derivatives *XIX* and *XX* was thus formed which are well differentiated on the basis of their mobility on silica gel thin layers and by their acetylation rates. The epimer *XX*, which moves faster, is acetylated relatively slowly to diacetate *XXII* the narrow multiplet of which ($W_{1/2}$ = 7 Hz) at 5·03 p.p.m. in the PMR spectrum indicates and equatorial 22-H. As in epimers with an equatorial hydroxy group (*XIX*) or acetoxy group (*XXI*) no significant shift of the 14α-methyl group signal can be observed either, these axial groups cannot be on $C_{(16)}$ (*cf.*[16]).

The exploitation of the Cotton effect of ketone *XXIII* for the determination of the annelation of the D/E cycles and thus also for the determination of the preferred side of diborane addition to anhydro derivative *X* was found to be unrealisable. It is evident from its ORD curve (Fig. 1, curve *1*) that its Cotton effect is not very distinct and is complex. Therefore we studied in detail the reaction of diborane with 3-deoxy derivative *VIII*. With this we were also able to isolate directly only one (*XVI*) of both possible (*XVI* or *XXVII*) hydroxy derivatives; its oxidation with chromium trioxide in pyridine gave ketone *XVII*, from the optical rotatory dispersion of which (Fig. 1, curve *2*) it is evident that it belongs to the same configurational series as ketone *XXIII*. The presence of the isomeric hydroxy derivative *XXVII* was proved in the mother liquors after crystallisation of hydroxy derivative *XVI* by their oxidation. In addition to ketone *XVII* the isomeric ketone *XXVIII* was also isolated, and according to preparative yields their ratio was 9 : 1. In contrast to ketones *XVII* and *XXIII* the isomeric ketone *XXVIII* has a simple negative Cotton effect (Fig. 1, curve *3*), *i.e.* it must have the reverse configuration on $C_{(17)}$.

Comparison of the ORD curves of steroid models[17] shows a striking similarity of the Cotton effect of ketone *XXVIII* and 5α-cholestan-4-one, and of Cotton effect of ketones *XVII* and *XXIII* and 5β-cholestan-4-one. From this it may be judged that ketone *XXVIII* has the rings D/E *trans* annelated and that the parent alcohol *XXVII* must have been formed by the (less preferred) addition to the double bond of diborane from the β side of anhydro derivative *VIII*; on the contrary, the reverse annelation (*i.e. cis*) of the cycles D/E in ketones *XVII* and *XXIII*, and the yield of the parent hydroxy derivatives *XVI* or *XIX* means that this double bond is much more easily attacked by diborane from the α side. There is some uncertainly in these conclusions owing to two facts: first, the model steroidal ketones are not substituted

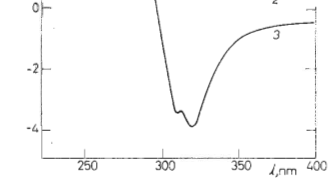


FIG. 1

Optical Rotation Dispersion Curves of Ketones *XVII* (*2*), *XXIII* (*1*) and *XXVIII* (*3*) in Dioxane

with an alkyl at $C_{(1)}$, and second, it was not yet proved that during the formation of anhydro derivatives *VIII* or *X* the original configuration at $C_{(18)}$ remains unchanged. The relative stability of their configuration at $C_{(17)}$ also seems to be against the proposed annelation of the D/E rings in ketones *XVII* and *XXIII* or *XXVIII* as we have shown by equilibration of ketones *XVII* and *XXVIII*, the equilibrium is shifted distinctly (88%) in favour of ketone *XVII*, *i.e.* the proposed *cis*-annelation of the rings D/E seems energetically more favourable ($-\Delta G = 1{\cdot}2$ kcal/mol) than the *trans*-annelation (*XXVIII*). This reversal of the relative stability of 1-decalones – as known[18] from the relation of 5α- or 5β-cholestan-4-ones – must be a consequence of sterical interactions of the equatorial isopropyl chain at $C_{(19)}$. The solution of the configuration at $C_{(18)}$ and the effect of the side chain on the stability of the D/E annelation will be described in our subsequent paper.

EXPERIMENTAL

The melting points were determined on a Kofler block and are not corrected. Optical rotation was measured in chloroform on an automatic polarimeter (ETL-NPL, Bendix Ericsson) with $a \pm 2°$ accuracy. The infrared spectra were measured in chloroform on IKS-14, ÚPT-ČSAV, Brno, UR-10, and Unicam SP-200 spectrophotometers. The ultraviolet spectra were measured in ethanol (unless otherwise stated) on a Unicam SP-700 apparatus. Proton magnetic resonance was measured with a Varian HA-100 instrument, in deuteriochloroform, using tetramethylsilane as internal reference; chemical shifts are given in p.p.m., δ-scale. Optical rotatory dispersion was recorded with a JASCO-ORD/UV-5 machine, in dioxan, and the mass spectra on a MCh-1303 apparatus. For chromatography neutral alumina of activity II according to Brockmann, or silica gel according to Pitra (30–60μ particle size) were employed. Analytical samples were dried at 100°C and reduced pressure (0·1–1 Torr) over phosphorus pentoxide for 10 hours. Under "conventional work-up" we understand: dilution of the reaction mixture with water, extraction of the product from this mixture with ether, repeated washing of the extract with water, dilute hydrochloric acid (1 : 4), water, and 5% sodium carbonate. All solutions were dried over anhydrous sodium sulfate. The identity of the compounds was determined by mixture melting points, optical rotation, thin-layer chromatography and infrared spectra.

3β-Acetoxy-28-tosyloxylupane (*VI*)

p-Toluenesulfonyl chloride (34·0 g) was added in portions to a solution of 33·7 g of 3β-acetoxy-28-lupanol (*V*) in 130 ml of pyridine and the mixture was allowed to stand for 6 days at room temperature. After the conventional working up and concentration of the ethereal solution 27·3 g (61%) of tosylate *VI* crystallised out, m.p. 174–176°C, $[\alpha]_D$ −3° (*c* 0·66). IR spectrum: 1607, 1366, 1178, 958, 856, 840, 815 (*p*-toluenesulfonyl), 1730, 1260 (CH_3COO) cm^{-1}. For $C_{39}H_{60}O_5S$ (640·9) calculated: 73·08% C, 9·44% H, 5·00% S; found: 73·14% C, 9·51% H, 5·02% S.

28-Tosyloxylupan-3β-ol (*IV*)

A solution of 42·0 g of acetate *VI* in benzene (150 ml) was mixed with an ethanolic solution of 5·0 g of potassium hydroxide and the mixture was refluxed for 6 hours. After dilution of the reaction mixture with water and extraction with ether the ethereal layer was washed with water

and dried. On concentration of the extract and addition of ethanol 34·9 g (89%) of hydroxy derivative *IV* crystallised out, m.p. 185—186°C which on further crystallisation from benzene–ethanol rose to 187·5—188·5°C; $[\alpha]_D$ −12° (*c* 0·54), IR spectrum: 1607, 1365, 1177, 958, 855, 842, 815 (*p*-toluenesulfonyl), 3640, 3480, 1042, 1027 (OH) cm^{-1}. For $C_{37}H_{58}O_4S$ (598·9) calculated: 74·20% C, 9·76% H, 5·35% S; found: 74·22% C, 9·80% H, 5·35% S.

28-Tosyloxylupan-3-one (*VII*)

To a suspension of 34·0 g of hydroxy derivative *IV* in 600 ml of acetone Jones'reagent was added dropwise under constant stirring until the colour of the excess reagent persisted. After 1/4 hour's standing at room temperature the mixture was diluted with water, extracted with ether, and — after conventional working up — the neutral fraction was crystallised from ether–methanol. Yield 31·0 g (91%) of oxo derivative *VII*, m.p. 177—180°C. Further crystallisation from a mixture of benzene and ethanol brought about a rise in the melting point to 180—182°C, $[\alpha]_D$ 6° (*c* 0·56). IR spectrum: 1606, 1364, 1176, 960, 855, 842, 815 (*p*-toluenesulfonyl), 1701 (CO) cm^{-1}. For $C_{37}H_{56}O_4S$ (596·9) calculated: 74·45% C, 9·46% H, 5·37% S; found: 74·62% C, 9·58% H, 5·40% S.

3β-Acetoxy-19α-isopropyl-28,29,30-trinor-18α-olean-17(22)-ene (*X*)

a) *Dehydration of* 3-O-*acetyldihydrobetulin* (V) *with phosphorus pentachloride*: Acetate *V* (7·94 g) was added in small portions and under shaking to a suspension of 7·0 g of phosphorus pentachloride in 500 ml of light petroleum, and the mixture allowed to stand at room temperature overnight. The undissolved residue was filtered off and the light petroleum solution was washed with water and 5% sodium carbonate in water. The organic layer was filtered through a layer of alumina and evaporated. Crystallisation of the residue from benzene–ethanol gave 4·20 g (55%) of crude anhydro acetate *X* of m.p. 195—203°C which after four crystallisations from ethyl acetate rose to 207·5°C, $[\alpha]_D$ −31° (*c* 1·40). IR spectrum: 1722, 1375, 1259 (CH_3COO), 1672 (C=C) cm^{-1}. PMR spectrum: 0·84 (4α-CH_3 + 4β-CH_3), 0·855 (10β-CH_3), 0·87 d, J = 6·2 Hz (19α-$CH(CH_3)_2$), 0·95 (14α-CH_3), 1·05 (8β-CH_3), 2·035 (3β-$OCOCH_3$), 4·49 m (3α-H), 5·325 m, $W_{1/2}$ = 9 Hz (22-H). For $C_{32}H_{52}O_2$ (468·7) calculated: 81·99% C, 11·18% H; found: 81·71% C, 11·20% H.

b) *Solvolysis of tosylate* VI: A solution of 6·60 g of tosylate *VI* in 40 ml of dimethylaniline was refluxed for 4 hours. After cooling and working up the product was crystallised from chloroform–methanol to yield 4·41 g (92%) of acetate *X* which on further crystallisation from ethyl acetate gave an analytical sample identical with the preparation prepared under *a*). Hydrolysis of 0·63 g of acetate *X* by three hours'boiling with a solution of 0·2 g of potassium hydroxide in benzene–ethanol gave 0·52 g of hydroxy derivative *IX*, of m.p. 179—180·5°C (chloroform–hexane), $[\alpha]_D$ −47° (*c* 1·33). IR spectrum: 3620, 3470, 1032 (OH), 1675 (C=C) cm^{-1}. PMR spectrum: 0·765 (4β-CH_3), 0·84 (10β-CH_3), 0·87 d, J = 6·2 Hz (19α-$CH(CH_3)_2$), 0·95 (14α-CH_3), 0·98 (4α-CH_3), 1·06 (8β-CH_3), 3·20 m (3α-H), 5·32 m, $W_{1/2}$ = 10 Hz (22-H). For $C_{30}H_{50}O$ (426·7) calculated: 84·44% C, 11·81% H; found: 84·20% 11·74% H.

3-Oxo-19α-isopropyl-28,29,30-trinor-18α-olean-17(22)-ene (*XI*)

a) *Oxidation of hydroxy derivative* IX: Chromium trioxide (1·20g) was added in several portions to a solution of 2·04 g of hydroxy derivative *IX* in 40 ml of pyridine and the mixture allowed to stand at room temperature for 5 days. After the conventional working up crystallisation from

chloroform–methanol of the crude product gave 1·53 g (75%) of 3-oxo derivative *XI*, m.p. 224 to 225°C, $[\alpha]_D$ −14° (*c* 1·13) IR spectrum: 1·701 (C=O), 1430 (α-CH_2) cm^{-1}. PMR spectrum: 0·87 d, $J = 6·0$ Hz (19α-$CH(CH_3)_2$), 0·94 bs (10β-CH_3), 0·985 (14α-CH_3), 1·03 (4β-CH_3), 1·07 (4α-CH_3), 1·08 (8β-CH_3), 5·335 m, $W_{1/2} = 10$ Hz (22-H). For $C_{30}H_{48}O$ (424·7) calculated: 84·84% C, 11·39% H; found: 85·04% C, 11·58% H.

b) *Solvolysis of tosylate* VII. The solvolysis of 32·0 g of tosylate *VII* by boiling in 110 ml of dimethylaniline and further working up was carried out as in the case of tosylate *VI*. Crystallisation from methanol gave 12·8 g (56%) of oxo derivatives *XI*. An analytical sample prepared by further crystallisation from chloroform–methanol and hexane was identical with the preparation prepared under *a*).

19α-Isopropyl-28,29,30-trinor-18α-olean-17(22)-ene (*VIII*)

a) *Reduction of 3-oxo derivative* XI: Hydrazine hydrate (85%; 6 ml) followed by ethanol was added to a solution of 1·04 g of oxo derivative *XI* in benzene (10 ml) until a homogeneous solution was obtained. The mixture was refluxed for 5 hours, concentrated to half its volume, and 2 ml of 85% hydrazine hydrate, 20 ml of diethylene glycol, and 1·9 g of potassium hydroxide were added to it and the mixture slowly heated to 220°C and kept at this temperature for 3 hours. Further conventional work-up gave 1·18 g of crude product which was dissolved in benzene, the solution filtered through a layer of alumina, evaporated and the residue crystallised from chloroform–methanol. Yield 0·87 g (64%) of 3-deoxy derivative *VIII*, m.p. 179–182°C. An analytical sample was prepared by additional crystallisation (chloroform–ethyl acetate, chloroform–methanol) and it had m.p. 181·5–182·5°C, $[\alpha]_D$ −47° (*c* 1·20). IR spectrum: 1674 (C=C) cm^{-1}. PMR spectrum: 0·80 (4β-CH_3), 0·84 bs (4α-CH_3 + 10β-CH_3), 0·88 d, $J = 6·0$ Hz (19α-$CH(CH_3)_2$), 0·945 (14α-CH_3), 1·065 (8β-CH_3), 5·29 m (22-H). For $C_{30}H_{50}$ (410,7) calculated: 87·73% C, 12·27% H; found: 87·81% C, 12·40% H.

b) *Solvolysis of tosylate* III: The soivolysis of tosylate *III* (1·51 g) in boiling dimethylaniline (5 ml) and further working up were carried out as in the preceeding cases. A product was obtained (0·58 g; 55%) which on crystallisation (chloroform–methanol) gave 0·39 g of an analytical sample of anhydro derivative *VIII*, identical with the preparation prepared under *a*).

28-Lupanol (*I*)

Methyl ester of lupan-28-oic acid[13] (2·20 g) was dried at 110°C and refluxed with excess ethereal lithium aluminum hydride for 3 hours. After the decomposition of excess hydride with ethyl acetate and further conventional work-up the product was crystallised from methanol. Yield 1·82 g (88%) of 28-lupanol (*I*), m.p. 177–177·5°C, $[\alpha]_D$ −20° (*c* 1·45). IR spectrum: 3630, 1026 OH) cm^{-1}. For $C_{30}H_{52}O$ (428·7) calculated: 84·04% C, 12·23% H; found: 83·84% C, 12·14% H. The mother liquors were evaporated to dryness and the residue (0·38 g) acetylated in the usual manner with a mixture of acetic anhydride and pyridine. Yield 0·35 g of acetate *II*, m.p. 170–171°C (methanol), $[\alpha]_D$ −20° (*c* 1·20). IR spectrum: 1727, 1248 (CH_3COO) cm^{-1}. For $C_{32}H_{54}O_2$ (470·75) calculated: 81·64% C, 11·56% H; found: 81·13% C, 11·11% H.

28-*p*-Toluenesulfonyloxylupane (*III*)

p-Toluenesulfonyl chloride (0·53 g) was added in portions to a solution of 1·26 g of 28-lupanol (*I*) in pyridine and the mixture allowed to stand at room temperature for 2 days. After working up the product was crystallised from light petroleum and from chloroform–methanol to yield

1·64 g (95%) of the ester *III* of m.p. 170—171°C, $[\alpha]_D$ −11° (*c* 1·53). IR spectrum: 1602, 1178, 958, 856, 843, 818 (*p*-toluenesulfonyl) cm^{-1}. For $C_{37}H_{58}O_3S$ (582·9) calculated: 76·23% C, 10·03% H, 5·50% S; found: 76·04% C, 9·86% H, 5·51% S.

3β-Acetoxy-19α-isopropyl-28,29,30-trinor-17α,18α-oleanane (*XIV*)

A solution of 0·5 g of anhydro acetate *X* in 50 ml of ether was hydrogenated on Adams platinum catalyst. After filtration off of the catalyst and concentration of the ethereal solution methanol was added from which 0·44 g (88%) of dihydro derivative *XIV* crystallised out, m.p. 253—258°C. An analytical sample was prepared by double crystallisation from a mixture of chloroform and methanol and it had m.p. 266—268°C, $[\alpha]_D$ 44° (*c* 0·82). IR spectrum: 1725, 1260 (CH_3COO) cm^{-1}. PMR spectrum: 0·85 (4α-CH_3 + 4β-CH_3), 0·855 d, J = 6·5 Hz and 0·865 d, J = 6·5 Hz (19α-$CH(CH_3)_2$), 0·88 (10β-CH_3), 0·92 (14α-CH_3), 1·03 (8β-CH_3), 2·03 (3β-$OCOCH_3$), 4·49 m (3α-H). For $C_{32}H_{54}O_2$ (470·75) calculated: 81·64% C, 11·56% H; found: 81·97% C, 11·87% H. On hydrolysis of acetate *XIV* with benzene–ethanolic potassium hydroxide solution by 3 hour's refluxing and the usual working up 0·17 g (70%) of hydroxy derivative *XIII* were obtained, m.p. 212—214°C (chloroform–methanol), $[\alpha]_D$ 38° (*c* 0·92). IR spectrum: 3630, 3400, 1025 (OH) cm^{-1}. PMR spectrum: 0·76 (4β-CH_3), 0·84 (10β-CH_3), 0·84 d, J = 6·3 Hz and 0·85 d, J = = 6·3 Hz (19α-$CH(CH_3)_2$), 0·915 (14α-CH_3), 0·96 (4α-CH_3), 1·02 (8β-CH_3), 3·21 m (3α-H).

19α-Isopropyl-28,29,30-trinor-17α,18α-oleanan-3-one (*XV*)

To a solution of 0·14 g of hydroxy derivative *XIII* in a mixture of benzene and acetic acid a solution of 0·10 g of chromium trioxide in acetic acid was added dropwise and the mixture allowed to stand at room temperature for one day. After a conventional working up 0·04 g (29%) of 3-oxo derivative *XV* were obtained, m.p. 199—203°C (chloroform–methanol), $[\alpha]_D$ 64° (*c* 0·43). IR spectrum: 1702 (C=O), 1428 (α-CH_2) cm^{-1}. PMR spectrum: 0·845 d, J = 6·1 Hz and 0·855 d, J = 6·1 Hz (19α-$CH(CH_3)_2$), 0·94 (14α-CH_3), 0·95 (10β-CH_3), 1·03 (4β-CH_3), 1·07 (4α-CH_3 and 8β-CH_3), 2·47 m (2-H_2). For $C_{30}H_{50}O$ (426·7) calculated: 84·44% C, 11·81% H; found: 84·15% C, 11·60% H.

19α-Isopropyl-28,29,30-trinor-17α,18α-oleanane (*XII*)

A solution of 0·14 g of unsaturated hydrocarbon *VIII* was hydrogenated in acetic acid on Adams catalyst. After the conventional working up and crystallisation from chloroform–methanol 0·12 g (85%) of dihydro derivative *XII* of m.p. 177—184°C were obtained. Further crystallisation from ethyl acetate and 2-butanone increased the melting point to 188—192°C, $[\alpha]_D$ 41° (*c* 0·62). PMR spectrum: 0·805 (4β-CH_3), 0·845 d, J = 6·3 Hz and 0·855 d, J = 6·3 Hz (19α-$CH(CH_3)_2$), 0·85 (4α-CH_3 + 10β-CH_3), 0·935 (14α-CH_3), 1·03 (8β-CH_3). For $C_{30}H_{52}$ (412·7) calculated: 87·30% C, 12·70% H; found: 87·28% C, 12·65% H.

3β-Acetoxy-19α-isopropyl-28,29,30-trinor-17α,18α-oleanan-22α-ol (*XIX*)

Diborane evolved from 3·2 g of boron trifluoride etherate and 0·52 g of sodium borohydride was introduced with a nitrogen stream into a solution of 4·0 g of acetate *X* in tetrahydrofuran. When the saturation was finished the reaction mixture was allowed to stand at room temperature overnight and the solution then mixed with a solution of 1·0 g of potassium hydroxide in 50 ml of ethanol and 16·2 ml of 30% hydrogen peroxide. The mixture was agitated for three hours, diluted with ether, and washed with water. After the usual working up of the ethereal extract

5·2 g of a residue were obtained which was separated chromatographically on 250 g of alumina. The first 200 ml of benzene eluate contained 0·52 g of the starting acetate *X*, a further 900 ml of ether eluted 2·78 g (67%) of hydroxy derivative *XIX*. After crystallisation from a mixture of benzene and ethanol it had m.p. 237—240°C, $[\alpha]_D$ 48° (*c* 1·20). IR spectrum: 1723, 1263 (CH_3COO), 3620, 3490, 1035 (OH) cm^{-1}. PMR spectrum: 0·85 (4α-CH_3 + 4β-CH_3), 0·86 d, J = 6·3 Hz and 0·88 d, J = 6·3 Hz (19α-$CH(CH_3)_2$), 0·87 (10β-CH_3), 0·95 (14α-CH_3), 1·01 (8β-CH_3), 2·02 (3β-$OCOCH_3$), 3·865 m, $W_{1/2}$ = 27 Hz (22β-H), 4·475 m (3α-H). For $C_{32}H_{54}O_3$ (486·75) calculated: 78·96% C, 11·18% H; found: 78·66% C, 11·06% H. Further elution with 300 ml of ether containing 20% of methanol gave 0·86 g of diol *XVIII*, m.p. 256—259°C, $[\alpha]_D$ 45° (*c* 0·62), which was identical with the product of hydrolysis of acetate *XIX*.

3β,22α-Dihydroxy-19α-isopropyl-28,29,30-trinor-17α,18α-oleanane (*XVIII*)

A solution of 100 mg of acetate *XIX* in benzene was refluxed with a solution of 50 mg of potassium hydroxide in ethanol. After conventional working up the product was crystallised from a mixture of chloroform–methanol, then from 2-butanone and from a mixture of benzene–hexane until the melting point was constant, *i.e.* 257·5—259°C, $[\alpha]_D$ 46° (*c* 1·20). IR spectrum: 3620, 3425, 1032 (OH) cm^{-1}. For $C_{30}H_{52}O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 80·89% C, 11·55% H.

3β,22α-Diacetoxy-19α-isopropyl-28,29,30-trinor-17α,18α-oleanane (*XXI*)

Acetylation of 0·32 g of monoacetate *XIX* was carried out with a mixture of 2 ml of pyridine and 1 ml of acetic anhydride at room temperature for one day. After the conventional working up crystallisation of the residue from chloroform–methanol afforded 0·35 g (92%) of diacetate *XXI*, m.p. 213·5—215°C, $[\alpha]_D$ 58° (*c* 1·33). IR spectrum 1727, 1260 (CH_3COO) cm^{-1}. PMR spectrum: 0·845 (4α—CH_3 + 4β-CH_3), 0·86 d, J = 6·0 Hz and 0·88 d, J = 6·0 Hz (19α-CH.$(CH_3)_2$), 0·87 (10β-CH_3), 0·93 (14α-CH_3), 1·045 (8β-CH_3), 2·01 and 2·03 (2 × CH_3COO), 4·48 m (3α-H), 5·15 m, $W_{1/2}$ = 22 Hz (22β-H). For $C_{34}H_{56}O_4$ (528·8) calculated: 77·22% C, 10·67% H; found: 77·10% C, 10·69% H.

3β-Acetoxy-19α-isopropyl-28,29,30-trinor-17α,18α-oleanan-22-one (*XXIII*)

A solution of 50 mg of chromium trioxide in acetic acid was added dropwise at room temperature and with stirring to a solution of 0·20 g of hydroxy derivative *XIX* in acetic acid and the mixture allowed to stand for 2 hours. Excess chromium trioxide was reduced with methanol and the mixture worked up. Crystallisation from a mixture of benzene and ethanol gave 0·10 g (53%) of oxoacetate *XXIII*, m.p. 260—262°C, $[\alpha]_D$ 67° (*c* 0·55). ORD: $[\Theta]_{322}$ +1935°, $[\Theta]_{315}$ +1680° $[\Theta]_{309}$ +1985°, $[\Theta]_{303}$ +1528°, $[\Theta]_{300}$ +1832°, $[\Theta]_{295}$ +1680°. IR spectrum: 1721, 1250 (CH_3COO), 1713 (C=O), 1422 (α-CH_2) cm^{-1}. PMR spectrum: 0·84 bs (4α-CH_3 + 4β-CH_3 + + 10β-CH_3), 0·885 (14α-CH_3), 0·93 (8β-CH_3), 0·965 d, J = 6·5 Hz (19α-$CH(CH_3)_2$), 2·03 (3β-$OCOCH_3$), 4·45 m (3α-H). For $C_{32}H_{52}O_3$ (484·7) calculated: 79·28% C, 10·81% H; found: 79·04% C, 11·00% H. To a solution of 50 mg of ketone *XXIII* in pyridine 50 mg of hydroxylamine hydrochloride were added and the mixture heated for 4 hours on a water bath. After the conventional working up and crystallisation from chloroform–methanol 30 mg of oxime *XXIV* were obtained, m.p. 222·5—224·5°C, $[\alpha]_D$ 66° (*c* 1·20). IR spectrum: 3585, 3300 (=N—OH), 1724, 1260 (CH_3COO) cm^{-1}. For $C_{32}H_{53}NO_3$ (499·75) calculated: 76·90% C, 10·69% H, 2·80% N; found: 77·00% C, 10·50% H, 2·93% N.

Ethylene dithioketal XXV: 1·5 ml of acetic acid, 0·5 ml of ethanedithiol, and 0·5 ml of boron trifluoride etherate were added to 40 mg of ketone *XXIII*. After mild heating of the mixture on a water bath methanol was added and the separated substance filtered off with suction and crystallised several times from a mixture of ether an light petroleum. Dithioketal *XXV* (10 mg) was obtained, m.p. 207—209·5°C, $[\alpha]_D$ −6° (*c* 0·23). IR spectrum: 1721, 1257 (CH_3COO) cm^{-1}. For $C_{34}H_{56}O_2S_2$ (560·9) calculated: 72·80% C, 10·06% H; found: 72·98% C, 9·87% H.

3β-Acetoxy-19α-isopropyl-28,29,30-trinor-17α,18α-oleanan-22β-ol (*XX*)

Sodium borohydride (0·27 g) was added to a solution of 0·27 g of ketone *XXIII* in a mixture of benzene (20 ml) and methanol (20 ml) and the mixture allowed to stand at room temperature for two days. After the working up the residue (0·25 g) was separated by chromatography on 20 g alumina. Elution with 110 ml benzene gave 0·24 g (89%) of hydroxyacetate *XX* which after crystallisation from chloroform–methanol had m.p. 267—268°C, $[\alpha]_D$ 35° (*c* 1·55). IR spectrum: 1724, 1261 (CH_3COO), 3620, 3425, 1032 (OH) cm^{-1}. PMR spectrum: 0·84 (4α-CH_3 + + 4β-CH_3), 0·87 (10β-CH_3), 0·87 d, J = 6 Hz (19α-CH(CH_3)$_2$), 0·93 (14α-CH_3), 1·01 (8β-CH_3), 2·03 (3β-OCOCH_3), 3·825 bs, $W_{1/2}$ = 6 Hz (22α-H), 4·48 m (3α-H). For $C_{32}H_{54}O_3$ (486·75) calculated: 78·96% C 11·18% H; found: 78·81% C, 11·38% H. Acetylation of hydroxyacetate *XX* (120 mg) with a mixture of acetic anhydride (2 ml) and pyridine (3 ml) on a water bath (100°C) for 6 hours and working up of the mixture gave diacetate *XXII*, m.p. 253—254·5°C (ethyl acetate), $[\alpha]_D$ 20° (*c* 0·69). IR spectrum: 1725, 1259 (CH_3COO) cm^{-1}. PMR spectrum: 0·85 (4α CH_3 + + 4β-CH_3), 0·87 d, J = 6 Hz (19α-CH(CH_3)$_2$), 0·89 (10β-CH_3), 0·925 (14α-CH_3), 1·07 (8β--CH_3), 2·03, 2·08 (2 × CH_3COO), 4·50 m (3α-H), 5·03 m, $W_{1/2}$ = 7 Hz (22α-H). For $C_{34}H_{56}O_4$ (528·8) calculated: 77·22% C, 10·67% H; found: 77·31% C, 10·95% H.

19α-Isopropyl-28,29,30-trinor-17α,18α-oleanan-22α-ol (*XVI*)

Into a solution of 4·0 g of anhydro derivative *VIII* in 150 ml of diglyme diborane was introduced at room temperature for 90 minutes. After 2·5 days standing the solution was again saturated with diborane at 50—60°C for 60 minutes, cooled, and additioned with a solution of 1 g of potassium hydroxide in 50 ml of ethanol. Hydrogen peroxide (30%; 16·2 ml) was added dropwise to the mixture which was then stirred for 3 hours. After dilution with water the mixture was extracted with ether, the ethereal layer was repeatedly washed with water and dried. After distillation off of the solvents *in vacuo* the residue was separated by chromatography on 80 g of alumina; 490 ml of benzene eluted 3·86 g of crude product which on repeated crystallisation from ethyl acetate gave 2·07 g (50%) of hydroxy derivative *XVI* of m.p. 191—195°C, or 218—219°C, $[\alpha]_D$ 51° (*c* 0·42). IR spectrum: 3610, 3460, 1060, 1030 (OH) cm^{-1}. PMR spectrum: 0·80 (4β-CH_3), 0·845 (4α-CH_3 + 10β-CH_3), 0·85 d, J = 6·4 Hz and 0·88 d, J = 6·4 Hz (19α-CH(CH_3)$_2$), 0·96 (14α-CH_3), 1·01 (8β-CH_3), 3·86 m, $W_{1/2}$ = 25 Hz (22β-H). For $C_{30}H_{52}O$ (428·7) calculated: 84·04% C, 12·23% H; found: 84·00% C, 11·93% H.

19α-Isopropyl-28,29,30-trinor-17α,18α-oleanan-22-one (*XVII*)

Chromium trioxide (1·00 g) in 150 ml of pyridine was added to a solution of 1·90 g of hydroxy derivate *XVI* in 60 ml of pyridine and the mixture alowed to stand at room temperature for 5 days. After addition of methanol and working up ketone *XVII* (1·63 g; 86%) was obtained which after several crystallisations form cyclohexane afforded 1·28 g of analytically pure material, m.p. 225—227°C, $[\alpha]_D$ 61° (*c* 0·62). ORD: $[\Theta]_{321}$ 1410°, $[\Theta]_{315}$ 1079°, $[\Theta]_{308,5}$ 1451°, $[\Theta]_{304}$ 1079°, $[\Theta]_{298,5}$ 1258°, $[\Theta]_{294,5}$ 1120°, $[\Theta]_{275}$ 1532°. UV spectrum (tetrahydrofuran);

λ_{max} 292 nm, log ε = 1·44. IR spectrum: 1705 (C=O), 1430 (α-CH_2) cm^{-1}. PMR spectrum: 0·79 (4β-CH_3), 0·82 (10β-CH_3), 0·84 (4α-CH_3), 0·89 (14α-CH_3), 0·94 (8β-CH_3), 0·97 d, J = 6·5 Hz (19α-CH(CH_3)$_2$), 2·50 bt (probably 17α-H). For $C_{30}H_{50}O$ (426·7) calculated: 84·44% C, 11·81% H; found: 84·29% C, 11·65% H.

19α-Isopropyl-28,29,30-trinor-18α-oleanan-22-one (*XXVIII*)

The residue (1·83 g) of the mother liquors after crystallisation of hydroxy derivative *XVI* was oxidised in pyridine with chromium trioxide in the same manner as in the preparation of ketone *XVII*. The crude product when crystallised from cyclohexane and from chloroform–methanol mixture gave 0·75 g of ketone *XVII* of m.p. 223—226°C, $[\alpha]_D$ 59° (*c* 0·55). The residue of the combined mother liquors after crystallisation was chromatographed on 50 g of silica gel. Elution with 80 ml of cyclohexane containing 1% of ether gave 0·15 g of ketone *XVII*, m.p. 224—226°C (benzene–ethanol), $[\alpha]_D$ 59° (*c* 0·60); further 30 ml of the same solvent mixture eluted 80 mg of a mixture of ketones *XVII* and *XXVIII*, and the next 80 ml of the same mixture eluted 0·28 g of ketone *XXVIII*. Crystallisation form benzene–ethanol gave 0·25 g of a product of m.p. 199 to 202°C, $[\alpha]_D$ −25° (*c* 0·59). ORD: $[\Theta]_{400}$ −363°, $[\Theta]_{316,5}$ −3935°, $[\Theta]_{309,5}$ − 3 385°C, $[\Theta]_{307}$, −3 510°, $[\Theta]_{295,5}$ 0°, $[\Theta]_{272}$ 4900°, $[\Theta]_{240}$ 3630°. UV spectrum (tetrahydrofuran): λ_{max} 292 nm log ε 1·42. IR spectrum: 1706 (C=O) cm^{-1}. PMR spectrum: 0·80 (4β-CH_3), 0·83 d, J = 6·5 Hz and 0·89 d, J = 6·5 Hz (19α-CH(CH_3)$_2$), 0·85 (4α-CH_3 + 10β-CH_3), 0·925 (8β-CH_3), 1·00 (14α-CH_3). For $C_{30}H_{50}O$ (426·7) calculated: 84·44% C, 11·81% H; found: 84·51% C, 10·90% H.

Equilibration of Ketones *XVII* and *XXVIII*

A 0·4N methanolic solution of potassium hydroxide (10 ml) was added to a solution of 70 mg of ketone *XVII* in 10 ml of benzene and the mixture allowed to stand at 20°C for two days. After dilution with ether and addition of water the ethereal layer was separated, washed with water and dried. The residue (66 mg) had in two subsequent measurements $[\alpha]_D$ 50·6° (*c* 0·79) or $[\alpha]_D$ 51·3° (*c* 0·91). Equilibration of ketone *XXVIII* was carried out in an analogous manner. The mixture of epimeric ketones *XVII* and *XXVIII* formed had $[\alpha]_D$ 51·2° (*c* 0·87).

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