ELIMINATION REACTION OF THE ANGULAR HYDROXYMETHYL GROUP OF THE LUPANE SKELETON*

A. Vystrčil[a], V. Křeček[a] and M. Buděšínský[b]

[a] *Department of Organic Chemistry, Charles University, 128 40 Prague 2,*
[b] *Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, 166 10 Prague 6*

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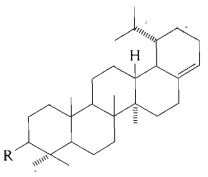
Comparison of the optical rotatory dispersion of the described ketones and steroidal models proved that in ketone *III* the configuration 18α,19βH remained unchanged, *i.e.* that the formation of anhydro derivatives *I* and *II* is also independent of these centers. According to the Cotton effect of bromo ketones *XX* and *XXI* it follows that *1)* in ketones *XI* and *XIV* the D/E rings are *cis*-annelated, *i.e.* that in anhydro derivatives *I* or *II* and in enolacetate *XVIII* the double bond 17(22) is much better accessible from the α-side than from the β-side, *2)* in ketone *XVI* (*XVII*) and in bromo ketone *XXI* the D/E rings are *trans*-annelated; the attack of the double bond 17 (22) from the β-side in anhydro derivative *I* and enolacetate *XVIII* could be proved only during the addition of diborane or bromine. From the relative changes of the chemical shifts in the PMR spectra of the described compounds the probable conformations of the cycles D and E could be proposed in dependence of their annelation and substitution.

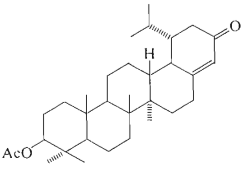
After the determination of the structure of anhydrobetulin and its derivatives described in the first part of this series[1] it was necessary to confirm the considered steric relations, *i.e.* to prove first whether a change in configuration at $C_{(18)}$ and $C_{(19)}$ does not take place during the actual preparation of the described anhydro derivatives *I* and *II*. For this purpose such a derivative is utilizable for diagnosis, which is derived from the given anhydro derivative (*I* or *II*) without the introduction of a further asymmetric center, for example unsaturated ketone *III*. Its preparation was carried out by oxidation of acetate *II* with chromium trioxide in acetic acid. Two neutral products were thus formed of which one was identical with ketone *XIV* described in the first part[1] and the second is unsaturated ketone *III* the structure of which is substantiated below. From the acid oxidation products seco-acid *VI* was isolated which was formed evidently on oxidative cleavage of acetate *II* at the site of the double bond. This acid was converted to methyl ester *VII* which was further characterized as 3-hydroxy derivative *IV* and oxime *V*. The structure of these seco derivatives *IV*–*VII* was proposed on the basis of their spectroscopic properties and further evidence.

* Part XXXVI in the series Triterpenes; Part XXXV: This Journal *39*, 2961 (1974).

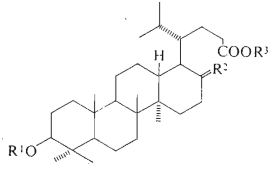
The structure of unsaturated ketone *III* is substantiated by the following properties: UV absorption (λ_{max} 248 nm, log ε 4·13) is in agreement with the theoretically computed[2] value (244 ± 5 nm). IR absorption, measured in tetrachloromethane for quantitative evaluation, gives a ratio $r^i = 4{\cdot}5$ and a shift $\Delta\nu = 46\ cm^{-1}$, which represents values agreeing with those of the *s-trans* form of α,β-unsaturated ketones[3]. In the PMR spectrum a singlet at 5·73 p.p.m. due to hydrogen signal at $C_{(22)}$ and a multiplet at 2·30 p.p.m. due to the $C_{(20)}H_2$ group, the signals of which are split by the $C_{(19)}$ hydrogen, may be identified. From the opposite transcription of formula *III* it is evident that if the configuration 18α,19βH is preserved, then the annelation and the substitution of its cycles D and E is equal as in cycles A and B in 1β-alkyl--3-oxo-19-nor-4,5-unsaturated steroids. Of the described derivatives 1β-methyl--19-norpregn-4-ene-3,20-dione[4,5] is most suitable; it has the same course of the ORD curve as ketone *III*, so that both compounds must have all elements of chirality



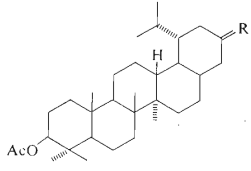
I, R = H
II, R = OAc



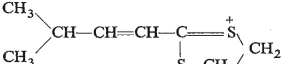
III



IV, R^1 = H, R^2 = O, $R^3 = CH_3$
V, R^1 = H, R^2 = NOH, $R^3 = CH_3$
VI, R^1 = Ac, R^2 = O, R^3 = H
VII, R^1 = Ac, R^2 = O, $R^3 = CH_3$



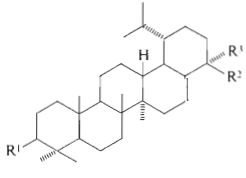
VIII, R = O
IX, R = SCH_2CH_2S



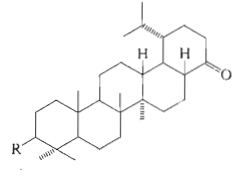
X

determining their Cotton effect identical. Hence, in the unsaturated ketone *III* and in the starting acetate *II* the original configuration 18α,19βH is preserved. The same conclusion can be arrived at in the following manner: hydrogenation of unsaturated ketone *III* gives saturated ketone *VIII* which has a negative Cotton effect, similarly as derivatives of 1β-methyl-5β-pregnan-3-one[6,7], while all isomeric 3-oxo derivatives with different configuration on $C_{(1)}$ and $C_{(5)}$ (*i.e.* 1α-methyl-5α-cholestan-3-one[8], 1α-methyl-5β-cholestan-3-one[8], 1β-methyl-17β-acetoxy-5α-androstan-3-one[9]) display a positive Cotton effect. The formation of saturated ketone *VIII* also means that in unsaturated ketone *III* too the double bond 17 (22) is more easily accessible from the α side. Further, from ketone *VIII* dithioketal *IX* was prepared in the mass spectrum of which the fragment $m/e = 173$, belonging to ion *X*, is significant. Its formation may be considered as the final corroboration of the structural formulations mentioned.

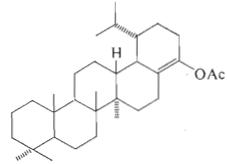
Our further step was the proof of configuration on $C_{(17)}$ in epimeric 22-oxo derivatives *XI* and *XVI*, or *XIV* and *XVII*. If this proof is to be independent of auxiliary models, such a substituent should be introduced in $C_{(17)}$ which would have the same configuration as the hydrogen atom in the parent ketone, and which would overwhelmingly determine the resulting Cotton effect. These requirements are best fulfilled by the introduction of a halogen at $C_{(17)}$, by addition to the corresponding enolacetate. According to the described analogies[10,11] we first carried out the enolacetylation of ketone *XI* with isopropenylacetate under catalysis of *p*-toluenesulfonic



XI, $R^1 = H$, $R^2 + R^3 = O$
XII, $R^1 = R^3 = OAc$, $R^2 = H$
XIII, $R^1 = R^2 = OAc$, $R^3 = H$
XIV, $R^1 = OAc$, $R^2 + R^3 = O$
XV, $R^1 = OAc$, $R^2 + R^3 = NOH$

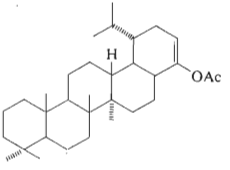


XVI, R = H
XVII, R = OAc

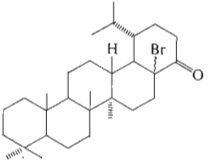


XVIII

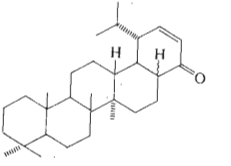
acid. However, it was observed, that under these conditions an inseparable mixture of enolacetates is formed (IR spectrum: 1743, 1238 (CH_3COO), 1703, 1687 (C=C) cm^{-1}; PMR spectrum: multiplet at 5·25 p.p.m. with a relative intensity corresponding to less than one proton). Under the effect of acetic anhydride and a catalytic amount of *p*-toluenesulfonic acid ketone *XI* or the above mentioned mixture of enolacetates is transformed to a single enolacetate. According to IR spectra (the PMR spectrum does not display a signal of a proton on unsaturated carbon atom) the latter compound should have the structure *XVIII*. From the characteristics of the inseparable mixture of enolacetates prepared in the first manner it may be concluded that acid catalysed enolacetylation of ketone *XI* with isopropenylacetate gives rise to isomeric enolacetate *XIX* in addition to enolacetate *XVIII*. Similarly as in the addition of diborane to the 17 (22) double bond in anhydro derivative *I* (*cf.*[1]) the addition of bromine in pyridine to the double bond of enolacetate *XVIII* also took place from both sides; epimeric bromo ketones *XX* and *XXI* were formed, from the preparative yields of which (3 : 1) it is evident that the formation of the more easily eluable epimer *XX* is preferred. For the determination of the conformation of bromine at $C_{(17)}$ we made use of the following spectroscopic criteria: From the IR absorption it follows that the more easily eluted bromo ketone *XX*, when compared with the parent ketone *XI*, has its carbonyl band absorption shifted by $+7\ cm^{-1}$, and the more strongly adsorbed bromo ketone *XXI* displays in comparison with ketone *XVI* a difference of $+2\ cm^{-1}$; these differences are acceptable for an axial conformation of bromine[12]. Their absorption in the UV region also points to the same



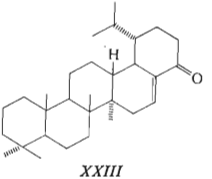
XIX



XX, 17α — Br
XXI, 17β — Br

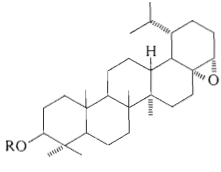


XXII

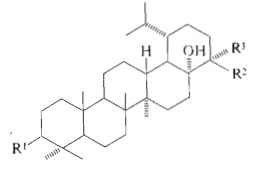


XXIII

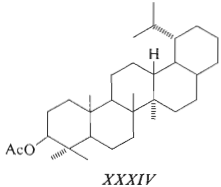
conclusion, because both bromo ketones show a bathochromic shift of the carbonyl absorption maximum (*XX*: $\Delta\lambda = 20$ nm, *XXI*: $\Delta\lambda = 17$ nm) and simultaneously a 3 to 4 fold increase in the molar extinction coefficient[13]. The same shifts are displayed by the extremes of the ORD curves of ketone *XVI* and bromo ketone *XXI*, under simultaneous increase in amplitude[14–16]; in the pair of ketone *XI* and bromo ketone *XX* these values cannot be read accurately because ketone *XI* has an indistinct and complex Cotton effect. All these data show that in bromo ketones *XX* and *XXI* bromine assumes an axial – or more accurately non-coplanar – conformation with respect to the carbonyl group plane. From the sign of the Cotton effect it is evident that in bromo ketone *XX* bromine at $C_{(17)}$ has α-configuration and in bromo ketone *XXI* β-configuration. The comparison of the ORD curves of these bromo ketones and of 5-bromo-5α- or 5β-cholestan-4-one[17] also leads to the same conclusion. By this a direct proof is given that the double bond 17(22) in enolacetate *XVIII* is more accessible from the α-side for the bromine addition than from the β-side. In an attempt at chemical proof of the structure of bromo ketones *XX* and *XXI* we carried out their dehydrobromination with lithium chloride in dimethylformamide[18]. It was shown that both bromo ketones (*XX*, *XXI*) are converted by this reaction to the same mixture of unsaturated ketones, the structure of which was proposed on the basis of these facts: Ketone *XXII* absorbs in the UV region at 229 nm, $\log \varepsilon = 4{\cdot}15$ and the theoretically calculated value[2] is 227 ± 5 nm. The IR absorption measurement in tetrachloromethane for quantitative evaluation – gave



XXIV R = H
XXV R = Ac



XXVI, $R^1 = R^2 = H$, $R^3 = OH$
XXVII, $R^1 = R^3 = H$, $R^2 = OH$
XXVIII, $R^1 = R^2 = H$, $R^3 = OAc$
XXIX, $R^1 = H$, $R^2 + R^3 = O$
XXX, $R^1 = R^3 = OH$, $R^2 = H$
XXXI, $R^1 = OAc$, $R^2 = OH$, $R^3 = H$
XXXII, $R^1 = R^2 = OAc$, $R^3 = H$
XXXIII, $R^1 = R^3 = OAc$, $R^2 = H$



XXXIV

the ratio $r^i = 37$ and the difference $\Delta\nu = 56\ cm^{-1}$, which confirms the *s-trans* form of the α,β-unsaturated ketone[3] unambiguously. The PMR spectrum proves the presence of the fragment —CH—CH=CH—C—. The formation of this unsaturated ketone is analogous to the dehydrobromination of steroidal bromo ketones, taking place by 1,4-elimination from the corresponding enol[19,20]. The isomeric unsaturated ketone *XXIII* could not be isolated in a pure state and therefore the proposed structure need not be definite. The structural proposal for *XXIII* is based, *inter alia*, on the UV absorption (λ_{max} 246 nm, $\log \varepsilon = 3{\cdot}78$; theoretically calculated[2] value: λ_{max} 242 ± 5 nm) and the IR absorption.

Further information on the relative accessibility of the double bond 17(22) was expected from the epoxidation course of anhydroacetate *II*. We were able, however, to isolate only one of the two possible epoxides, *i.e.* epoxide *XXV* which was also characterized as hydroxy derivative *XXIV*. On chromatography of crude epoxide *XXV* we also isolated a fraction which we consider to be a mixture of ketones *XIV* and *XVII*. From this mixture we succeeded in separating by repeated crystallization almost pure ketone *XIV* which was freed of the last traces of impurities only after its conversion to oxime *XV*. In an attempt at chromatographic purification of epoxide *XXV* we isolated in addition to a mixture of ketones *XIV* and *XVII* also a much more polar product for which we propose the structure of trans diol *XXXI* on the basis of its spectra and analogies from the literature[21]; its formation can be interpreted by a contact reaction of epoxide *XXV* with alumina[21–23]. For further characterization diol *XXXI* was converted to diacetate *XXXII*. In order to be able to further evaluate the effect of 17,22-*trans*-diol and 17,22-*cis*-diol systems on the signals of the 14α-methyl group and 19α-isopropyl group in the PMR spectra we carried out *cis*-dihydroxylation of anhydro derivatives *I* and *II* by the addition of osmium tetroxide and subsequent reduction of the adduct with lithium aluminum hydride. The diol *XXVI* or triol *XXX* were thus formed, respectively, which were further acetylated to acetate *XXVIII* or diacetate *XXXIII*, respectively. Oxidation of diol *XXVI* with chromium trioxide in pyridine gave ketol *XXIX* which was found identical with the product of a similarly performed oxidation of *trans*-diol *XXVII* prepared by us earlier[22]. As this proves that diols *XXVI* and *XXVII* differ by the configuration of the 22-hydroxy group only, we were able to apply the correlation of these epimers also to diacetates *XXXII* and *XXXIII*. The positive Cotton effect of ketol *XXIX* need not be decisive for the configuration at $C_{(17)}$ because numerous exceptions from octant rule are known[24] in α-ketols.

Finally we tried to determine approximately the conformations of the rings D and E in the described derivatives. As was mentioned in the preceding paper[1] the 17β-ketone *XVI* is energetically less advantageous, due to the large steric interaction of the isoptopyl side chain. This interaction should lead to a limitation of its free

rotation, which may be manifested by an accentuation of the non-equivalence (difference in chemical shifts) of both methyl groups of the isopropyl substituent. This difference is in the 17β-ketone *XVI* 0·06 p.p.m., and in the corresponding 17β-bromo ketone *XXI* even 0·1 p.p.m., while in 17α-ketones *XI* and *XIV* both methyl groups of the side chain appear as a single six-proton doublet. The methyl groups of the side chain of 17α-bromo ketone *XX* also produce a different chemical shift (0·04 p.p.m.) which is explicable by 1,3-interaction of the isopropyl chain with the bulky bromine atom located on the same side of the cycle. In the case of the classical chair conformation of this ring this interaction should be very pronounced and the affecting of the isopropyl group signals should therefore be much stronger. The observed small difference in chemical shifts may thus be considered as a consequence of the deviation of the conformation of the E-ring from the classical chair conformation in 17α-bromo ketone *XX*. Further conclusions may be reached by comparing the PMR spectra of 22α-acetoxy derivative *XII* and the 22-epimer *XIII* with those of corresponding 22-acetoxy derivatives substituted at $C_{(17)}$ with a hydroxy group, *i.e.* with acetates *XXXIII* and *XXXII*: when compared with the unsubstituted derivative *XXXIV* the chemical shift of the 14α-methyl group signal does not change substantially in those 22-acetoxy derivatives which are not substituted at $C_{(17)}$, and that without regard to the configuration at $C_{(22)}$ (*XII*, *XIII*). The introduction of a hydroxy group into this position is connected with a different change of this signal: for 22α-acetoxy derivative *XXXIII* it makes +0·075 p.p.m. and for 22β-acetoxy derivative *XXXII* it is +0·12 p.p.m.. This can be explained by the fact that in hydroxy derivatives *XXXII* and *XXXIII* the D-ring exists in boat conformation, causing the 17α-hydroxy group to come close to the 14α-methyl group[25].

From an analysis of models and from the mentioned spectral characteristics it may be judged that the conformation of cycles D and E in derivatives formed by addition to the double bond 17 (22), (from the α-side) in anhydro compounds *I* and *II* will not be equal in all instances. While in *trans*-transoid-*cis*-perhydrophenanthrene the most advantageous conformation is that with all cycles in the chair form[26], a boat conformation of ring E (*XX*), or ring D, or both rings simultaneously (*XXXII*, *XXXIII*), may be supposed in some derivatives described here which have their D/E rings *cis*-annelated, *i.e.* so that 19α-isopropyl group would not be axial with respect to the ring E and that at the same time its non-bonding interactions with methylene group $C_{(12)}$ would be decreased. This D-boat-E-boat form is a rather flexible formation because in addition to the 4 edge forms it also makes possible a series of transition forms thus enabling the system to react dynamically even to weak effects of the substituents. In derivatives with *trans*-annelated D/E rings the D ring will be more stable in the chair conformation, while the ring E will be present in some of the possible boat conformations, due to the large non-bonding interaction of the 19α-isopropyl group.

EXPERIMENTAL

The melting points were determined on a Kofler block and they 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 solutions (unless stated otherwise) on an IKS-14 spectrometer, on an instrument of the Institute of Apparatus Technology, Czechoslovak Academy of Sciences, Brno, and on UR-10 and Unicam SP-200 apparatuses. The ultraviolet spectra were measured in ethanolic solution (unless otherwise stated) on a Unicam SP-700 spectrophotometer. The proton magnetic resonance was recorded with a Varian HA-100 machine in deuteriochloroform with tetramethylsilane as internal standard; chemical shifts are given in p.p.m., δ-scale. Optical rotatory dispersion was measured on a JASCO-ORD/UV-5 apparatus in dioxan and the mass spectra with a MCh-1303 spectrometer. For chromatography neutral alumina according to Brockmann, activity grade II, or silica gel according to Pitra (30—60 μ) were used. The samples for analysis were dried at 100°C and reduced pressure (0·1 to 1 Torr) over phosphorus pentoxide for 10 hours. Under the conventional working up the following procedure is understood: dilution of the reaction mixture with water, extraction of the product with ether, repeated washing of the extract with water, dilute hydrochloric acid (1 : 4), water and eventually 5% sodium carbonate. The identity of the preparations was determined on the basis of mixture melting point, optical rotation, thin-layer chromatography and infrared spectra.

Oxidation of Acetate *II*

A solution of 1·0 g of chromium trioxide in acetic acid was added over 2 hours dropwise and under stirring to a solution of 4·0 g of acetate *II* in a mixture of benzene and acetic acid. The reaction mixture was then additioned with methanol, diluted with ether, and extracted with water and 5% sodium carbonate solution. After the ethereal layer was dried and the solvent evaporated, 1·3 g of a neutral fraction were obtained. The sodium carbonate extract was acidified with dilute hydrochloric acid to Congo, extracted with ether, and the extract washed with water and dried. Evaporation of ether gave 3·3 g of an acid fraction. The neutral fraction was chromatographed on alumina (150 g); 320 ml of benzene eluted 0·32 g of a substance which after crystallization from chloroform–methanol had m.p. 261—264°C, $[\alpha]_D$ 65° (*c* 0·52) and was identified as ketone *XIV* (see[1]). Further elution with 750 ml of benzene gave 0·31 g of unsaturated ketone *III*. After crystallization (chloroform–methanol, ethyl acetate) it melted at 264—267°C, $[\alpha]_D$ −67° (*c* 0·58). ORD: $[\Phi]_{345}$ 0°, $[\Phi]_{253}$ −60750°, $[\Phi]_{243}$ 0°, $[\Phi]_{210}$ 74250°. UV spectrum, ethanol: λ_{max} 248 nm (log ε 4·13); cyclohexane: λ_{max} 236 nm (log ε = 4·20). IR spectrum, chloroform: 1660, 1632 (C=C—C=O), 1428 (α-CH_2), 1721, 1259 (CH_3COO) cm^{-1}; tetrachloromethane (*c* 0·068M): ν_s (C=C—C=O) 1682 cm^{-1}, $\varepsilon' = 391$, $\nu_{1/2} = 28$ cm^{-1}, $A = 10950$; ν_{as}(C=C—C=O) 1636 cm^{-1}; $\varepsilon' = 87$, $\nu_{1/2} = 19$ cm^{-1}, $A = 1650$. PMR spectrum: 0·81—0·87 bs (4α-CH_3 + + 4β-CH_3 + 10β-CH_3),0·84 d, $J = 6$ Hz (19α-$CH(CH_3)_2$), 0·93 (8β-CH_3), 1·12 (14α-CH_3), 2·02 (3β-$OCOCH_3$), 2·30 m(20-H_2), 4·475 (3α-H), 5·73 (22-H). For $C_{30}H_{50}O_3$ (482·7) calculated: 79·62% C, 10·44% H; found: 79·42% C, 10·46% H. The acid fraction was dissolved in excess ethereal diazomethane solution and allowed to stand overnight. After evaporation to dryness the residue (2·48 g) was crystallized from chloroform–methanol. Methyl ester *VII* had m.p. 150—154°C, $[\alpha]_D$ 32° (*c* 1·33). IR spectrum: 1725, 1257 (CH_3COO), 1725, 1455, 1197, 1176 ($COOCH_3$) cm^{-1}. The hydrolysis of crude acetate *VII* (2·4 g) was carried out by 6 hours' refluxing with a solution of potassium hydroxide in benzene–ethanol mixture. After acidification of the reaction mixture with dilute hydrochloric acid to Congo, acid *VI* was precipitated and extracted with ether. The extract was washed with water, dried and evaporated to dryness.

The residue was dissolved in excess ethereal diazomethane solution and allowed to stand overnight. After evaporation of excess diazomethane solution the residue (1·71 g) was again dissolved in ether and filtered through a layer of alumina, and the filtrate evaporated. The chromatographically pure residue (0·91 g) was crystallized from heptane–acetone affording 170 mg of hydroxy ester *IV*, m.p. 61—64°C, $[\alpha]_D$ 20° (*c* 0·66). IR spectrum: 3·625, 3450, 1035 (OH), 1730, 1456, 1200, 1176 ($COOCH_3$) cm^{-1}. For $C_{31}H_{52}O_4$ (488·7) calculated: 76·18% C, 10·72% H; found: 76·19% C, 11·08% H. The preparation of oxime *V* was carried out by 4 hours' heating of 70 mg of hydroxy ester *IV* with 70 mg of hydroxylamine hydrochloride in pyridine on a water bath. After the conventional work-up and double crystallization from benzene–heptane 50 mg of oxime *V* were obtained, m.p. 197—199°C, $[\alpha]_D$ −8° (*c* 0·48). IR spectrum: 1734, 1457, 1178, 1150 ($COOCH_3$), 3610, 3350, 1027, 925 (OH, =N—OH) cm^{-1}. For $C_{31}H_{53}NO_4$ (503·7) calculated: 73·91% C, 10·61% H, 2·78% N; found: 74·19% C, 10·54% H, 3·02% N.

3β-Acetoxy-19α-isopropyl-28,29,30-trinor-17α,18α-oleanan-21-one (*VIII*)

A solution of 0·11 g of unsaturated ketone *III* in ethyl acetate was hydrogenated on palladium on charcoal at normal pressure. After filtration off of the catalyst the filtrate was concentrated to afford 50 mg of ketone *VIII*, m.p. 275—277°C, $[\alpha]_D$ 48° (*c* 0·46). ORD $[\Phi]_{350}$ 260°, $[\Phi]_{326}$ 0°, $[\Phi]_{317}$ −586°, $[\Phi]_{309}$ −66°, $[\Phi]_{307.5}$ −130°, $[\Phi]_{300}$ 911°, $[\Phi]_{275}$ 3318°, $[\Phi]_{250}$ 3448°. IR spectrum: 1723, 1260 (CH_3COO), 1712 (CO) cm^{-1}. For $C_{32}H_{52}O_3$ (484·7) calculated: 79·28% C, 10·81% H; found: 79·21% C, 10·96% H.

Ethylene Dithioketal *IX*

0·3 ml of ethanedithiol and 0·1 ml of boron trifluoride etherate were added to a solution of 30 mg of ketone *VIII* in 3 ml of acetic acid and the mixture allowed to stand at room temperature for 2 days. The separated crystals were filtered off under suction and recrystallized from a mixture of ether and light petroleum. Yield 15 mg of dithioketal *IX*, m.p. 244·5—246°C, $[\alpha]_D$ 46° (*c* 0·37). IR spectrum: 1722, 1258 (CH_3COO) cm^{-1}. For $C_{34}H_{56}O_2S_2$ (560·9) calculated: 72·80% C, 10·06% H; found: 72·90% C, 10·01% H.

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

a) Reaction of ketone XI *with isopropenylacetate.* *p*-Toluenesulfonic acid (50 mg) was added to a solution of 0·21 g ketone *XI* in 15 ml of freshly distilled isopropenylacetate and the mixture was heated at a rate permitting 1/10 of the total volume to be distilled off over 2 hours. The mixture was then refluxed for 7·5 hours. After vacuum evaporation of excess isopropenyl acetate the residue was dissolved in ether, the solution washed with water and 5% sodium hydrogen carbonate solution, dried and concentrated. A mixture of enolacetates *XVIII* and *XIX* (0·20 g) crystallized on addition of methanol, m.p. 142—147°C, $[\alpha]_D$ 13° (*c* 0·59). IR spectrum: 1743, 1238 (CH_3COO), 1703, 1687 (C=C) cm^{-1}. PMR spectrum: 2·10 bs ($22\text{-}OCOCH_3$), 5·25 m (21-H). A solution of 0·15 g of a mixture of enolacetates *XVIII* and *XIX* in 12 ml of acetic anhydride was mixed with 50 mg of *p*-toluenesulfonic acid and refluxed for 2 hours. After further working up the product was crystallized from a mixture of ether and methanol. Yield 90 mg of enolacetate *XVIII*, m.p. 159—160°C, $[\alpha]_D$ 5° (*c* 0·62), identical with a preparation obtained in the following manner.

b) *Reaction of ketone* XI *with acetic anhydride.* A solution of 0·16 g of ketone *XI* and 40 mg of *p*-toluenesulfonic acid in 10 ml of acetic anhydride was refluxed for 4 hours. After further

conventional work-up and crystallization from a mixture of ether and ethanol 0·12 g (68%) of enol-acetate *XVIII* were obtained, m.p. 160—161·5°C, $[\alpha]_D$ 5° (*c* 0·64). IR spectrum: 1741, 1238 (CH_3COO), 1703 (C=C) cm^{-1}. PMR spectrum: 0·80 (4β-CH_3), 0·85 bs (4α-CH_3 + 10β-CH_3), 0·89 d, J = 6·5 Hz (19α-$CH(CH_3)_2$), 0·965 (14α-CH_3), 1·06 (8β-CH_3), 2·10 (22-$OCOCH_3$). For $C_{32}H_{52}O_2$ (468·7) calculated: 81·99% C, 11·18% H; found: 81·96% C, 11·45% H.

Bromination of Enolacetate *XVIII*

A solution of bromine (94 mg; 1·1 mol) in acetic acid was added dropwise and under stirring to a solution of 0·25 g of enolacetate *XVIII* in 5 ml of pyridine and 50 ml of acetic acid and the mixture allowed to stand for one hour in darkness. The mixture was diluted with ether, washed with water and 5% sodium hydrogen carbonate solution, dried and evaporated. The crude product was dissolved in benzene and chromatographed on silica gel (75 g); benzene (170 ml) eluted 0·13 g of bromo ketone *XX* which after crystallization from a mixture of benzene and hexane melted at 152—155°C under decomposition, $[\alpha]_D$ 8° (*c* 0·62). ORD: $[\Phi]_{400}$ −380°, $[\Phi]_{339.5}$ −3965°, $[\Phi]_{320}$ 0°, $[\Phi]_{290}$ 7500°, $[\Phi]_{270}$ 6960°, $[\Phi]_{260}$ 7170°. UV spectrum, tetrahydrofuran: λ_{max} 312 nm (log ε = 1·98); IR spectrum: 1712 (CO) cm^{-1}. PMR spectrum: 0·785 (4β-CH_3), 0·81 (10β-CH_3), 0·83 bs (4α-CH_3 + 14α-CH_3), 0·96 d, J = 6·7 Hz and 1·00 d, J = 6·7 Hz (19α-$CH(CH_3)_2$), 1·052 (8β-CH_3), 2·55—3·00 m (approx. 21-H_2). For $C_{30}H_{49}BrO$ (505·6) calculated: 71·26% C, 9·77% H; found: 70·95% C, 9·74% H. Further 50 ml of benzene eluted from the column 20 mg of a mixture of bromo ketones *XX* and *XXI*, and the next 130 ml of benzene eluted 40 mg of bromo ketone *XXI* which after crystallization from benzene–hexane melted at 147—157°C under decomposition, $[\alpha]_D$ 53° (*c* 0·43). ORD: $[\Phi]_{400}$ 1021°, $[\Phi]_{332.5}$ 3975°, $[\Phi]_{310}$ 0°, $[\Phi]_{285}$ −4090°, $[\Phi]_{250}$ −2500°. UV spectrum, tetrahydrofuran: λ_{max} 309 nm (log ε = 1·99). IR spectrum: 1708 (CO) cm^{-1}. PMR spectrum: 0·80 d, J = 6·8 Hz and 0·90 d, J = 6·8 Hz (19α-$CH(CH_3)_2$), 0·81 (4β-CH_3), 0·86 (4α-CH_3), 0·87 (10β-CH_3), 0·94 (14α-CH_3), 1·125 (8β-CH_3). For $C_{30}H_{49}BrO$ (505·6) calculated: 71·26% C, 9·77% H; found: 71·49% C, 10·02% H.

Dehydrobromination of Bromo Ketones *XX* and *XXI*

Lithium chloride (0·16 g) was added to a solution of 0·16 g of bromo ketone *XX* in dimethylformamide and the mixture was refluxed for 4 hours. After cooling the mixture was diluted with ether, washed with water and evaporated after drying. Dehydrobromination of bromo ketone *XXI* (0·05 g) was carried out in the same manner. As the same mixtures of products was obtained from both bromo ketones, they were combined (0·18 g) and chromatographed on silica gel (10 g). Elution with 150 ml of cyclohexane gave 90 mg of unsaturated ketone *XXII* which after a triple crystallization from a benzene–cyclohexane mixture had m.p. 226—228°C, $[\alpha]_D$ −58° (*c* 0·37). UV spectrum: λ_{max} 229 nm (log ε = 4·15). IR spectrum: 1675, 1632 (C=C—C=O) cm^{-1}; tetrachloromethane (*c* 0·1256M): ν_s(C=C—C=O) 1683 cm^{-1}, ε' = 503, $\nu_{1/2}$ = 25 cm^{-1}, A = 12 600; ν_{as}(C=C—C=O) 1627 cm^{-1}, ε' = 13·5, $\nu_{1/2}$ ≈ 17 cm^{-1}, A = 230. PMR spectrum: 0·78, 0·80 (2 × CH_3), 0·84(2 × CH_3), 0·97 (CH_3), 1·02 d, J = 6·5 Hz (19α-$CH(CH_3)_2$), 2·65 bt (probably 17-H), 5·945 bd, $J_{21,20}$ = 10·0 Hz, $J_{21,19}$ and $J_{21,17} \neq 0 < 1$ Hz (21-H), 6·815 bddd, $J_{20,21}$ = 10·0 Hz, $J_{20,19}$ = 5·5 Hz, $J_{20,18\text{ or }17}$ = 1·4 Hz (20-H). For $C_{30}H_{48}O$ (424·7) calculated: 84·84% C, 11·39% H; found: 84·85% C, 11·30% H. Further elution with cyclohexane (60 ml) gave 50 mg of unsaturated ketone *XXIII*, which after triple crystallization from a mixture of benzene and heptane had m.p. 174—176°C, $[\alpha]_D$ 31° (*c* 0·38). UV spectrum: λ_{max} 246 nm (log ε = 3·78). IR spectrum: 1665, 1638 (C=C—C=O) cm^{-1}. PMR spectrum: 0·81 (CH_3), 0·86 (2 × CH_3), 0·92 d, J = 7·0 Hz and 0·955 d, J = 7·0 Hz (19α-$CH(CH_3)_2$),0·93, 0·95 (2 × CH_3), 6·39 bp, $J_{16,15}$ = 4·8 and 2·5 Hz, $J_{16,18}$ = 2·5 Hz (16-H).

Epoxidation of Acetate *II*

a) A 1·2 molar excess of perbenzoic acid solution in chloroform was added to a solution of 1·0 g of acetate *II* in chloroform, cooled in a refrigerator and allowed to stand in a refrigerator overnight. The mixture was washed with 5% sodium carbonate solution and water, dried and evaporated in a vacuum to dryness. The residue (1·2 g) was chromatographed on alumina (50 g); 110ml of benzene eluted a substance (0·41 g) which after crystallization from hexane, cyclohexane and acetone afforded 180 mg of epoxide *XXV*, m.p. 180–182°C, $[\alpha]_D$ 47° (*c* 0·59). IR spectrum: 1726, 1262 (CH_3COO), 1156, 908 (epoxide) cm^{-1}. For $C_{32}H_{52}O_3$ (484·7) calculated: 79·28% C, 10·81% H; found: 79·08% C, 10·87% H. With further 80 ml of benzene 0·25 g of a mixture of ketones *XIV* and *XVII* were eluted. Double crystallization from benzene–ethanol and chloroform–methanol gave 0·22 g of ketone *XIV*; when 0·20 g of hydroxylamine hydrochloride were added to its solution in pyridine and the mixture heated on a water bath for 5 hours and worked up, a product was obtained which after crystallization from chloroform gave oxime *XV* (0·16 g) identical with a preparation described earlier[1].

b) A reaction mixture (1·47 g) prepared in the same manner by epoxidation of acetate *II* was chromatographed on 150 g of alumina. Elution with 500 ml of benzene containing 10% of ether gave 0·49 g of a mixture of ketones *XIV* and *XVII*. Further 500 ml of a mixture of ether with 10% of methanol eluted 1·03 g of a substance which on crystallisation from ethyl acetate gave 0·16 g of diol *XXXI*, m.p. 273–276°C, $[\alpha]_D$ 26° (*c* 0·74). IR spectrum: 1725, 1261 (CH_3COO), 3620, 3430, 1030 (OH) cm^{-1}. For $C_{32}H_{54}O_4$ (502·75) calculated: 76·44% C, 10·83% H; found: 76·06% C, 10·62% H. On acetylation of 0·1 g of diol *XXXI* with a mixture of 2 ml of pyridine and 1 ml of acetic anhydride at room temperature for one week (using the conventional working up) 0·09 g (83%) of acetyl derivative *XXXII* were obtained, m.p. 271–273°C (chloroform–methanol, ethyl acetate), $[\alpha]_D$ 14° (*c* 0·42). IR spectrum: 1725, 1259 (CH_3COO), 3600, 3500, 1034 (OH) cm^{-1}. PMR spectrum: 0·85 (4α-CH_3 + 4β-CH_3), 0·86 d, J = 6·4 Hz and 0·91 d, J = 6·4 Hz (19α-CH(CH_3)$_2$), 0·89 (10β-CH_3), 1·01 (8β-CH_3), 1·04 (14α-CH_3), 2·03 (3β-OCOCH_3), 2·085 (22β-OCOCH_3), 4·49 m (3α-H), 4·70 μm, $W_{1/2}$ = 6·8 Hz (22α-H). For $C_{34}H_{56}O_5$ (544·8) calculated: 74·96% C, 10·36% H; found: 75·12% C, 10·48% H.

19α-Isopropyl-28,29,30-trinor-17α,18α-oleanan-3β,17,22α-triol (*XXX*)

0·10 g of osmium tetroxide were added to a solution of 0·17 g of acetate *II* in 40 ml of ether and the mixture allowed to stand at room temperature in darkness for 4 days. Excess ethereal lithium aluminum hydride solution was then added to it and the mixture was refluxed for 2 hours. After decomposition of excess hydride and further working up the product was crystallized from benzene. Yield 0·09 g (50%) of triol *XXX*, m.p. 261–263°C, $[\alpha]_D$ 27° (*c* 0·51). IR spectrum: 3620, 3460, 1047, 1037, 1015 (OH) cm^{-1}. Acetylation of 50 mg of triol *XXX* by a procedure similar to the preparation of diacetate *XXXII* gave 50 mg of acetyl derivative *XXXIII*, m.p. 242–245°C (ether–hexane), $[\alpha]_D$ 39° (*c* 0·67). IR spectrum: 1725, 1253 (CH_3COO), 3580, 3435, 1058, 1032 (OH) cm^{-1}. PMR spectrum: 0·84 (4α-CH_3 + 4β-CH_3), 0·85 d, J = 6·4 Hz and 0·92 d, J = = 6·4 Hz (19α-CH(CH_3)$_2$), 0·875 (10β-CH_3), 0·99 (14α-CH_3), 1·01 (8β-CH_3), 2·035 (3β-OCOCH_3), 2·065 (22α-OCOCH_3), 4·48 m (3α-H), 5·135 dd, J_{vic} = 10·0 Hz + 4·6 Hz (22β-H). For $C_{34}H_{56}O_5$ (544·8) calculated: 74·95% C, 10·36% H; found: 74·71% C, 10·20% H.

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

Dihydroxylation of 0·15 g of anhydro derivative *I* with osmium tetroxide (0·1 g) was carried out in the same manner as the preparation of triol *XXX*. Yield 0·12 g (74%) of diol *XXVI*, m.p.

250—253°C (benzene), $[\alpha]_D$ 35° (*c* 0·44). IR spectrum: 3595, 3420, 1050, 1021 (OH) cm^{-1}. PMR spectrum: 0·80 (4β-CH_3), 0·85 (4α-CH_3 + 10β-CH_3), 0·85 d, J = 6·5 Hz and 0·915 d, J = 6·5 Hz (19α-$CH(CH_3)_2$), 0·98 (14α-CH_3), 1·02 (8β-CH_3), 1·57 bs (17α-OH + 22α-OH), 3·77 m (22β-H). For $C_{30}H_{52}O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 81·15% C, 12·02% H. Acetylation of 40 mg of diol *XXVI*, carried out in the conventional manner, gave 20 mg (46%) of monoacetate *XXVIII*, m.p. 217—219°C (hexane), $[\alpha]_D$ 37° (*c* 0·43). IR spectrum: 1728, 1250 (CH_3COO), 3580, 3425, 1058, 1032 (OH) cm^{-1}. PMR spectrum: 0·80 (4β-CH_3), 0·84 (4α-CH_3 + 10β-CH_3), 0·85 d, J = 6·6 Hz and 0·92 d, J = 6·6 Hz (19α-$CH(CH_3)_2$), 1·01 (8β-CH_3 + 14α-CH_3), 2·06 (22α-$OCOCH_3$), 5·13 dd, J_{vic} = 10·3 Hz and 4·7 Hz (22β-H). For $C_{32}H_{54}O_3$ (486·8) calculated: 78·96% C, 11·18% H; found: 78·73% C, 11·19% H.

17-Hydroxy-19α-isopropyl-28,29,30-trinor-17α,18α-oleanan-22-one (*XXIX*)

Chromium trioxide (70 mg) was added to a solution of 70 mg of diol *XXVI* in 15 ml of pyridine and the mixture was allowed to stand at room temperature for 5 days. After the conventional working up acid reaction products were separated and discarded. By crystallization of the neutral fraction from ether–light petroleum and ether–hexane 10 mg of ketone *XXIX* were obtained, m.p. 244—245°C $[\alpha]_D$ 44° (*c* 0·20). ORD: $[\Phi]_{400}$ 700°, $[\Phi]_{336.5}$ 1995°, $[\Phi]_{303}$ 376°, $[\Phi]_{250}$ 2270°. IR spectrum: 1710 (CO), 1050 (OH) cm^{-1}; ketone *XXIX* is identical with a preparation prepared by us earlier[22].

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