PHOTOOXIDATION OF (20*R*)- AND (20*S*)-29-LUPANOL DERIVATIVES*

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The preferred rotamers of the side chain in (20*R*)- or (20*S*)-29-lupanol derivatives enable a selective functionalization of this skeleton in dependence on the configuration at $C_{(20)}$. On photooxidation of (20*R*)-hydroxy derivative *II* two isomeric epoxy derivatives are formed, *IV* and *V*. Their structure was demonstrated on the basis of spectral data and their oxidation to corresponding lactones *VI* and *VII*. When acetolysed epoxy derivative *IV* gave two unsaturated triacetates, *VIII* and *IX*. Photooxidation of (20*S*)-hydroxy derivative *XII* takes place predominantly under formation of nor-derivatives *XIV*, *XVII* and *XX*. To a lesser extent epoxy derivative *XXI* is also formed the structure of which follows from its oxidation to lactone *XXII* and keto acid *XXIII*.

In preceding papers[1,2] we described the functionalization of the lupane skeleton by radical transfer from the side chain ($C_{(20)}$) into position $C_{(12)}$ and we determined the dependence of this reaction on the configuration 20*S*. Therefore, we were further interested in how the effect of configuration at $C_{(20)}$ would manifest itself on the radical transfer from a functional group more remote by an additional covalent bond from this centre, *i.e.* on $C_{(29)}$. For such a system an attack on some of the tertiary carbons of the skeleton cannot be excluded, so that Barton's reaction would give only limited information. Therefore, for the solution of the metioned dependence radicalic oxidation of (20*R*)- or (20*S*)-29-lupanol derivatives *II* or *XII*, resp., has been made use of under conditions which we found suitable earlier[3] during the functionalization of 28-lupanol derivatives; radicalic oxidation initiated with dibenzoyl peroxide[4] was found less suitable in orienting experiments.

The starting hydroxy derivatives *II* and *XII* were prepared in the described manner[5]. During the separation of the reaction mixture we isolated another product in addition to them, the composition of which, as well as its IR spectrum (3635, 1730, 1262 cm^{-1}) and PMR spectrum (2·03, s, 3 H, $OCOCH_3$), corresponds to the monoacetate of the parent triol *I* or *X*. From the chemical shifts of the signals of protons at $C_{(3)}$ (4·49, m, 1 H), $C_{(28)}$ (3·31, d, 1 H; 3·79, d, 1 H) and $C_{(29)}$ (3·42, d, 2 H) it follows that the acetoxy group must be bound in the position 3β. The comparison of the chemical shift of the doublet of the $C_{(20)}$-methyl group (0·80 p.p.m.) with the

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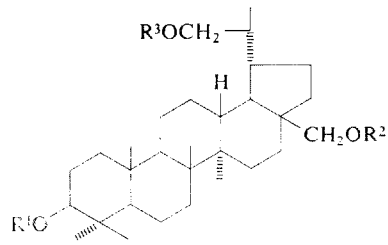
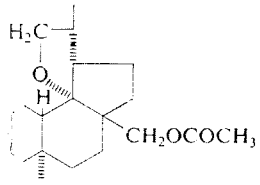
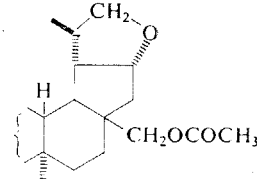
values found for 20*S*-diacetate *XII* or 20*R*-diacetate *II* (0·81 p.p.m. or 0·96 p.p.m. respectively) led to the assumption that the isolated substance is 3-O-acetyl derivative of the 20*S*-triol *X*, *i.e.* *XI*. This assumption was confirmed by acetylation of monoacetate *XI* and diacetate *XII* in the usual manner. In both cases an identical triacetate *XIII* was formed. Monoacetate *XI* was further characterized by converting it to triol *X* hydrolytically. For the completion of the proof of configuration 20*S* and for the completion of the series of $C_{(20)}$-epimeric lupane derivatives diacetate *II* was further acetylated to triacetate *III*. The molecular rotation differences and the changes of chemical shifts in the PMR spectra of triacetates *III* or *XIII* are in agreement with earlier[5] derived differentiations of $C_{(20)}$-epimers. The formation of monoacetate *XI* under the given conditions may be explained by partial hydrolysis of diacetate *XII*



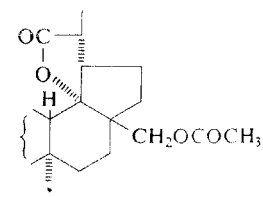
I, $R^1 = R^2 = R^3 = H$
II, $R^1 = R^2 = COCH_3$, $R^3 = H$
III, $R^1 = R^2 = R^3 = COCH_3$



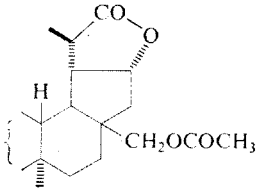
IV



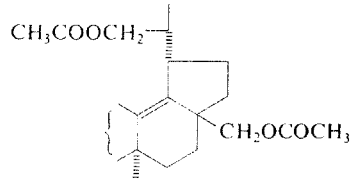
V



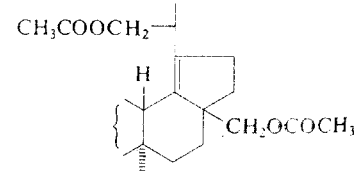
VI



VII

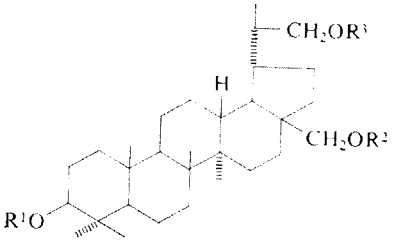


VIII

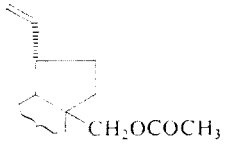


IX

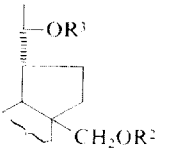
only. As an analogous partial hydrolysis of the epimeric diacetate *II* was not observed, it may be supposed that a side chain with the configuration 20*S* is preferred in such a conformation in which it may accelerate the hydrolysis of the 28-acetoxy group (see partial hydrolysis of betulin diacetate[6]). Information on the conformation of the side chain are included in vicinal coupling constants $J_{19,20}$ and $J_{20,29}$. However, from the PMR spectrum of diacetate *XII* in deuteriochloroform the values of the required coupling constants cannot be obtained with a sufficient accuracy because



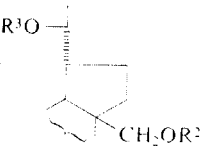
X, $R^1 = R^2 = R^3 = H$
XI, $R^1 = COCH_3$, $R^2 = R^3 = H$
XII, $R^1 = R^2 = COCH_3$, $R^3 = H$
XIII, $R^1 = R^2 = R^3 = COCH_3$



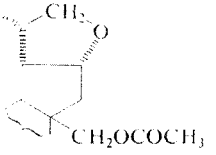
XIV



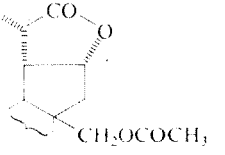
XV, $R^1 = R^2 = R^3 = H$
XVI, $R^1 = R^2 = COCH_3$, $R^3 = H$
XVII, $R^1 = R^2 = R^3 = COCH_3$



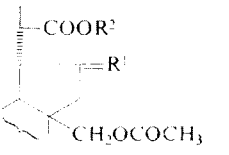
XVIII, $R^1 = R^2 = R^3 = H$
XIX, $R^1 = R^2 = COCH_3$, $R^3 = H$
XX, $R^1 = R^2 = R^3 = COCH_3$



XXI



XXII



XXIII, $R^1 = O$, $R^2 = H$
XXIV, $R^1 = O$, $R^2 = CH_3$
XXV, $R^1 = H_2$, $R^2 = CH_3$

the $C_{(29)}$-protons afford a deceptively simple spectrum of two overlapping doublets, enabling the determination of the sum $J_{20,29} = 14$ Hz only, while the protons on $C_{(19)}$ and $C_{(20)}$ are hidden.

On photooxidation of (20*R*)-hydroxy derivative *II* two isomeric epoxy derivatives, *IV* and *V*, were obtained in 51% or 8% yield, respectively. The structure of the main product, *IV*, follows from the following data: According to its IR spectrum the product contains instead of the original hydroxy group a tetrahydrofuran cycle (1 052 cm^{-1}) which according to the PMR spectrum contains the oxygen atom between the 29--methylene group (3·09, dd, 1 H; 3·86, t, 1 H) and the fully substituted carbon. As according to other signals (Table I) skeletal changes can be practically excluded, the epoxyde ring must be closed between the positions $C_{(29)}$ and $C_{(18)}$. From the comparison of the chemical shifts of the 28-methylene group protons and of those of the 8β- and 14α-methylene groups in the starting substance *II* and the product *IV* it follows that no change in annelation of the cycles D and E took place during the reaction, *i.e.* that the epoxidic bond has configuration 18α. In order to bring about a chemical proof of the proposed structure we first oxidized epoxy derivative *IV*; thus we obtained lactone *VI* in a lower yield (34%); its IR spectrum (1 759 cm^{-1}) confirms the butanolide grouping. In its PMR spectrum the $C_{(29)}$-protons disappear and the signal of one —CH—CO— proton newly appears, due to the $C_{(20)}$-hydrogen, as a pentet at 2·94 p.p.m. with $J_{20,19} = 7$ Hz, corresponding to the proposed geometry. The presence of the lactone carbonyl manifests itself by a distinct downfield shift of the doublet of the $C_{(20)}$-methyl ($\Delta\delta = +0{\cdot}25$ p.p.m.), in contrast to substance *II*. In a further experiment aiming at a chemical proof of the structure of epoxy derivative *IV* we carried out its acid catalysed acetolysis and obtained thus a mixture of two unsaturated triacetates with a tetrasubstituted double bond, to which we assigned the structures *VIII* (50%) and *IX* (25%). As neither of the two triacetates isomerize under the conditions of acid catalysis, they must have arisen by side reactions under elimination of 13β-H or 19β-H. The structures *VIII* and *IX* are based on the speculative structural interpretation of the shifts observed in the PMR spectra. While in the spectrum of derivative *IX* the downfield signal of the $C_{(20)}$-hydrogen (sextet at 3·40 p.p.m.) protrudes from the methylene protons envelope, in the case of derivative *VIII* the signal is similarly protruding which must belong to the $C_{(19)}$--hydrogen (multiplet at 2·78 p.p.m.). As in both epimeric saturated triacetates *III* and *XIII* the hydrogens at $C_{(19)}$ and in $C_{(20)}$ lie at substantially higher field and are under the envelope, we interprete the observed downfield shift of these protons in unsaturated triacetates *VIII* and *IX* by the presence of an allylic double bond, *i.e.* in 13(18) or 18(19), respectively. The by-product of the photooxidation of hydroxy derivative *II* also contains an intramolecular ether bond (IR: 1 074 cm^{-1}) which according to its PMR spectrum connects the 29-methylene group (3·74, dd, 1 H; 3·87, dd, 1 H; $J_{29,29} = 9$ Hz) with the carbon atom carrying one proton (4·66, q, 1 H) with three, approximately equal, vicinal couplings of *J* approximately equal to 7 Hz,

in the grouping —CH_2—CH(OR)—CH—. From the theoretically possible positions, suitable for the closing of the epoxide ring, *i.e.* $C_{(12)}$ and $C_{(21)}$, only the position 21α fulfils the geometrical conditions of the observed splitting of the —CH—O— proton signal. In agreement with the proposed structure *V* the epoxide gave on oxidation the five-membered lactone *VII* (IR: 1 759 cm^{-1}) in 74% yield; its carbonyl in the PMR spectrum shifts the doublet of $C_{(20)}$—CH_3 and the quartet of $C_{(21)}$—H distinctly downfield ($\Delta\delta = +0{\cdot}33$ or $\Delta\delta = +0{\cdot}32$, respectively). According to the preparative results it is evident that the side chain of the (20*R*)-hydroxy derivative *II* assumes two different conformations in the transition state of the cyclisation. The prevailing conformation is geometrically close to the basic state of the starting hydroxy derivative *II* with synclinal $C_{(19)}$—H and $C_{(20)}$—H, leading to epoxide *IV*. The second, less energetically favoured conformation, with synclinal $C_{(19)}$—H and $C_{(20)}$—CH_3 leads to epoxide *V*. On closing of the epoxide ring the methyl on $C_{(20)}$ does not enter an environment substantially different from that of the starting hydroxy derivative *II*, and, therefore, the change in its chemical shift, connected with cyclisation, is also small.

The conformation of the side chain in epimeric (20*S*)-29-hydroxy derivative *XII* is less advantageous for the formation of the transition state of intramolecular cyclisation, as evident from the structures and relative representation of the products isolated. Three of the isolated products are 30-norderivatives *XIV*, *XVII* and *XX*, the identification of which was carried out by comparison with authentic samples prepared by us earlier[7,8]. They represent at least 47% of the conversion of the starting hydroxy derivative *XII*; of this 30-nor-20(29)-lupene derivative *XIV* represents 15%. From further 30-nor-20-acetoxy derivatives (32%) we isolated directly triacetate *XVII* only, with unchanged 20*S* configuration. The presence of epimeric 20*R*-triacetate *XX* was demonstrated by hydrolysis of the mixture of triacetates and the separation of the mixture of triols *XV* and *XVIII* formed. Their weight ratio (5·5 : 1) indicates that during the formation of 30-nortriacetates *XVII* and *XX* the original 20*S* configuration remains predominantly preserved. To the last isolated product of photooxidation of hydroxy derivative *XII* (yield 14%) we assign the structure of epoxide *XXI* for the following reasons: Similarly as in epoxy derivative *V* in this case too the tetrahydrofuran nucleus (IR: 1 088 cm^{-1}) is closed between the positions $C_{(29)}$ (PMR: 3·60, dd, 1 H; 3·77, dd, 1 H; $J_{29,29} = 9$ Hz) and $C_{(21)}$ (PMR: 4·51, m, 1 H). However, after this cyclisation the $C_{(20)}$-methyl appears in an environment rather different from that of the starting hydroxy derivative *XII*, as evident from the chemical shift change of its doublet ($\Delta\delta = +0{\cdot}16$). From the models it follows that it is fixed in the proximity of the position $C_{(12)}$, which probably leads to conformational deformations of the ring E and of the tetrahydrofuran ring in consequence of steric interactions. In agreement with this idea the oxidation of epoxide *XXI* affords

the expected lactone *XXII* in a low yield only (28%). Its absorption in the infrared region (1765 cm^{-1}) and the changes of the chemical shifts of the doublet of $C_{(20)}$—CH_3 ($\Delta\delta$ = +0·31) and the multiplet $C_{(21\alpha)}$—H ($\Delta\delta$ = +0·47) confirm the structure of the starting epoxide *XXI*. The second oxidation product is the keto acid *XXIII* (27%), characterized as methyl ester *XXIV*. Its structure follows primarily from its PMR spectrum in which the signals of the 29-methylene group disappeared and the singlet of $COOCH_3$ (3·74 p.p.m.) newly appeared; also the multiplet of $C_{(20)}$—H (2·68 p.p.m.), shifted downfield, and the protons in the vicinity of the keto group, *i.e.* a broad doublet due to $C_{(19)}$—H (2·99 p.p.m.) and the doublet of one proton of the isolated 22-methylene group (2·46 p.p.m.) with a characteristic J_{gem} = 17 Hz (the second $C_{(22)}$—H is overlapped at about 1·85 p.p.m. and it was proved by tickling experiments). The position of the carbonyl on $C_{(21)}$ is further confirmed by its anisotropic shielding effect following from the comparison of the PMR spectra of keto ester *XXIV* and the corresponding deoxo derivative *XXV* (ref.[5]); a distinct downfield shift of the $C_{(19)}$—H signal ($\Delta\delta$ = +0·69), a weaker downfield shift for the $COOCH_3$ group ($\Delta\delta$ = +0·13) and for $C_{(28)}$—H_2 ($\Delta\delta$ = +0·18 or +0·12), and a small upfield shift of $C_{(20)}$—CH_3 ($\Delta\delta$ = −0·02) and $C_{(20)}$—H ($\Delta\delta$ = −0·04). The observed Cotton effect of the keto group in *XXIV*, *i.e.* the position of the CD-curve maximum (303 nm) and the distinct ellipticity (Φ = 13430) lead to the same conclusion. The formation of the keto acid *XXIII* can be explained by the opening of the butanolide ring of lactone *XXII* during the oxidation (in consequence of the above mentioned conformational deformations) and by the oxidation of the hydroxy acid formed to keto acid *XXIII*.

EXPERIMENTAL

The melting points were determined on a Kofler block. Optical rotations were measured in chloroform (unless stated otherwise) on an automatic polarimeter ETL-NPL (Bendix-Ericsson) with a ±2° precision. The infrared spectra were measured in chloroform (unless otherwise stated) on a UR-20 (Zeiss, Jena) instrument. The PMR spectra were measured in deuteriochloroform on a Varian HA-100 apparatus (at 100 MHz, using tetramethylsilane as internal reference). The PMR data are given in Table I. The circular dichroism curve was recorded with a Roussel-Jouan Dichrographe 185 in dioxan. For chromatography neutral alumina (Reanal, activity II) and silica gel (Spolana, Neratovice) were used. For the preparation of preparative silica gel plates silica gel G according to Stahl was employed (for a 20 × 20 cm plate 10 g were sufficient). Under the conventional working up the following procedure is meant: dilution of the reaction mixture with water, extraction of the product from this mixture with ether, repeated washing of the ethereal extract with water and 5% sodium carbonate solution. All solutions were dried over anhydrous sodium sulfate. Samples for analysis were dried over phosphorus pentoxide at 100°C and 0·1—1 Torr pressure for 12 hours. The identity of the samples was determined on the basis of their mixture melting points with reference samples, optical rotation, thin-layer chromatography, and infrared spectra.

(20*S*)-3β-Acetoxylupane-28,29-diol (*XI*)

The product (3·20 g) obtained during the preparation of alcohols *II* and *XII* according to[5] was separated by chromatography on 320 g of alumina; 1150 ml of benzene containing 10% of ether eluted 1·23 g of alcohol *II*, 450 ml of benzene with 20% of ether eluted 0·40 g of a mixture of alcohols *II* and *XII*, 1000 ml of the same solvent mixture eluted 0·77 g of alcohol *XII*. Ether containing 10% of methanol (1000 ml) eluted 0·53 g of diol *XI*, m.p. 298–300°C (chloroform–methanol), $[\alpha]_D$ −5° (*c* 0·61). IR spectrum: 3635, 1029 (OH), 1730, 1262, 1029 (CH_3COO) cm^{-1}. For $C_{32}H_{54}O_4$ (502·8) calculated: 76·44% C, 10·83% H; found: 76·20% C, 11·00% H.

(20*S*)-Lupane-3β,28,29-triol (*X*)

Acetate *XI* (50 mg) was hydrolysed in refluxing ethanolic potassium hydroxide solution for 7 hours. After the conventional work-up crystallization from ethanol gave 35 mg of triol *X*, m.p. 307–309°C, $[\alpha]_D$ −19° (*c* 0·37, dimethyl sulfoxide). IR spectrum (nujol): 3625, 3355, 1048, 1032 (OH) cm^{-1}. For $C_{30}H_{52}O_3$ (460·7) calculated: 78·20% C, 11·38% H; found: 78·06% C, 11·38% H.

(20*S*)-3β,28,29-Triacetoxylupane (*XIII*)

a) Alcohol *XII* (50 mg) was heated with 2 ml of pyridine and 1 ml of acetic anhydride on a water bath for 3 hours. After dilution with water the mixture was extracted with ether, the extract washed with dilute hydrochloric acid (1 : 4), water and 5% sodium carbonate solution. Yield, 40 mg of triacetate *XIII*, m.p. 186·5–187·5°C (ether–hexane), $[\alpha]_D$ +2° (*c* 0·89). IR spectrum: 1730, 1254, 1030 (CH_3COO) cm^{-1}. For $C_{36}H_{58}O_6$ (586·8) calculated: 73·68% C, 9·96% H; found: 73·73% C, 9·96% H.

b) Acetylation of 100 mg of diol *XI* was carried out in the same manner as under *a*). Yield, 100 mg of triacetate *XIII*, m.p. 186·5–187·5°C (ether–hexane), $[\alpha]_D$ −2° (*c* 0·85), which was identical with a sample prepared as under *a*).

(20*R*)-3β,28,28-Triacetoxylupane (*III*)

Acetylation of 50 mg of alcohol *II* was carried out under the same conditions as in the case of alcohol *XII*. Triacetate *III* (40 mg) was obtained which had m.p. 170–170·5°C (ether–hexane), $[\alpha]_D$ −25° (*c* 0·90). IR spectrum: 1730, 1258, 1030 (CH_3COO) cm^{-1}. For $C_{36}H_{58}O_6$ (586·8) calculated: 73·68% C, 9·96% H; found: 73·80% C, 10·05% H.

Photooxidation of (20*R*)-3β,28-Diacetoxylupan-29-ol (*II*)

Calcium carbonate (2 g) and lead tetra-acetate (5 g) were suspended in a solution of 1·0 g of alcohol *II* in 200 ml of cyclohexane and the stirred mixture was refluxed and irradiated under nitrogen with a 500 W lamp for 4 hours. After filtration and the conventional working up the crude product (1 g) was separated chromatographically on 130 g of alumina. Elution with benzene (200 ml) gave 0·51 g (51%) of epoxy derivative *IV*, m.p. 269–271°C (chloroform–methanol), $[\alpha]_D$ +4° (*c* 0·91). IR spectrum: 1052 (C—O—C), 1732, 1260, 1035 (CH_3COO) cm^{-1}. For $C_{34}H_{54}O_5$ (542·8) calculated: 75·23% C, 10·03% H; found: 74·97% C, 10·11% H. A mixture of benzene with 5% of ether (80 ml) eluted 70 mg of a mixture of substances which were not identified. Further elution with the same mixture of solvents (120 ml) gave 80 mg (8%) of epoxy derivative *V*. M.p. 225–227°C (benzene–ethanol), $[\alpha]_D$ +2° (*c* 0·45). IR spectrum: 1099, 1074 (C—O—C), 1730,

1260, 1036 (CH_3COO) cm^{-1}. For $C_{34}H_{54}O_5$ (542·8) calculated: 75·23% C, 10·03% H; found: 75·41% C, 9·82% H. The same mixture of solvents (120 ml) gave 20 mg of a mixture of substances which were not identified. Elution with benzene with 20% of ether (450 ml) eluted 190 mg of alcohol *II*.

(20*R*)-3β,28-Diacetoxylupan-29→18α-olide (*VI*)

A solution of chromium trioxide (100 mg) in 10 ml of acetic acid was added to a solution of 100 mg of epoxy derivative *IV* in 5 ml of acetic acid and the mixture allowed to stand at room temperature overnight. After an additional two hours' heating at 40°C methanol was added and the mixture worked up in the usual manner, affording 100 mg of a product which was further separated chromatographically on 15 g of alumina. Benzene (15 ml) eluted 20 mg of epoxy derivative *IV* from the column. Further elution with benzene containing 3% of ether (120 ml) gave 35 mg of lactone *VI*, m.p. 288—291°C (ether–hexane), $[\alpha]_D$ −9° (*c* 0·45). IR spectrum: 1759, 1194 (γ-lactone), 1732, 1260, 1040 (CH_3COO) cm^{-1}. For $C_{34}H_{52}O_6$ (556·8) calculated: 73·34% C, 9·41% H; found: 73·21% C, 9·49% H.

(20*R*)-3β,28-Diacetoxylupan-29→21α-olide (*VII*)

To a solution of 80 mg of epoxy derivative *V* in 5 ml of acetic acid a solution of 80 mg of chromium trioxide in 10 ml of acetic acid was added and the mixture allowed to stand at room temperature for 24 hours. After addition of methanol and the conventional working up 80 mg of product were obtained which was separated chromatographically on a preparative silica gel plate in benzene–ether 4 : 1. Yield 60 mg of lactone *VII*, m.p. 239—241°C (ether–methanol), $[\alpha]_D$ +16° (*c* 0·73). IR spectrum: 1759, 1189(γ-lactone), 1728, 1252, 1032 (CH_3COO) cm^{-1}. For $C_{34}H_{52}O_6$ (556·8) calculated: 73·34% C, 9·41% H; found: 73·08% C, 9·38% H.

Acetolysis of (20*R*)-3β,28-Diacetoxy-18α,29-epoxylupane (*IV*)

A solution of 130 mg of epoxy derivative *IV* in 30 ml of acetic anhydride and 40 mg of *p*-toluenesulfonic acid was refluxed for 7 hours. The mixture was evaporated in vacuo and worked up in the conventional manner. The residue (130 mg) was separated by chromatography on 35 g of silica gel. A mixture of light petroleum with 10% of ether (120 ml) eluted 35 mg of the starting epoxy derivative *IV*. Further elution with the same mixture of solvents (200 ml) gave 70 mg of triacetate *VIII*, m.p. 185—187°C (ether–methanol), $[\alpha]_D$ −42° (*c* 0·76). IR spectrum: 1730, 1260, 1033 (CH_3COO) cm^{-1}. For $C_{36}H_{56}O_6$ (584·8) calculated: 73·93% C, 9·65% H; found: 74·15% C, 9·81% H. Further elution with the same mixture of solvents (240 ml) afforded 35 mg of triacetate *IX*, m.p. 191—193°C (ether–methanol), $[\alpha]_D$ −2° (*c* 0·54). IR spectrum: 1732, 1260, 1036 (CH_3COO) cm^{-1}. For $C_{36}H_{56}O_6$ (584·8) calculated: 73·93% C, 9·65% H; found: 73·79% C, 9·84% H.

Attempt at Isomerization of (20*R*)-3β,28,29-Triacetoxy-13(18)-lupene (*VIII*)

A solution of 30 mg of triacetate *VIII* in 6 ml of acetic anhydride containing 10 mg of *p*-toluenesulfonic acid was refluxed for 8 hours. The mixture was concentrated in a vacuum and worked up in the conventional manner. The residue (30 mg) was separated by chromatography on a silica gel plate, using heptane–ether 3 : 2 as the developing solvent. Yield 10 mg of triacetate *VIII*, m.p. 183—185°C (ether–methanol) $[\alpha]_D$ −41° (*c* 0·66). Triacetate *IX* was not found.

TABLE I

Characteristic Parameters of Proton Magnetic Resonance Spectra

In $CDCl_3$ with TMS as internal reference; all parameters were obtained by first order analysis. Chemical shifts are given with a ± 0·005 p.p.m. and the coupling constants with a ± 0·2 Hz or ±0·5 Hz (indicated with the symbol ≈) accuracy. For the assignment of methyl signals see ref.[11].

Compound	Chemical Shifts (in p.p.m.) and Coupling Constants (in Hz)											
	4α-Me	4β-Me	10β-Me	8β-Me	14α-Me	20-Me[a]	3α-H	28-H_2[b]	29-H_2	$J_{29,29}$	$J_{29,20}$	Other protons
II	0·85	0·85	0·85	1·05	0·96	0·96	4·46	3·78; 4·21	3·41; 3·78	≈10	≈ 8	2·01 (2 × OAc)
III	0·85	0·85	0·86	1·05	0·96	0·93	4·48	3·80; 4·24	3·89; 4·15	10·8	7·3; 5·3	2·03; 2·05; 2·06 (3 × OAc)
IV	0·83	0·83	0·83	1·07	1·02	0·92	4·45	3·68; 4·30	3·09; 3·86	7·6	11·2; 7·4	2·01; 2·05 (2 × OAc)
V	0·85	0·85	0·88	1·05	0·96	0·98	4·48	3·70; 4·20	3·47; 3·87	≈ 9	≈ 5; 2·5	2·03; 2·05 (2 × OAc), 4·66 (21β-H)
VI	0·85	0·85	0·85	1·11	1·07	1·17	4·48	3·74; 4·33	— —	—	— —	2·02; 2·08 (2 × OAc), 2·56 (19β-H) 2·94 (20-H), $J_{20,19} \approx 7$
VII	0·85	0·85	0·88	1·04	0·95	1·31	4·48	3·74; 4·14	— —	—	— —	2·03; 2·07 (2 × OAc), 2·25—2·55 (19β-H + 20-H), 4·98 (21β-H)
VIII	0·85	0·87	0·90	1·13	1·00	0·96	4·51	3·72; 3·97	3·66; 3·95	≈10	≈10; 3·5	2·03; 2·05; 2·05 (3 × OAc), 2·78 (19β-H)
IX	0·84	0·84	0·91	1·07	0·91	0·94	4·50	3·50—4·15		[c]	≈ 7; ≈ 7	2·04; 2·05; 2·05 (3 × OAc), 3·40 (20-H)
XI	0·85	0·85	0·85	1·03	0·96	0·80	4·49	3·31; 3·79	3·42	[c]	≈ 7·5; ≈7·5	2·03 (1 × OAc)
XII	0·85	0·85	0·85	1·05	0·96	0·81	4·48	3·81; 4·26	3·40	[c]	6·9; 6·9	2·01 (2 × OAc)
XIII	0·85	0·85	0·85	1·05	0·95	0·83	4·50	3·78; 4·27	3·84	[c]	≈ 7; ≈ 7	2·04; 2·04; 2·05 (3 × OAc)
XXI	0·85	0·85	0·87	1·05	1·01	0·97	4·48	3·77; 4·31	3·60; 3·77	9·0	2·5; 4·5	2·03; 2·05 (2 × OAc), 4·51 (21β-H)
XXII	0·85	0·85	0·88	1·07	1·00	1·28	4·50	3·76; 4·27	— —	—	— —	2·04; 2·08 (2 × OAc), 4·98 (21β-H)
XXIV	0·86	0·86	0·88	1·10	1·05	1·02	4·49	3·98; 4·37	— —	—	— —	2·02; 2·05 (2 × OAc), 3·74 (COOMe) 2·46 (22-H), $J_{22,22} \approx 17$, 2·68 (20-H) $J_{20,19} \approx 3·5$, 2·99 (19β-H), $J_{19,18} \approx 11$

[a] Doublets with $J_{30,20} = 6—7$ Hz; [b] two doublets $J_{28,28} = 10·5—11·5$ Hz; [c] indeterminable value.

Attempt at Isomerization of (20*R*)-3β,28,29-Triacetoxy-18(19)-lupene (*IX*)

The reaction was carried out with 40 mg of triacetate *IX* under the same same conditions as in the case of triacetate *VIII*. After chromatography of the residue (40 mg) on a preparative silica gel plate in heptane–ether 4 : 1 triacetate *IX* was isolated (20 mg). M.p. 189–192°C (ether–methanol), $[\alpha]_D$ −5° (*c* 0·83). Triacetate *VIII* was not found.

Photooxidation of (20*S*)-3β,28-Diacetoxylupan-29-ol (*XII*)

The reaction was carried out with 500 mg of alcohol *XII* analogously as in the case of alcohol *II*, with the difference that the reaction time was prolonged to 6 hours. The residue (500 mg) was separated by chromatography on 100 g of silica gel. Elution with light petroleum containing 5% of ether (630 ml) gave 90 mg of crude nor derivative *XIV* which was purified by thin-layer chromatography on a thin-layer silica gel plate with 5% silver nitrate in heptane–ether 4 : 1. Nor-derivative *XIV* (70 mg) was obtained in a 15% yield. It was crystallized twice from ether and methanol, and eventually hexane, (m.p. 181–183°C, $[\alpha]_D$ +5° (*c* 1·92)), and it was identical with an authentic sample[7]. Further elution with light petroleum containing 10% of ether (210 ml) eluted 50 mg of a mixture of nor-derivatives *XIV*, *XVII* and *XX*. Using the same mixture of solvents (700 ml) 170 mg (32%) of a mixture of epimeric nor-derivatives *XVII* and *XX* was eluted. After six-fold crystallization from methanol nor-derivative *XVII* was obtained with m.p. 185–187°C, $[\alpha]_D$ +7° (*c* 0·29). IR spectrum: 1729, 1260, 1035 (CH_3COO) cm^{-1}. Literature[8] gives m.p. 186–188°C, $[\alpha]_D$ +6·6°. Elution with light petroleum containing 20% of ether (420 ml) afforded 70 mg (14%) of epoxy derivative *XXI*, m.p. 261–263·5°C (chloroform–methanol), $[\alpha]_D$ −7° (*c* 0·62). IR spectrum: 1088 (C—O—C), 1730, 1260, 1036 (CH_3COO) cm^{-1}. For $C_{34}H_{54}O_5$ (542·8) calculated: 75·23% C, 10·03% H; found: 75·28% C, 9·76% H.

Hydrolysis of the Mixture of (20*R*) and (20*S*)-3β,20,28-Triacetoxy-30-nor-lupanes (*XVII* and *XX*)

A mixture of epimeric triacetates *XVII* and *XX* (170 mg) was heated with an ethanolic solution of potassium hydroxide for 6 hours. After the usual working up the mixture of triols (170 mg) was separated by preparative chromatography on a silica gel plate, using a four-fold development in chloroform. From the faster zone 20 mg of triol *XVIII* were eluted with chloroform, m.p. 238–240°C (acetone–light petroleum), $[\alpha]_D$ −21° (*c* 0·63, dioxan). It was identical with an authentic sample prepared by the procedure described below. From the slower zone 110 mg of triol *XV* were eluted with chloroform, m.p. 315–318°C (ethanol), $[\alpha]_D$ −19° (*c* 0·75, dioxan). It was identical with an authentic specimen prepared by the procedure described below.

(20*R*)-30-Norlupane-3β,20,28-triol (*XVIII*)

Diacetate[9] *XIX* (100 mg) was refluxed with an ethanolic potassium hydroxide solution for four hours and the mixture was worked up in the conventional manner. Crystallization of the product from ethanol and acetone–light petroleum gave triol *XVIII* (45 mg) of m.p. 241–242°C, $[\alpha]_D$ −22° (*c* 0·58, dioxan). IR spectrum (nujol): 3360, 1032 (OH) cm^{-1}. For $C_{29}H_{50}O_3$ (446·7) calculated: 77·97% C, 11·28% H; found: 77·72% C, 11·26% H.

(20*S*)-30-Norlupane-3β,20,28-triol (*XV*)

Hydrolysis of 100 mg of diacetate[9] *XVI* under the same conditions as in the acetate *XIX* gave a product which after crystallization from ethanol gave 50 mg of triol *XV*, m.p. 318–319·5°C,

$[\alpha]_D$ −20° (*c* 0·56, dioxan), IR spectrum (nujol): 3605, 3460, 3400, 1074, 1028 (OH) cm^{-1}. Literature[10] gives m.p. 315—319°C, $[\alpha]_D$ −19·2° (dioxan).

Oxidation of (20*S*)-3β,28-Diacetoxy-21α,29-epoxylupane (*XXI*)

A solution of 70 mg of chromium trioxide in 5 ml of acetic acid was added to 70 mg of epoxy derivative *XXI* dissolved in 20 ml of acetic acid and the mixture was allowed to stand at room temperature for 24 hours. After addition of methanol, dilution with water, and extraction with ether the product was separated by partitioning between ether and 5% sodium carbonate solution to a neutral (30 mg) and an acid fraction (40 mg). The neutral material was separated by preparative chromatography on a silica gel plate in heptane–ether 1 : 1. In addition to the starting epoxy derivative *XXI* 20 mg of lactone *XXII* were obtained, which had m.p. 265—267·5°C (chloroform–methanol), $[\alpha]_D$ −14° (*c* 0·29). IR spectrum: 1765, 1205 (γ-lactone), 1732, 1260, 1039 (CH_3COO) cm^{-1}. For $C_{34}H_{52}O_6$ (556·8) calculated: 73·34% C, 9·41% H; found: 73·11% C, 9·50% H. Crystallization of the acid fraction from ether gave 20 mg of acid *XXIII*, m.p. 265 to 269°C, $[\alpha]_D$ +71° (*c* 0·82). IR spectrum: 3300—2500 (COOH), 1740—1713 (CO), 1250, 1031 (CH_3COO), 1409 (α-CH_2) cm^{-1}.

On esterification of acid *XXIII* (15 mg) 12 mg of methyl ester *XXIV* were obtained, m.p. 284—286°C, $[\alpha]_D$ +70° (*c* 0·86). IR spectrum: 1740—1730 (CO), 1432, 1056, 1030 ($COOCH_3$), 1250, 1030 (CH_3COO), 1407 (α-CH_2) cm^{-1}. Circular dichroism: $\Delta\varepsilon$ +4·07 (303 nm) (*c* 0·038). For $C_{35}H_{54}O_7$ (586·8) calculated: 71·64% C, 9·28% H; found: 71·37% C, 9·30% H.

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