PHOTO-OXIDATION OF 28-LUPANOL AND ITS DERIVATIVES*

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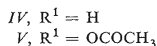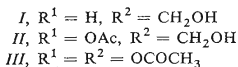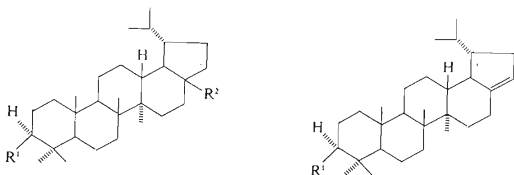
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On photo-oxidation of 28-lupanol (*I*) both unsaturated 28-nor-hydrocarbons *IV* and *VI*, and 13β,28-epoxylupane (*XIII*) are formed. During the photo-oxidation of 3β-acetoxy-28-lupanol (*II*) in addition to analogous derivatives *V*, *VI* and *XVI* 3β,17β(?)-diacetoxy-28-norlupane (*III*) was isolated also. The structure of olefins *IV* and *VI* was derived by their conversion to hydroxy derivatives *VII* or *X* and *XII*, resp., and further to oxo derivatives *VIII* or *XI*, respectively. From epoxy derivatives *XIII* and *XV* 12-lupene derivatives *XIX* or *XX*, resp., were prepared, which were transformed to lupan-12-one derivative *XXII*. Thus the first method for partial synthesis of lupane derivatives substituted in the ring C was found. The PMR spectra of newly prepared derivatives and their CD curves are also discussed.

While the natural triterpenes with oleanane or ursane skeleton always contain a double bond in the position 12 (13) (*cf.*[1]), no 12-lupene derivative is known as yet. The number of described natural lupane derivatives with a substituted ring C is also limited[2-5]. Therefore we investigated the preparation and the properties of these derivatives.

The functionalisation of the ring C in lupane derivatives was carried out using the 28-hydroxymethyl group, namely photo-oxidation[6] of 28-lupanol (*I*) and its 3β-acetoxy derivative *II*. Thus from 28-lupanol (*I*) we obtained a mixture from

$$I, \text{ R}^1 = \text{H, R}^2 = \text{CH}_2\text{OH}$$
$$II, \text{ R}^1 = \text{OAc, R}^2 = \text{CH}_2\text{OH}$$
$$III, \text{ R}^1 = \text{R}^2 = \text{OCOCH}_3$$

$$IV, \text{ R}^1 = \text{H}$$
$$V, \text{ R}^1 = \text{OCOCH}_3$$

which we isolated 28-nor-16-lupene (*VI*), 28-nor-17(22)-lupene (*IV*) and 13β,28-
-epoxylupane (*XIII*) the structures of which we demonstrated in the manner described
below. Functionalisation by means of the "hypoiodite reaction"[7] was not successful:
Thus, from 3β-acetoxy-28-lupanol (*II*) 28-nor derivative *V* was obtained as the sole
isolatable product. Its structure was proved by the further proved structures of 28-nor
derivatives *IV* and *VI*.

In the PMR spectra of hydrocarbons *IV* and *VI* the signal of protons on $C_{(28)}$ is
missing. They have only a single vinyl proton (*IV* and *V*: $\delta = 5\cdot1$ (bs), *VI*: $\delta = 5\cdot25$ (m)
p.p.m.). While the double bond in the hydrocarbon *IV* causes only a small shift of
the signal of one of the side chain methyls ($\Delta\delta = +0\cdot06$ p.p.m.), its effect on the
8β-methyl group in the isomeric hydrocarbon *VI* is clearly evident ($\Delta\delta = -0,1$ p.p.m.).
For the determination of the double bond position the 28-nor derivatives *IV* and *VI*
were converted by the Brown method to corresponding hydroxy derivatives that were
further oxidized to oxo derivatives with the carbonyl group in the position of the
original trisubstituted olefinic carbon. Thus from 28-norlupene *IV* hydroxy derivative
VII was obatained. In its PMR spectrum the hydrogen adjacent to the secondary
hydroxyl group appears as a quartet ($\delta = 4\cdot03$ p.p.m., $J_{vic} = 8 + 8 + 8$ Hz). Ketone
VIII shows a 1725 cm^{-1} frequence in the carbonyl region, that belongs to the region
of carbonyl groups in five-membered cycles. From the PMR it follows that the car-
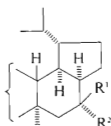bonyl affects by the sphere of the paramagnetic shift primarily the signal of one of
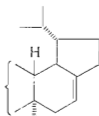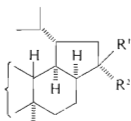
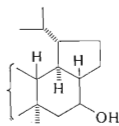*VII*, R^1 = H, R^2 = OH
*VIII*, R^1 + R^2 = O

VI
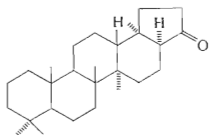
IX

X, R^1 = H, R^2 = OH
XI, R^1 + R^2 = O

XII

the angular methyls, 8β or 14α $(\Delta\delta = +0.19$ p.p.m.$)$. These findings comply with the position of the original double bond 17 (22) only. As ketone *VIII* in chloroform does not undergo equilibration under the effect of hydrogen bromide, it must possess a stable annelation of the cycles D and E, which is in substituted 1-hydrindanones *cis*[8]. Its distinctly positive Cotton effect excludes according to the octant rule the *trans* fusion; λ_{max} $(\Delta\varepsilon)$: 297 nm (2.13), 306·5 nm (2.13), 318 nm (1.13). A case of a very good agreement with the proposed structure *VIII* is given[9] for the analogous derivative of trinorhopanone *IX* (Table I).

In contrast to 28-norlupene *IV* diastereoisomeric hydroxy derivatives *X* and *XII* are formed in a 3 : 1 ratio by Brown's method from 28-nor derivative *VI*. Their difference may be caused merely by a reversed sterical course of the addition of diborane. In the PMR spectrum of hydroxy derivative *X* the downfield shift of one angular methyl is striking $(\Delta\delta = +0.12$ p.p.m.$)$. In analogy to 16α-lupanol derivatives[11] this shift is caused by 1,3-diaxial interaction of the hydroxy group with the 14α-methyl group; this determines both the position of the original double bond in nor derivative *VI* and the position and configuration of the hydroxy group and the annelation of the rings D/E in hydroxy derivative *X*. In order to confirm the position hydroxy derivative *X* was oxidized to ketone *XI*. Its IR spectrum absorbs in the carbonyl region at 1692 cm^{-1} which is in the region of absorption of carbonyl in a six-membered ring. In its PMR spectrum the shielding of one of the angular methyl group is evident $(\Delta\delta = -0.07$ p.p.m.$)$. For the definitive structural deduction it is essential that ketone *XI* has a distinct negative Cotton effect $\left(\lambda_{max}\ (\Delta\varepsilon)\ 294\ \text{nm}\right.$ $\left(-7.01\right))$. From the octant diagram it again follows that only 16-oxo derivative with *cis* D/E ring annelation can display such a distinct negative Cotton effect. The proposed structures *VI*, *X* and *XI* are therefore substantiated. Thus we consider that the position of the double bond in 28-nor derivatives *IV* and *VI* is definitively established. The structure of the isomeric hydroxy derivative *XII* was proposed only on the basis of its method of preparation and its spectroscopic properties, due to the low yield.
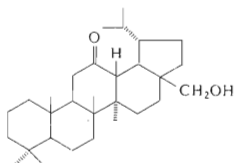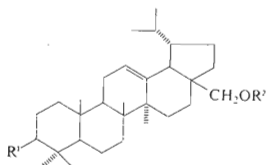

XIX, R^1 = H, R^2 = OH
XX, R^1 = OAc, R^2 = COCH$_3$
XXI, R^1 = H, R^2 = COCH$_3$

XXII

TABLE I
Correlation of the Optical Properties of Ketones *VIII* and *IX*

Optical property	*VIII*	*IX* (ref.[10])
$[M]_D$, $CHCl_3$	515°	538°
$\nu(CO)$, $CHCl_3$, cm^{-1}	1 725	1 729
CD, λ_{max} ($\Delta\varepsilon$)	297 nm (2·13), 306·5 (2·13)	—
Dioxan	318 (1·13)	
ORD, dioxan	peak 321 trough 303 cm $a = +57$	peak 322 trough 305 nm $a = +49$

The structure of the cyclic ether *XIII* was proposed on the basis of the spectral data and chemical conversions. According to the IR spectrum the new ether bond is characterised by an absorption band at $1019\ cm^{-1}$ and according to PMR spectra it must be connected with a tetrasubstituted carbon atom; assuming an unchanged cyclic skeleton only positions $C_{(19\beta)}$ and $C_{(13\beta)}$ satisfy this requirement. As the 19β,28--epoxylupane system (*XVIII*) is known[12] the same epoxide bridge in ether *XIII* may be excluded on the basis of the PMR spectra. While 19β,28-epoxy bond shifts especially the signals of the side chain, the effect of the epoxy bond in ether *XIII* is limited to the distinct downfield shift ($\Delta\delta = +0\cdot2$ p.p.m.) of the 8β-methyl group. Therefore it must be bridged with the position 13β. For the confirmation of this assumption ether *XIII* was oxidized to lactone *XIV*. Its lactone ring must be five-
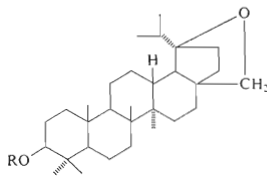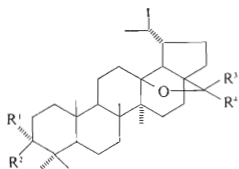
XIII, $R^1 = R^2 = R^3 = R^4 = H$
XIV, $R^1 = R^2 = H$, $R^3 + R^4 = O$
XV, $R^1 = R^3 = R^4 = H$, $R^2 = OH$
XVI, $R^1 = R^3 = R^4 = H$, $R^2 = OCOCH_3$
XVII, $R^1 + R^2 = O$, $R^3 = R^4 = H$

XVIII

membered $(v_{(CO)}$ 1765 cm^{-1}) and situated so that the shielding cone of the carbonyl hits the 8β-methyl group·($\Delta\delta = -0·06$ p.p.m.) and passes the 14α methyl group ($\Delta\delta = +0·130$ p.p.m.). The final assignment of all signals was done on the basis of the comparison of the PMR spectra of the prepared derivatives $XV-XVII$.

Photo-oxidation of 3β-acetoxy-28-lupanol (*II*) gave a mixture from which the analogous ether *XVI*, a mixture of unsatutated nor derivatives analogous to derivatives *IV* and *VI* (which could not be separated), and also the saturated nor derivative *III* were isolated. One acetoxy group of the latter compound is bound in the position 3β ($\delta = 2·03$ (3H, s) and 4·49 (1 H, p.p.m.) while the other ($\delta = 1·92$ (3H, s) p.p.m.) must be bound to a quaternary carbon atom. On the basis of the relative changes of other PMR signals we consider the structure *III* as probable.

For a further proof of the position of the ether bond of epoxides *XIII* and *XVI* their acetolysis with acetic anhydride and *p*-toluenesulfonic acid was carried out in good yield giving rise to unsaturated acetoxy derivatives for which we propose the structures *XXI* or *XX*, resp. The reasons are the following: The new double bond is undoubtedly trisubstituted ($\delta = 5·14$ (1H, bt) p.p.m., $J_1 + J_2 = 8$ Hz) and located so that the signals of the angular methyl groups in 8β and 14α are shifted under its influence in opposite directions ($\Delta\delta = -0·022$ or $+0·14$ p.p.m. resp.). Under the effect of hydrogen peroxide in acidic medium and subsequent base catalysed hydrolysis acetate *XXI* is transformed to keto alcohol *XXII* the keto group of which is in a six-membered ring ($v_{(CO)}$ 1710 cm^{-1}), and from the PMR spectrum of which it may be seen that the signal of the 8β-methyl group is distinctly shifted downfield ($\delta = 0·26$ p.p.m.). From this it may be judged that the double bond of the unsaturated acetate *XXI* must be in the position 12 (13) and hence the carbonyl group of the keto alcohol *XXII* formed by subsequent conversion must be in the position $C_{(12)}$. As this carbonyl gives a negative Cotton effect (λ_{max} ($\Delta\varepsilon$): 296 nm ($-1·61$)) the rings C/D must be *trans* fused. This Cotton effect is in agreement with the values of the Cotton effect in derivatives of lupan-12-one in which the keto group position was proved indirectly only[4,14].

EXPERIMENTAL

The melting points were measured on a Kofler block and they were not corrected. Optical rotation was measured in chloroform on an automatic polarimeter ETL-NPL (Bendix-Ericsson) with a ±2° accuracy. The IR spectra were measured in chloroform on an apparatus constructed in the Institute for Apparatus Technology, Brno, and a UR-20 from Zeiss, Jena. The PMR spectra were measured in deuteriochloroform, using tetramethylsilane as internal reference, on a Varian HA-100 apparatus; the chemical shifts are given in p.p.m., δ-scale. The circular dichroism curves were measured in dioxan on a Roussel-Jouan Dichrographe. Samples for analysis were dried at 100°C and 0·1 Torr over P$_2$O$_5$ for 8—12 hours. The reaction mixtures were worked up by extraction with ether, repeated washing with water, hydrochloric acid (1 : 4), sodium carbonate (5%) and water. The ethereal layer was dried over sodium sulfate, filtered and evaporated to dryness.

The residue was crystallised or chromatographed on neutral alumina (Reanal, act. II according to Brockmann) or on silica gel (30—60 µ), or on silica gel with 10% of silver nitrate.

Photo-oxidation of 28-Lupanol (*I*)

In a solution of 28-lupanol (*I*) (1·9 g) in cyclohexane (400 ml) lead tetraacetate (10·4 g) was suspended and the mixture refluxed, stirred and irradiated with a 500 W lamp for 6 hours. After filtration and dilution with water the mixture was extracted with ether and the extract worked up in the usual manner. The yellow oil (1·9 g) was chromatographed on alumina (110 g). Elution with light petroleum gave 950 mg of a mixture of hydrocarbons *IV* and *VI*, light petroleum–benzene (9 : 1) mixture eluted 260 mg of 13β,28-epoxylupane (*XIII*), m.p. 189—191°C (benzene–n-heptane), $[\alpha]_D +13°$ (*c* 0·63). IR spectrum: 1019 (C—O—C) cm^{-1}. PMR spectrum: 0·80 (4β-CH$_3$); 0·805 d + 0·865 d, $J_{vic} = 6·5$ Hz (CH(CH$_3$)$_2$); 0·85 (4α-CH$_3$); 0·875 (10β-CH$_3$, $J_{1.r.} = 0·4$ Hz); 1·025 (14α-CH$_3$, $J_{1.r.} = 0·6$ Hz), 1·24 (8β-CH$_3$); 3·465 bd + 3·62 d, $J_{1.r.} = 1$ Hz, $J_{gem} = 7·6$ Hz(C$_{(28)}$H$_2$) p.p.m. For C$_{30}$H$_{50}$O (426·7) calculated: 84·44% C, 11·81% H; found: 84·25% C, 11·67% H. The mixture of hydrocarbons *IV* and *VI* was separated by chromatography on silica gel (75 g) impregnated with silver nitrate using cyclohexane as eluent. 28-Nor-16-lupene (*VI*) 200 mg, m.p. 158—160°C (n-heptane), $[\alpha]_D +45°$ (*c* 0·58). appeared first in the eluate. PMR spectrum: 0·824 d + 0·900 d, $J = 6·5$ Hz (CH(CH$_3$)$_2$); 0·86 (4β-CH$_3$, 10β-CH$_3$); 0·94 (4α-CH$_3$, 14α-CH$_3$, 8β-CH$_3$); 5·25 m, W 1/2 = 9 Hz (C$_{(16)}$—H) p.p.m. Second 28-nor-17(22)-lupene (*IV*) (400 mg) was eluted, m.p. 165—167°C (n-heptane), $[\alpha]_D -18·2°$ (*c* 0·63). PMR spectrum: 0·77 dd + 0·845 d, $J_{gem} = 6·5$ Hz, $J_{1.r.} = 1$ Hz (CH(CH$_3$)$_2$); 0·804 (4β-CH$_3$); 0·845 (4α-CH$_3$); 0·851 (10β-CH$_3$); 0·941 (14α-CH$_3$); 1·013 (8β-CH$_3$); 5·1 m W 1/2 = = 5 Hz (C$_{(22)}$—H) p.p.m. For C$_{29}$H$_{48}$ (396·7) calculated: 87·80% C, 12·20% H; found: 87·94% C, 12·09% H.

28-Nor-17α-lupan-22α-ol (*VII*)

A solution of olefin *IV* (220 mg) in 40 ml of tetrahydrofuran was saturated with diborane at room temperature for 30 minutes. After three hours' standing at room temperature the mixture was evaporated to dryness and dissolved in 25 ml of tetrahydrofuran. Potassium hydroxide (1·5 g) dissolved in 5 ml of ethanol was added, followed by dropwise addition of 5 ml of 30% hydrogen peroxide, and the mixture stirred for one hour. After evaporation to dryness it was worked up as described above. Chromatography on alumina (15 g) with benzene–ether (9 : 1) gave 110 mg of alcohol *VII*, m.p. 140—150°C (benzene–ethanol), $[\alpha]_D +40°$ (*c* 0·68). IR spectrum: 1064 1083, 3458, 3605 (—OH) cm^{-1}. PMR spectrum: 0·795 (4β-CH$_3$); 0·845 d + 0·835 d, $J = 6·5$ Hz (CH(CH$_3$)$_2$); 0·845 (4α-CH$_3$ 10β-CH$_3$); 0·905 (14α-CH$_3$); 0·945 (8β-CH$_3$); 7·34 s (OH); 4·03 bq, $J_{vic} = 8 + 8$ Hz (C$_{(22\beta)}$—H) p.p.m.

28-Nor-17α-lupan-22-one (*VIII*)

To a solution of 45 mg of alcohol *VII* in 25 ml of dimethylformamide solid chromium trioxide (50 mg) and a drop of concentrated sulfuric acid were added and the mixture allowed to stand at room temperature for 24 hours. It was then precipitated with 20 ml of water and extracted with ether. The extract was worked up as described above. The obtained ketone *VIII* (40 mg) had m.p. 208—209°C (chloroform–n-heptane), $[\alpha]_D + 125°$ (*c* 0·352). IR spectrum: 1405(α-CH$_2$), 1725 (C=O) cm^{-1}. PMR spectrum: 0·79 (4β-CH$_3$), 0·849 (4α-CH$_3$, 10β-CH$_3$, 8β-CH$_3$), 0·92 (14α-CH$_3$), 0·90 d + 0·93 d, $J = 6$Hz (CH(CH$_3$)$_2$) p.p.m. Circular dichroism: (dioxan, *c* 0·09) λ_{max} (Δε) 297 nm (2·13), 306·5 nm (2·13), 318 nm (1·13). For C$_{29}$H$_{48}$O (412·6) calculated: 84·40% C, 11·72% H; found: 85·14% C, 11·55% H.

28-Nor-17α-lupan-16α-ol (*X*) and 28-Nor-17β-lupan-16β-ol (*XII*)

A solution of olefin *VI* (160 mg) in 30 ml of tetrahydrofuran was saturated with diborane for 30 minutes and worked up as in the case of the hydroboration of olefin *IV*. The crude product was chromatographed on alumina (16 g). Elution with benzene–ether (19 : 1) afforded 60 mg of alcohol *X*, m.p. 177°C, $[\alpha]_D +7°$ (*c* 0·67). IR spectrum: 3520 (OH) cm^{-1}. PMR spectrum: 0·79 (4β-CH$_3$); 0·828 (10β-CH$_3$); 0·83 d + 0·87 d, $J = 6·5$ Hz (CH(CH$_3$)$_2$); 0·85 (4α-CH$_3$); 0·94 (8β-CH$_3$); 1·085 (14α-CH$_3$); 3·725 m, $J_1 = J_2 = 5·6$ Hz, $J_3 = 7·6$ Hz (16β-H) p.p.m. For C$_{29}$H$_{50}$O (414·7) calculated: 83·99% C, 12·15% H; found: 83·72% C, 12·31% H. Further elution gave 20 mg of 28-nor-17β-lupan-16β-ol (*XII*), m.p. 210—212°C (chloroform–ethanol), $[\alpha]_D +10°$ (*c* 0·53). PMR spectrum: 0·80 (4β-CH$_3$); 0·835 d, $J = 6·5$ Hz (CH(CH$_3$)$_2$); 0·85 (4α-CH$_3$, 10β-CH$_3$); 0·92 (14α-CH$_3$); 0·975 (8β-CH$_3$); 4·08 m, $J_1 = J_2 = 6·5$ Hz, $J_3 = 10$ Hz (16α-H) p.p.m.

28-Nor-17α-lupan-16-one (*XI*)

To a solution of alcohol *X* (45 mg) in 25 ml of dimethylformamide chromium oxide (50 mg) and 1 drop of concentrated sulfuric acid were added and the mixture was treated and worked up as in the case of the oxidation of alcohol *VII*. The obtained ketone *XI* (30 mg) had m.p. 206—208°C (benzene–n-heptane), $[\alpha]_D -40°$ (*c* 0·18). IR spectrum: 1414 (α-CH$_2$), 1692 (C=O) cm^{-1}. PMR spectrum: 0·80 (4β-CH$_3$); 0·82 d + 0·86 d, $J = 6·5$ Hz (CH(CH$_3$)$_2$); 0·86 (4α-CH$_3$, 10β-CH$_3$); 0·89 (14α-CH$_3$); 1·025 (8β-CH$_3$); 2·3—2·6 m (C$_{(17)}$—H) p.p.m. CD (dioxan, *c* 0·02): λ_{max} ($\Delta\varepsilon$) 294 nm (−7·01).

Lupan-28→13β-olide (*XIV*)

To a solution of 13β,28-epoxylupane (*XIII*) (300 mg) in acetic acid (30 ml) chromium oxide (420 mg) dissolved in acetic acid (20 ml) was added dropwise under stirring and the mixture heated at 50°C for one hour. After addition of 20 ml of methanol the mixture was evaporated to dryness and worked up as above. Chromatography on alumina (20 g) with benzene gave 100 mg of lactone *XVI*, m.p. 245—247°C (benzene–ethanol), $[\alpha]_D -10°$ (*c* 0·67). IR spectrum: 1765 (γ-lactone) cm^{-1}. PMR spectrum: 0·805 (4β-CH$_3$); 0·82 d + 0·86 d, $J = 6·5$ Hz (CH(CH$_3$)$_2$); 0·86 (4α-CH$_3$); 0·88 (10β-CH$_3$); 1·155 (14α-CH$_3$); 1·18 (8β-CH$_3$) p.p.m. For C$_{30}$H$_{48}$O$_2$ (440·7) calculated: 81·76 C, 10·98% H; found: 81.79% C, 11·21% H.

Photo-oxidation of 3β-Acetoxy-28-lupanol (*II*)

a) Photo-oxidation of acetate *II* (2 g) was first carried out in the same manner as the photo-oxidation of alcohol *I*. After the usual work-up the reaction mixture was separated on alumina (120 g). Cyclohexane eluted a mixture of isomeric 28-nor derivatives similar to *IV* and *VI*, which, however, could not be separated. In subsequent fractions 3β-acetoxy-13β,28-epoxylupane (*XVI*) (300 mg) was eluted, m.p. 198—200°C (benzene–ethanol), $[\alpha]_D +20°$ (*c* 0·63). IR spectrum: 1025, 1265, 1730 (CH$_3$COO), 1025 (C—O—C) cm^{-1}. PMR spectrum: 0·844 (4α-CH$_3$); 0·844 (4β-CH$_3$); 0·845 t, $J = 6·5$ Hz (CH(CH$_3$)$_2$); 0·90 (10β-CH$_3$); 1·002 (14α-CH$_3$); 1·239 (8β-CH$_3$); 2·03 (3β-CH$_3$COO); 3·47 bd +3·62 d, $J_{gem} = 7·5$ Hz (C$_{(28)}$H$_2$); 4·49 m (3α-H) p.p.m. For C$_{32}$H$_{52}$O$_3$ (484·7) calculated: 79·28% C, 10·81% H; found: 79·10% C, 10·92% H.

Hydrolysis of acetate *XVI* (120 mg) with 5% potassium hydroxide solution in benzene–ethanol (1 : 1) under reflux for 2 hours and a conventional work-up gave 100 mg of 3β-hydroxy-13β,28-epoxylupane (*XV*), m.p. 206—208°C (n-heptane), $[\alpha]_D +9°$ (*c* 0·655). IR spectrum: 1025 (C—O——C), 3485, 3625 (OH) cm^{-1} PMR spectrum: 0·768 (4β-CH$_3$); 0·834 t, $J = 6—6·5$ Hz (CH(CH$_3$)$_2$);

0·878 (10β-CH_3); 0·975 (4α-CH_3); 1·010 (14α-CH_3); 1·239 (8β-CH_3); 3·2 m (3α-H); 3·47 bd +3·63 d, J_{gem} = 7·5 Hz ($C_{(28)}H_2$) p.p.m. For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·54% C, 11·14% H.

Oxidation of hydroxy derivative *XV* by a method described in the preparation of ketones *VIII* or *XI* gave ketone *XVII* of m.p. 193—196°C (chloroform—methanol), $[\alpha]_D$ +32° (*c* 0·20). IR spectrum: 1027 (C—O—C), 1705 (C=O) cm^{-1}. PMR spectrum: 0·81 d + 0·88 d, J = 6·5 Hz (CH(CH$_3$)$_2$); 1·00 (4α-CH_3); 1·04 (4β-CH_3, 10β-CH_3); 1·09 (14α-CH_3); 1·30 (8β-CH_3); 3·475 d +3·65 d, J_{gem} = 8 Hz ($C_{(28)}H_2$) p.p.m.

b) In a quartz flask 1 g of acetoxy derivative *II* was dissolved in 100 ml of benzene, 620 mg of pyridine were added and 2·7 g of lead tetraacetate suspended and the mixture was stirred at room temperature and under irradiation with a TESLA THK 101 UV lamp[6] for 2 hours. After filtration and working up in the conventional manner the product was chromatographed on 60 g of alumina with light petroleum. First an inseparable mixture of 28-nor derivatives (250 mg) was eluted, epoxide *XVI* (150 mg) and 3β,17β(?)-diacetoxy-28-nor-lupane (*III*) (100 mg) of m.p. 215—217°C (benzene—ethanol), $[\alpha]_D$ +27° (*c* 0·315). IR spectrum: 1030, 1259, 1723 (CH$_3$COO) cm^{-1}. PMR spectrum: 0·845 m (4α-CH_3, 4β-CH_3, 10β-CH_3, CH(CH$_3$)$_2$); 0·933 (14α-CH_3); 1,026 (8β-CH_3); 1·92 s (17β-CH$_3$COO); 2·03 s (3β-CH$_3$COO); 4·49 m (3α-H) p.p.m.

c) *Hypoiodite reaction*[7]: In a solution of 690 mg of acetoxy derivative *II* in 300 ml of cyclohexane 2·9 g of lead tetraacetate were suspended and the mixture refluxed and irradiated with a 500 W lamp. Iodine (500 mg) was then added gradually over 20 minutes. After decoloration of the reaction mixture (45 min) 1·5 g of calcium carbonate were added and the mixture irradiated under heating and stirring for 15 hours. The mixture was filtered, evaporated to dryness and worked up as above. Chromatography on silica gel (50 g) gave 190 mg of 3β-acetoxy-28-nor-17(22)-lupene (*V*), m.p. 167—169°C (chloroform—methanol), $[\alpha]_D$ +4° (*c* 0·57). PMR spectrum: 0·83 d + 0·905 d, J = 6·5 Hz (CH(CH$_3$)$_2$); 0·86 (4α-CH_3, 4β-CH_3, 10β-CH_3); 0·94 (14α-CH_3); 1·005 (8β-CH_3); 2·03 (3β-CH$_3$COO); 4·48 m $C_{(3\alpha)}$—H); 5·1 bs, W 1/2 = 6 Hz ($C_{(22)}$—H) p.p.m. For $C_{31}H_{50}C_2$ (454·7) calculated: 81·88% C, 11·08% H; found: 81·85% C, 11·25% H.

12-Lupen-28-ol (*XIX*)

A mixture of 25 ml of acetic anhydride, 100 mg of ether *XIII* and 30 mg of *p*-toluenesulfonic acid was heated at 100°C for 2 hours, evaporated to dryness and worked up as above. Acetate *XXI* (80 mg) was obtained, m.p. 118—119°C (light petroleum), $[\alpha]_D$ −4° (*c* 0·56). PMR spectrum: 0·74 d + 0·86 d, J = 6·7 Hz (CH(CH$_3$)$_2$); 0·813 (4β-CH_3); 0·861 (4α-CH_3); 0·951 (10β-CH_3); 1·009 (8β-CH_3); 1·14 (14α-CH_3); 2·00 (28-CH$_3$COO); 3·72 d + 3·92 dd, J_{gem} = 11 Hz, $J_{1.r.}$ = = 1·5 Hz ($C_{(28)}H_2$); 5·10 bt ($C_{(12)}$—H) p.p.m. Acetate *XXI* (50 mg) was converted to unsaturated alcohol *XIX* (40 mg) by base catalysed hydrolysis, m.p. 168—170°C (ether—ethanol), $[\alpha]_D$ −6° (0·62). IR spectrum: 3580 (OH) cm^{-1}. PMR spectrum: 0·75 d + 0·88 d, J = 6·6 Hz (CH(CH$_3$)$_2$); 0·828 (4β-CH_3); 0·877 (4α-CH_3); 0·971 (10β-CH_3); 1·025 (8β-CH_3); 1·164 (14α-CH_3); 3·19 d + + 3·50 d, J_{gem} = 11 Hz, $J_{1.r.}$ = 1·5 Hz ($C_{(28)}H_2$); 5·13 m ($C_{(12)}$—H) p.p.m. For $C_{30}H_{50}O$ (426·7) calculated: 84·44% C, 11·81% H; found: 84·52% C, 11·73% H.

3β,28-Diacetoxy-12-lupene (*XX*)

Ether *XVI* (300 mg) was acetolysed analogously as ether *XIII*. The reaction gave 220 mg of diacetate *XX*, m.p. 203—206°C (benzene—ethanol), $[\alpha]_D$ −3° (*c* 0·655). IR spectrum: 1033, 1261, 1731 (CH$_3$COO) cm^{-1}. PMR spectrum: 0·755 d + 0·874 d, J = 6·6 Hz (CH(CH$_3$)$_2$) 0·871 (4α-CH_3, 4β-CH_3); 0·989 (10β-CH_3); 1·018 (8β-CH_3); 1·132 (14α-CH_3); 2·03 (3β-CH$_3$COO),

2·03 (28-CH$_3$COO); 3·73 d + 3·94 bd, $J_{gem} = 11·5$ Hz (C$_{(28)}$H$_2$) 4·52 m (C$_{(3\alpha)}$—H); 5·14 bt, $J_1 = J_2 = 8$ Hz (C$_{(12)}$—H) p.p.m. For C$_{34}$H$_{54}$O$_4$ (526·8) calculated: 77·52% C, 10·32% H; found: 77·73% C, 10·46% H.

28-Hydroxy-12-lupanone (*XXII*)

To a solution of acetate *XXI* (230 mg) in acetic acid (20 ml) 30% hydrogen peroxide (2·5 ml) was added dropwise and the mixture stirred at 100°C for one hour. After evaporation and working up in the usual manner the oily residue (200 mg) was hydrolysed with 5% potassium hydroxide in benzene–ethanol (1 : 1) under reflux for 2 hours. After the working up as above 180 mg of crude product were obtained. Chromatography on alumina (5 g) with benzene gave 100 mg of keto alcohol *XXII*, m.p. 271—272°C (benzene–ethanol), $[\alpha]_D -9°$ (*c* 0·443). IR spectrum: 1028, 1710 (C≕O), 3480, 3635 (OH) cm^{-1}. PMR spectrum: 0·783 d + 0·924 d, $J = 7$ Hz (CH(CH$_3$)$_2$); 0·820 (4β-CH$_3$); 0·855 (4α-CH$_3$, 10β-CH$_3$); 0·911 (14α-CH$_3$); 1·290 (8β-CH$_3$); 3·36 d + 3·72 d, $J_{gem} = 11$ Hz (C$_{(28)}$H$_2$) p.p.m. Circular dichroism (dioxan, *c* 0·07): λ_{max} ($\Delta\varepsilon$) 296 nm (−1·61).

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