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STEREOCHEMISTRY OF DEHYDRATION OF ISOMERIC 20-HYDROXY-30-NORDERIVATIVES OF LUPANE

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On reaction of (20*R*)-3β,28-diacetoxy-30-norlupan-20-ol (*II*) with phosphorus oxychloride or tosyl chloride in pyridine olefin *IV* is formed predominantly in addition to a small amount of chloro derivative *VII*. The (20*S*)-isomer *III* gives under the same conditions predominantly chloro derivative *XVIII* and olefins *VI* and *XIX*. The steric course of these reactions is discussed and on its basis the assignment of the configurations to alcohols *II* and *III* is confirmed. The structure of olefin *IV* was deduced from its isomeration to olefin *V*, transformation to the unsaturated ketone *XIV*, diene *X*, and 20-acetoxy-19β,28-epoxy derivative *XIII*; by this the configuration of 20-hydroxy-30-norderivatives in the lupane series and 19β,28-epoxylupane series was also correlated.

In the preceding paper[1] we demonstrated that on oxidation of betulin diacetate (*I*) with performic acid and subsequent partial hydrolysis of the 20-formyloxy derivatives formed it is possible to prepare both 20-hydroxy-30-norderivatives *II* and *III*, isomeric in their side chain. The configuration of these alcohols at $C_{(20)}$ was determined[2] by comparison of the physical data of a series of 30-norlupane derivatives; to the less polar isomer *II* (m.p. 230°C, *XXa* in ref.[1]) the 20*R* configuration was assigned, while to the more polar isomer *III* (m.p. 260°C, *XXb* in ref.[1]) the configuration 20*S* was assigned. In this paper the configuration at $C_{(20)}$ is confirmed independently on the basis of the different course of the reactions of 20-hydroxy derivatives *II* and *III* with phosphorus oxychloride or tosyl chloride in pyridine.

When the (20*R*)-isomer *II* was submitted to the reaction with phosphorus oxychloride in boiling pyridine olefin *IV* was obtained as the main product. According to thin-layer chromatography the mother liquors contained traces of additional olefins *V* and *VI*, further a chloro derivative which, however, could not be chromatographically separated from the olefin *IV*. Therefore the mother liquors were epoxidated with perbenzoic acid, and from the mixture obtained chloro derivative *VII* and epoxides *VIII* and *IX* were isolated chromatographically. When the dehydration was carried out with phosphorus oxychloride at −5°C the presence of olefins *V* and *VI*

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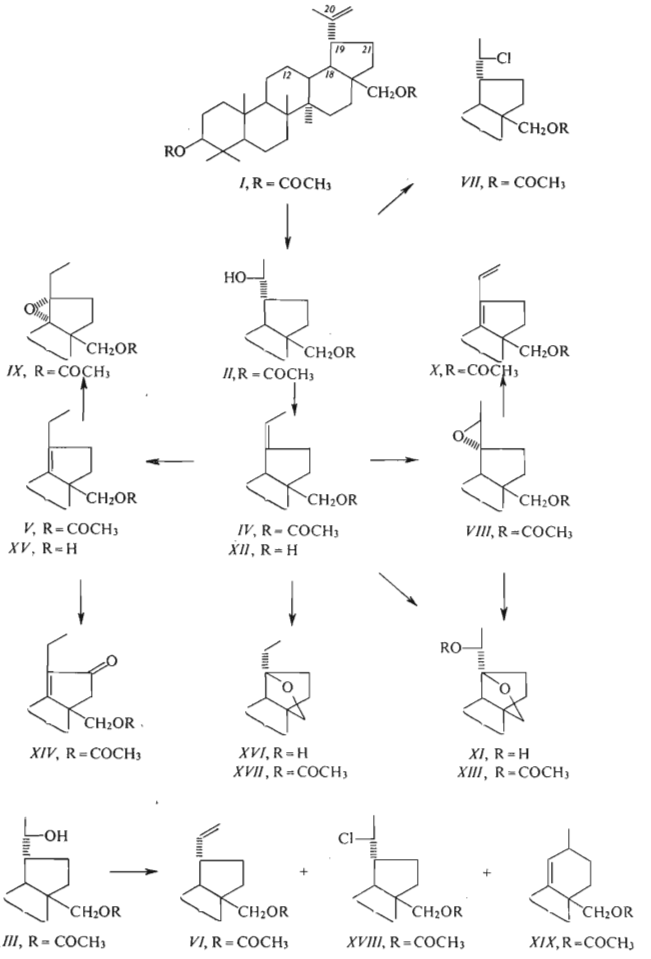
could not be determined. On reaction of hydroxy derivative *II* with tosyl chloride in boiling pyridine or at 20°C olefin *IV* was obtained again, containing traces of olefins *V* and *VI* and chloro derivative *VII*.

The structure of olefins *IV* and *V* follows from the following series of reactions and from the PMR spectra. The spectrum of olefin *IV* contains a signal of an olefinic hydrogen apparent as a broad unresolved quadruplet. The doublet of the methyl group on the double bond could be identified only when using double resonance, because it is unusually broad and overlapped by the methylene group signals. An unequivocal confirmation of the structure *IV* followed from the spectra of epoxide *VIII* where the signals of the methyl group (doublet 1·23 p.p.m., $J = 5$ Hz) and the methine hydrogen (quadruplet 3·07 p.p.m.) are clearly resolved. Epoxide *VIII* afforded diene *X* under the effect of boron trifluoride etherate; according to UV spectra this diene is conjugated. In the PMR spectrum signals of three olefinic hydrogens forming an isolated ABX system are present; the coupling constants obtained by a complete analysis of this system according to[3] ($J_{gem} = 2$ Hz, $J_{trans} = 17$ Hz, $J_{cis} = 11$ Hz) correspond according to an analogous case[4] to the presence of a vinyl group. Diene *X* was also prepared[2] by an independent route from the dehydrogenation products of betulinic acid with mercuric acetate. In alkaline medium diol *XI* was formed from epoxide *VIII*; the same diol was also obtained under the effect of perbenzoic acid on the unsaturated diol *XII* which was prepared by alkaline hydrolysis of diacetate *IV*. The diacetate *XIII* prepared on acetylation of diol *XI* was not identical with the starting diacetyl epoxide *VIII*. Its PMR spectrum contains in addition to the signals corresponding to the CH_3CH—O group also an AB system with a long range coupling (doublet 3·315 p.p.m. and a doublet of doublets 3·95 p.p.m., $J_{gem} = 7$ Hz, $J_{l.r.} = 2{\cdot}5$ Hz) characteristic of the $—C_{(28)}H_2—O—$ group in 19β,28-epoxy derivatives of lupane[4]. It was further established that diacetate *XIII* is identical with the diacetate prepared earlier from the products of dehydrogenation of betulin with mercuric acetate, for which the presence of a 19β,28-epoxy group was proved[4]. From this it follows that both in alkaline hydrolysis of epoxy diacetate *VIII* and in direct epoxidation of the free diol *XII* opening of the epoxide ring takes place under participation of the oxygen function in the position 28 from the β-side, similarly as in analogous epoxides of the taraxastane series[5]. The configuration of the epoxide group at $C_{(19)}$ in epoxide *VIII* must therefore be α, as may also be expected on the basis of an easier attack of the peracid from the sterically less hindered α-side.

The olefin *IV* is not stable and it isomerises easily on heating or under the effect of formic acid to the stable derivative *V* which according to its PMR spectrum does not contain an olefinic hydrogen; the presence of an ethyl group is indicated by a signal of one of the methyls, which forms a triplet. For a further confirmation of the structure olefin *V* was oxidized with chromium trioxide in acetic acid; two products were thus obtained, of which one was identical with epoxide *IX* prepared on reaction of olefin *V* with perbenzoic acid. The second product was the α,β-un-

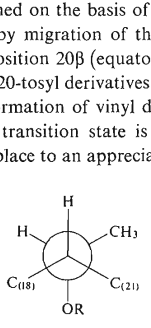

20
19
21
12
18
CH2OR
RO
I, R = COCH3
Cl
CH2OR
VII, R = COCH3
HO
CH2OR
II, R = COCH3
O
CH2OR
IX, R = COCH3
CH2OR
X, R = COCH3
CH2OR
V, R = COCH3
XV, R = H
CH2OR
IV, R = COCH3
XII, R = H
O
CH2OR
VIII, R = COCH3
O
CH2OR
XIV, R = COCH3
O
CH2OR
XVI, R = H
XVII, R = COCH3
RO
O
XI, R = H
XIII, R = COCH3
OH
CH2OR
III, R = COCH3
CH2OR
VI, R = COCH3
Cl
CH2OR
XVIII, R = COCH3
CH2OR
XIX, R = COCH3

saturated ketone *XIV* ($\lambda_{max}^{cyclohexane}$ 235 nm), five-membered according to IR analysis (1705 cm^{-1}), with a methylene group in the α-position (1413 cm^{-1}). From the PMR spectrum the presence of an ethyl group on a double bond is clearly evident (triplet 0·975 p.p.m., quadruplet 2·35 p.p.m., J = 7 Hz), as well as one of the hydrogens in the α-position to the carbonyl group, which shows only a geminal coupling (doublet 2·47 p.p.m., J_{gem} = 18 Hz), and a hydrogen in allylic position (13βH; doublet of doublets 2·86 p.p.m., J_1 = 4 Hz, J_2 = 12 Hz); hence structure *XIV* must be assigned to this ketone. The same course of oxidation with chromium trioxide was also observed in other 18-lupene derivatives[6,7]. Isomerisation of diol *XII* with formic acid and subsequent alkaline hydrolysis of the formates formed gave a mixture of two products. One of them was identified as diol *XV*, because it gave diacetate *V* on acetylation, the second is formulated as *XVI* because it gives monoacetate *XVII* which according to IR spectra contains an ether oxygen in a cycle (C—O—C: 1014 cm^{-1}).

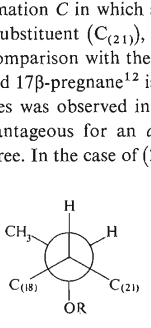
In contrast to (20*R*)-hydroxy derivative *II*, when (20*S*)-isomer *III* was reacted with phosphorus oxychloride in boiling pyridine a mixture of products was obtained in which chloro derivative *XVIII* and a mixture of olefins were present in a 1 : 1 ratio. From the olefinic fraction derivative *VI* was obtained by chromatography on silica gel with silver nitrate as the main component (25% of the original mixture of products); the residue is composed of a chromatographically unresolvable mixture from which another olefin, *XIX* (4%), was isolated by crystallisation. The same mixture of products was also formed from hydroxy derivative *III* under the effect of tosyl chloride in pyridine at 20°C and at boiling temperature. On reaction with phosphorus oxychloride at −5°C a mixture of chloro derivative *XVIII* and olefin *VI* was obtained; the presence of further olefins could not be proved. Chloro derivative *XVIII* is not an intermediate in the formation of olefins, because under the effect of boiling pyridine or a mixture of pyridine and phosphorus oxychloride it remains unchanged. The structure of olefin *VI* is based on the proof of a vinyl group by means of IR and PMR spectra. In comparison with diene *X* the three olefinic protons form a more complex system in which in addition to a coupling between the olefinic hydrogens (J_{gem} = 2 Hz, J_{trans} = 17 Hz, J_{cis} = 9·8 Hz) a coupling of the hydrogen at $C_{(20)}$ with the neighbouring 19β-hydrogen (J_{vic} = 8 Hz) is also evident. For the further isolated olefin we propose structure *XIX*, because its PMR spectrum contains a doublet of the methyl group and a singlet of the olefinic hydrogen (5·13 p.p.m., $W_{1/2}$ 5 Hz). The low value of the coupling constant (between the olefinic hydrogen and the adjacent methine hydrogen), manifested by a mere broadening of the signal of the olefinic hydrogen (determined by double resonance), shows that the methine hydrogen is pseudoaxial and hence, the configuration of the methyl group at $C_{(20)}$ must be β. Both chloro derivatives *VII* and *XVIII* contain a $CH_3-CHCl-$ group according to PMR spectra, showing that they have an unrearranged skeleton and that they are epimeric at $C_{(20)}$. In view of the fact that on substitution of the —$OPOCl_2$

and —OTos groups by chloride anion under the above mentioned conditions a Walden rearrangement may be expected[8-10], we propose configuration 20*S* for the isomer *VII* and configuration 20*R* for the isomer *XVIII*. This assignment is supported by the comparison of the PMR spectra with other derivatives of 30-norlupane, isomeric at $C_{(20)}$ (ref.[2]).

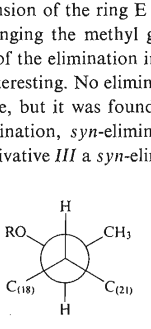
The results of the elimination reactions corroborate the correctness of the assignment[2] of the configurations of alcohols *II* and *III*. It is known[8,11,12] that on dehydration with the mentioned reagents a transition state is favoured in which the departing group and hydrogen are in *anti*-periplanar conformation; elimination takes place under formation of the more substituted olefin if other sterical requirements are fulfilled. In (20*R*)-hydroxy derivative *II* the transition state for *anti*-elimination (see conformation A), is more favoured, as there is not interaction between the bulky group on $C_{(20)}$ and the methylene group in position 12. Therefore olefin *IV* with methyl group *trans* to $C_{(18)}$ is formed as the main product. On the basis of the same conformation the formation of derivative *V* from hydroxy derivative *II* may also be explained, *i.e.* by migration of the 19β-hydrogen on $C_{(20)}$ and elimination of the proton in *anti*-periplanar position (18αH). However in view of the easy isomerisation of derivative *IV* to *V* it cannot be excluded that the formation of a small amount of olefin *V* is a subsequent process, *i.e.* occurring during the working up of the reaction mixture. In the case of the (20*S*)-isomer *III* the transition state for an *anti*-elimination (conformation *B*) is infavourable due to the interaction of the methyl group with the methylene group in position 12 causing the olefin with the exocyclic double bond not to be formed. Substitution is prefeued instead (chloro derivative *XVIII*); further elimination of the proton from the methyl group (vinyl derivative *VI*) and rearrangement (*XIX*) take place. The formation of derivative *XIX* may be explained on the basis of conformation *C* in which an expansion of the ring E takes place by migration of the *anti*-substituent ($C_{(21)}$), thus bringing the methyl group into position 20β (equatorial). Comparison with the results of the elimination in isomeric 20-tosyl derivatives 17α- and 17β-pregnane[12] is also interesting. No elimination and formation of vinyl derivatives was observed in this case, but it was found that if the transition state is disadvantageous for an *anti*-elimination, *syn*-elimination takes place to an appreciable degree. In the case of (20*S*)-derivative *III* a *syn*-elimina-



A



B



C

R = —$POCl_2$ or Tos

tion would lead to olefin *IV*, which, however, was not found in the mixture of products. Another difference consists in the fact that in the case of steroids both *trans* and *cis*-olefins[12] are formed, while in the case of 30-norlupane derivatives the isomer with the methyl group in *cis* position with respect to $C_{(18)}$ was not obtained. The decisive factor here is evidently the interaction of the *cis*-substituent with the 12-methylene group. In the case of dehydration of 20-hydroxylupane derivatives an isopropenyl derivative is also formed exclusively, but not the derivative with an exocyclic double bond[13–15], while in analogous 22-hydroxy derivatives of the hopane series[16–20] and in 4-hydroxy-A-neo-triterpenes[21,22] the formation of an exocyclic olefin is commonly observed. Similarly, in the case of 20-oxo-30-nor derivatives of lupane no enol derivatives with a double bond in the position 19(20) could be obtained[23]. The only presently known example of the formation of a 19-ene with a *cis*-substituent is the preparation of 20,20-diphenyl-29,30-dinor-19-lupene[24–26].

Finally, it should be stated that the sequence of the stereospecific reactions *II* → *IV* → *VII* → *XI* → *XIII* represents a correlation of $C_{(20)}$-isomeric 20-hydroxy-30-norderivatives between the 3β,28-diacetoxylupane and 3β-acetoxy-19β,28-epoxylupane series[4]; hence, configuration 20*R* must correspond to derivative *XIII*, which is in agreement with the results of spectral measurements[2].

EXPERIMENTAL

The melting points were determined on a Kofler block. Optical rotations were measured in chloroform solution on an ETL-NPL polarimeter (Bendix Ericsson), with a ±1—2° error. The infrared spectra were measured in chloroform on a model apparatus of the Institute for Apparatus Technique, Czechoslovak Academy of Sciences, Brno; the ultraviolet spectra were measured in cyclohexane on a Unicam SP-700 spectrophotometer. The PMR spectra were measured in deuteriochloroform on a Varian HA-100 spectrometer, using tetramethylsilane as internal standard; the chemical shifts are given in p.p.m. For column chromatography neutral alumina (Reanal, act. II) and neutral silica gel (Spolana) was used, for thin-layer chromatography silica gel according to Stahl as well as the same silica gel with 4% silver nitrate were employed. If a melting point under decomposition is mentioned in the text the decomposition was confirmed by thin-layer chromatography of the melt. Samples for analysis were dried over phosphorus pentoxide at 100°C and 1—2 Torr pressure, for 8—12 h.

Dehydration of (20*R*)-3β,28-Diacetoxy-30-nor-20-lupanol (*II*)

a) To a boiling solution of hydroxy derivative *II* (1·0 g, see[1]) in pyridine (30 ml) a solution of phosphorus oxychloride (10 ml) in pyridine (30 ml) was added dropwise over 10 minutes. The mixture was allowed to cool down to 20°C over 20 min and then decomposed with ice and extracted with ether. The ethereal solution was washed with water, dilute hydrochloric acid, and a sodium carbonate solution and dried over sodium sulfate. After distillation off of ether the crude product (0·85 g) was obtained, $[\alpha]_D$ +39° (*c* 0·8) which according to thin-layer chromatography on silver nitrate impregnated silica gel contained in addition to olefin *IV* also traces of olefins *V* and *VI* and gave a positive Beilstein test for halogen. Crystallisation from n-heptane gave 3β,28-diacetoxy-30-nor-19-lupene (*IV*, 0·55 g), m.p. 204—207°C, $[\alpha]_D$ +45° (*c* 0·7). IR spectrum: 1729, 1255 cm^{-1} (CH_3COO). PMR spectrum: 0·845 ($2 \times CH_3$), 0·875; 0·98 and 1·04 ($3 \times CH_3$), 1·52 bd, J = 6 Hz (20-CH_3), 2·02 ($2 \times CH_3COO$), 3·54 d and 4·14 bd, J = 11·5 Hz (28-H_2), 4·48 m (3α-H), 5·35 bq (20-H). For $C_{33}H_{52}O_4$ (512·7) calculated: 77·29% C, 10·22% H; found: 77·06% C, 10·35% H. The mother liquors after crystallisation of the olefin *IV* were epoxid-

ated with perbenzoic acid (0·25 g) in chloroform (9 ml) at 0°C for 15 h. The solution was filtered through a column of alumina on the top of which a layer of moist sodium hydrogen carbonate was placed. After evaporation of chloroform the residue was chromatographed on alumina. Elution with a light petroleum–ether mixture 7 : 1 and crystallisation from a mixture of chloroform and light petroleum gave (20*S*)-3β,28-diacetoxy-20-chloro-30-norlupane (*VII*, 40 mg), m.p. 263—265°C, $[\alpha]_D$ −4° (*c* 2·1). IR spectrum: 1735, 1259 cm^{-1} (CH_3COO). PMR spectrum: 0·845 (2 × CH_3), 0·865, 0·925, and 1·045 (3 × CH_3), 1·405 d, J = 6·5 Hz (20-CH_3), 2·03 and 2·05 (2 × CH_3COO), 3·78 d and 4·28 bd, J = 11 Hz (28-H_2), 4·35—4·55 m (3α-H and 20-H, overlapped). For $C_{33}H_{53}ClO_4$ (549·2) calculated: 72·16% C, 9·70% H; found: 72·23% C, 9·55% H. With a light petroleum–ether mixture 5 : 1 epoxide *IX* was eluted (30 mg), m.p. 245—247°C (chloroform–n-heptane), $[\alpha]_D$ +23° (*c* 0·55), identical with the preparation described below. On further elution with the same mixture only the epoxide *VIII* was obtained. If the reaction was carried out with phosphorus oxychloride (2 ml) in pyridine (17 ml) at −5°C for 2·5 h, hydroxy derivative *II* (250 mg) afforded 90 mg of crude *IV*, $[\alpha]_D$ +40°, which according to thin-layer chromatography did not contain olefins *V* and *VI*. Crystallisation from light petroleum gave olefin *IV* (80 mg), m.p. 203—207°C, $[\alpha]_D$ +44° (*c* 0·6).

b) A solution of hydroxy derivative *II* (0·6 g) and tosyl chloride (1·8 g) in pyridine (20 ml) was allowed to stand at room temperature for 30 days. After working up as under *a*) the mixture (0·59) was chromatographed on alumina. A mixture of light petroleum and ether (7 : 1) eluted olefin *IV* (0·51 g), accompanied by a small amount of olefins *V* and *VI* and chloro derivative *VII*. Crystallisation from heptane gave olefin *IV* (0·20 g), m.p. 203—207°C, $[\alpha]_D$ +47° (*c* 0·7), identical with the preparation described under *a*). From the mother liquors after epoxidation, using a working up as under *a*), chloro derivative *VII* (20 mg) was isolated, m.p. 262—265°C (n-heptane), $[\alpha]_D$ −4° (*c* 0·9), identical with the preparation described under *a*), as well as epoxy derivatives *VIII* and *IX*. Further elution with a mixture of light petroleum and ether 5 : 1 gave a non-crystalline product (60 mg) which according to IR spectra contained a tosyloxy group. IR spectrum: 1734, 1259 (CH_3COO), 1609, 1180, 1155, 1095 cm^{-1} (tosyloxy group). The same products, with the exception of the tosylate, were obtained on dehydration of hydroxy derivative *II* (0·48) with tosyl chloride (0·9 g) in pyridine (30 ml) by 5 h reflux.

Dehydration of (20*S*)-3β,28-Diacetoxy-30-nor-20-lupanol (*III*)

a) Reaction of alcohol *III* (0·41 g) with phosphorus oxychloride (4 ml) in boiling pyridine (26 ml) under the same conditions as in the case of alcohol *II* gave a mixture of products (0·37 g) which was chromatographically separated on alumina. Elution with light petroleum–ether mixture 7 : 1 gave a mixture of olefins (0·18 g). The same mixture further eluted (20*R*)-3β,28-diacetoxy-20-chloro-30-norlupane (*XVIII*, 0·17 g), m.p. 248—250°C (chloroform–methanol), $[\alpha]_D$ −20° (*c* 1·1). IR spectrum: 1729, 1258 cm^{-1} (CH_3COO). PMR spectrum: 0·85 (3 × CH_3), 0·98 and 1·04 (2 × CH_3), 1·43 d, J = 6 Hz (20-CH_3), 2·02 and 2·05 (2 × CH_3COO), 3·78 d and 4·23 bd, J = 11 Hz (28-H_2), 4·48 m (3α-H), 4·30—4·40 m (20-H, superimposed by other signals). For $C_{33}H_{53}ClO_4$ (549·2) calculated: 72·16% C, 9·70% H; found: 72·00% C, 9·56% H. The mixture of olefins was chromatographed on silica gel with silver nitrate using a mixture of light petroleum and ether (7 : 1) for elution. A chromatographically inseparable fraction (60 mg) was eluted which was crystallised repeatedly from chloroform–methanol and ether–light petroleum to afford 3β,28-diacetoxy-29-nor-18-oleanene (*XIX*, 15 mg), m.p. 245—250°C, $[\alpha]_D$ +12° (*c* 0·7). IR spectrum: 1730, 1260 cm^{-1} (CH_3COO). PMR spectrum: 0·835 (2 × CH_3), 0·77, 0·89 and 1·06 (3 × CH_3), 0·925 d, J = 7 Hz (20β-CH_3), 2·00 and 2·02 (2 × CH_3COO), 3·95 d and 4·19 d, J = 11 Hz (28-H_2), 4·43 m (3α-H), 5·13 bs, $W_{1/2}$ = 5 Hz (19-H). Double resonance: irradiation at 2·15 causes the doublet at 0·925 to collapse and also the sharpening of the singlet at 5·13 p.p.m.

For $C_{33}H_{52}O_4$ (512·7) calculated: 77·29% C, 10·22% H; found: 77·50% C, 10·39% H. Using the same solvent mixture 3β,28-diacetoxy-30-nor-20(29)-lupene (*VI*, 90 mg) was eluted, m.p. 187·5–190°C (chloroform–methanol), $[\alpha]_D$ +6° (*c* 1·5). IR spectrum: 1732, 1255 (CH_3COO), 3090, 1646, 1000, 913 cm^{-1} (CH_2=CH–). PMR spectrum: 0·84 (3 × CH_3), 0·945 and 1·03 (2 × CH_3), (2·02 and 2·05 (2 × CH_3COO), 3·82 d and 4·25 bd, J = 11 Hz (28-H_2), 4·47 m (3α-H), 4·87 dd (29′-H), 4·78 dd (29-H), 5·70 m (20-H), $J_{29,29'}$ = 2 Hz, $J_{20,29}$ = 9·8 Hz, $J_{20,29'}$ = 17 Hz, $J_{19,20}$ = 8 Hz. For $C_{33}H_{52}O_4$ (512·7) calculated: 77·29% C, 10·22% H; found: 77·55% C, 10·34% H. If the reaction of the hydroxy derivative *III* (0·27 g) with phosphorus oxychloride (2·5 ml) was carried out in pyridine (19 ml) at −5°C for 4 h a product (80 mg) was obtained, which according to thin-layer chromatography contained chloro derivative *XVIII* and olefin *VI*; the presence of olefin *XIX* could not be detected. On crystallisation from a mixture of chloroform and methanol chloro derivative *XVIII* was obtained (40 mg), m.p. 249–251°C, $[\alpha]_D$ −19° (*c* 0·21), identical according to its IR spectrum with the chloro derivative described above. Chloro derivative *XVIII* was recovered unchanged after 2 hours refluxing in pyridine or a mixture of pyridine and phosphorus oxychloride 5 : 1; according to thin-layer chromatography on silica gel with silver nitrate not a trace of olefin *VI* or *XIX* was formed.

b) A solution of alcohol *III* (0·24 g) and tosyl chloride (0·6 g) in pyridine (15 ml) was refluxed for 5 h and worked up as under *a*). From the crude product (0·23 g) chloro derivative *XVIII* (110 mg) was obtained by chromatography on alumina and silica gel with silver nitrate as under *a*). Its melting point was 247–249°C (chloroform–methanol), $[\alpha]_D$ −19° (*c* 0·76), the IR spectrum identical with those of the above described preparations. Further, olefin *VI* (40 mg) was obtained, m.p. 185–187°C (chloroform–n-heptane), $[\alpha]_D$ +5° (*c* 0·7), identical according to its IR spectrum with the above mentioned substance, as well as a mixture of olefins, which according to thin-layer chromatography on silica gel with silver nitrate contained derivative *XIX* as the main component. On reaction of alcohol *III* (0·12 g) with tosyl chloride (0·44 g) in pyridine (5 ml) at room temperature for 30 days and using the same isolation procedure as in the preceding case chloro derivative *XVIII* (60 mg), m.p. 246–249°C (chloroform–methanol), and olefin *VI* (15 mg), m.p. 184–187°C (chloroform–n-heptane) were obtained. Both were identical with authentic specimens according to their IR spectra. In the olefinic fraction derivative *XIX* was also present according to thin-layer chromatography, but it was not isolated. On chromatography on alumina a non-crystalline tosylate (20 mg) was eluted with light petroleum–ether mixture (1 : 1) which was not obtained in the preceding reaction; IR spectrum: 1736, 1264 (CH_3COO), 1610, 1192, 1179, 1155, 1100 cm^{-1} (tosyloxy group).

(20*R*)-3β,28-Diacetoxy-19α,20-epoxy-30-norlupane (*VIII*)

A solution of olefin *IV* (0·1 g) and perbenzoic acid (0·11 g) in chloroform (7 ml) was allowed to stand at 0°C for 15 h and it was then filtered through a small alumina column with a small layer of moist sodium hydrogen carbonate on top of it. Epoxide *VIII* (0·1 g) was obtained, m.p. 220–225°C (chloroform–methanol), $[\alpha]_D$ +20° (C 0·9). IR spectrum: 1730, 1254 cm^{-1} (CH_3COO). PMR spectrum: 0·84 (3 × CH_3), 0·97 and 1·015 (2 × CH_3), 1·23 d, J = 5 Hz (20-CH_3), 2·015 and 2·05 (2 × CH_3COO), 3·07 q, J = 5 Hz (20-H), 3·66 d and 4·24 bd, J = 11 Hz (28-H_2), 4·47 m (3α-H). For $C_{33}H_{52}O_5$ (528·9) calculated: 74·96% C, 9·91% H; found: 75·06% C, 9·96% H.

3β,28-Diacetoxy-30-nor-18,20(29)-lupadiene (*X*)

To a solution of epoxide *VIII* (0·13 g) in ether (15 ml) boron trifluoride etherate (1 ml) was added and the mixture allowed to stand for 22 h at room temperature. It was then washed with a 5% sodium hydrogen carbonate solution and water and the solution was dried over sodium sulfate.

The crude product was chromatographed on silica gel. On elution with a mixture of light petroleum and ether 10 : 1 diene *X* was obtained (80 mg), m.p. 198–210°C (under decomposition, chloroform–methanol or n-heptane), $[\alpha]_D$ +49° (*c* 0·55). UV spectrum: λ_{max} 240 nm, log ε 4·26, 247 nm, log ε 4·31, 256 nm, log ε 4·13. IR spectrum: 1733, 1260 (CH_3COO), 3110, 1635, 910 cm^{-1} (diene). PMR spectrum: 0·845 (2 × CH_3), 0·885, 0·905 and 1·09 (3 × CH_3), 2·03 and 2·04 (2 × CH_3COO), 4·07 (28-H_2), 4·50 m (3α-H), 5·04 (29′-H), 5·01 (29-H), 7·02 (20-H), $J_{20,29'}$ = = 17 Hz, $J_{20,29}$ = 11 Hz, $J_{29,29'}$ = 2 Hz. For $C_{33}H_{50}O_4$ (510·7) calculated: 77·60% C, 9·87% H; found: 77·47% C, 9·88% H.

3β,28-Dihydroxy-30-nor-19-lupene (*XII*)

A solution of olefin *IV* (0·15 g) and sodium hydroxide (0·30 g) in a mixture of benzene and ethanol 1 : 1 was refluxed for 1 h, then diluted with water and extracted with ether. The ethereal solution was washed with water and dried over sodium sulfate. Diol *XII* (0·11 g) was obtained, m.p. 199–204°C (under decomposition, benzene–ethanol), $[\alpha]_D$ +52° (*c* 0·69). IR spectrum: 3610, 3460 (O–H), 1024 (C–O–H) cm^{-1}. For $C_{29}H_{48}O_2$ (428·7) calculated: 81·25% C, 11·29% H; found: 81·36% C, 11·25% H. Acetylation with acetic anhydride and pyridine 1 : 1 at room temperature gave diacetate *IV*, m.p. 210–213°C (ether–light petroleum), $[\alpha]_D$ +42° (*c* 0·77), identical according to IR spectra with the starting olefin *IV*.

(20*R*)-3β,28-Diacetoxy-30-nor-19β,28-epoxylupane (*XIII*)

a) A solution of epoxide *VIII* (0·16 g) and sodium hydroxide (0·50 g) in a mixture of benzene and ethanol 1 : 1 (20 ml) was refluxed for 2 h. After dilution of the reaction mixture with water the product was extracted with ether and dried by filtration through an alumina layer. On crystallisation from a chloroform–n-heptane mixture diol *XI* (0·11 g) was obtained, m.p. 223–224°C. For $C_{29}H_{48}O_3$ (444·7). CH_3OH calculated: 75·58% C, 11·00% H; found: 75·73% C, 11·19% H. Acetylation with acetic anhydride and pyridine 1 : 1 at room temperature transformed diol *XI* to diacetate *XIII*, m.p. 281–282°C (chloroform–methanol), $[\alpha]_D$ +34° (*c* 0·69), according to IR spectrum, mixture melting point, and thin-layer chromatography data identical with the sample mentioned in paper[4]. PMR spectrum: 0·84 (2 × CH_3), 0·86, 0·91 and 1·00 (3 × CH_3), 1·235 d, *J* = 6 Hz (20-CH_3), 2·015 and 2·03 (2 × CH_3COO), 3·315 d and 3·95 d, with fine splitting, J_{gem} = = 7 Hz, $J_{1,r.}$ = 2·5 Hz (28-H_2), 4·48 m (3α-H), 5·04 q, *J* = 6 Hz (20-H).

b) A solution of diol *XII* (80 mg) and perbenzoic acid (85 mg) in chloroform (10 ml) was allowed to stand at 0°C for 17 h. After filtration through a small column of alumina with a layer of moist sodium hydrogen carbonate on top of it, evaporation and crystallisation from chloroform–methanol epoxy diol *XI* (40 mg) was obtained, m.p. 223–224°C. On acetylation as under *a*) diacetate *XIII* was obtained, m.p. 281–282°C, $[\alpha]_D$ +34° (*c* 0·8), identical according to IR spectra and mixture melting point with the preparation obtained under *a*).

Isomerization of Olefin *IV*

a) To a solution of olefin *IV* (0·46 g) in chloroform (20 ml) formic acid (20 ml) was added and the mixture allowed to stand at room temperature for 48 h. The mixture was diluted with water and extracted with ether, the extract was washed with a sodium hydrogen carbonate solution and water and dried by filtration through a layer of alumina. The crude product (0·44 g) was chromatographed on alumina. Benzene eluted 3β,28-diacetoxy-30-nor-18-lupene (*V*; 0·41 g), m.p. 210–213°C (chloroform–n-heptane), $[\alpha]_D$ +11° (*c* 0·7). IR spectrum: 1727, 1259 cm^{-1} (CH_3COO). PMR spectrum: 0·845 (2 × CH_3), 0·895 (2 × CH_3), 1·065 (CH_3), 0·965 t, *J* = 7·5 Hz

(20-CH_3), 2·035 (2 × CH_3COO), 4·01 (28-H_2), 4·50 m (3α-H). For $C_{33}H_{52}O_4$ (512·7) calculated: 77·29% C, 10·22% H; found: 76·98% C, 10·38% H.

b) Olefin *IV* was heated at 250—270°C for 1 h; the melt was dissolved in light petroleum and the solution filtered through a small column of alumina. Crystallisation of the residue from n-heptane gave olefin *V*, m.p. 209—212°C, $[\alpha]_D$ +13° (*c* 1·8), identical according to IR spectra with the preparation obtained under *a*).

Isomerization of Diol *XII* with Formic Acid

To a solution of diol *XII* (0·12 g) in chloroform (4 ml) 98% formic acid (4 ml) was added and the mixture allowed to stand at room temperature for 48 h. The reaction mixture was diluted with water, extracted with ether, and the extract washed with sodium carbonate solution and water, and dried over alumina. The crude product (0·12 g) was hydrolysed with sodium hydroxide (0·15 g) in benzene–ethanol 1 : 1 (15 ml) for 1 h. After the usual working up the crude product was chromatographed on alumina. Elution with light petroleum–ether 2 : 1 gave 3β-hydroxy-30-nor-19β,28-epoxylupane (*XVI*; 60 mg), m.p. 226—229°C (chloroform–methanol); IR spectrum: 3610 (OH), 1010 (C—O—C) cm^{-1}. For $C_{29}H_{48}O_2$ (428·7) calculated: 81·25% C, 11·29% H; found: 81·35% C, 11·69% H. Hydroxy ether *XVI* was acetylated by acetic anhydride and pyridine 1 : 1 at room temperature to afford 3β-acetoxy-30-nor-19β,28-epoxylupane (*XVII*), m.p. 239 to 242°C (chloroform–methanol), $[\alpha]_D$ +36° (*c* 0·80). IR spectrum: 1728, 1257 (CH_3COO), 1014 cm^{-1} (C—O—C). For $C_{31}H_{50}O_3$ (470·7) calculated: 79·10% C, 10·71% H; found: 79·47% C, 10·85% H. The same solvent mixture eluted diol *XV* (50 mg), m.p. 180—187°C (decomp., chloroform–methanol), $[\alpha]_D$ −20° (*c* 0·64). IR spectrum: 3610, 1025 cm^{-1} (C—O—H). For $C_{29}H_{48}O_2$ (428·7). CH_3OH calculated: 78·20% C, 11·38% H; found: 78·54% C, 11·45% H. Acetylation as in the preceding case gave diacetate *V*, m.p. 208—212°C, $[\alpha]_D$ +12° (*c* 1·2), identical according to IR spectrum with an authentic specimen.

Oxidation of Olefin *V*

a) To a solution of olefin *V* (0·27 g) in acetic acid (100 ml) a solution of chromium trioxide (0·14 g) in a mixture of acetic acid (42 ml) and water (4·5 ml) was added and the mixture allowed to stand at room temperature for 23 h. Methanol and water were added to the reaction mixture and the product extracted with ether. The extract was washed with sodium carbonate solution and water and dried by filtration through a layer of alumina. The mixture of products (0·23 g) was separated on alumina. Elution with benzene gave 3β,28-diacetoxy-18α,19α-epoxy-30-norlupane (*IX*; 80 mg), m.p. 245—246·5°C (chloroform–heptane), $[\alpha]_D$ +25° (*c* 0·6). IR spectrum: 1732 m 1255 cm^{-1} (CH_3COO). PMR spectrum: 0·845 (2 × CH_3), 0·89, 0·98 and 1·10 (3 × CH_3), 1·05 t, $J \sim 7$ Hz (20-CH_3), 2·03 (2 . CH_3COO), 3·95 d and 4·46 d, J = 11 Hz (28-H_2), 4·50 m (3α-H). For $C_{33}H_{52}O_5$ (528·7) calculated: 74·96% C, 9·91% H; found: 74·95% C, 9·73% H. With a mixture of benzene and ether, 9 : 1, 3β-,28-diacetoxy-30-nor-18-lupen-21-one (*XIV*; 60 mg) was eluted, m.p. 258—261°C (methanol). UV spectrum: λ_{max} 235 nm, log ε 4·22. IR spectrum: 1739, 1246 (CH_3COO), 1705, 1620 (C=C—C=O), 1413 cm^{-1} (CH_2CO). PMR spectrum: 0·855 (2 × CH_3), 0·93 (2 × CH_3), 1·16 (CH_3), 0·975 t, J = 7 Hz (20-CH_3), 2·35 q, J = 7 Hz (20-H_2), 1·97 and 2·03 (2 × CH_3CO), 2·47 d, J = 18 Hz (22ξ-H), 2·86 dd, J_1 = 4 Hz, J_2 = = 12 Hz (13β-H), 4·08 d and 4·30 d, J = 11 Hz (28-H_2), 4·50 m (3α-H). For $C_{33}H_{50}O_5$ (526·7) calculated: 75·24% C, 9·57% H; found: 75·26% C, 9·71% H.

b) A solution of olefin *V* (40 mg) and perbenzoic acid (30 mg) in chloroform was allowed to stand at room temperature for 17 h, then diluted with water, extracted with benzene, and the

extract washed with 5% Na_2CO_3 and water and dried over sodium sulfate. Crystallisation from n-heptane gave epoxide *IX*, m.p. 245·5—247·5°C, $[\alpha]_D$ +24° (*c* 0·50), according to IR spectra identical with the sample obtained under *a*).

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