REACTION OF 30-NOR- 19(20)-LUPENE DERIVATIVES WITH BROMINE*

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The reaction of 30-nor-19-lupene-3β,28-diol (*I*) with bromine gives bromo ether *III*; from the corresponding diacetate *II* diene *IX*, unsaturated alcohols *VII* and *VIII* and hydroxy ketone *XII* were obtained as products of conversion of the primarily formed dibromo derivative *VI*, depending on the reaction conditions. The structure and configuration of unsaturated alcohols *VII* and *VIII* at $C_{(20)}$ is based on ^1H and ^{13}C NMR spectra and the different course of their reaction with peracid.

In the large majority of presently known natural triterpenes of lupane series the side chain on $C_{(19)}$ has α-configuration (19β*H*-series). Recently several lupane derivatives have been described in which the side chain has a less favourable β-configuration (19α*H*-series)[1-3]. Our recently published synthesis of 19α*H* compounds (for example 19α*H*-lupeol acetate and similar substances)[4] is based on the addition of diborane to the exocyclic double bond in position 19(20) in derivatives of 30-norlupane. Among other addition reactions which were investigated in connection with the preparation of 19α*H*-lupane compounds we mention in this paper the reaction of 30-nor-19-lupene derivatives *I* and *II* with bromine. The preparation of the starting compounds *I* and *II* is described in ref.[5].

Reaction of diol *I* with bromine in acetic acid gave as the sole product bromo ether *III* which when acetylated afforded monoacetate *IV*. The structure of compound *IV* follows from its ^1H NMR spectrum which displays signals characteristic of CH$_2$—O--group in the ether bridge of 19β,28-epoxy derivatives of lupane[6] (doublet at 3·39 and doublet of doublets at 4·00 ppm, $J_{gem} = 7·3$ Hz, $J_{1,r.} = 2·8$ Hz) and also signals of the CH$_3$—CHBr-group (quadruplet at 4·32 and a three-proton doublet at 1·68 ppm, $J = 6·9$ Hz). The formation of bromo ether *III* can be explained by assuming that the attack of bromine on the double bond takes place from the α-side, similarly as the attack of peracids[5] and diborane[4], and that the free hydroxyl group in the position 28

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participates in the opening of the bromonium ion under formation of 19β.28-epoxide bridge. On the basis of this reaction course and the known[5] E-configuration of the double bond in compound *I* configuration 20R can be proposed for compounds *III* and *IV*.

The reaction of diacetate *II* with bromine or pyridinium bromide perbromide leads to various products, in dependence on the reaction medium. The primary product of the addition, dibromo derivative *VI*, was obtained in the reaction of diacetate *II* with pyridinium bromide perbromide in pyridine. In its mass spectrum the molecular ion was not present, and the ion with the highest mass corresponded to a loss of a molecule of hydrogen bromide and acetic acid from the original dibromo derivative. Further, the main fragments correspond to the fragments found in the case of unsaturated alcohols *VII* and *VIII*. The presence of two bromine atoms in compound *VI* is indicated by the ^{13}C NMR spectrum in which signals of sp^2 carbon atoms which would correspond to unsaturated monobromo derivative were not found. In agreement with structure *VI* the signals of six quaternary carbon atoms (80·2; 47·0; 43·4; 41·1; 37·8 and 37·2 ppm) were detected in the spectrum by a noise off-resonance decoupling experiment, of which the downfield signal (80·2 ppm) may be assigned to the $C_{(19)}$ atom, carrying the bromine atom. The second carbon atom ($C_{(20)}$) carrying the bromine atom gives a doublet at 59·5 ppm. In the ^{1}H NMR spectrum in deuteriochloroform the signals of the CH_3CHBr-group (1·99 (d) and 4·63 (q) ppm, $J = 6·7$ Hz) are overlapped by the signals of the acetate methyls, 3α-hydrogen and 28-methylene group. Their identification was carried out by double resonance, partially relaxed Fourier transform spectra and measurement in hexadeuteriobenzene and its mixture with deuteriochloroform. It is worth mentioning that according to the NMR spectra dibromo derivative *VI* is pure, *i.e.* a single isomer was obtained of the four possible; however, it cannot be decided on the basis of spectral data which are the configurations on $C_{(19)}$ and $C_{(20)}$.

Dibromo derivative *VI* is unstable, as evident from its easy conversion to dienes and substitution derivatives of allylic type. Under the effect of methanol dibromo derivative *VI* gives rise to the known[5] diene *IX* and a chromatographically inseparable mixture of methoxy derivatives *V*, isomeric at $C_{(20)}$. From the ^{1}H NMR spectrum of this mixture it is evident that both isomers differ in the chemical shifts of the methoxyl group (3·16 and 3·21 ppm); one of the isomers has the hydrogens of the $C_{(28)}H_2$-group almost equivalent, while in the second the chemical shift of both hydrogens differs by 0·12 ppm, similarly as in the case of isomeric alcohols *VII* and *VIII*. The reaction of dibromo derivative *VI* with water in pyridine or dioxane gave diene *IX* and unsaturated alcohols *VII* and *VIII*, differing in configuration in the position 20 (for their structure and configuration see below).

During the reaction of diacetate *II* with bromine in anhydrous dioxane or ether an elimination of hydrogen bromide was observed. The mixture of products formed was converted to a separable mixture of stable substances under the effect of water,
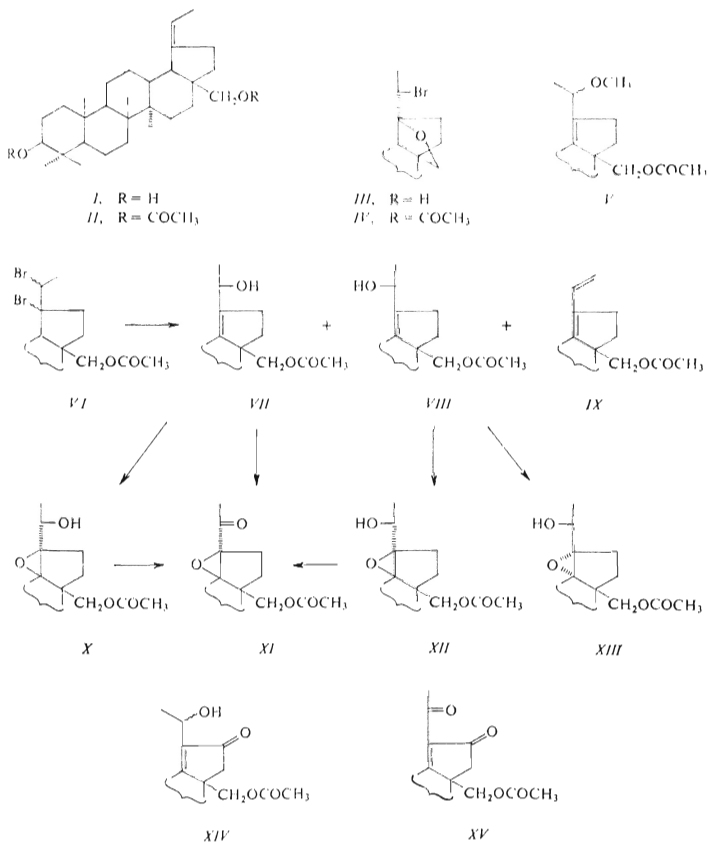
from which diene IX and hydroxy derivatives VII and $VIII$ were isolated. When using acetic acid as solvent in the reaction of diacetate II with bromine, a mixture of unidentified dienes, unsaturated alcohols VII and $VIII$ and an inseparable mixture of their 20-0-acetyl derivatives was obtained. In the reaction of diacetate II in aqueous dioxane different compounds are formed than in anhydrous medium. Hydroxy ketone XIV was isolated as the major product from the mixture of the products. Under these reaction conditions evidently various combinations of addition and elimination reactions, allylic substitution and oxidation take place. The structure of hydroxy ketone XIV is based on its IR spectrum (unsaturated five-membered ketone, 1 680 and 1 615 cm^{-1}) and the ^{1}H NMR spectrum, containing the signals of the CH_3— —CH(OH)— (1·385 (d) and 4·96 (q) ppm, $J = 6·3$ Hz) and two doublets of the $C_{(22)}H_2$ group (2·06 and 2·47 ppm, $J = 19·0$ Hz, for analogy see ref.[5]). Oxidation of hydroxy ketone XIV with chromium trioxide gave diketone XV, containing according its IR spectrum an unsaturated dicarbonyl system (1 705, 1 680, 1 615 cm^{-1}); in its ^{1}H NMR spectrum the singlet of the methyl keto group (2·36 ppm) and two doublets of the protons on $C_{(22)}$ (2·13 and 2·55 ppm, $J = 19·0$ Hz) are present.

It is interesting that in none of the mentioned reactions of diacetate II with bromine could derivatives of type IV be found, containing ether bridges between $C_{(19)}$ and $C_{(28)}$ which are formed in the reaction of diol I. Hence the acetoxy group in the position 28 does not participate in this case, even though in analogous reactions of the 20(21)-double bond in 18α,19βH-ursene derivatives the acetoxy group from position 28 did participate[7] to a considerable extent (about 50%).

In the ^{13}C NMR spectra of both unsaturated alcohols VII and $VIII$ the signals of the carbon atoms of the tetrasubstituted double bond were located at 141 and 138 ppm and a doublet of $C_{(20)}$ at 64 ppm. The spectra of both isomers are practically the same, maximum differences in chemical shifts amount to about 0·4 ppm. The ^{1}H NMR spectra confirm the presence of the CH_3—CH(OH)— group and they are similar in both isomers; in contrast to saturated 20R and 20S 20-hydroxylupane derivatives[8] the shifts of hydrogen atoms in the position 20 do not differ. The most significant difference between the isomers VII and $VIII$ is in the signals of the $C_{(28)}H_2$—O— group: while the isomer VII gives a singlet (similarly as the unsubstituted derivative with the double bond in position[5] 18(19)), in the isomer $VIII$ the hydrogen atoms of the $C_{(28)}H_2$-group are non-equivalent and their chemical shifts differ by 0·1 ppm.

The unsaturated alcohol VII when reacted with 3-chloroperoxybenzoic acid gives rise to epoxy alcohol X as the sole product, from the isomeric alcohol $VIII$ two epoxy alcohols, XII and $XIII$, are formed in comparable amounts. Both epoxy alcohols X and XII give epoxy ketone XI on oxidation with chromium trioxide. The β-configuration of the epoxy group in derivatives $X - XII$ follows both from the known[9-11] preference of the β-attack of peracids on 18(19) double bond, and from the comparison of the ^{1}H NMR spectra and optical rotations of epoxy alcohols XII and $XIII$. According to ref.[9] both doublets of the $C_{(28)}H_2$ group in 18β,19β-epoxylupane deri-

vatives containing the 28-acetoxy group are shifted downfield in comparison with 18α,19α-epoxy derivatives; the chemical shift of the protons of the $C_{(28)}H_2$-group in epoxy alcohol *XII* (3·93 and 4·46 ppm) indicates the 18β,19β-configuration, while in epoxy alcohol *XIII* (3·85 and 4·18 ppm) the 18α,19α-configuration of the epoxide

I,   R = H
II,   R = COCH₃

III,   R = H
IV,   R = COCH₃

V

VI   *VII*   *VIII*   *IX*

X   *XI*   *XII*   *XIII*

XIV   *XV*

group. The molecular rotation difference between epoxy alcohols $XIII$ and XII $(M_D(XIII) - M_D(XII) = +95°)$ also corresponds, according to lit.[4] to the β-configuration of the side chain on $C_{(19)}$ in derivative $XIII$ and to the α-configuration in derivative XII.

The assignment of the configuration on $C_{(20)}$ in unsaturated alcohols VII and $VIII$ and in epoxy alcohols X, XII and $XIII$ has been carried out in the following three manners:

a) According to earlier formulated rules[8] for the mobility of isomeric 30-nor-20--hydroxylupane derivatives in thin-layer chromatography it follows that the more polar isomers VII and X have 20S configuration and the less polar isomers $VIII$ and XII the 20R configuration.

b) It is known[8], that in the ^1H NMR spectra of 30-nor-20-hydroxylupane derivatives which have the 19α-side chain, the signal of $C_{(20)}H$ is shifted upfield in the case of 20R-isomers, in comparison with the 20S-isomers. This rule also applies for substances which have an oxygen atom[8] in position 19β; its application onto 18β,19β--epoxy alcohols X and XII indicates the 20R-configuration for compound XII (quadruplet $C_{(20)}H$ at 4·09 ppm) and the 20S-configuration of compound X (quadruplet at 4·15 ppm).

c) The same configuration on $C_{(20)}$ can be derived on the basis of the known geometry of the transition state in the epoxidation of unsaturated alcohols with peracids (see ref.[12] and the references therein). According to molecular models the conformation $VIIA$ of the side chain may be expected preferentially in the epoxidation of the 20S-isomer VII where the complex of the hydroxy group with the peracid is oriented from the β-side. On the contrary, the hydroxy group of the 20R-isomer $VIII$ (in conformation $VIIIA$) should enhance the formation of α-epoxide. The orientation of the side chain with the terminal methyl group in close proximity of the methylene group on $C_{(12)}$ ($VIIB$, $VIIIB$) is in both alcohols improbable. Hence, the preferred geometry of the transition state ($VIIA$) in the 20S-isomer supports the
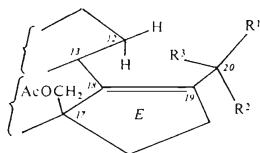
$VIIA$, $R^1 = OH$, $R^2 = CH_3$, $R^3 = H$
$VIIB$, $R^1 = H$, $R^2 = OH$, $R^3 = CH_3$
$VIIIA$, $R^1 = CH_3$, $R^2 = OH$, $R^3 = H$
$VIIIB$, $R^1 = OH$, $R^2 = H$, $R^3 = CH_3$

formation of β-epoxide which is also formed on attack of peracids on 18(19)-un-saturated lupene derivatives without a hydroxyl on $C_{(20)}$ (refs[9-11]), while in the 20R--isomer it competes with this attack. The unambiguous formation of β-epoxide X from 20S-isomer VII and the more complex course of epoxidation of the 20R-isomer VIII, during which both isomeric epoxides XII and XIII were obtained, correspond to the mentioned tendencies.

The isomeric unsaturated alcohols VII and VIII also differ in the reaction with chromium trioxide or pyridinium chlorochromate. Oxidation of the 20S-isomer VII gives epoxy ketone XI as the only product, while the 20R-isomer VIII gives under the same conditions a mixture of acid and neutral products. Among the neutral products epoxy ketone XI could be identified by thin-layer chromatography and diketone XV was isolated. In this oxidation the chromate complex[13] enhanced the epoxidation, in the 20S-isomer in which the complex can assume a suitable orientation (VIIA) for the attack of the double bond from the β-side. In the case of the 20R-isomer the course of the reaction is again more complex and allylic oxidation also takes place. For the comparison, in the 18-lupene derivatives without a 20-hydroxy group allylic oxidation takes place to the same extent as the epoxidation of the double bond[5].

EXPERIMENTAL

The melting points were measured on a Kofler block and they are not corrected. Optical rotations were measured in chloroform on an automatic polarimeter ETL/NPL (Bendix-Erics-son) with a $\pm 2°$ accuracy. The infrared spectra were measured in chloroform on a UR 20 (Zeiss, Jena) spectrophotometer. The NMR spectra were measured in deuteriochloroform, the chemical shifts are given in ppm δ-scale, using tetramethylsilane as reference. The ^1H NMR spectra were measured on a Varian HA-100 spectrometer (100 MHz, internal reference tetramethyl-silane) and a Tesla BS 487A (80 MHz, internal reference hexamethyldisiloxane). For the identifi-cation of the signals the spectra were also measured in mixture of deuteriochloroform and hexa-deuteriobenzene, while for the identification of the —$C_{(20)}$H—CH_3 group signals, decoupling was used. The ^{13}C NMR spectra were measured on a FX-60 (JEOL, 15 MHz) spectrometer, ope-rating in FT-mode; chemical shifts were calculated from the digitally obtained differences of addresses; the multiplicity of the signals was determined by means of single frequency off reso-nance decoupling, or also noise off resonance decoupling. The number and the multiplicity of the signals corresponds to the structure of the substances measured. The mass spectra were measured on a Varian MAT-311 instrument. The energy of the ionizing electrons was 70 eV and the ionizing electron current was 1 mA; the temperature of the ion source was 200°C and the temperature of the direct inlet system was 130—200°C. The identity of the samples prepared in different ways was checked by thin-layer chromatography on silica gel according to Stahl and the infrared spectra. The analytical samples were dried over phosphorus pentoxide under reduced pressure at 100°C.

Reaction of 30-nor-19(20)lupene-3,28-diol (I) with Bromine

A solution of bromine (0·12 g) in acetic acid (3 ml) was added under stirring to a solution of lupe-nediol I (0·3 g) in acetic acid (10 ml) at 14°C. After 2 min water was added and the separated pro-

duct was filtered off under suction, dissolved in ether and the solution filtered through a layer of alumina. After evaporation of ether and crystallization from heptane $(20R)$-20-bromo-19β,28--epoxy-30norlupan-3β-ol (III; 0·25 g) was obtained, m.p. 204—208°C, $[\alpha]_D$ −19°. IR spectrum: 3 630, 1 049, 1 010, 990 cm^{-1}. For $C_{29}H_{47}BrO_2$ (507·6) calculated: 68·61% C, 9·33% H; found: 68·93% C, 9·52% H.

Acetate IV was prepared from hydroxy derivative III using a mixture of acetic anhydride and pyridine in a 1 : 1 ratio, at room temperature. After decomposition of the reaction mixture with water the product was extracted with ether, the etheral solution was washed with water and filtered through a layer of alumina. Acetate IV had m.p. 247—250°C (chloroform–heptane), $[\alpha]_D$ −6°. IR spectrum: 1 730, 1 260, 1 031, 1 009, 985 cm^{-1}. ^{1}H NMR spectrum (100 MHz): 0·85 (2 × × CH$_3$), 0·88; 0·93 and 1·02 (3 × CH$_3$); 1·68 d ($J = 6·9$ Hz; C$_{(20)}$CH$_3$), 2·03 (CH$_3$COO), 3·39 d and 4·00 dd ($J_{gem} = 7·3$ Hz, $J_{1,r} = 2·8$ Hz; C$_{(28)}$H$_2$), 4·32 q ($J = 6·9$ Hz; C$_{(20)}$H), 4·49 m (C$_{(3)}$H). For $C_{31}H_{49}BrO_3$ (549·6) calculated: 67·74% C, 8·96% H; found: 67·94% C, 9·03% H.

Reaction of 3β,28-Diacetoxy-30-nor-19(20)-lupene (II) with Pyridinium Bromide Perbromide

a) In pyridine: A solution of diacetate II (0·4 g) and pyridinium bromide perbromide (0·33 g) in pyridine (25 ml) was allowed to stand at room temperature for 70 h, then diluted with water and extracted with ether. The ethereal solution was washed with dilute sulfuric acid, water and dried over sodium sulfate. Evaporation of ether gave 0·35 g of 3β,28-diacetoxy-19ξ,20ξ-dibromo--30-norlupane (VI), which was rapidly crystallized from a mixture of ether and methanol to give a product melting at 164—166°C (decomp.), $[\alpha]_D$ +48°. IR spectrum: 1 730, 1 260 cm^{-1}. ^{1}H NMR spectrum (80 MHz): 0·85 (2 × CH$_3$), 0·88, 1·06 and 1·10 (3 × CH$_3$), 1·99 d ($J = $ $= 6·7$ Hz; C$_{(20)}$H$_3$), 2·03 and 2·06 (2 × CH$_3$COO), 4·42 d and 4·59 d ($J = 11$ Hz; C$_{(28)}$H$_2$) 4·45 m (C$_{(3)}$H), 4·63 q ($J = 6·7$ Hz; C$_{(20)}$H). ^{13}C NMR spectrum: 171·0 and 171·3 (2 × C=O), 81·0 d (C$_{(3)}$), 80·2 (C$_{(19)}$), 62·5 t (C$_{(28)}$), 59·5 d (C$_{(20)}$). Mass spectrum, m/z (%): 532 (0·2), 530 (0·2), 510 (13), 450 (21), 437 (100), 390 (11), 377 (22), 187 (75). For $C_{33}H_{52}Br_2O_4$ (672·6) calculated: 58·89% C, 7·74% H; found: 60·07% C, 8·01% H.

b) In dioxane: A solution of pyridinium bromide perbromide (0·8 g) in pyridine (2 ml) was added to a solution of diacetate II (0·9 g) in anhydrous dioxane (25 ml) at room temperature and the mixture was stirred at the same temperature for 30 min. After pouring it into a sodium hydrogen carbonate solution a precipitate was formed which was filtered off under suction, dissolved in ether and the ethereal extract was dried over sodium sulfate. The residue, which decomposed on thin-layer chromatography, was dissolved in dioxane (10 ml), water (3 ml) and solid sodium hydrogen carbonate (0·3 g) were added and the mixture was heated on a water bath for 15 min. The mixture was diluted with water and extracted with ether. After washing the extract with water and drying over sodium sulfate, the extract was evaporated and the residue (0·9 g) chromatographed on silica gel. Elution with benzene afforded diene IX (0·11 g), m.p. 208—212°C, identical with an authentic specimen[5], and then a mixture of unidentified substances (0·08 g). Benzene–ether 4 : 1 mixture eluted $(20R)$-3β,28-diacetoxy-30-nor-18(19)-lupen-20-ol ($VIII$; 0·21 g), m.p. 199 to 203°C (chloroform, heptane), $[\alpha]_D$ +25°. IR spectrum: 3 620, 1 730, 1 260 cm^{-1}. ^{1}H NMR spectrum (100 MHz): 0·85 (2 × CH$_3$), 0·91, 0·92 and 1·075 (3 × CH$_3$), 1·21 d ($J = 6·4$ Hz; C$_{(20)}$CH$_3$), 1·56 (OH), 3·98 d and 4·08 d ($J = 11$ Hz; C$_{(28)}$H$_2$), 4·50 m (C$_{(3)}$H), 5·07 q ($J = $ $= 6·4$ Hz; C$_{(20)}$H); after addition of trichloroacetyl isocyanate: 1·36 d (C$_{(20)}$CH$_3$), 6·19 q (C$_{(20)}$H), 8·30 bs (NH). ^{13}C NMR spectrum: 171·3 and 171·0 (2 × C=O), 141·4 and 138·4 (C=C), 80·8 d (C$_{(3)}$), 66·9 t (C$_{(28)}$), 64·3 d (C$_{(20)}$). Mass spectrum, m/z (%): 528 (M$^+$: 0·8), 510 (8), 450 (26), 439 (55), 437 (50), 395 (10), 377 (29), 303 (14), 189 (100). For $C_{33}H_{52}O_5$ (528·7) calculated: 74·96% C, 9·91% H; found: 75·15% C, 10·09% H. Using the same eluent mixture the

mixture of both isomeric hydroxy derivatives VII and $VIII$ (0·3 g) was eluted first and then (20S)--3β,28-diacetoxy-30-nor-18(19)-lupen-20-ol (VII; 0·14 g), m.p. 232–233°C (chloroform, heptane), $[\alpha]_D +6°$, IR spectrum: 3 620, 1 730, 1 260 cm⁻¹. ¹H NMR spectrum (100 MHz): 0·85 (2 × × CH₃), 0·86, 0·91 and 1·08 (3 × CH₃), 1·29 d ($J = 6·3$ Hz; C₍₂₀₎CH₃) 1·55 (OH; disappears after addition of CD₃COOD), 2·05 (2 × CH₃COO), 4·06 s (C₍₂₈₎H₂), 4·50 m (C₍₃₎H), 5·07 q ($J = 6·3$ Hz; C₍₂₀₎H). ¹³C NMR spectrum: 171·4 and 171·0 (2 × C=O), 140·9 and 138·3 (C=C), 80·8 d (C₍₃₎), 66·9 t (C₍₂₈₎), 64·2 d (C₍₂₀₎). Mass spectrum, m/z (%): 528 (M⁺, 1), 510 (6), 450 (15), 439 (23), 437 (22), 377 (15), 303 (13), 189 (100). For C₃₃H₅₂O₅ (528·7) calculated: 74·96% C, 9·91% H; found: 74·86% C, 10·11% H. When anhydrous ether was used instead of dioxane the same mixture of products was obtained under the given reaction conditions.

Reaction of 3β,28-Diacetoxy-30-nor-19(20)-lupene (II) with Bromine

a) In dioxane: A solution of bromine (0·25 g) in dioxane (6 ml) was added to a mixture of diacetate II (0·85 g) and sodium hydrogen carbonate (0·8 g) in dioxane (60 ml) and the mixture was stirred at room temperature for 2 h. After pouring into a sodium hydrogen carbonate solution the precipitated substance was filtered off under suction, washed with water, dissolved in ether and the solution dried over sodium sulfate. After evaporation of the solvent the residue was analysed and found to contain in addition to hydroxy derivatives VII and $VIII$ also a considerable amount of nonpolar substances which decomposed on thin-layer chromatography. Therefore the mixture was converted using aqueous dioxane to a mixture capable of chromatography in the same manner as in the preceding case. Chromatography on silica gel gave diene IX (0·2 g), m.p. 197–206°C, (20S)-hydroxy derivative VII (0·15 g), m.p. 232–233°C, and (20R)-hydroxy derivative $VIII$ (0·15 g), m.p. 198–202°C, all identical with authentic specimens, and 0·3 g of mixed fractions.

b) In acetic acid: A solution of bromine (0·36 g) in acetic acid (3 ml) was added dropwise under stirring to a solution of diacetate II (1·0 g) and sodium acetate (0·17 g) in acetic acid (70 ml), cooled at 14°C. After a further 3 minutes the mixture was poured into water and the formed precipitate filtered off under suction, washed with water, dissolved in chloroform and the solution dried over sodium sulfate. By chromatography of the residue (1·1 g) on silica gel a mixture of dienes was obtained (0·58 g), in which diene IX predominated, according to TLC on argented silica gel. Further, an inseparable mixture of acetylated alcohols VII and $VIII$ (0·30 g) was obtained by chromatography. IR spectrum: 1 730, 1 260 cm⁻¹. The (20 R)-alcohol $VIII$ (0·17 g) followed, with m.p. 199–203°C, $[\alpha]_D +26°$, and then a mixture of (20R) and (20S)-hydroxy derivatives VII and $VIII$ (0·15 g) and finally the (20S)-isomer VII (0·18 g) m.p. 230–233°C, $[\alpha]_D +7°$, identical with the samples described above.

c) In aqueous dioxane: A solution of bromine (0·08 g) in dioxane (8 ml) was added at room temperature and under stirring to a mixture of diacetate II (0·28 g) and sodium hydrogen carbonate (0·22 g) in dioxane (20 ml) and water (1 ml). After 10 min stirring the mixture was poured into water, the precipitate was filtered off, washed with water, dissolved in ether and the solution was dried over sodium sulfate. A mixture of several substances (0·25 g) was obtained, which differed according to TLC from the products obtained under the conditions described above. Chromatography on silica gel gave the major product of the mixture, hydroxy ketone XIV (0·05 g), m.p. 249–252°C (ether, heptane), $[\alpha]_D +33°$. IR spectrum: 3 520, 1 730, 1 680, 1 615, 1 260 cm⁻¹. ¹H NMR spectrum (80 MHz): 0·85 (2 × CH₃), 0·92, 0·99 and 1·15 (3 × CH₃), 1·385 d ($J = = 6·3$ Hz; C₍₂₀₎CH₃), 1·97 and 2·03 (2 × CH₃COO), 2·06 d and 2·47 d ($J = 19$ Hz; C₍₂₂₎H₂), 3·99 d and 4·43 d ($J = 11$ Hz; C₍₂₈₎H₂), 4·45 m (C₍₃₎H), 4·96 q ($J = 6·3$ Hz; (C₍₂₀₎H). Mass spectrum, m/z (%): 542 (M⁺, 10), 464 (4), 449 (4), 439 (3), 263 (100), 261 (95), 235 (8). For C₃₃H₅₀O₆ (542·7) calculated: 73·03% C, 9·29% H; found: 72·88% C, 9·45% H.

Reaction of Dibromo Derivative *VI*

a) *With water in pyridine*: A solution of dibromo derivative *VI* (0·5 g) in a mixture of pyridine (70 ml) and water (30 ml) was refluxed for 1 h, then diluted with water and the precipitated product filtered off under suction. After its dissolution in chloroform the solution was filtered through a layer of alumina. The residue (0·36 g) was chromatographed on silica gel, to obtain diene *IX* (0·07 g), m.p. 208—212°C, (20*R*)-alcohol *VIII* (0·12 g), m.p. 200—203°C, a mixture of (20*R*) and (20*S*)-isomers *VII* and *VIII* (0·03 g), and finally (20*S*)-alcohol *VII* (0·14 g), m.p. 232—233 °C; all the substances were identical with the corresponding samples obtained by other procedures.

b) *With methanol*: A solution of bromo derivative *VI* (0·05 g) in methanol (5 ml) and sodium hydrogen carbonate (0·05 g) were refluxed for 10 min. After evaporation of the solvent the product was chromatographed on silica gel. This gave diene *IX* (0·01 g), m.p. 206—210°C, identical with an authentic sample, and then a mixture of methoxy derivatives *V* (0·03 g). IR spectrum: 1 730, 1 260, 1 092, 1 032 cm^{-1}. ^{1}H NMR spectrum (80 MHz): 0·84 (3 × CH$_3$), 0·90 and 1·08 (2 × × CH$_3$), 1·25 d ($J =$ 6·5 Hz; (C$_{(20)}$CH$_3$), 2·03 (2 × CH$_3$COO), 3·16 and 3·21 (CH$_3$O), 4·04 s and 3·95 d and 4·07 d ($J =$ 11 Hz; C$_{(28)}$H$_2$), 4·50 m (C$_{(3)}$H and C$_{(20)}$H). Mass spectrum, *m/z* (%): 542 (M$^+$; 5), 510 (30), 469 (100), 450 (28), 437 (38), 390 (10), 377 (33).

Reaction of (20*S*)-3β,28-Diacetoxy-30-nor-18(19)-lupen-20-ol (*VII*) with 3-Chloroperbenzoic Acid

A mixture of (20*S*)-alcohol *VII* (0·11 g), sodium hydrogen carbonate (0·14 g) and 3-chloroperbenzoic acid (0·10 g) in dichloromethane (8 ml) was stirred at room temperature for 1·5 h, then shaken with 1 ml of a saturated sodium hydrogen sulfite and filtered through a layer of alumina with sodium hydrogen carbonate. After evaporation of the solvent under reduced pressure (20*S*)-3β,28-diacetoxy-18β,19β-epoxy-30-norlupan-20-ol (*X*; 0·1 g), m.p. 267—270°C (ether, heptane), [α]$_D$ +25·5°, was obtained. IR spectrum: 3 610, 1 730, 1 260 cm^{-1}. ^{1}H NMR spectrum (100 MHz): 0·845 (2 × CH$_3$), 0·895, 0·975 and 1·105 (3 × CH$_3$), 1·325 d ($J =$ 6·4 Hz; C$_{(20)}$CH$_3$), 2·04 and 2·05 (2 × CH$_3$COO), 3·85 d and 4·45 d ($J =$ 10·5 Hz; C$_{(28)}$H$_2$), 4·15 q ($J =$ 6·4 Hz; C$_{(20)}$H), 4·48 m (C$_{(3)}$H). Mass spectrum, *m/z* (%): 544 (M$^+$; 7), 484 (9), 281 (35), 263 (85), 221 (32), 212 (25), 203 (52), 189 (100). For C$_{33}$H$_{52}$O$_6$ (544·7) calculated: 72·75% C, 9·62% H; found: 72·60% C, 9·68% H.

Reaction of (20*R*)-3β,28-Diacetoxy-30-nor-18(19)-lupen-20-ol (*VIII*) with 3-Chloroperbenzoic Acid

A mixture of (20*R*)-alcohol *VIII* (0·11 g), sodium hydrogen carbonate (0·15 g) and 3-chloroperbenzoic acid (0·10 g) in dichloromethane (9 ml) was stirred at room temperature for 2·5 h. After working up as in the preceding case the mixture of the products was separated by chromatography on alumina. The following products were eluted: epoxy ketone *XI* (0·01 g), m.p. 214—216°C, identical with the preparation described later; (20*R*)-3β,28-diacetoxy-18β,19β-epoxy-30-norlupan--20-ol (*XII*; 0·06 g), m.p. 232—233°C (ether, heptane), [α]$_D$ + 23·5°. IR spectrum: 3 630, 1 730, 1 260, 1 090, 1 038 cm^{-1}. ^{1}H NMR spectrum (80 MHz): 0·85 (2 × CH$_3$), 0·89, 1·11 and 1·125 (3 × CH$_3$), 1·30 d ($J =$ 6·3 Hz; C$_{(20)}$CH$_3$), 2·03 and 2·04 (2 × CH$_3$COO), 3·93 d and 4·46 d ($J =$ 11 Hz; C$_{(28)}$H$_2$), 4·10 q ($J =$ 6·3 Hz; C$_{(20)}$H). Mass spectrum, *m/z* (%): 544 (M$^+$; 17), 484 (11), 439 (15), 281 (30), 263 (100), 221 (30), 212 (30), 203 (57), 189 (87). For C$_{33}$H$_{52}$O$_6$ (544·7) calculated: 72·75% C, 9·62% H; found: 72·49% C, 9·80% H. As a further component (20*R*)-3β,28-diacetoxy-18α,19α-epoxy-30-norlupan-2-ol (*XIII*; 0·03 g) was eluted, m.p. 216—217°C (ether, heptane), [α]$_D$ +40°. IR spectrum: 3 630, 1 730, 1 260, 1 108, 1 039 cm^{-1}. ^{1}H NMR spectrum (80 MHz): 0·85 (2 × CH$_3$), 0·87, 1·06 and 1·11 (3 × CH$_3$), 1·23 d ($J =$

= 6·5 Hz; C$_{(20)}$CH$_3$). 2·03 and 2·07 (2 $\times$ CH$_3$COO). 3·84 d and 4·18 d (J = 11 Hz; C$_{(28)}$H$_2$). 4·11 q (J = 6·5 Hz; C$_{(20)}$H), 4·47 m (C$_{(13)}$H). Mass spectrum, m/z (%): 544 (M$^+$; 8), 484 (6), 281 (16), 263 (71), 221 (16), 203 (46), 212 (15), 189 (100). For C$_{33}$H$_{52}$O$_6$ (544·7) calculated: 72·75% C, 9·62% H; found: 72·53% C, 9·69% H.

3β,28-Diacetoxy-18β,19β-epoxy-30-norlupan-20-one (XI)

a) *From (20R)-epoxy alcohol* XII: Chromium trioxide adsorbed on alumina (0·4 g) was added to a solution of (20R)-epoxy alcohol XII (0·03 g) in 0·5 ml of benzene and the mixture was allowed to stand at room temperature for 30 h. Epoxy ketone XI (0·03 g) was then eluted with ether, m.p. 215—217°C (ether, heptane), [α]$_D$ +3°. IR spectrum: 1 729, 1 714, 1 425, 1 260, 1 030 cm^{-1}. ^{1}H NMR spectrum (100 MHz): 0·84 (2 $\times$ CH$_3$), 0·87, 0·955 and 1·07 (3 $\times$ CH$_3$), 2·03 and 2·05 (2 $\times$ CH$_3$COO), 2·29 (C$_{(20)}$CH$_3$), 3·98 d and 4·37 d (J = 11 Hz; C$_{(28)}$H$_2$), 4·45 m (C$_{(3)}$H). Mass spectrum, m/z (%): 542 (M$^+$; 7), 482 (9), 292 (10), 279 (47) 261 (28), 249 (11), 203 (47), 201 (33), 189 (100). For C$_{33}$H$_{50}$O$_6$ (542·7) calculated: 73·03% C, 9·29% H; found: 72·81% C, 9·50% H.

b) *From (20S)-epoxy alcohol* X: A solution of (20S)-epoxy alcohol X (0·04 g) in acetic acid (5 ml) was allowed to stand with an excess of chromium trioxide for 30 min at room temperature. Methanol was added, followed by water and the precipitated product was filtered of with suction. After dissolution in chloroform the solution was filtered through a layer of alumina. Epoxy ketone XI was obtained (0·04 g), m.p. 214—216°C, [α]$_D$ +4°, identical with the sample obtained under a). On oxidation of epoxy alcohol X under the conditions given under a) the unreacted starting material was regenerated.

c) *From (20S)-alcohol* VII: 0·02 g of (20S)-alcohol VII were oxidized under the conditions given under b). The epoxy ketone XI obtained (0·02 g), m.p. 210—213°C and [α]$_D$ +4°, was identical with an authentic specimen.

Reaction of (20R)-3β,28-Diacetoxy-30-nor-18(19)-lupen-20-ol (VIII) with Chromium Trioxide

A solution of (20R)-alcohol VIII (0·11 g) in acetic acid (10 ml) was allowed to stand with an excess of chromium trioxide at room temperature for 10 min. After addition of methanol and water the product was extracted with ether, the extract washed with sodium hydrogen carbonate solution and water and dried over sodium sulfate. Chromatography on silica gel gave the following defined substances: epoxy ketone XI (0·01 g), an unidentified substance (0·02 g), m.p. 292—296°C (ether, heptane), [α]$_D$ +60°, and diketone XV (0·01 g), m.p. 217—224°C, identical with the preparation described below.

3β,28-Diacetoxy-30-nor-18(19)-lupene-20,21-dione (XV)

A solution of hydroxy ketone XIV (0·02 g) in acetic acid (3 ml) was allowed to stand with an excess of chromium trioxide at room temperature for 15 min and then methanol and water were added to it. The precipitated product was extracted with ether and the extract washed with a sodium hydrogen carbonate solution and water and dried over sodium sulfate. Crystallization from a mixture of ether and heptane gave diketone XV (0·015 g), m.p. 223—227°C, [α]$_D$ −23°. IR spectrum: 1 730, 1 705, 1 680, 1 615, 1 260 cm^{-1}. ^{1}H NMR spectrum (80 MHz): 0·85 (2 $\times$ $\times$ CH$_3$), 0·905, 0·975 and 1·14 (3 $\times$ CH$_3$), 2·03 (2 $\times$ CH$_3$COO), 2·13 d and 2·55 d (J = 19 Hz; C$_{(22)}$H$_2$), 2·36 (C$_{(20)}$CH$_3$), 4·08 d and 4·43 d (J = 11 Hz; C$_{(28)}$H$_2$), 4·45 m (C$_{(3)}$H). Mass spectrum, m/z (%): 540 (M$^+$; 2), 277 (100), 263 (56), 223 (36), 217 (29), 190 (79), 189 (97). For C$_{33}$H$_{48}$O$_6$ (540·7) calculated: 73·30% C, 8·95% H; found: 73·01% C, 9·07% H.

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