

REACTION OF 30-NOR-18-LUPENE DERIVATIVES WITH BROMINE AND PERACIDS

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Received March 21, 1983

The reaction of diol *I* and diacetate *II* with one mole of bromine gives rise, depending on conditions, to isomeric dienes *III*–*V* and *IX* or to derivatives substituted in position 21 (*VII*, *VIII*). On reaction of diacetate *II* with two moles of bromine in acetic acid 21,22-disubstituted compounds *XI* and *XII* were obtained. Diene *V* is the intermediate in the formation of dienes *IV* and *IX* and derivatives *XI* and *XII*. Epoxidation of the 18(19)-double bond in compounds *I* and *II* takes place from the β -side and leads to epoxides *XIV* and *XV*.

In connection with the preparation of lupene derivatives which have a β -oriented side chain at C₍₁₉₎ we described in earlier papers^{1–3} the course of the addition reactions (diborane, peracids and bromine) to the exocyclic 19(20) double bond in derivatives of 30-nor-19-lupene. In this paper we present some results of similar additions (bromine, peracids) to the endocyclic double bond in the position 18(19) in 30-nor-18-lupene derivatives *I* and *II*. The preparation of the starting diol *I* and diacetate *II* is described in ref.².

The reaction of diol *I* and diacetate *II* with bromine led to mixtures of labile substances, from which only some products could be isolated, depending on the reaction conditions, solvent and the work-up method. In some instances the products of the decomposition of the primarily formed substances were identified only on the basis of the ¹H NMR spectra of the mixtures formed. After the reaction of diol *I* with one equivalent of bromine in acetic acid the least polar product – diene *III* – was isolated from the mixture. Its structure is in agreement with the UV spectrum (236 nm, ϵ 7 500) and ¹H NMR spectrum, where a signal of the hydrogen atom in the position 12 is present at 5.35 ppm (triplet, $\Sigma J \sim 7.5$ Hz); similar values are also given in literature^{4–6} for an analogous heteroannular *cisoid* diene.

The reaction of diacetate *II* with one equivalent of pyridinium bromide perbromide in pyridine gave predominantly diene *V*. Its structure follows from its UV absorption (256 nm, ϵ 3 900) and the presence of an AB system of protons in the positions 21 and 22 (6.22 and 6.32 ppm, $J = 5.5$ Hz) in its ¹H NMR spectrum (for an analogy

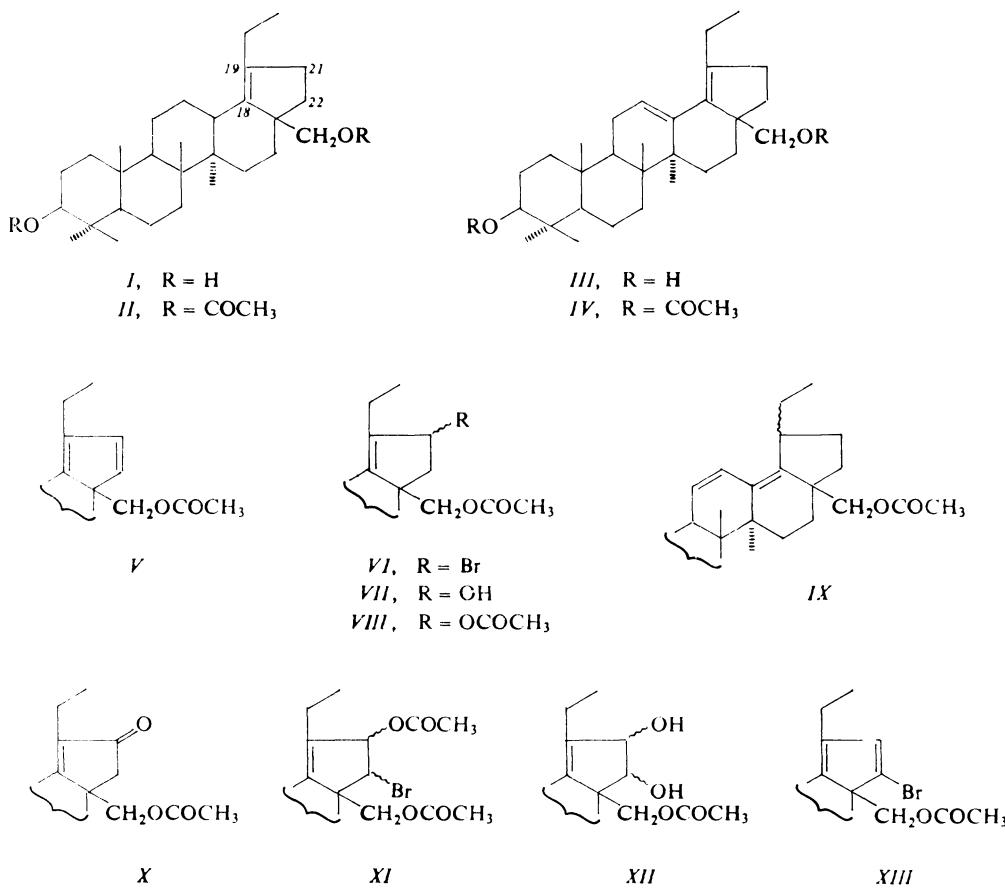
* Part LXX in the series Triterpenes; Part LXIX: This Journal 48, 3444 (1983).

see ref.⁷). Under the influence of aqueous hydrobromic acid diene *V* is isomerized to the *ciosid* diene *IV* (236 nm, ϵ 7 500, a broad triplet of $C_{(12)}H$ at 5.32 ppm, $J \sim 7.5$ Hz). In the mass spectrum of all the dienes mentioned, *i.e.* *III*–*V*, the ions which could be formulated as *a* were found as the main fragments, which lead to a highly abundant ion of *m/z* 187 after the loss of radical CH_2OR . The mass spectra of these compounds also agree with the spectra of analogous derivatives with an isopropyl group in position 19, published in ref.⁷.

During the reaction of diacetate *II* with one equivalent of bromine in acetic acid a product crystallizes out directly from the reaction mixture, which contains bromine and which is according to its 1H NMR spectrum a mixture of several compounds. The presence of the signals in the 5.1–5.3 ppm region, which might correspond to olefinic hydrogens or the hydrogens of the $CHBr$ type, and the substitution reactions suggest that it is a mixture of isomeric bromo derivatives of allylic type (for example 21-bromo derivatives *VI*, isomeric at $C_{(21)}$, and the isomers with the 19(21) double bond and bromine on $C_{(18)}$). According to 1H NMR spectrum a small amount of diene *V* and derivative *XI* is also present in the mixture. The product is unstable and it cannot be purified and characterized, its 1H NMR spectrum changes rapidly with time. After 20 h, when the decomposition is over, the spectrum contains signals characteristic of diene *IV* and two doublets of doublets (5.58 ppm, $J = 10.7$ and 1.4 Hz; 6.19 ppm, $J = 10.7$ and 3 Hz). According to analogies^{8,9} these values are typical of hydrogens in positions 11 and 12 in 11,13(18)-dienes of type *IX*. The UV spectrum also corresponds to a mixture of diene *IV* (235 nm) and heteroannular *transoid* diene *IX* (243, 251 and 261 nm, for analogy see refs^{5,6}). On heating of the crystalline mixture of the bromo derivatives of the allylic type with sodium hydrogen carbonate in aqueous dioxane a mixture of 21-hydroxy derivatives *VII*, isomeric at $C_{(21)}$ was formed, which on oxidation with pyridinium chlorochromate adsorbed on alumina afforded the known² α,β -unsaturated ketone *X*. If the reaction of diacetate *II* with bromine in acetic acid is carried out in the presence of sodium acetate, bromine is substituted under formation of 21-acetoxy derivatives *VIII*, isomeric in the position 21. In the 1H NMR spectrum of this mixture the signals $C_{(21)}H$ of both isomers are evident: doublet of doublets at 5.58 ppm ($J \sim 6$ and 3 Hz) and a broad triplet ($\sum J \sim 14$ Hz). Acetates *VIII* eliminate a molecule of acetic acid easily (for example on standing in a chloroform solution, during the measurement of the 1H NMR spectrum in C^2HCl_3 , or on heating in aqueous dioxane) under formation of the homoannular diene *V*. In the mass spectra of acetyl derivatives *VIII* and hydroxy derivatives *VII* the abundance of molecular ions is very low and after the loss of acetic acid or water, the fragmentation corresponds to the fragmentation of diene *V*.

In the reaction of diacetate *II* with two equivalents of bromine in acetic acid bromohydrin acetate *XI* separates from the reaction mixture as the main product. From the filtrate a mixture of products was obtained from which dihydroxy derivative *XII* was isolated. Bromohydrin acetate *XI* is also formed on reaction of diene *V*

with bromine in acetic acid. On reduction with zinc in acetic it gives back the diene *V*. Bromohydrin acetate *XI* eliminates a molecule of acetic acid easily: in the mass spectrum its molecular ion does not appear, but $[M - \text{CH}_3\text{COOH}]$ is evident in it (*m/z* 588 and 590), on pyrolysis at 200°C or heating in pyridine it is converted to bromodiene which we formulate as *XIII* on the basis of its UV spectrum (272 nm, ϵ 5 700), ^1H NMR spectrum (singlet of $\text{C}_{(21)}\text{H}$ at 6.27 ppm) and analogy⁷. An elimination of hydrogen bromide under formation of enol acetate or unsaturated ketone *X* was not observed.



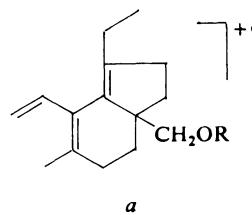
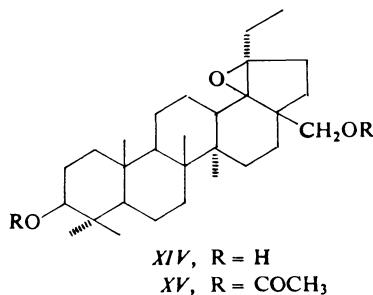
Compounds *V*–*XIII* have $3\beta\text{-OCOCH}_3$ group.

The structure of bromohydrin acetate *XI* follows from the above mentioned reactions, especially from its formation from diene *V* (1,2- or 1,4-addition followed

by substitution under allylic rearrangement leads to an acetoxy group in position 21) and from NMR spectra. ^1H NMR spectrum confirms the presence of three acetate groups (a six-proton singlet at 2.03 ppm and a three-proton singlet at 2.09 ppm) and hydrogen atoms in positions 21 and 22, forming an AB system (doublets at 5.20 and 4.83 ppm, resp., the assignment was checked by decoupling and tickling experiments). The doublet 21-H (5.20 ppm) is broadened owing probably to the long-range coupling with a homoallylic 13β -H or $\text{C}_{(20)}\text{H}_2$ group. In the ^{13}C NMR spectrum the signals are evident of the carbon atoms of the tetrasubstituted double bond (singlets at 142.4 and 137.7 ppm) and doublets $\text{C}_{(21)}$ and $\text{C}_{(22)}$ at 67.1 and 61.7 ppm. The signal at 67.1 ppm was assigned on the basis of selective decoupling to the doublet at 5.20 ppm in the ^1H NMR spectrum, the signal at 61.7 ppm to the doublet at 4.83 ppm. The structure of dihydroxy derivative *XII* is based on the ^1H NMR spectrum (singlets of $\text{C}_{(21)}\text{H}$ and $\text{C}_{(22)}\text{H}$ at 3.89 and 4.17 ppm), IR spectrum and mass spectrum where significant fragments correspond to the loss of a hydrogen radical and to subsequent gradual elimination of water molecule and two acetic acid molecules from $[\text{M}-1]^+$. The low values of the vicinal coupling constant of the protons in positions 21 and 22 in bromohydrin acetate *XI* (3.2 Hz) and in dihydroxy derivative *XII* (~ 0 Hz) indicate a *trans*-configuration of the functional groups. However from the data known so far no decision can be made between both possible *trans*-isomers.

The course of the addition of bromine to the 18(19)-double bond of 30-nor-18-lupene derivatives may be rationalized in assuming that the primarily formed unsaturated bromo derivatives of the allylic type (*VI* and similar) react, depending on conditions, either by substitution, under formation of 21-substituted derivatives (*VII*, *VIII*), or by elimination of hydrogen bromide, under formation of diene *V*. In the presence of the hydrogen bromide formed isomerization of diene *V* to hetero-annular dienes *IV* and *IX* takes place (a mutual isomerization of similar dienes in acid medium has already been observed⁵⁻⁷). The addition of further bromine to diene *V* with the assistance of the solvent or subsequent substitution then leads to 21,22-disubstituted derivatives *XI* and *XII*. Hence, the addition of bromine to the 18(19)-double bond may be used for the introduction of an oxygen-containing substituent into position 21 which is also substituted in some natural triterpenes of the lupane series (for example stellatogenin, thurberogenin¹⁰).

In an earlier paper² we mentioned that on oxidation of diacetate *II* with perbenzoic acid or chromium trioxide 18,19-epoxy derivative is formed which we formulated incorrectly as $3\beta,28$ -diacetoxy- $18\alpha,19\alpha$ -epoxy-30-norlupane. On reaction of diol *I* with perbenzoic acid we have now prepared epoxy diol which according to its IR spectrum contains an intramolecular hydrogen bond between the 28-hydroxy group and the epoxide oxygen (3537 cm^{-1}), so that it must be formulated as $18\beta,19\beta$ -epoxy diol *XIV*. Since on acetylation of epoxy diol *XIV* epoxy diacetate *XV* is formed which is identical with the substance obtained on epoxidation of diacetate *II* according



to ref.², and on alkaline hydrolysis or reduction with lithium aluminum hydride epoxy diol *XIV* is regenerated from epoxy diacetate *XV*, the configuration of the epoxy group in diacetate *XV* must also be β . The attack of the peracids on the 18(19)-double bond in 30-norlupene derivatives thus takes place from the β -side, similarly as in substances with the isopropyl group on C₍₁₉₎ (see^{4,11}). It is interesting that the exocyclic double bond in the position 19(20) in 30-norderivatives of lupane is attacked from the α -side exclusively¹⁻³.

EXPERIMENTAL

The melting points were measured on a Kofler block and they are not corrected. Optical rotations were measured in chloroform on an automatic ETL/NPL polarimeter (Bedix-Ericsson) with a $\pm 2^\circ$ accuracy. The infrared spectra were measured in chloroform on a UR 20 spectrophotometer (Zeiss, Jena). The ultraviolet spectra were measured in cyclohexane on a SP-700 (Unicam) spectrophotometer. The NMR spectra were measured in deuteriochloroform, the chemical shifts are given in ppm (δ -scale, with tetramethylsilane as reference). The ¹H NMR spectra were measured on a TESLA BS 487A spectrometer (80 MHz, internal standard hexamethyl-disiloxane); the ¹³C NMR spectrum was measured on an FX-60 spectrometer (JEOL, 15 MHz), operating in FT-mode. 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.

30-Nor-12,18-lupadiene-3 β ,28-diol (*III*)

Diol *I* (0.16 g) was dissolved in warm acetic acid (20 ml) and the solution was cooled to 14°C. At this temperature a solution of bromine (0.06 g) in acetic acid (2.5 ml) was added to it under stirring. After 1 min the mixture was diluted with water and the precipitated product was filtered off under suction. The least polar component (0.11 g) was isolated from it by chromatography on silica gel. On repeated crystallization of the product from ether-light petroleum and chloroform-heptane mixtures diene *III* was obtained, m.p. 137—140°C, $[\alpha]_D +170^\circ$. IR spectrum: 3 630, 3 500, 1 650 cm⁻¹. UV spectrum: λ_{max} 236 nm, ϵ 7 500. ¹H NMR spectrum: 0.80 (CH₃) 0.99 (3 \times CH₃), 1.26 (CH₃), 3.24 m (C₍₃₎H), 3.40 s (C₍₂₈₎H₂), 5.35 bt, $\Sigma J \sim 7.5$ Hz (C₍₁₂₎H). Mass spectrum, *m/z* (%): 426 (M⁺; 5), 408 (2), 395 (100), 377 (3), 295 (2), 255 (3), 189 (20), 187 (23). For C₂₉H₄₆O₂ (426.7) calculated: 81.10% C, 11.18% H; found: 81.37% C, 11.17% H.

Reaction of Diacetyl Derivative *II*

a) *With pyridinium bromide perbromide in pyridine:* A solution of diacetate *II* (0.28 g) and pyridinium bromide perbromide (0.21 g) in pyridine (20 ml) was allowed to stand at room temperature for 20 h, then diluted with water and extracted with chloroform. The extract was washed with water and dried over sodium sulfate. From the residue (0.2 g) the least polar product was separated by chromatography on silica gel, *i.e.* 3 β ,28-diacetoxyl-30-nor-18,21-lupadiene (*V*; 0.12 g), m.p. 216–219°C (ether, heptane), $[\alpha]_D$ –125°. IR spectrum: 1730, 1260 cm^{-1} . UV spectrum: λ_{max} 256 nm, ϵ 3900. ^1H NMR spectrum: 0.74 (CH_3), 0.85 ($2 \times \text{CH}_3$), 0.92 and 1.14 ($2 \times \text{CH}_3$), 1.06 t, $J \approx 7.5$ Hz ($\text{C}_{(20)}-\text{CH}_3$), 2.03 ($2 \times \text{CH}_3\text{COO}$), 3.44 d and 4.39 d, $J = 11$ Hz ($\text{C}_{(28)}\text{H}_2$), 4.49 m ($\text{C}_{(3)}\text{H}$), 6.22 d and 6.32 d, $J = 5.5$ Hz ($\text{C}_{(21)}\text{H}$ and $\text{C}_{(22)}\text{H}$). Mass spectrum, m/z (%): 510 (M^+ ; 10), 450 (15), 437 (18), 390 (8), 260 (9), 249 (9), 247 (18), 189 (60), 187 (100). For $\text{C}_{33}\text{H}_{50}\text{O}_4$ (510.7) calculated: 77.60% C, 9.87% H; found: 77.32% C, 10.08% H.

b) *With one equivalent of bromine in acetic acid:* A solution of bromine (0.04 g) in acetic acid (1.5 ml) was added to a solution of diacetate *II* (0.13 g) in acetic acid (8 ml), cooled at 14°C. After 10 min standing at room temperature the separated mixture of bromo derivatives was suction-dried and washed with ether. The product (a mixture of bromo derivatives, 0.1 g) had m.p. 192–210°C, under decomposition, and $[\alpha]_D$ –60°. It also gave a positive Beilstein test. The ^1H NMR spectrum changes in time and after 20 h it contains in addition to the signals of diene *IV* also the signals of diene *IX*: 3.90 bs ($\text{C}_{(28)}\text{H}_2$), 5.58 dd, $J_1 = 10.7$ Hz, $J_2 = 1.5$ Hz ($\text{C}_{(12)}\text{H}$), 6.19 dd, $J_1 = 10.7$ Hz, $J_2 = 3$ Hz ($\text{C}_{(11)}\text{H}$). The sample after the measurement of the ^1H NMR spectrum was freed of coloured components by chromatography on alumina and crystallized from methanol. The mixture of dienes *IV* and *IX* obtained had m.p. 196–207°C, UV spectrum: λ_{max} (ϵ): 235 nm (14 000), 243 nm (15 000), 251 nm (13 000) and 261 nm (8 000). The crystalline mixture of bromo derivatives (0.15 g), prepared by the mentioned method was immediately dissolved in dioxane, water and sodium hydrogen carbonate were added and the mixture refluxed for 5 min. After dilution with water a precipitate separated which was filtered off under suction and chromatographed on silica gel. As the main fraction (0.1 g) a mixture of isomeric 3 β ,28-diacetoxyl-30-nor-18-lupene-21-ols (*VII*) with m.p. 212–218°C (benzene–heptane), $[\alpha]_D$ +20° was obtained. IR spectrum: 3564, 3620, 1727, 1255 cm^{-1} . ^1H NMR spectrum, 3.86 d and 4.13 d, $J = 11$ Hz, 3.79 d and 4.38 d, $J = 11$ Hz (two AB systems of $\text{C}_{(28)}\text{H}_2$), 2.03 ($\text{C}_{(3)}-\text{OCOCH}_3$), 2.015 and 2.05 ($\text{C}_{(28)}-\text{OCOCH}_3$), 4.48 m ($\text{C}_{(3)}\text{H}$), 4.30–4.70 m ($\text{C}_{(21)}\text{H}$, overlapped by other signals). Mass spectrum, m/z (%): 528 (M^+ ; 2), 510 (8), 468 (3), 455 (6), 450 (13), 437 (12), 390 (5), 263 (14), 260 (9), 247 (18), 189 (50), 187 (100). For $\text{C}_{33}\text{H}_{52}\text{O}_5$ (528.7) calculated: 74.96% C, 9.91% H; found: 74.67% C, 9.71% H. A chloroform solution of the mixture of hydroxy derivatives *VII* (0.03 g) was adsorbed on alumina impregnated with pyridinium chlorochromate (0.3 g); after 45 min ketone *X* was eluted (0.03 g) with m.p. 258 to 259°C (chloroform, methanol; lit.² gives m.p. 258–261°C), $[\alpha]_D$ –38°, which according to TLC, IR and ^1H NMR spectra was identical with an authentic sample.

c) *With one equivalent of bromine in the presence of sodium acetate:* A solution of bromine (0.06 g) in acetic acid (2.3 ml) was added under stirring to a solution of diacetate *II* (0.2 g) and sodium acetate (0.06 g) in acetic acid (12 ml) kept at 14°C. After 10 min the mixture was diluted with water, the precipitated compound was filtered off under suction, dissolved in ether and the solution was filtered through a layer of alumina. A chromatographically inseparable mixture of isomers of 3 β ,21,28-triacetoxyl-30-nor-18-lupene (*VIII*; 0.02 g) was obtained. IR spectrum: 1726, 1256 cm^{-1} . ^1H NMR spectrum: 2.02, 2.03 and 2.05 ($3 \times \text{CH}_3\text{COO}$), 4.13 s and 4.01 d, 4.32 d, $J \sim 11$ Hz ($\text{C}_{(28)}\text{H}_2$), 5.58 dd $J_1 \sim 6$ Hz, $J_2 \sim 3$ Hz, and 5.72 bt, $J \sim 14$ Hz ($\text{C}_{(21)}\text{H}$), 4.50 m.

(C₍₃₎H). The spectrum changes with time, after 20 h it is identical with the spectrum of diene *V*. Mass spectrum, *m/z* (%): 570 (M⁺; 0.5), 510 (14), 450 (19), 437 (25), 390 (7), 260 (8), 249 (8), 247 (18), 189 (54), 187 (100). For C₃₅H₅₄O₆ (570.7) calculated: 73.64% C, 9.54% H; found: 73.24% C, 9.42% H.

A mixture of triacetyl derivatives *VIII* (0.06 g) was dissolved in aqueous dioxane and refluxed for 15 min. After dilution with water the precipitate formed was filtered off under suction, dissolved in chloroform and the solution dried over sodium sulfate. The product (0.05 g) had m.p. 218–223°C, [α]_D – 125°, UV spectrum: λ_{max} 253 nm, ε 3 900. According to TLC and the ¹H NMR spectrum it was identical with diene *V*.

d) With two equivalents of bromine: Diacetate *II* (1.0 g) was dissolved in warm acetic acid (60 ml), the solution cooled to 14°C and a solution of bromine (0.6 g) in acetic acid (6 ml) was added to it under stirring at the same temperature. After 5 min stirring the precipitate formed was suction-dried and washed twice with ether. The 3β,21ξ,28-triacetoxy-22ξ-bromo-30-nor-18-lupene thus obtained (*XI*; 0.75 g) had m.p. 178–181°C (under decomposition), [α]_D – 47°. IR spectrum: 1 730, 1 650, 1 256, 1 035, 985 cm^{–1}. ¹H NMR spectrum: 0.85 (2 × CH₃), 0.90, 0.91, and 1.11 (3 × CH₃), 1.05 t, *J* = 7.3 Hz (C₍₂₀₎CH₃), 2.03 (2 × CH₃COO), 2.09 (CH₃COO), 4.26 s (C₍₂₈₎H₂), 4.50 = (C₍₃₎H), 4.83 d, *J* = 3.2 Hz (C₍₂₂₎H), 5.20 bd, *J* = 3.2 Hz (C₍₂₁₎H). ¹³C NMR spectrum: 170.9 s (C=O), 142.4 s and 137.7 s (C=C), 80.7 d (C₍₃₎), 67.1 d (C₍₂₁₎), 64.1 t (C₍₂₈₎), 61.7 d (C₍₂₂₎). The multiplicity of other signals, determined by single frequency off resonance decoupling, corresponds to the total number of quaternary, methine, methylene and methyl carbon atoms. Mass spectrum, *m/z* (%): 590 (2), 588 (2), 530 (1), 528 (1), 517 (1), 515 (1), 509 (4), 449 (9), 389 (4), 344 (4), 329 (2), 189 (30), 43 (100). For C₃₅H₅₅BrO₆ (651.6) calculated: 64.50% C, 8.50% H; found: 64.15% C, 8.29% H. The filtrate after the separation of bromohydrin acetate *XI* was diluted with water, the separated product was filtered off under suction, washed with water, dissolved in benzene and the solution dried over sodium sulfate. After evaporation of benzene under reduced pressure an oily mixture (0.3 g) was obtained from which 3β,28-diacetoxy-30-nor-18-lupene-21ξ,22ξ-diol (*XII*; 0.04 g), was obtained by repeated crystallization from ether and benzene-heptane mixture. M.p. 263–265°C, [α]_D + 14°. IR spectrum: 3 560, 1 728, 1.256, 1 035, 1 045 cm^{–1}. ¹H NMR spectrum: 0.85 (2 × CH₃), 0.895, 1.09 and 1.11 (3 × CH₃), 1.09 t, *J* = 7.2 Hz (C₍₂₀₎CH₃), 2.03 and 2.06 (2 × CH₃COO), 3.89 bs and 4.17 bs (C₍₂₂₎H and C₍₂₁₎H), 4.26 d and 4.44 d, *J* = 11 Hz (C₍₂₈₎H₂), 4.49 m (C₍₃₎H). Mass spectrum, *m/z* (%): 544 (M⁺; C₃₃H₅₂O₆; 2), 543 (2), 526 (4), 525 (C₃₃H₄₉O₅; 6), 483 (6), 482 (8), 465 (C₃₁H₄₅O₃; 12), 453 (15), 439 (7), 423 (4), 405 (7), 189 (100). For C₃₃H₅₂O₆ (544.7) calculated: 72.75% C, 9.62% H; found: 72.50% C, 9.39% H.

Reaction of Diene *V*

*a) A solution of bromine (0.025 g) in acetic acid (0.03 ml) was added under cooling at 14°C and stirring to a solution of diene *V* (0.07 g) in acetic acid (5 ml) and the stirring was continued at room temperature for 10 min. The precipitated product was filtered off under suction and washed with ether. The bromohydrin acetate *XI* (0.05 g) thus obtained had m.p. 179–182°C (decomp.) and according to mass and ¹H NMR spectra it was identical with the sample mentioned above.*

*b) A drop of 48% hydrobromic acid was added to a solution of diene *V* (0.03 g) in chloroform (4 ml) and the mixture was allowed to stand at room temperature for 24 h. The solution was filtered through a layer of alumina and the filtrate concentrated. The residue was crystallized from heptane to give diene *IV* (0.025 g), m.p. 145–150°C. UV spectrum: λ_{max} 236 nm, ε 7 500, ¹H NMR spectrum: 0.85–1.25 (methyl signals), 2.03 (2 × CH₃COO), 3.78 d and 3.93 d, *J* =*

δ = 11 Hz ($C_{(28)}H_2$), 4.50 m ($C_{(3)}H$), 5.32 bt, $\Sigma J \sim 7.5$ Hz ($C_{(12)}H$). Mass spectrum, m/z (%) 510 (M^+ ; 9), 450 (10), 437 (100), 377 (10), 260 (9), 247 (15), 189 (44), 187 (88).

Reaction of Bromohydrin Acetate *XI*

a) Compound *XI* (0.1 g) was heated at 200°C for 4 min and the pyrolysate was chromatographed on silica gel impregnated with silver nitrate. As the main fraction $3\beta,28$ -diacetoxy- 22 -bromo- 30 , $18,21$ -lupadiene (*XIII*; 0.05 g) was eluted, m.p. 169–176°C (hexane), $[\alpha]_D$ – 120°. IR spectrum: 1 728 with an inflection at 1 707, 1 615, 1 256, 1 040 cm^{-1} . UV spectrum: λ_{max} 272 nm, ϵ 5 700. 1H NMR spectrum: 0.76 (CH_3), (0.85) ($2 \times CH_3$), 0.92 and 1.16 ($2 \times CH_3$), 1.05 t, $J = 7.5$ Hz ($C_{(20)}CH_3$), 1.92 and 2.02 ($2 \times CH_3COO$), 2.37 q, ($J = 7.5$ Hz ($C_{(20)}H_2$)), 3.99 d and 4.40 d, $J = 11.3$ Hz ($C_{(28)}H_2$), 4.48 m ($C_{(3)}H$), 6.27 s ($C_{(21)}H$). Mass spectrum, m/z : 590, 588 (M^+). For $C_{33}H_{49}BrO_4$ (589.7) calculated: 67.20% C, 8.39% H; found: 66.93% C, 8.10% H.

b) Compound *XI* (0.06 g) in pyridine (3 ml) was refluxed for 1 h, diluted with water and extracted with ether. The ethereal extract was washed with dilute hydrochloric acid, water, and dried over sodium sulfate. Chromatography of the residue on argentated silica gel gave bromo derivative *XIII* (0.03 g), m.p. 167–174°C, $[\alpha]_D$ – 125°, which according to TLC and IR spectrum was identical with the sample described above.

c) A solution of *XI* (0.1 g) in benzene (10 ml) was added dropwise to a boiling mixture of acetic acid (20 ml) and zinc powder (1.1 g). After 30 min refluxing the mixture was cooled, zinc filtered off and washed with ether, and the filtrate diluted with water and extracted with ether. The extract was washed with water and sodium carbonate and dried over sodium sulfate. After evaporation of ether and crystallization from heptane diene *V* (0.09 g) was obtained, m.p. 216–219°C, $[\alpha]_D$ – 123°, identical according to TLC and IR, UV and 1H NMR spectra with the sample described above.

18 β ,19 β -Epoxy- 30 -norlupane- $3\beta,28$ -diol (*XIV*)

a) A solution of diol *I* (0.17 g) and perbenzoic acid (~0.3 g) in benzene (10 ml) was allowed to stand at 0°C for 18 h, then solid sodium carbonate was added and after 15 min standing the solution was filtered through a layer of alumina. The epoxy diol *XIV* obtained (0.17 g) had m.p. 234–238°C (under decomposition; chloroform, heptane), $[\alpha]_D$ + 26°. IR spectrum: 3 620, 3 500, 1 035 cm^{-1} ; $\nu_{(OH)}$ in CCl_4 ($2.8 \cdot 10^{-3}$ mol l^{-1}): 3 635 (ϵ 70), shoulder at 3 624, 3 537 cm^{-1} (ϵ 53), the shape of the spectrum does not change on dilution. For $C_{29}H_{48}O_3$ (444.7) calculated: 78.32% C, 10.88% H; found: 78.20% C, 10.87% H. When acetylated with acetic anhydride in pyridine at room temperature epoxy diol *XIV* afforded epoxy diacetate *XV*, m.p. 246–248°C, $[\alpha]_D$ + 24°, according to TLC and IR spectrum identical with a sample prepared as in ref.².

b) Epoxy diacetate *XV* (0.2 g) was refluxed for 2 h with a 2.5% solution of potassium hydroxide in a mixture of benzene (10 ml) and ethanol (10 ml). After dilution with water the mixture was extracted with ether, the extract was washed with water, dried over sodium sulfate and evaporated. The residual epoxy diol *XIV* (0.2 g) had m.p. 232–235°C (under decomposition), $[\alpha]_D$ + 26°, which according to TLC and IR spectrum was identical with the sample described above. The same epoxy diol *XIV* (0.3 g) was also obtained when epoxy diacetate *XV* (0.3 g) was refluxed with an excess of lithium aluminum hydride in ether for 17 h and worked up as in the preceding case.

The elemental analyses were carried out in the analytical laboratory of our department under the direction of Dr J. Zelinka. For the measurement of the ^{13}C NMR spectrum the authors thank Dr J. Urban, Microbiological Institute, Czechoslovak Academy of Sciences, Prague.

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Translated by Ž. Procházka.