# PREPARATION OF 12,20-DISUBSTITUTED LUPANE DERIVATIVES*

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Ketoester *I* was reduced to diol *VI*. The higher reactivity of its primary hydroxy group was made use of for the preparation of 12α-hydroxy derivatives *VII*, *VIII* and *X* the oxidation of which led to oxo derivatives *XII*, *XIII* and *XIV*. The reduction of the 12-oxo group in compounds *XII* and *XIV* with lithium aluminum hydride takes place stereospecifically under formation of 12α--hydroxy derivatives *VII* and *X*, while on reduction with sodium in 1-propanol corresponding 12β-hydroxy derivatives *XV* and *XVI* are also formed. Reduction of the unsaturated ketone *XVII* with sodium borohydride gave unsaturated alcohols *XVIII* and *XX*. As acetoxy ketone *XXIV* was obtained from olefin *XIX* in a 12% yield only, its alternative preparation was carried out from acetoxy ketone *XXXIV via* the intermediates *XXXII*, *XXXV*, *XXVIII* and *XXXI* in an overall yield of 27%. The structures of the derivatives of 12-lupene (*III*, *V*, *XVII*, *XIX* and *XXI*), 12-lupanol (*II*, *VII*, *X*, *XV*, *XXXI* and *XXVII*) and 12-lupanone (*I*, *XII*, *XIII*, *XIV*, *XXIII*, *XXIV*, *XXXIII* and *XXXIV*) were confirmed by the analysis of their $^1$H-NMR spectra.

In a previous communication[1] we investigated polar interactions of the substituents in the position 20 and in the ring C in 30-nor- or 29,30-dinorlupane derivatives. As the presence of oxygen-containing substituents in the posions 3 and 28 complicates the interpretation of spectral measurements, and as it was impossible in some cases to obtain the substances in pure state, we decided to prepare a series of derivatives of 12-lupene, 12-lupanol and 12-lupanone with various substituents in the position 20. Derivatives of 12-lupanone[2,3] (*I* and *XXXIV*) and 12-lupene[2] (*III* and *XVII*) were used as starting substances.

Reduction of the unsaturated ester *III* with lithium aluminum hydride afforded hydroxy derivative *IV*, characterized as acetate *V*. Hydroxy ester *II* was reduced with lithium aluminum hydride to diol *VI*; this diol is also formed on reduction of keto ester *I*. Partial methylation of diol *VI* gives hydroxy ether *VII* which was oxidized to 12-oxo derivative *XII*. Reduction of ketone *XII* with lithium aluminum hydride gives the alcohol *VII* alone; the epimeric alcohol *XV* was prepared by reduction of ketone *XII* with sodium in 1-propanol when both alcohols are formed in a 1 : 1 ratio. The configuration of the hydroxyl group in both epimeric alcohols *VII* and *XV* is confirmed by the analysis of their $^1$H-NMR spectra (Table I). In the spectrum of compound

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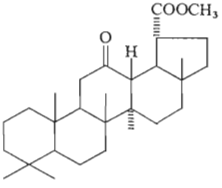
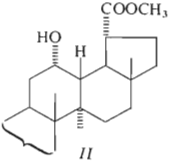
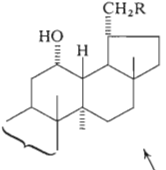


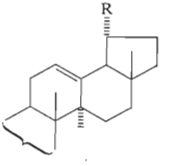

*I*



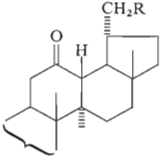

*II*



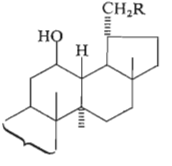

*VI*, R = OH
*VII*, R = $OCH_3$
*VIII*, R = OAc
*IX*, R = $OSO_2CH_3$
*X*, R = H




*III*, R = $COOCH_3$
*IV*, R = $CH_2OH$
*V*, R = $CH_2OAc$




*XI*, R = OH
*XII*, R = $OCH_3$
*XIII*, R = OAc
*XIV*, R = H




*XV*, R = $OCH_3$
*XVI*, R = H

*VII* the axial hydroxyl group in the position 12 causes a downfield shift of the 14α-$CH_3$ signal; the width of the multiplet ($W \approx 10$ Hz) of the proton in the position 12 confirms its equatorial orientation. In the spectrum of compound *XV* the width of the multiplet ($W \geqq 20$ Hz) of the proton in the position 12 confirms its axial orientation. From the IR spectra of both hydroxy ethers *VII* and *XV* it follows that in both substances an intramolecular hydrogen bond is formed between the hydroxyl group and the oxygen of the ether group.

On partial acetylation of diol *VI* monoacetate *VIII* was prepared which was then oxidized to ketone *XIII*, prepared earlier[4] from the products of Barton's reaction of the nitrite derived from 29,30-dinorlupan-20-ol. Hydrolysis of acetoxy ketone *XIII* gave hydroxy ketone *XI*. When diol *VI* was reacted with methanesulfonyl chloride in pyridine under cooling, monomesylate *IX* was formed which reacted[5] with sodium iodide and zinc dust in 1,2-dimethoxyethane to afford alcohol *X*. Oxidation of alcohol *X* led to ketone *XIV* the reduction of which with sodium in 1-propanol gave epimeric alcohols *X* and *XVI* in a 1 : 3 ratio. The effect of the substitution of the position 19α to the ratio of the epimeric alcohols formed in this reduction of 12-oxo derivatives is interesting. While for the polar substituent $CH_2OCH_3$ (ketone *XII*) the ratio of the formed alcohols *VII* and *XV* is 1:1, in the reduction of the ketone with the non-polar substituent $CH_3$ (ketone *XIV*) the equatorial alcohol *XVI* prevails over the axial alcohol *X* in a 3 : 1 ratio.

Reduction of the unsaturated ketone *XVII* with sodium borohydride gave two epimeric unsaturated alcohols differing in their polarity on thin-layer chromatography; the less polar epimer *XVIII* predominated in a 8 : 5 ratio over the more polar epimer *XX*. Their acetylation afforded corresponding acetates *XIX* and *XXI*. In order to propose their absolute configuration at $C_{(20)}$ empirical rules were made use of that were derived[6,7] for corresponding saturated derivatives *XLVII*–*L*: *a*) the less polar alcohol *XLVII* has the configuration 20*R*; *b*) the acetate with a higher value of molecular rotation has the configuration 20*S*; *c*) in the $^1$H-NMR spectra of acetates the 20*R* epimer *XLVIII* has $J_{19,20}$ (~0 Hz) lower than the 20*S* epimer *L* (+4·1 Hz). From these empirical rules the 20*R* configuration can be derived both for substance *XVIII* (less polar in thin-layer chromatography) and substance *XXIX* ($M_D = -98°$, $J_{19,20} = +1{\cdot}8$ Hz). For compounds *XX* (more polar in thin-layer chromatography), and *XXI* ($M_D = +45°$, $J_{19,20} = +6{\cdot}3$ Hz) the derived configuration is 20*S*. In order to confirm the proposed 20*S* configuration of acetate *XXI* its independent preparation was carried out by dehydration of compound *XXVII* with methanesulfonyl chloride-in pyridine. Compound *XXVII* is formed as the only product in the sodium borohydride reduction of the known[3] acetoxy ketone *XXXIV* with a 20*S* configuration.

When the unsaturated acetate *XIX* was reacted with hydrogen peroxide in acetic acid[8,9] ketone *XXIV* was obtained in merely a 12% yield. Therefore another synthesis was devised, starting from the known[3] acetoxy ketone *XXXIV*. When its acetate

group was hydrolyzed hydroxy ketone *XXXII* was obtained which was oxidized with Jones reagent to diketone *XXXV*. On reduction of diketone *XXXV* with lithium aluminum hydride two products were obtained; according to IR spectral measurements the reduction of both carbonyl groups took place. The ratio of the yields of

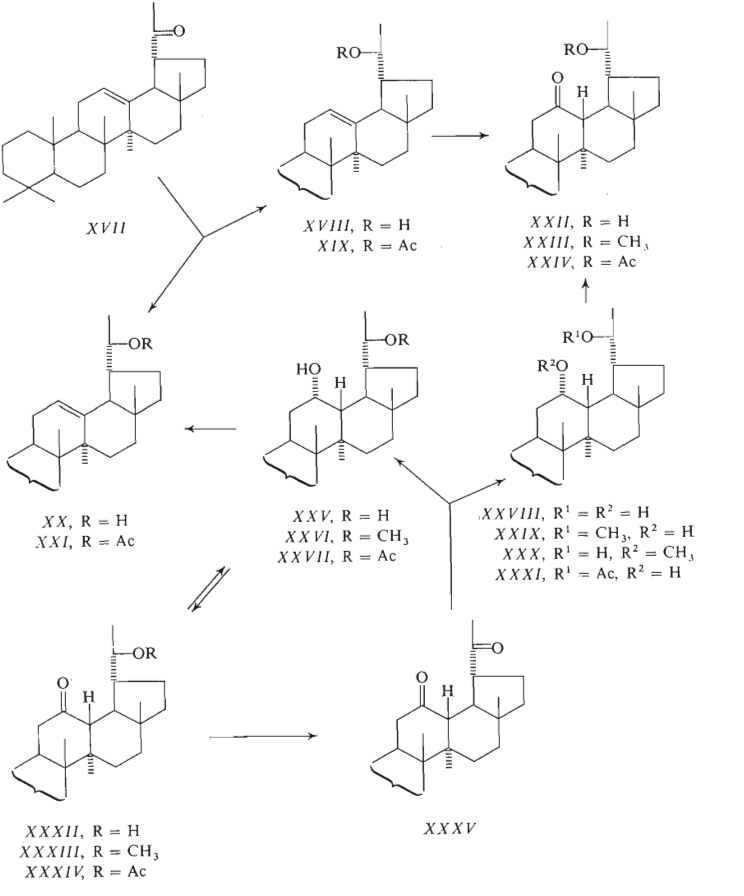


TABLE I
Methyl Signals of the $^1$H-NMR Spectra[a]

| Compound | 4α-$CH_3$ | 4β-$CH_3$ | 8β-$CH_3$ | 10β-$CH_3$ | 14α-$CH_3$ | 17β-$CH_3$ |
|---|---|---|---|---|---|---|
| | | | Reference compounds | | | |
| *XXXVI* | 0·837 | 0·795 | 1·023 | 0·837 | 0·959 | 0·751 |
| *XXXVII* | 0·829 | 0·789 | 1·020 | 0·840 | 0·973 | 0·778 |
| *XLI* | 0·849 | 0·804 | 1·047 | 0·849 | 0·906 | 0·766 |
| *XLIII* | 0·846 | 0·800 | 1·041 | 0·846 | 0·903 | 0·772 |
| *XLVI* | 0·848 | 0·802 | 1·042 | 0·848 | 0·923 | 0·744 |
| *XLVIII* | 0·838 | 0·794 | 1·034 | 0·838 | 0·860 | 0·753 |
| *L* | 0·843 | 0·800 | 1·038 | 0·843 | 0·908 | 0·761 |
| | | | Derivatives of 12-lupanone | | | |
| *I* | 0·859 | 0·825 | 1·241 | 0·895 | 0·842 | 0·744 |
| *XII* | 0·858 | 0·825 | 1·287 | 0·920 | (0·796) | (0·785) |
| *XIII* | 0·857 | 0·823 | 1·280 | 0·914 | (0·795) | (0·785) |
| *XIV* | 0·858 | 0·822 | 1·288 | 0·919 | 0·822 | 0·760 |
| *XXIII* | 0·861 | 0·828 | 1·295 | 0·918 | 0·848 | 0·751 |
| *XXIV* | 0·852 | 0·815 | 1·272 | 0·898 | (0·787) | (0·770) |
| *XXXIII* | 0·860 | 0·827 | 1·292 | 0·923 | 0·797 | 0·797 |
| *XXXIV* | 0·854 | 0·821 | 1·277 | 0·911 | (0·781) | (0·774) |
| | | | Derivatives of 12-lupanol | | | |
| *II* | 0·856 | 0·806 | 1·027 | 0·872 | 1·238 | 0·762 |
| *VII* | 0·857 | 0·812 | 1·034 | 0·884 | 1·203 | 0·758 |
| *X* | 0·863 | 0·816 | 1·047 | 0·892 | 1·193 | 0·746 |
| *XV* | 0·856 | 0·812 | 1·087 | (0·899) | (0·887) | 0·799 |
| *XXVII* | 0·861 | 0·812 | 1·034 | 0·881 | 1·168 | 0·746 |
| *XXXI* | 0·853 | 0·806 | 1·044 | 0·880 | 1·158 | 0·739 |
| | | | Derivatives of 12-lupene | | | |
| *III* | 0·869 | 0·819 | 1·002 | 0·955 | 1·154 | 0·628 |
| *V* | 0·872 | 0·824 | 1·008 | 0·965 | 1·097 | 0·629 |
| *XVII* | 0·870 | 0·820 | 0·999 | 0·950 | 1·166 | 0·650 |
| *XIX* | 0·869 | 0·821 | 1·010 | 0·963 | 1·065 | 0·615 |
| *XXI* | 0·873 | 0·824 | 1·015 | 0·971 | 1·085 | 0·620 |

[a] Accuracy of the measurement ±0·003 ppm; singlets; the values in parentheses are assigned tentatively and they can be mutually interchanged.

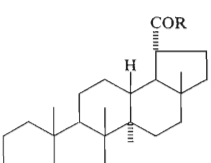
both products is 6 : 1 according to preparative chromatography, in favour of the less polar product. The more polar product is identical with 12α,(20*S*)-diol *XXV* which was obtained by hydrolysis of monoacetate *XXVII*. Acetylation of the less polar product *XXVIII* gave monoacetate *XXXI*. Its proposed structure with the configurations 12α and 20*R* is confirmed by its $^1$H-NMR spectrum (Table I). The absolute configuration at $C_{(20)}$ follows from the fact that compounds *XXVII* and *XXXI* represent epimers differing by configuration on $C_{(20)}$. As the monoacetate *XXVII* has configuration 20*S* the monoacetate *XXXI* must have configuration 20*R*. Monoacetate *XXXI* was oxidized with Jones's reagent to acetoxy ketone *XXIV* in a 27% overall yield, calculated with acetoxy ketone *XXXIV* as a basis. Hydrolysis of acetoxy ketone *XXIV* afforded hydroxy ketone *XXII*.

Partial methylation of diol *XXV* gave monomethyl ether *XXVI* which was oxidized to methoxy ketone *XXXIII*. Partial methylation of diol *XXVIII*, which was carried out under much more vigorous conditions, gave two products, *XXIX* and *XXX*, in an approximately 5 : 2 ratio. According to their IR spectra both compounds were methylated on one hydroxy group only. As oxidation of the less polar product *XXIX* gave 12-oxolupane derivative *XXIII*, substance *XXIX* must have the structure of 12α-hydroxy-20-methoxy derivative. Hence, for compound *XXX* the structure 12α-methoxy-20-hydroxy derivative must be accepted.

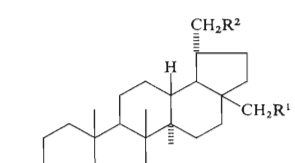
In our previous work[1–4] we found that the introduction of a keto or a hydroxy group into the position 12 distinctly affects the chemical shifts of the signals of the methyl group in the positions 8β, 10β and 14α. In derivatives of 12-lupene considerable differences were found[8–10] in chemical shifts of the methyl signals in the positions 10β, 14α and 17β in comparison with corresponding saturated derivatives (with *trans* annelation of the rings C and D). Characteristic parameters of the $^1$H-NMR spectra of reference substances of compounds *XXXVI*, *XXXVII* and *XLII* and *L* were taken from literature[3,4]; compound *XLVIII* was prepared according to ref.[7]. Compounds *XLI* and *XLVI* were prepared from the known[4] dinoralcohol *XXXVIII*.

The reaction of compound *XXXVIII* with methyl iodide and silver oxide gave methyl ether diacetate *XXXIX* the hydrolysis of which gave rise to dihydroxy methyl ether *XL* which was converted to methyl ether *XLI* by Huang–Minlon reduction of the corresponding 3,28-dioxo derivative. On reaction with methanesulfonyl chloride dinoralcohol *XXXVIII* gave mesylate *XLIII* the reduction of which with zinc and sodium iodide in 1,2-dimethoxyethane[5] gave compound *XLIV*. When hydrolyzed the latter compound afforded diol *XLV* from which the hydrocarbon *XLVI* was prepared *via* the corresponding 3,28-dioxo derivative.

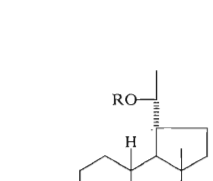
The methyl signals of the $^1$H-NMR spectra are given in Table I, while other characteristic signals, confirming the proposed structures, are given under Experimental. The changes of the chemical shifts of the methyl signals are related to the corres-



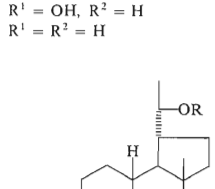

*XXXVI*, R = $OCH_3$
*XXXVII*, R = $CH_3$




*XXXVIII*, $R^1$ = OAc, $R^2$ = OH
*XXXIX*, $R^1$ = OAc, $R^2$ = $OCH_3$
*XL*, $R^1$ = OH, $R^2$ = $OCH_3$
*XLI*, $R^1$ = H, $R^2$ = $OCH_3$
*XLII*, $R^1$ = H, $R^2$ = OAc
*XLIII*, $R^1$ = OAc, $R^2$ = $OSO_2CH_3$
*XLIV*, $R^1$ = OAc, $R^2$ = H
*XLV*, $R^1$ = OH, $R^2$ = H
*XLVI*, $R^1$ = $R^2$ = H




*XLVII*, R = H
*XLVIII*, R = Ac




*IL*, R = H
*L*, R = Ac

ponding reference substances: In the case of 12-oxo and 12-hydroxy derivatives to corresponding deoxy derivatives, and in the case of the derivatives of 12-lupene to corresponding saturated derivatives with a *trans* annelation of the C and D ring. In derivatives of 12-lupanone a downfield shift of the signals of 8β-$CH_3$ (0·22 to 0·25 ppm) and 10β-$CH_3$ (0·06–0·07 ppm) and an upfield shift of the signal of 14α-$CH_3$ (0·07–0·12 ppm) were found. A further characteristic signal in the 12--lupanone derivatives is the doublet of 13β-H (2·58–2·78 ppm, $J_{13,18}$ = 10 to 11·5 Hz). In the case of compounds *XII* and *XIV* the analysis of the ABX system of the protons bound in the positions 11α, 11β and 9α made it possible to obtain the coupling constant values, $J_{11\alpha,11\beta} = -12$ Hz, $J_{9\alpha,11\alpha} = +3{\cdot}1$ Hz, and $J_{9\alpha,11\beta} = +14$ Hz, which are in good agreement with the values found for 12-oxolupane derivatives earlier[1,3,4].

For the differentiation between the two possible orientations of the hydroxyl group in the position 12 it is possible to make use of the value of the chemical shift of 14α-$-CH_3$ and the width of the multiplet of the signal of 12-H. In the case of 12α-hydroxy derivatives the 1,3-diaxial interaction causes a downfield shift of the 14α-$CH_3$ signal (0·26–0·30 ppm), the width of the 12β-H signal (10–11 Hz) corresponds[1] to its equatorial orientation. In the spectrum of 12β-hydroxy derivative *XV* the equatorial hydroxyl group practically does not affect the chemical shifts of the 8β-$CH_3$, 10β-$CH_3$ and 14α-$CH_3$ protons; the width of the 12α-H signal (>20 Hz) corresponds[2] to its axial orientation. The changes of the chemical shifts of the signals of 10β-$CH_3$ (downfield 0·11–0·13 ppm), 14α-$CH_3$ (downfield 0·18–0·20 ppm) and 17β-$CH_3$ (upfield 0·12–0·15 ppm) groups of 12-lupene derivatives correspond to the changes observed in 12-lupene derivatives earlier[8–10].

## EXPERIMENTAL

The melting points were determined on a Kofler block. Optical rotations were measured in chloroform on an automatic polarimeter ETL-NPL (Bendix–Ericsson) with a ± 1–2° accuracy. The infrared spectra were measured on UR-10 and UR-20 instruments (Zeiss, Jena, GDR). The $^1$H-NMR spectra were recorded on a Varian HA-100 (100 MHz) instrument in deuteriochloroform with tetramethylsilane as internal reference; the chemical shifts are given in ppm of δ-scale. Neutral alumina (Reanal, activity II) was used for column chromatography. For thin-layer chromatography silica gel G (Merck) was used. The reaction mixtures were worked up using the following procedures: *A*) The excess of hydride was decomposed with water and dilute hydrochloric acid (1 : 4), the product was extracted with ether, the extract washed with a saturated aqueous sodium hydrogen carbonate solution and water; *B*) the reaction mixture was poured onto ice, the separated product was filtered off under suction, washed with water and dried in a vacuum; *C*) the excess of oxidation reagent was decomposed with oxalic acid, the reaction mixture was poured into water, the product was extracted with ether, the extract washed with a saturated aqueous sodium hydrogen carbonate solution and water; *D*) the reaction mixture was diluted with a tenfold amount of ether and the organic phase was washed with water; *E*) the mixture was poured onto ice, the product was extracted with ether, the extract washed with dilute hydrochloric acid (1 : 4), then water, saturated aqueous sodium hydrogen carbonate solution, and water; *F*) the reaction mixture was poured into water, acidified with hydrochloric acid, extracted with ether, the extract was washed with saturated sodium hydrogen carbonate solution and water. Organic phases were dried over anhydrous sodium sulfate. Samples for analysis were dried over phosphorus pentoxide at 100°C and 13–133 Pa (0·1–1 Torr) for 8 to 12 h. The identity of the sample prepared in various ways was confirmed by comparison of their IR spectra, optical rotation values, thin-layer chromatography data and mixture melting point determinations.

20-Hydroxy-29,30-dinorlup-12-ene (*IV*)

Lithium aluminum hydride (200 mg) was added to a solution of 120 mg of unsaturated ester[2] *III* in 30 ml of tetrahydrofuran and the mixture was refluxed for 4 h under argon. The mixture was worked up using procedure *A*). The residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (7 : 3). Yield, 100 mg of alcohol *IV*, m.p. 148–150°C

(light petroleum), $[\alpha]_D$ −7·8° (*c* 0·64). IR spectrum (tetrachloromethane): 3638, 1022 (OH) $cm^{-1}$. For $C_{28}H_{46}O$ (398·7) calculated: 84·35% C, 11·63% H; found: 84·45% C, 11·49% H.

20-Acetoxy-29,30-dinorlup-12-ene (*V*)

Acetic anhydride (2 ml) was added to a solution of 65 mg of alcohol *IV* in 5 ml of pyridine and the mixture heated at 100°C for 3 h. After working up according to procedure *B*) the crude product was crystallized from methanol–ether to afford 45 mg of acetate *V*, m.p. 96—98°C, $[\alpha]_D$ −13·6° (*c* 0·70). IR spectrum (tetrachloromethane): 1738, 1239, 1030 ($CH_3COO$) $cm^{-1}$. $^1$H-NMR spectrum: 2·04 s ($CH_3COO$); 3·74 dd and 4·32 dd, $J_{gem} \approx -10·5$ Hz, $J_{vic_1} \approx 8·5$ Hz, $J_{vic_2} \approx$ ≈ 3·5 Hz (20-H); 5·23 mt, $W \approx 10$ Hz (12-H). For $C_{30}H_{48}O_2$ (440·7) calculated: 81·76% C, 10·98% H; found: 81·88% C, 11·11% H.

29,30-Dinorlupane-12α,20-diol (*VI*)

*a*) Lithium aluminum hydride (330 mg) was added to a solution of 220 mg of keto ester[2] *I* in 25 ml of tetrahydrofuran. After 6 h refluxing under argon the mixture was worked up using the procedure *A*). Crystallization of the residue from ether gave 190 mg of diol *VI*, m.p. 209 to 212°C, $[\alpha]_D$ +6·1° (*c* 0·57). IR spectrum (chloroform): 3609, 3564 (OH) $cm^{-1}$. For $C_{28}H_{48}O_2$ (416·7) calculated: 80·71% C, 11·61% H; found: 80·55% C, 11·80% H.

*b*) Lithium aluminum hydride (110 mg) was added to a solution of 35 mg of hydroxy ester[2] *II* in 20 ml of tetrahydrofuran, and the mixture refluxed under argon for 4 h. The mixture was worked up using procedure *A*). Crystallization of the residue from ether afforded 27 mg of diol *VI*, m.p. 210—213°C, $[\alpha]_D$ +6·4° (*c* 0·55).

20-Methoxy-29,30-dinorlupan-12α-ol (*VII*)

*a*) Methyl iodide (0·15 ml) was added to a suspension of 350 mg of sodium hydride in a solution of 200 mg of diol *VI* in 15 ml of tetrahydrofuran. After 15 min stirring at 45°C another 0·15 ml of methyl iodide was added and the mixture stirred at 45°C for another 15 min; the reaction was carried out under argon. The mixture was worked up using procedure *A*). Chromatography of the residue on two preparative silica gel plates (20 × 20 cm) in light petroleum–ether (4 : 1) gave 160 mg of hydroxy ether *VII*, m.p. 163—164°C (ether–methanol), $[\alpha]_D$ −18·5° (*c* 0·50). IR spectrum (chloroform): 1108 ($OCH_3$), 3470 (OH) $cm^{-1}$. $^1$H-NMR spectrum: 3·35 s ($OCH_3$); 3·42 dd and 3·63 dd, $J_{gem} \approx -9·5$ Hz, $J_{vic_2} \approx 2·9$ Hz (20-$H_2$); 4·05 mt, $W \approx 10$ Hz (12β-H). For $C_{29}H_{50}O_2$ (430·7) calculated: 80·87% C, 11·70% H; found: 80·58% C, 11·77% H.

*b*) Sodium (750 mg) was added over 2 h to a stirred and refluxing solution of 70 mg of ketone *XII* in a mixture of 10 ml of benzene and 15 ml of 1-propanol. After cooling the mixture was worked up according to procedure *F*). The residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (4 : 1). Elution of the zones containing the less polar substance with dichloromethane gave 32 mg of hydroxy ether *VII*, m.p. 163—164°C (ether–methanol).

*c*) Lithium aluminum hydride (30 mg) was added to a solution of ketone *XII* (10 mg) in tetrahydrofuran (5 ml) and refluxed under argon for 4 h. After working up according to procedure *A*) and crystallization of the residue from ether–methanol 6 mg of hydroxy ether *VII* were obtained, m.p. 162—164°C.

20-Acetoxy-29,30-dinorlupan-12α-ol (*VIII*)

Diol *VI* (210 mg) was dissolved in pyridine (4 ml) and acetic anhydride (1·1 ml) and allowed to stand in an ice-cold bath for 3 h. The mixture was worked up according to procedure *B*). Chromatography of the crude product on 2 preparative silica gel plates (20 × 20 cm) in light petroleum–ether (7 : 3) gave 150 mg of monoacetate *VIII*, m.p. 191–192°C (ether), $[\alpha]_D$ −10·5° (*c* 0·47). IR spectrum (chloroform): 1734, 1240, 1025 ($CH_3COO$), 3616, 3508 broad (OH) $cm^{-1}$. For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·63% C, 11·11% H.

29·30-Dinorlupan-12α-ol (*X*)

*a*) Methanesulfonyl chloride (1·4 ml) was added to a solution of 280 mg of diol *VI* in 14 ml of pyridine, cooled at −20°C. After 90 min standing at −5°C the reaction mixture was worked up according to procedure *E*). According to TLC the residue (320 mg) contained predominantly mesylate *IX*; its IR spectrum (tetrachloromethane): 3625, 3565 broad, 1039 (OH), 1347, 1178 ($CH_3SO_2O$) $cm^{-1}$. The residue was dissolved in 15 ml of 1,2-dimethoxyethane and 900 mg of sodium iodide and 780 mg of zinc dust were added to it. The mixture was refluxed under stirring for 2 h. After cooling it was filtered through a column of alumina (10 g) and the eluate evaporated. The residue was crystallized from a mixture of dichloromethane and acetone to afford 173 mg of alcohol *X*, m.p. 172–174°C, $[\alpha]_D$ −7·6° (*c* 0·52). IR spectrum (tetrachloromethane): 3630, 1042, 1029 (OH) $cm^{-1}$. $^1$H-NMR spectrum: 1·150 d, $J_{19,20}$ = 6·3 Hz (19α-$CH_3$); 4·07 q, $W \approx 10$ Hz (12β-H). For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 84·01% C, 11·99% H.

*b*) Sodium (2·5 g) was added into refluxing and stirred solution of 120 mg of ketone *XIV* in 10 ml of benzene and 40 ml of 1-propanol over 2 h. After cooling the mixture was worked up using procedure *F*). The residue was chromatographed on 2 preparative silica gel plates (20 × 20 cm) in light petroleum–ether (9 : 1). Elution of the zones containing the least polar zone gave 45 mg of the starting ketone *XIV*. On elution of the zones containing the substance of medium polarity 15 mg of alcohol *X* were obtained, m.p. 172–174°C, (dichloromethane–acetone).

20-Hydroxy-29,30-dinorlupan-12-one (*XI*)

Potassium hydroxide (70 mg) dissolved in 2 ml of ethanol was added to a solution of 50 mg of acetoxy ketone *XIII* in 2 ml of benzene and the mixture was allowed to stand at room temperature for 12 h. The reaction mixture was worked up using the procedure *D*). Crystallization of the residue from ether gave 32 mg of hydroxy ketone *XI*, m.p. 214–216°C. IR spectrum (tetrachloromethane): 1708 (C=O), 3553, 1043 (OH) $cm^{-1}$. For $C_{28}H_{46}O_2$ (414·7) calculated: 81·10% C, 11·18% H; found: 81·23% C, 11·11% H.

20-Methoxy-29,30-dinorlupan-12-one (*XII*)

*a*) Jones's reagent (0·3 ml) was added to a solution of 90 mg of hydroxy ether *VII* under stirring, and after 10 min stirring at room temperature the reaction mixture was worked up using procedure *C*). Crystallization of the residue from light petroleum gave 75 mg of ketone *XII*, m.p. 150–152°C, $[\alpha]_D$ −12·3° (*c* 0·41). IR spectrum (tetrachloromethane): 1708 (C=O), 2812, 1115 ($OCH_3$) $cm^{-1}$. $^1$H-NMR spectrum: 2·26 AB part of the ABX system, $J_{11\alpha,11\beta}$ = −12 Hz, $J_{9\alpha,11\alpha}$ = 3·9 Hz, $J_{9\alpha,11\beta}$ = 14 Hz (11-$H_2$); 2·76 d, $J_{13,18}$ = 11 Hz (13β-H); 3·30 s ($OCH_3$); 3·24 dd and 3·65 dd, $J_{gem} \approx -9$ Hz, $J_{vic_1} \approx 8$ Hz, $J_{vic_2} \approx 4$ Hz (20-$H_2$). For $C_{29}H_{48}O_2$ (428·7) calculated: 81·25% C, 11·29% H; found: 81·11% C, 11·11% H.

*b*) Jones's reagent (5 drops) was added to a solution of 12 mg of hydroxy ether *XV* in 1 ml of acetone and after 10 min stirring at room temperature the reaction mixture was worked up using procedure *C*). On crystallization of the residue from hexane 10 mg of ketone *XII* were obtained, m.p. 148–150°C, $[\alpha]_D$ −10° (*c* 0·52).

20-acetoxy-29,30-dinorlupan-12-one (*XIII*)

Jones's reagent (0·5 ml) was added into a solution of 60 mg of monoacetate *VIII* in 7 ml of dichloromethane and 7 ml of acetone and the mixture was stirred at room temperature for 10 min. It was then worked up according to procedure *C*). Chromatography of the residue on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (7 : 3) gave 55 mg of acetoxy ketone *XIII*, m.p. 149–152°C (ether), $[\alpha]_D$ −15·5° (*c* 0·55), identical with an authentic sample[4].

29,30-Dinorlupan-12-one (*XIV*)

*a*) Jones's reagent (0·5 ml) was added under stirring to a solution of 80 mg of alcohol *X* in a mixture of 10 ml of dichloromethane and 10 ml of acetone, and the mixture was stirred at room temperature for 10 min and then worked up according to procedure *C*). Crystallization of the residue from ether afforded 75 mg of ketone *XIV*, m.p. 195–196°C, $[\alpha]_D$ +16·5° (*c* 0·57). IR spectrum (tetrachloromethane): 1711 (C=O) $cm^{-1}$. $^1$H-NMR spectrum: 1·066 d, $J_{19,20}$ = = 6·0 Hz (19α-$CH_3$); 2·26 AB part of the ABX system, $J_{11\alpha,11\beta} = -12$ Hz, $J_{9\alpha,11\alpha} = 3{\cdot}1$ Hz, $J_{9\alpha,11\beta} = 14$ Hz (11-$H_2$); 2·72 d, $J_{13,18} = 11$ Hz (13β-H). For $C_{28}H_{46}O$ (398·7) calculated: 84·35% C, 11·63% H; found: 84·52% C, 11·55% H.

*b*) Jones's reagent (5 drops) was added to a solution of 15 mg of alcohol *XVI* in a mixture of 1 ml of dichloromethane and 1 ml of acetone and the mixture was stirred at room temperature for 10 min and then worked up according to procedure *C*). Crystallization of the residue from ether gave 8 mg of ketone *XIV*, m.p. 192–194°C.

20-Methoxy-29,30-dinorlupan-12β-ol (*XV*)

Elution of the zones containing the more polar substances (for the preparation of compound *VII* see procedure *b*)) gave 35 mg of oily hydroxy ether *XV*, $[\alpha]_D$ −19·4° (*c* 0·46). IR spectrum (tetrachloromethane): 1107 ($OCH_3$), 3473 broad (OH) $cm^{-1}$. $^1$H-NMR spectrum: 3·28 t and 3·48 dd, $J_{gem} \approx -9$ Hz, $J_{vic_1} \approx 9$ Hz. $J_{vic_2} \approx 3$ Hz (20-$H_2$); 3·35 s ($OCH_3$); 3·61 mt, $W \geqq$ $\geqq$ 20 Hz (12α-H). For $C_{29}H_{50}O_2$ (430·7) calculated: 80·87% C, 11·70% H; found: 80·67% C, 11·51% H.

29,30-Dinorlupan-12β-ol (*XVI*)

Elution of the zones containing the most polar substance (preparation of alcohol *X* procedure *b*)) gave 50 mg of alcohol *XVI*, m.p. 189–190°C (ether), $[\alpha]_D$ −22·8° (*c* 0·57). IR spectrum (tetrachloromethane): 3652, 3612 (OH) $cm^{-1}$. For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 84·05% C, 12·00% H.

(20*R*)-20-Hydroxy-30-nor-12-lupene (*XVIII*)

Sodium borohydride (300 mg) was added into a solution of norketone[2] *XVII* (150 mg) in benzene (6 ml) and methanol (6 ml) and allowed to stand at room temperature for 12 h. The reaction mixture was worked up using procedure *D*). The residue was chromatographed on 2 preparative

silica gel plates (20 × 20 cm) in light petroleum–ether (4 : 1). The zones containing the less polar substance were combined and eluted with dichloromethane. Yield, 80 mg of alcohol *XVIII*, m.p. 174–175°C (ether), $[\alpha]_D$ +5·2° (*c* 0·48). IR spectrum (tetrachloromethane); 3631 (OH) $cm^{-1}$. For $C_{29}H_{48}O$ (412·7) calculated: 84·40% C, 11·72% H; found: 84·23% C, 11·64% H.

(20*R*)-20-Acetoxy-30-nor-12-lupene (*XIX*)

A solution of 76 mg of alcohol *XVIII* in 4 ml of pyridine and 2 ml of acetic anhydride was heated at 100°C for 3 h and then the mixture worked up using procedure *B*). Crystallization of the crude product from ether afforded 82 mg of acetate *XIX*, m.p. 161–163°C, $[\alpha]_D$ −21·6° (*c* 0·78). IR spectrum (tetrachloromethane): 1737, 1247, 1031 ($CH_3COO$) $cm^{-1}$. $^1$H-NMR spectrum: 1·208 d, $J_{20,29}$ = 6·6 Hz (20-$CH_3$); 2·005 s ($CH_3COO$); 5·03 dq, $J_{20,29}$ = 6·6 Hz, $J_{20,19}$ = = 1·8 Hz (20-H); 5·10 mt, $W \leqq 11$ Hz (12-H). For $C_{31}H_{50}O_2$ (454·7) calculated: 81·88% C, 11·18% H; found: 81·62% C, 11·21% H.

(20*S*)-20-Hydroxy-30-nor-12-lupene (*XX*)

Elution of the combined zones, containing the more polar substance (preparation of alcohol *XVIII*), with dichloromethane gave 49 mg of alcohol *XX*, m.p. 147–150°C (hexane), $[\alpha]_D$ +1·3° (*c* 0·37). IR spectrum (tetrachloromethane); 3629, 3584 (OH) $cm^{-1}$. For $C_{29}H_{48}O$ (412·7) calculated: 84·40% C, 11·72% H; found: 84·34% C, 11·55% H.

(20*S*)-20-Acetoxy-30-nor-12-lupene (*XXI*)

*a*) Alcohol *XX* (40 mg) was acetylated in a mixture of 2 ml of pyridine and 1 ml acetic anhydride at 100°C for 3 h. The mixture was worked up using procedure *B*). Crystallization of the crude product from ether gave 40 mg of acetate *XXI*, m.p. 135–145°C/162–163°C, $[\alpha]_D$ +9·8° (*c* 0·56). IR spectrum (tetrachloromethane): 1734, 1249, 1058 ($CH_3COO$) $cm^{-1}$. $^1$H-NMR spectrum: 1·142 d, $J_{20,29}$ = 6·3 Hz (20-$CH_3$); 1·96 s ($CH_3COO$); 5·06 p, $J_{20,29}$ = 6·3 Hz, $J_{19,20} \approx 6{\cdot}3$ Hz (20-H); 5·36 mt, $W$ = 10 Hz (12-H). For $C_{31}H_{50}O_2$ (454·7) calculated: 81·88% C, 11·18% H; found: 81·55% C, 11·35% H.

*b*) Methanesulfonyl chloride (1 ml) was added to a solution of hydroxy acetate *XXVII* (30 mg) in pyridine (2 ml) and the mixture heated at 100°C for 90 min and then worked up using procedure *E*). Chromatography of the residue on a preparative silica gel plate (10 × 20 cm) in light petroleum–ether (9 : 1) gave 16 mg of acetate *XXI*, m.p. 163–166°C (ether), $[\alpha]_D$ +13° (*c* 0·42).

(20*R*)-20-Hydroxy-30-norlupan-12-one (*XXII*)

A solution of 16 mg of acetoxy ketone *XXIV* and 200 mg of potassium hydroxide in 4 ml of ethanol was refluxed for 6 h. The mixture was evaporated and the residue dissolved in ether and water, the aqueous phase was extracted with ether and the combined organic phases were washed with water (4×). Crystallization of the residue from ether gave 8 mg of hydroxy ketone *XXII*, m.p. 220–224°C. IR spectrum (tetrachloromethane): 1700 (C=O), 3538, 1045 (OH) $cm^{-1}$. For $C_{29}H_{48}O_2$ (428·7) calculated: 81·25% C, 11·29% H; found: 81·28% C, 11·36% H.

(20*R*)-20-Methoxy-30-norlupan-12-one (*XXIII*)

Hydroxy ether *XXIX* (27 mg) was dissolved in a mixture of acetone (3 ml) and dichloromethane (5 ml), and Jones's reagent (0·2 ml) was added to it. The mixture was stirred at room tempera-

ture for 5 min and worked up using procedure *C*). Crystallization of the residue from light petroleum gave 20 mg of methoxy ketone *XXIII*, m.p. 232–235°C, $[\alpha]_D$ −14° (*c* 0·63). IR spectrum trum (tetrachloromethane): 1711 (C=O), 1099, 1090 ($OCH_3$) $cm^{-1}$. $^1$H-NMR spectrum: 1·016 d, $J_{20,29}$ = 6·2 Hz (20-$CH_3$); 2·28 AB part of the ABX system, $J_{11\alpha,11\beta}$ = −12 Hz (11-$H_2$); 2·76 d, $J_{13,18}$ = 10·5 Hz (13β-H); 3·47 s ($OCH_3$); 3·93 bq, $J_{20,29}$ = 6·2 Hz, $J_{19,20} \leqq$ ≦ 1 Hz (20-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·33% C 11·24% H.

(20*R*)-20-Acetoxy-30-norlupan-12-one (*XXIV*)

*a*) A mixture of 2 ml of 30% hydrogen peroxide and 2 ml of acetic acid was added to a solution of 60 mg of olefin *XIX* in 5 ml of acetic acid at 100°C over 15 min and the mixture was allowed to stand at this temperature for 2 h. It was then worked up using procedure *F*). The residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (3 : 2). The zone containing the least polar substance was eluted with dichloromethane. Yield 8 mg of acetoxy ketone *XXIV*, m.p. 169–171°C (methanol), $[\alpha]_D$ −22·2° (*c* 0·36).

*b*) Jones's reagent (0·3 ml) was added to a solution of hydroxy acetate *XXXI* (20 mg) in acetone (3 ml), the mixture was stirred at room temperature for 5 min and then worked up using procedure *C*). Crystallization of the residue from methanol gave 15 mg of acetoxy ketone *XXIV*, m.p. 172–174°C, $[\alpha]_D$ −22·5° (*c* 0·75). IR spectrum (tetrachloromethane): 1735, 1249, 1042 ($CH_3COO$). 1711 (C=O) $cm^{-1}$. $^1$H-NMR spectrum: 1·172 d, $J_{20,29}$ = 6·4 Hz (20-$CH_3$); 2·08 s ($CH_3COO$); 2·27 AB part of the ABX system (11-$H_2$); 2·73 d, $J_{13,18} \approx$ 10 Hz (13β-H); 5·15 bq, $J_{20,29}$ = 6·4 Hz, $J_{19,20} \approx$ 1 Hz (20-H). For $C_{31}H_{50}O_3$ (470·7) calculated:79·10% C, 10·70% H; found: 79·12% C, 10·55% H.

(20*S*)-30-Norlupane-12α,20-diol (*XXV*)

*a*) A solution of potassium hydroxide (100 mg) in ethanol (2 ml) was added to a solution of hydroxy acetate *XXVII* (70 mg) in benzene (4 ml) and the mixture was allowed to stand at room temperature for 12 h. After working up according to procedure *D*) the residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (1 : 1) to afford 50 mg of diol *XXV*, m.p. 135–145°C/189–191°C (methanol), $[\alpha]_D$ +17·9° (*c* 0·58). IR spectrum (chloroform): 3620, 3560, 3270 broad (OH) $cm^{-1}$. For $C_{29}H_{50}O_2$ (430·7) calculated: 80·87% C, 11·70% H; found: 80·95% C, 11·63% H.

*b*) The zones containing the more polar substance (preparation of diol *XXVIII*) were combined and eluted with ether. Yield, 28 mg of diol *XXV*, m.p. 137–147°C/186–188°C (methanol), $[\alpha]_D$ +17·2° (*c* 0·49).

(20*S*)-20-Methoxy-30-norlupan-12α-ol (*XXVI*)

Methyl iodide (0·1 ml) was added to a suspension of sodium hydride (100 mg) in a solution of diol *XXV* (30 mg) in tetrahydrofuran (9 ml) and the mixture was stirred at 40°C for 30 min. Additional methyl iodide (0·01 ml) was added and the mixture was stirred at 40°C for another 30 min. The reaction was carried out under argon and the mixture was worked up using procedure *A*). Chromatography of the residue on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (4 : 1) gave 18 mg of hydroxy ether *XXVI*, m.p. 200–202°C (ether), $[\alpha]_D$ +4° (*c* 0·60). IR spectrum (tetrachloromethane): 1100 ($OCH_3$), 3615, 3445 (OH) $cm^{-1}$. For $C_{30}H_{52}$. $.O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 81·32% C, 11·65% H.

(20*S*)-20-Acetoxy-30-norlupan-12α-ol (*XXVII*)

Sodium borohydride (90 mg) was added to a solution of acetoxy ketone *XXXIV* (45 mg) in a mixture of benzene (2 ml) and methanol (2 ml) and the mixture was allowed to stand at room temperature for 12 h. After working up according to procedure *F*), the residue was crystallized from ether, affording 37 mg of hydroxy acetate *XXVII*, m.p. 225–226°C, $[\alpha]_D$ +23·6° (*c* 0·42). IR spectrum (chloroform): 1713, 1262, 1036 ($CH_3COO$), 3614 (OH) $cm^{-1}$. $^1$H-NMR spectrum: 1·222 d, $J_{20,29}$ = 6·4 Hz (20-$CH_3$); 1·99 s ($CH_3COO$); 4·15 mt, $W$ = 11 Hz (12β-H); 5·37 dq, $J_{20,29}$ = 6·4 Hz, $J_{20,19}$ = 3·8 Hz (20-H). For $C_{31}H_{52}O_3$ (472·8) calculated: 78·76% C, 11·09% H; found: 78·55% C, 11·25% H.

(20*R*)-30-Norlupane-12α,20-diol (*XXVIII*)

Lithium aluminum hydride (225 mg) was added to a solution of diketone *XXXV* (205 mg) in tetrahydrofuran (20 ml) and refluxed under argon for 90 min. After working up according to procedure *A*) the residue was chromatographed on 2 preparative silica gel plates (20 × 20 cm) in light petroleum–ether (1 : 1). The zones with the less polar substance were combined and eluted with dichloromethane. Yield, 163 mg of diol *XXVIII*, m.p. 180–184°C/205–207°C (light petroleum), $[\alpha]_D$ −4·4° (*c* 0·46). IR spectrum (chloroform): 3607, 3483 (OH) $cm^{-1}$. For $C_{29}H_{50}O_2$ (430·7) calculated: 80·87% C, 11·70% H; found: 80·94% C, 11·76% H.

(20*R*)-20-Methoxy-30-norlupan-12α-ol (*XXIX*)

Methyl iodide (0·5 ml) was added to a suspension of sodium hydride (200 mg) in a solution of diol *XXVIII* (70 mg) in tetrahydrofuran (12 ml) and the mixture was stirred at 40°C for 30 min. After addition of another 0·5 ml portion of methyl iodide the reaction mixture was stirred again at 40°C for 30 min. The operation was carried out under argon. The mixture was worked up using procedure *A*). The residue was chromatographed on a preparative silica gel plate (20 × × 20 cm) in light petroleum–ether (9 : 1). Elution of the zone containing the less polar substance gave 34 mg of hydroxy ether *XXIX*, m.p. 222–224°C (tetrachloromethane–acetone), $[\alpha]_D$ −18° (*c* 0·83). IR spectrum (tetrachloromethane): 1081 ($OCH_3$), 3520, 1032 (OH) $cm^{-1}$. For $C_{30}H_{52}O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 81·15% C, 11·66% H.

(20*R*)-12α-Methoxy-30-norlupan-20-ol (*XXX*)

The zones containing the more polar compound (preparation of hydroxy ether *XXIX*) were eluted with dichloromethane and 13 mg of hydroxy ether *XXX* were thus obtained, m.p. 232–234°C (light petroleum), $[\alpha]_D$ +9·2° (*c* 0·54). IR spectrum (tetrachloromethane): 1088 ($OCH_3$), 3545, 1048, 1019 (OH) $cm^{-1}$. For $C_{20}H_{52}O_2$ (444·7) calculated: 81·02% C, 11·79% H; found: 81·16% C, 11·66% H.

(20*R*)-20-Acetoxy-30-norlupan-12α-ol (*XXXI*)

Diol *XXVIII* (120 mg) in pyridine (4 ml) and acetic anhydride (1 ml) was heated at 80°C for 3 h and then worked up using procedure *E*). Chromatography of the residue on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (3 : 2) gave 70 mg of hydroxy acetate *XXXI*, m.p. 170–172°C (methanol), $[\alpha]_D$ −5·1° (*c* 0·59). IR spectrum (tetrachloromethane): 1723, 1257, 1045 ($CH_3COO$), 3608, 3503, 1031 (OH) $cm^{-1}$. $^1$H-NMR spectrum: 1·226 d, $J_{20,29}$ = = 6·3 Hz (20-$CH_3$); 2·045 s ($CH_3COO$), 3·99 mt, $W \approx 10$ Hz (12β-H); 5·18 q, $J_{20,29}$ = 6·3 Hz,

$J_{20,19} \approx 0$ Hz (20-H). For $C_{31}H_{52}O_3$ (472·8) calculated: 78·76% C, 11·09% H; found: 78·55% C' 11·25% H.

(20*S*)-20-Hydroxy-30-norlupan-12-one (*XXXII*)

A solution of potassium hydroxide (250 mg) in 2·5 ml of ethanol was added to a solution of acetoxy ketone *XXXIV* (250 mg) in benzene (5 ml) and allowed to stand at room temperature for 12 h. After working up according to procedure *D*) the residue was crystallized from ether, affording 205 mg of hydroxy ketone *XXXII*, m.p. 219—221°C, $[\alpha]_D$ −6·5° (*c* 0·46). IR spectrum (tetrachloromethane): 1708 (C=O), 3628, 3590, 3468 broad (OH) $cm^{-1}$. For $C_{29}H_{48}O_2$ (428·7) calculated: 81·25% C, 11·29% H; found: 81·36% C, 11·44% H.

(20*S*)-20-Methoxy-30-norlupan-12-one (*XXXIII*)

Jones's reagent (0·1 ml) was added to a solution of hydroxy ether *XXVI* (16 mg) in acetone (3 ml) and dichloromethane (3 ml), and stirred at room temperature for 5 min. After working up according to procedure *C*) the residue was chromatographed on a preparative silica gel plate (10 × 20 cm) in light petroleum–ether (5 : 1) to afford 14 mg of methoxy ketone *XXXIII*, m.p. 170—173°C (light petroleum), $[\alpha]_D$ −3° (*c* 0·73). IR spectrum (tetrachloromethane): 1711 (C=O) 1100 ($OCH_3$) $cm^{-1}$. $^1$H-NMR spectrum: 1·178 d, $J_{20,29}$ = 5·9 Hz (20-$CH_3$); 2·78 d, $J_{13,18}$ = = 11·5 Hz (13β-H); 3·20 s ($OCH_3$); 3·63 mt (20-H). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·56% C, 11·23% H.

30-Norlupane-12,20-dione (*XXV*)

Jones's reagent (1·5 ml) was added to a solution of hydroxy ketone *XXXII* (230 mg) in a mixture of dichloromethane (20 ml) and acetone (20 ml), and the mixture was stirred at room temperature for 6 min. It was then worked up using procedure *C*) and the residue was crystallized from light petroleum. Yield 220 mg of diketone *XXXV*, m.p. 186—188°C, $[\alpha]_D$ +9·2° (*c* 0·54). IR spectrum (tetrachloromethane): 1707 (C=O), 1707, 1369 ($CH_3CO$) $cm^{-1}$. For $C_{29}H_{46}O_2$ (426·7) calculated: 81·63% C, 10·87% H; found: 81·47% C, 10·92% H.

3β,28-Diacetoxy-20-methoxy-29,30-dinorlupane (*XXXIX*)

Silver oxide (950 mg) was added to a solution of alcohol[4] *XXXVIII* (200 mg) and methyl iodide (1 ml) in benzene (30 ml) and the mixture was refluxed for 10 h. After filtration through diatomaceous earth the filtrate was evaporated and the residue chromatographed on a column of alumina (15 g). Elution with light petroleum–ether (4 : 1) gave 114 mg of methyl ether *XXXIX*, m.p. 169—171°C (ether), $[\alpha]_D$ −26·5° (*c* 0·49). IR spectrum (chloroform): 1725, 1258, 1031 ($CH_3COO$), 2830, 1111 ($OCH_3$) $cm^{-1}$. For $C_{33}H_{54}O_5$ (530·8) calculated: 74·67% C, 10·25% H; found: 74·66% C, 10·07% H.

20-Methoxy-29,30-dinorlupane-3β,28-diol (*XL*)

A solution of potassium hydroxide (100 mg) in ethanol (10 ml) was added into a solution of diacetate *XXXIX* (110 mg) in benzene (5 ml) and refluxed for 6 h. After working up according to procedure *D*) the residue was crystallized from ether, giving 80 mg of diol *XL*, m.p. 234 to 236°C, $[\alpha]_D$ −41·1° (*c* 0·45). IR spectrum (chloroform): 3620, 1022 (OH), 1111 ($OCH_3$) $cm^{-1}$. For $C_{29}H_{50}O_3$ (446·7) calculated: 77·97% C, 11·28% H; found: 78·08% C, 11·11% H.

20-Methoxy-29,30-dinorlupane (*XLI*)

Pyridinium chlorochromate[11] (250 mg) was added to a solution of diol *XL* (80 mg) in dichloromethane (10 ml). After 2 h stirring at room temperature the mixture was filtered through a column of alumina (10 g) and the insoluble residue in the flask was washed with ether. The combined organic phases were evaporated in a vacuum and the residue dissolved in 15 ml of diethylene glycol. After addition of 2 ml of 100% hydrazine hydrate the mixture was refluxed for 2 h, cooled and additioned with 400 mg of potassium hydroxide in a minimum amount of water. Solvents were distilled off from the mixture (until the temperature rose to 220°C), the residual solution was further refluxed for 2 h and then worked up using procedure *F*). Chromatography of the residue on a preparative silica gel plate (20 × 20 cm) in light petroleum–ether (95 : 5) gave 40 mg of methyl ether *XLI*, m.p. 98—100°C (acetone), $[\alpha]_D$ −32·8° (*c* 0·61). IR spectrum (chloroform): 2815, 1111 ($OCH_3$) $cm^{-1}$. $^1$H-NMR spectrum: 3·01 t and 3·51 dd, $J_{gem}$ = −8·5 Hz, $J_{vic_1}$ = 8·5 Hz, $J_{vic_2}$ = 2·5 Hz (20-$H_2$); 3·30 s ($OCH_3$). For $C_{29}H_{50}O$ (414·7) calculated: 83·99% C, 12·15% H; found: 83·88% C, 12·30% H.

3β,28-Diacetoxy-29,30-dinorlupane (*XLIV*)

Methanesulfonyl chloride (0·5 ml) was added to a solution of alcohol[4] *XXXVIII* (100 mg) in pyridine (4 ml) cooled to −20°C and then allowed to stand at −5°C for 90 min. The reaction mixture was worked up using procedure *E*). The residue (110 mg) according to TLC contained predominantly the mesylate *XLIII*. IR spectrum (chloroform): 1725, 1253, 1029 ($CH_3COO$), 1338, 1173 ($CH_3SO_2O$) $cm^{-1}$. Sodium iodide (300 mg) and zinc dust (260 mg) were added to the residue dissolved in 4 ml of 1,2-dimethoxyethane, and the mixture was refluxed under stirring for 3 h. After dilution with ether (60 ml), filtration through a column of alumina (6 g) and crystallization of the residue from methanol diacetate *XLIV* (74 mg) was obtained, m.p. 181—185°C/200—202°C, $[\alpha]_D$ −20° (*c* 0·51). IR spectrum (tetrachloromethane): 1734, 1246, 1028 ($CH_3COO$) $cm^{-1}$. For $C_{32}H_{52}O_4$ (500·8) calculated: 76·75% C, 10·47% H; found: 76·59% C, 10·38% H.

29,30-Dinorlupane-3β,28-diol (*XLV*)

Potassium hydroxide (300 mg) dissolved in ethanol (15 ml) was added to a solution of diacetate *XLIV* (250 mg) in benzene (15 ml) and the mixture was refluxed for 5 h and worked up using procedure *D*). Crystallization of the residue from ether gave 180 mg of diol *XLV*, m.p. 245 to 248°C, $[\alpha]_D$ −25·5° (*c* 0·55). IR spectrum (chloroform): 3627, 3390 broad, 1020 (OH) $cm^{-1}$. For $C_{28}H_{48}O_2$ (416·7) calculated: 80·71% C, 11·61% H; found: 80·59% C, 10·82% H.

29,30-Dinorlupane (*XLVI*)

Hydrocarbon *XLVI* was prepared from 80 mg of diol *XLV* using the same procedure as for compound *XLI* from diol *XL*. The residue was chromatographed on a column of alumina (10 g). Elution with light petroleum gave 38 mg of hydrocarbon *XLVI*, m.p. 143—145°C (ether), $[\alpha]_D$ −20·8° (*c* 0·77). $^1$H-NMR spectrum: 0·988 d, $J_{19,20}$ = 6·2 Hz (19α-$CH_3$). For $C_{28}H_{48}$ (384·7) calculated: 87·42% C, 12·58% H; found: 87·59% C, 12·44% H.

(20*R*)-20-Acetoxy-30-norlupane (*XLVIII*)

Acetate *XLVIII* was prepared on acetylation of alcohol *XLVII* according to ref.[7]; m.p. 168 to 169°C (hexane–ether), $[\alpha]_D$ −14·8° (*c* 0·46). Literature[7] gives m.p. 166—168°C, $[\alpha]_D$ −15°.

$^1$H-NMR spectrum: 1·161 d, $J_{20,29}$ = 6·3 Hz (20-$CH_3$); 2·03 s ($CH_3COO$); 5·12 q, $J_{20,29}$ = = 6·3 Hz, $J_{20,19} \approx 0$ Hz (20-H).

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