FUNCTIONALIZATION OF THE LUPANE SKELETON THROUGH BARTON'S REACTION*

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It was found that the photolysis of 20-nitrosyloxy-29,30-dinorlupane derivatives *X* and *XIX* takes place under formation of 12-oximino-20-hydroxy derivatives *XX* and *XXIV*; aldehydes *VI* and *XVI* were isolated as by-products. The structure of 12-substituted 29,30-dinorlupane derivatives *XXI*, *XXII*, *XXV*, *XXVI*, *XXVIII* and *XXIX* has been determined by comparison of their PMR spectra with those of corresponding 12-substituted 30-norlupane derivatives. The basic information of the determination of the minimum distance of the interacting groups during Barton's reaction have also been determined.

In the preceding paper[1] we described the course of the photolysis of epimeric 20-nitrosyloxy-30-norlupane derivatives. The photolysis of 20*S* nitrites takes place under formation of 12-oximino-20-hydroxy derivatives, while the photolysis of epimeric 20*R* nitrites gives rise to a complex mixture which does not contain substances with an oximino group. It could be supposed that the reasons for the failure of Barton's reaction in the case of 20*R* nitrites are of sterical origin; the rotational barrier[2] of the side chain in 30-norlupane derivatives evidently does not permit the approach of the oxygen radical of the 20*R* configuration in the transition state to the necessary proximity of 12βH; although its approach to 21αH is possible, the minimum attainable distance necessary for the transfer of the hydrogen atom is evidently insufficient.** In order to prove these ideas derived from the models experimentally we investigated the course of Barton's reaction in 20-nitrosyloxy-29,30-dinorlupane (*XIX*) and its 3β,28-diacetoxy derivative *X*; the rotation of their $C_{(19)}$-$C_{(20)}$ bond is no longer so much hindered, so that by photochemical conversion both the position 12 and the position 21 could be functionalized.

As starting substances for the preparation of nitrites *X* and *XIX* we used dinoralcohols *VIII* and *XVII*. The key substance for the preparation of dinoralcohol *VIII* is dinoracid *III* which we prepared using the modification of a known procedure[3];

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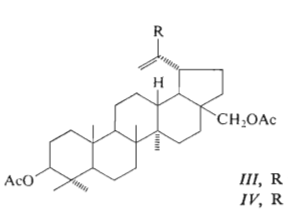
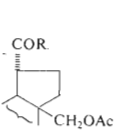
** It is necessary to consider the distance between the center of the oxygen radical and the center of the hydrogen atom. On Dreiding models the minimum distance of the oxygen radical from 12βH was found to be 1·5 Å and for the distance from 21αH it was 2 Å.

betulin diacetate *I* was oxidized with selenium dioxide to unsaturated aldehyde *II* which was degradated by oxidation with chromium trioxide to dinoracid *III*. For the selective reduction of the carboxyl functional group in the presence of 3β and 28 acetoxy groups we tried two different procedures. In the first dinoracid *III* was converted to chloride *V* which was reduced by Rosenmund reduction to dinoraldehyde *VI*. Reduction of dinoraldehyde *VI* with sodium borohydride gave dinoralcohol *VIII*. In the second procedure dinoracid *III* was converted on reaction with triethylamine and ethyl chloroformate to mixed anhydride *VII* the reduction of which[4,5] with sodium borohydride in aqueous tetrahydrofuran gave dinoralcohol *VIII*, further characterized as acetate *IX*. Both procedures give practically identical yields: for the main experiment the second procedure was made use of because it was experimentally less exacting.

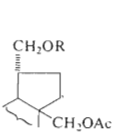
As the sequence of degradation reactions of the isopropenyl side chain, leading to dinoracid *III*, gives only a 14% yield, it was necessary to find a new, more advantageous, preparative method for the degradation of the side chain of the poorly accessible α-lupene (*XI*). As starting substance for the preparation of dinoracid *XIV* norketone *XII* was used, which can be prepared by a known procedure[6] from α-lupene (*XI*) in a 71% yield. By condensation of norketone *XII* with ethyl formate in the presence of sodium hydride hydroxymethylene ketone *XIII* was obtained; the latter was oxidized with chromium trioxide in acetic acid to dinoracid *XIV* isolated in the form of its methyl ester *XV*; its total yield (calculated per *XI*) is 34%. Reduction of methyl ester *XV* with lithium aluminum hydride gave dinoralcohol *XVII* which was characterized as acetate *XVIII*. The authors of paper[7] described the formation of corresponding aldehydes during the photolysis of nitrites of primary alcohols; hence, we supposed that noraldehydes *VI* or *XVI* would be formed as by-products in the photolysis of nitrites *X* or *XIX*, respectively. The authentic samples of dinoraldehydes *VI* or *XVI* were prepared on oxidation of dinoralcohols *VIII* and *XVII* with a mixture of dimethyl sulfoxide and N,N'-dicyclohexylcarbodiimide under catalysis with pyridinium trifluoroacetate[8]. Under the effect of gaseous nitrosyl chloride on



I, R = CH_3
II, R = CHO



III, R = OH
IV, R = OCH_3
V, R = Cl
VI, R = H
VII, R = $OCOOC_2H_5$



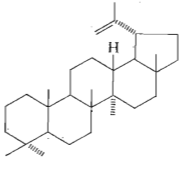
VIII, R = H
IX, R = Ac
X, R = NO

dinoralcohols *VIII* or *XVII* at −20°C in pyridine corresponding nitrites *X* or *XIX*, resp., were obtained.

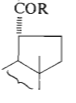
Using the photolysis of nitrite *X* a mixture was obtained from which the following substances were isolated chromatographically: dinoraldehyde *VI* in 24% yield, dinoralcohol *VIII* in 24% yield, and an oxime to which we assign the structure *XX* in 37% yield. Similarly, from nitrite *XIX* dinoraldehyde *XVI* was obtained in 21% yield, dinoralcohol *XVII* in 29% yield, and the oxime of the supposed structure *XXIV* in 27% yield. Acetylation of oximes *XX* or *XXIV* gave N—O—, 20-O-diacetyl derivatives *XXI* or *XXV*, respectively, which can be partially hydrolysed to 20-O-acetyl--oximes *XXII* and *XXVI*, resp. On reaction of oxime *XXII* with nitrous acid in acetic acid nitrimine *XXIII* was obtained which was converted on boiling with aqueous dioxan to ketone *XXVIII*. Ketone *XXIX* was prepared in the same manner from oxime *XXVI* *via* nitrimine *XXVII*.

The structure of the products of functionalization was determined by the analysis of their spectra and comparison of the measured values with those measured for corresponding 30-norlupane derivatives[1]. In the IR spectrum of oxime *XXIV* the valence vibration of 12-hydroxyimino group ($\nu_{(OH)}$ 3587 cm^{-1})* is practically the same as the vibration of 12-hydroxyimino group in the spectrum of 20-O-acetyloxime *XXVI* ($\nu_{(OH)}$ 3592 cm^{-1}),* while the valence vibrations of 20-hydroxy group ($\nu_{(OH)}$ 3228 and 3121 cm^{-1})* display an appreciable shift to lower frequenceies in comparison to the valence vibration of 20-hydroxy group of dinoralcohol *XVII* ($\nu_{(OH)}$ 3632 cm^{-1}).* This shift is caused by a strong intramolecular hydrogen bond between the 20-hydroxy group and 12-oximino group; a similar intramolecular hydrogen bridge was also observed in the spectrum of the corresponding 30-norlupane derivative[1].

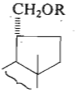
In the PMR spectra of oximes and their acetates *XXI*, *XXII*, *XXV* and *XXVI* the double bond C=N causes a downfield shift of the signals of 8β and 10β methyl groups (Table I). The determined values of the shifts are in good agreement with the



XI



XII, R = CH_3
XIII, R = C=CHOH
XIV, R = OH
XV, R = OCH_3
XVI, R = H



XVII, R = H
XVIII, R = Ac
XIX, R = NO ,

* Measured on a grating spectrophotometer Unicam SP 700 in $2 \cdot 10^{-3}$ M solutions in tetrachloromethane.

values measured for analogous 30-norlupane derivatives[1]. The signal of proton 13β again appears as a doublet with a coupling constant of 10–11 Hz. The proton 11α (*X*) forms with the protons 11β(A) and 9α(B) an ABX system; in the spectra of compounds *XXI*, *XXII* and *XXV* its *X* part has the form of a broadened doublet. In the spectra of substance *XXVI* the *X* part is composed of 6 lines; after integration of the record the values of interaction constants could be computed: $J_{AX} = -11{\cdot}9 \pm \pm 2$ Hz, $J_{BX} = 3{\cdot}2 \pm 2$ Hz and $J_{AB} = 13 \pm 1$ Hz. These values are again in good agreement with those calculated from the spectra of the corresponding 30-nor-lupane derivative[1].

In the PMR spectra of both 12-lupanone derivatives, *XXVIII* and *XXIX*, a downfield shift of 8β and 10β methyl signals was observed, as well as an upfield shift of

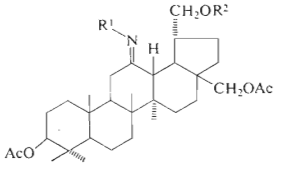
TABLE I

Chemical Shifts (δ-scale, p.p.m.) and Coupling Constants (Hz) of the PMR spectra of 12-Substituted Lupane Derivatives

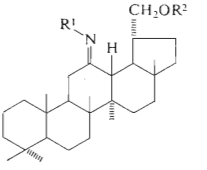
Compound	8βCH$_3$ Δ[a]	10βCH$_3$ Δ[a]	14αCH$_3$ Δ[a]	13βH	11αH	$J_{13,18}$
IX	1·049 0·000	0·864 0·000	0·922 0·000	—	—	—
XXI	1·213 −0·164	0·932 −0·068	0·932 −0·010	2·64d	3·13bd	11·0
XXII	1·197 −0·148	0·933 −0·069	0·856 +0·066	2·50d	3·30bd	10·5
XXVIII	1·299 −0·250	0·946 −0·082	0·814 +0·108	2·77d	—	11·1
XVIII	1·041 0·000	0·846 0·000	0·903 0·000	—	—	—
XXV	1·195 −0·154	0·911 −0·065	0·911 −0·008	2·59d	3·13bd	11·0
XXVI	1·179 −0·138	0·908 −0·062	0·837 +0·066	2·45d	3·30[b]	10·8
XXIX	1·280 −0·239	0·914 −0·068	0·795 +0·108	2·74d	2·21[c]	10·7

[a] Δ-Values in compounds *XXI*, *XXII* and *XXVIII* are referred to substance *IX* as standard; in compounds *XXV*, *XXVI* and *XXIX* they are referred to substance *XVIII* as standard. The sign — means a downfield shift of the signal; [b] X part of an ABX system, from the spectrum the position of all 6 lines can be read; [c] AB part of the ABX system, the value of the chemical shift was calculated.

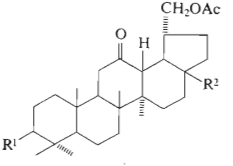
the 14α-CH_3 signal (Table I); such changes of signals of the methyl groups are characteristic[1,9] of 12-oxolupane derivatives. In the spectrum of ketone *XXIX* a multiplet was found (2·25 p.p.m.) corresponding to two protons in α-position to the carbonyl group, 11α and 11β. This multiplet forms 5 lines of the partly degenerated AB part of the ABX system. From the spectrum the magnitudes $|J_{AB}| = 12$ Hz and $J_{AX} + J_{BX} = 17{\cdot}6$ Hz may be read, which are in very good agreement with the values measured for an analogous 30-norlupane derivative[1]. The exact calculation of the magnitude of the interaction constants J_{AX} and J_{BX} is impossible due to the reasons described in paper[10]. Further proofs of the proposed structures of both ketones may be obtained from the IR spectra and CD curves. In the IR spectrum of ketone *XXIX* there is an absorption band of a carbonyl (1 706 cm^{-1}) in the region of the absorption of six-membered and higher ketones; in the spectrum of ketone *XXVIII* this band is superimposed by intensive bands of the acetate groups. The position and the magnitude of the extremes on the CD curve of ketone *XXVIII* ($\Delta\varepsilon = -1{\cdot}50$ at 293 nm) corresponds to the values measured for 12-lupanone derivatives described earlier[1,9,11]. From the analogous course of Barton's reaction in derivatives of 20-nitro-



XX, $R^1 = OH$, $R^2 = H$
XXI, $R^1 = OAc$, $R^2 = Ac$
XXII, $R^1 = OH$, $R^2 = Ac$
XXIII, $R^1 = NO_2$, $R^2 = Ac$



XXIV, $R^1 = OH$, $R^2 = H$
XXV, $R^1 = OAc$, $R^2 = Ac$
XXVI, $R^1 = OH$, $R^2 = Ac$
XXVII, $R^1 = NO_2$, $R^2 = Ac$



XXVIII, $R^1 = OAc$, $R^2 = CH_2OAc$
XXIX, $R^1 = H$, $R^2 = CH_3$

syloxy-29,30-dinorlupane and (20*S*)-nitrosyloxy-30-norlupane it may be concluded that their transition states are very similar, especially in the first step of the reaction when the transfer of 12βH from the carbon atom to the oxygen radical takes place. Hence, the methyl group on $C_{(20)}$ in (20*S*)-nitrosyloxy-30-norlupane does not prevent the turning of the oxygen radical in the direction of 12βH. In the case of (20*R*)-nitrosyloxy-30-norlupane, which does not afford products with an oxime group during Barton's reaction, the methyl group prevents the rotation of the oxygen radical to the proximity of 12βH; the methyl groups should assume an antiperiplanar position with respect to 19βH. This conformation is evidently energetically less favourable than the synclinal one, which is assumed by the methyl group in the transition state of the epimeric nitrite 20*S* (Fig. 1).

The attack of the position 21, *i.e.* the transfer of 21αH to the oxygen radical, requires in 20*S* nitrite such a rotation of the side chain as would bring the methyl group on $C_{(20)}$ to an appreciable proximity of 12βH. The oxygen radical generated from (20*R*)-nitrosyloxy-30-norlupane could attack the position 21; in the transition state of the first reaction step (transfer of hydrogen atom) the methyl group on $C_{(20)}$ should assume a synperiplanar conformation with respect to 19βH, and this transition state surely would be less energetically exacting than the above-mentioned transition state for the configuration 20*S*. As in Barton's reaction of (20*R*)-nitrosyloxy-30-norlupane no product with an oxime group was isolated, it could be supposed that the minimum distance between the oxygen radical and 21αH (approx. 2 Å) is too large for a hydrogen atom transfer. This supposition was now fully corroborated by the above experiments with the photolysis of 20-nitrosyloxy-29,30-dinorlupane which lacks a methyl group on $C_{(20)}$ which might prevent the attack of the position 21. However, as the product of the functionalization of the position 21 has not been isolated,

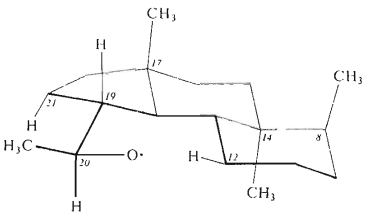


FIG. 1

The Supposed Transition State of Barton's Reaction (transfer of the 12βH to the oxygen radical of the 20*S* nitrite)

In the hypothetic transition state of 20*R* nitrite 20-CH_3 and 20-H are exchanged.

it can be supposed that the limit distance for the hydrogen atom transfer to the oxygen radical is less than 2 Å.

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 $\pm 1-2°$ accuracy. The infrared spectra were measured in chloroform using a UR-20 (Zeiss, Jena, GDR) instrument; the ultraviolet spectra were measured on a Unicam SP-700 spectrophotometer. Circular dichroism curves were registered on a Roussel-Jouan Dichrographe 185 in dioxan. The PMR spectra were recorded in deuteriochloroform with tetramethylsilane as internal standard, using a Varian HA-100 instrument (substance *VI* was measured on a Tesla 80-MHz apparatus); the chemical shifts are given in p.p.m., δ-scale, and for the description of the ABX systems the same symbols were used as in paper[12]. For column chromatography neutral alumina was used (Reanal, act. II) and silica gel (Spolana, Neratovice); for thin-layer chromatography silica gel G (Merck) was employed. The working up of the ethereal solutions in the conventional manner was carried out by washing with dilute hydrochloric acid (1 : 4), water, saturated sodium hydrogen carbonate, and water. For drying anhydrous sodium sulfate was used. Samples for analysis were dried over phosphorus pentoxide at 80°C and 0·1—1 Torr for 8—12 hours. The identity of the samples, prepared in various ways was checked by mixture melting point determination, optical rotation measurement and thin-layer chromatography and infrared spectra.

3β,28-Diacetoxy-29,30-dinorlupan-20-oic Acid (*III*)

Chromium trioxide (5·7 g) in 150 ml of acetic acid (90%) was added to a solution of 4·6 g of aldehyde[3] *II* in 280 ml of acetic acid at 90°C over 1·5 h and the mixture was heated at the same temperature for 30 minutes. After cooling to room temperature excess chromium trioxide was decomposed by addition of 30 ml of methanol. After evaporation of the majority of acetic acid in a vacuum the residue was diluted with water, the reaction mixture was adjusted to pH 4 with potassium hydrogen carbonate, and extracted with ether. The extract was washed with water and dried over sodium sulfate. The residue was chromatographed on a silica gel column (120 g). Light petroleum–acetone mixture (9 : 1) eluted 2·1 g of amorphous acid *III*. Methyl ester *IV* (diazomethane); m.p. 163-167°C, $[\alpha]_D$ −16° (*c* 1·23). Literature[13] gives m.p. 161 to 164°C, $[\alpha]_D$ −15·3°.

3β,28-Diacetoxy-29,30-dinorlupan-20-al (*VI*)

a) A solution of 500 mg of acid *III* in 5 ml of thionyl chloride (cooled to −20°C) was allowed to stand at room temperature for 2 days. Excess thionyl chloride was eliminated by repeated distillation with benzene in a vacuum. Crystallization from hexane gave 450 mg of chloride *V*, m.p. 177—182°C, $[\alpha]_D$ −12·3° (*c* 0·65). IR spectrum: 1733, 1258, 1037 (CH_3COO), 1798 (COCl) cm^{-1}. A suspension of 150 mg of 5% palladium on charcoal in 37 ml of xylene was bubbled through with hydrogen and simultaneously 7 ml of xylene were distilled off. A solution of 450 mg of chloride *V* in 10 ml of xylene was added to the above suspension and hydrogen was introduced into the mixture at 140°C for 5 hours. Nitrogen was then introduced to eliminate hydrogen, the mixture was cooled, the catalyst filtered off and the filtrate evaporated *in vacuo*. The residue was chromatographed on a column of alumina (50 g). Light petroleum–ether (4 : 1) mixture eluted 370 mg of aldehyde *VI*, m.p. 165—170°C under decomposition; (light petroleum), $[\alpha]_D$ −3·2°

(*c* 0·62). IR spectrum: 1730, 1260, 1035 (CH_3COO), 2830, 2730, 1730 (CHO) cm^{-1}. CD: 300 nm ($\Delta\varepsilon$ +0·45) (*c* 0·097). PMR spectrum: 0·848 bs (3 . CH_3); 0·979 s; 1·038 s (2 . CH_3); 2·01 s; 2·04 s (2 . CH_3COO); 3·75 d and 4·26 d, J_{gem} = 11 Hz (28-H_2); 4·48 mt (3αH); 9·50 d, J = 4·3 Hz (CHO). For $C_{32}H_{50}O_5$ (514·7) calculated: 74·67% C, 9·79% H; found: 74·49% C, 9·58% H.

b) 0·008 ml of trifluoroacetic acid and 0·016 ml of pyridine were added to a solution of 100 mg of alcohol *VIII* and 88 mg of N,N'-dicyclohexylcarbodiimide in 2 ml of benzene and 2 ml of dimethyl sulfoxide and the mixture allowed to stand at room temperature for 20 hours. The unreacted N,N'-dicyclohexylcarbodiimide was hydrated with a solution of 27 mg of anhydrous oxalic acid in 0·5 ml of methanol. After 15 minutes' standing at room temperature the mixture was diluted with ether (20 ml), the separated N,N'-dicyclohexylurea was filtered off and the filtrate washed with water (5 times). The residue was chromatographed on a column of alumina (15 g). A mixture of light petroleum and ether (4 : 1) eluted 76 mg of aldehyde *VI*, m.p. 166 to 171°C, under decomposition (light petroleum), $[\alpha]_D$ −0·6° (*c* 1·54).

3β,28-Diacetoxy-29,30-dinorlupan-20-ol (*VIII*)

a) A solution of 0·361 ml of ethyl chloroformate in 5 ml of tetrahydrofuran was added dropwise and under stirring at -20°C into a solution of 1·93 g of acid *III* and 0·526 ml of triethylamine in 40 ml of tetrahydrofuran. The mixutre was stirred for 45 min at room temperature and the separated triethylamine hydrochloride was filtered off and the filtrate evaporated *in vacuo*. Yield 1·93 g of amorphous mixed anhydride *VII*. IR spectrum: 1735, 1260, 1035 (CH_3COO), 1822, 1735 (COOCO) cm^{-1}. The residue was dissolved in 40 ml of tetrahydrofuran and added dropwise over 15 minutes, under stirring and cooling with ice, to a suspension of 450 mg of sodium borohydride in 8 ml of water. After 4 hours' stirring at room temperature the mixture was poured into dilute hydrochloric acid (1 : 10) and the product extracted with ether. The extract was worked up in the usual manner. Before evaporation the solution was filtered through a column of alumina (50 g). The residue was crystallized from dichloromethane–hexane mixture. Yield 1·05 g of alcohol *VIII*, m.p. 243—246°C, $[\alpha]_D$ −18·9 (*c* 0·64). IR spectrum: 1730, 1260, 1035 (CH_3COO), 3635 (OH) cm^{-1}. For $C_{32}H_{52}O_5$ (516·7) calculated: 74·37% C, 10·14% H; found: 74·67% C, 10·34% H.

b) Sodium borohydride (240 mg) was added into a solution of 370 mg of aldehyde *VI* in a mixture of 8 ml benzene and 16 ml methanol and the mixture was allowed to stand at room temperature overnight. After concentration to 1/3 of its volume *in vacuo* the mixture was poured into dilute hydrochloric acid (1 : 10) and the product extracted with ether. After working up the obtained residue (330 mg) was chromatographed on alumina (30 g). Benzene–acetone (4 : 1) mixture eluted 270 mg of dinoralcohol *VIII*, m.p. 241—243°C (dichloromethane–hexane), $[\alpha]_D$ −17·8° (*c* 0·67).

3β,20,29-Triacetoxy-29,30-dinorlupane (*IX*)

A solution of 160 mg of alcohol *VIII* in a mixture of 3 ml of pyridine and 1·5 ml of acetic anhydride was allowed to stand at room temperature for 3 days. The mixture was poured onto ice and the product extracted with ether. The extract was worked up and the residue (160 mg) was crystallized from methanol, yield 120 mg of acetate *IX*, m.p. 161—163°C, $[\alpha]_D$ −18·6°. Literature[13] gives m.p. 162—164°C, $[\alpha]_D$ −21°. PMR spectrum: 0·845 s (2 . CH_3); 0·864 s; 0·922 (2 . CH_3); 1·049 s (8βCH_3); 2·035 s (2 . CH_3COO); 2·055 s (CH_3COO); 3·70 dd and 4·24 dd, J_{gem} = 10·6 Hz, J_{vic_1} = 7·2 Hz, J_{vic_2} = 3 Hz, (20-H_2); 3·78 d and 4·26 d, J_{gem} = 11·5 H_2 (28-H_2); 4·49 mt (3αH).

3β,28-Diacetoxy-20-nitrosyloxy-29,30-dinorlupane (*X*)

An excess of nitrosyl chloride was distilled over into a solution of 200 mg of alcohol *VIII* in 5 ml of pyridine at −20° and under stirring (until the orange colour of the mixture persisted). After 10 minutes' stirring at −20°C and 5 minutes' standing at room temperature the mixture was poured into water and the product was extracted with ether. The extract was washed with water (5 times), dried and evaporated in a vacuum, the residual pyridine was evaporated by repeated distillation with light petroleum under reduced pressure. Yield 180 mg of nitrite *X*, m.p. 170 to 173°C, under decomposition (hexane), $[\alpha]_D$ −10·3° (*c* 1·35). IR spectrum: 1730, 1260, 1035 (CH_3COO), 1650, 1612 (ONO) cm^{-1}. UV spectrum (tetrahydrofuran): λ_{max} 323 nm (ε 53·3), 333 nm (ε 69·9), 344 nm (ε 90·8), 357 nm (ε 102·0), 370 nm (ε 84·9), 382 nm (ε 41·2).

29-Hydroxymethylene-30-norlupan-20-one (*XIII*)

A solution of 1·9 g of ketone *XII* and 8·3 ml of ethyl formate in 100 ml of benzene was added to a suspension of 2·6 g of sodium hydride in 40 ml of benzene over 5 minutes under stirring which was continued under nitrogen and at room temperature for another 44 hours. The unreacted sodium hydride was decomposed with ethanol and water, the mixture was poured into dilute hydrochloric acid (1 : 4) and the product extracted with ether. The extract was washed with water until neutral and evaporated. The residue crystallized out on addition of light petroleum, m.p. 155—160°C. Yield 1·7 g of crude hydroxymethylene ketone *XIII*. A sample for analysis was obtained by double crystallization from light petroleum, m.p. 159—162°C, $[\alpha]_D$ −49·6° (*c* 0·77). IR spectrum: 1632, 1593 (COCH=CHOH) cm^{-1}. UV spectrum (cyclohexane): λ_{max} 271 nm (log ε 3·94). For $C_{30}H_{48}O_2$ (440·7) calculated: 81·76% C, 10·98% H; found: 81·51% C, 11·05% H.

Methyl Ester of 29,30-Dinorlupan-20-oic Acid (*XV*)

A solution of chromium trioxide (5 g) in 20 ml of 70% acetic acid was added at 90°C over 15 minutes to a solution of 2 g of crude hydroxymethylene ketone *XIII* in 120 ml of acetic acid and the mixture heated at 90°C under occasional shaking for 5 hours; after cooling to room temperature 10 g of an anhydrous sodium acetate were added and acetic acid was distilled off in a vacuum. The residue was dissolved in ether and water, the phases were separated and the aqueous layer extracted with ether. The combined ethereal layers were washed with water, saturated sodium pyrosulfite solution, sodium hydrogen carbonate solution, and water. The residue was dissolved in 50 ml of benzene and additioned with excess ethereal diazomethane solution, and the mixture was allowed to stand at room temperature for 15 minutes. The unreacted diazometane was evaporated in vacuo together with the solvents. The residue was chromatographed on a column of alumina (200 g). A mixture of light petroleum and ether (97 : 3) eluted 1·05 g of methyl ester *XV*, m.p. 190—192°C (hexane), $[\alpha]_D$ −20° (*c* 1·03). Literature[14] gives m.p. 192°C, $[\alpha]_D$ −21°.

29,30-Dinorlupan-20-al (*XVI*)

Trifluoroacetic acid (0·008 ml) and pyridine (0·016 ml) were added to a solution of 80 mg of alcohol *XVII* and 88 mg of N,N'-dicyclohexylcarbodiimide in 2 ml of benzene and 2 ml of dimethyl sulfoxide and the mixture was allowed to stand at room temperature for 20 hours. The mixture was worked up as in the case of aldehyde *VI*. The residue was chromatographed on a column of alumina (10 g). A mixture of light petroleum and ether (96 : 4) eluted 40 mg of aldehyde *XVI*, m.p. 150—160°C (hexane) under decomposition, $[\alpha]_D$ +2·7° (*c* 0·74). IR spectrum: 2830, 2730, 1730 (CHO) cm^{-1}. For $C_{28}H_{46}O$ (398·6) calculated: 84·35% C, 11·63% H; found: 84·72% C, 11·87% H.

29,30-Dinorlupan-20-ol (*XVII*)

A solution of 480 mg of methyl ester *XV* in 15 ml of tetrahydrofuran was added to a suspension of 1 g of lithium aluminum hydride in 60 ml of tetrahydrofuran and the mixture was refluxed for 6 hours. After cooling the excess hydride was decomposed with ethyl acetate and water, and the mixture was poured into dilute hydrochloric acid (1 : 4) and the product extracted with ether. The extract was washed with saturated ammonium sulfate solution, sodium hydrogen carbonate solution and again with saturated ammonium sulfate solution. The residue was dissolved in dichloromethane and filtered through a column of alumina (10 g). Yield 440 g of amorphous alcohol *XVII*, $[\alpha]_D$ −18·6° (*c* 0·86). IR spectrum: 3630 (OH) cm^{-1}. For $C_{28}H_{48}O$ (400·7) calculated: 83·93% C, 12·08% H; found: 84·10% C, 12·01% H.

20-Acetoxy-29,30-dinorlupane (*XVIII*)

Alcohol *XVII* (60 mg) was acetylated with a mixture of 2 ml of pyridine and 1 ml of acetic anhydride at room temperature for 3 days. The mixture was worked up in the same manner as in the case of acetate *IX*. Yield 55 mg of acetate *XVIII*, m.p. 121—123°C (acetone), $[\alpha]_D$ −27·9° (*c* 0·82). IR spectrum: 1730, 1245, 1033 (CH_3COO) cm^{-1}. PMR spectrum: 0·772 s; 0·800 s (2 . CH_3); 0·846 s (2 . CH_3); 0·903 s (CH_3); 1·041 s (8βCH_3); 2·03 s (CH_3COO); 3·70 dd and 4·26 dd, J_{gem} = 10·45 Hz, J_{vic_1} = 8·6 Hz, J_{vic_2} = 2·5 Hz (20-H_2). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·47% C, 11·22% H.

Photolysis of Nitrite *X*

A solution of 950 g of nitrite *X* (dried by vacuum distillation with benzene) in 100 ml of benzene was photolysed in a sial flask using a UV lamp (Tesla THK 101) for 6 hours. The photolysis was carried out under nitrogen at 15—16°C. After evaporation of benzene in a vacuum the residue was chromatographed on silica gel (100 g column). Light petroleum–ether mixture (4 : 1) eluted 220 mg of aldehyde *VI*, m.p. 168—173°C, under decomposition (light petroleum), $[\alpha]_D$ −2·6° (*c* 0·87). Light petroleum–ether mixture (3 : 2) eluted 220 mg of alcohol *VIII*, m.p. 242—245°C (dichloromethane–hexane), $[\alpha]_D$ −18·2° (*c* 0·97). Further elution with the same mixture of solvents gave 350 mg of crude oxime *XX*, m.p. 268—278°C under decomposition (hexane–ether). IR spectrum: 1728, 1260, 1035 (CH_3COO), 3590, 1666 (C═NOH), 3240, 3130 (OH) cm^{-1}.

3β,20,28-Triacetoxy-12(*E*)-acetoxyimino-29,30-dinorlupane (*XXI*)

Acetic anhydride (10 ml) was added into a solution of 330 mg of oxime *XX* in 16 ml of pyridine and the mixture heated at 40°C for 24 hours. The mixture was poured onto ice and the product extracted with ether. The ethereal extract was worked up in the conventional manner. The residue was chromatographed on a silica gel column (35 g) with a mixture of light petroleum and ether (3 : 2). The first eluate weighed 280 mg (oil) and it consisted of acetate oxime *XXI*, $[\alpha]_D$ +61·5° (*c* 0·65). IR spectrum: 1730, 1260, 1035 (CH_3COO), 1760, 1650 (C═NOOCCH_3). PMR spectrum: 0·859 s (2 . CH_3); 0·932 s (2 . CH_3); 1·213 s (8βCH_3): 1·99 s; 2·045 s; 2·075 s; 2·13 s (4 . CH_3COO); 2·64 d, J = 11 Hz (13βH); 3·13 bd, $J \approx$ 12 Hz, X part of an ABX system (11αH); 3·82 d and 4.29 d, J_{gem} = 11 Hz (28-H_2); 3·96 dd and 4·64 dd, J_{gem} = 11 Hz, J_{vic_1} = 7·5 Hz, J_{vic_2} = 3·0 Hz (20-H_2); 4·48 mt (3αH). For $C_{36}H_{55}NO_8$ (629·8) calculated: 68·65% C, 8·80% H, 2·22% N; found: 68·31% C, 9·09% H, 2·09% N.

3β,20,28-Triacetoxy-12(*E*)-hydroxyimino-29,30-dinorlupane (*XXII*)

A solution of 250 mg of acetate oxime *XXI* in 5 ml of benzene was introduced into a column of alumina (20 g) and allowed to stand at room temperature overnight. Elution with chloroform gave 210 mg of oily oxime *XXII*, $[\alpha]_D$ +73·5° (*c* 0·69). IR spectrum: 1735, 1263, 1036 (CH_3COO), 3597, 3440, 1668 (C=NOH) cm^{-1}. PMR spectrum 0·856 s (3 . CH_3); 0·933 s (CH_3); 1·197 s (8βCH_3); 2·01 s; 2·03 s; 2·065 s (3 . CH_3COO); 2·50 d, J = 10·5 Hz (13βH); 3·30 bd, $J \approx 10$ Hz, X part of an ABX system (11αH); 3·60 to 4·60 broad mt (28-H_2, 20-H_2, 3αH). For $C_{34}H_{53}NO_7$ (587·8) calculated: 69·47% C, 9·09% H, 2·38% N; found: 69·33% C, 9·25% H, 2·25% N.

3β,20,28-Triacetoxy-29,30-dinorlupane-12-one (*XXVIII*)

A saturated aqueous solution of sodium nitrite (10 ml) was added dropwise over one hour to a solution of 170 mg of oxime *XXII* in 20 ml of acetic acid and the mixture was stirred at room temperature for one hour. Another 5 ml of saturated sodium nitrite solution were added over one hour to the mixture which was stirred for one hour and then poured into water and the product extracted with dichloromethane. The extract was washed with water, sodium hydrogen carbonate solution and water. Evaporation of the solvent *in vacuo* gave 132 mg of crude nitrimine *XXIII*, IR spectrum: 1733, 1255, 1036 (CH_3COO), 1638, 1570, 1319 (C=NNO_2) cm^{-1}. The residue was disolved in a mixture of 17 ml of dioxan and 10 ml of water and the solution was refluxed for 4·5 hours. The mixture was poured into water and the product extracted with dichloromethane. The residue was chromatographed on a column of alumina (20 g) using a light petroleum–ether mixture (1 : 1). Yield 60 mg of ketone *XXVIII*, $[\alpha]_D$ −8·3° (*c* 0·61). IR spectrum: 1732, 1260, 1035 (CH_3COO), 1715 inflexion (CO) cm^{-1}. PMR spectrum: 0·814 s (CH_3); 0·866 s (2 . CH_3); 0·946 s (CH_3); 1·299 s (8βCH_3); 2·01 s; 2·035 s; 2·07 s (3 . CH_3COO); 2·77 d, J = 11·1 Hz (13βH 3·75 d and 4·24 d, J_{gem} = 11·5 Hz (28-H_2); 3·96 dd and 4·42 dd, J_{gem} = 11 Jz, J_{vic_1} = 7 Hz); J_{vic_2} = 3·5 Hz (20-H_2); 4·48 mt (3αH). CD (dioxan): 293 nm ($\Delta\varepsilon$ −1·50). For $C_{34}H_{52}O$ (572·8) calculated: 71·29% C, 9·15% H; found: 71·45% C, 9·35% H.

Photolysis of Nitrite *XIX*

Excess nitrosyl chloride was distilled into a solution of 450 mg of alcohol *XVII* in 10 ml of pyridine at −20°C and under stirring until an orange colour persisted. After 10 minutes' stirring at −20°C and 5 minutes' standing at room temperature the mixture was worked up in the same manner as in the case of nitrite *X*. Yield 440 mg of an oily nitrite *XIX*; IR spectrum: 1638 (ONO) cm^{-1}. A solution of 430 mg of nitrite *XIX* (dried by vacuum distillation with benzene) in 50 ml of benzene was photolysed in a sial flask using a UV lamp (Tesla THK 101) for 6 hours. The photolysis was carried out under nitrogen at 15—16°C. After evaporation of benzene under reduced pressure the residue was chromatographed on a silica gel column (50 g). A mixture of light petroleum and ether (95 : 5) eluted 90 mg of aldehyde *XVI*, m.p. 150—158°C (ether) under decomposition, $[\alpha]_D$ +1·2° (*c* 1·46). Light petroleum–ether mixture (85 : 15) eluted 120 mg of amorphous alcohol *XVII*, $[\alpha]_D$ −17·5° (*c* 0·78). Further elution with the same solvent mixture eluted 123 mg of oxime *XXIV*, m.p. 270—280°C under decomposition; (ether), IR spectrum: 3590, 1665 (C=NOH), 3250, 3130 (OH) cm^{-1}.

20-Acetoxy-12(*E*)-acetoxyimino-29,30-dinorlupane(*XXV*)

Oxime *XXIV* (123 mg) was acetylated with a mixture of 6 ml of pyridine and 4 ml of acetic anhydride at 40°C for 24 hours. The mixture was worked up in the same manner as the reaction mixture after acetylation of oxime *XX*. Chromatography on a preparative silica gel thin-layer

plate (30 . 20 cm) in hexane– ether (4 : 1) gave 108 mg of an oily acetate oxime *XXV*, $[\alpha]_D$ +51·6° (*c* 1·45). IR spectrum: 1731, 1260, 1030 (CH_3COO), 1761, 1646 (C=NOOCCH$_3$) cm^{-1}. PMR spectrum: 0·810 s (2 . CH_3); 0·847 s (CH_3); 0·911 s (2 . CH_3); 1·195 s (8βCH_3); 1·985 s; 2·14 s (2 . CH_3COO); 2·59 d, J = 11 Hz (13βH); 3·13 bd, J 10 Hz, X part of an ABX system (11αH); 3·94 dd and 4·63 dd, J_{gem} = 10·4 Hz, J_{vic_1} = 8 Hz, J_{vic_2} = 4 Hz (20-H_2). For $C_{32}H_{51}NO_4$ (513·7) calculated: 74·81% C, 10·01% H, 2·73% N; found: 74·98% C, 9·78% H, 2·56% N.

20-Acetoxy-12(*E*)-hydroxyimino-29,30-dinorlupane (*XXVI*)

A solution of 80 mg of acetate oxime *XXV* in 3 ml of benzene was introduced into a column of alumina (10 g) and allowed to stand at room temperature overnight. Elution with chloroform yielded 59·3 mg of amorphous oxime *XXVI*, $[\alpha]_D$ +64·5° (*c* 0·44); IR spectrum: 1722, 1265, 1031 (CH_3COO), 3600, 1662 (C=NOH) cm^{-1}. PMR spectrum: 0·810 s (2 . CH_3); 0·837 s (2 . CH_3); 0·908 s (CH_3); 1·179 s (8βCH_3); 2·01 s (CH_3COO); 2·45 d, J = 10·8 Hz (13βH); 3·30, X part of an ABX system ($J_{AX} + J_{BX}$) = 8·7 Hz, 2($D_+ - D_-$) = 3·8 Hz, 2($D_+ + D_-$) = = 30·8 Hz (11αH); 4·07 dd and 4·37 dd, J_{gem} = 10·6 Hz, J_{vic_1} = 6·6 Hz, J_{vic_2} = 3·3 Hz (20-H_2). For $C_{30}H_{49}NO_3$ (471·7) calculated: 76·38% C, 10·47% H, 2·97% N; found: 76·25% C, 10·50% H, 2·77% N.

20-Acetoxy-29,30-dinorlupan-12-one (*XXIX*)

Saturated aqueous sodium nitrite solution (5 ml) was added over 1 hour into a solution of 100 mg of oxime *XXVI* in 3 ml of dichloromethane and 11 ml of acetic acid and the mixture was stirred at room temperature for one hour. An additional 2·5 ml of the same sodium nitrite solution were added over one hour to the mixture and the stirring was continued at room temperature for another hour. The reaction mixture was then poured into water and the product extracted with dichloromethane. The extract was washed with water, a sodium hydrogen carbonate solution and water. The residue was dissolved in 12 ml of dioxan, 5 ml of water were added and the solution refluxed for 10 hours. The mixture was poured into water and extracted with dichloromethane. The residue was chromatographed on a preparative silica gel plate (20 × 20 cm) in a mixture of light petroleum and ether (7 : 3). Yield, 40 mg of amorphous ketone *XXIX*. IR spectrum: 1723, 1253, 1030 (CH_3COO), 1706 (CO) cm^{-1}. PMR spectrum: 0·785 s; 0·795 s; 0·823 s; 0·857s; 0·914 s (5 . CH_3); 1·280 s (8βCH_3); 2·00 s (CH_3COO); 2·25, AB part of an ABX system, $|J_{AB}|$ = = 12 Hz, 2 D_+ = 19·4 Hz, 2 D_- ≈12 Hz, ($J_{AX} + J_{BX}$) = 17·6 Hz (11-H_2); 2·74 d, J = 10·7 Hz (13 H); 3·95 dd and 4·44 dd, J_{gem} = 10·6 Hz, J_{vic_1} = 8 Hz, J_{vic_2} = 4 Hz.

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