TRITERPENES. XXXII.*

ABSOLUTE CONFIGURATION AT $C_{(20)}$ IN 29-SUBSTITUTED LUPANE DERIVATIVES

A. VYSTRČIL, V. POUZAR and V. KŘEČEK

Department of Organic Chemistry, Charles University, 128 40 Prague 2

Received April 6th, 1973

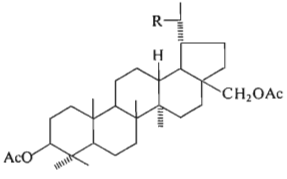
The absolute configuration of aldehydes *Ia*, *Ib*, epimeric at $C_{(20)}$ has been established by Baeyer–Villiger oxidation to noralcohols *IIa*, *IIb* of known configuration. Acids *Va*, *Vb*, alcohols *VIa*, *VIb*, and homoketones *XIIa*, *XIIb* were correlated with these aldehydes. Chemical shifts of protons $C_{(20)}$—H and $C_{(30)}$—H_3 can be differentiated in dependence on the configuration 20*R* or 20*S* resp., in the same manner as in the case of alcohols *IIa*, *IIb*. The changes of molar rotations are also consistent in both series of epimeric derivatives. The restriction of the rotation of the $C_{(20)}$—$C_{(29)}$ bond, evident from the circular dichroism curves of aldehydes *Ia*, *Ib*, increases with the substitution of the aldehydic hydrogen by a methyl group, *i.e.* homoketones *XIIa*, *XIIb*.

In the preceding papers[1,2] the absolute configuration on the asymmetric centre $C_{(20)}$ of 20-hydroxy-30-norlupane derivatives *IIa*, *IIb* has been established. This was utilised for the determination of the configuration on the asymmetric centre $C_{(20)}$ of lupane derivatives substituted with various substituents in the position 29. A possibility of a direct correlation is offered by Baeyer–Villiger oxidation of aldehydes *Ia* or *Ib*. We first tried to prepare them according to ref.[3] by rearrangement of epoxides *III*. On epoxidation of betulin diacetate (*IV*) a mixture of two epimeric epoxides *III* was formed which could not be separated. Rearrangement of this mixture (epoxides *III*) gave a mixture of aldehydes *Ia* and *Ib*. These aldehydes, though different in thin-layer chromatography, could not be separated preparatively on silica gel or alumina, due to oxidation and isomerisation. Therefore aldehydes *Ia* and *Ib* had to be prepared in a different manner. As starting material acids *Va* and *Vb* or alcohols *VIa* and *VIb* came into consideration. Single epimers of these derivatives can be separated chromatographically.

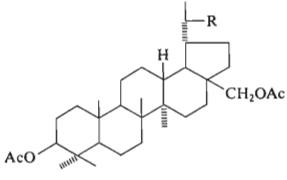
Acids *Va* and *Vb* were prepared according to ref.[4] by oxidation of betulin diacetate (*IV*) with chromium trioxide in acetic acid and they were separated chromatographically on silica gel. Alcohols *VIa* and *VIb* were prepared on reduction of a mixture of aldehydes *Ia* and *Ib* and separation on alumina. For the preparation of aldehydes

* Part XXXI: This Journal *38*, 3648 (1973).

Ia and *Ib* we first chose acids *Va* and *Vb* which seemed more advantageous. Acids *Va*, *Vb* were transformed to imidazolides[5] *VIIa* and *VIIb* that may be reduced[6] to corresponding aldehydes *Ia* and *Ib* in reaction with lithium tris(tert-butoxy)hydridoaluminate. Another possibility was the Rosenmund reduction of chlorides of acids *VIIIa* and *VIIIb*. Both these methods led in the case of the dextrorotatory acid *Vb* to a single aldehyde, *Ib*, but in the case of the levorotatory acid *Va* a mixture of both epimers *Ia* and *Ib* was formed. For the preparation of the second epimer *Ia* we had to start with alcohol *VIa* which on oxidation[7,8] gave pure aldehyde *Ia*; analogously, from the epimeric alcohol *VIb* an aldehyde was formed which was identical with aldehyde *Ib* prepared from the dextrorotatory acid *Vb*. A complete correlation of these derivatives was confirmed by oxidation of aldehydes *Ia*, *Ib* to corresponding acids *Va*, *Vb*, further by oxidation of alcohols *VIa*, *VIb* to the same acids *Va*, *Vb*, by reduction of aldehydes *Ia*, *Ib* to alcohols *VIa*, *VIb*, and by reduction of acids *Va*, *Vb* according to[9] to the same respective alcohols *VIa*, *VIb*.



a, 20 *R*

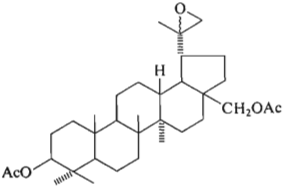


b, 20 *S*

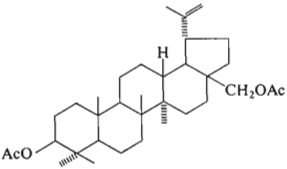
I, R = CHO
II, R = OH
V, R = COOH
VI, R = CH_2OH

VII, R = 
VIII, R = COCl
IX, R = $COOCH_3$
X, R = $CONHC(CH_3)_3$

XI, R = $CONHCH_3$
XII, R = $COCH_3$
XIII, R = $CH_2OOCC_6H_5$
XIV, R = $COOCOOC_2H_5$
XV, R = $COCHN_2$



III



IV

Baeyer–Villiger oxidation of aldehydes *Ia*, *Ib* afforded corresponding norformyloxy derivatives which may be easily partially hydrolysed by adsorption on alumina and standing[3] to noralcohols *IIa* or *IIb*, resp. The reaction was carried out with both epimers. Negatively rotating aldehyde *Ia* gave noralcohol *IIa* as the sole product and the positively rotating aldehyde *Ib* gave noralcohol *IIb* exclusively. Therefore aldehyde *Ia* must have the configuration 20*R* and aldehyde *Ib* the configuration 20*S*. According to the above mentioned chemical correlations the acid *Va* and alcohol *VIa* also belong to the 20*R* series, while the corresponding epimers *Vb* and *VIb* belong to the 20*S* series.

In order to compare the molar rotations and the PMR spectra of these compounds known methyl esters[4] *IXa*, *IXb*, tertbutylamides *Xa*, *Xb*, and methylamide *XIb*, were prepared from both epimeric acids *Va*, *Vb*, while from chlorides *VIIIa* and *VIIIb* both epimetic homoketones *XIIa*, *XIIb* were prepared according to[10]. Benzoates *XIIIa*, *XIIIb* were prepared from alcohols *VIa* and *VIb*. From Table I it is evident that all the derivatives display the same sign of the differences of molar rotations between the 20*R* and 20*S* epimers. In the case of alcohols *VIa*, *VIb* this difference decreases due probably to the absence of a chromophore in the proximity of the chiral center $C_{(20)}$. In all epimeric pairs the derivatives with 20*S* configuration have higher melting points than the corresponding derivatives with 20*R* configuration (with the exception of aldehydes *Ia*, *Ib* which melt under decomposition).

We endeavoured to explain the conformational relationship in the side chain of these substances by interpretation of the PMR spectra and CD curves of aldehydes *Ia*, *Ib* and homoketones *XIIa*, *XIIb*. From the PMR spectra of the measured derivatives it follows that for the configuration 20*R* (in comparison with the configuration

TABLE I

Molecular Rotation Differences Between the Derivatives of 20*R* and 20*S* Configuration

$C_{(20)}$—	M_D		ΔM_D
	20*R*	20*S*	
—COOH (*V*)	−246°	+ 61°	+307°
—$COOCH_3$ (*IX*)	−281°	+ 97°	+378°
—COCl (*VIII*)	−161°	+ 78°	+239°
—$CONHC(CH_3)_3$ (*X*)	−222°	+ 74°	+296°
—$CONHCH_3$ (*XI*)	—	+ 80°	—
—CHO (*I*)	−103°	+ 70°	+173°
—$COCH_3$ (*XII*)	− 67°	+169°	+236°
—CH_2OH (*VI*)	− 76°	− 44°	+ 32°
—$CH_2OOC_6H_5$ (*XIII*)	−123°	+ 58°	+181°

20*S*) the downfield shift of the 20-CH_3 signal and the lower value of the coupling constant between 20-H and 19β-H is characteristic (Table II). As these values agree with those from paper[2] we consider that the proportions of conformers of the side chain in single epimers are analogous to those in the case of 30-norlupane derivattives[2]: in 20*R* epimers $C_{(29)}$ assumes an *anti*-periplanar conformation with respect to 19β-H, while in 20*S* epimers $C_{(29)}$ assumes with respect to 19β-H an approximately *syn*-periplanar conformation which brings the carbonyl group of these derivatives (*Ib*, *XIIb*) in interaction with $C_{(12)}$. This interaction appreciably hinders free rotation of the $C_{(20)}$—$C_{(29)}$ bond which has an increase in absolute values of Δε of aldehyde *Ib* (+1·36 at 299 nm) and homoketone *XIIb* (+2·52 at 292 nm) as a consequence, in comparison with their epimers *Ia* (−0·33 at 310 nm) and *XIIa* (+0·31 at 294 nm).

TABLE II

Chemical Shifts 20—CH_3 (δ, p.p.m.) and *J* Constants Between 20-H and 19-H

$C_{(20)}$	20-CH_3		$J_{20,19}$(Hz)	
	20*R*	20*S*	20*R*	20*S*
—$COOCH_3$ (*IX*)	1·111	1·043	≠ 0 < 1·5	3·1
—$COCH_3$ (*XII*)	1·126	0·977	≠ 0 < 1·5	3·4
—CH_2OH (*VI*)	0·958	0·808	—	—

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 ± 2° accuracy. The IR spectra were measured in chloroform on a UR-20 spectrophotometer, or in tetrachloromethane on a Unicam SP-700 apparatus. The PMR spectra were measured in deuteriochloroform with tetramethylsilane as internal standard, using a Varian HA-100 or Tesla 80 MHz apparatus; the chemical shifts are given in p.p.m., δ-scale. Circular dichroism curves were recorded on a Rousel-Jouan dichrographe 185 in dioxan. For chromatography neutral alumina (Reanal, activity II) and silica gel (Spolana, Neratovice) was employed. For the preparation of preparative silica gel plates silica gel G according to Stahl was used (10 g per 20 × 20 cm plate). For washing organic extracts dilute hydrochloric acid (1 : 4) and a 5% sodium carbonate were used. The organic solutions were dried over anhydrous sodium sulfate. Samples for analysis were dried over phosphorus pentoxide at 100°C and 0·1—1 Torr for 8—12 h. The identity of the samples was determined by mixed melting points, optical rotation, thin-layer chromatography and infrared spectra.

3β,28-Diacetoxy-(20*R*)-lupan-29-oic Acid (*Va*)

a) To a solution of 10·0 g of betulin diacetate (*IV*) in 400 ml of acetic acid a solution of 6·5 g of chromium trioxide in 100 ml of 90% acetic acid were added dropwise at 65—70°C over one hour under stirring. The solution was stirred for 20 minutes at the same temperature and 20 ml

of methanol were added. The product was precipitated by addition of 550 ml of a 0·2M-HCl solution, then filtered off under suction and washed with water. After dissolution in ether it was separated by extraction with 5% sodium carbonate to neutral (1·85 g) and acid (6·76 g) fraction. Chromatography of the acid fraction on 120 g of silica gel with benzene containing 2% of ether (800 ml) as eluent gave 2·56 g of acid *Va*. Crystallisation from ether–hexane and from acetone gave a product of m.p. 239—241°C, $[\alpha]_D$ −44° (*c* 0·68). IR spectrum: 3525, 3300—2800, 1717 (COOH), 1731, 1260, 1034 (CH_3COO) cm^{-1}. For $C_{34}H_{54}O_6$ (558·8) calculated: 73·08% C, 9·74% H; found: 72·88% C, 9·64% H.

b) To a solution of 30 mg of aldehyde *Ia* in 3 ml of acetone 0·5 ml of Jones reagent were added and the mixture stirred at room temperature for 20 minutes. The excess oxidant was decomposed by addition of 2 ml of methanol, the mixture was diluted with water and the product extracted with ether. The extract was washed with water, evaporated to dryness and the residue crystallised from acetone. Yield, 20 mg of acid *Va*, m.p. 235—237°C, $[\alpha]_D$ −42° (*c* 0·61).

c) 70 mg of alcohol *VIa* were djssolved in 10 ml of acetone and additioned dropwise with Jones reagent to persistent excess. After 10 minutes standing at room temperature methanol was added to the mixture. The mixture was extracted with ether and the extract washed with water. Crystallisation of the residue from a mixture of ether and hexane and from acetone gave 40 mg of acid *Va*, m.p. 237—240°C, $[\alpha]_D$ −44° (*c* 0·63).

3β,28-Diacetoxy-(20*S*)-lupan-29-oic Acid (*Vb*)

a) On further elution after acid *Va* (see preparation of acid *Va* by method *a*) with the same solvent mixture (1 500 ml) 2·70 g of acid *Vb* were obtained. By repeated crystallisation from a mixture of ether and hexane a product was obtained of m.p. 204/254—259°C, $[\alpha]_D$ +11° (*c* 0·65). IR spectrum: 3530, 3300—2800, 1718 (COOH), 1735, 1258, 1036 (CH_3COO) cm^{-1}. For $C_{34}H_{54}O_6$ (558·8) calculated: 73·08% C, 9·74% H; found: 73·19% C, 9·66% H.

b) The reaction was carried out in the same manner as in the case of aldehyde *Ia*, starting from 30 mg of aldehyde *Ib*. The residue was crystallised from hexane. Yield, 15 mg of acid *Vb*, m.p. 204/253—258°C, $[\alpha]_D$ +12° (*c* 0·68).

c) The reaction was carried out analogously as for alcohol *VIa*, starting from 70 mg of alcohol *VIb*. By crystallisation of the residue from a mixture of ether and hexane 50 mg of acid *Vb* were obtained, m.p. 203/251—256°C, $[\alpha]_D$ +11° (*c* 0·65).

Derivatives of 3β,28-Diacetoxy-(20*R*)-lupan-29-oic Acid

Methyl ester IXa: To 100 mg of acid *Va* excess diazomethane solution in ether was added. After evaporation of the solvent and crystallisation from ether–hexane mixture 80 mg of methyl ester *IXa* were obtained, m.p. 213—215°C, $[\alpha]_D$ −49° (*c* 0·50). Literature[4] gives m.p. 212—213°C, $[\alpha]_D$ −48·0°. IR spectrum: 1730, 1442, 1180, 1037 ($COOCH_3$), 1730, 1260, 1037 (CH_3COO) cm^{-1}. PMR spectrum: 0·836 (2 × CH_3); 0·856, 0·928; 1·035 (3 × CH_3); 1·111 d, $J_{30,20} = 6·7$ Hz (20-CH_3); 2·01, 2·02 (2 × CH_3COO); 2·74 bq, $J_{20,30} = 6·7$ Hz, $J_{20,19} \neq 0 < 1·5$ Hz (20-H); 3·65 ($COOCH_3$), 3·75 d and 4·21 bd, $J_{gem} \approx 11$ Hz (28-H_2); 4·47 m (3α-H).

Chloride VIIIa: 500 mg of acid *Va* were dissolved in 5 ml of thionyl chloride, one drop of pyridine was added and the obtained solution was refluxed for 30 minutes. After evaporation in a vacuum and several crystallisations from benzene–light petroleum 130 mg of chloride *VIIIa* of m.p. 195—198°C were obtained, $[\alpha]_D$ −28° (*c* 0·98). IR spectrum: 1800 (COCl), 1735, 1260, 1036 (CH_3COO) cm^{-1}. For $C_{34}H_{53}ClO_5$ (577·2) calculated: 70·74% C, 9·26% H; found: 70·58% C, 9·15% H.

Tert-butylamide Xa: To a solution of 400 mg of chloride *VIIIa* in 10 ml of benzene 260 mg of tert-butylamine were added and allowed to stand for 72 hours at room temperature. The solution was evaporated *in vacuo*, the residue dissolved in ether and the solution washed with dilute hydrochloric acid and water. Chromatography of the residue (400 mg) on 45 g of silica gel with light petroleum with 20% of ether (250 ml) gave 200 mg of amorphous tert-butylamide *Xa*, $[\alpha]_D$ −36° (*c* 0·66). IR spectrum: 3450, 1674, 1510, 1258, ($CONHC(CH_3)_3$), 1630, 1258, 1034 (CH_3COO) cm^{-1}.

Derivatives of 3β,28-Diacetoxy-(20*S*)-lupan-29-oic Acid

Methyl ester IXb: The preparation of the methyl ester *IXb* was carried out from 80 mg of acid *Vb* in the same manner as in the case of methyl ester *IXa*. Crystallisation from a mixture of ether and hexane afforded 40 mg of methyl ester *IXb*, m.p. 234–236°C, $[\alpha]_D$ +17° (*c* 0·86). Literature[4] gives m.p. 234–236°C, $[\alpha]_D$ +18·9°. IR spectrum: 1730, 1442, 1185, 1036 ($COOCH_3$), 1730, 1260, 1036 (CH_3COO) cm^{-1}. PMR spectrum: 0·835 (2 × CH_3); 0·853, 0·945, 1·038 (3 × CH_3); 1·043 d, $J_{30,20}$ = 6·8 Hz (20-CH_3); 2·01, 2·03 (2 × CH_3COO); 2·30 m (19-H); 2·72 dq, $J_{20,30}$ = = 6·8 Hz, $J_{20,19}$ = 3·1 Hz (20-H), 3·61 ($COOCH_3$); 3·80d and 4·25 bd J_{gem} = 11 Hz (28-H_2); 4·47 m (3α-H).

Chloride VIIIb: The preparation of chloride *VIIIb* was carried out from 500 mg of acid *Vb* by the same procedure as in the case of chloride *VIIIa*. On repeated crystallisations from benzene–light petroleum mixture 50 mg of chloride *VIIIb* were obtained, m.p. 229–232°C, $[\alpha]_D$ +14° (*c* 0·74). IR spectrum: 1794 (COCl), 1735, 1260, 1035 (CH_3COO) cm^{-1}. For $C_{34}H_{53}ClO_5$ (577·2) calculated: 70·74% C, 9·26% H; found: 70·96% C, 9·21% H.

tert-Butylamide Xb: tert-Butylamide *Xb* was prepared from 420 mg of chloride *VIIIb* applying the same procedure as for the preparation of tert-butylamide *Xa*. Chromatography of the residue (420 mg) on 30 g of alumina (elution with 100 ml of benzene) gave 240 mg of amorphous tert-butylamide *Xb*, $[\alpha]_D$ +12° (*c* 0·65). IR spectrum: 3450, 1678, 1511, 1260 ($CONHC(CH_3)_3$), 1730, 1260, 1034 (CH_3COO) cm^{-1}.

Methylamide XIb: 510 mg of chloride *VIIIb* were dissolved in 50 ml of benzene saturated with methylamine. After an additional one hour's saturation with methylamine the solution was allowed to stand at room temperature for 72 hours. After evaporation of the solvent under reduced pressure the residue was dissolved in benzene and the solution was washed with dilute hydrochloric acid and water. Chromatography of the residue (510 mg) on 55 g of alumina (elution with 125 ml of benzene containing 10% of ethyl acetate) afforded 300 mg of methylamide *XIb*. On crystallisation from a mixture of chloroform and methanol a product was obtained of m.p. 237–238°C, $[\alpha]_D$ +14° (*c* 0·68). IR spectrum: 3470, 1670, 1533, 1259 ($CONHCH_3$), 1730, 1259, 1035 (CH_3COO) cm^{-1}. For $C_{35}H_{57}NO_5$ (571·8) calculated: 73·51% C, 10·05% H, 2·45% N; found: 73·68% C, 9·99% H, 2·44% N.

3β,28-Diacetoxy-(20*R*)-lupan-29-al (*Ia*)

To a suspension of 120 mg of chromium trioxide and 100 mg of anhydrous magnesium sulfate in 6 ml of dichloromethane 0·193 ml of pyridine in 1 ml of dichloromethane was added under stirring and cooling with ice. The mixture was stirred under cooling for another 20 minutes and the mixture with the complex formed was additioned with 105 mg of alcohol *VIa* in 3 ml of dichloromethane. The mixture was stirred for 30 minutes under cooling and an additional 30 minutes at room temperature under argon. The mixture was decomposed with sodium carbonate solution and the product extracted with ether. The extract was washed with dilute hydro-

chloric acid, sodium hydrogen carbonate solution, and water. Crystallisation of the residue from hexane gave 70 mg of aldehyde *Ia*; m.p. 202—211°C under decomposition; $[\alpha]_D$ −19° (*c* 0·69) IR spectrum: 1730, 1260, 1035 (CH_3COO), 2830, 2740, 1730 (CHO) cm^{-1}. Circular dichroism: $\Delta\varepsilon$ −0·33 (310 nm) (*c* 0·082). For $C_{34}H_{43}O_5$ (542·8) calculated: 75·23% C, 10·03% H; found: 75·13% C, 10·36% H.

3β,28-Diacetoxy-(20*S*)-lupan-29-al (*Ib*)

a) To a solution of 1·36 g imidazole in 15 ml tetrahydrofuran 0·42 ml of thionyl chloride was added at −10°C over one minute. The mixture was stirred at −10°C for 10 minutes and the separated imidazole hydrochloride was filtered off under nitrogen. Acid *Vb* (400 mg) was added to the filtrate and the mixture was allowed to stand at room temperature overnight. After pouring it into water a product separated which was extracted with ether. Evaporation *in vacuo* gave 320 mg of crude imidazolide *VIIb*. IR spectrum: 1730, 1260, 1035 (CH_3COO), 1735 (CON) cm^{-1}. To a solution of 320 mg imidazolide *VIIb* in 6 ml of tetrahydrofuran 600 mg of lithium tris-(tert-butoxy)hydridoaluminate were added and the mixture stirred for 3 hours and poured into dilute hydrochloric acid (1 : 10). The product was extracted with ether, the extract washed with water, sodium hydrogen carbonate solution, and water. According to thin-layer chromatography the residue contained aldehyde *Ib* and traces of compounds *Vb*, *VIb* and *VIIb*. The residue was chromatographed on a preparative silica gel plate. Yield, 50 mg of aldehyde *Ib*. After crystallisation from hexane a product was obtained of m.p. 203—210°C (under decomp.) $[\alpha]_D$ +16° (*c* 0·47). IR spectrum: 1725, 1260, 1035 (CH_3COO), 2830, 2720, 1725 (CHO) cm^{-1}.

b) Palladium catalyst (60 mg 5% Pd/C) was suspended in 20 ml of toluene and 5 ml of the solvent were distilled off while bubbling hydrogen gas through. To this suspension a solution of chloride *VIIIb* in 10 ml toluene was added (prepared from 200 mg of acid *Vb*). Hydrogen was introduced into the solution at 110°C for 2 hours. After rinsing with nitrogen the mixture was cooled, the catalyst filtered off and the filtrate evaporated *in vacuo*. After crystallisation from hexane and ether 100 mg of aldehyde *Ib* were obtained, m.p. 206—210°C (under decomp.) $[\alpha]_D$ +13° (*c* 0·62). Circular dichroism: $\Delta\varepsilon$ +1·36 (299 nm) (*c* 0·067). For $C_{34}H_{54}O_5$ (542·8) calculated: 75·23% C, 10·03% H; found: 75·27% C, 10·19% H.

c) Oxidation of alcohol *VIb* was carried out from 105 mg of alcohol *VIb* in the same manner as in the case of alcohol *VIa*. Crystallisation of the residue from hexane gave 80 mg of aldehyde *Ib*, m.p. 205—211°C, under decomp. $[\alpha]_D$ +13° (*c* 0·58).

3β,28-Diacetoxy-(20*R*)-lupan-29-ol (*VIa*)

a) To a solution of 2·90 g of a mixture of epimeric aldehydes *Ia* and *Ib* (prepared according to[3]) in 150 ml of ethyl acetate 3·0 g of lithium tris(tert-butoxy)hydridoaluminate were added and the mixture allowed to stand at room temperature for 4 hours. The mixture was decomposed with dilute hydrochloric acid and extracted with ether. The extract was washed with dilute hydrochloric acid and water and evaporated. The residue (2·80 g) was separated by chromatography on 300 g of alumina; elution with 900 ml of benzene containing 3% of ether gave 1·18 g of alcohol *VIa*. On crystallisation from a mixture of chloroform and methanol a product was obtained, m.p. 235—236°C, $[\alpha]_D$ −14° (*c* 0·65). IR spectrum: 3635 (OH), 1730, 1260, 1032 (CH_3COO); 2·79 . 10^{-3} M solution in tetrachloromethane: 3637 cm^{-1}, $\varepsilon^a = 62$, $\nu_{1/2} = 19$ cm^{-1}, B = 1840; 3623 cm^{-1}, $\varepsilon^a = 9$, $\nu_{1/2} = 10$ cm^{-1}, B = 140 (OH). PMR spectrum: 0·853 bs (3 × CH_3); 0·956, 1·046 (2 × CH_3); 0·958 d, $J_{30,20} = 6{\cdot}6$ Hz (20-CH_3), 2·01 (2 × CH_3COO); 3·41 dd and 3·775 bd, $J_{gem} = 10$ Hz (29-H_2); 3·775 d and 4·21 bd, $J_{gem} = 11$ Hz (28-H_2); 4·46 m (3α-H). For $C_{34}H_{56}O_5$ (544·8) calculated: 74·95% C, 10·36% H; found: 75·25% C, 10·27% H.

b) To a solution of 30 mg of aldehyde *Ia* in 4 ml of tetrahydrofuran cooled at 0°C 60 mg of lithium tris(tert-butoxy)hydridoaluminate were added and the mixture stirred at room temperature for 2 hours. After decomposition with dilute hydrochloric acid the product was extracted with ether, the extract washed with a solution of sodium hydrogen carbonate and water. From the residue a product was isolated by preparative thin-layer chromatography on silica gel. Yield 23 mg. After crystallisation from a mixture of chloroform and methanol the m.p. was 233—235°C.

c) To a solution of 270 mg of acid *Va* in 5 ml of tetrahydrofuran a solution of 0·070 ml of triethylamine in 1 ml of tetrahydrofuran was added followed by dropwise addition, over 30 minutes, of a solution of 0·048 ml of ethyl chloroformate in 1 ml of tetrahydrofuran. The addition was carried out at −5°C and under stirring and the mixture was stirred for another 30 minutes at the same temperature. The separated triethylamine hydrochloride was filtered off, the filtrate evaporated to dryness at +10°C *in vacuo* (oil pump). The yield of the amorphous mixed anhydride *XIVa* was 270 mg. IR spectrum: 1730, 1260, 1035 (CH_3COO), 1820, 1740 (COOCO) cm^{-1}. The residue was dissolved in 6 ml of tetrahydrofuran and added dropwise and under stirring over 30 minutes to a suspension of 50 mg of sodium borohydride in 1 ml of water (liberation of CO_2). The mixture was stirred for another 2·5 hours and decomposed with dilute hydrochloric acid. The product was extracted with ether, the extract washed with sodium hydrogen carbonate solution and water. The residue was chromatographed on 3 preparative silica gel thin-layer plates in hexane–ether 1 : 1. Yield 210 mg, m.p. 230—232°C, $[\alpha]_D$ −15° (*c* 0·57).

3β,28-Diacetoxy-(20*S*)-lupan-29-ol (*VIb*)

a) By further elution with the same solvent mixture (1400 ml) after the elution of the alcohol *VIa* 0·74 g of alcohol *VIb* were obtained. Repeated crystallisation from chloroform–methanol gave a product of m.p. 252—252·5°C, $[\alpha]_D$ −8° (*c* 0·64). IR spectrum: 3635 (OH), 1730, 1260, 1035 (CH_3COO) cm^{-1}; 2·06. 10^{-3} M solution in tetrachloromethane: 3641 cm^{-1}, $\varepsilon^a = 73$, $\nu_{1/2} = 16$ cm^{-1}, B = 1840; 3624 cm^{-1}, $\varepsilon^a = 15$, $\nu_{1/2} = 14$ cm^{-1}, B = 320 (OH). PMR spectrum: 0·850 bs (3 × CH_3); 0·960, 1·049 (2 × CH_3); 0·808 d, $J_{30,20} \approx 6{\cdot}5$ Hz (20-CH_3); 2·01 (2 × CH_3COO); 3·40 d, $J_{vic} = 6{\cdot}9$ Hz (29-H_2); 3·81 d and 4·26 bd, $J_{gem} = 11$ Hz (28-H_2); 4·475 m (3α-H). For $C_{34}H_{56}O_5$ (544·8) calculated: 74·95% C, 10·36% H; found: 75·06% C, 10·24% H.

b) The reduction of aldehyde *Ib* (30 mg) was carried out in the same manner as in the case of aldehyde *Ia*. From the residue alcohol *VIb* (20 mg) was obtained on chromatography on a preparative thin-layer plate (silica gel). M.p. 248—250°C (chloroform–methanol).

c) The preparation of mixed anhydride *XIVb* was carried out from 270 mg of acid *Vb* in the same manner as in the case of acid *Va*. The reaction yielded 265 mg of amorphous mixed anhydride *XIVb*. IR spectrum: 1730, 1260, 1035 (CH_3COO), 1820, 1740 (COOCO) cm^{-1}. The reduction of this anhydride was carried out in the same manner as in the case of anhydride *XIVa*. The residue was chromatographed on three preparative thin-layer silica gel plates in hexane–ether 1 : 1. Yield 220 mg of alcohol *VIb*, m.p. 248—251°C, $[\alpha]_D$ −8° (*c* 0·72).

3β,28-Diacetoxy-29-benzoyloxy-(20*R*)-lupane (*XIIIa*)

To a solution of 100 mg of alcohol *VIa* in 5 ml of pyridine 0·3 ml of benzoyl chloride were added and the reaction mixture allowed to stand at room temperature for 24 hours. After decomposition with water the mixture was extracted with ether. The extract was washed with dilute hydrochloric acid, water and sodium carbonate solution. Crystallisation of the residue (100 mg) from hexane afforded 60 mg of benzoate *XIIIa*, m.p. 186·5—188·5°C, $[\alpha]_D$ −19° (*c* 0·59). IR spectrum: 1718,

1610, 1592, 1280 (C_6H_5COO), 1730, 1261, 1032 (CH_3COO) cm^{-1}. For $C_{41}H_{60}O_6$ (648·9) calculated: 75·88% C, 9·32% H; found: 76·04% C, 9·29% H.

b) The mother liquors (4·3 g) after crystallisation of the mixture of alcohols *VIa* and *VIb* were dissolved in 15 ml of pyridine and the solution was additioned with 3 ml of benzoyl chloride. The mixture was allowed to stand at room temperature for 48 hours and then decomposed with water. After extraction with ether the extract was washed with dilute hydrochloric acid, water and sodium carbonate solution. A part of the residue (500 mg) was separated chromatographically on 60 g of alumina; 50 ml of light petroleum with 15% of ether eluted 70 mg of benzoate *XIIIa*. Repeated crystallisation from hexane gave a product of m.p. 187—188·5°C, $[\alpha]_D$ −18° (*c* 0·76).

3β-28-Diacetoxy-29-benzoyloxy-(20*S*)-lupane (*XIIIb*)

Further elution, after benzoate *XIIIa* was eluted, with the same mixture of solvents (80 ml) afforded 70 mg of benzoate *XIIIb*. Repeated crystallisation from a mixture of chloroform and hexane gave a product of m.p. 201·5—203·5°C, $[\alpha]_D$ +9 (*c* 0·69). IR spectrum: 1720, 1610, 1592, 1279 (C_6H_5COO), 1730, 1260, 1032 (CH_3COO) cm^{-1}. For $C_{41}H_{60}O_6$ (648·9) calculated: 75·88% C, 9·32% H; found: 75·84% C, 9·26% H.

Baeyer–Villiger Oxidation of Aldehyde *Ia*

Aldehyde *Ia* (20 mg) and *m*-chloroperbenzoic acid (32 mg) were dissolved in 2 ml of 1,2-dichloroethane and allowed to stand at room temperature for 3 days. After evaporation of the solvent the residue was dissolved in 10 ml of benzene and applied on a column of 5 g of alumina. After two days standing the product was eluted with benzene–ether 1 : 1. The residue was crystallised from ether. Yield 12 mg of noralcohol *IIa*, m.p. 229—232°C, $[\alpha]_D$ −11° (*c* 0·68).

Baeyer–Villiger Oxidation of Aldehyde *Ib*

a) Aldehyde *Ib* (30 mg) and *m*-chloroperbenzoic acid (30 mg) were dissolved in 4 ml of 1,2-dichloroethane and allowed to stand at room temperature for 3 days. After evaporation of the solvent in a vacuum the residue was dissolved in benzene and put on a column of 5 g of alumina. After 2 days standing the product was eluted with a mixture of benzene and ether 2 : 3. The residue was crystallised from chloroform–methanol. Yield 20 mg of nor alcohol *IIb*, m.p. 258—260°C, $[\alpha]_D$ −12° (*c* 0·56).

b) To a solution of 30 mg of aldehyde *Ib* in 0·3 ml of chloroform 0·15 ml of 99% formic acid and 0·08 ml of 30% hydrogen peroxide were added and the mixture stirred for 5 hours at room temperature. After pouring it into water it was extracted with chloroform and the extract washed with sodium hydrogen carbonate solution and water. The residue was dissolved in benzene and introduced onto a column of 10 g of alumina. After 2 days standing the product was eluted with a benzene–ether mixture (2 : 3). The residue was crystallised from a mixture of ethyl acetate and methanol. Yield 15 mg of alcohol *IIb*, m.p. 260—263°C, $[\alpha]_D$ −10° (*c* 0·49).

3β,28-Diacetoxy-29a-homo-(20*R*)-lupan-29-one (*XIIa*)

Chloride *VIIIa* (170 mg) was dissolved in 15 ml of benzene and the solution added dropwise over 10 minutes at −20°C to a solution of diazomethane in ether (prepared from 5 g of N-nitroso-N-methylurea). The mixture was allowed to stand overnight at room temperature and the excess diazomethane and the solvents were evaporated under reduced pressure. After the addition of hexane and evaporation under reduced pressure amorphous diazoketone *XVa* was obtained.

IR spectrum: 1730, 1260, 1035 (CH_3COO), 3130, 2115, 1645 ($COCHN_2$) cm^{-1}. A solution of diazoketone *XVa* in 20 ml of chloroform was shaken with 12·5 ml of 56% hydriodic acid. The chloroform layer was washed with a saturated potassium iodide solution and water, saturated sodium thiosulfate solution and water. The residue was crystallised from ether. Yield 125 mg of homoketone *XIIa*, m.p. 216–219°C, $[\alpha]_D$ −12° (*c* 0·61). IR spectrum: 1730, 1260, 1035 (CH_3COO), 1700 (CO)cm^{-1}. PMR spectrum: 0·849 (2 × CH_3); 0·870, 0·934, 1·052 (3 × CH_3); 1·126 d $J_{30,20}$ = 7·2 Hz (20-CH_3); 2·04, 2·05 (2 × CH_3COO); 2·15 ($COCH_3$), 3·77 d and 4·22 bd J_{gem} = 11 Hz (28-H_2); 2·86 bq $J_{20,30}$ = 7·2 Hz $J_{20,19} \neq 0 < 1{\cdot}5$ Hz (20-H); 4·48 m (3α-H). For $C_{35}H_{56}O_5$ (556·8) calculated: 75·49% C, 10·14% H; found: 75·20% C, 9·83% H.

3β,28-Diacetoxy-29*a*-homo-(20*S*)-lupan-29-one (*XIIb*)

The preparation of diazoketone *XVb* was carried out with 170 mg of chloride *VIIIb* in the same manner as in the case of diazoketone *XVa*. IR spectrum: 1730, 1260, 1035 (CH_3COO), 3125, 2115, 1647 ($COCHN_2$) cm^{-1}. The conversion of diazoketone *XVb* to homoketone *XIIb* was also carried out as in the case of diazoketone *XVa*. The residue was crystallised from ether. Yield 130 mg of homoketone *XIIb* of m.p. 268–272°C, $[\alpha]_D$ +30·5° (*c* 0·62). IR spectrum: 1730, 1260, 1035 (CH_3COO), 1710 (CO) cm^{-1}. PMR spectrum: 0·853 (2 × CH_3); 0·875, 0·972 (2 × CH_3); 0·977 d $J_{29,20}$ = 6·9 Hz (20-CH_3); 1·069 (CH_3); 2·04, 2·06 (2 × CH_3COO); 2·12 ($COCH_3$), 2·77 dq $J_{20,19}$ = 3·4 Hz, $J_{20,29}$ = 6·9 Hz (20-H); 3·71d and 4·29 bd J_{gem} = 11 Hz (28-H_2), 4·48 m (3α-H). For $C_{35}H_{56}O_5$ (556·8) calculated: 75·49% C, 10·14% H; found: 75·35% C, 9·99% H.

For elemental analyses we thank the staff of the analytical laboratory, Department of Organic Chemistry, Charles University, for the measurement of IR spectra our thanks are due to Dr J. Pecka of the same laboratory. We thank Dr M. Budějínský and Dr I. Frič, Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, for the PMR spectra and circular dichroism measurements.

REFERENCES

1. Klinotová E., Hovorková N., Klinot J., Vystrčil A.: This Journal *38*, 1179 (1973).
2. Vystrčil A., Blecha Z.: This Journal, in press.
3. Klinot J., Hovorková N., Vystrčil A.: This Journal *35*, 1105 (1970).
4. Ruzicka L., Brenner M.: Helv. Chim. Acta *23*, 1325 (1940).
5. Staab H. A., Walther G.: Ann. *657*, 98 (1962).
6. McMorris T. C.: J. Org. Chem. *35*, 459 (1970).
7. Ratcliffe R., Rodehorst R.: J. Org. Chem. *35*, 4000 (1970).
8. Henrick C. A., Schaub F., Siddall J. B.: J. Am. Chem. Soc. *94*, 5374 (1972).
9. Ishizumi K., Koga K., Yamada S.: Chem. Pharm. Bull. (Tokyo) *16*, 492 (1968).
10. Barber G. W., Hrenstein M.: J. Org. Chem. *19*, 1758 (1954).

Translated by Ž. Procházka.