FUNCTIONALIZATION OF 3β,28-LUPANEDIOL DIACETATE WITH CHROMIUM(VI) OXIDE*

Jan SEJBAL[a], Jiří KLINOT[a], Miloš BUDĚŠÍNSKÝ[b] and Jiří PROTIVA[a]

[a] *Department of Organic Chemistry, Charles University, 128 40 Prague 2*
[b] *Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Science, 166 10 Prague 6*

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Dedicated to Professor Alois Vystrčil on the occasion of his 70th birthday.

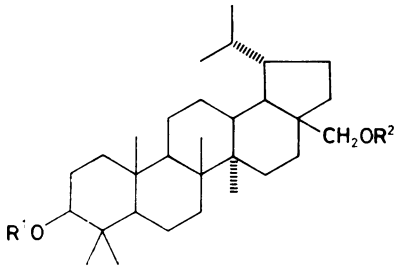
The oxidation of 3β,28-lupanediol diacetate (*I*) with chromium(*VI*) oxide gives low yields of products with functional groups in the ring E as products of hydroxylation at the 19β position (*IV*, *VI*, and *IX*) and the 11-ketone *VII* which has been transformed into other lupane derivatives with an oxygen functional group at 11 position (*VIII*, *XIII*—*XV*) or with a 9(11)-double bond (*XVI*, *XVII*). Structure of the compounds prepared has been verified by their ^{1}H and ^{13}C NMR spectra as well as by their mass spectra.

Again and again new triterpenes with functional groups at unusual positions are found in natural materials. With lupane derivatives quite common is the presence of oxygen functional groups at 3β and 28 positions and a double bond 20(30); in other positions substituents are less common and the respective compounds are found in nature only sporadically. In the present paper we have tried to prepare lupane derivatives with functional groups in less common positions using the radical functionalization of 3β,28-lupanediol diacetate (*I*).

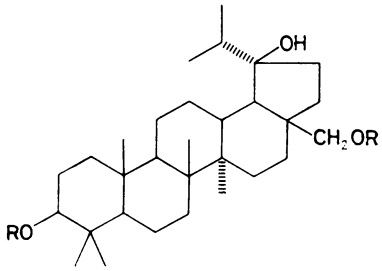
From literature it is known that application of selective radical reagents introduces functional groups only into the 19 position of diacetate *I*: dry ozonation[1] and the reaction with 3-chloroperbenzoic acid[2] give the 19β-hydroxy derivative *IV*, the reaction with peroxyacetic acid[3] gives a mixture of 19β-hydroxy derivative *IV* and 18β,19β-epoxy-3β,28-lupanediol diacetate (*XII*). Now we have used chromium(VI) oxide as a less selective radical reagent[4] which often attacks also secondary carbon atoms. The functionalizations with chromium(VI) oxide are usually carried out in acetic acid at room temperature. However, the diacetate *I* does not react at these conditions. If the reaction mixture is heated at 100°C, then a complex mixture of products is formed out of which only the nonpolar products were studied in detail.

* Part XCVII in the series on Triterpenes; Part XCVI: Collect. Czech. Chem. Commun. *56*, 2917 (1991).

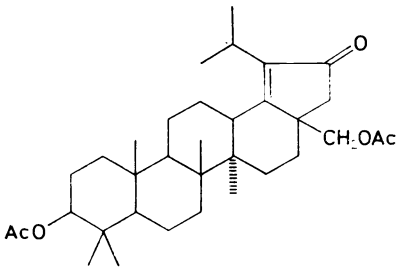
More than one half of the starting diacetate *I* underwent destruction; the evaporation residue after extraction of the dilute reaction mixture with ether corresponds only to 44% of the weight of the starting diacetate *I*. It was possible by chromatography to obtain three pure substances beside the unreacted starting diacetate *I* (13%), and other two substances were isolated from the chromatographic fractions



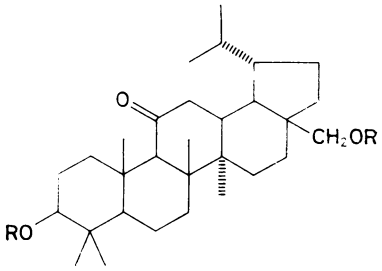
I, $R^1 = R^2 = Ac$
II, $R^1 = R^2 = H$
III, $R^1 = H$; $R^2 = Ac$



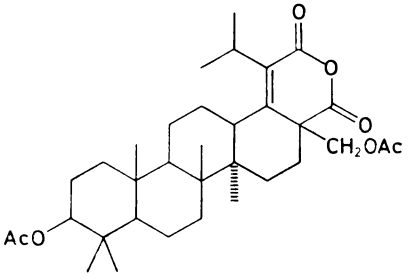
IV, R = Ac
V, R = H



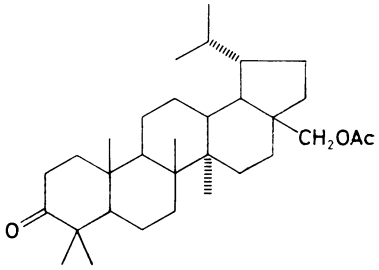
VI



VII, R = Ac
VIII, R = H



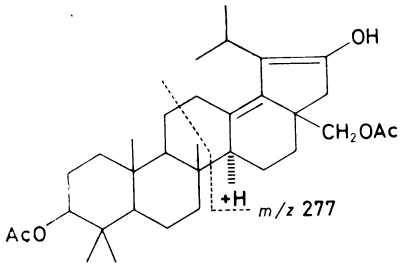
IX



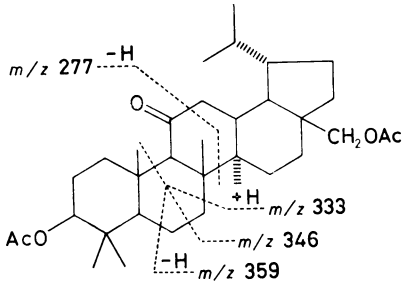
X

and identified after reduction with hydrides. The remaining fractions (denoted as *A*, *B*, *C* in Experimental) were chromatographically unresolvable and were not analyzed further; the corresponding ^{1}H NMR spectra indicate that they are mixtures.

The most highly populated product which was obtained in the yield of 3% was the unsaturated ketone *VI*. Its IR spectrum (1 693 and 1 603 cm^{-1}) indicates a five-membered cyclic unsaturated ketone. Its ^{1}H NMR spectrum shows a heptuplet H-20 at δ 3·18 characteristic of lupane derivatives with 18(19) double bond[3] and a doublet at δ 2·39 (J = 18·9 Hz) which can be assigned to one of the hydrogen atoms at C-22 which form an AB system at the α position to carbonyl. In the ^{13}C NMR spectrum (Table I) the signals of quaternary carbon atoms at δ 170·73, 146·65, and 207·55 confirm the presence of the fragment C=C—C=O. The most intensive ion of the mass spectrum is that at m/z 277 formed by fragmentation of the ring C between the pairs of atoms C-11, C-12 and C-8, C-14 with a hydrogen transfer from the neutral fragment to the rings D and E. Its formation can be explained on the basis of twofold allylic splitting of enol form *VIa*. For comparison the ketone *VI* was prepared by reaction of the 18-olefin *XI* with chromium(VI) oxide according to the analogies in ref.[5]; the epoxide *XII* described earlier[3] is a side product of the reaction.



VIa



VII

The presence of the heptuplet H-20 at δ 3·26 in the ^{1}H NMR spectrum of another isolated compound (*IX*) indicates a close connection with the previous derivative. The bands at 1 789 and 1 720 cm^{-1} in the IR spectrum together with the signals of two olefinic and two carbonyl (beside the acetate carbons) carbon atoms in the ^{13}C NMR spectrum (δ 151·58, 135·38, 159·30, and 169·78) indicate an unsaturated six-membered cyclic anhydride. Compound *IX* is also formed as the only product from the oxidation of ketone *VI* with chromium(VI) oxide at the conditions of the functionalization.

Another derivative present – according to TLC and ^{1}H NMR spectrum – in one fraction was 19β-hydroxy derivative *IV*. It could not be purified chromato-

graphically, and alkaline hydrolysis of the fraction failed, too. Only after reduction of the fraction with lithium tetrahydridoaluminate it was possible to isolate the

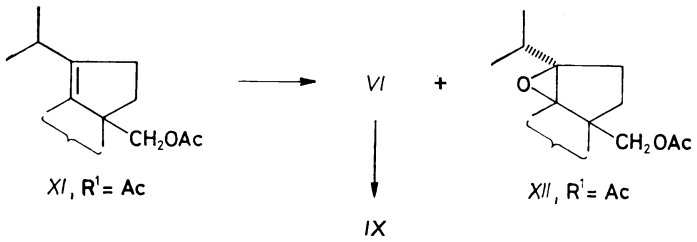
TABLE I

Carbon-13 chemical shifts of lupane derivatives *I*, *IV*, *VI*, *VII*, *IX*, *XIV* and *XVI*

Carbon	*I*	*IV*	*VI*	*VII*	*IX*	*XIV*	*XVI*
1	38·32	38·33	38·45	36·29	38·58	38·48	38·93
2	23·64	23·65	23·50	23·34	23·59	23·53	24·22
3	80·84	80·90	80·57	80·52	80·54	80·81	80·61
4	37·74	37·77	37·65	37·73	37·80	37·73	37·98
5	55·27	55·33	55·29	54·45	55·65	56·22	52·18
6	18·13	18·17	17·99	17·79	17·94	18·41	18·16
7	34·15	34·22	34·69	33·04	33·80	35·99	33·79
8	40·87	41·06	41·25	44·91	42·46	41·35	40·69
9	49·90	49·99	50·85	63·89	52·18	53·09	153·51
10	36·96	37·00	37·00	37·81	37·08	38·18	37·31
11	20·76	20·63	21·18	210·51	22·27	67·14	116·37
12	26·76	25·86	27·36	45·39	28·22	37·54	28·96
13	37·06	36·92	42·33	38·42	43·55	31·78	33·33
14	42·79	42·99	45·32	42·77	44·36	43·03	42·47
15	26·87	26·93	27·64	26·53	27·07	27·11	27·11
16	29·79	30·48	32·53	29·52	30·01	29·76	29·33
17	46·39	46·46	47·55	46·64	53·37	46·53	46·21
18	48·05	50·43	170·73[a]	47·72	151·58	47·88	48·66
19	44·45	85·09	146·65	43·99	135·38	44·39	45·39
20	29·38	33·75	25·04	28·96	28·07	29·61	29·25
21	21·54	33·54	207·55	21·41	159·30	21·64	21·54
22	34·59	34·88	45·36	34·29	169·78	34·57	34·18
23	27·89	27·92	27·79	27·89	27·82	28·12	27·96
24	16·47	16·47	16·42	16·53	16·44	16·54	16·52
25	16·00[a]	16·07[a]	15·77	16·18	16·35	18·08	16·15[a]
26	16·06[a]	16·16[a]	19·84	18·27	19·43	19·35	16·42[a]
27	14·57[b]	14·78	16·74	14·49	16·92	15·10	24·86
28	62·78	63·19	66·73	62·21	66·68	62·74	62·78
29	14·86[b]	17·35	16·74	14·72	20·41	14·89	14·91
30	22·88	18·72	20·47	22·69	22·13	22·84	22·92
OAc:							
C=O	170·91	171·00	170·81[a]	170·82	170·12	171·04	170·01
	171·55	171·34	171·73[a]	171·26	170·94	171·56	171·65
CH_3	21·29	21·30	21·18	21·20	21·28	21·29	21·34
	21·02	21·08	20·58	20·91	20·49	21·03	21·07

[a,b] The assignment of signals with the same letters may be interchanged.

3β,19β,28-triol *V* which gave the original diacetate *IV* on acetylation. This compound is known[1-3] and its formation can be explained by a direct attack of the 19 position. It is a likely precursor of the two above-mentioned compounds *VI* and *IX*: it can be presumed that at the given conditions a water molecule is eliminated from compound *IV*, and the olefin *XI* formed undergoes allylic oxidation to give the ketone *VI* which is further oxidized to anhydride *IX*. The formation of 18-olefin *XI* from 19β-hydroxy derivative *IV* by action of $POCl_3$ is described in ref.[3]; both the oxidations were confirmed experimentally (Scheme 1). 3β,28-Lupanediol 28-acetate (*III*) was obtained after reduction from another fraction (containing, according to ^{1}H NMR and TLC, the 3-oxo derivative *X* as the predominant component) like in the previous case.



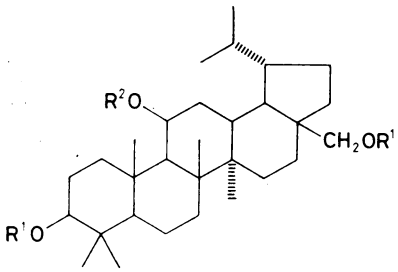
SCHEME 1

Another product of the oxidation of diacetate *I* with chromium(VI) oxide was the 11-oxo derivative *VII* whose structure was determined on the basis of the following spectral data and reactions: The IR spectrum indicates a six-membered saturated ketone (1 700 cm^{-1}). The ^{1}H NMR spectrum shows the hydrogen signals 3α-H and 2 × H-28 (4·47 m, 3·77 d, and 4·24 d) which are only little affected as compared with the starting diacetate *I* (4·46 m, 3·80 d, and 4·25 d), which excludes the carbonyl group at the positions 1, 2, and 16. The position 6 can be excluded with regard to the unchanged chemical shifts of the methyl groups 4α-CH_3 and 4β-CH_3. The mass spectrum does not correspond the known[6] fragmentation of 12-oxo and 16-oxo triterpenoids. The triterpenoids with a ketonic group at 7 position are reduced with hydrides to give epimeric 7-hydroxy derivatives[7], whereas the ketone *VII* gives the triol *XIII* as the only product on reduction with lithium tetrahydridoaluminate. Also the ^{13}C NMR spectrum agrees with the structure of 11-oxo derivative: the signals of carbon atoms at all positions except 9, 11, 12 are very little affected as compared with those of the starting diacetate *I*.

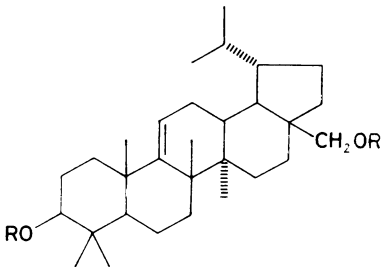
Also the mass spectra of the 11-oxo derivative *VII* and the therefrom prepared (by hydrolysis) diol *VIII* are in accordance with the suggested structure and correspond to the fragmentation mechanism given in ref.[8] for 11-oxo derivatives of the types *XXI* and *XXII*. The dominant splitting is that of the ring C giving the ions *m/z* 277 and 235 with the diacetate *VII* and diol *VIII*, respectively. In the case of diol

VIII this ion splits off carbon monoxide to give the ion of *m/z* 207. Other significant splittings are the fragmentations of the ring B leading to the fragments with *m/z* 359, 346, and 333 (from the diacetate *VII*) and *m/z* 317 and 304 (from diol *VIII*).

The 11-oxo derivative *VII* is only little reactive. It does not form the oxime by heating with pyridine solution of hydroxylamine, and it does not react with isopropenyl acetate, ethyl orthoformate, and 3-chloroperbenzoic acid. The reduction with sodium tetrahydridoborate does not give a uniform product, that with lithium tetrahydridoaluminate gives triol *XIII*. Triol *XIII* gives a mixture of diacetate *XIV* and triacetate *XV* on acetylation with acetic anhydride in pyridine; the triacetate *XV* can be prepared from triol *XIII* directly by heating with acetanhydride. In the ^{1}H NMR spectra the proton 11-H gives a narrow multiplet (the sum of coupling constants 6–7 Hz) corresponding to an equatorial hydrogen atom, which, together with the analogy for the stereochemistry of reduction of 11-oxo derivative[8], enables the assignment of 11β configuration to the derivatives *XIII*–*XV*.



XIII, $R^1 = R^2 = H$
XIV, R^1 = Ac ; R^2 = H
XV, $R^1 = R^2$ = Ac



XVI, R = Ac
XVII, R = H

The reaction of 11β-hydroxy derivative *XIV* with phosphorus(V) trichloride oxide gives only one unsaturated derivative *XVI* whose hydrolysis gave diol *XVII*. The ^{1}H NMR spectra of both the compounds show one olefinic proton (δ 5·26 dd, J' = = 4·3 Hz, J'' = 2·8 Hz) and indicate compounds with 9(11) double bond. In accordance with this structure the ^{13}C NMR spectrum of compound *XVI* shows two signals of olefinic carbon atoms of a trisubstituted double bond (δ 153·51 and 116·37).

The mass spectra of the 11β-hydroxy derivatives exhibit – as the main type of splitting – decomposition of the ring C with formation of the ions *m/z* 279 and 237 from the diacetate *XIV* and triol *XIII*, respectively. The most intensive ions in the mass spectra of both 9(11)-unsaturated derivatives (*m/z* 276 and 234 from compounds *XVI* and *XVII*, respectively) come from the retro-Diels–Alder splitting of the ring C. The 11β-triacetate *XV* shows no molecular ion in its mass spectrum:

TABLE II

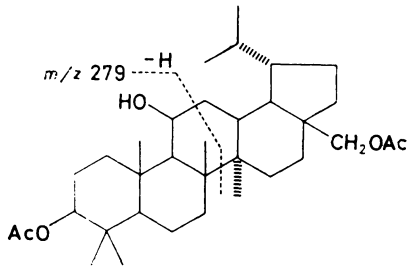
Proton NMR parameters of 11-substituted lupane derivatives and the reference compounds

Compound	4α-Me	4β-Me	10β-Me	8β-Me	14α-Me	20-Me's[a] (29-H_2)	OAc	3α-H[b]	11-H[c]	28-H_2[d] (17-Me)
11-oxo:										
VII	0·85	0·87	1·21	1·01	1·18	0·77; 0·84	2·04; 2·06	4·47	—	3·77; 4·24
VIII	0·99	0·80	1·20	0·99	1·20	0·77; 0·84	—	3·16	—	3·29; 3·69
XXI[e]	[f]	0·86	1·23	1·02	1·16	1·70; (4·72 m)	2·05	4·53	—	(0·77 s)
XXII[e]	1·06	1·06	1·38	1·06	1·19	1·70; (4·72 m)	—	—	—	(0·80 s)
11β-OH:										
XIV	0·84	0·87	1·36	1·38	0·94	0·78; 0·86	2·05; 2·06	4·46	4·30	3·89; 4·30
XIII	0·97	0·80	1·37	1·37	0·94	0·77; 0·86	—	3·19	4·30	3·31; 3·78
XXIII[e]	0·84	0·84	1·37	1·37	0·94	[f]; (4·65 m[h])	2·04	4·65[h]	4·30	(0·84 s)
XXIV[e]	0·94	0·79	1·32	1·32	0·96	1·68; (4·58—4·71 m)	—	3·18	4·24	(0·79 s)

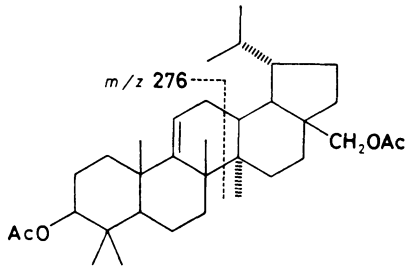
11β-OAc:										
XV	0·84	0·83	1·10	1·35	0·96	0·75; 0·83	2·04; 2·06(2)	4·48	5·40	3·86; 4·30
XXV[e]	0·83	0·83	1·25[g]	1·35	0·95	[f] ; (4·65 m[h])	2·04(2)	4·65[h]	—	(0·85 s)
9(11)-en:										
XVI	0·87	0·88	1·16	1·25	0·87	0·80; 0·86	2·05; 2·06	4·47	5·26	3·86; 4·26
XVII	0·99	0·80	1·14	1·24	0·90	0·80; 0·86	—	3·19	5·27	3·33; 3·80
Reference compounds:										
I	0·85	0·84	0·86	1·04	0·95	0·77; 0·84	2·03; 2·04	4·46	[i]	3·80; 4·25
II	0·97	0·77	0·84	1·03	0·97	0·77; 0·84	—	3·18	[i]	3·31; 3·78
XVIII	0·85	0·85	0·85	1·03	0·94	1·69; (4·57 + 4·69 m)	2·03	4·47	[i]	(0·78 s)
XIX	0·98	0·77	0·85	1·05	0·95	1·69; (4·57 + 4·69 m)	—	3·21	[i]	(0·79 s)
XX	1·07	1·03	0·95	1·07	0·95	1·69; (4·57 + 4·69 m)	—		[i]	(0·80 s)

[a] Doublets with $J \approx 7{\cdot}0$ Hz; [b] multiplet with $\sum J \approx 16$ Hz; [c] multiplet with $\sum J = 7-10$ Hz; [d] doublets with $J = 11{\cdot}0-11{\cdot}8$ Hz; [e] data taken from ref.[8]; [f] ref.[8] gives data for 6 methyl signals only; [g] probably incorrect value (not used for substituent effect calculation); [h] overlapping signals; [i] not found.

it splits off acetic acid and its further fragmentation is almost the same as that of the 9(11)-unsaturated derivative *XVI*.



XIV



XVI

Table II summarizes important parameters of ^{1}H NMR spectra of the newly prepared 11-substituted and 9(11)-unsaturated derivatives together with the structural assignment of the signals of methyl protons. For comparison the table also presents the data of analogous 11-substituted lupane derivatives *XXI–XXIV* taken from ref.[8] (with our assignment of the methyl signals). Table III shows the average values of the substituent effects connected with introduction of the 11-oxo, 11β-hydroxy groups and 9(11)-double bond into the lupane skeleton. Considered are all the compounds given in Table II, compounds *I*, *II*, *XVIII–XX* being taken as the reference substances (their ^{1}H NMR parameters are given in Table II, too). The substituent effects on chemical shifts of methyl groups found by us agree with the effect of spatially similarly oriented functional groups and multiple bonds on methyl signals in steroids[9].

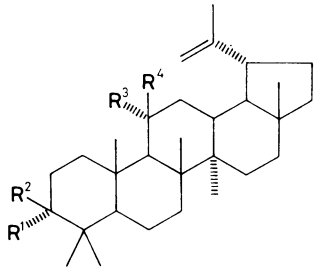
The assignment of ^{13}C NMR spectra is based on the experimental assignment of carbon signals according to the number of attached hydrogen atoms, arguments following from the generally known relations between chemical shifts and structural features, and particularly from the structural assignment of carbon atoms in lupane

TABLE III

Substituent effects on methyl protons in lupane derivatives

Substituents	4α-Me	4β-Me	10β-Me	8β-Me	14α-Me	20-Me's	
11-oxo	0·00	0·03	0·37	−0·03	0·23	0·00	0·00
11β-OH	−0·02	0·02	0·51	0·33	−0·02	0·00	0·02
11β-OAc	−0·01	−0·01	0·24	0·21	0·01	−0·02	−0·01
$\Delta^{9(11)}$	0·02	0·04	0·30	0·21	−0·08	0·03	0·02

described in ref.[10]. At first the signals in spectrum of the starting diacetate *I* were assigned to make the interpretation easier.



XVIII, $R^1 = R^3 = R^4 = H$; $R^2 = OAc$
XIX, $R^1 = R^3 = R^4 = H$; $R^2 = OH$
XX, $R^1 + R^2 = O$; $R^3 = R^4 = H$
XXI, $R^1 = H$; $R^2 = OAc$; $R^3 + R^4 = O$
XXII, $R^1 + R^2 = O$; $R^3 + R^4 = O$
XXIII, $R^1 = R^3 = H$; $R^2 = OAc$; $R^4 = OH$
XXIV, $R^1 = R^3 = H$; $R^2 = R^4 = OH$
XXV, $R^1 = R^3 = H$; $R^2 = R^4 = OAc$

The lupane derivatives with a functional group at the 11 position prepared in the present work obviously are the first derivatives of this type obtained by synthetic procedures. Their structure was confirmed by a combination of various methods. So far only a few natural lupane triterpenes with an oxygen functional group at 11α position have been isolated[11–13], and also known is one triterpene with an OH group at 11β position[8]. The paper[14] describes the isolation of 3-oxo-9(11)--lupene-28-oic acid and 3-oxo-9(11)-lupene-28-al from several species of the *Senecio* genus. Both these derivatives were transformed by reduction into the same diol which was ascribed the structure of 9(11)-lupene-3β,28-diol. However, the physical constants and spectral data of this diol are considerably different from those of the 9(11)-unsaturated diol prepared in the present work (the differences are 61°C and 70° in the m.p. and $[\alpha]_D$, respectively), which leads to a conclusion that the structures of the whole series of 9(11)-lupene derivatives described in ref.[14] are incorrect. From the chemical shifts of methyl groups published in the paper[14] not only for the 9(11)-lupene derivatives mentioned but also for a series of 12-lupene derivatives it can even be concluded that they obviously are not triterpenoids with the lupane skeleton.

EXPERIMENTAL

The melting temperatures were determined with a Kofler apparatus and are not corrected. The optical rotations were determined in chloroform using an automatic polarimeter ETL-NPL

(Bendix–Ericsson) with the accuracy of $\pm 2°$ (concentration 0·4—0·8). The IR spectra were measured in chloroform using a PE 684 apparatus (Perkin–Elmer). The wavenumbers are given in cm^{-1}. The ^1H NMR spectra were measured with a Tesla BS 487 A apparatus (80 MHz, CW mode) in deuteriochloroform using hexamethyldisiloxane as the internal standard (the chemical shifts were referred to tetramethylsilane according to the relation $\delta(HMDS) = 0{\cdot}063$ and were rounded off to two decimals) or with a Varian XL-200 apparatus (200 MHz, FT mode) in deuteriochloroform with tetramethylsilane as the internal standard. The chemical shifts and coupling constants (in Hz) were obtained by the analysis of the first order. The ^{13}C NMR spectra were measured with the Varian XL-200 apparatus (50·31 MHz, attached proton test technique). in deuteriochloroform. The chemical shifts were referenced to the solvent signal and recalculated according to the relation $\delta(CDCl_3) = 77{\cdot}00$. The mass spectra were measured with a Varian MAT 311 apparatus, the ionizing electron energy of 70 eV. The direct inlet temperatures varied within the limits from 150 to 180°C. The UV spectra were measured with a Unicam SP-700 apparatus in cyclohexane. The CD spectrum was measured with a dichrograph I Roussel-Jouan 185 in dioxane.

The identity of samples prepared by different procedures was verified by TLC, IR and ^1H NMR spectra. The thin layer chromatography was carried out on silica gel plates G (Merck), detection by spraying with a 10% sulfuric acid solution and heating or on Silufol plates (Kavalier, Votice), detection with 5% ethanolic molybdophosphoric acid and heating. The preparative thin layer chromatography was carried out on Kieselgel 60 G (Merck), the column chromatography with silica gel Silpearl (Kavalier, Votice). "Usual processing" involved pouring of the reaction mixture onto water, extraction of the products in ether, successive washing of the ethereal layer with water, diluted hydrochloric acid, water, saturated solution of sodium hydrogen carbonate, water, drying with sodium sulfate, and evaporation of the solvent under reduced pressure. For analyses the samples were dried in vacuum over phosphorus pentoxide at room temperature.

The starting compounds *I* and *XI* were prepared according to refs[15,16].

Oxidation of Diacetate *I* with Chromium(VI) Oxide

A mixture of 40 g diacetate *I*, 50 g chromium(VI) oxide, and 600 ml acetic acid was heated at 100°C 20 min and then cooled. The separated starting diacetate was collected by suction and mixed with a solution of 15 g chromium(VI) oxide in 200 ml acetic acid and again heated at 100°C 20 min. The combined solutions were concentrated to 100 ml and submitted to the above-mentioned usual processing. The evaporation residue (17·5 g) was submitted to chromatography on a silica gel column (260 g) with a 15 : 1 mixture of petroleum ether and ether. We obtained successively:

a) 5·2 g starting diacetate *I*.

b) 0·65 g (1·5%) 3β,28-dihydroxylupan-11-one diacetate (*VII*) recrystallized from ethanol, m.p. 271—272°C (sublimation about 250°C), $[\alpha]_D$ +19°. IR spectrum: 1 726 and 1 252 (OAc), 1 700 (C=O), 1 031 (C—O—C). ^1H NMR spectrum (200 MHz) and ^{13}C NMR spectrum, (Tables I and II). Mass spectrum, *m/z* (%): 542 (17, M^+ $C_{34}H_{54}O_5$), 527 (2), 482 (41, $C_{32}H_{50}O_3$); 469 (11, $C_{31}H_{49}O_3$), 467 (8), 439 (10), 409 (12), 359 (16, $C_{23}H_{35}O_3$), 346 (27), 333 (8), 277 (86, $C_{17}H_{25}O_3$), 249 (14), 191 (74), 190 (67), 189 (100), 95 (95). CD spectrum: λ_{max} 309 nm, $\Delta\varepsilon = -0{\cdot}5$. For $C_{34}H_{54}O_5$ (542·8) calculated: 75·23% C, 10·03% H; found: 75·44% C, 10·05% H.

c) 0·12 g chromatographically unseparable fraction *A*.

d) 0·07 g chromatographically unseparable fraction which according to its ^1H NMR spectrum predominantly contains 28-hydroxy-3-lupanone acetate (*X*). Reduction of this fraction

with 20 mg sodium tetrahydridoborate in 10 ml methanol and (after 20 min) the usual processing followed by TLC (10 g silica gel plate, petroleum ether–ether 2 : 1) gave 55 mg (0·15%) 3β,28--lupanediol 28-acetate (*III*), m.p. 243–245°C, $[\alpha]_D$ +21°, identical with the authentic sample[17]

e) 2·5 g chromatographically unseparable fraction *B*.

f) 0·2 g chromatographically unseparable fraction. This fraction was refluxed with 30 mg lithium tetrahydridoaluminate in 20 ml ether 20 min, whereafter ethyl acetate was added, the reaction mixture was poured onto ice and dilute hydrochloric acid and submitted to the usual processing followed by column chromatography (20 g silica gel, petroleum ether–ether 10 : 1) to give 85 mg (0·24%) 3β,19β,28-lupanetriol (*V*) recrystallized from methanol; m.p. 288–290°C (sublimation about 255°C), $[\alpha]_D$ −11°. IR spectrum: 3 611 and 3 526 (OH), 1 026, 994. ^{1}H NMR spectrum (80 MHz): 0·78 s, 0·87 s, 0·92 s, 0·98 s, and 1·06 s (5 × CH_3); 3·19 m, 1 H (3α-H); 3·34 d, 1 H and 3·73 d, 1 H (2 × H-28, J = 10·5 Hz). Mass spectrum, *m/z* (%): 442 (10, M^+ − 18), 427 (11), 411 (21), 207 (60), 203 (100), 189 (92). For $C_{30}H_{52}O_3$ (460·7) calculated: 78·20% C, 11·38% H; found: 78·12% C, 11·33% H. The acetylation of triol *V* with acetanhydride in pyridine at room temperature (30 h) gave the diacetate *IV* identical with the authentic sample prepared[3]. For the ^{13}C NMR spectrum of the diacetate *IV* see Table I.

g) 3·8 g chromatographically unseparable fraction *C*.

h) 0·18 g (0·42%) 3β,28-dihydroxy-21,22-secolup-18(19)-ene-21,22-dioic anhydride diacetate (*IX*) recrystallized from acetone; m.p. 315–320°C (above 260° slow decomposition with liberation of a gas), $[\alpha]_D$ +87°. IR spectrum: 1 789, 1 720 (anhydride), 1 741, 1 254 (OAc), 1 626 (C=C). ^{1}H NMR spectrum (200 MHz): 0·85 s, 0·85 s, 0·90 s, 0·91 s, 1·11 s, 1·14 d (J = 7·0) and 1·31 d (J = 7·0), 7 × 3 H (7 × CH_3); 2·01 s, 3 H, and 2·05 s, 3 H (2 × OAc); 2·53 dt, 1 H (J' = 14·4, J'' = J''' = 3·5); 2·72 dd, 1 H (J' = 3·1, J'' = 12·3); 3·26 heptuplet, 1 H (H-20, J = 7·0); 3·90 d, 1 H, and 4·54 d, 1 H (2 × H-28, J = 11·0), 4·47 m, 1 H (H-3α). ^{13}C NMR spectrum in Table I. Mass spectrum, *m/z* (%): 570 (0·2), 555 (0·2), 528 (18), 510 (13), 495 (11), 468 (35), 453 (15), 425 (14), 407 (9), 406 (9), 265 (11), 203 (43), 189 (100). For $C_{34}H_{50}O_7$ (570·7) calculated: 71·55% C, 8·83% H; found: 71·45% C, 8·91% H.

i) 1·1 g (2·7%) 3β,28-dihydroxy-18-lupen-21-one diacetate (*VI*) recrystallized from a mixture chloroform–methanol, m.p. 198–201°C (a change of modification at 150°C), $[\alpha]_D$ −34°. IR spectrum: 1 731, 1 252, 1 245 (OAc), 1 693 (C=O), 1 603 (C=C), 1 038, 1 030 (C–C–C). ^{1}H NMR spectrum (200 MHz): 0·85 s, 0·86 s, 0·93 s, 0·94 s, 1·16 s, 1·17 d (J = 6·5), 1·21 d (J = 6·5), 7 × 3 H (7 × CH_3); 2·00 s, 3 H, 2·05 s, 3 H (2 × OAc); 2·39 d, 1 H (H-22, J = 18·9); 2·87 dd, 1 H (J' = 11·9, J'' = 4·1); 3·18 heptuplet, 1 H (H-20, J = 6·6); 4·06 d, 1 H, 4·34 d, 1 H (2 × H-28, J = 10·9); 4·49 m, 1 H (3α-H). ^{13}C NMR spectrum in Table I. Mass spectrum, *m/z* (%): 540 (19), 525 (3), 480 (18), 465 (6), 437 (6), 277 (100), 189 (48). UV spectrum, $\lambda_{max}(\varepsilon)$: 244 (20 200), 286·5 (1 060). For $C_{34}H_{52}O_5$ (540·8) calculated: 75·51% C, 9·69% H; found: 75·59% C, 9·79% H.

Oxidation of Olefin *XI* with Chromium(VI) Oxide

A solution of 380 mg olefin *XI* in 100 ml acetic acid was treated with a solution of 250 mg chromium(VI) oxide in 2 ml water and the mixture was left to stand at room temperature overnight, whereafter it was submitted to the usual processing. The evaporation residue was submitted to chromatography on 30 g silica gel with a mixture of petroleum ether and ether (10 : 1) to give successively 80 mg (20%) epoxide *XII* identical with the authentic sample prepared according to ref.[3] and 150 mg (30%) unsaturated ketone *VI* identical with the compound obtained in the previous experiment.

Oxidation of Ketone *VI* with Chromium(VI) Oxide

A mixture of 0·3 g unsaturated ketone *VI*, 0·4 g chromium(VI) oxide, and 5 ml acetic acid was refluxed 1 h, whereafter it was submitted to the usual processing. The evaporation residue (230 mg) was submitted to column chromatography (25 g silica gel, mixture of petroleum ether and ether (6 : 1)) to give successively 105 mg (33%) anhydride *IX* identical with the compound obtained by the oxidation of diacetate *I* and 90 mg starting ketone *VI*. An increase in reaction time reduces the amounts of both compounds.

3β,28-Dihydroxy-11-lupanone (*VIII*)

A solution of 35 mg 11-oxo derivative *VII* in 1 ml benzene was added to a solution of 50 mg potassium hydroxide in 5 ml ethanol, and the resulting mixture was refluxed 2 h, whereafter it was submitted to the usual processing. The recrystallization of the evaporation residue from a mixture of chloroform and methanol gave 23 mg (78%) derivative *VIII* with m.p. 294—295°C (at 280°C the modification is changed from plates to prisms), $[\alpha]_D$ −21°. IR spectrum: 3 619 (OH), 1 701 (C=O). ^{1}H NMR spectrum (80 MHz) in Table II. Mass spectrum, *m/z* (%): 458. (20), 456 (7), 443 (5), 440 (7), 427 (17), 415 (6), 317 (31), 304 (18), 235 (64), 207 (35), 191 (100), 189 (54), 177 (90), 95 (86). For $C_{30}H_{50}O_3$ (458·7) calculated: 78·55% C, 10·99% H; found: 78·38% C, 11·09% H.

3β,11β,28-Lupanetriol (*XIII*)

A solution of 100 mg ketone *VII* in 20 ml ether was treated with 100 mg lithiumtetrahydridoaluminate, and the reaction mixture was refluxed 30 min. Then the excess hydride was decomposed with ethyl acetate, the reaction mixture was poured in dilute hydrochloric acid, extracted with ether and submitted to usual processing. The evaporation residue was recrystallized twice from acetone to give 65 mg (77%) triol *XIII*, m.p. 266—268°C, $[\alpha]_D$ −7°. IR spectrum: 3 550 to 3 630 (OH). ^{1}H NMR spectrum (80 MHz) in Table II. Mass spectrum, *m/z* (%): 460 (M^+, 2·5), 442 (35), 411 (51), 227 (80), 191 (100), 177 (70). For $C_{30}H_{52}O_3$ (460·7) calculated: 78·20% C, 11·38% H; found: 78·03% C, 11·49% H.

Acetylation of Triol *XIII*

a) A solution of 20 mg triol *XIII* in 0·6 ml acetanhydride was refluxed 10 min. After cooling the solution gave 20 mg (75%) crystalline 3β,11β,28-lupanetriol triacetate (*XV*), m.p. 218—220°C, $[\alpha]_D$ +35°. IR spectrum: 1 723, 1 252 (OAc), 1 032. ^{1}H NMR spectrum (80 GHz) in Table II. Mass spectrum, *m/z* (%): 526 (M^+ − 60, 10), 511 (9), 466 (100), 451 (16), 423 (14), 406 (10), 391 (12), 383 (8), 363 (7), 330 (9), 279 (9), 276 (12), 216 (24), 203 (32), 189 (45). For $C_{36}H_{58}O_6$ (586·8) calculated: 73·68% C, 9·96% H; found: 73·68% C, 10·12% H.

b) A solution of 80 mg triol *XIII* in 5 ml pyridine was treated with 0·5 ml acetanhydride and the reaction mixture was left to stand at room temperature 18 h. Then it was poured onto ice and submitted to the usual processing. The evaporation residue was submitted to TLC (10 g silica gel, petroleum ether and ether 3 : 1). On recrystallization from a benzene–heptane mixture the less polar fraction gave 22 mg (22%) triacetate *XV*, m.p. 217—220°C, identical with the compound prepared sub *a*). The more polar fraction was recrystallized from a benzene–ethanol mixture to give 63 mg (66%) 3β,11β,28-lupanetriol 3,28-diacetate (*XIV*), m.p. 320—322°C (a change in modification from plates to prisms about 270°C), $[\alpha]_D$ +3°. IR spectrum: 3 580 to 3 650 (OH), 1 724, 1 255 (OAc). ^{1}H NMR spectrum (200 MHz) in Table II, ^{13}C NMR spectrum

in Table I. Mass spectrum, *m/z* (%): 544 (1), 526 (16), 511 (3), 484 (7), 466 (23), 451 (14), 423 (8), 406 (5), 391 (10), 363 (5), 344 (7), 330 (4), 279 (75), 191 (100). For $C_{34}H_{56}O_5$ (544·8) calculated: 74·95% C, 10·36% H; found: 75·22% C, 10·59% H.

9(11)-Lupene-3β,28-diol (*XVII*) and Diacetate *XVI*

A solution of 35 mg 11β-hydroxy derivative *XIV* in 2 ml pyridine was cooled to 0°C and treated with 0·5 ml phosphorus(V) trichloride oxide. The reaction mixture was left to stand at room temperature 6 h and then heated at 100°C 2 h. After cooling it was poured onto ice and submitted to the usual processing. The recrystallization of the evaporation residue from a chloroform–methanol mixture gave 23 mg (68%) 9(11)-lupene-3β,28-diol diacetate (*XVI*), m.p. 217 to 220°C, $[\alpha]_D$ +38°. IR spectrum: 1 722, 1 255 (OAc), 1 030, 987. ^{1}H NMR spectrum (200 MHz) in Table II, ^{13}C NMR spectrum in Table I. Mass spectrum, *m/z* (%): 526 (13, M^+), 511 (12), 466 (35), 451 (27), 423 (10, $C_{29}H_{43}O_2$), 330 (10, $C_{22}H_{34}O_2$), 276 (72), 216 (75, $C_{16}H_{24}$), 203 (37), 201 (100), 189 (48), 177 (44). For $C_{34}H_{54}O_4$ (526·8) calculated: 77·52% C, 10·33% H; found: 77·49% C, 10·17% H.

The hydrolysis of 16 mg diacetate *XVI* by 2 h boiling with 2 ml 1% sodium hydroxide solution in methanol and subsequent usual processing and recrystallization from a benezene–ethanol mixture gave 9 mg (67%) 9(11)-lupene-3β,28-diol (*XVII*), m.p. 262—264°C (about 230°C the plates change into prisms), $[\alpha]_D$ +16°. IR spectrum: 3 620 (OH), 1 022, 922. ^{1}H NMR spectrum (200 MHz) in Table I. Mass spectrum, *m/z* (%): 442 (60), 427 (32), 424 (17), 395 (29), 235 (83), 177 (100). For $C_{30}H_{50}O_2$ (442·7) calculated: 81·39% C, 11·38% H; found: 81·33% C, 11·26% H.

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