Tetrahedron. Vol. 29, pp. 13 to 20. Pergamon Press 1973. Printed in Great Britain

STUDIES ON CONSTITUENTS OF *ABIES GRANDIS*

THE STRUCTURES AND ABSOLUTE STEREOCHEMISTRY OF CYCLOGRANDISOLIDE AND EPICYCLOGRANDISOLIDE, NOVEL CYCLOPROPANE TRITERPENE LACTONES*[,1]

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(*Received in the USA* 12 *June* 1972; *Received in the UK for publication* 28 *August* 1972)

Abstract—The light petroleum extract of grand fir [*Abies grandis* (Dougl.) Lindl.] was found to contain two novel triterpene lactones. The first compound, named cyclograndisolide, was shown by chemical and spectroscopic considerations and finally confirmed by X-ray analysis to be (23 *R*)-3α-methoxy-9,19-cyclo-9β-lanost-24-ene-26,23-olide (**6**). The second component, epicyclograndisolide was isomeric with the first and was assigned as (23 *S*)-3α-methoxy-9,19-cyclo-9β-lanost-24-ene-26,23-olide (**10**).

As part of a long range study aimed at the eventual utilization of chemicals found in the bark of coniferous species an examination of the extractives of grand fir [*Abies grandis* (Dougl.) Lindl.], was undertaken.[2,3] The bark for the present study was obtained from a one hundred year old tree growing on the University of British Columbia campus. The air-dried ground bark was extracted with light petroleum and the resultant extract was subjected to successive column chromatography on alumina and finally preparative layer chromatography on silica gel. In this manner two novel cyclopropane triterpene lactones, which were named cyclograndisolide and eipcyclograndisolide, were isolated and their structures elucidated.

The major compound, cyclograndisolide, possessed the molecular formula, $C_{31}H_{48}O_3$, as established by high resolution mass spectrometry and elemental analysis. The IR bands at 1745 and 1660 cm^{-1} and the UV absorption (λ_{max}^{MeOH} 209 nm (log ε4·33)) suggested an α,β-unsaturated-γ-lactone system already known in abieslactone, a triterpene lactone previously isolated from the related species *Abies mariesii* Masters[4] and *A. amabilis* (Dougl.) Forbes.[5] The NMR spectrum revealed, among its characteristic signals, one proton multiplets at τ3·02 (J = 1·7 Hz) and τ5·05, a three proton singlet (τ6·70, OMe), a one proton triplet (τ7·18, J = 1·8 Hz, equatorial H geminal to OMe), a triplet for a vinylic Me group (τ8·10, J = 1·7 Hz), signals for five C-Me groups (τ8·98 − 9·14) and a pair of one proton doublets at τ9·50 and 9·68 (J = 4·0 Hz) characteristic of cyclopropane protons.

By analogy with abieslactone[4] the vinylic Me group was assigned to the α-position of the α,β-unsaturated-γ-lactone, whilst signals at τ3·02 and 5·05 were assigned to the β and γ protons in this system.

The CD curve of cyclograndisolide revealed a weak peak at 250 nm ([θ] + 377°) and a strong negative value at lower wavelengths ($[\theta]_{220} = -31{,}500°$), whilst the ORD curve of this compound had a trough, $[\Phi]_{225} = -26{,}700°$. Again by analogy with abieslactone, the *R* configuration was assigned to the γ position of the lactone.

The position of the cyclopropane ring could not be established from the spectral evidence but most cyclopropanoid triteroenes[6] and the Buxus alkaloids[7] are based on a cycloartane skeleton thereby providing some suggestion for a possible placement of this ring.

The chemistry of cycloartenol has been well studied.[8,9] It was known that treatment of cycloartenyl acetate (**2**) with gaseous hydrogen chloride in chloroform resulted in the opening of the cyclopropane ring with the formation of a mixture of olefins in which the 9(11)-ene isomer is in predominance. If the implied relationship between the most attractive postulate for cyclograndisolide (**6**) and the published structure for abieslactone (**1**) was correct, the acid reaction on the former should yield

*Financial support from the National Research Council of Canada is gratefully acknowledged.

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the latter as a major component. However, when gaseous hydrogen chloride was passed into a chloroform solution of cyclograndisolide the product isolated was not the expected abieslactone. In the NMR spectrum of abieslactone the C(11) olefinic proton resonates at τ4·48 while the olefinic proton of the new product, which we have called grandisolide, was seen at τ4·80. This latter value was in much better agreement with the reported value of 4·75 for the C(11) olefinic proton of the etianic ester (**3**)[10] and 4·81 for this proton in lanost-9(11)-ene-3β-yl acetate (**4**).

The other intriguing aspect of the NMR spectrum of grandisolide was that the chemical shifts of the C-Me groups (τ8·95 − 9·36) were in a different range than those observed in abieslactone (τ8·90 − 9·08).[4]

The chemical shifts of the Me groups of certain families of triterpenes have been the object of considerable systematic study.[11–13] Also the changes in chemical shift caused by various functional groups in these systems are well documented. Thus it is possible to calculate the expected chemical shifts of the Me groups in these triterpene systems.

The facts available to this point suggested that cyclograndisolide was a member of the cycloartane family, hence grandisolide would be a member of the lanostane family. The position of the OMe group was not known but the most logical site would be at C(3). The change in chemical shifts of the Me groups caused by a 3α-OMe function is not reported but should be closely approximated by the change in chemical shifts caused by a 3α-OH group for which information is available. Since the α,β-unsaturated-γ-lactone system of cyclograndisolide would, as in the case of abieslactone, form part of the side chain, its effect was assumed to be negligible. The change in chemical shifts caused by a C9(11) double bond in the lanostene series has been reported[10] and from all of the mentioned data it is possible to calculate the expected chemical shifts for the Me groups in an appropriate lanostene derivative. Table 1 illustrates the comparison of such a calculation with the values observed for grandisolide.

As can be seen the similarities are quite striking. This result provided further evidence for the general structural features present in grandisolide and thereby in cyclograndisolide.

At this stage it was clearly desirable to establish the relationship, if any, between grandisolide and abieslactone. Indeed when abieslactone was treated with gaseous hydrogen chloride in chloroform in the manner used for cyclograndisolide, a reaction product identical in all respects (m.p., mixed m.p., TLC and IR) with grandisolide was obtained. This established the suspected relationship between the two series and strengthened the argument that grandisolide possesses the tetracyclic system characteristic of the lanostane family.

Table 1. Comparison of resonance frequencies of Me groups in lanost-9(11)-en-3α-ol(**5**) and grandisolide (**1**)

	Methyl groups				
	30	31	19	18	32
Lanost-9(11)-en-3α-ol(**5**) calculated	9·11	9·02	8·89	9·34	9·24
Grandisolide (**1**) observed	9·12	9·02	8·95	9·36	9·26

On the evidence presented thus far the most likely structure for grandisolide was **1** thereby suggesting that abieslactone cannot possess the previously assigned structure.[4] On this basis cyclograndisolide could be represented by the alternatives **6** or **7** since both upon treatment with acid could lead to the 9(11)-ene system favoured for grandisolide.

The quantities of cyclograndisolide available precluded further extensive chemical investigations. It was therefore decided that a detailed mass spectrometric study may reveal further evidence in support of **6** or **7**. For this purpose the known cyclopropane system present in the cycloartenol family was first investigated. The mass spectra of cycloartenol and some of its derivatives have been determined by several workers.[14,15] The presence of the 9,19 cyclopropane ring is manifested in the mass spectra by the appearance of an ion peak having an even mass number. The position of the peak is unaffected by the substitution pattern at C(4) or by the oxygen function at C(3). It is, however, shifted by varying the substitution in the side chain. Two proposals for the origin of this fragment have been advanced. One proposal envisages loss of ring A including the C(19) carbon (path i),[14] while the other envisages loss of ring A with inclusion of C(6) but not with the C(19) carbon (path ii).[15] Without proper labelling studies these two paths cannot be distinguished. Regardless of the path followed, the resulting fragment (ion e) for cycloartenol or cycloartenyl acetate has a value of *m/e* 286.

In order to compare our subsequent results under closely identical conditions, the spectrum of cycloartenyl acetate was run on our instrument and a summary of the results obtained is presented in Fig 1 and Table 2. In general the observed fragmentation pattern agrees well with the published data[14,15] but its presentation here allows a clear comparison with that obtained for cyclograndisolide.

When the difference in functionality at C(3) and in the side chain is taken into account, the mass spectrum of cyclograndisolide (Fig 2) is remarkably similar to cycloartenyl acetate. A direct comparison of the relevant fragments is provided in Table 2 and a summary of the fragmentation modes is shown in Fig 3.

The striking similarities of the mass spectra of cycloartenyl acetate and cyclograndisolide coupled with the other chemical and spectral evidence presents a convincing argument for the presence of a

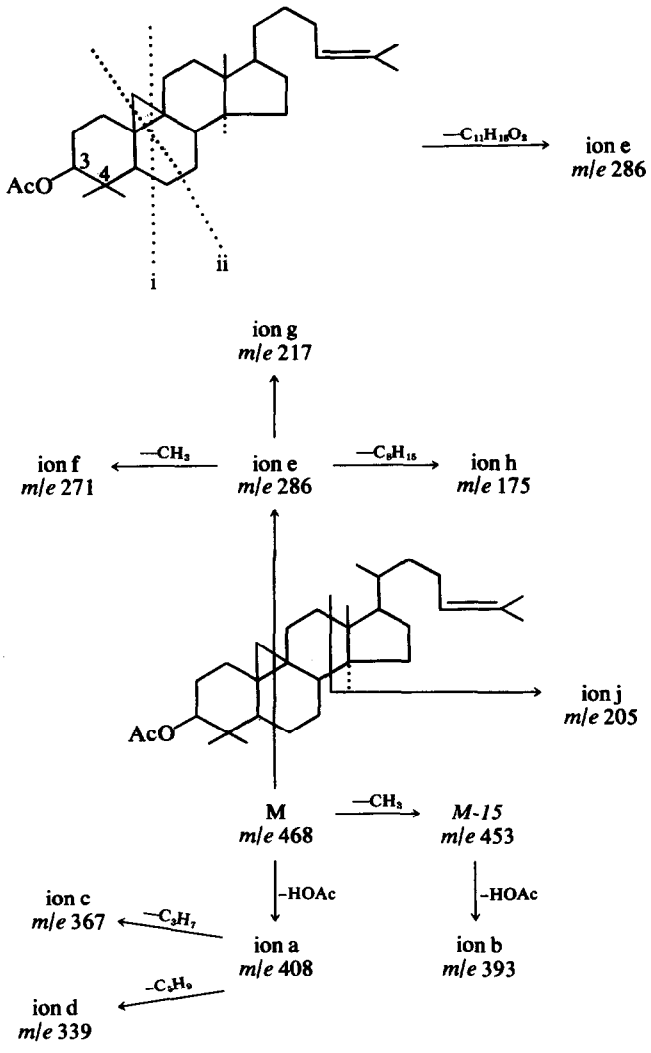


Fig 1. Summary of mass spectral fragmentation of cycloartenyl acetate

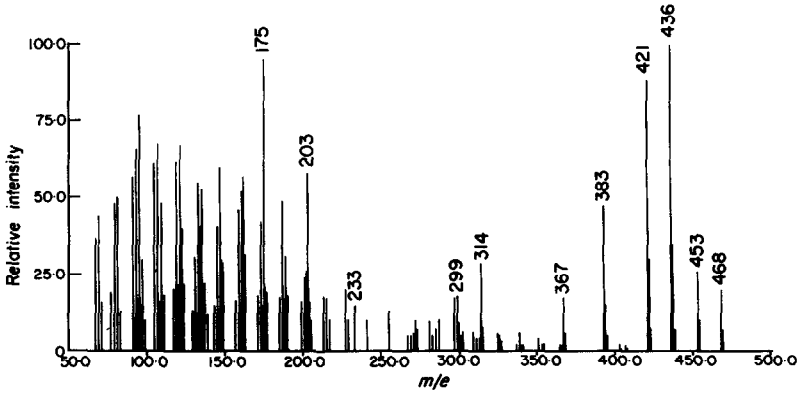


Fig 2. Mass spectrum of cyclograndisolide.

Table 2. Mass spectral comparison of cycloartenyl acetate and cyclograndisolide

Ion	m/e	Cycloartenyl Acetate metastable observed		m/e	Cyclograndisolide metastable observed		composition*
M	468			468			$C_{31}H_{48}O_3$
M-15	453	M → M-15,	438·1	453	M → M-15,	438·1	$C_{30}H_{45}O_3$
a	408	M → a,	356·2	436			$C_{30}H_{44}O_2$
b	393	M-15 → b,	341·1	421	a → b,	406·4	$C_{29}H_{41}O_2$
		a → b,	378·8				
c	367	a → c,	328·8	393	a → c,	354·2	$C_{27}H_{37}O_2$
d	339	a → d,	281·8	367			$C_{25}H_{35}O_2$
e	286			314			$C_{31}H_{30}O_2$
f	271	e → f,	256.9	299			$C_{20}H_{27}O_2$
h	175			175			
j	205	a → j,	102·9	233			$C_{15}H_{21}O$

*Obtained from high resolution mass spectrometry on cyclograndisolide.

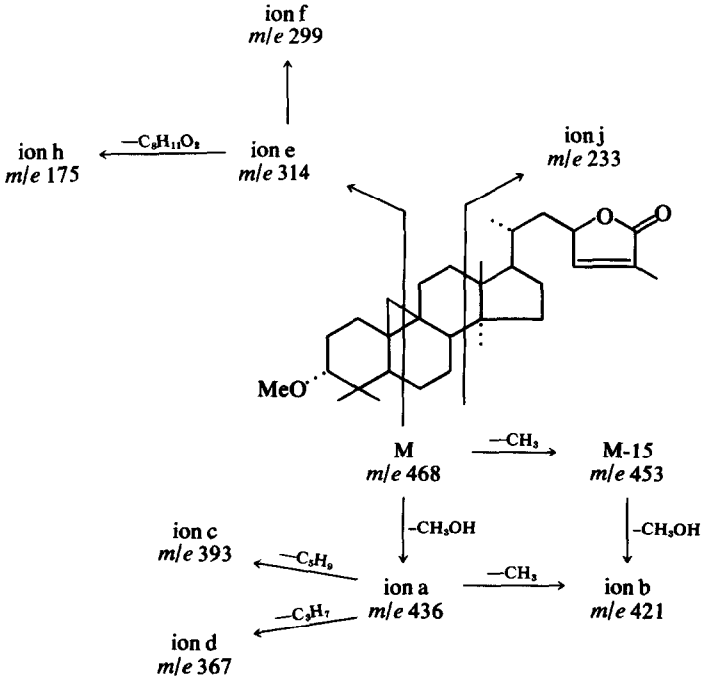
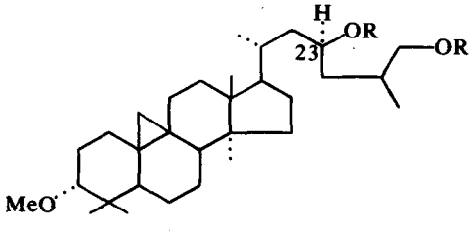


Fig 3. Summary of mass spectral fragmentation of cyclograndisolide

9,19 cyclopropane system. On the basis of all the evidence presented the structure 6 can be assigned for cyclograndisolide.



8: R = H
9: R = COC_6H_4Br

Since rather heavy reliance on spectral data was necessary in deducing this structure, it was decided to submit a derivative of this molecule for X-ray analysis.

To this end cyclograndisolide was reduced under mild conditions to give dihydrocyclograndisolide (24,25 double bond reduced in **6**), whose NMR spectrum still contained the resonances for the cyclopropane protons. The mass spectral fragmentation of dihydrocyclograndisolide was like that of cyclograndisolide with ions containing the lactone ring now being observed at two mass units higher than in the latter compound.

Dihydrocyclograndisolide could be reduced with lithium aluminium hydride to give a diol (**8**). The

The CD curve of epicyclograndisolide had a shoulder at 250 nm ($[\theta] = 1708°$) with no other maxima being observed above 220 nm ($[\theta]_{220} = 39{,}140°$). The ORD curve revealed a peak at 225 nm ($[\Phi] = 22{,}640°$). The positive nature of both of these measurements suggests that the configuration about the lactone is opposite to that of cyclograndisolide and therefore the *S* configuration is assigned at C(23).

The close similarity of epicyclograndisolide to cyclograndisolide was further established when the mass spectrum of each was compared. In fact the fragmentation patterns for both substances were *identical*. Because of the limited amount of eipcyclograndisolide isolated, further chemical work was not possible but the spectral evidence provides a strong case for the structural assignment as (23 *S*)-3 α-methoxy-9,19-cyclo-9β-lanost-24-ene-26,23-olide (**10**).

EXPERIMENTAL

Throughout this work Merck silica gel G with added fluorescent indicator was used as adsorbent in TLC. The chromatograms, 0·3 mm in thickness, were air dried and activated in an oven at 100° for 3 hr. The chromatograms were developed in chloroform and sprayed with $SbCl_5$ in CCl_4 (1:2) unless otherwise noted.

For preparative layer chromatography a thicker layer (0·5 mm) of adsorbent was utilized with 0·01% Rhodamine 6G added as indicator.[17] Spraying with $SbCl_5$ was done only along one edge or not at all as detection of bands was possible with UV light in most instances.

Column chromatography was performed on either Woelm silica gel or neutral alumina. The preferred adsorbent was deactivated alumina (Activity III) prepared by the addition of water as directed by the manufacturers.

The NMR spectra were determined in $CHCl_3$ or $CDCl_3$ at either 60 MHz using a Jeolco C-60, Varian A-60, or a Varian T-60 instrument or at 100 MHz using a Varian HA-100 instrument. The positions of all NMR resonances are given in the Tiers τ scale with TMS as internal standard set at 10·0 units. For multiplets the τ values given represent the center of the signal.

Mass spectra were obtained on an AEI MS9 high resolution mass spectrometer or, where noted, on an Atlas CH4 spectrometer. High resolution molecular weight determinations were determined on the MS9 spectrometer.

IR spectra were obtained on Perkin-Elmer model 21, 137, or 457 instruments. The samples were usually measured as KBr pellets, unless otherwise indicated. The positions of absorption maxima are quoted in wave numbers (cm^{-1}).

UV absorptions were measured in MeOH or EtOH on Cary model 11 or model 15 spectrophotometers.

A Jasco model UV/ORD/CD 5 spectropolarimeter was used to measure the CD and ORD curves using methanol or dioxane as solvent.

M.p.'s were determined on a Kofler block and are uncorrected.

Elemental analyses were performed by Mr. P. Borda, University of British Columbia.

Extraction of grand fir bark. Bark was obtained from a 100 year old grand fir tree growing on the campus of the University of British Columbia. The bark was air dried and ground in a Wiley mill to pass through a 3 mm sieve. The ground bark was extracted for 24 hr in a large glass Soxhlet extractor. The extract was taken to dryness to provide a crude extract in a yield of 0·8% based on the air dried weight of bark extracted.

Chromatography of crude extract. The crude extract (26·7 gms) was chromatographed on alumina (450 gms) into a number of fractions as shown below. The compounds subsequently isolated from each fraction are shown for clarity.

Chromatography of fraction G. Fraction G (2·77 gm) was chromatographed on alumina (200 gm). Elution with 20% benzene in light petroleum (400 ml) gave Fraction M (770 mg) subsequently shown to contain epimanool, fatty alcohol, and lactones. Further elution with 50%

Fraction	Solvent (volume, mls)	Weight, mgs	Compounds
A	light petroleum (200)	690	hydrocarbons
B	light petroleum (100)	228	hydrocarbons, sterol ester
C	light petroleum (200)	263	sterol ester
D	light petroleum (200)	450	sterol and wax ester
E	light petroleum (500)	994	wax ester, 2 unknowns
F	10% benzene in light petroleum (500) 20% benzene in light petroleum (400)	826	unidentified
G	30% benzene in light petroleum (400) 50% benzene in light petroleum (300)	1444	fatty alcohol, epimanool, lactones
H	60% benzene in light petroleum (400)	909	fatty alcohol, β-sitosterol
I	60% benzene in light petroleum (300)	1016	β-sitosterol, ferulic ester
J	benzene (400)	1925	β-sitosterol, ferulic ester, 2 unknowns
K	ether (500) methanol (500)	5004	ferulic ester
	Total recovery	13·75 gms.*	

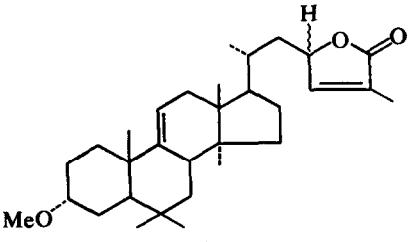
*Resin and fatty acids present in crude extract were irreversibly adsorbed on the alumina

NMR spectrum of the latter revealed that the cyclopropane ring was still intact and it was clear that the diol still contained all the asymmetric centers of the original natural product.

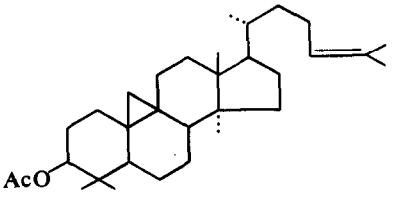
Treatment of the diol with *p*-bromobenzoyl chloride in pyridine gave the bis-*p*-bromobenzoate (**9**). The NMR spectrum of this derivative contained the resonances for the cyclopropane ring and for eight aromatic protons. In addition elemental analysis and ions in the mass spectrum at *m/e* 838, 840 and 842 confirmed that the bis derivative had been obtained.

The X-ray analysis of **9** will be reported in detail elsewhere. It is pertinent to indicate that the analysis confirms the presence of the 9,19 cyclopropane ring and establishes the absolute configuration at C(23) as well as the various asymmetric centers shown in **9**. Hence, cyclograndisolide has the structure and absolute stereochemistry as shown in structure **6** and is (23 *R*)-3α-methoxy-9,19-cyclo-9β-lanost-24-ene-26,23-olide. With the structure of cyclograndisolide established, grandisolide is (23 *R*)-3α-methoxylanosta-9(11), 24-diene-26,23-olide (**1**) as suggested earlier. Hence, the structure originally proposed for abieslactone[4] is incorrect. More recent investigations in our laboratory[16] have now settled the structure and absolute configuration of abieslactone as (23 *R*)-3α-methoxy-5α,9β-lanosta-7,24-dien-26,23-olide.

The second component, named, epicyclograndisolide, was isolated at the same time as cyclograndisolide and appeared to be an isomer of this substance. Elemental analysis and high resolution mass spectrometry established the molecular formula as $C_{31}H_{48}O_3$. The IR and UV spectral properties were similar to those of cyclograndisolide. The NMR spectrum exhibited signals for the cyclopropane protons (τ9·50 and 9·68, J = 4 Hz), the vinylic methyl (τ8·12) as an apparent triplet (J = 1·7 Hz), an equatorial proton (7·20, J = 1·8 Hz) geminal to a OMe group (τ6·72), the γ proton of the α,β-unsaturated-γ-lactone as a multiplet (5·90) and the β proton of the lactone ring as an apparent quintet (2·98, J = 1·7 Hz). The differences of note from the spectrum of cyclograndisolide is the slight downfield shift of the β olefinic proton of the lactone and the slight upfield shifts of the γ proton and the vinylic Me group.



1



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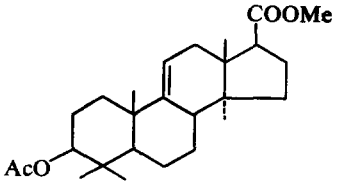

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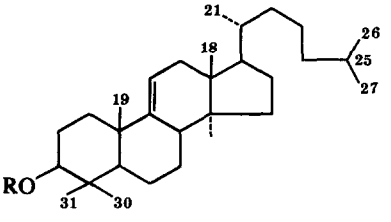
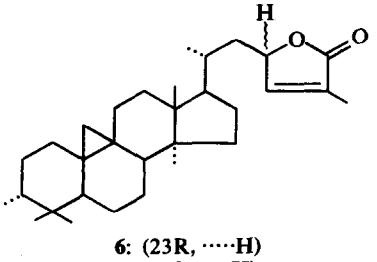
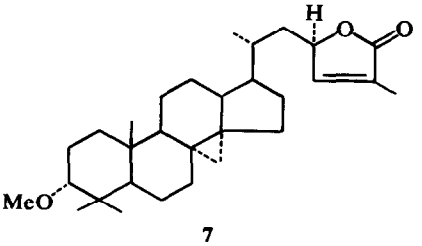


4: R = Ac
5: R = H



6: (23R, ····H)
10: (23S, ——H)



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benzene in light petroleum (400 ml) gave Fraction N (860 mg) subsequently shown to contain lactones and fatty alcohol. Finally elution with benzene (600 ml) gave Fraction O (950 mg) containing fatty alcohol and lactones.

Chromatography of fraction M. Fraction M (500 mg) was chromatographed on alumina (50 gm). Elution with 20% benzene in light petroleum (250 ml) gave Fraction P (80 mg). Further elution with 40% benzene in light petroleum (500 ml) gavr Fraction Q (400 mg).

Fraction P. Fraction P was a pale yellow oil. IR (neat) 3300 (OH), 3065 (vinyl), 1635 (C=C), 1410, (990) 915 (vinyl), 878 (terminal methylene), 1383 and 1365 (gem dimethyl). NMR (60 MHz) 4·15 (1 H, qu, J = 17·5 Hz, J = 10·5 Hz), 4·880)1H, qu, J = 10·5 Hz, J = 1·5 Hz), 5·05 (1H, qu, J = 10·5 Hz, J = 1·5 Hz), 5·26 and 5·55 (2H, mu, exocyclic methylene), 8·79 (CH_3—C—OH), and 9·17, 9·23, and 9·36 (angular Me).

Fraction P (80 mg) was treated with freshly prepared 3,5-dinitrobenzoyl chloride (80 mg) in pyridine (2 ml) for 3 days at room temp. The pyridine was removed *in vacuo*. The residue was dissolved in CH_2Cl_2, washed with water, dried over $NaSO_4$, and evaporated. Crystallization of this residue from CH_2Cl_2—MeOH gave needles m.p. 116–118°, mixed m.p. with authentic epimanoyl-3,5-dinitrobenzoate 116–118°.

Fraction Q. Fraction Q (400 mg) was obtained from Fraction M as a white low melting waxy solid. TLC showed the presence of at least 3 compounds R_f 0·35, 0·25, 0·17). NMR (60 MHz) had resonances at 3·0, 5·0, 6·7, and 8·1 similar to abieslactone[4] in addition to broadened singlet at 8·7 assigned to methylene protons of a long chain fatty alcohol.

Removal of fatty alcohol from fraction Q. A methanolic soln (4 ml) of Fraction Q (200 mg) was heated to reflux and urea (2 gm) was added followed by 1 ml benzene. The soln was allowed to cool slowly and was left standing for 2 days before filtering off the crystalline urea complex. The complex was washed twice with $CHCl_3$ (2 ml) and the combined filtrate was taken to dryness. The filtrate residue was partitioned between water and CH_2Cl_2 and the organic layer separated, washed with water, and dried over $NaSO_4$. Evaporation of the solvent gave a white solid (85 mg) which contained by TLC two compounds, cyclograndisolide and eipcyclograndisolide (R_f 0·35 and 0·25).

The urea complex was dissolved in water and extraction with CH_2Cl_2 gave, upon drying and evaporation, the fatty alcohol as a low melting wax (R_f 0·17).

Purification of fraction N. Fraction N (500 mg) was dissolved in hot MeOH and left to cool for 4 hr after which time a white solid (120 mg) was removed by filtration. This solid was found to be fatty alcohol and not further examined. The filtrate was concentrated to 4 ml and urea (2 gm) added and the soln was warmed to reflux to dissolve the urea; benzene (1 ml was added and the soln left to crystallize for 2 days. Removal of the urea complex by filtration and evaporation of the filtrate gave a residue which was partitioned between water and CH_2Cl_2. The organic layer was washed with water, dried over $NaSO_4$, and evaporated to give a residue of cyclograndisolide and epicyclograndisolide (250 mg).

Purification of Fraction O. Fraction O (950 mg) was dissolved in hot MeOH and left to cool for 4 hr after which time fatty alcohol (505 mg) was removed by filtration. The filtrate was concentrated to 4 ml and urea (2 gm) was added and dissolved at reflux, benzene (1 ml) was added. After 2 days the urea complex was removed by filtration and the filtrate evaporated to give a residue which was partitioned between water and CH_2Cl_2. The CH_2Cl_2 layer was washed with water, dried ($NaSO_4$), and evaporated to give a residue of cyclograndisolide and epicyclograndisolide (185 mg).

Preparative layer chromatography of cyclograndisolide and epicyclograndisolide. The mixture containing these compounds (85 mg) was dissolved in $CHCl_3$ (0·3 ml) and applied to a preparative layer chromatogram (20 × 60 cm). The plate was developed in $CHCl_3$ and three bands were visible when the chromatogram was examined under UV light. The bands were scraped off the plate and extracted with $CHCl_3$. The top band (R_f 0·67) was of small amount (2 mg) and was not examined. The second band (R_f 0·40) was the major band (35 mg) and was cyclograndisolide when examined by TLC. The third band (R_f 0·25) overlapped the second band and contained both cyclograndisolide and epicyclograndisolide (22 mg). Re-chromatography on preparative layer chromatograms as before gave pure cyclograndisolide (3 mg) and pure epicyclograndisolide (15 mg).

Cyclograndisolide (**6**). This substance from the preparative layer chromatography was passed rapidly through a short column of alumina with benzene to remove most of the orange color which came from the Rhodamine 6G dye. Crystallization from MeOH gave a white solid m.p. 191–193°. ORD (*c*, 0·0368 in dioxane) $[\phi]_{300}$ −890°, $[\phi]_{250}$ −4,670°, $[\phi]_{225}$ −26,700°, $[\phi]_{220}$ −18,000°. CD (*c*, 0·0368 in dioxane) $[\theta]_{270}$ +120°, $[\theta]_{250}$ +370°, $[\theta]_{235}$ 0°, $[\theta]_{225}$ −12,600°, $[\theta]_{215}$ −44,000°. IR (KBr) 1745 (lactone CO), 1665 (C=C). UV λ_{max}^{MeOH} 209 mμ (log ε 4·33). NMR (100 MHz) in $CDCl_3$, TMS lock 3·02 (1H, apparent tr, J = 1·7 Hz, H—C=C—C=O), 5·05 (1H, mt, H—C—O), 6·72 (3H, si, OMe), 7·20 (1H, tr, J = 1·8 Hz, equatorial H—C—OMe), 8·10 (3H, apparent tr, J = 1·7 Hz, vinylic Me), 8·98, 9·02, 9·07, 9·14 (5 C-Me's); in $CHCl_3$, $CHCl_3$ lock 3·02 unobservable, 5·05–9·14 region as before, 9·50 and 9·68 (2H, pair of doublets, J = 4 Hz, cyclopropane protons). Mass spectrum *m/e* 468 (M), 453 (M-15), 436 (M-32), 421 (M-47), and 314. (Found: C, 79·43; H, 10·17; $C_{31}H_{48}O_3$ requires: C, 79·44; H, 10·32%); high resolution: 468·365 $C_{31}H_{48}O_3$ requires: 468·360, 453·333 $C_{30}H_{45}O_3$ requires: 453·336, 436·334 $C_{30}H_{44}O_2$ requires: 436·334, 421·311 $C_{29}H_{41}O_2$ requires: 421·311, 393·278 $C_{27}H_{37}O_2$ requires: 393·279, 367·265 $C_{25}H_{35}O_2$ requires: 367·264, 339·229 $C_{23}H_{31}O_2$ requires: 339·232, 314·227 $C_{21}H_{30}O_2$ requires: 314·224, 299·204 $C_{20}H_{27}O_2$ requires: 299·201, 272·179 $C_{18}H_{24}O_2$ requires: 272·178, 233·154 $C_{15}H_{21}O_2$ requires: 233·154.

Epicyclograndisolide (**10**). The substance from preparative layer chromatography was passed rapidly through a short column of alumina with benzene to remove most of the orange color which came from the Rhodamine 6G dye. Crystallization from MeOH gave a white solid m.p. 193–194°. ORD (*c*, 0·0434 in dioxane) $[\phi]_{450}$ +53°, $[\phi]_{300}$ +2,370°, $[\phi]_{250}$ +6,420°, $[\phi]_{225}$ +22,640°, $[\phi]_{220}$ +10,780°. CD (*c*, 0·0434 in dioxane) $[\theta]_{270}$ +462°, $[\theta]_{260}$ +1030°, $[\theta]_{255}$ +1424°, $[\theta]_{250}$ +1700°, $[\theta]_{245}$ +1850°, $[\theta]_{215}$ +39,140°. IR (KBr) 1740 (CO), 1660 (C=C). UV λ_{max}^{MeOH} 210 mμ (log ε 4·15). NMR (100 MHz) in $CDCl_3$ TMS lock 2·98 (1H, apparent tr, J = 1·7 Hz), 5·10 (1H, mu, H—C—O), 6·72 (3H, s, O—Me), 7·20 (1H, tr, J = 1·7 Hz, equatorial H—C—OMe), 8·12 (3H, tr, J = 1·7 Hz, vinylic Me), 8·98, 9·02, 9·07, 9·14 (5 C-Me's); in $CHCl_3$ with $CHCl_3$ lock 2·98 resonance unobservable. 5·10–9·14 region as before, 9·50 and 9·68 (2H, pair of doublets, J = 4 Hz, cyclopropane protons). Mass spectrum *m/e* 468 (M), 453 (M-15), 436

(M-32), 421 (M-47) and 314. (Found C, 79·32; H, 10·20; $C_{31}H_{48}O_3$ requires: C, 79·44; H, 10·32%; high resolution 468·363 $C_{31}H_{45}O_3$ requires: 468·360).

Grandisolide (1). Cyclograndisolide (33 mg) was dissolved in dry $CHCl_3$ (5 ml) and HCl, dried by passing through conc HSO_4, was bubbled through for 2 hr. Evaporation of the $CHCl_3$ gave grandisolide which was one spot on TLC. Crystallization from acetone gave a white solid m.p. 212–214°. IR (KBr) 1740 (lactone CO), 1665 (C=C). NMR ($CDCl_3$, 100 MHz) 3·02 (1H, apparent tr, J = 1·7 Hz, H—C=C—C=O), 4·80 (1H, m, H—C=C), 5·05 (1H, m, H—C—O), 6·72 (3H, s, OMe), 7·20 (1H, tr, J = 1·7 Hz, equitorial, H—C—OMe), 8·10 (3H, tr, J = 1·7 Hz, vinylic Me), 8·95, 9·02, 9·12, 9·29, 9·36 (6 C-Me's). Mass spectrum (*m/e*) 468, 453, 436, 421. (Found C, 79·34; H, 10·36; $C_{31}H_{48}O_3$ requires: C, 79·44; H, 10·32%).

Acid catalyzed isomerization of abieslactone. Abieslactone (35 mg) was dissolved in dry $CHCl_3$ (5 ml) and dry HCl was bubbled through the soln for 2 hr. Evaporation of the $CHCl_3$ gave a white solid which was one spot on TLC, m.p. 195–207°. NMR (100 MHz) 3·02 (1H, apparent tr, J = 1·7 Hz, H—C=C—C=O), 4·80 (non-integral, m, H—C=C), 5·05 (1H, m, H—C—O), 6·72 (3H, s, OMe), 7·20 (1H, tr, J = 1·7 Hz), 8·10 (3H, tr, J = 1·7 Hz, vinylic Me), 8·94, 9·02, 9·07, 9·12, 9·14, 9·30, and 9·34 (18H, C-Me's). Repeated crystallizations from acetone gave m.p. 212–214°, mixed m.p. with grandisolide 212–214°. IR (KBr) 1740 (lactone CO) 1665 (C=O); superimposable with IR of grandisolide.

Dihydrocyclograndisolide. Cyclograndisolide (50 mg) in THF (10 ml) was hydrogenated over 10% Pd-C (50 mg) at room temp for 2 hr. The catalyst was removed by filtration and the filtrate evaporated and crystallized from EtOAc m.p. 198–199°. IR (KBr) 1770 (lactone CO). NMR (60 MHz) 5·50 (1H, m, H—C—O), 9·50 and 9·68 (2H, pair of doublets, J = 4 Hz). Mass spectrum (*m/e*) 470 (M), 455 (M-15), 438 (M-32), 423 (M-47), and 316. (Found C, 79·00; H, 10·81; $C_{31}H_{50}O_3$ requires: C, 79·10; H, 10·71%).

Dihydrocyclograndisolide diol (8). Dihydrocyclograndisolide (30 mg) in THF (10 ml) was stirred with LAH (10 mg) for 18 hr. A small amount of water was added and the solvent was evaporated. The residue was carefully acidified with dil HCl and extracted with ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a white residue. Column chromatography on alumina (1 gm) of the residue and elution with ether gave the diol, crystallization from light petroleum–ether gave a white solid m.p. 133–134°. IR (KBr) 3540, 3350 (OH). NMR (60 MHz) 6·2–6·6 (3H, overlapping multiplets, H—C—OH, CH_2—OH) 8·97, 9·03, 9·06, 9·10 (6 C-Me's) 9·50 and 9·68 (2H, pair of doublets, J = 4 Hz, cyclopropane protons). Mass spectrum (*m/e*) 474 (M), 459 (M-15), 456 (M-18), 442 (M-32), 438 (M-36). (Found C, 78·58; H, 11·35; $C_{31}H_{54}O_3$ requires: C, 78·43; H, 11·46%).

Bis-p-bromobenzoate of dihydrocyclograndisolide diol (9). Dihydrocyclograndisolide diol (8) (10 mg) and freshly crystallized *p*-bromobenzoyl chloride (15 mg) were dissolved in dry pyridine and left at room temp for 2 days. The pyridine was removed *in vacuo* and the residue dissolved in CH_2Cl_2 and washed with water, 5% $NaHCO_3$ aq, water and dried over $NaSO_4$. Evaporation of the solvent and crystallization from light petroleum gave the bis-*p*-bromobenzoate (9) as a white solid m.p. 154–156°. IR (KBr) 1720 (ester CO). NMR (60 MHz) 1·9–2·4 (8H, aromatic protons), 9·50 and 9·68 (2H, pair of doublets, J = 4 Hz, cyclopropane protons). Mass spectrum (*m/e*) 838, 840, 842 (M). (Found C, 64·10; H, 7·32; $C_{45}H_{60}O_5Br_2$ requires: C, 64·29; H, 7·17%).

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