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TRITERPENES OF *CALOPHYLLUM INOPHYLLUM* LINN*

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Abstract—Friedelin (Ia) and three new triterpenes of the friedelin group have been isolated from the leaves of *Calophyllum inophyllum*. The three new compounds, canophyllal (Ib), canophyllol (Ic) and canophyllic acid (IVa) have been inter-related and their structures established by a direct correlation with oleanenic lactone (XI).

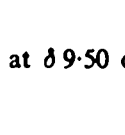
CALOPHYLLUM INOPHYLLUM Linn. (Guttiferae) is a tree commonly found in the coastal regions of South India. The seed oil is used in Indian medicine for the cure of rheumatism and skin affections.[1] The chemical constituents of the nuts have been extensively investigated[2] and three compounds with a 4-phenylcoumarin skeleton, calophyllic acid, calophyllolide and inophyllolide have been isolated and their structures established.[3]

Mitra[4] isolated calophyllic acid, calophyllolide and a new polyene acid, named inophyllic acid. Pillay and Das[5] isolated calophyllic acid and two new acids, calophenic acid, $C_{22}H_{22}O_5$, and inophenic acid, $C_{24}H_{34}O_6$, for which no structures were proposed.

We wish to report here the chemical investigation of the leaves collected at Madras. Three new triterpenes of the friedelin type have been isolated and their structures established.

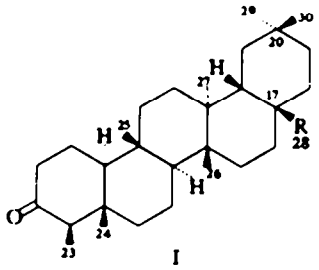
Extraction of the leaves with hexane yielded a solid mixture of triterpenes. Chromatography of this over silica gel yielded four crystalline compounds, A, B, C and D in the increasing order of polarity.

Compound A was identified as friedelin (Ia) by direct comparison with an authentic sample.

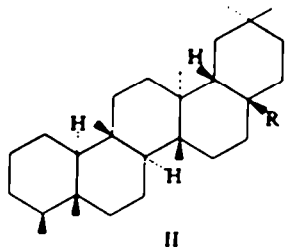
Compound B analysed for $C_{30}H_{48}O_2$. The mass spectrum showed a weak molecular ion peak at *m/e* 440 and a prominent peak at *m/e* 411 indicating the loss of an angular formyl group. Its IR spectrum showed peaks at 2785 and 1718 cm^{-1} (aldehyde) and 1710 cm^{-1} (six or higher-membered ring ketone). The NMR spectrum of the compound showed a sharp singlet (1H) at δ 9·50 due to the  group,

* Contribution No. 83 from CIBA Research Centre.

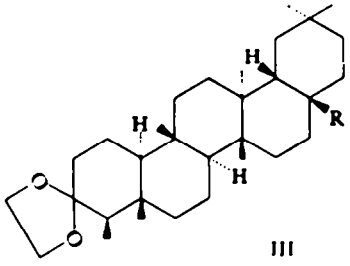
[1] K. M. Nadkarni, *Indian Materia Medica* **1**, 236 (1954).
[2] A. Ormancy-Potier, A. Buzas and E. Lederer, *Bull. Soc. Chim. Fr.* 577 (1951).
[3] J. Polonsky, *Bull. Soc. Chim. Fr.* 1079 (1957) and papers cited therein.
[4] C. Mitra, *J. Sci. Ind. Res. India* **16E**, 120, 167 (1957).
[5] P. P. Pillay and K. G. Das, *Bull. Res. Inst. Univ. Kerala* **5**, 53 (1957), *Chem. Abstr.* **53**, 1134 (1959).



I

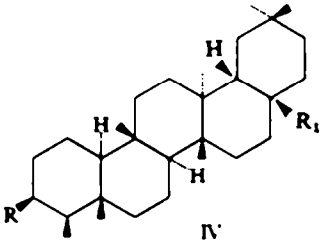


II

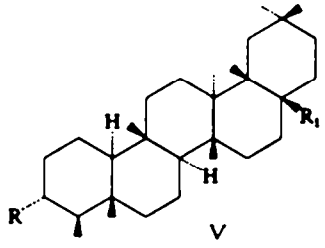


III

a: R = Me
b: R = CHO
c: R = CH_2OH
d: R = CH_2OAc
e: R = CH_2OTS
f: R = CH_2OCOCF_3
g: R = CO_2H
h: R = CO_2Me



IV



V

a: R = OH; R_1 = CO_2H
b: R = OH; R_1 = CO_2Me
c: R = OAc; R_1 = CO_2H
d: R = OAc; R_1 = CO_2Me

seven C—Me groups and no olefinic protons. The compound, shown to be a keto-aldehyde, has been named canophyllal.

Compound C, which is the major component, analysed for $C_{30}H_{50}O_2$. Its mass spectrum showed a weak molecular ion peak at *m/e* 442. A strong peak at *m/e* 411 suggests the elimination of an angular hydroxymethyl group. Its IR spectrum showed bands at 3620 cm^{-1} (OH) and 1700 cm^{-1} (six or higher-membered ring ketone). Its NMR spectrum showed the presence of seven C—Me groups and the absence of olefinic protons. A two-proton singlet at δ 3·65 is due to the methylene of the primary alcoholic group. The compound, shown to be a keto-alcohol, has been named canophyllol. It forms an acetate, m.p. 170–171°, and a tosylate, m.p. 201°. Reduction with sodium borohydride gives a diol, m.p. 247–249°. Wolff-Kishner reduction of canophyllol gives desoxocanophyllol, m.p. 246–247°, which yields an acetate, m.p. 168–169°, and a tosylate, m.p. 173–175°.

Oxidation of canophyllol with pyridine–chromium trioxide gave the corresponding keto-aldehyde which proved to be identical with naturally occurring canophyllal.

Wolff-Kishner reduction of canophyllal yielded friedelane (IIa) showing that the compounds belong to the friedelin group of triterpenes. The position of the keto group was indicated to be C_3 since the ORD curve of canophyllol, which showed a negative Cotton effect, was practically superposable on that of friedelin.[6] This was confirmed in the following manner. The ethylene ketal of canophyllol, on oxidation with pyridine–chromium trioxide, gave the ketal-aldehyde. Wolff-Kishner reduction of this followed by cleavage of the protecting group yielded friedelin (Ia) identical in all respects with an authentic sample. In canophyllol and canophyllal, therefore, a Me group of friedelin is replaced by a hydroxymethyl and a formyl group respectively.

Canophyllol was converted into the O-trifluoroacetyl derivative, m.p. 72–73°, with remarkable ease by just dissolution in trifluoroacetic acid. The methylene protons of the hydroxymethyl group in canophyllol which appeared at δ 3·65 in $CDCl_3$ solution were seen as a quartet centred at δ 4·65 in trifluoroacetic acid solution.

Compound D, analysed for $C_{30}H_{50}O_3$ (mol wt. by mass spectrum 458). It yields an acetate, m.p. 314–316°. With diazomethane it gives a Me ester, m.p. 240–241°, which on acetylation gives a Me ester acetate, m.p. 270–271°. Compound D, obviously a hydroxy acid, has been named canophyllic acid.

Canophyllic acid was correlated with canophyllal in two ways. LAH reduction of methyl canophyllate yielded an amorphous diol. Oxidation of this with pyridine–chromium trioxide gave canophyllal identical with the naturally occurring keto-aldehyde. Secondly, oxidation of canophyllal with acetone–potassium permanganate and esterification of the product with diazomethane gave a keto-ester identical with a sample prepared by pyridine–chromium trioxide oxidation of methyl canophyllate. In canophyllic acid, therefore, a carboxyl group replaces the aldehyde of canophyllal and a secondary alcohol group replaces the C_3 ketone.

The stereochemistry of the OH at C_3 in canophyllic acid was settled by reduction of the keto-ester, methyl dehydrocanophyllate. Reduction with sodium borohydride gave a mixture consisting of 80% of methyl canophyllate and 20% of a more polar isomer. Reduction with sodium and n-propanol on the other hand gave predominantly methyl 3-*epi*-canophyllate. In view of the known behaviour of friedelin towards reducing agents, the hydroxyl in canophyllic acid should be β (axial).

The position of the hydroxymethyl group in canophyllol and hence of the aldehyde in canophyllal and the carboxyl in canophyllic acid was determined as follows. The hydroxymethyl in canophyllol replaces one of the eight Me groups of friedelin. Of these C_{23} can be ruled out since canophyllol is stable to refluxing 5% ethanolic KOH and also since the aldehyde proton in canophyllal appears as a sharp singlet in its NMR spectrum. C_{24} and C_{25} were ruled out by comparison of the physical properties of canophyllol and its derivatives with those of the known C_{24}[7] and C_{25}[8] hydroxy derivatives of friedelin (Table 1). Their non-identity was confirmed by direct comparison of acetyldesoxocanophyllol with 24-acetoxyfriedelane and of acetylcanophyllol with 25-acetoxyfriedelan-3-one.

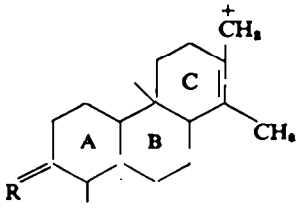
The mass spectra of canophyllol, acetylcanophyllol and canophyllal show strong

[6] C. Djerassi, *Optical Rotatory Dispersion* p. 100 McGraw-Hill, N.Y. (1960).
[7] J. L. Courtney and W. Stern, *Tetrahedron Letters* 1607 (1965).
[8] J. L. Courtney, C. G. MacDonald and J. S. Shannon, *Tetrahedron Letters* 173 (1963).

TABLE 1

Compound	m.p.	$[\alpha]_D$
Canophyllol	280–282°	−21·22°
24-Hydroxyfriedelan-3-one	—	—
25-Hydroxyfriedelan-3-one	301–305°	−20°
O-Acetylcanophyllol	170–171°	−31·35°
24-Acetoxyfriedelan-3-one	—	—
25-Acetoxyfriedelan-3-one	175–176°	−25°
Canophyllal	263–265°	−16·02°
Friedelan-3-one-24-al	—	—
Friedelan-3-one-25-al	306–310°	−60°
Desoxocanophyllol	246–247°	+22·03°
24-Hydroxyfriedelane	238–241°	+23°
25-Hydroxyfriedelane	223–226°	+21°
O-Acetyldesoxocanophyllol	168–169°	+5·75°
24-Acetoxyfriedelane	173–175°	+19°
25-Acetoxyfriedelane	143–145°	+13°
Desoxocanophyllal	263–265°	+26·27°
Friedelan-24-al	180–182°	+25°
Friedelan-25-al	287–290°	−34°

peaks at *m/e* 273 shifted to *m/e* 259 in the spectra of the desoxo derivatives. Deuteration of acetylcanophyllol gave a d_3-derivative in which the *m/e* 273 peak was shifted to *m/e* 276. In the light of the known fragmentation pattern of friedelin[9], the *m/e* 273 fragment should be represented by VIa and the *m/e* 259 peak by VIb. This indicates the presence of only one oxygen atom in rings A, B and C and limits the position of the OH group in canophyllol to C_{23}, C_{29} (α-CH_2OH) and C_{30} (β-CH_2OH).



a: R = O

b: R = H_2

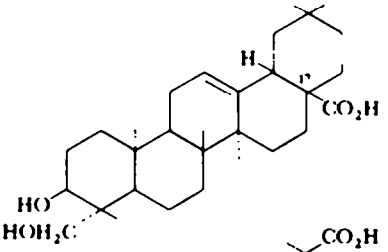
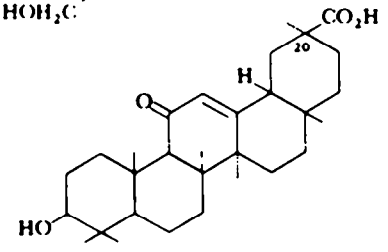
VI

A comparative study of the pK°_{MCS} values of canophyllic acid, O-acetylcanophyllic acid and dehydrocanophyllic acid with those of some known acids of the oleanane group (Table 2) indicates that the carboxyl group of canophyllic acid is attached to C_{17} and not C_{20}.

In compounds with the normal Δ^{12}-oleanane skeleton, Djerassi and Monsimer[10] have observed a significant difference in the ease of saponification with 5·7 and 10% methanolic KOH of the esters bearing the methoxycarbonyl group at C_{17}, $C_{20}(\alpha)$ and $C_{20}(\beta)$. They observed that the ease of hydrolysis was in the order $C_{20}(\alpha)$-CO_2Me(eq.) > $C_{20}(\beta)$-CO_2Me(axial) > C_{17}-CO_2Me. Methyl canophyllate and

[9] J. L. Courtney and J. S. Shannon, *Tetrahedron Letters* 13 (1963).

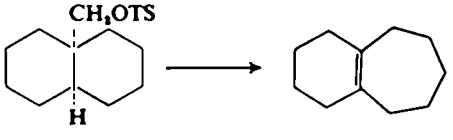
TABLE 2

Compound	Structure	pK^{*}_{MCS}
Canophyllic Acid	IVa	9·15
O-Acetylcanophyllic acid	IVc	8·85
Dehydrocanophyllic acid	I g	9·02
Hederagenin acid		8·50
β-Glycyrrhetinic acid		7·68

methyl dehydrocanophyllate are extremely resistant to alkaline hydrolysis, being recovered quantitatively after refluxing with 10% methanolic KOH. They required very vigorous conditions for hydrolysis (Experimental). This observation also indicates that the carboxyl group in canophyllic acid is attached to C_{17}.

Reaction of friedelane with N-bromosuccinimide has been reported to give friedel-18-ene.[11] An attempt to use this reaction to get chemical evidence for the location of the hydroxymethyl group in canophyllol was, however, unsuccessful. O-Acetyl-desoxocanophyllol was recovered after treatment with NBS under the usual conditions. Use of more drastic conditions gave only intractable material.

Dauben and Rogan[12] have observed that acetolysis of *cis*-9-decalylcarbinyl tosylate (VII) yields the hydrocarbon (VIII). Acetolysis of canophyllol tosylate under

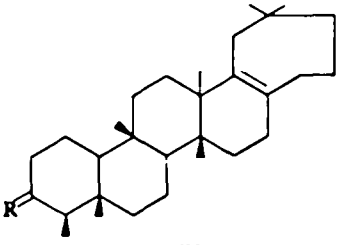


VII VIII

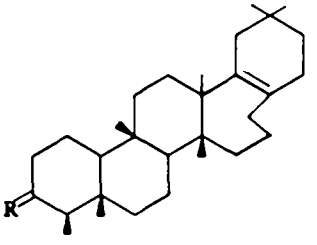
the same conditions gave a compound $C_{30}H_{48}O$ (mol. wt. by mass spectrum 424), m.p. 228–230°. Acetolysis of desoxocanophyllol tosylate similarly gave a hydrocarbon, $C_{30}H_{50}$ (mol. wt. by mass spectrum 410), m.p. 165°. The NMR spectra of both compounds showed the absence of olefinic protons. The hydrocarbon, on treatment

[10] C. Djerassi and H. G. Monsimer, *J. Am. Chem. Soc.* **79**, 2901 (1957).
[11] V. V. Kane and R. Stevenson, *Tetrahedron* **15**, 223 (1961).
[12] W. G. Dauben and J. B. Rogan, unpublished results quoted in A. Streitwieser Jr., *Solvolytic Displacement Reactions* p. 136. McGraw-Hill, N.Y. (1962).

with perbenzoic acid, forms an epoxide, m.p. 260–263°. It is evident that the solvolysis products contain a tetrasubstituted double bond and have to be assigned structures IXa and IXb or Xa and Xb. If the tosyloxymethyl group were attached to C_{20}, acetolysis would be expected to yield a compound containing at least one olefinic proton. The results thus lend further support to the ring D/E angular location of the hydroxymethyl group.



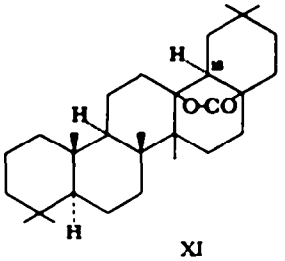
IX



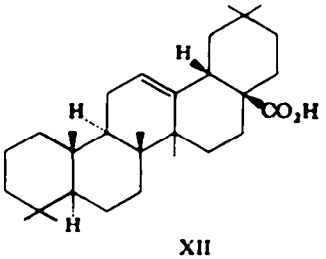
X

a: R = O
b: R = H_2

Direct confirmation of this was achieved by correlating canophyllic acid with a compound of known structure derived from oleanolic acid. Treatment of methyl canophyllate with hydrogen chloride in phenol gave, in analogy with the backbone rearrangement of friedelan-3β-ol to olean-13(18)-ene,[13] a γ-lactone, $C_{30}H_{48}O_2$, m.p. 350–352° (dec), ν_{max} 1755 cm^{-1}. The NMR spectrum of the compound showed the absence of olefinic protons and methoxyl. The lactone, also obtained from canophyllic acid under the same conditions, was found to be identical in all respects (mixed m.p., IR spectra, optical rotation) with a sample of oleanenic lactone (XI) prepared by treatment of γ-oleanenic acid[14] (XII) with hydrogen chloride in phenol. The C_{18}-hydrogen in the lactone is assigned the more stable configuration since the



XI



XII

lactone is recovered after treatment with HCl in refluxing acetic acid. Barton and Holness[15] have observed that under the conditions, the 18-n-lactone of oleanolic acid acetate is isomerised to the 18-isolactone acetate.

The carboxyl group in canophyllic acid should hence be attached to C_{17} leading to structures Ib, Ic and IVa for canophyllal, canophyllol and canophyllic acid respectively. These three compounds represent growing additions to the class of oxygenated

[13] E. J. Corey and J. J. Ursprung, *J. Am. Chem. Soc.* **78**, 5041 (1956).
[14] P. Bilham and A. R. Kon, *J. Chem. Soc.* 552 (1941).
[15] D. H. R. Barton and N. J. Holness, *J. Chem. Soc.* 78 (1952).

friedelin derivatives. Courtney *et al.*[16,17] have isolated several friedelin-type compounds from *Siphonodon australe* bearing oxygen functions in the "x" (C_{21} or C_{22}, more likely the latter) and "y" (C_{24}) position. The "x" and "y" positions have been assigned on the basis of a systematic study of the mass spectra of the compounds and their deuterium-labelled derivatives.[8,9]

EXPERIMENTAL

M.ps are uncorrected. IR spectra were taken as KBr discs using a Perkin-Elmer model 421 spectrophotometer. Optical rotations, unless otherwise specified, were measured in 2–3% sols in chf at 24°. NMR spectra were determined in $CDCl_3$ on a Varian A-60 spectrometer. Hexane refers to the fraction, b.p. 60–80°.

1. *Extraction of* Calophyllum inophyllum *and isolation of the triterpenes.* The dried, powdered leaves (30 kg) were extracted 3 times with cold hexane. The green solid left after removal of the solvent was triturated with fresh hexane (200 ml) and filtered. This was dissolved in hot benzene and left overnight at room temp. The solid that separated was filtered and crystallized from chf–MeOH to yield *canophyllic acid* IVa (0·3 g) as prisms, m.p. 312°, $[\alpha]_D$ +20·89° (*c* 2·35, pyridine), ν_{max} 1690 cm^{-1}. (Found: C, 78·99; H, 10·79. $C_{30}H_{46}O_3$ requires: C, 78·55; H, 10·99%.) Mol. wt. by mass spectrum 458.

The benzene soln was evaporated, the residue filtered in benzene through alumina and the product crystallized from EtOH. The solid (6 g) thus obtained was dissolved in hexane containing the minimum amount of benzene and chromatographed over silica gel (200 g). The column was eluted successively with hexane, benzene–hexane (1:3), benzene–hexane (1:1), benzene and finally with benzene–MeOH (9:1). The fractions were examined by TLC and like fractions combined.

The hexane eluate contained only fatty material. The earlier fractions of the benzene–hexane (1:3) eluate yielded, after crystallization from chf–MeOH, Ia (0·3 g), m.p. and mixed m.p. with an authentic sample, 262–263°, $[\alpha]_D$ −22·45°. The IR spectra of the two samples were also identical. (Found: C, 84·09; H, 11·90. Calc. for $C_{30}H_{50}O$. C, 84·44; H, 11·81%.) Mol. wt. by mass spectrum 426.

The later fractions of the benzene–hexane (1:3) eluate yielded *canophyllal* Ib (0·2 g) which crystallized from chf–MeOH as needles, m.p. 263–265°, $[\alpha]_D$ −16·02°, ν_{max} 2785, 1718, 1710 cm^{-1}. (Found: C, 81·59; H, 10·66. $C_{30}H_{46}O_3$ requires: C, 81·76; H, 10·98%.) Mol. wt. by mass spectrum 440.

The benzene–hexane (1:1) eluate yielded *canophyllol* Ic (2·5 g) which crystallized from chf–MeOH as needles, m.p. 280–282°, $[\alpha]_D$ −21·22°, ν_{max} 3620, 1700 cm^{-1}. (Found: C, 81·11; H, 11·51. $C_{30}H_{48}O_3$ requires: C, 81·39; H, 11·38%.) ORD data (*c* 2%, dioxan): $[\alpha]_{600}$ −25°, $[\alpha]_{318}$ −1100°, $[\alpha]_{315}$ +1460°, $[\alpha]_{300}$ +880°. Mol. wt. by mass spectrum 442.

The benzene–MeOH eluate yielded canophyllic acid (0·1 g), m.p. 312°, identical with the benzene-insoluble material mentioned earlier.

2. *Acetylcanophyllol* (Id). Canophyllol (0·2 g) was heated with pyridine (0·2 ml) and Ac_2O (2 ml) for 5 hr at 60°. The soln was poured on water and the precipitated solid filtered and crystallized from chf–MeOH to yield the *acetate* (0·15 g), m.p. 170–171°, $[\alpha]_D$ −31·35°, ν_{max} 1735, 1700 cm^{-1}. (Found: C, 79·09; H, 10·57. $C_{32}H_{52}O_3$ requires: C, 79·28; H, 10·81%.) Mass spectrum: *m/e* 484, 469, 466, 424, 411, 393, 273. Its m.p. was depressed to 150° on admixture with a sample of 25-acetoxyfriedelan-3-one, m.p. 176–179° (kindly supplied by Dr. Courtney).

3. *Canophyllol tosylate* (Ie). A soln of canophyllol (1 g) in pyridine (9 ml) was treated with *p*-toluenesulphonyl chloride (1 g). The soln was heated at 60–70° for 2 hr and then left overnight at room temp. Decomposition with water and extraction with chf gave the *tosylate* (0·9 g) which crystallized from chf–MeOH as needles, m.p. 201°. (Found: C, 74·62; H, 9·07. $C_{37}H_{54}O_4S$ requires: C, 74·46; H, 9·46%.)

4. *Trifluoroacetylcanophyllol* (If). A soln of canophyllol (0·3 g) in trifluoroacetic acid (2 ml) was allowed to stand at room temp overnight. It was diluted with water and extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with water, $NaHCO_3$aq, again water, dried (Na_2SO_4) and evaporated. Crystallization of the residue from chf–MeOH gave the *trifluoroacetate*, m.p. 72–73°, ν_{max} 1780, 1710 cm^{-1}. (Found: C, 71·82; H, 9·34. $C_{32}H_{49}O_3F_3$ requires: C, 71·34; H, 9·17%.)

[16] J. L. Courtney and R. M. Gascoigne, *J. Chem. Soc.* 2115 (1956).

[17] J. L. Courtney, R. M. Gascoigne and A. Z. Szumer, *J. Chem. Soc.* 2119 (1956).

5. $NaBH_4$ *reduction of canophyllol.* $NaBH_4$ (0·1 g) was added to a warm soln of canophyllol (0·1 g) in dioxan (5 ml). The soln was kept overnight at 50–55° and decomposed with dil AcOH. The ppt was filtered off, washed with water, dried and crystallized from chf–MeOH to yield the *diol* (70 mg), m.p. 247–249°. (Found: C, 81·11; H, 11·67. $C_{30}H_{52}O_3$ requires: C, 81·02; H, 11·79 %.)

6. $NaBH_4$ *reduction of acetylcanophyllol.* Acetylcanophyllol (50 mg) in dioxan (2 ml) was reduced with $NaBH_4$ (50 mg). The product was chromatographed over a short column of silica gel. The fraction eluted by chf crystallized from chf–MeOH as *needles*, m.p. 224–226°. (Found: C, 78·41; H, 11·05. $C_{32}H_{54}O_3$ requires: C, 78·96; H, 11·18%.)

7. *Pyridine–chromium trioxide oxidation of canophyllol.* To a well-stirred, ice-cooled suspension of pyridine–chromium trioxide complex (prepared from 0·6 g CrO_3 and 6 ml pyridine) was added a soln of canophyllol (1 g) in pyridine (6 ml). The mixture was stirred for 3 hr at 0° and for 8 hr more at room temp. Benzene (50 ml) was added, the supernatant liquid decanted and the residue washed well with hot benzene. The combined benzene soln was washed well with water, dil. HCl, $NaHSO_3$aq, finally with water, dried (Na_2SO_4) and evaporated. The residue crystallized from chf–MeOH as needles (0·6 g), m.p. 262–264°, undepressed by admixture with a sample of naturally occurring canophyllal. The IR and NMR spectra of the two samples were also identical. (Found: C, 81·28; H, 10·64. $C_{30}H_{48}O_3$ requires: C, 81·76; H, 10·98%.)

8. *Desoxocanophyllol* (IIc). A mixture of canophyllol (1 g), hydrazine hydrate (98%, 4 ml) and EtONa (3·3 g Na in 45 ml EtOH) was heated in a sealed tube at 160° for 14 hr. It was cooled, poured into water and extracted with chf. The chf soln was washed with water, dried (Na_2SO_4) and evaporated. The residue crystallized from chf–MeOH as *needles* (0·75 g), m.p. 246–247°, $[\alpha]_D$ +22·03°, ν_{max} 3500 cm^{-1}. (Found: C, 83·84, H, 11·79. $C_{30}H_{52}O$ requires: C, 84·04; H, 12·23%.) Mol. wt. by mass spectrum 428.

9. *Acetyldesoxocanophyllol* (IId). Acetylation of desoxocanophyllol by the pyridine–Ac_2O method gave the *acetate*, m.p. 168–169°, $[\alpha]_D$ +5·75°. (Found: C, 81·88, H, 11·33. $C_{32}H_{54}O_3$ requires: C, 81·64; H, 11·56%.) Its m.p. was depressed to 135 ~ 145° on admixture with a sample of 24-acetoxyfriedelane, m.p. 173–175° (kindly supplied by Dr. Courtney). Mass spectrum: *m/e* 470, 455, 410, 397, 395, 259.

10. *Desoxocanophyllol tosylate* (IIe). A soln of desoxocanophyllol (0·4 g) in pyridine (4 ml) was heated with *p*-toluenesulphonyl chloride (0·6 g) at 60–70° for 2 hr and then left overnight at room temp. Working up gave the *tosylate* (0·4 g), needles (from chf–MeOH), m.p. 173–175°. (Found: C, 76·37; H, 10·28. $C_{37}H_{58}O_5S$ requires: C, 76·24; H, 10·03%.)

11. *Pyridine–chromium trioxide oxidation of desoxocanophyllol.* Desoxocanophyllol (0·2 g) in pyridine (2 ml) was oxidized with pyridine–CrO_3 complex (prepared from 0·2 g CrO_3 and 2 ml pyridine). Working up yielded the *aldehyde* (IIb), needles (from chf–MeOH), m.p. 263–265°, $[\alpha]_D$ +26·27°, ν_{max} 2700, 1720 cm^{-1}. (Found: C, 84·51; H, 11·75. $C_{30}H_{50}O$ requires: C, 84·44; H, 11·81%.)

12. *Wolff-Kishner reduction of canophyllal.* A mixture of canophyllal (0·6 g), hydrazine hydrate (98%, 3 ml) and EtONa (2 g Na in 30 ml EtOH) was heated in a sealed tube at 170° for 16 hr. Working up gave IIa (0·3 g), flakes (from benzene), m.p. 246–247°, undepressed by admixture with an authentic sample of friedelane prepared by Wolff-Kishner reduction of friedelin; $[\alpha]_D$ +18·70°. (Found: C, 86·82; H, 12·75. Calc. for $C_{30}H_{52}$: C, 87·30; H, 12·70%.)

13. *Ethylene ketal of canophyllol* (IIIc). A soln of canophyllol (1 g) and ethylene glycol (2 ml) in benzene (100 ml) containing *p*-toluenesulphonic acid (0·1 g) was refluxed for 8 hr using a Dean-Stark water-separator. The benzene soln was washed with Na_2CO_3aq, water, dried (Na_2SO_4) and evaporated. The residue crystallized from chf–MeOH as *needles* (0·9 g), m.p. 325° (dec). (Found: C, 78·67; H; 11·07. $C_{32}H_{54}O_3$ requires: C, 78·96; H, 11·18%.)

14. *Pyridine–chromium trioxide oxidation of canophyllol ethylene ketal.* The above ketal (0·9 g) was oxidized with pyridine–CrO_3 (prepared from 0·4 g CrO_3 and 4 ml pyridine) and worked up to yield the *ketal-aldehyde* (IIIb), needles (from chf–MeOH), m.p. 321–323° $[\alpha]_D$ +11·60°. (Found C, 79·17; H, 10·83. $C_{32}H_{52}O_3$ requires: C, 79·28; H, 10·81%.)

15. *Wolff-Kishner reduction of the ketal-aldehyde* (IIIb). A mixture of IIIb (1 g), hydrazine hydrate (98%, 3 ml) and EtONa (3 g Na in 30 ml EtOH) was heated in a sealed tube at 160–170° for 14 hr. Working up gave *desoxycanophyllol ethylene ketal* (IIIa), needles (from chf–MeOH), m.p. 306–308°. (Found: C, 81·19; H, 11·19. $C_{32}H_{54}O_2$ requires: C, 81·64; H, 11·56%.)

16. *Hydrolysis of desoxycanophyllol ethylene ketal.* A soln of the above ketal (0·2 g) and *p*-toluenesulphonic acid (0·2 g) in acetone (150 ml) was refluxed for 12 hr, evaporated *in vacuo* and digested with Na_2CO_3aq. The solid obtained was filtered off, dried and chromatographed over silica gel in hexane. Elution with 1:1 benzene–hexane gave friedelin (0·1 g), m.p. and mixed m.p. with an authentic sample, 260–262°. The optical rotations and IR spectra of the two samples were also identical.

17. *Acetylcanophyllic acid* (IVc). Canophyllic acid (0·15 g) was refluxed for 2 hr with anhyd AcONa (0·1 g), glacial AcOH (4 ml) and Ac_2O (3 ml). The soln was concentrated *in vacuo* till a ppt appeared. MeOH (10 ml) was added and the mixture refluxed for 2 hr more. Dilution with water gave a solid which crystallized from chf–MeOH as *needles*, m.p. 314–316°. (Found: C, 76·86; H, 10·41. $C_{36}H_{48}O_4$ requires: C, 76·75; H, 10·47%.)

18. *Methyl canophyllate* (IVb). A suspension of canophyllic acid (0·6 g) in MeOH (20 ml) was treated with excess ethereal diazomethane. The solvents were evaporated *in vacuo* and the residue filtered through a column of silica gel in chf. The product crystallized from chf–MeOH as *needles*, m.p. 240–241°, $[\alpha]_D$ +2·75°, ν_{max} 1720 cm^{-1}. (Found: C, 78·61; H, 10·99. $C_{31}H_{48}O_3$ requires: C, 78·76; H, 11·09%.) Acetylation of methyl canophyllate (pyridine–Ac_2O method) yielded the *acetate* (IVd), needles (from chf–MeOH), m.p. 270–271°, $[\alpha]_D$ +30·48°, ν_{max} 1730, 1715 cm^{-1}. (Found: C, 76·66; H, 10·78. $C_{33}H_{46}O_4$ requires: C, 76·99; H, 10·57%.)

19. *Canophyllal from methyl canophyllate.* A soln of methyl canophyllate (0·5 g) in dioxan (15 ml) was added to a suspension of LAH (2 g) in dioxan (20 ml). The mixture was refluxed with stirring for 6 hr and decomposed with ether and water. The ether soln was dried (Na_2SO_4) and evaporated to yield the diol (0·4 g) as an amorphous solid. A soln of the diol (0·4 g) in pyridine (5 ml) was added to pyridine–CrO_3 complex (prepared from 0·5 g CrO_3 and 5 ml pyridine) and the mixture stirred overnight at room temp. Working up gave canophyllal, m.p. and mixed m.p. with the naturally occurring material, 260–262°, $[\alpha]_D$ −21·15°. (Found: C, 81·32; H, 10·90. $C_{30}H_{46}O_2$ requires: C, 81·76; H, 10·98%.) The two samples had identical IR spectra.

20. *Pyridine–chromium trioxide oxidation of methyl canophyllate:* Methyl canophyllate (0·1 g) was oxidized with pyridine–CrO_3 (prepared from 0·1 g CrO_3 and 2 ml pyridine). Working up gave the *keto-ester* (Ih), needles (from chf–MeOH), m.p. 247–249°, $[\alpha]_D$ −29·27°, ν_{max} 1718, 1710 cm^{-1}. (Found: C, 79·17; H, 10·95. $C_{31}H_{46}O_3$ requires: C, 79·10; H, 10·71%.)

21. *Permanganate oxidation of canophyllal.* A soln of canophyllal (0·6 g) in acetone (100 ml) was treated with $KMnO_4$ (1·5 g). The soln was refluxed with stirring for 2 hr, evaporated *in vacuo* and the residue treated with dil. H_2SO_4 and $NaHSO_3$. The ppt was filtered off, dried, suspended in MeOH and treated with excess ethereal diazomethane. The soln was evaporated *in vacuo* and the residue crystallized from chf–MeOH to give the *keto* ester (Ih), m.p. 247–249°. (Found: C, 78·94; H, 10·89. $C_{31}H_{46}O_3$ requires: C, 79·10, H, 10·71%.) Its m.p. was undepressed by admixture with a sample of the keto-ester prepared by pyridine–CrO_3 oxidation of methyl canophyllate. The IR spectra of the two samples were also identical.

22. $NaBH_4$ *Reduction of the keto ester* (Ih). A soln of the above keto ester (0·1 g) in dioxan (5 ml) was treated with $NaBH_4$ (0·2 g). The soln was kept at 45–50° for 1 hr and then left overnight at room temp. The soln was concentrated *in vacuo*, treated with dil. AcOH and extracted with chf. The product, which was shown by TLC to consist of 2 compounds in the ratio 4:1, was chromatographed over silica gel in benzene soln. The major product which was less polar crystallized from chf–MeOH as needles, m.p. and mixed m.p. with methyl canophyllate, 239–240°. The two samples had identical IR spectra and TLC behaviour. The more polar fraction was identical with the product of Na–n-propanol reduction described below.

23. *Sodium and propanol reduction of the keto-ester* (Ih). A boiling soln of the keto-ester (0·25 g) in n-propanol (40 ml) was treated gradually with Na (2 g) during a period of 30 min. The soln was refluxed for 30 min more, evaporated *in vacuo*, treated with dil. HCl and extracted with chf. The residue from the chf extract was chromatographed over silica gel in benzene soln. The product (Vb) crystallized from chf–MeOH as *needles* (0·23 g), m.p. 229–230°, $[\alpha]_D$ +1·95°, ν_{max} 1720 cm^{-1}. It differed from methyl canophyllate in the IR spectrum as well as in its TLC behaviour. (Found: C, 78·64; H, 10·96. $C_{31}H_{48}O_3$ requires: C, 78·76; H, 11·09%.) Acetylation of the hydroxyester by pyridine–Ac_2O gave the *acetate* (Vd), needles (from chf–MeOH), m.p. 295–296°, $[\alpha]_D$ −16·61°, ν_{max} 1735, 1720 cm^{-1}. (Found: C, 76·99; H, 10·51. $C_{33}H_{46}O_4$ requires: C, 76·99; H, 10·57%.)

24. *Saponification of methyl canophyllate* (IVb). Methyl canophyllate (0·5 g) was refluxed for

18 hr with KOH (13 g) in ethylene glycol (50 ml). The soln was diluted with water and extracted with ether to remove any unhydrolysed ester. The aq. soln was acidified and extracted with ether. The product crystallized form chf–MeOH as prisms, m.p. and mixed m.p. with canophyllic acid, 312°.

25. *Saponification of methyl dehydrocanophyllate* (Ih). The keto ester (0·3 g) was refluxed for 18 hr with KOH (8 g) in ethylene glycol (30 ml) and worked up to yield the *keto-acid* (Ig) (0·2 g), m.p. 310°, ν_{max} 1700 cm^{-1}. (Found: C, 78·35; H, 11·10. $C_{30}H_{48}O_3$ requires: C, 78·89; H, 10·59.)

26. *Acetolysis of canophyllol tosylate.* A soln of Ie (1 g) and AcONa (0·6 g) in AcOH (80 ml) was heated at 95° for 3 hr, concentrated *in vacuo* and diluted with water. The ppt was filtered off, dried and chromatographed over silica gel in benzene–hexane (1:1). The product (IXa or Xa) crystallized from chf–MeOH as *needles* (0·3 g), m.p. 228–230°, $[\alpha]_D$ −23·21°. (Found: C, 85·02; H, 11·62. $C_{30}H_{48}O$ requires: C, 84·84; H, 11·39%.) Mass spectrum: *m/e* 424, 409.

27. *Acetolysis of desoxocanophyllol tosylate.* The tosylate IIe (1 g) was heated in AcOH (90 ml) with AcONa (1 g) at 90–95° for 3 hr. Working up as above gave the *hydrocarbon* (IXb or Xb) as needles, m.p. 165°, $[\alpha]_D$ +23·29°. (Found: C, 87·54; H, 12·26. $C_{30}H_{50}$ requires: C, 87·73; H, 12·27%.) Mass spectrum: *m/e* 410, 395, 260.

28. *Epoxidation of the above hydrocarbon.* The above IXb or Xb (0·4 g) was treated with 20 ml perbenzoic acid soln in chf (containing 30 mg peracid per ml) and allowed to stand at 5° for 4 days. The soln was washed well with Na_2CO_3aq, water, dried (Na_2SO_4) and evaporated. The product crystallized from CH_2Cl_2–MeOH as *needles*, m.p. 260–263°. (Found: C, 83·98; H, 11·80. $C_{30}H_{48}O$ requires: C, 84·44; H, 11·81%.)

29. *Oleanenic lactone* (XI) *from methyl canophyllate.* A soln of the ester (1·3 g) in phenol (10 g) was saturated with dry HCl gas and maintained at saturation by slow passage of HCl at 110° for 45 min. The soln was cooled, heated with 70 ml of 10% aq KOH and extracted with CH_2Cl_2. The CH_2Cl_2 extract was washed with water, dried (Na_2SO_4) and evaporated. The residue crystallized from chf–hexane to give *oleanenic lactone* (XI) as needles (0·35 g), m.p. 350–352° (dec), $[\alpha]_D$ +20·62°, ν_{max} 1755 cm^{-1}. (Found: C, 81·73; H, 10·82. $C_{30}H_{46}O_2$ requires: C, 81·76; H, 10·98%.) The lactone was recovered unchanged after refluxing in AcOH with con HCl according to the conditions described.[16]

30. *Oleanenic lactone from canophyllic acid.* A soln of canophyllic acid (0·6 g) in phenol (6 g) was saturated with dry HCl at 110° for 45 min. Working up gave *oleanenic lactone* (0·2 g), m.p. and mixed m.p. with the sample obtained from the ester, 350–352° (dec). The IR spectra of the two samples were also identical.

31. *γ-oleanenic acid.* This was prepared by the method of Bilham and Kon.[14] A mixture of methyl oleanonate (1·5 g), hydrazine hydrate (98%, 4 ml) and EtONa (0·5 g Na in 25 ml EtOH) was heated in a sealed tube at 160° for 15 hr. The soln was poured into water and extracted with ether. The aq. soln was acidified and extracted with ether to yield XII (0·7 g). Crystallization from AcOEt gave needles, m.p. 272°.

32. *Oleanenic lactone from γ-oleanenic acid.* A soln of XII (0·2 g) in phenol (4 ml) was saturated with dry HCl at 110° for 45 min. The soln was cooled, poured into 50 ml of 5% KOHaq and extracted with CH_2Cl_2. Chromatography of the product over silica gel in benzene followed by crystallization from CH_2Cl_2–hexane gave *oleanenic lactone* (0·1 g), m.p. 350–352° (dec), undepressed by admixture with a sample of the lactone obtained from canophyllic acid. The two samples had also identical IR spectra and TLC behaviour. (Found: C, 81·74; H, 11·37. $C_{30}H_{46}O_2$ requires: C, 81·76; H, 10·98%.)

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