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CHEMICAL CONSTITUENTS OF *GLOCHIDION HOHENACKERI**

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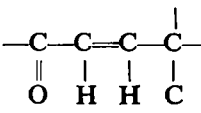
Abstract—From the bark and roots of *Glochidion hohenackeri* (Euphorbiaceae), in addition to the known 3-epi-lupeol, two new triterpenes glochidone and glochidiol have been isolated and assigned structures I and VIIIa respectively. The stereochemistry of the hydroxyl groups in glochidiol has been determined by the partial synthesis of three of the four possible stereoisomers of the dihydrodiol diacetate (Vd, VId and VIId) which all differ from dihydroglochidiol diacetate (VIIId).

Glochidion hohenackeri (Euphorbiaceae), is a tree very common on the west coast of India. In this paper investigations on the triterpene constituents of the bark and roots of the plant are reported.

The hexane extract of the bark yielded a gum which on chromatography gave a crystalline ketone, m.p. 164–165°, $[\alpha]_D$ +73·41°, which we have named glochidone. The gummy material in the polar fractions was found to consist of a mixture of two triterpene alcohols. Acetylation of this mixture and chromatography of the product yielded two crystalline acetates. One was found to be a monoacetate, m.p. 163°, $[\alpha]_D$ −6·91°; the other a diacetate, m.p. 253–256°, $[\alpha]_D$ +20·82°. The alcohol corresponding to the latter has been named glochidiol. In subsequent isolations, instead of chromatography, it was found more convenient to acetylate the gum obtained by evaporation of the hexane extract. From the roots of the plant, glochidone and glochidiol diacetate were obtained in somewhat lower yield.

Glochidone has the molecular formula $C_{30}H_{46}O$ (mol. wt. by mass spectrum 422) and is an α,β-unsaturated ketone, λ_{max} 228 mμ (log ε 4·00), ν_{max} 1660 cm^{-1} (α,β-unsaturated ketone), 885 cm^{-1} (=CH_2). Its NMR spectrum shows the presence of six tertiary C—CH_3, one vinyl C—CH_3, a two-proton doublet at δ 4·65 (=CH_2, J = 6 c/s) and a pair of one-proton doublets each at δ 5·75 (J = 10 c/s) and δ 7·09 (J = 10 c/s) indicating the presence of the grouping  Catalytic hydrogenation of glochidone yielded lupan-3-one identical in all respects with an authentic sample. Glochidone hence possesses the structure and stereochemistry shown in I.

The monoacetate, m.p. 163°, has the molecular formula $C_{32}H_{52}O_2$ (mol. wt. by mass spectrum 468). On alkaline hydrolysis it gave an amorphous alcohol. Oxidation of the latter with Jones reagent furnished lupen-3-one (mixed m.p., IR spectrum).

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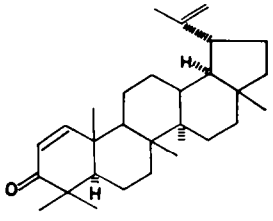
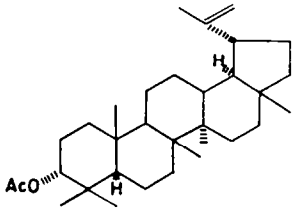
Catalytic reduction of the acetate gave a dihydro derivative. This was hydrolysed to the alcohol and then oxidized with CrO_3 to yield lupan-3-one. The acetate is hence 3-epi-lupeol acetate (II). 3-Epi-lupeol has previously been obtained from plants of the Burseraceae family.[1]

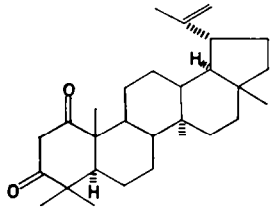
Glochidiol diacetate has the molecular formula $C_{34}H_{54}O_4$ (mol. wt. by mass spectrum 526). Its IR spectrum shows bands at 1725 cm^{-1} (ester), 1630 and 880 cm^{-1} (=CH_2). Catalytic reduction yielded a dihydro derivative. Alkaline hydrolysis of glochidiol diacetate gave an amorphous diol which could not be cleaved by periodic acid showing that it was not a 1,2-diol. On being subjected to Jones oxidation, the diol yielded a 1,3-diketone (III), m.p. 197–200°, $[\alpha]_D$ +101·7°, λ_{max} 256 mμ (log ε 3·97), ν_{max} 1718, 1696 cm^{-1}. Oppenauer oxidation of glochidiol yielded an α,β-unsaturated ketone, $C_{30}H_{46}O$, which was found to be identical with glochidone (I). This suggests that glochidiol has the structure IV. Formation of glochidone from this would involve oxidation of the C_3-OH followed by β-elimination of the OH at C_1. The stereochemistry of the OH groups in IV remained to be settled. Stereospecific synthesis of three (Vd, VId and VIId) of the four possible stereoisomers (Vd, VId, VIId and VIIId) of the dihydrodiol diacetates showed them to be different from dihydroglochidiol diacetate. Dihydroglochidiol diacetate hence possesses the stereochemistry shown in VIIId, glochidiol itself being represented by VIIIa.



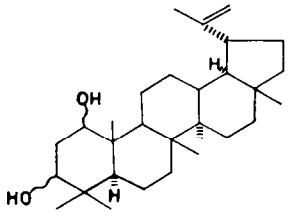
I



II



III

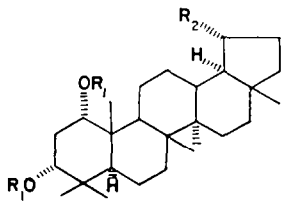


IV

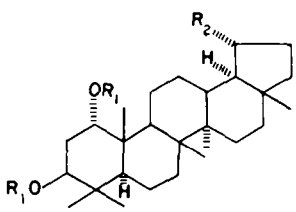
Treatment of glochidone with alkaline hydrogen peroxide gave the epoxide (IX), m.p. 181–183°, which on catalytic hydrogenation yielded X, m.p. 223–225°. LAH reduction of X yielded a mixture of diols which were separated by chromatography on alumina. The less polar fraction afforded the 1α,3α-diol (Vb), which yielded the diacetate (Vd). The more polar fraction afforded the 1α,3β-diol (VIb) which yielded on acetylation the diacetate (VId). LAH4 reduction of IX similarly gave two diols (Va and VIa) which yielded the diacetates Vc and VIc respectively.

The diketone (III) on reduction with LAH4 or NaBH4 yielded the 1α,3β-diol (VIa). However, with Na and propanol, it yielded the 1β,3β-diol (VIIa) acetylation of which furnished the diacetate (VIIc). Catalytic hydrogenation of VIIc gave VIId.

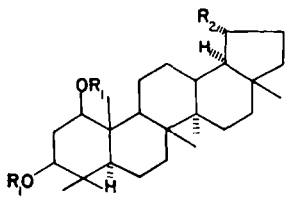
[1] B. Tursch and E. Tursch, *Bull. Soc. Chim. Belges* **70**, 585 (1961).



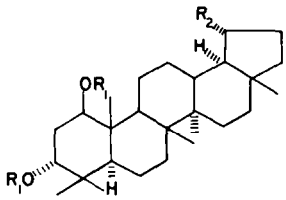
V



VI



VII

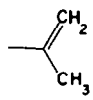


VIII

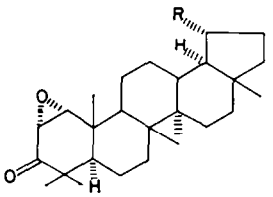
a : R_1 = H ; R_2 =

b : R_1 = H ; R_2 =

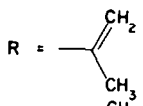
c : R_1 = Ac ; R_2 =



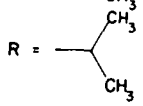
d : R_1 = Ac ; R_2 =



IX



X



The m.ps and optical rotations of the stereoisomeric dihydrodiols and their diacetates are summarized below:

Diol				Diacetate		
	Compound	m.p.	$[\alpha]_D$	Compound	m.p.	$[\alpha]_D$
1α,3α	Vb	250°	−16·06°	Vd	158–160°	
1α,3β	VIb	236–238°	−6·4°	VId	238–242°	+9·80°
1β,3β	VIIb	amorph.		VIId	223–226°	−6·48°
1β,3α	VIIIb	262–263°	−29·39°	VIIId	210–211°	−30·68°

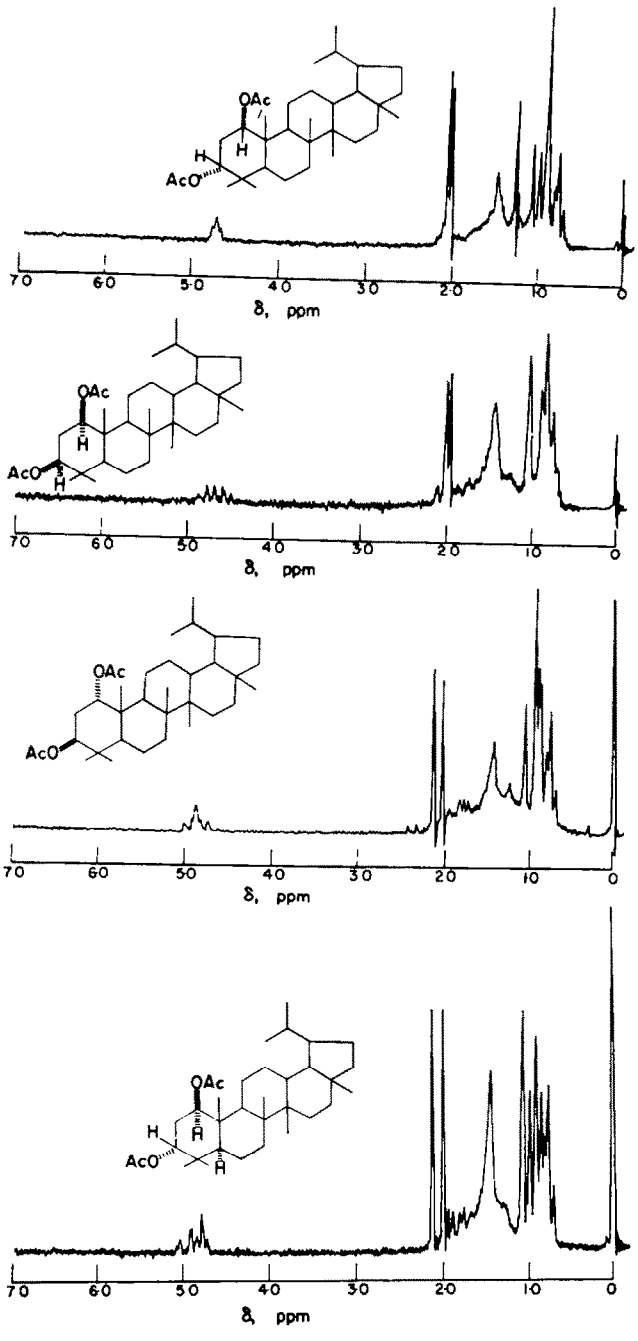

OAc
H
AcO
H
7·0
6·0
5·0
4·0
3·0
2·0
1·0
0
δ, ppm
OAc
AcO
H
H
7·0
6·0
5·0
4·0
3·0
2·0
1·0
0
δ, ppm
OAc
AcO
7·0
6·0
5·0
4·0
3·0
2·0
1·0
0
δ, ppm
OAc
H
AcO
H
H
7·0
6·0
5·0
4·0
3·0
2·0
1·0
0
δ, ppm

FIG. 1

The NMR spectra of the dihydrodiol diacetates (Vd, VId, VIId and VIIId) are presented in Fig. 1. As reported by Williams and Bhacca,[2] the J_{ae} values denoting the coupling of an axial proton on the carbon atom bearing the electronegative substituent to an equatorial proton were observed to be of the order of 6 c/s whereas J_{ea} values denoting the analogous coupling in which the proton on the electronegatively substituted carbon atom is equatorial were of the order of 2–3 c/s.

EXPERIMENTAL

M.ps are uncorrected. IR spectra were taken in CH_2Cl_2 using a Perkin–Elmer model 421 spectrophotometer. Optical rotations refer to 2–3% solutions in $CHCl_3$ at 24°. NMR spectra were determined in $CDCl_3$ on a Varian A-60 spectrometer. Hexane used had b.p. 60–80°. Neutral alumina was used for chromatography.

Extraction of Glochidion hohenackeri *bark and isolation of components.* The dried ground bark (5 kg) was extracted 3 times with cold hexane. The residue obtained by evaporation of hexane was treated with acetic anhydride (120 ml) and pyridine (50 ml) and left overnight at room temp. The mixture was poured into water and extracted with $CHCl_3$. The $CHCl_3$ solution was washed with dil. HCl, water, $NaHCO_3$aq and again with water, dried (Na_2SO_4) and evaporated. The residue (70 g) was chromatographed in hexane over alumina. The hexane eluate yielded a solid which crystallized from $CHCl_3$–MeOH to give *glochidone* (9 g), needles, m.p. 164–165°, $[\alpha]_D$ +73·41°, ν_{max} 1660, 885 cm^{-1}, λ_{max} 228 mμ (log ϵ 4·00). (Found: C, 84·72; H, 10·65. $C_{30}H_{46}O$ requires: C, 85·24; H, 10·97%.) Subsequent elution of the column with benzene–hexane (1:1) and then with benzene yielded 3-epi-lupeol acetate (0·8 g), m.p. 163°, $[\alpha]_D$ −6·91°, ν_{max} 1720, 1635, 880 cm^{-1}. (Found: C, 82·06; H, 11·25. Calc. for $C_{32}H_{52}O_2$; C, 81·99; H, 11·18%). Later fractions of the benzene eluate yielded *glochidiol diacetate* (8·5 g). Crystallization from $CHCl_3$–MeOH gave needles, m.p. 253–256°, $[\alpha]_D$ +20·82°, ν_{max} 1725, 1630, 880 cm^{-1}. (Found: C, 77·34; H, 10·21. $C_{34}H_{54}O_4$ requires; C, 77·52; H, 10·33%.) Elution of the column with $CHCl_3$–MeOH yielded only gums.

The MeOH extract of the bark after removal of tannins and acetylation yielded, after chromatography, more glochidiol diacetate (3 g).

When the residue from the hexane extract was chromatographed without being acetylated, the only crystalline compound obtained was glochidone since the free alcohols epi-lupeol and glochidiol were both amorphous.

The hexane extract of the roots (5 kg) after acetylation and chromatography yielded glochidone and glochidiol diacetate.

Dihydroglochidone (lupan-3-one). Glochidone (0·25 g) in acetic acid (10 ml) was reduced with H_2 at atm. press. in presence of 10% Pd–C (50 mg). The catalyst was filtered off, the solvent evaporated *in vacuo* and the residue crystallized from $CHCl_3$–MeOH to give dihydro-glochidone (0·2 g), $[\alpha]_D$ +14·41°, m.p. 208–209°, undepressed by admixture with an authentic sample of lupan-3-one. (Found: C, 84·48; H, 11·85. Calc. for $C_{30}H_{52}O$: C, 84·04; H, 12·23%.) The IR spectra of the two samples were also identical.

Hydrolysis of 3-epi-lupeol acetate. A solution of the acetate (1 g) in dioxan (30 ml) was refluxed with 7% methanolic KOH for 4 hr. The solution was evaporated *in vacuo*, the residue diluted with water and extracted with $CHCl_3$ to yield the alcohol as a gum.

Jones oxidation of 3-epi-lupeol. The above alcohol (0·4 g) was oxidized with Jones reagent and the product crystallized from $CHCl_3$–MeOH to yield lupen-3-one, m.p. and mixed m.p. with an authentic sample, 170°. The IR spectra of the two samples were identical.

Dihydro-3-epi-lupeol acetate. 3-Epi-lupeol acetate (0·2 g) in acetic acid (10 ml) was hydrogenated in presence of PtO_2 (40 mg) to yield the dihydroacetate, m.p. 164°, $[\alpha]_D$ −46·32°. (Found: C, 81·24; H, 11·27. $C_{32}H_{54}O_2$ requires: C, 81·64; H, 11·56%.)

Chromic acid oxidation of dihydro-epi-lupeol. The dihydroacetate was hydrolysed with KOH to yield dihydro-epi-lupeol as a gel. The alcohol (1·3 g) in acetic acid (10 ml) was treated with a solution of CrO_3 (0·4 g) in acetic acid (10 ml) and left overnight at room temp. Dilution with water gave a solid (0·8 g) which crystallized from CH_2Cl_2–MeOH to yield needles, m.p. 207–208°, undepressed by admixture with authentic lupan-3-one.

[2] D. H. Williams and N. S. Bhacca, *J. Amer. Chem. Soc.* **86**, 2742 (1965).

Dihydroglochidiol diacetate. A solution of glochidiol diacetate (1 g) in acetic acid (30 ml) was reduced with H_2 at atm. press. in presence of PtO_2 (0·1 g). The catalyst was filtered off, the solvent evaporated *in vacuo* and the residue crystallized from $CHCl_3$–MeOH to give needles, m.p. 210–211°, $[\alpha]_D$ −30·68°. (Found: C, 77·77; H, 10·38. $C_{34}H_{56}O_4$ requires: C, 77·22; H, 10·67%.)

Hydrolysis of glochidiol diacetate. The diacetate (2 g) was refluxed for 2 hr with 7% methanolic KOH (40 ml). The MeOH was evaporated *in vacuo*, the residue diluted with water and extracted with CH_2Cl_2 to yield glochidiol (1·7 g) as an uncrystallizable gum.

Hydrolysis of dihydroglochidiol diacetate. Dihydroglochidiol diacetate was hydrolysed as above to yield *dihydroglochidiol* which crystallized from $CHCl_3$–MeOH as needles, m.p. 262–263°, $[\alpha]_D$ −29·39°. (Found: C, 81·24; H, 11·77. $C_{30}H_{52}O_2$ requires: C, 81·02; H, 11·79%.)

Jones oxidation of glochidiol. A solution of glochidiol (2 g) in acetone (30 ml) was cooled to 0° and treated with excess of Jones reagent. After 5 min, acetone saturated with SO_2 was added, followed by K_2CO_3aq, and ether. The ether layer was washed with K_2CO_3aq water, dried (Na_2SO_4) and evaporated to yield the *diketone* (III) needles (from hexane), m.p. 196–200°, $[\alpha]_D$ +101·71°, λ_{max} 256 mμ (log ϵ 3·97). (Found: C, 82·58; H, 10·52. $C_{30}H_{46}O_2$ requires: C, 82·13; H, 10·57%.)

Oppenauer oxidation of dihydroglochidiol. A solution of dihydroglochidiol (0·53 g) in toluene (5 ml) was refluxed with Al isopropoxide (2·5 g) and cyclohexanone (7 ml) at 120° for 1 hr. The mixture was cooled, decomposed with water and extracted with ether. The ether extract was washed with 20% NaOHaq, then with water and excess cyclohexanone removed by distillation with steam. The residue was extracted with $CHCl_3$, the $CHCl_3$ extract dried (Na_2SO_4) and evaporated. The solid obtained crystallized from $CHCl_3$–MeOH to give *lup-1-ene-3-one* (0·35 g), m.p. 177–179°, λ_{max} 228 mμ. (Found: C, 84·63; H, 11·67. $C_{30}H_{48}O$ requires: C, 84·84; H, 11·39%.)

Oppenauer oxidation of glochidiol. The diol (1 g) was oxidized in the above manner and the product chromatographed in benzene over alumina. The first 25 ml fraction gave 0·3 g of a solid which was crystallized from $CHCl_3$–MeOH to give needles, m.p. 165–166°, undepressed by admixture with a sample of glochidone. The UV and IR spectra of the two samples were identical.

Glochidone epoxide. A solution of glochidone (2 g) in dioxan (80 ml) was treated with 1N NaOH (30 ml) and 30% H_2O_2 (15 ml) and stirred for 2 days. Dilution with water gave a solid which crystallized from MeOH to yield the *epoxide* (2 g), m.p. 181–183°. (Found: C, 82·27; H, 10·71. $C_{30}H_{46}O_2$ requires: C, 82·13; H, 10·57%.)

LAH *reduction of glochidone epoxide.* The above epoxide (2 g) was reduced with LAH (2 g) in THF (75 ml) and worked up as usual. The solid obtained was crystallized once from MeOH and 3 times from $CHCl_3$–MeOH to yield *needles* (Va; 600 mg), m.p. 256–257°, $[\alpha]_D$ +28·03°. (Found: C, 81·14; H, 11·28. $C_{30}H_{50}O_2$ requires: C, 81·39; H, 11·38%.) Its *acetate* (Vc) (pyridine-acetic anhydride method), crystallized from MeOH, had m.p. 124–126°. (Found: C, 77·49; H, 10·20. $C_{34}H_{54}O_4$ requires: C, 77·52; H, 10·33%.)

The MeOH mother liquor was evaporated to dryness and the residue chromatographed in benzene over alumina. Elution with $CHCl_3$ gave solids which were followed by TLC. Like fractions were combined, acetylated with pyridine and acetic anhydride and the *acetate* (VIc) crystallized from MeOH to yield needles (800 mg), m.p. 230–234°, $[\alpha]_D$ +46·57°. (Found: C, 77·82; H, 10·19. $C_{34}H_{54}O_4$ requires: C, 77·52; H, 10·33%.)

LAH *reduction of lup-29-ene-1,3-dione.* The diketone (III; 100 mg) was reduced with LAH (100 mg) in THF (60 ml). The amorphous product obtained was acetylated and the acetate chromatographed in benzene over alumina. Elution with benzene gave a solid which was repeatedly crystallized from MeOH to yield needles, m.p. 230–234°, undepressed by admixture with the acetate mentioned above.

$NaBH_4$ *reduction of lup-29-ene-1,3-dione.* A solution of III (0·3 g) in MeOH (30 ml) was refluxed for 12 hr with $NaBH_4$ (0·1 g) and worked up in the usual way. The product was acetylated and the acetate purified by chromatography. Crystallization of the product from $CHCl_3$–MeOH gave needles, m.p. 234–235°, undepressed by admixture with the acetate obtained by the LAH method.

Dihydroglochidone epoxide. Glochidone epoxide (1 g) was hydrogenated in acetic acid solution using PtO_2 catalyst. The solid obtained crystallized from $CHCl_3$–MeOH to give the *dihydroepoxide*, m.p. 223–225°, $[\alpha]_D$ +67·52°. (Found: C, 81·38; H, 11·26. $C_{30}H_{48}O_2$ requires; C, 81·76; H, 10·98%.)

LAH *reduction of dihydroglochidone epoxide.* The above dihydroepoxide (2 g) was reduced with LAH (2 g) in THF (100 ml) and worked up as usual. The solid obtained (1·8 g) was chromatographed in benzene over alumina (60 g). The column was eluted with $CHCl_3$ and 10 ml fractions

collected. Like fractions were combined after being checked by TLC. Fractions 2–6 gave 878 mg of a *diol* (Vb) which crystallized from $CHCl_3$–MeOH as needles (740 mg), m.p. 250°, $[\alpha]_D$ −16·06°. (Found: C, 81·10; H, 12·10. $C_{30}H_{52}O_2$ requires: C, 81·02; H, 11·79%.) Its *acetate* (Vd), crystallized from MeOH, had m.p. 158–160°. (Found: C, 77·79; H, 10·86. $C_{34}H_{56}O_4$ requires: C, 77·72; H, 10·67%.) Fractions 8 to 25 in the chromatography gave 741 mg of a second *diol* (VIb), m.p. 236–238° (from MeOH), $[\alpha]_D$ −6·4°. (Found: C, 81·18; H, 12·16. $C_{30}H_{52}O_2$ requires: C, 81·02; H, 11·79%.) This gave VId (680 mg), m.p. 238–242° from $CHCl_3$–MeOH), $[\alpha]_D$ +9·80°. (Found: C, 77·10; H, 10·69. $C_{34}H_{56}O_4$ requires: C, 77·22; H, 10·67%.)

Sodium and propanol reduction of lup-29-ene-1,3-dione. A solution of III (0·3 g) in boiling *n*-propanol (50 ml) was treated with Na (3·5 g) portionwise over a period of 40 min. Heating was continued for 30 min more and the reaction mixture worked up as usual. The product was acetylated with pyridine and acetic anhydride and the acetate purified by chromatography. Crystallization from MeOH gave needles, m.p. 212–214°, $[\alpha]_D$ +31·53°. (Found: C, 77·72; H, 10·42. $C_{34}H_{56}O_4$ requires: C, 77·22; H, 10·67%.)

Catalytic hydrogenation of the above acetate. The above acetate (180 mg) was hydrogenated in acetic acid solution over PtO_2 and the solid obtained crystallized 3 times from MeOH as needles, m.p. 223–226°, $[\alpha]_D$ −6·48°. (Found: C, 77·04; H, 10·97. $C_{34}H_{58}O_4$ requires: C, 76·93; H, 11·01%.)

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