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THE STRUCTURE AND STEREOCHEMISTRY OF OLIVERIC ACID

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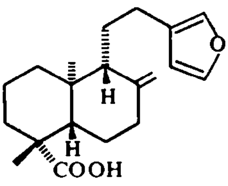
Abstract:—The structure and stereochemistry of oliveric acid, a principal constituent of the trunk resin of *Daniellia oliveri*, have been established as in **2a**.

THE Caesalpiniae, *Daniellia oliveri* (Amherstiae), is a large tropical tree which exudes copious amounts of a copal when damaged in the trunk area. The copals of several other Amherstiae are utilized commercially as varnishes because they harden upon exposure to air. This process is invariably accompanied by a decrease in solubility in organic solvents and has been attributed to oxidation and polymerization of the resin constituents.

Investigations of several fresh Amherstiae copals have shown that these resins are rich sources of bicyclic diterpenes. Thus far, more than two dozen alcohols, aldehydes, and acids possessing the labdane[1-6] or backbone rearranged labdane skeleton[7,8] have been characterized.

We presently report work which establishes the structure and absolute stereochemistry of a new diterpene diacid which is a principal constituent of the trunk copal of *D. oliveri*[9]. Previous investigations of this copal[1] resulted in the isolation and characterization of daniellic acid, **1**.*



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The new diterpenic diacid, oliveric acid, was isolated from the crude copal by precipitation as the triethanolamine salt. Elemental analysis of this salt indicated the empirical formula of oliveric acid to be $C_{20}H_{32}O_4$. Catalytic hydrogenation of the triethanolamine salt of oliveric acid revealed the presence of one double bond. This double bond is a 1,1-disubstituted ethylene type as evident from the IR spectrum of

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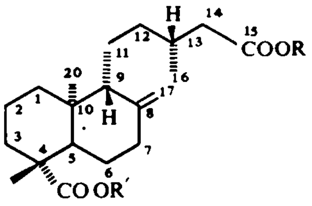
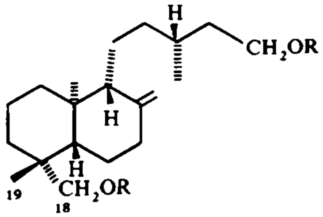
* However it must be noticed that daniellic acid **1** and oliveric acid **2a** have never been found together in the same sample or resin. The sample containing oliveric acid was provided to us by Professor Aubreville (Paris), who confirmed the botanic source as being *Daniellia oliveri* in both cases.

oliveric acid which shows absorption at 1645 and 890 cm^{-1} and produces formaldehyde upon ozonolysis.

Treatment of oliveric acid, **2a**, with etheral diazomethane gave the diester, **2b**. The NMR spectrum of the diester was readily interpreted in terms of the skeleton of structure **2b**. Thus, there are four 3-hydrogen singlets δ 0·48, 1·15, 3·60 and 3·64 evident in the spectrum. The two high field singlets are attributable to the quaternary Me groups at C-10 and C-4 respectively, whereas the low field singlets are due to ester methoxyls. A prominent 3-hydrogen doublet (J=5·5 Hz) signal centered at δ 0·94 was attributed to the C-13 Me whereas the two one-hydrogen signals at δ 4·48 and δ 4·84 are typical of C-17 hydrogens of $\Delta^{8,17}$ labdenes[5].



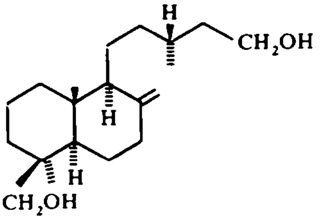
2a: R=R'=H
b: R=R'=CH_3
c: R=H, R'=CH_3



3a: R=H
b: R=OSO_2-tol-*p*

The hindered nature of one of the carbomethoxy groups in **2b** was indicated by its resistance to hydrolysis. Thus, refluxing **2b** in 0·1 N ethanolic potassium hydroxide for a half hour gave an acid ester (**2c**) which was unchanged even after refluxing in 2N alcoholic base for 4 hours. The location of the carbomethoxy groups *axial* at C-4 and at C-15 as well as the presence of the $\Delta^{8(17)}$—labdene skeleton in **2b** was further indicated upon reduction of the diester to the diol **3a** with LAH.

The NMR spectrum of this diol is indistinguishable from that of the known[10] diterpene, imbricatadiol, **4**.



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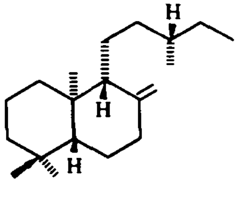
The ORD curves (plain) of **3a** and **4** are opposite in sign; otherwise, little difference in their optical rotatory power was detectable. These two criteria suggest a mirror image relationship. However, since the X-ray powder diffraction diagrams and IR spectra of **3a** and **4** do reveal differences, the two compounds are not mirror images. The identity of the NMR spectra and similarity of optical rotatory power of **3a** and **4** are readily explained if these two diols are *enantiomeric* at every asymmetric center except C-13. The absolute configuration at this carbon would have little observable effect on the chemical shifts of the hydrogens in these compounds and might not be expected to affect the optical rotatory power significantly. The absolute stereochemistry at C-5, C-9, C-10 and C-13 of **3a** was determined as follows. The diol, **3**, was converted to the ditosylate, **3b** which was subsequently reduced with LAH to the known[11] olefin **5**. An examination of the NMR spectrum of **5** revealed the presence of three quarternary Me groups at δ 0·65, 0·78 and 0·85 as well as signals at δ 4·38 and 4·68 due to a $>C{=}CH_2$ group. The IR spectrum of **5** shows olefinic absorptions at 1640 and 888 cm^{-1}. The specific rotation of **5** was (within experimental error) identical to that reported for this compound. Oxidation of **5** (osmium tetroxide in pyridine) gave the crystalline 8,17-diol, **6**. Comparison of the 8,17-diol, **6**, obtained from **3a**, with an authentic sample[11] by mixture m.p. gave no depression.



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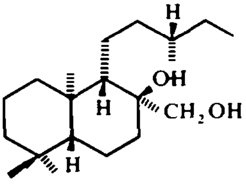

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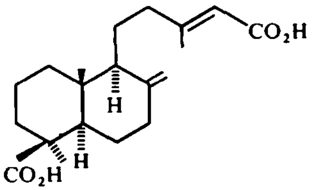
Oliveric acid, **2a**, thus belongs to the class of antipodal (10α) labdene diterpenes possessing the 13 (**R**) configuration in which the skeleton and C_{13} configuration are identical to the diterpenes of the Amherstiae, *Eperua falcata* but different in C_{13} configuration from those found in *T. verrucosum*[5].* The large number of labdene and backbone rearranged labdene diterpenes encountered in the copals of the Amherstiae indicate that these skeletons are characteristic of this tribe although there appears to be no obvious taxonomic significance attributable to the C_{10} or C_{13} configuration.



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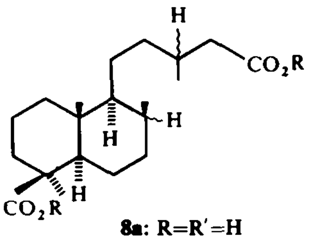

8a: R=R′=H
b: $R=R'=CH_3$
c: $R=H, R'=CH_3$

EXPERIMENTAL

Analyses were carried out by the Strasbourg Division of the Service Central de microanalyse of the CNRS. M.ps were determined with a Reichert m.p. microscope. Rotations were determined in $CHCl_3$. IR spectra: Beckman IR 5-A instrument; NMR spectra: Varian A-60 instrument in $CDCl_3$, using TMS as

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* A correlation with agathic acid **7**, through the tetrahydro derivative, **8**, has been described in a preliminary communication[9]. This leaves undefined the configuration at C-13. Experimental details are given below.

an internal standard. Mol wts: MS-9 instrument. using an ionization energy of 70 eV and inlet temp. of 100–150°.

Isolation of oliveric acid (*enantio*-13β*H*-lab-8 (17) -en-15, 19-dioic acid), **2a**. Treatment of an acetone soln of the copal of *D. oliveri* with an acetone soln of triethanolamine gave, upon standing for several hours, fine needles of the triethanolamine salt of **2a**. Several recrystallizations from MeOH gave m.p. 142° $[\alpha]_D$ −2° (*c*=1, EtOH). (Found: C, 64·13; H, 9·90; N, 3·00. Calcd. for $C_{26}H_{47}O_7N$: C, 64·30; H, 9·76; N, 2·88%).

Hydrogenation of the triethanolamine salt of oliveric acid—A soln of 491 mg triethanolamine salt of oliveric acid in 10 ml EtOH was stirred for 1 hr under H_2 in the presence of 5% Pt-C. After this time H_2 uptake had ceased (25 ml). The soln was concentrated and the product crystallized from EtOH to give m.p. 160°. The IR spectrum of the reduction product exhibited no absorption at 1645 or 890 cm^{-1}. (Found: C, 64·20; H, 10·26; N, 3·03. Calcd. for $C_{26}H_{49}O_7N$: C, 64·03; H, 10·13; N, 2·87%).

Hydrogenation of agathic acid. A soln of 334 mg agathic acid in 10 ml EtOH was hydrogenated at atm. press. in the presence of 5% Pt-C. After the uptake of 50 ml H_2 the product was isolated in the usual manner as an amorphous solid. It was then treated with one equiv. (150 mg) triethanolamine in 2 ml acetone. After several hr a crystalline triethanolamine salt precipitated (40% of the theoretical amount), probably the salt of one of the C-13 diastereoisomers of **7a**; recrystallized from MeOH it had m.p. 160–161°. Its IR spectrum (KBr) was identical with that of the triethanolamine salt of dihydro-oliveric acid. ORD curve (plain): $[\alpha]_D$ +32°, $[\alpha]_{270}$ +257° (*c*, 0·1; dioxan). ORD of the triethanolamine salt of dihycrooliveric acid: $[\alpha]_D$ −28°; $[\alpha]_{270}$ −261° (*c*, 0·1; dioxan).

Tetrahydroagathic acid (**8a**). The triethanolamine salt, obtained above, was shaken with 20 ml 0·1 HCl and 10 ml ether. The normal workup of the ethereal layer left an amorphous solid. Its IR spectrum showed no difference with that of dihydro-oliveric acid, obtained in the same way from its triethanolamine salt (see above).

Tetrahydroagathic acid dimethylester **8b** *and monomethylester* **8c**. The esterification of **8a** was carried out with ethereal diazomethane and the resulting dimethylester (liquid) **8b** saponified in 0·1 N ethanolic KOH for ½ hr, giving the acid-ester **8c**. Both **8b** and **8c** had IR spectra (CCl_4) indistinguishable from those of the corresponding mono- and dimethylesters obtained in the same way from dihydrooliveric acid.

Ozonolysis of **2a**. Ozonolysis of **2a** (100 mg) in 10 ml dichloromethane containing 5 ml pyridine, followed by the usual workup, gave formaldehyde (isolated as the dimedone derivative) and a ketodiacid (isolated as an oil) which exhibited a positive Cotton effect in its ORD curve: $[\alpha]_D$−70°. $[\alpha]_{308}$+ 1337°, $[\alpha]_{270}$ −1957° (min) (dioxan *c*= 0·2) ν_{max} 1710 and 1725 cm^{-1}.

Esterification of **2a**. An ether soln of **3a** (600 mg) was treated with ethereal diazomethane. After 1 hr the ether was evaporated and the residue filtered through a neutral alumina column to give the diester **2b**; $\nu_{max}^{CS_2}$ 1735, 1645, 1160 and 890 cm^{-1}; $[\alpha]_D$ −61° (c, 0·7).

Reduction of **2b** *to* **3a**. Treatment of an ether soln of **2b** (600 mg) with excess LAH for 24 hr followed by the usual workup gave 502 mg of **3a**, which crystallized from light petroleum, m.p. 107–108°, $[\alpha]_D$ −28° (*c*. 1·3); ν_{max}^{KBr} 3380, 1645, 1062, 1030, 970, 886 and 850 cm^{-1}; NMR δ 4·82 (1, s, C_{17}), 4·52 (1, s, C_{17}). 3·69 (2. t. J=6 Hz. C_{15}). 3·57 (2. doub. Δν=23 Hz. J=12Hz. C_{18})[*]. 0·99 (3. C_{19}. Me). 0·91 (3, d, J = 5 Hz, C_{16}, Me) and 0·66 (3, C_{20}, Me). (Found: Lit.[10] for **4**, m.p. 113–114·5 and 114–116°; $[\alpha]_D$ + 26°. C, 77·91; H, 11·88 Calc. for $C_{20}H_{36}O_2$: C, 77·86; H, 11·76.

Preparation of **3b**. The ditosylate, **3b**, was prepared by treatment of **3a** (450 mg) with excess *p*-toluenesulfonyl chloride in benzene containing pyridine. After 2 days the solvent was evaporated and the diester was isolated as a gum by filtration of the crude reaction mixture through silica gel; ν_{max}^{film} 1640, 1590. 1320, (SO_2), 1175 (SO_2), 1087, 951, 886, 842, 813, 680 and 651cm^{-1}; NMR δ 7·95–7·24 (4). 4·79(1, s, C_{17}), 4·45 (1, s, C_{17}), 3·91 (2, t, J=6 Hz, C_{15}), 3·58 (2, doub, Δν=23Hz, J=11Hz, C_{18}), 0·97(3, C_{19}, Me) and 0·63(3, C_{20}, Me).

Reduction of **3b**. The ditosylate, **3b**, prepared above, was reduced with LAH in ether. Work up in the usual manner yielded 50 mg of **5** which was purified by chromatography on silica gel impregnated with $AgNO_3$. The olefin, **5**, was isolated as on oil, $[\alpha]_D$ −40° (*c*, 2·3). (Found mol. wt. by mass spec. 276 Calc. for $C_{20}H_{36}$: mol. wt., 276); Lit.[11] for **5**, $[\alpha]_D$ −39°.

Oxidation of **5** *with* OsO_4. A soln of **5** (20 mg) in 2 ml dry pyridine containing 100 mg OsO_4 was

[*] A detailed analysis of the chemical shifts of C-18 and C-19 hydroxymethylene as well as C-18, C-19 and C-20 Me hydrogens in diterpenes is given in Ref. 12.

allowed to stand for 1 day. The excess OsO_4 was destroyed by the addition of $NaHSO_3$ aq. The soln was extracted with ether, filtered through silica gel and evaporated to give 15mg of **6**. After several crystallizations from light petroleum, **6** had m.p. 119–120°. m.mp. with authentic sample[11] (m.p. 121–122°) was 119–121°. (Lit.[11] for **6**, m.p. 121–122°).

Acknowledgments—We wish to thank Professor P. R. Jefferies for a sample of **6**, Professor K. Bruns for the IR and NMR comparison of **3a** and imbricatadiol and Professor R. Weiss (Strasbourg) for the X-ray powder diffraction diagrams of **3a** and **4**.

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