ON TERPENES. CCXXIV.*

THE STRUCTURE OF MYLIOL, A TETRACYCLIC SESQUITERPENIC ALCOHOL FROM THE LIVERWORT *Mylia taylorii* (HOOK.) GRAY**

V.BENEŠOVÁ, P.SEDMERA, V.HEROUT and F.ŠORM

Institute of Organic Chemistry and Biochemistry, Czechoslovak Academy of Sciences, Prague 6

Received May 13th, 1972

The major component of the n-pentane extracts of the liverwort *Mylia taylorii* (HOOK.) GRAY is a tetracyclic sesquiterpenic alcohol–myliol ($C_{15}H_{22}O$), to which we assigned the structure *I* on the basis of its chemical degradation and the PMR spectral analysis.

In addition to other substances[1] we isolated from n-pentane extract of the liverwort *Mylia taylorii* (HOOK.) GRAY as the major component a sesquiterpenic alcohol to which we gave the name myliol. In a preliminary communication[2] we assigned the structure *I* to this compound of m.p. 110–111°C. In this communication we present more detailed data confirming the previously proposed structure of myliol.

According to its mass spectrum and elemental analysis it has the composition $C_{15}H_{22}O$ (M^+ 218). Its IR spectrum shows the maxima for —OH group and exomethylene group vibrations. The PMR spectrum of myliol contains overlapping multiplets of three protons in the 0·2–0·6 p.p.m. region, singlets of three tertiary methyl groups at 0·93 (3 H) and 1·06 p.p.m. (6 H), a one-proton multiplet at 4·73 p.p.m., and two doublets at 5·04 (J = 2·8 Hz) and 5·14 p.p.m. (J = 2·4 Hz). The assignment of the most upfield multiplets to the cyclopropane protons is obvious. In view of the presence of a single O atom in the molecule the multiplet at 4·73 p.p.m. may be considered as due to a proton of the OCH type. This assignment is confirmed by the greater width of this multiplet in the spectrum measured in hexadeuteriodimethyl sulfoxide and to its narrowing after the addition of CD_3COOD. The signals at 5·04 and 5·14 p.p.m. belong to two olefinic protons. The coupling of both these protons with the proton of the OCH type was proved by double resonance experiments. The noise decoupled ^{13}C NMR spectrum contains only three singlets in the low-field region at 160·2, 105·9 and 80·1 p.p.m.; the remaining signals are located in the region of aliphatic and alicyclic carbon atoms. By off-resonance decoupling

* Part CCXXIII: This Journal *38*, 739 (1973).

** Components of Liverworts, Part IX:, Part VIII: Phytochemistry *12*, 211 (1973).

it was shown that the signal at 160·2 p.p.m. belongs to the quaternary carbon, the signal at 105·9 p.p.m. to the carbon carrying two hydrogen atoms, and the signal at 80·1 p.p.m. to the carbon atom with a single hydrogen; these data, together with the chemical shifts of these signals, lead to their assignment to the atoms of the $>C=$, $=CH_2$, and CH—O type. The absence of further signals in this region excludes the possibility of a tetrasubstituted double bond. From these facts it follows that in the molecule of myliol only one double bond is present – an exomethylene one, and that the additional deficit of hydrogen, following from the constitutional formula, is due to the presence of cycles in the molecule.

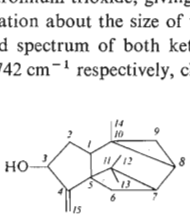
Having solved the nature of the double bond, it is now possible to interpret the decoupling experiments in the PMR spectra in favour of the localization of the secondary hydroxy group: it is in the allylic position to the exomethylene double bond. The PMR spectrum of acetyl derivative *II*, $C_{17}H_{24}O_2$ (M^+ 260) also agrees with these conclusions as it contains multiplets of three cyclopropane protons between 0·10 and 0·70 p.p.m., singlets of three tertiary methyl groups at 0·95 (3 H) and 0·99 p.p.m. (6 H), a singlet of the acetyl group at 2·06 p.p.m., a multiplet of the —CHO—C— proton at 5·68 p.p.m., and the signals of two exomethylene protons

at 5·06 p.p.m. (doublet, J = 1·3 Hz) and 5·09 p.p.m. (broad singlet). The existence of only one double bond in myliol is further confirmed by its hydrogenation by which two dihydro derivatives are formed both in ethanol and acetic acid, (*IIIa*, *IIIb*), of the composition $C_{15}H_{24}O$ (M^+ 220), which can be separated chromatographically owing to their differing polarity. In their IR spectra there remain[3] the absorptions of the hydroxy group, of the cyclopropane hydrogens at 3055 cm^{-1}, pointing to an unsubstituted methylene group, and of the geminal dimethyl group.

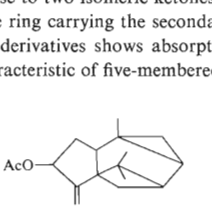
The PMR spectrum of the less polar dihydro derivative *IIIa* contains three signals of the three strongly coupled protons located in the 0·25–0·90 p.p.m., region, the singlets of the three tertiary methyl groups at 0·99, 1·01, and 1·28 p.p.m., a doublet of the secondary methyl group (J = 7·5 Hz) at 1·04 p.p.m., mutually overlapping multiplets of two protons in the 2·3 and 2·7 p.p.m. region, and a multiplet of the methine OCH proton (splittings 9 Hz, 9 Hz and 2·4 Hz). The proton on the carbon carrying the hydroxy group is coupled to both protons in the 2·3–2·7 p.p.m. multiplet; both coupling constants are equal to 9 Hz. An INDOR experiment proved that one of these protons is responsible for the 7·5 Hz splitting of the secondary methyl group signal. The second proton shows a 10 Hz coupling to the proton at 1·61 p.p.m. which is in turn coupled to the OCH proton (J = 2·4). The constant J = = 16 Hz may be considered as due to geminal coupling between the protons of the CH_2 group (confirmed by the PMR spectra of keto derivatives *IVa*, *IVb*); thus, the mentioned facts permit the formulation of the partial structure CH_3—CH—CH(OH)·.CH_2—. The multiplets of protons in the highest field, assigned to the cyclopropane

ring protons, do not change their shape on irradiation of the remaining part of the spectrum, which indicates that either there are no hydrogen atoms on the neighbouring carbons, or, if there are some, their vicinal couplings are small or of zero magnitude. The PMR spectrum of the more polar dihydroderivative *IIIB* has similar features: a three-proton system at 0·25–0·90 p.p.m., singlets of three tertiary methyl groups at 0·96 (6 H) and 1·04 p.p.m. (3 H), a doublet of the secondary methyl group at 1·08 p.p.m. (J = 6·8 Hz), a two-proton multiplet in the 2·0–2·4 p.p.m. region, and a multiplet of the OCH proton at 3·77 p.p.m. (splittings 8·5, 9, and 9 Hz).

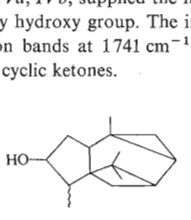
Oxidation of both dihydro derivatives *IIIa* and *IIIb* with a mixture of pyridine and chromium trioxide, giving rise to two isomeric ketones *IVa*, *IVb*, supplied the information about the size of the ring carrying the secondary hydroxy group. The infrared spectrum of both keto derivatives shows absorption bands at 1741 cm^{-1} and 1742 cm^{-1} respectively, characteristic of five-membered cyclic ketones.



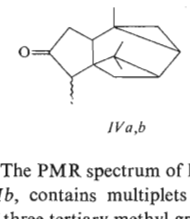
I



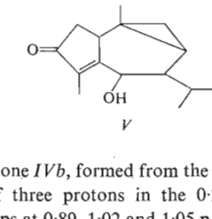
II



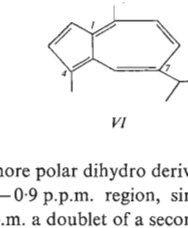
IIIa,b



IVa,b



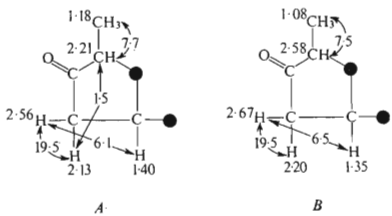
V



VI

The PMR spectrum of ketone *IVb*, formed from the more polar dihydro derivative *IIIb*, contains multiplets of three protons in the 0·2–0·9 p.p.m. region, singlets of three tertiary methyl groups at 0·89, 1·02 and 1·05 p.p.m. a doublet of a secondary methyl at 1·18 p.p.m. (J = 7·7 Hz), a doublet at 1·40 p.p.m. (J = 6·1 Hz), a doublet of doublets at 2·13 p.p.m. (J = 19·5 and 1·5 Hz), a doublet of doublets at 2·56 p.p.m. (J = 19·5 and 6·1 Hz) and a doublet of quartets at 2·21 p.p.m. (J = 7·7 and 1·5 Hz). The extreme value of the coupling constant[3] (J = 19·5 Hz) of the protons at 2·13 and 2·56 p.p.m. permits the assignment of these two signals to the geminal protons in a CH_2 group in the α-position to the carbonyl group. Since the keto group was formed from the alcoholic group located in the allylic position to the exomethylene double bond, the methine proton of the secondary methyl group is also vicinal to the carbonyl group. The coupling constant 1·5 Hz between this proton and one of the protons of the CH_2—CO— group (δ 2·13 p.p.m.) may also be considered as a through-carbonyl coupling. The interaction (J = 6·1 Hz) between the proton at 1·40 p.p.m.

and one of the —CH_2—CO— group protons may be interpreted most easily as a vicinal coupling. This is also supported by the weak, but detectable coupling of this proton to the second proton of this group. From the fact that both the methine proton of the secondary methyl group and the proton at 1·4 p.p.m. are coupled only to the protons of the CH_2—CO— group it may be inferred that the remaining atom of the five-membered ring is a quaternary one. The observed multiplicity of the methine proton signal at the five-membered ring junction (δ 1·40 p.p.m.) shows that the other carbon atom in its neighbourhood is quaternary as well (Scheme 1-*A*). The interpretation of the PMR spectrum of the second ketone *IVa* is similar. This spectrum contains signals of cyclopropane protons in the 0·2–0·9 p.p.m. region, singlets of three tertiary methyl groups at 0·89, 1·03, and 1·09 p.p.m., a doublet of a secondary methyl group at 1·15 p.p.m. (J = 7·5 Hz), a doublet at 1·35 p.p.m. (J = 6·5 Hz), a doublet at 2·20 p.p.m. (J = 19·5 Hz), a quartet at 2·58 p.p.m. (J = 7·5 Hz, detectable through-carbonyl coupling to the 2·20 p.p.m. proton), and a doublet of doublets at 2·67 p.p.m. (J = 19·5 and 6·5 Hz), see Scheme 1-*B*.



A *B*

SCHEME 1

In view of the proof of a single double bond and the presence of a cyclopropane ring in the molecule of myliol the molecular composition of this alcohol indicates a tetracyclic skeleton, very rare among sesquiterpenoids. According to a complex analysis of the IR and PMR spectra of myliol and its derivatives this alcohol is exceptional in structure among the tetracyclic skeletal systems described up to the present time. For the determination of the magnitude of the two remaining rings in the molecule of myliol and for the general skeletal arrangement its selenium dehydrogenation was very informative. As the sole product S-guaiazulene was isolated in a very good yield.

Hence, the structure of myliol should be derived from the guaiane skeleton. The arrangement of the substituents on the five-membered ring of this skeleton was already determined above. Further rings may be formed only by a suitable connection of the remaining carbon atoms. One of these rings must be three-membered

and should contain a methylene and a methine group. The tertiary methyl group is bound to the $C_{(10)}$ of the guaiane skeleton which should be quaternary, in agreement with the above mentioned inferences. This means that at this position one of the as yet unidentified rings should be fused. A cyclopropane ring of the required properties may be formed only by connecting the atoms $C_{(8)}$ and $C_{(10)}$. The formation of the isopropyl group may be explained only by the rupture of the bond from going from the $C_{(11)}$-atom which in myliol and its derivatives carries a geminal dimethyl group. As the isopropyl group in the guaiane skeleton is bound to $C_{(7)}$, the only remaining alternative for the formation of the last ring is the connection of the $C_{(11)}$ and $C_{(5)}$ atoms, the latter of which should be quaternary. The resulting structure of myliol is expressed by formula *I*.

The structure of the conjugated hydroxy ketone *V* can also be explained on the basis of structure (*I*); the latter was isolated in low yield as a side product of the oxidation of the less polar dihydro derivative *IIIa*. Its composition is $C_{15}H_{22}O_2$ (M^+ 234). The IR spectrum of this compound displays the characteristic bands of a conjugated carbonyl group, of a CH_2 group in α-position to a carbonyl, of a hydroxyl group and a double bond. Its PMR spectrum contains signals in the 0·6—0·85 p.p.m. region, a doublet at 1·01 p.p.m. (J = 6·6 Hz, 6 H), a singlet of a tertiary group at 1·25 p.p.m. a three-proton doublet (J = 2·1 Hz) at 1·74 p.p.m., and a single-proton multiplet at 3·38 p.p.m.. In view of the band of the OH group in the IR spectrum and of the presence of two oxygen atoms in the molecule, the multiplet at 3·38 p.p.m. may be assigned to the methine proton on the carbon carrying the secondary hydroxy group. The coupling of this proton to the doublet at 1·74 p.p.m., assigned to the olefinic methyl was demonstrated by double resonance. The signals in the 0·6—0·85 p.p.m. region indicate that the cyclopropane ring remained preserved, while the six-proton doublet at 1·01 p.p.m. may be interpreted as a signal of isopropyl methyls. In view of the structure of myliol the structure expressed by formula *V* may be assigned to this compound.

EXPERIMENTAL

The melting points were determined on a Kofler block. The IR spectra were measured in tetrachloromethane by means of a Zeiss UR 10 spectrophotometer. The UV spectra were taken on a CF 4 apparatus (Optica, Milano). The mass spectra were measured on a MS 902 spectrometer. The NMR spectra were recorded with a Varian HA-100 spectrometer. Silica gel for column chromatography was prepared according to Pitra and Štěrba[4], and, unless stated otherwise, it was deactivated by the addition of 10% of water.

Myliol (*I*)

Myliol was isolated[1] from the n-pentane extract of the liverwort *M. taylorii* (HOOK.) GRAY. After crystallisation from n-pentane it had m.p. 110—111°C and a molecular weight 218 (by mass spectrometry). IR spectrum: OH 3510 cm^{-1}; $CH_2{=}C\lesssim$ 896, 1651, 3060 cm^{-1}, possibly also cyclopropane under the frequencies of $CH_2{=}C\lesssim$; UV spectrum: λ_{max_1} 220 nm (log ε 3·70); λ_{max_2} 275—280 nm (log ε 2·43—2·44). For $C_{15}H_{22}O$ (218·3) calculated: 82·51% C, 10·16% H, 0·49% H act.; found: 82·40% C, 9·95% H, 0·49% H act.

Acetyl derivative II: To a solution of myliol (0·1 g) in pyridine (20 ml) acetic anhydride (20 ml) was added dropwise and the mixture allowed to stand at room temperature overnight. The oily product isolated in the conventional manner was filtered through a small column of inactive, neutral alumina, yielding a product of mol. weight 260 (mass spectrometry). IR spectrum: CH_3.

.COO 1738, 1248 cm^{-1}; CH_2=C< 896, 1651, 3060 cm^{-1}. For $C_{17}H_{24}O_2$ (260·3) calculated: 78·42% C, 9·29% H; found: 78·22% C, 9·15% H.

Dihydro derivatives IIIa, IIIb: A solution of myliol (1·20 g) in ethanol (20 ml) or in acetic acid (20 ml) was hydrogenated in the presence of a platinum catalyst (0·30 g). The hydrogenation ceased when the amount of absorbed hydrogen corresponded to the saturation of one double bond. The product, isolated in the conventional manner weighed 1·10 g and on a silica gel thin-layer plate it gave two spots (*IIIa* — R_F 0·15; *IIIb* — R_F 0·29). The mixture of dihydro derivatives was separated chromatographically on a 100-fold amount of silica gel. The combined chromatographic fractions eluted from the column with benzene were evaporated and crystallised from benzene. Pure dihydro derivative *IIIa* had m.p. 77—78°C and mol. weight 220 (mass spectrometry). IR spectrum: OH 3620 cm^{-1}; C—O 993, 1010, and 1018 cm^{-1}; cyclopropane 3050 cm^{-1}; gem. dimethyl 1374, 1387 cm^{-1}; UV spectrum: λ_{max_1} 210 nm (log ε 2·81); λ_{max_2} 245 to 250 nm (log ε 1·80); for $C_{15}H_{24}O$ (220·3) calculated: 81·76% C, 10·98% H, 0·54% H act.; found: 81·76% C, 10·92% H, 0·50% H act. As the more polar product dihydro derivative *IIIb* (0·55) was eluted. It crystallised from n-pentane, giving a product of m.p. 81—84°C and a mol. weight 220 (mass spectrometry). IR spectrum: OH 3610 cm^{-1}; C—O 1013 and 1037 cm^{-1}; cyclopropane 3055 cm^{-1}; gem. dimethyl 1377, 1386 cm^{-1}; UV spectrum: λ_{max_1} 210 nm (log ε 3·12); λ_{max_2} 240—252 nm (log ε 2·27); for $C_{15}H_{24}O$ (220·3) calculated: 81·76% C, 10·98% H, 0·45% H act.; found: 81·69% C, 10·97% H, 0·49% H act.

Dihydromylione *IVa*

To a solution of dihydromyliol *IIIa* (0·40 g) in pyridine (10 ml) a solution of chromium trioxide (0·23 g) in pyridine (2 ml) was added dropwise and the mixture allowed to stand at room temperature overnight. The product of oxidation (0·32 g), isolated in the conventional manner, was distilled in a Hickmann flask at 90—110°C (bath temp.) and 0·01 Torr. On a thin-layer chromatogram (silica gel), developed in benzene–ether 9 : 1, the product contained in addition to the expected dihydro derivative *IVa* (R_F 0·88) also another component (R_F 0·38) which displayed in its IR spectrum a frequency characteristic of a conjugated ketone (1661 cm^{-1}). On chromatography on a hundred-fold amount of silica gel both components were separated. Dihydro derivative *IVa* had the following frequencies in its IR spectrum: a ketone carbonyl group in a five-membered ring at 1741 cm^{-1}; CH_2 in α-position to the carbonyl at 1414 cm^{-1}; cyclopropane 3055 cm^{-1}. For $C_{15}H_{22}O$ (218·3) calculated: 82·51% C, 10·16% H; found: 82·33% C, 10·56% H. The second component (0·015 g) was the ketone *V* which after crystallisation from light petroleum had m.p. 98—100°C and mol. weight 234 (mass spectrometry). IR spectrum (KBr pellet): conjugated ketone carbonyl 1661 cm^{-1}; CH_2 in α-position to the carbonyl 1412 cm^{-1}; C=C 1604 cm^{-1}; OH 3265 cm^{-1}; UV spectrum: λ_{max} 263 nm (log ε 2·63).

Dihydromylione *IVb*

From dihydromyliol *IIIb* (0·55 g) keto derivative *IVb* (0·40 g) was prepared by the method described for the isomer *IIIa*. Its mol.weight was 218 (mass spectrometry). IR spectrum: ketone carbonyl in a five-membered ring 1742 cm^{-1}; CH_2 in α-position to the carbonyl 1411 cm^{-1}; cyclopropane 3055 cm^{-1}; UV spectrum: λ_{max} 265 nm (log ε 2·73). For $C_{15}H_{22}O$ (218·3) calculated: 82·51% C, 10·16% H; found: 82·63% C, 10·30% H.

S-Guaiazulene (*VI*)

A mixture of myliol (0·1 g) and an equal amount of selenium was heated at 280°C for 5 minutes. After cooling the azulene formed was extracted with light petroleum and the solution filtered

through a small column of alkaline alumina (act. II). After evaporation of the solvent and addition of trinitrobenzene an addition compound of the azulene was prepared, m.p. 147·5°C, which melted undepressed with an authentic specimen of S-guaiazulene trinitrobenzenate.

For the identification of the plant material we thank Dr J. Váňa, Department of Botany, Charles University, Prague. The infrared spectra were measured by Mrs K. Matoušková and interpreted by Dr S. Vašíčková. The ultraviolet spectra were measured by Mr P. Formánek. The microanalyses were carried out in the Analytical Laboratory of this Institute by Mrs V. Rusová and Mrs M. Kabelíková under the direction of Dr J. Horáček. The mass spectra were measured and interpreted by Dr L. Dolejš. Technical assistance was provided by Miss K. Verešová. We express our gratitude to all those mentioned.

REFERENCES

1. Benešová V., Hoang Minh Châu, Herout V.: Phytochemistry, in press.
2. Benešová V., Sedmera P., Herout V., Šorm F.: Tetrahedron Letters *1971*, 2679.
3. Cahill R., Cookson R. C., Crabb T. A.: Tetrahedron *25*, 4711 (1969).
4. Pitra J., Štěrba J.: Chem. listy *56*, 544 (1962).

Translated by Ž. Procházka.