# ON TERPENES. CCXXVIII.*

# THE STRUCTURE OF THE SESQUITERPENIC LACTONE SILEROLIDE

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For silerolide the structure expressed by the alternative formulae *IIa* and *IIb* has been proposed, mainly on the basis of its chemical correlation with laserolide (*IV*).

Many years ago we investigated the sesquiterpenic lactones present in the roots and the rhizomes of *Laserpitium siler* L. ssp. *siler* of Bulgarian origin. We isolated two sesquiterpenic lactones and we gave the crystalline one the name montanolide (*I*). Some years ago we described its structure[1]. The second lactone the non-crystalline one – to which we gave the name silerolide (*II*) was obtained in a relatively low yield which sufficed at that time only for a few transformations and did not allow us to deduce its structure. In the mentioned communication[1] we only described the isolation of silerolide (*II*), the preparation of its crystalline derivative tetrahydrosilerolide *III*, the IR spectra of both *II* and *III* and the mass spectra of *III*. We were unable to procure additional plant material from which silerolide (*II*) could be isolated again. In spite of these difficulties we were able to elucidate recently the structure of silerolide on the basis of previously prepared substances by chemical correlation with lasolide[2] (*IV*) which we isolated from the roots of *Laser trilobum* (L). BORKH. and the structure of which we determined recently[2].

We observed that the hydroxyketo lactone *V* prepared from lasolide[2] (*IV*) is according to PMR and IR spectra and mixture melting point identical with the compound which we obtained by saponification of tetrahydrosilerolide *III* and the oxidation of the formed lactonediol *VI* with chromium trioxide. From the mentioned facts it followed that silerolide (*II*) is based on selinane skeleton containing a γ-lactone group closed up at $C_{(6)}$, one esterified tertiary hydroxyl at $C_{(11)}$ and one esterified secondary hydroxy group at $C_{(1)}$. For the determination of the structure of silerolide (*II*) we still needed to determine the position of the skeletal double bond, the character

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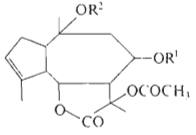
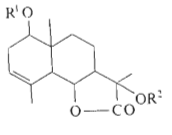
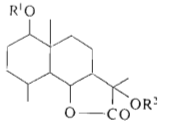
and the location of the acylating α,β-unsaturated $C_5$-acid residue. We deduced the position of the mentioned double bond from the PMR spectrum of lactonediol *VII* which was obtained on hydrolysis of silerolide (*II*). The PMR spectrum of substance *VII* (100 MHz, $CDCl_3$) indicated the presence of a methyl group on a trisubstituted double bond (C<u>H</u>=C(C,C): 5·32 p.p.m.; C<u>H</u>—C=CH: 1·86 p.p.m.; proved by decoupling experiments), which, in the case of the selinane skeleton of silerolide (*II*), proves unambiguously the position of the double bond between $C_{(3)}$ and $C_{(4)}$. We no longer had the native compound at our disposal for the measurement of the PMR spectrum, but the PMR spectrum of tetrahydrosilerolide *III* excluded the presence of α-methylbutyric and n-valeric acids. From this fact it followed that the α,β-unsaturated residue of the $C_5$-acid in silerolide is that of β-methylcrotonic (senecioic) acid. A further experiment which would lead to the determination of the positions of the ester groups could not be performed in view of the inaccessibility of the starting material. From the sum of all the mentioned data two alternative formulae, *IIa* and *IIb*, follow for the structure of silerolide.







*I*; $R^1 = CO.CH{=}C(CH_3)_2$, $R^2 = H$

*IIa*; $R^1 = CO.CH{=}C(CH_3)_2$, $R^2 = CO.CH_3$

*III*; $R^1$ } {$CO.CH_2.CH(CH_3)_2$, $R^2$ } {$CO.CH_3$

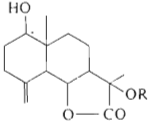
*X*; $R^1 = CO.C(CH_3){=}CH.CH_3$, $R^2 = H$

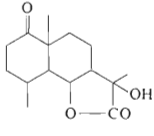
*IIb*; $R^1 = CO.CH_3$, $R^2 = CO.CH{=}C(CH_3)_2$

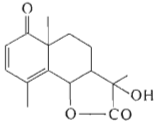
*VI*; $R^1 = R^2 = H$

*XI*; $R^1 = CO.C(CH_3){=}CH.CH_3$, $R^2 = CO.CH_3$

*VII*; $R^1 = R^2 = H$





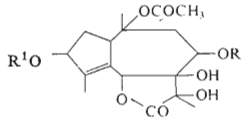


*IV*; R = $CO.C(CH_3){=}CH.CH_3$

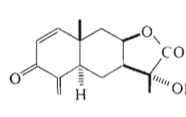
*V*

*VIII*

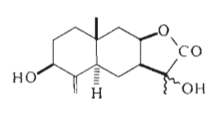
It is worth mentioning that on oxidation of lactone *VII* with chromium trioxide in pyridine we obtained lactone *VIII* the structure of which followed from its composition $C_{15}H_{18}O_4$ ($M^+$ 262), IR spectrum indicating the presence of a γ-lactone group (1 770 $cm^{-1}$), conjugated keto group (1 670 $cm^{-1}$) and a hydroxy group (3 450 and 3 600 $cm^{-1}$), and from the UV spectrum ($\lambda_{max}$ 271 nm, log ε 3·8; $\lambda_{max}$ 315 nm, log ε 3·0).




*IX*; $R^1$ = CO.CH($CH_3$).$CH_2$.$CH_3$
R = CO.C($CH_3$) = CH.$CH_3$




*XII*




*XIII*

According to its structure silerolide (*II*) is closely related to lasolide[2] (*IV*) which was isolated from the roots of *Laser trilobum* (L.) Borkh.[3] belonging to the same family (*Umbelliferae*) and the same tribe (*Laserpitineae*) as the parent species of silerolide (*II*). The close relationship of both mentioned species (*Laser trilobum* and *Laserpitium siler*) is further evidenced by the fact that trilobolide (*IX*) was found[3–5] in the roots of both species. *Laserpitium siler* of Bulgarian origin on one hand and of Slovenien origin on the other differ – if sesquiterpenic lactones in their roots are taken for comparison – in the fact that Bulgarian plants contain sesquiterpenic lactones esterified in addition to acetic acid with β-methylcrotonic acid (senecioic acid) exclusively [montanolide[1] (*I*), silerolide (*II*)], while the plants of Slovenian origin contain sesquiterpenic lactones esterified with acetic and α-methylisocrotonic (angelic) acids only [isomontanolide[6] (*X*), acetylisomontanolide[6] (*XI*), trilobolide[4,5] (*IX*)].

As regards native sesquiterpenic lactones of the selinane type, several ones were detected in the species of *Compositae* family, while in the species of *Umbelliferae* five selinanolides[7–10] were found up to now in addition to silerolide (*II*) and lasolide[2] (*IV*). Among the mentioned first group of selinanolides only farinosin[11,12] (*XII*) and hybrifarin[13] (*XIII*), and among the second only lasolide[2] (*IV*) and silerolide (*II*), contain an oxygen-containing substituent on $C_{(11)}$ of the selinanolide skeleton.

## EXPERIMENTAL

The melting points were determined on a Kofler block and were not corrected. Alumina for column chromatography was neutral, act. III. The IR spectra were measured in chloroform on a Unicam SP-200 spectrophotometer and the UV spectrum in ethanol on a FC 4 spectrophotometer (Optica, Milano). The PMR spectra were measured with a Varian HA 100 apparatus. Mass spectra were recorded on a MCH 1303 and AEI MS 902 spectrograph.

### Lactonediol *VI*

*a*) Tetrahydrosilerolide *III* (50 mg) in 3 ml of a 5% methanolic potassium hydroxide was allowed to stand at room temperature for 20 hours. The solvent was distilled off under reduced pressure and the residue acidified by 5% sulfuric acid and extracted with ether. The ethereal extract was worked up in the conventional manner, affording lactonediol *VI* (30 mg), m.p. 132–133°C (ethyl acetate–diisopropyl ether). For $C_{15}H_{24}O_4$ (268·3) calculated: 67·14% C, 9·02% H, 0·75% H act. (2); found: 67·33% C, 9·12% H, 0·82% H act.: IR spectrum: 3550, 3450 (hydroxyl), 1765 (γ-lactone), 1470, 1395, 1350, 1320, 1250, 1135, 1110, 1020, 1000, 990, 980, 925 $cm^{-1}$.

*b*) Unsaturated lactonediol *VII* (93 mg) in 8 ml acetic acid was mixed with 12·2 mg of $PtO_2$ and hydrogenated. Consumption was 14 ml of hydrogen (21·5°C, 730 Torr) which corresponds to 1·3 double bonds. The usual work-up gave lactonediol *VI* (70 mg) of m.p. 143—145°C which had an identical IR spectrum as, and melted undepressed with, the lactonediol *VI* prepared from tetrahydrosilerolide *III*. The difference in the melting points of lactonediol *VI* prepared from tetrahydrosilerolide *III* and that prepared from the unsaturated lactonediol *VII* are probably due to differing ratios of $C_{(4)}$-epimers.

Ketolactone *V*

Lactonediol *VI* (60 mg) was mixed with a suspension of 300 mg of chromium trioxide in 3 ml of pyridine and allowed to stand at room temperature for 20 hours. The mixture was diluted with water and extracted with ether. The combined ethereal extracts were worked up in the usual manner affording ketolactone *V* (40 mg), m.p. 210—211°C (benzene), For $C_{15}H_{22}O_4$ (266·3) calculated: 67·65% C, 8·33% H, 0·38% H act.; found: 67·76% C, 8·30% H, 0·46% H act. IR spectrum: 3550, 3450 (hydroxyl), 1770 (γ-lactone), 1705 (ketone), 1470, 1390, 1135, 1105, 1015, 970 $cm^{-1}$. Mixture melting point with ketolactone *V* prepared from lasolide[2] (*IV*) was undepressed.

Unsaturated Lactonediol *VII*

Silerolide (*II*; 700 mg) and 20 ml of a 5% methanolic potassium hydroxide were mixed and allowed to stand at room temperature for 16 hours. After a similar working up as mentioned for lactonediol *VI* unsaturated lactonediol *VII* (320 mg) was obtained, melting at 184—185°C (ethyl acetate). For $C_{15}H_{22}O_4$ (266·3) calculated: 67·65% C, 8·33% H, 0·78% H act. (2); found: 67·52% C, 8·17% H, 0·77% H act. IR spectrum: 3600, 3450 (hydroxyl), 1765 (γ-lactone), 1460, 1395, 1350, 1320, 1130, 1095, 1080, 1050, 1025, 1010, 980, 945, 920 $cm^{-1}$.

Ketolactone *VIII*

Unsaturated lactonediol *VII* (150 mg) was mixed with a suspension of 500 mg of chromium trioxide in 8 ml pyridine and allowed to stand at room temperature for 20 hours. The mixture was worked up as in the case of ketolactone *V*, affording ketolactone *VIII* (100 mg) of m.p. 215°C (diisopropyl ether). For $C_{15}H_{18}O_4$ (262·3) calculated: 68·69% C, 6·92% H, 0·38% H act.; found: 68·40% C, 7·23% H, 0·44% H act. IR spectrum: 3590, 3450 (hydroxyl), 1770 (γ-lactone), 1670 (conjugated ketone), 1735 (double bond), 1590, 1460, 1390, 1125, 1105, 1025, 990 $cm^{-1}$. UV spectrum: $\lambda_{max}$ 271 nm (log ε 3·8), $\lambda_{max}$ 315 (log ε 3·0).

*The elemental analyses were carried out in the analytical department of our Institute by Mrs V. Rusová, Mrs M. Kabelíková, Mrs E. Sýkorová and Mr V. Štěrba (head Dr J. Horáček). The IR spectra were measured by Mrs S. Holubová and the UV spectrum by Mr P. Formánek. The mass spectra were recorded by Dr A. Trka (head Dr L. Dolejš). We express our gratitude to all of them.*

REFERENCES

1. Holub M., Popa D. P., Samek Z., Herout V., Šorm F.: This Journal *35*, 3296 (1970).
2. Holub M., Samek Z.: This Journal *38*, 1428 (1973).
3. Holub M., De Groote R., Herout V., Šorm F.: This Journal *33*, 2911 (1968).
4. Holub M.: Unpublished results.
5. Holub M., Samek Z., De Groote R., Herout V., Šorm F.: This Journal *38*, 1551 (1973).
6. Holub M., Motl O., Samek Z., Herout V.: This Journal *37*, 1186 (1972).
7. Serkerov S. V.: Chim. Prir. Sojed. *1971*, 590.
8. Serkerov S. V.: Chim. Prir. Sojed. *1971*, 667.
9. Serkerov S. V.: Chim. Prir. Sojed. *1972*, 63.
10. Serkerov S. V.: Chim. Prir. Sojed. *1972*, 176.
11. Geissman T. A., Mukherjee R.: J. Org. Chem. *33*, 656 (1968).
12. Herz W., Subramanian P. S., Geissman T. A.: J. Org. Chem. *33*, 3743 (1968).
13. Bjeldanes L. F., Geissman T. A.: Phytochemistry *10*, 1079 (1971).

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