

**RELATIVE AND ABSOLUTE CONFIGURATION OF THE
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Received January 17th, 1975

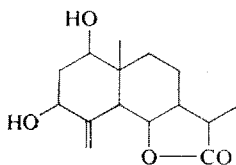
For erivanin, isolated now from *Tanacetum balsamita* L., the relative and the probable absolute configuration expressed by formula III has been derived on the basis mainly of ¹H-NMR spectroscopy and circular dichroism measurements.

In connection with a systematic study of sesquiterpenic lactones from *Compositae* we also investigated the species *Tanacetum balsamita* L. From the above-ground part of this plant we isolated substance I of the composition C₁₅H₂₂O₄. From the IR spectrum and a detailed analysis of the ¹H-NMR spectrum it followed that it is a sesquiterpenic dihydroxy lactone of the selinane type the structure of which may be expressed by formula I. Structure I was proposed earlier¹ for erivanin which was isolated from *Artemisia fragrans* WILLD. var. *erivanica* BESS. (*Compositae*). From the comparison of the melting points of substance I isolated by us and its diacetate with those of erivanin and its diacetate, and from the comparison of specific rotations and spectral data it follows that the substance I isolated by us is identical with erivanin.

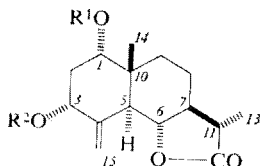
To our knowledge conclusions on the stereochemistry of its molecule were not described either in the original paper on erivanin¹ or in any subsequent publication. Therefore we studied this question and came to the conclusion that erivanin has the relative configuration represented by formula II. The relative stereostructure of erivanin follows directly from the observed distribution of the chemical shifts and the coupling constant values of erivanin and its derivatives III–V (Table I). On the basis of the comparison of these data with the well known ¹H-NMR data of selinanolides it may be supposed that the homocyclic-system is *trans*-annelated, that it possesses the steroidal chair conformation of both homocyclic rings, 1,3-diaxial configuration of the hydroxyl groups, and a *trans*-annelated γ -lactone ring.

* Part CCXL in the series on Terpenes; Part CCXXXIX: Arch. Pharm., in press.

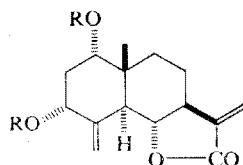
Hence, the relative configuration of erivanin corresponds to one of both 11,13-dihydro derivatives of ludovicin B (VI) (ref.²). Dihydro derivatives of ludovicin B have not yet been described, but the correspondence with erivanin follows from the PMR data for protons H_1 , H_3 , H_{14} , H_{15} and H_5 of both native substances, as well as of their diacetates II and VII (ref.²). For the methyl group on $C_{(11)}$ we propose the relative



I



- II, $R^1 = R^2 = H$
 III, $R^1 = R^2 = COCH_3$
 IV, $R^1 = R^2 = CONHCO.CCl_3$
 V, $R^1 = H$; $R^2 = COC_6H_5$



- VI, $R = H$
 VII, $R = COCH_3$

configuration α on the basis of the vicinal coupling constant $J_{11,13} = 6.6 \text{ Hz}$, cf.^{3,4} For the determination of the absolute configuration we tried to prepare 1-monobenzoate of erivanin, but we only isolated its 3-monobenzoate V which is not suitable for the application of the benzoate rule. The information on absolute configuration of the molecule of erivanin was obtained from the CD of the lactonic chromophore. The measured value, $\Delta\epsilon + 1.3$, suggests according to the sector rule,⁵ the *R*-configuration of the substituents on $C_{(11)}$ as probable. In this sense formula III would also express the absolute configuration of erivanin; hence the latter would belong to the usual series of selinanolides with the β -configuration of the $C_{(7)}-C_{(11)}$ bond.

Erivanin, which has been isolated so far from two species of *Compositae* of the *Anthemideae* tribe, corresponds in its structure of a lactone of selinanoline type (synonyms santanolide or eudesmanolide) to the assumptions expressed in several review articles^{6,7} on the importance of the presence of sesquiterpenic lactones in plants as a chemotaxonomic sign. This tribe is especially characteristic of the occurrence of this type of lactones; this is also evident, among other facts, from the frequent occurrence of the longest known substance of this type – santonin. Guaianolides can be expected less frequently in this tribe. The only exception to this assumption is still the presence of the cadinanolide arteannuin from *Artemisia annua* L.,⁸ which is unique among sesquiterpenic lactones.

TABLE I
Characteristic Parameters of the $^1\text{H-NMR}$ Spectra

Compound ^a	H ₁	H ₃	H ₅	H ₆	H ₁₃	H ₁₄	H ₁₅	H _{15'}
<i>I</i> ^{b,c,d}	3.36 $J_{1,2} \cong J_{1,2'} \cong 3 J_{3,2}$	4.39 ^{e,f} $J_{3,2'} = J_{3,2} = 2.8$	3.01 $J_{5,6} = 11.0$	4.05 $J_{6,5} = 10.7$ $J_{6,7} = 9.7$	1.23 (6.7)	0.80	5.16 ^e $J_{15,5} = 1.2$ $J_{15',5} = 1.8$ $2J = 1.0$	5.01 ^e $J_{15',5} = 1.8$ $2J = 1.0$
<i>II</i> ^{g,h}	3.41	4.45	3.30 $J_{5,6} = 11.0$	4.05 $J_{6,5} \cong 10.5$ $J_{6,7} \cong 10.5$	1.09 (6.8)	0.69	5.05 $\sum J = 1.4$	4.98 $\sum J = 1.6$
<i>III</i> ^{b,c,i}	4.59 $J_{1,2} \cong J_{1,2'} \cong 3$	5.38 ^j	3.01 $J_{5,6} = 11.0$	4.01 $J_{6,5} = 11.0$ $J_{6,7} = 9.6$	1.25 (6.5)	0.96	5.34 ^k	5.26 ^l
<i>IV</i> ^{b,c,m}	4.91 $J_{1,2} \cong J_{1,2'} \cong 3 J_{3,2} \cong 3$	5.58 $J_{3,2'} \cong 3$	2.96 $J_{5,6} = 11$	4.03 $\sum J = 21$	1.24 (6.5)	0.99	5.47 ^k	5.26 ^l
<i>V</i> ^{b,c,n}	3.45	5.75	3.00 $J_{5,6} = 11$	4.03 $\sum J = 21$	1.24 (6.5)	0.88	5.40 ^k	5.20 ^l

^a First-order data, chemical shifts in δ scale, splittings in Hz (in parentheses if not otherwise stated); measured on Varian HA-100 (compounds *III*, *IV*) and on a prototype of Czechoslovak 80 Mc (compounds *II*, *V*) instrument. ^b In deuteriochloroform. ^c Internal standard tetramethylsilane. ^d $\text{H}_2 \sim 2.11$ ($J_{2,2'} \cong 15$, $J_{2,1} = J_{2,3} = 2.6$); $\text{H}_2' \sim 1.92$ ($J_{2,2'} \cong 15$, $J_{2,1} = J_{2,3} = 3.0$); $\text{H}_7 \sim 1.65$; $\text{H}_{11} \sim 2.30$. ^e $J_{3,15} \gg \gg J_{3,15'}$. ^f $J_{1,3} \neq 0$. ^g In pentadeuteriopyridine; internal standard hexamethyldisiloxane; δ (HMDSb) = 0.06. ^h H_2 2.20 ($J_{2,2'} = 15$, $J_{2,1} = J_{2,3} = 2.5$); H_2' 1.89 ($J_{2,2'} = 15$, $J_{2,1} = J_{2,3} = 3.0$); $\text{H}_7 \sim 1.55$, $\text{H}_{11} \sim 2.31$; 1-OH: 5.42 ($J = 8.5$). ⁱ CH_3CO 2.00; 2.10. ^j Partly overlapping with signal of $\text{H}_{15'}$. ^k Broadened singlet. ^l Broadened doublet. ^m H_2 , $\text{H}_2' \sim 2.29$; $\text{H}_{11} \sim 2.29$; NH 9.10; 8.73. ⁿ Poorly resolved spectrum.

EXPERIMENTAL

Isolation of Erivanin (*III*)

The above-ground part of *Tanacetum balsamita* L. (3.5 kg) was worked up as described earlier^{9,10} and a lactone fraction (3.8 g) was obtained which was chromatographed on a silica gel column (200 g). Elution with chloroform-acetone (9:1) gave a mixture from which erivanin (*III*) was isolated by fractional crystallization, m.p. 203–204°C, $[\alpha]_D^{20} +98.1^\circ$ (*c* 0.053; methanol). IR (in chloroform; cm^{-1}): 3600, 3510 (hydroxyl), 1770 (γ -lactone), 1645 (double bond). Mass: 278 (M^+). CD (methanol): $\Delta\epsilon_{218} +1.3$. For $\text{C}_{15}\text{H}_{22}\text{O}_4$ (266.3) found: 67.76% C, 8.37% H, 0.68% H act.; calculated: 67.65% C, 8.33% H, 0.86% H act.

Erivanin 3-Monobenzoate (*V*)

4 drops of benzoyl chloride were added under stirring to a cooled solution of erivanin (40 mg) in 2 ml of pyridine and the mixture was allowed to stand at room temperature for 24 hours. After the usual working up a fraction was obtained (53 mg) from which 3-monobenzoate *V* was obtained by chromatography on silica gel in the form of a non-crystalline product, $[\alpha]_D^{20} +23.7^\circ$ (0.063; methanol). IR (in chloroform; cm^{-1}): 3595, 3535, 3435 (hydroxyl), 1770 (γ -lactone), 1658 (double bond), 1722, 1268 (benzoate). Mass: 370 (M^+), 352 (M-18), 265 (M-105), 248 (M-122), 122 ($\text{C}_6\text{H}_5\text{COOH}$), 105 ($\text{C}_6\text{H}_5\text{CO}^+$), 77 (C_6H_5^+). For $\text{C}_{22}\text{H}_{26}\text{O}_5$ (370.4) found: 71.22% C, 7.12% H, 0.36% H act.; calculated: 71.33% C, 7.07% H, 0.27% H act. CD (methanol): $\Delta\epsilon_{230} -5.8$.

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Translated by Ž. Procházka.