

## SPECIALIA

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### (+)- $\alpha$ -Selinene, and Enantiomeric Eudesmane from *Chiloscyphus polyanthus* (L.) Corda<sup>1</sup>

Recently a number of liverworts (Hepaticae) have been shown to elaborate unusual sesquiterpenes in high yield. Among these have been several representatives of novel skeletons; e.g. bazzanene<sup>2</sup>, myliol<sup>3</sup>, and the barbatenes<sup>4</sup>. Another feature is the occurrence of previously unknown enantiomers of sesquiterpenes common in higher plants<sup>5</sup>.

In light of these interesting findings, we have, in collaboration with Dr. S. HUNECK<sup>6</sup>, begun a systematic examination of the sesquiterpene constituents of the volatile extracts of liverworts. One of the first samples studied was the steam-distilled ether extract of *Chiloscyphus polyanthus* (L.) Corda prepared by Dr. HUNECK, in part due to a report of the isolation of chiloscyphone from this species. Chiloscyphone has been assigned structure I on the basis of ORD and NMR studies<sup>9</sup>.

**Materials and methods.** The plant sample was collected by Dr. S. HUNECK (Institut für Biochemie der Pflanzen der D.A.W., Weinberg) in Sachsen. Ether extraction of the ground air-dried material afforded a 0.77% yield of essential oil after steam distillation. The components of the oil were partially separated by chromatography on AgNO<sub>3</sub>-Al<sub>2</sub>O<sub>3</sub> using a cyclohexane-benzene gradient. The column chromatographic and subsequent preparative gas chromatographic purifications were monitored by analytical GC<sup>10</sup> on two stationary phases Apiezon-L (ApL) and Carbowax 20M (C-20M). The isolated compounds were examined by the usual spectral methods: NMR (60 and 100 MHz,  $\delta = 0.0$  for TMS), optical rotatory dispersion (ORD) (c, 0.2 pentane), IR (film), and CD (1–10 mM pentane). Samples for CD determination are filtered through Al<sub>2</sub>O<sub>3</sub> (Woelm, activity I, basic) using pentane just before use.

Comparison samples of  $\alpha$ -selinene were obtained from 2 sources: commercial oil of sweet flag (*Acorus calamus*) and the olefin mixture resulting from stirring 9 ml of

$\beta$ -selinene ( $[\alpha]_D = +32^\circ$ , from celery seed oil) with 3 ml of formic acid for 36 h. In each case, AgNO<sub>3</sub>-Al<sub>2</sub>O<sub>3</sub> chromatography gave fractions enriched in  $\alpha$ -selinene. Final purification was effected by preparative gas chromatography. A comparison sample of 5,10-*epi*- $\alpha$ -selinene<sup>11</sup> was the gift of Dr. KLEIN.

**Results and discussion.** The hydrocarbon portion of the essential oil showed at least 20 sesquiterpene components on gas chromatography. Of these, 5 were present in significant amounts. The retention data for these and some authentic samples are collected in Table I.

Thus far, only the compounds responsible for peaks Nos. 6, 11, and 14 have been isolated in pure state. Component No. 11 was confirmed as  $\beta$ -barbatene<sup>12</sup> from the correspondence of the NMR-, IR-, and CD-spectra<sup>4</sup>. Component No. 6 is a novel tricyclic sesquiterpene. The NMR-spectrum [5.02 (1-vinyl-H), 2.03 (3 allylic-H), and 0.85–1.06 ppm (4 CH<sub>3</sub> signals)] was different from those of the known substances otherwise fitting the spectrum.

Component No. 14 was tentatively identified as  $\alpha$ -selinene by direct NMR- and GC-comparison of the dienes and their hydrogenation products. However a comparison of the observed rotation data with that of authentic  $\alpha$ -selinene samples was hampered by the low and un-reproducible rotation values obtained for different authentic  $\alpha$ -selinene samples. This, together with the

Table I. Retention indices<sup>10</sup> of *Chiloscyphus polyanthus* sesquiterpenes

peak No.	Oil (%)	ApL $\delta$ 190°	$\delta$ 155°	C-20M $\delta$ 150°
2	4	1424	1407	
6	7	1479.5	1454	1613
9	5	1518	1498	1700.5
11	16	1535.5	1503	1690.5
14	48	1559	1536.5	1751.5
$\beta$ -barbatene		1534.5	1502.5	1689.5
$\alpha$ -selinene (II)		1557.5	1535	1753
5,10- <i>epi</i> -selinene (III)			1581	

<sup>1</sup> This work has been supported, in part, by a National Institutes of Health grant No. GM-18143.

<sup>2</sup> S. HAYASHI and A. MATSUO, *Experientia* 25, 1139 (1969). – A. MATSUO, *Tetrahedron* 27, 2757 (1971).

<sup>3</sup> V. BENESOVA, P. SEDMERA, V. HEROUT and F. SORM, *Tetrahedron Lett.* 1971, 2679.

<sup>4</sup> N. H. ANDERSEN, C. R. COSTIN, C. M. KRAMER, Y. OHTA and S. HUNECK, *Phytochemistry*, submitted for publication.

<sup>5</sup> *Frullania dilatata* produces an enantiomeric santonin-related lactone<sup>7</sup>; *Scapania* species produce (–)-longifolene<sup>8</sup>.

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<sup>7</sup> H. KNOCH, G. OURISSON, G. W. PEROLD, J. FOUSSEREAU and J. MALEVILLE, *Science* 166, 239 (1969).

<sup>8</sup> S. HUNECK and E. KLEIN, *Phytochem.* 6, 383 (1967).

<sup>9</sup> S. HAYASHI, A. MATSUO and T. MATSUURA, *Tetrahedron Lett.* 1969, 1599; A. MATSUO and S. HAYASHI, 1970, 1289. – A. MATSUO, *Tetrahedron* 28, 1203 (1972).

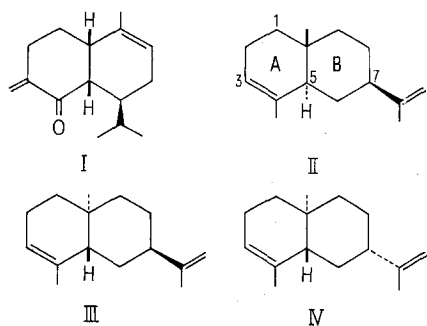
<sup>10</sup> N. H. ANDERSEN and M. S. FALCONE, *J. Chromatog.* 44, 52 (1969).

<sup>11</sup> E. KLEIN and W. ROJAN, *Tetrahedron Lett.* 1970, 279.

<sup>12</sup>  $\beta$ -Barbatene, a novel tricyclic sesquiterpene common to liverworts that is presently under investigation, was first found in *Barbilioxiphzia* species<sup>4</sup>, and has now been found in *Scapania undulata* and *Bazzania trilobata* (N. H. ANDERSEN and S. HUNECK, *Phytochemistry* 12, in press), see note <sup>3</sup>.

Table II. Spectral data for various  $\alpha$ -selinenes

	NMR data ( $\delta$ )			ORD		
$\alpha$ -selinene	10-CH <sub>3</sub>	=C-CH <sub>3</sub>	=C-H	$[\alpha]_D$	$[\alpha]_{300}$	Trend
from $\beta$ -selinene	0.79 <sup>2</sup>	1.57 1.71	4.67 5.28	-16°	-71°	-ve
from <i>Acorus calamus</i>	0.80 <sup>7</sup>	1.58 1.73	4.66 5.26	+6°	-60°	-ve
<i>Ch. polyanthus</i> No. 14	0.80	1.57 1.72	4.65 5.25	+7.8°	+74°	+ve
5,10- <i>epi</i> - $\alpha$ -selinene	0.84	1.58 1.72	4.84 5.26	+2.1°		?

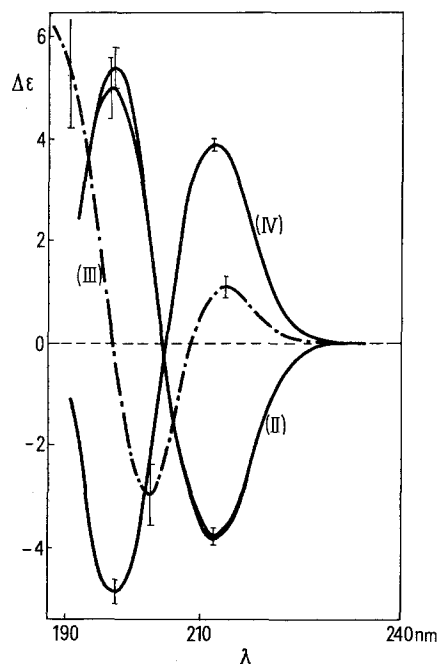


report that 10-*epi*-selinenes afford eudesmane on hydrogenation<sup>13</sup>, apparently via epimerization at C-7 prior to reduction, suggested that component No. 14 is 5,10-*epi*- $\alpha$ -selinene (III) or the enantiomer of  $\alpha$ -selinene (IV). In order to allow a definitive assignment we obtained authentic 5,10-*epi*- $\alpha$ -selinene<sup>11</sup> for direct comparison. The NMR spectral characteristics and rotation data are collected in Table II. The epimeric selinenes proved to be

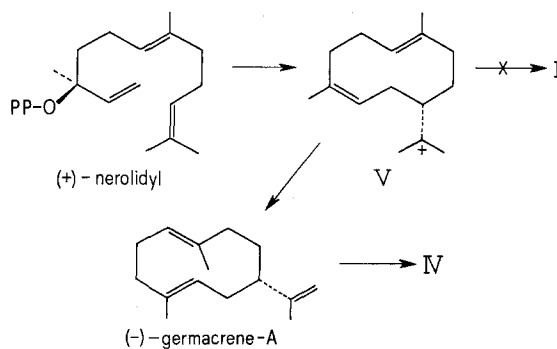
distinguishable by NMR-spectroscopy, lending further support for assigning structure IV to the selinene from *Chiloscyphus*.

The only acceptable proof of enantiomeric relationship is chiroptical spectra that display reflection symmetry about zero. Clearly the ORD data, particularly in the vicinity of the sodium D-line do not allow such a conclusion. Over the past 5 years, we have encountered many cases of this sort in sesquiterpene structure elucidation, i.e. cases in which minor impurities (< 3%) drastically alter  $[\alpha]_D$  values. For this reason we now rely on circular dichroism in the 240–185 nm energy span for characterizing chiral olefins from natural sources<sup>14</sup>.

The CD-spectra of the selinenes encountered in this study are reproduced in the Figure. The two  $\alpha$ -selinene (II) samples gave identical traces within experimental error, even though they had  $[\alpha]_D$  values of opposite sign. The enantiomeric nature of  $\alpha$ -selinene from the liverwort oil (IV) is established beyond doubt by its CD spectrum. In this case the 2 cotton effects observed are due to the  $\Delta^3$  olefinic bond<sup>15</sup>; the signs are determined by the skew sense of ring A<sup>16</sup>. It is worth noting that the CD-spectrum of the epimeric selinene (III) is distinctly different, reflecting conformational transmission of the strain associated with the axial isopropenyl group at C-7.



CD-spectra of authentic  $\alpha$ -selinene (II),  $\alpha$ -selinene ex *Chiloscyphus polyanthus* (IV), and authentic 5,10-*epi*- $\alpha$ -selinene (III).



<sup>13</sup> H. SULSER, J. R. SCHERER and K. L. STEVENS, *J. org. Chem.* **36**, 2422 (1971).

<sup>14</sup> N. H. ANDERSEN, C. R. COSTIN, D. D. SYRDAL and D. P. SVEDBERG, *J. Am. chem. Soc.*, **95**, 2049 (1973).

<sup>15</sup> The spectra are not drastically altered by selective hydrogenation of the isopropenyl double bond.

<sup>16</sup> See ref. <sup>14</sup> for a discussion of the relationship between local symmetry and CD sign for olefinic bonds.

Selinene IV is the first enantiomeric selinene isolated from a plant source<sup>17</sup>, and the third case of liverworts yielding previously unknown enantiomers of sesquiterpenes common in higher plants<sup>5</sup>. This contrasts to the nearly universal presence of 7 $\beta$ -isopropyl groups in higher plant products<sup>18</sup>. Further studies of the more primitive plants should thus reveal the phylogeny of vascular plants and the point in evolution at which this exceptional consistency in absolute configuration<sup>18</sup> developed.

<sup>17</sup> (-)-Germacrene-A and some related selinenes have however been isolated from marine invertebrates: A. J. WEINHEIMER, W. W. YOUNGBLOOD, P. H. WASHECHECK, T. K. B. KARNS and L. S. CIERESZKO, *Tetrahedron Lett.* 1970, 497.

<sup>18</sup> N. H. ANDERSEN, *Phytochemistry* 9, 145 (1970).

<sup>19</sup> N. H. ANDERSEN and D. D. SYRDAL, *Tetrahedron Lett.* 1972, 2455. See ref. <sup>18</sup> and also N. H. ANDERSEN and D. D. SYRDAL, *Tetrahedron Lett.* 1970, 2277.

Assuming the applicability of the framework of biogenetic conjecture for higher plants<sup>19</sup> (as seems likely due to the general similarities between liverwort and e.g. conifer sesquiterpene oils) the following can be proposed: Clearly intermediate V cannot yield cadalane structure I, the structure proposed for chiloscypnone, suggesting the need for further studies on the configuration of that substance.

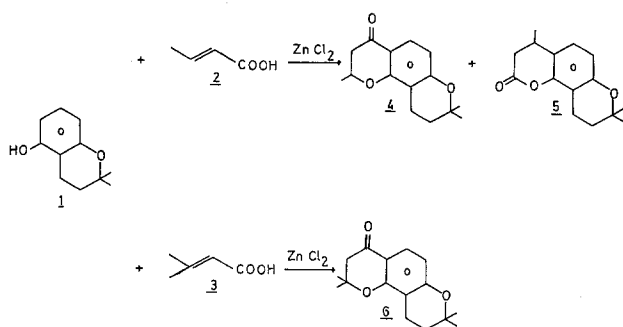
*Zusammenfassung.* Nachweis des optischen Isomeren eines Sesquiterpens im Lebermoos *Chiloscyphus polyanthus* mit (+)- $\alpha$ -Selinen als Hauptanteil.

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## Synthesis of Chromanones from 5-Hydroxy-2,2-Dimethylchroman and $\alpha,\beta$ -Unsaturated Acids

The acid-catalysed condensation of polyphenols with  $\alpha,\beta$ -unsaturated acids is a valuable synthetic method for the preparation of 4-chromanones<sup>1,2</sup>. During studies aimed at the synthesis of rotenoids, we investigated the reaction of 5-hydroxy-2,2-dimethylchroman<sup>3</sup> with  $\alpha,\beta$ -unsaturated acids in the presence of Friedel-Craft catalysts. 5-Hydroxy-2,2-dimethylchroman (**1**) reacted with crotonic acid (**2**) in the presence of zinc chloride to yield a mixture of two products, 9,10-dihydro-2,8,8-trimethyl-8H-[1]pyrano[2,3-h]chroman-4-one (**4**) and 9,10-dihydro-4,8,8-trimethyl-8H-[1]pyrano[2,3-h]chroman-2-one (**5**) separated by column chromatography. Reaction of the phenol **1** with  $\beta,\beta$ -dimethylacrylic acid (**3**) afforded only the chroman-4-one compound 9,10-dihydro-2,2,8,8-tetramethyl-8H-[1]pyrano[2,3-h]chroman-4-one (**6**).



Distinction between 2-chromanones and 4-chromanones can be made by IR. The carbonyl frequency falls in the range of 1760–1740  $\text{cm}^{-1}$  (lactone) for 2-chromanones, while lower frequencies arise in the 4-chromanones by the effect of conjugation (1680–1650  $\text{cm}^{-1}$ ). The NMR-spectra showed sharp signals for each gem-dimethyl group in **4**, **5** and **6**. The methylene and methine protons of the chromanon ring appeared as an ABX pattern for compound **4** and as an ABC pattern for compound **5**. One of the aromatic protons of **4** and **6** exhibited a large deshielding effect of  $\pm 0.8$  ppm by the anisotropy of the carbonyl function. The most prominent peak in the mass spectrum of **5** arose from a retro-Diels-Alder reaction with

hydrogen shift in the pyrano ring ( $m/e$  191). Another retro-Diels-Alder fragmentation occurred in the chromanon ring affording an ion ( $m/e$  204) of moderately large relative intensity, followed by another retro-Diels-Alder fragmentation ( $m/e$  149 and 148). The minor pathway involved loss from  $M^+$  of a methyl radical and the consecutive expulsions of methyl radicals and CO or vice versa from the ion  $m/e$  204.

Compound **4**:  $\nu_{\text{max}}$  (KBr) 1675 (CO); 1600, 1440 and 815  $\text{cm}^{-1}$  (aromatic)  $\delta$  ( $\text{CCl}_4$ ) 1.31 (3H, s,  $\text{CH}_3$ ); 1.32 (3H, s,  $\text{CH}_3$ ); 1.49 (3H, d, J 6.0 cps,  $\text{CH}_3$ ); 1.75 (2H, t, J 7.2 cps,  $\text{CH}_2$ ); 2.45 (1H, dxd, J 14 cps, J 7 cps, CH); 2.61 (2H, t, J 7.2 cps,  $\text{CH}_2$ ); 4.3–4.6 (1H, m, CH); 6.34 (1H, d, J 9 cps, Ar-H); 7.56 (1H, d, J 9 cps, Ar-H).  $m/e$  246(68) 231(10) 191(100) 149(45) 148(15).

Compound **5**:  $\nu_{\text{max}}$  (KBr) 1760 (CO); 1620, 1440, 830 (aromatic)  $\delta$  ( $\text{CCl}_4$ ) 1.29 (3H, d, J 6 cps,  $\text{CH}_3$ ); 1.32 (6H, s,  $2 \times \text{CH}_3$ ); 1.76 (2H, t, J 7 cps,  $\text{CH}_2$ ); 2.3–2.6 (2H, m,  $\text{CH}_2$ ); 2.76 (2H, t, J 7 cps,  $\text{CH}_2$ ); 2.9–3.1 (1H, m, CH); 6.42 (1H, d, J 8.1 cps, Ar-H); 6.82 (1H, d, J 8.1 cps, Ar-H);  $m/e$  246(51) 231(50) 204(22) 191(100) 190(30) 175(25) 161(23) 149(75) 148(19).

Compound **6**:  $\nu_{\text{max}}$  (KBr) 1675 (CO); 1595, 1580, 815  $\text{cm}^{-1}$  (aromatic)  $\delta$  ( $\text{CCl}_4$ ) 1.33 (6H, s,  $2 \times \text{CH}_3$ ); 1.44 (6H, s,  $2 \times \text{CH}_3$ ); 1.76 (2H, t, J 6.1 cps,  $\text{CH}_2$ ); 2.52 (2H, s,  $\text{CH}_2$ ); 2.59 (2H, t, J 6.1 cps,  $\text{CH}_2$ ); 6.30 (1H, d, J 9 cps, Ar-H); 7.52 (1H, d, J 9 cps, Ar-H);  $m/e$  260(100) 245(85) 204(30) 189(34) 176(24) 149(64).

*Zusammenfassung.* Die Synthese von 2- und 4-Chromanonen aus 5-Hydroxy-2,2-dimethylchroman und Crotonsäure oder  $\beta,\beta$ -Dimethylacrylsäure wird beschrieben.

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<sup>1</sup> M. MIYANO and M. MATSUI, *Chem. Ber.* 91, 397 (1958).

<sup>2</sup> A. S. R. ANJANEYULI, *Current Sci.* 37, 513 (1969).

<sup>3</sup> R. VERHÉ, PhD Thesis, State University of Ghent 1972.