

## ON TERPENES. CCXXI.\*

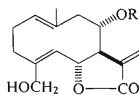
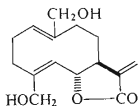
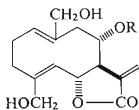
THE STRUCTURE OF ALATOLIDE, A SESQUITERPENIC LACTONE  
FROM *Jurinea alata* CASS.B.DROŽDŽ<sup>a</sup>, Z.SAMEK<sup>b</sup>, M.HOLUB<sup>b</sup> and V.HEROUT<sup>b</sup><sup>a</sup>Biological-Pharmaceutical Institute, Medical Academy,  
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The isolation of a new sesquiterpenic lactone — alatolide — from the leaves of *Jurinea alata* CASS. is described. Its structure, represented by formula I, was derived mainly on the basis of a detailed analysis of its PMR spectrum.

In connection with the study of sesquiterpenic lactones present in the species of the *Carduinae* subtribe<sup>1</sup> we also investigated the species *Jurinea alata* CASS. From its leaf substance I, m.p. 59–61°C,  $[\alpha]_D^{25} +64.4^\circ$ , composition C<sub>19</sub>H<sub>26</sub>O<sub>6</sub>, containing two active hydrogen atoms in the molecule, has been isolated earlier<sup>1</sup>. The native substance I, to which we gave the name alatolide, was not identical with any of the two sesquiterpenic lactones isolated up to now from the species of *Jurinea* genus (albicolide (II) from *J. albicaulis*<sup>2</sup> and jurineolide (III) from *J. cyanoides*<sup>3</sup>) or any other sesquiterpenic lactone described so far.

The structure of alatolide was derived on the basis of its IR, mass, and PMR spectra: The IR spectrum of alatolide contained absorption bands at 3430 and 3605 cm<sup>-1</sup> (OH group), 1757, 1400 and 1150 cm<sup>-1</sup> (methylene-γ-lactone), 1723 cm<sup>-1</sup> (ester group), and 1652 cm<sup>-1</sup> (double bond). The mass spectrum of the native sub-



I, R = CO.CH(CH<sub>3</sub>)<sub>2</sub>  
 III, R = CO.C(CH<sub>3</sub>)=CH.CH<sub>2</sub>OH

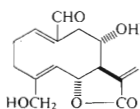
II  
 IV, R = CO.C(=CH<sub>2</sub>).CHOH.CH<sub>2</sub>OH  
 V, R = CO.C(=CH<sub>2</sub>).CH<sub>2</sub>OH

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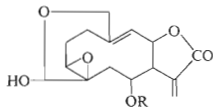
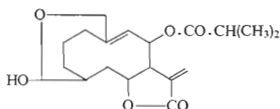
stance *I* contained a pseudomolecular peak of  $m/e$  332 (350–18) and fragments of  $m/e$  244 (350–18–88), 226 (350–18–88–18), 71 ( $C_3H_7CO^+$ ). The PMR spectrum of alatolide (*I*) (in deuteriodimethyl sulfoxide added with deuteriochloroform) displayed characteristic features of the germacranolide skeleton and it was very similar to that of jurineolide<sup>3</sup> (*III*). It differed from it only in the presence of characteristic signals of the *O*-isobutyryl group (two doublets of secondary methyl groups at 1.06 and 1.12 p.p.m., with  $J = 7$  Hz;  $\alpha$ -H at 2.54 p.p.m.; confirmed by a double-resonance experiment). Therefore it was possible to suppose that alatolide differs from jurineolide (*III*) only in the character of the *O*-acyl group bound to  $C_{(8)}$ . This supposition was further corroborated by a detailed analysis of the PMR spectra, using decoupling and exchange experiments from which followed these characteristic parameters (chemical shifts in  $\delta$ -TMS-scale, splittings in Hz):  $H_{(13)}$ : 6.11 dd ( $J_{13,7} = 3.5$ ,  $J_{13,13'} = 0.9$ );  $H_{(13')}$ : 5.66 dd ( $J_{13',7} = 3,3$ ,  $J_{13',13} = 0.9$ );  $H_{(1)}$ : 4.90 bm;  $H_{(5)}$ : 4.92 bd ( $J_{5,6} \cong 10$ );  $H_{(6)}$ : 5.18 dd ( $J_{6,5} \cong 10$ ,  $J_{6,7} \cong 7$ );  $H_{(7)}$ : 3.22 m ( $J_{7,6} \cong J_{7,8} \cong 7$ );  $H_{(8)}$ : 5.10 m; OH: 4.67 t ( $J \cong 5$ );  $H_{(14)}$  and  $H_{(15)}$ : 3.69–4.15 (overlapping of two AB-parts of ABX-systems, lowfield proton  $H_{(15)}$  at 4.03 p.p.m. as doublet with typical  $^2J \cong 13.5$ ). The observed parameters of protons bound to  $C_{(5)}$ ,  $C_{(6)}$ ,  $C_{(7)}$ ,  $C_{(8)}$ ,  $C_{(13)}$  and  $C_{(15)}$  are practically identical with the corresponding parameters of the PMR spectra of cnicin<sup>4</sup> (*IV*) and onopordopicrin<sup>5</sup> (*V*) and therefore it may be assumed that the molecule of alatolide has the same sterical arrangement at the mentioned carbon atoms as both mentioned substances, *IV* and *V*, the steric arrangement of which is described<sup>4,5</sup>. From these facts it follows that the molecule of alatolide has the stereostructure expressed by formula *I*. The same conclusion may also be made for jurineolide (*III*) the stereostructure of which was not fully elucidated in the original paper<sup>3</sup>. As for the mentioned paper<sup>3</sup> we may add that the presence of the ester-bound  $\gamma$ -hydroxytiglic acid in the molecule of jurineolide (*III*) also follows directly from the chemical shift of  $\beta$ -H, the correct value of which is 6.76 p.p.m.

The absolute configuration of alatolide (*I*) was deduced in the following manner: the CD curve of alatolide displays a negative Cotton effect at 262 nm. with  $[\theta] -4390^\circ$ . According to Geissman and coworkers<sup>6,7</sup> the negative dichroic band in the region about 255 nm in  $C_{(6)}$ -lactones with a conjugated exocyclic bond and a  $\beta$ -oriented  $C_{(7)}-C_{(11)}$  bond corresponds to the *trans*-fused  $\gamma$ -lactone group. The negative Cotton effect of the lactonic chromophore of alatolide (*I*) may thus be due in principle either to a *trans*-lactone with an absolute configuration  $\beta H_{(6)}$ ,  $\alpha H_{(7)}$  or to a *cis* lactone with  $\beta H_{(6)}$ ,  $\beta H_{(7)}$ . In view of the fact that from the PMR spectrum it follows – as was said above – that the molecule of alatolide contains a *trans*-annulated  $\gamma$ -lactone ring, the negative dichroic band of the lactonic chromophore of alatolide also determines its absolute configuration expressed by formula *I*. A similar consideration also applies for albicolide<sup>2</sup> (*II*) and for jurineolide<sup>3</sup> (*III*) the CD curves<sup>3</sup> of which have the same course as the CD curve of alatolide.

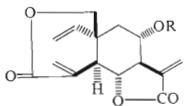
From the chemosystematical point of view the presence of a lactone of germacranolide type in *J. alata* is in agreement with the classification of this species in the *Cynareae* tribe (synonymum *Cardueae*, ref.<sup>8</sup> for example). Only in a relatively small number of genera of this tribe, as for example in *Saussurea*<sup>9</sup>, *Cynara*<sup>10</sup>, and similar genera, the formation of substances of a higher biogenetical degree (*i.e.* the formation of guaianolides) takes place. However, it is remarkable that in the case of alatolide from *J. alata*, as well as in the case of the two native substances studied earlier, *i.e.* albicolide from *J. albicaulis* and jurineolide from *J. cyanoides*,



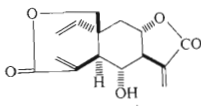
VI

VII, R = CO.C(=CH<sub>2</sub>).CH<sub>3</sub>VIII, R = CO.C(=CH<sub>2</sub>).CH<sub>2</sub>OH

IX

X, R = CO.C(=CH<sub>2</sub>).CH<sub>2</sub>OH

XI, R = H



XII

its germacrenolide basis has both its methyl groups bound to the double bonds of the ten-membered ring, oxidized to primary hydroxy groups. The native sesquiterpene lactones which contain both mentioned methyl groups in oxidized form were already described, as for example urospermal<sup>11</sup> (VI), vernolide<sup>12</sup> (VII), hydroxy-vernolide<sup>13</sup> (VIII), and vernomygdin<sup>14</sup> (IX) from the germacranolide group, and vernodalin<sup>14</sup> (X), vernolepin<sup>15</sup> (XI), and vernomenin<sup>15</sup> (XII) from the group of eleanolides. Of course, the presence of two primary hydroxy groups bound to C<sub>(14)</sub> and C<sub>(15)</sub> was hitherto observed only in alatolide (I), albicolide (II), and jurineolide (III), the parent plants of which are species of the *Jurinea* genus. Therefore it may be provisionally supposed that for the *Jurinea* genus germacrenolides with two primary hydroxy groups bound to C<sub>(14)</sub> and C<sub>(15)</sub> are typical, although the corroboration of this conclusion requires an analysis of a larger series of species of the mentioned genus.

## EXPERIMENTAL

The melting point was determined on a Kofler block and it was not corrected. The IR spectrum was measured on a Zeiss UR-10 spectrophotometer. The PMR spectra were measured with a Varian HA-100 apparatus and the mass spectrum with a AEI MS 902 spectrograph. Circular dichroism was measured on a Roussel-Jouan Dichrographe CD-185.

## Alatolide (I)

Dry leaves of *Jurinea alata* CASS. (1.0 kg) were worked up in the described manner<sup>1</sup> to yield 1.9 g of alatolide of m.p. 59–61°C and  $[\alpha]_D^{25} + 64.4^\circ$ . For  $C_{19}H_{26}O_6 \cdot H_2O$  (368.4) calculated: 61.94% C 7.66% H, 0.54% H act.; found: 61.89% C and 62.11% C, 7.67 and 7.62% H, 0.68% H act. CD (methanol):  $[\theta]_{330} \pm 0^\circ$ ,  $[\theta]_{262} - 4390^\circ$ ,  $[\theta]_{250} \pm 0^\circ$ ,  $[\theta]_{220} + 120\,680^\circ$ ;  $[\theta]_{208} \pm 0^\circ$ .

The elemental analysis was determined in the analytical department, Institute of Organic Chemistry and Biochemistry, by Mrs V. Rusová and Mrs L. Pejchalová. The mass spectrum was measured by Dr K. Ubik, the infrared spectrum by Mrs K. Matoušková, and optical rotation by Mrs J. Šafaříková. We express our thanks to all those mentioned, as well as to Miss H. Němcová and Miss D. Szmania for technical assistance.

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