8α-HYDROXYBALCHANIN — A NEW SESQUITERPENIC LACTONE FROM *Leucanthemella serotina* (L.) TZVEL.*

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For the sesquiterpenic lactone isolated from *Leucanthemella serotina* (L.) TZVEL., called 8α-hydroxybalchanin, the structure *I*, including relative and absolute configuration, was derived on the basis of IR, CD and mass spectra and mainly ^{1}H NMR spectroscopy.

In connection with the systematic study of sesquiterpenic lactones of the *Compositae* family we also investigated the species *Leucanthemella serotina* (L.) TZVEL (synonymum *Chrysanthemum serotinum* L. and *Tanacetum serotinum* SCH. BIP.; tribe *Anthemideae*, subtribe *Chrysanthemineae*). From its aerial parts we isolated a lactonic fraction in the described manner[1], from which we obtained by chromatography on silica gel also compound *I*, m.p. 80–82°C, $[\alpha]_D^{20}$ +150·6° and composition $C_{15}H_{20}O_4$, for which we propose the name 8α-hydroxybalchanin. The IR spectrum of this substance evidenced the presence of a γ-lactone group (1 768 and 1 132 cm^{-1}), a hydroxy group (3 616 and 3 490 cm^{-1}) and a double bond (1 672 cm^{-1}). The mass spectrum had molecular peak m/e 264 and characteristic fragments 246 (M – 18) and 228 (M – 18 – 18). The CD spectrum had a maximum at 257 nm with $\Delta\varepsilon$ –0·72.

The ^{1}H NMR spectrum of compound *I* (Table I) detected the presence of two tertiary methyl groups of which one is bound to an sp^3 carbon (δ 0·90, d, J = 0·7 Hz) and the second to an sp^2 carbon (δ 1·84, bs). Further the signals for an exomethylene group were found in the spectrum (δ 6·17 dd and 5·98 dd, $J \approx$ 3·0 and 0·7 Hz), of an olefinic hydrogen on a trisubstituted double bond (δ 5·36 um) and of two secondary hydroxy groups (CH—O hydrogens at δ 3·70 dd, J = 9·8 and 6·5 Hz and 4·10 dt, J = 11, 10·4 and 4·5 Hz). An *in situ* reaction with trichloroacetyl isocyanate[2,3] gave bis-trichloroacetylcarbamoyl derivative *II*. Its ^{1}H NMR spectrum (Table I) showed the signals of two NH hydrogens (δ 8·50 and 8·55) and characteristic acylation shifts of the CH—O protons to δ 5·04 dd and 5·33 dt. A number of de-

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TABLE 1

^{1}H NMR Parameters of 8α-hydroxybalchanin (*I*) and bis-trichloroacetylcarbamate *II*

Compound	Chemical shifts[a]													
	$H_{(1)}$	$H_{(2)}$	$H_{(2')}$	$H_{(3)}$	$H_{(5)}$	$H_{(6)}$	$H_{(7)}$	$H_{(8)}$	$H_{(9)}$	$H_{(9')}$	$H_{(13)}$	$H_{(13')}$	$H_{(14)}$	$H_{(15)}$
I	3·70	2·35	2·00	5·36	2·35	3·98	2·57	4·10	2·35	1·27	6·17	5·98	0·90	1·84
II	5·04	2·60	2·17	5·42	2·60	5·07	2·91	5·33	2·44	1·51	6·21	5·64	1·11	1·88

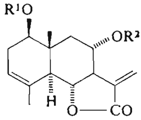
	Coupling constants[a]													
	$J_{1,2}$	$J_{1,2'}$	$J_{2,2'}$	$J_{2,3}$	$J_{2,3'}$	$J_{5,6}$	$J_{6,7}$	$J_{7,8}$	$J_{7,13}$	$J_{7,13'}$	$J_{8,9}$	$J_{8,9'}$	$J_{9,9'}$	$J_{13,13'}$
I	6·5	9·8	[b]	[b]	[b]	11·4	10·8	10·4	3·15	3·0	4·5	11·0	12·6	0·75
II	6·8	9·6	[b]	[b]	[b]	11·4	10·8	10·9	2·8	2·6	4·5	10·7	12·5	0·75

[a] Measured on Varian XL 200 in deuteriochloroform; tetramethylsilane as internal standard; chemical shifts in δ and coupling constants in Hz.

[b] Coupling constants could not be determined due to overlapping of signals or unsufficient resolution of lines following from non-zero long-range couplings $J_{2,5'}$, $J_{2',5'}$, $J_{2,15'}$ $J_{2',15}$ and $J_{3,15}$. Observed coupling $J_{9',14}$ was 0·7 Hz both in *I* and *II*.

coupling experiments and a detailed analysis of the ^{1}H NMR spectra of compounds *I* and *II* led to the assignment of all hydrogens (Table I) and to a proposal of the eudesmanolide (selinanolide) skeleton with a $C_{(6)}$-γ-lactone ring, hydroxyls in the positions $C_{(1)}$ and $C_{(8)}$ and a double bond between $C_{(3)}$ and $C_{(4)}$. The *trans*-configuration of the lactone is in agreement with the high value of $J_{6,7} = 10 \cdot 8$ for the diaxial arrangement of hydrogens on $C_{(6)}$ and $C_{(7)}$ and with the values of allylic couplings of the exomethylene hydrogens ($J_{7,13} = 3 \cdot 15$ and $J_{7,13'} = 3 \cdot 0$ Hz) in compound *I*. The high values of $J_{5,6} = 11 \cdot 4$ and $J_{7,8} = 10 \cdot 4$ Hz correspond to the *trans*-diaxial arrangement of the hydrogens on a six-membered ring and they also determine the relative arrangement of the substituents in position $C_{(5)}$, $C_{(6)}$ or $C_{(7)}$ and $C_{(8)}$. Such a distinct upfield acylation shift of one of the exomethylene hydrogens ($\Delta\delta_H$ is $-0 \cdot 34$ for $H_{(13')}$ and $+0 \cdot 04$ ppm for $H_{(13)}$) in bis-trichloroacetylcarbamate *II* is plausible merely for the hydroxy group in the position 8α (sterical proximity of OH and $H_{(13')}$). The coupling constants $J_{8,9} = 4 \cdot 5$ and $J_{8,9'} = 11 \cdot 0$ Hz also define the steric arrangement around the $C_{(8)}$—$C_{(9)}$ bond and permit the configurational assignment of both $C_{(9)}$-hydrogens $H_{(9)}$ as 9β and $H_{(9')}$ as 9α hydrogen. At the same time, only the observed σ-interaction ^4J of the $C_{(10)}$-methyl ($J = 0 \cdot 7$ Hz) with $H_{(9')}$ is in agreement with the axial position of $H_{(9')}$. Under the assumption of a β-configuration of the $C_{(10)}$-methyl and the *trans*-annelation of the six-membered rings – in agreement with the above mentioned facts – the hydroxyl in the position $C_{(1)}$ should have β-configuration, *i.e.* it should be *cis* oriented with respect to the $C_{(10)}$-methyl, on the basis of the following arguments. According to the coupling constants and the widths of the signals of protons in positions 1, 2 and 3 the corresponding six-membered ring assumes a twist-chair $_1T^{10}$ or envelope E^{10} conformation. In these the observed $J_{1,2} = 6 \cdot 5$ and $J_{1,2'} = 9 \cdot 8$ Hz are compatible only with the β-configuration of the hydroxyl on $C_{(1)}$, with the dihedral angles of hydrogens in positions 1 and 2 approximately 30 and 150 with $H_{(2)}$ as 2α and $H_{(2')}$ as 2β-hydrogens. For an α-configuration of the hydroxyl on $C_{(1)}$ the angle relations would correspond to values approximately 30 and 90°. The clear downfield acylation shift of the $C_{(10)}$-methyl ($\Delta\delta_H = 0 \cdot 21$ ppm) in bis-trichloroacetylcarbamate *II* is in agreement with the gauche arrangement of $C_{(1)}$—OH and $C_{(10)}$—CH_3 with 1β-OH configuration of compound *I* (ref.[3]).

We determined the absolute configuration of the investigated compound *I* on the basis of the rule deduced by Geissman and co-workers[4,5], evaluating the maximum at 257nm with $\Delta\varepsilon$ $-0 \cdot 72$ in the CD spectrum of lactone *I*. The negative sense of this maximum, belonging to the exomethylene-γ-lactone grouping shows that the absolute configuration on $C_{(7)}$ is R, when taking into account that we have demonstrated on the basis of ^{1}H NMR spectroscopy that the grouping discussed is bound to $C_{(6)}$ and $C_{(7)}$ and that it is *trans*-annelated with the six-membered homocycle. The structure of the lactone studied is thus represented by formula *I*, *i.e.* 8α-hydroxybalchanin[6].



I: $R^1 = R^2 = H$
II: $R^1 = R^2 = CONHCOCCl_3$
III: $R^1 = H$; $R^2 = COCH_2C(OH)(CH_3)_2$
IV: $R^1 = H$, $R^2 = COC(CH_3){=}CHCH_2OH$

In connection with the isolation of 8α-hydroxybalchanin (*I*) from the species *Leucanthemella serotina* (L.) TZVEL. it is important to mention the preliminary communication by Yugoslav authors[7] who isolated from the same species growing wild in the neighbourhood of Belgrade, two sesquiterpenic lactones which they called beogradolide A and B and for which they derived the structures represented by formulae *III* and *IV*. These native substances differ from 8α-hydroxybalchanin (*I*) merely by the esterification of the secondary hydroxyl group bound to $C_{(8)}$.

From the point of view of the distribution of skeletal types of sesquiterpenic lactones in lower taxons of *Compositae* the presence of 8α-hydroxybalchanin (*I*), or of lactones *III* and *IV*, based on eudesmanolide (selinanolide) skeleton, in the species *Leucanthemella serotina* (L.) TZVEL. corresponds to the conclusions already described on the distribution of sesquiterpenic lactones of the mentioned type in the tribe *Anthemideae*[8].

EXPERIMENTAL

The melting point was determined on a Kofler block and it was not corrected. The mass spectrum was measured on an AEI 902 spectrometer. The IR spectrum was measured in chloroform on a Zeiss UR 20 (Jena) spectrophotomer. The CD spectrum was measured with a Roussel--Jouan Dichrographe CD 185 and the optical rotation was determined with an objective polarimeter Perkin–Elmer in methanol.

Isolation of 8α-Hydroxybalchanin (*I*)

From the dried above-ground part of *Leucanthemella serotina* (L.) TZVEL. (100 g), the voucher of which is deposited in the herbarium of the Department of Medicinal Plants, Academy of Medicine, Poznan, Poland, under the number RL 4/79, a lactone fraction (310 mg) was obtained in the described manner[1], which was chromatographed on 20 g of silica gel, using chloroform and further mixtures of chloroform and acetone in 9 : 1, 4 : 1 and 3 : 1 ratios for elution. From the fractions eluted with the last mentioned mixture 8α-hydroxybalchanin (*I*; 80 mg) was obtained, m.p. 80—82°C (chloroform–diethyl ether), $[\alpha]_D^{20} + 150{\cdot}6°$ (*c* 0·29) and the composition $C_{15}H_{20}O_4$. IR spectrum (in cm^{-1}): 1 768, 1 132 (γ-lactone), 1 672 (double bond), 3 616, 3 490 (hydroxyl). Mass spectrum (*m/e*): 264 (M), 246 (M—18), 228 (M—18—18). CD spectrum (nm, Δε): 257, —0·72; 210 (sh), +9·9. For $C_{15}H_{20}O_4$ (264·3) calculated: 68·16% C, 7·63% H, 0·76% H act.; found: 68·10% C, 7·83% H, 0·60% H act.

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