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SESQUITERPENE LACTONES OF NEW STEREOSTRUCTURAL TYPES FROM LASER TRILOBUM[1]

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Abstract: The newly established structures of sesquiterpene lactones from Laser trilobum showed that these lactones belong among the new stereostructural types of germacranolides, guaianolides, eudesmanolides and elemanolides.

From the roots of Laser trilobum (L.) BORKH. (Umbelliferae family, tribe Laserpitieae) we isolated earlier[2] laserolide (m.p. 140-141°C, $[\alpha]_D^{20}$ -234, $C_{22}H_{30}O_6$) and derived its basic structure[3]. Now we propose for it on the basis of its ^{1}H NMR spectrum (Table 1), and on the basis of its X-ray structural analysis, a corrected structure including the relative configuration represented by I. We determined its absolute configuration by making use of the benzoate rule[4], according to the molecular rotation of the pair of compounds II and III, for the chiral centre $C_{(6)}$ and the pair IV and V for the chiral centre $C_{(8)}$. We derived the absolute configuration at $C_{(11)}$ for some laserolide derivatives by means of CD, using the sector rule[5]. The absolute configuration of laserolide (I) was also supported by its CD spectrum (225 nm, $\Delta\varepsilon$ -32.8), similarly as in the case of ursiniolides A, B and C[6,7]. Hence, laserolide (I) belongs to the relatively recently described stereostructural group of germacranolides, characterized by the 6αH,7αH-germacra-(E) 1(10),(E) 4-dien-6,12-olide basis[6,7]. Laserolide (I) is the first described native substance from the species of the Umbelliferae family, belonging to that stereostructural group. From the plant material studied we also isolated isolaserolide (m.p. 125-127°C, $[\alpha]_D^{20}$ +81.1, $C_{22}H_{30}O_6$)[2]. According to the chemical correlation with laserolide (I) we proposed for it a structure[8] which we want to correct now on the basis of detailed analysis of the ^{1}H NMR spectrum (Table 1) and in connection with the new structure of laserolide (I) to structure VI, expressing both relative and absolute configuration. Isolaserolide (VI) is thus the first native representative of the new stereostructural series of elemanolides, characterized by the 5βH,6αH,7αH,10αCH_3-elema-1,3-dien-6,12-olide basis. From the mentioned plant material we now isolated 8-deacetoxylaserolide (m.p. 105-107°C, $[\alpha]_D^{20}$ -138.6, $C_{20}H_{28}O_4$) to which we assigned the structure VII, including the relative and absolute configuration, according to its ^{1}H NMR (Table 1), mass, IR and CD spectrum. This substance belongs to the mentioned group of 6αH,7αH-germacra-(E)1(10),(E)4-dien-6,12-olides[6,7], too. Further, we also obtained isolasolide (m.p. 120-121°C, $[\alpha]_D^{20}$ -62.3, $C_{20}H_{28}O_5$) for which we inferred on the basis of ^{1}H NMR (Table 1) mass, IR and CD spectrum, the structure VIII, expressing its relative and absolute configuration. According to its structure, this sesquiterpene lactone belongs to the new stereostructural group of eudesmanolides, with the 5βH, 6αH,7αH,10αCH$_3$-eudesman-6,12-olide basis[9]. According to the spectral correlation of isolasolide (VIII) with the earlier isolated lasolide[2] we derived the full stereostructure IX even for this lactone. Lasolide (IX) is thus a further representative of the new stereostructural group of eudesmanolides already mentioned[9]. In addition to these lactones we isolated from the plant material studied also four guaianolides of the slovanolide type (1βH,5βH,6αH,7αH-guaian-6,12-olide)[10], i.e. 8α-(2′-methyl)butyroyloxy-10β,11α-diacetoxyslov-3-enolide (X; m.p. 126-127°C, $C_{24}H_{34}O_8$), 10β-hydroxy-11α-angeloyloxyslov-3-enolide (XI; m.p. 186-189°C, $C_{20}H_{28}O_5$), further the non-crystalline 2β-(2′-methyl)butyroyloxy-8α-angeloyloxy-10β-hydroxy-11α-acetoxyslov-3-enolide (XII; $[\alpha]_D^{20}$ -66.4, $C_{27}H_{38}O_9$), and 2β-angeloyloxy-8α-(2′-methyl)butyroyloxy-10β,11α-diacetoxyslov-3-enolide (archangelolide; XIII), the isolation of which from the root of Laserpitium archangelica WULF. and its basic structure we described earlier[11]. For all the mentioned guaianolides we propose, mainly on the basis of a detailed analysis of their ^{1}H NMR spectra (Table 1), mass, IR and CD spectra, the structures X-XIII, including relative and absolute configurations. For the further guaianolide trilobolide, the isolation[2] and the basic structure of which we described earlier[12], we derived the stereostructure XIV, mainly on the basis of the ^{1}H NMR spectra of the native substance (Table 1) and a number of its derivatives. The structure XIV is in full agreement with the result of an X-ray structural analysis of trilobolide, carried out by Kutschabsky and co-workers[13].

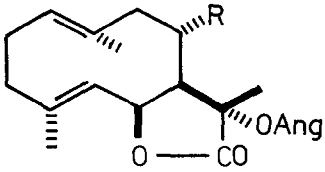
From the structures of the mentioned sesquiterpene lactones of the Laser trilobum species, e.g. from the relationship of the lactones VII and VIII and VI and XI, or I and VI, it follows that the biogenesis of these substances takes place, up from a certain stage, in a stereostructural way different from the biogenesis of common germacranolides, guaianolides, eudesmanolides and elemanolides in the species of the Compositae family.

Table 1 PROTON CHEMICAL SHIFTS (COUPLING CONSTANTS) OF SESQUITERPENE LACTONES I, VI–XIV

Proton	I	VI	VII	VIII	IX	X	XI	XII	XIII	XIV
H-1	5.11 m	5.94 dd (17.5; 10.8)	4.93 m (9.9;6.2; 1.5(4x)	3.49 dd (9.8;6.4)	3.44 bd (11.0;≠0)	2.73 m (10.9;7.1; 5.9;1.5)	2.57 m	3.29 dd (7.5;3.9)	3.32 dd (7.9;3.5)	4.45 b
H-2	1.90 - 2.40	5.10 dd (17.5; 0.7)	1.59 - 2.22	1.67 - 2.33	1.40 - 2.40	2.10 - 2.30	1.75 - 2.50	5.80 m	5.83 m (3.5;2.4; 1.4(4x)	2.52 dt (14.7;8.6; 8.6)
H-2'		5.04 dd (10.8; 0.7)						—	—	1.62 dt (14.7; 6.0;4.5)
H-3		5.05 m (1.4(3x); 1.0)		5.31 m	2.40 ddd (13.7; 4.8;2.4)	5.57 m (1.5(5x)	5.49 m (1.5(5x)	5.66 m	5.66 m (2.4;1.8; 1.5(3x)	5.58 m
H-3'		4.76 m (1.0; 0.7(3x)		—	1.40 - 2.40	—	—	—	—	—
H-5	4.74 bd (1.5(3x); 10.3)	2.16 d (12.3)	4.79 bd (1.5(3x); 10.7)	1.67 - 2.33		2.56 dd (11.6;5.8)	2.79 m	3.07 m	3.05 m (11.9;7.9; 1.8;1.4)	—
H-6	5.38 dd (10.3;9.4)	5.08 dd (12.3;9.9)	5.43 dd (10.6;8.9)	4.74 dd (9.8;6.4)	5.03 dd (11.0;9.3)	4.72 dd (11.6;9.9)	5.39 dd (11.8;9.3)	4.64 dd (11.8;9.3)	4.82 dd (11.9;9.7)	5.68 b
H-7	3.72 dd (11.3;9.4)	3.37 dd (9.9;7.7)	3.11 dt (9.7;8.9; 3.8)	3.18 bq	3.34 m (4.7(2x); 9.4)	3.62 dd (11.0; 9.9)	3.23 dd (11.4; 9.3)	3.04 dd (10.5; 9.3)	3.62 dd (11.2; 9.7)	—
H-8	5.28 dt (11.3; 10.8;4.0)	5.26 ddd (9.6;7.7; 3.8)	1.59 - 2.22	1.67 - 2.33	1.40 - 2.40	5.59 ddd (11.0; 10.0;0.9)	1.75 - 2.50	5.70 dt (11.1; 10.5;2.2)	5.62 dt (11.2; 10.9;2.6)	5.66 t (3.8;3.4)
H-8'	—	—				—		—	—	—
H-9	2.86 bd (14.0;≠0)	2.00 dd (13.9; 3.8)				2.59 ddd (15.0; 1.7;0.9)		2.59 dd (15.5; 2.2)	2.60 dd (15.2; 2.6)	3.20 dd (14.7; 3.4)
H-9'	1.84 dd (14.0; 10.8)	1.49 dd (13.9; 9.6)				1.95 dd (15.0; 10.2)		2.12 dd (15.4; 11.1)	2.06 dd (15.2; 10.9)	2.08 dd (14.7; 3.8)
H-13	1.52 s	1.60 s	1.54 s	1.51 s	1.61 s	1.53 s	1.49 s	1.58 s	1.58 s	1.47 s
H-14	1.40 bd (1.3;≠0)	1.04 s	1.41 d (1.5)	0.76 s	0.75 s	1.56 s	1.19 s	1.43 s	1.43 s	1.31 s
H-15	1.74 d (1.5)	1.82 dd (1.4;0.7)	1.73 d (1.5)	1.79 dt (2.5; 1.2(2x)	5.05 b 4.95 b	1.89 dt (2.5; 1.7(2x)	1.86 dt (2.4; 1.6(2x)	1.92 b	1.95 dd (1.2;1.5)	1.90 b
Ac:	2.07 s	2.05 s	—	—	—	2.10 s 2.06 s	—	2.05 s	2.08 s 2.02 s	1.97 s
Mebu:										
CH^a	—	—	—	—	—	2.31 m	—	2.36 m	2.33 m	2.34 m
2-CH_3^{b}	—	—	—	—	—	1.15 d	—	1.18 d	1.15 d	1.14 d
CH_2^{c}	—	—	—	—	—	1.71 m 1.45 m	—	1.73 m 1.45 m	1.72 m 1.46 m	1.69 m 1.43 m
3-CH_3^{d}	—	—	—	—	—	0.94 t	—	0.91 t	0.93 t	0.90 t
Ang:										
2-CH_3^{e}	1.93 p	1.90 p	1.91 p	1.81 p	1.89 p	—	1.88 p	1.86 p	1.87 p	1.91 p
CH^f	6.20 qq	6.20 qq	6.18 qq	6.09 qq	6.17 qq	—	6.15 qq	6.05 qq	6.05 qq	6.11 qq
3-CH_3^{g}	2.04 dq	2.01 dq	2.01 dq	1.92 dq	2.00 dq	—	1.99 dq	1.95 dq	1.95 dq	2.01 dq

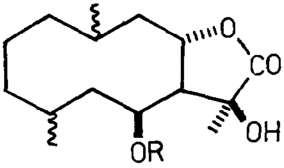
[a] J=7(5x); [b] J=7; [c] J=13.5;7(4x); [d] J=7.4(2x); [e] J=1.5(4x); [f] J=7.3(3x);1.5(3x); [g] J=7.3;1.5(3x)

Ac = CH_3COO ; Mebu = $C_2H_5CH(CH_3)COO$; Ang = $CH_3CH{=}C(CH_3)COO$ (Z)



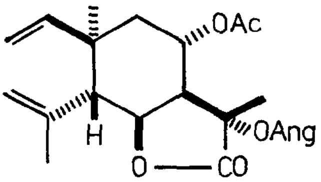
I: R=OAc

VII: R=H

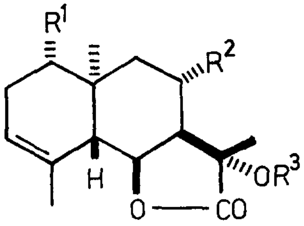


II: R=H

III: R=Bzl



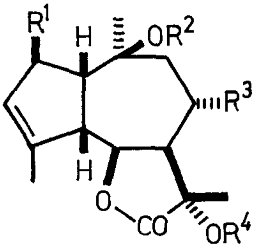
VI



IV: R^1,R^3=H;R^2=OH

V: R^1,R^3=H;R^2=OBzl

VIII: R^1=OH;R^2=H;R^3=Ang

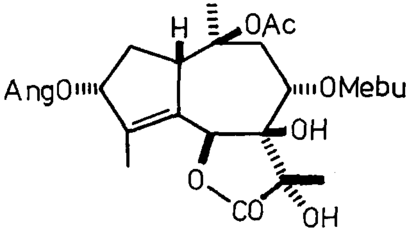


X: R^1=H;R^2,R^4=Ac;R^3=OMebu

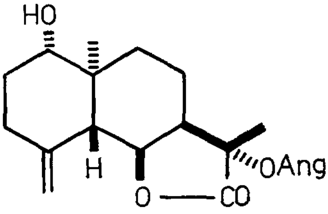
XI: R^1,R^2,R^3=H;R^4=Ang

XII: R^1=OAng;R^2=Ac;R^3=OMebu;R^4=H

XIII: R^1=OAng;R^2,R^4=Ac;R^3=OMebu



XIV



IX

Ac = $COCH_3$; Ang = $COC(CH_3)=CHCH_3$ (Z);

Mebu = $COCH(CH_3)CH_2CH_3$; Bzl = COC_6H_5

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