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SESQUITERPENE LACTONES OF THE UMBELLIFERAE*

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Key Word Index—Umbelliferae; sesquiterpene lactones; new stereostructural types; biogenesis; chemotaxonomy.

Abstract—A survey of sesquiterpene lactones from the species of Umbelliferae is presented. The structures based on predominantly undescribed stereostructural types were derived for the majority of these lactones.

INTRODUCTION

At present the number of described sesquiterpene lactones† isolated from members of the Umbelliferae amounts to about 100. While studying them systematically, we have found recently that practically all the sesquiterpene lactones of this family so far described are based on new stereostructural types.

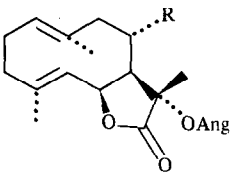
* Part 292 in the series "On Terpenes". For Part 291 see *Collect. Czech. Chem. Commun.* (1986) **51**, 1323.

† 'Sesquiterpene lactones' here means those substances only the lactone carbonyl of which can be derived by oxidation of the methyl of the isopropyl group of the basic sesquiterpene carbon skeleton.

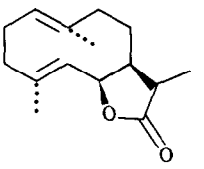
RESULTS

Germacranolides

So far in the species of Umbelliferae five germacranolides have been identified, among which laserolide (**1**) [1, 2], 8-deacetoxylaserolide (**2**) [3] and gallicolide (**3**) [4], isolated from the tribe Laserpitieae, belong according to their structure to the new stereostructural type of germacranolide which we described recently. It is based on the fundamental skeleton 6*R*,7*S*-germacra-*E*1(10),*E*(4)-dien-6,12-olide (**4**) [5, 6]. We confirmed the structure of this new stereostructural type by X-ray analysis of ursiniolide A (**5**) [7] and laserolide (**1**) [8]. The further two germacranolides described, isolated from *Smyrnium rotundifolium* Mill. (tribe Smyrnieae), i.e. 1β,10α-epoxy-4-methoxy-8-hydroxyglechomanolide (**6**) and 1β,10α-epoxy-4-methoxyglechomanolide (**7**), still do not have their complete relative and absolute configurations de-



1 R = OAc
2 R = H
3 R = OMebu



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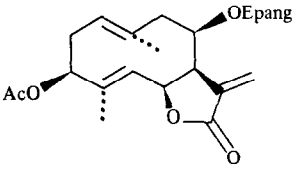

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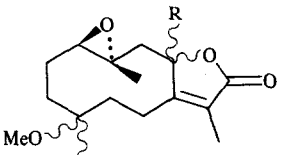
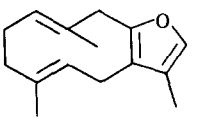


6 R = OH
7 R = H



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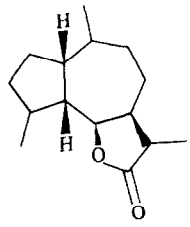
termined. It is possible that they are artifacts formed from the furodiene **8**, which was also detected in the same plant material [9].

Guaianolides

As regards guaianolides, we have demonstrated that the predominant lactones of this type, isolated from the species of Umbelliferae—especially from the tribes Laserpitieae and Peucedaneae—belong to the new stereostructural type which we have also described [10] and the fundamental skeleton is 1*S*,5*R*,6*R*,7*S*-guaian-6,12-olide (**9**) or slovanolide [11]. We confirmed the structure of this new type of guaianolide by X-ray analysis of the ketolactone **10** [12] which we prepared from 8α-angeloyloxy-10β,11α-diacetoxyslov-3-enolide (**11**) [10], and by the correct interpretation [12] of the X-ray data of the lactone from *Laserpitium marginatum* [13] leading to the correct structure **12** for this compound [12]. About 20 natural sesquiterpene lactones can be classed as slovanolides, which we isolated from *Laserpitium siler* [10,11,14], *L. archangelica* [15] and *Laser trilobum* [3], all being derived from 8α,10β,11α-trihydroxyslov-3-enolide (**13**), 2β,8α,10β,11α-tetrahydroxyslov-3-enolide (**14**) or 4α,8α,10β,11α-tetrahydroxyslov-2-enolide (**15**). Grilactone (**16**) also belongs in this group. Its structure was proved by X-ray structural analysis [16] several years ago and completed by us by its absolute configuration [17]. The guaianolides such as 8-deangeloylshairidin (**17**) [18], guillonein (**18**) [19] and others are structurally closely related to the slovanolides. The structure for the natural lactones **17** and **18** (including absolute configur-



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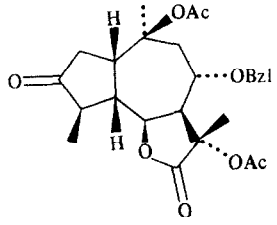

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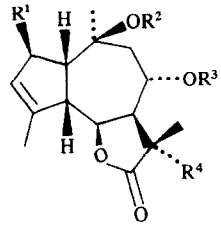
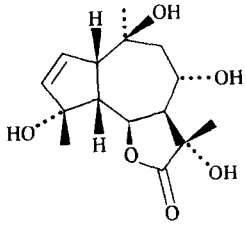


11 R^1 = H, R^2 = Ac; R^3 = Ang; R^4 = OAc
12 R^1, R^4 = H; R^2 = Ac; R^3 = Ang
13 R^1, R^2, R^3 = H; R^4 = OH
14 R^1, R^4 = OH; R^2, R^3 = H



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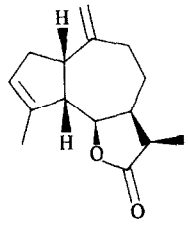

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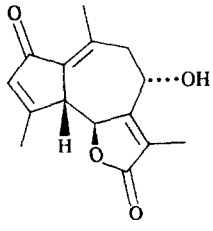

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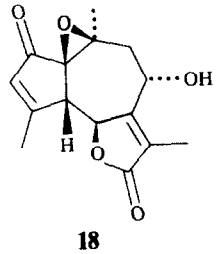

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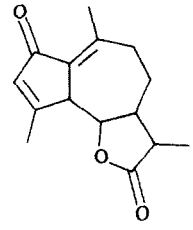

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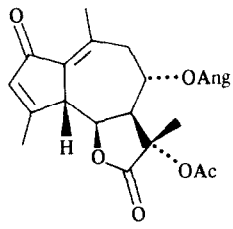

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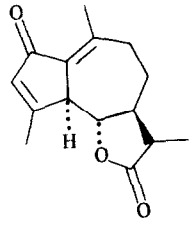

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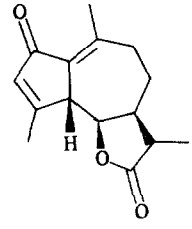
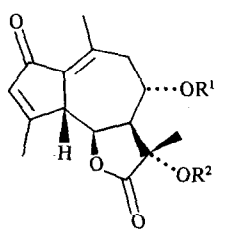


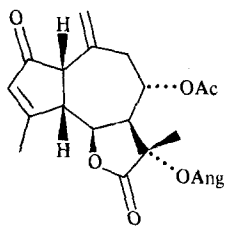
22

ation) was derived by X-ray analysis [19, 20]. In connection with the study of guaianolides with the basic structure **19** we solved the structure of 2-oxo-8α-angeloyloxy-11α-acetoxyguai-1(10),3-dien-6,12-olide [21] (4-acetoxypruteninone-10 [22], laferin [23]) by means of X-ray structural analysis, assigning it formula **20** [21]. Simultaneously we also demonstrated that according to the differing values of δH-6 and $J_{9,9'}$ the lactones with the basic stereostructure **21** can be differentiated from the lactones based on stereostructure **22**. On the basis of these facts we revised the originally derived structures for talasin A [23] (evidently identical with 4-angeloyloxypruteninone-10 [22]), talasin B [23], malafil [24–26], malafilin [24–26], malafilinin [25, 26], giferolide [25], ferugolide [25], gigantolide [25], olgin [23], oferin [23], olgoferin [23] and fegvolide [26] to the formulae **23–34** [21]. Similarly we have also revised the structures of acetoxyisopruteninone-10 [22], prutenin [22], ferulidin [27] and badkhysin [27] to **35–38** [21].

Among the guaianolides of the Umbelliferae, trilobolide (**39**) [28, 29] and evidently the entire group of guaianolides of the genus *Thapsia* [30–32], e.g. thapsigargin (**40**) and thapsigargicin (**41**), represent exceptions. In these compounds, the γ-lactone ring is *trans*-annellated to the seven-membered ring, as was demonstrated by us by X-ray diffraction analysis of trilobolide (**39**) [33], as well as by a group of German authors [34] and Danish authors by X-ray analysis of the epoxide **42** [30]. In the case of trilobolide (**39**) we determined its absolute configuration [33] which is identical to that derived by Christensen and



23 R^1, R^2 = Ang
24 R^1 = Ang; R^2 = iBu
25 R^1 = Bzl (3,4-OMe); R^2 = Sen
26 R^1 = Bzl (3,4-OMe); R^2 = Ac
27 R^1 = Bzl; R^2 = Ac
28 R^1 = Bzl; R^2 = Sen
29 R^1 = Bzl (4-OMe); R^2 = Sen
30 R^1 = Bzl (4-OMe); R^2 = Ac
31 R^1 = Mac; R^2 = Ac
32 R^1 = Mac; R^2 = iBu
33 R^1, R^2 = Mac
34 R^1 = Bzl (3,4-OMe); R^2 = Ang



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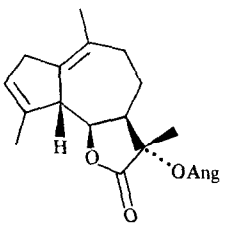

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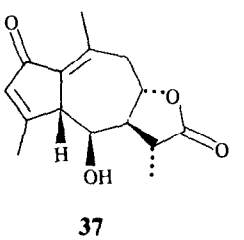

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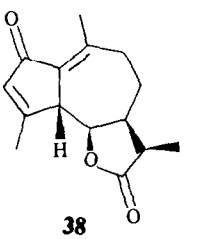

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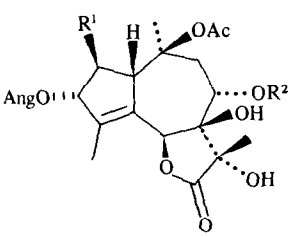
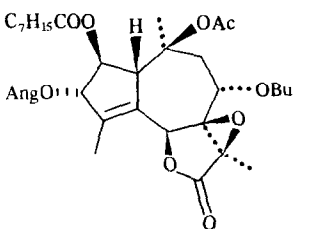


39 R^1 = H; R^2 = Mebu
40 R^1 = $OCOC_7H_{15}$; R^2 = Bu
41 R^1 = $OCOC_5H_{11}$; R^2 = Bu



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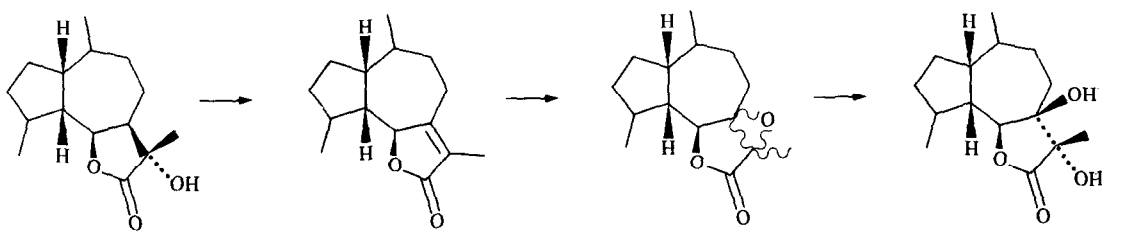
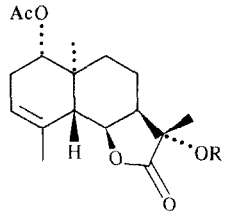
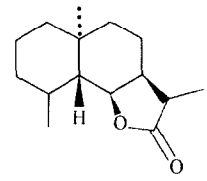


Scheme 1

Norup in a different way [35], and which confirms that its C-7–C-11 bond has the opposite configuration to that in the majority of sesquiterpene lactones. According to other structural evidence (for example proving the configurations of 1βH, 10βOAc, 8α-acyloxy and 6αH groups trilobolide (**39**) and the *Thapsia* guaianolides [30–32] are closely related to the slovanolides. One of the possible inversion routes to the configuration of the C-7–C-11 bond starts from the slovanolide precursor, as indicated in Scheme 1.



44 R = Ang
45 R = Sen



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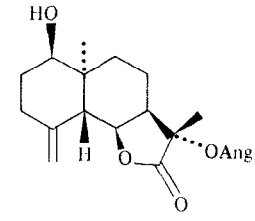

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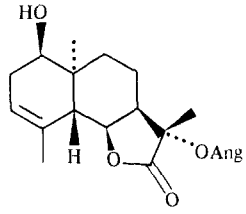

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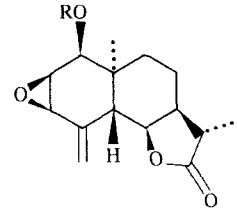
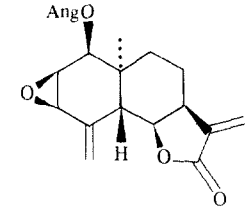


48 R = Ang
53 R = H



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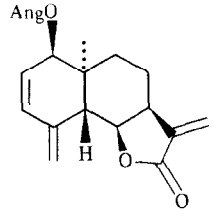

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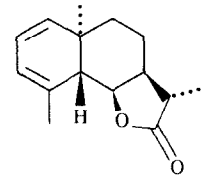

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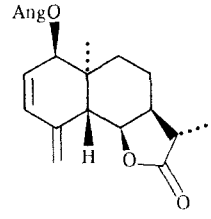

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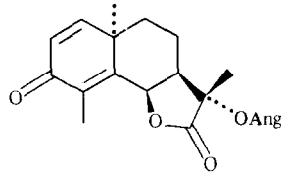

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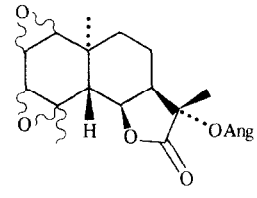

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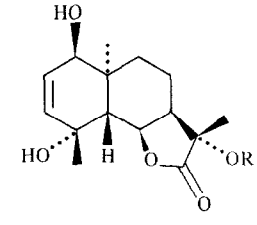
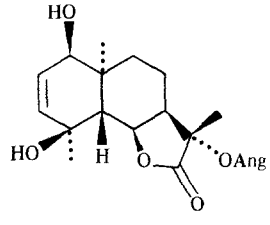


56 R = Ang
57 R = H



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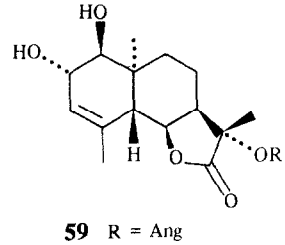
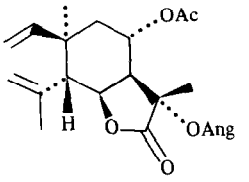


59 R = Ang
60 R = H



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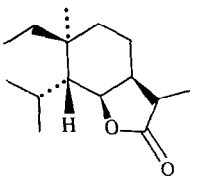

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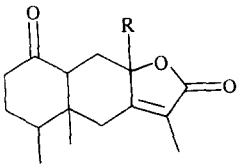
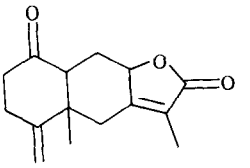


63 R = OH
64 R = H



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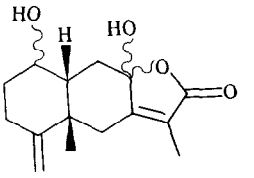

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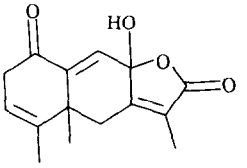

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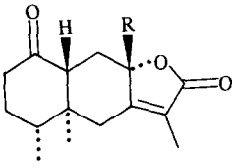
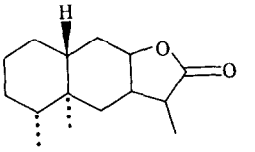


68 R = OH
69 R = H



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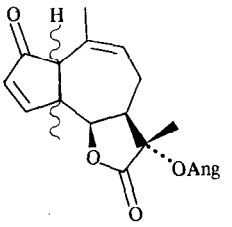


71

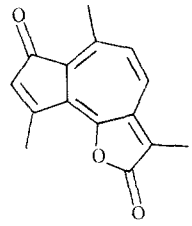
Eudesmanolides

The group of eudesmanolides (selinanolides) from the Umbelliferae, especially from the tribe Laserpitieae, contain a new stereostructural type, represented by the basic structure 5βH,6αH,7αH,10αMe-eudesman-6,12-olide (**43**) with the 7*S*-configuration. This is found in isosilerolide (**44**) [36], silerolide (**45**) [37], lasolide (**46**) [37] and isolasolide (**47**) [3]. We correlated these lactone configuration by chemical means and by ^{1}H NMR spectroscopy [37]. We also confirmed this new stereostructural type of eudesmanolide by X-ray analysis in the case of isosilerolide (**44**) [38].

Similarly as with the guaianolides, we also found among the eudesmanolides that 6,12-eudesmanolides with a *trans*- and *cis*-annellated γ-lactone ring may be distinguished on the basis of δH-6 and $J_{6,7}$ values in their ^{1}HNMR spectra [37]. On the basis of these values, we therefore revised the stereostructures of earlier described eudesmanolides isolated from members of the Umbelliferae, especially from the tribe Peucedaneae. Thus badkhysidin, badkhysinin, dehydro-oopodin, feropodin, oopodin and oxylactone (see ref. [39]), should now be represented by formulae **48–53** [37]. For decipienins A, B, D, E, F, G and H, isolated from *Melanoselinum decipiens* (Schrader-Wendl.) Hoffm. (tribe Laserpiticae) [40–42], the value of δH-6 in their ^{1}H NMR spectra indicates a *cis*-annellation of the γ-lactone ring with respect to the six-membered homocycle. Some evidence, especially the δH-7 shift to higher field on esterification of the hydroxyl group at C-11, indicates an opposite configuration at C-11 to that which has been published [40–42]. Therefore we assume that decipienins A, B, D, E, F, G and H should have structures represented by formulae **54–60** [37].

Elemanolides

Only a single elemanolide has beeen detected so far in the family, i.e. isolaserolide (**61**) in *Laser trilobum* [28], the structure of which, including relative and absolute configuration, follows from the chemical correlation with laserolide (**1**) [43]. Isolaserolide (**61**) is the first representative of the stereostructural type derived from



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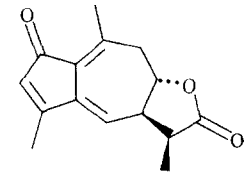

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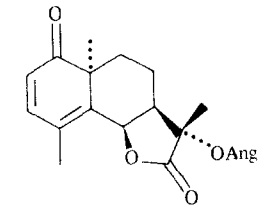

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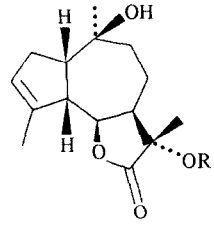
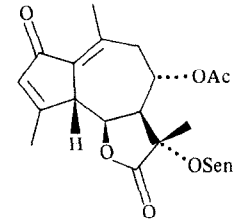


77 R = Sen
80 R = Ang



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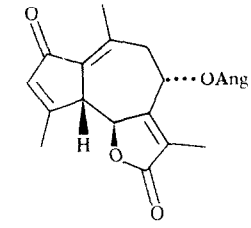

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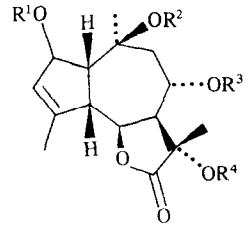
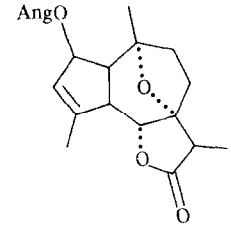


78 R^1 = Ang; R^2 = Ac; R^3 = Mebu; R^4 = H
79 R^1 = Ang; R^2, R^4 = Ac; R^3 = Mebu
88 R^1 = H; R^2, R^4 = Ac; R^3 = Ang



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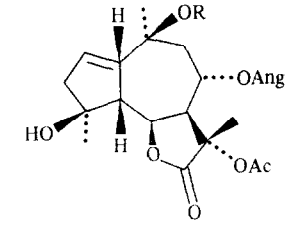
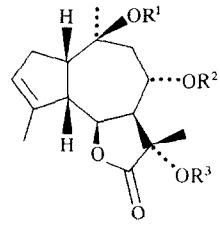
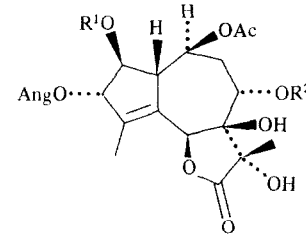


87 R = H
89 R = Ac



81 R^1, R^3 = Ac; R^2 = Mebu
83 R^1 = H; R^2 = Ang; R^3 = Ac
84 R^1 = Ac; R^2, R^3 = Ang
85 R^1 = H; R^2, R^3 = Ang
86 R^1, R^2 = H; R^3 = Ac
90 R^1, R^3 = Ac; R^2 = H
91 R^1, R^3 = Ac; R^2 = iBu
92 R^1 = H; R^2 = iBu; R^3 = Ac
93 R^1 = H; R^2 = Mebu; R^3 = Ac
94 R^1 = H; R^2 = Sen; R^3 = Ac



95 R^1 = Ang; R^2 = Bu
96 R^1 = iVal; R^2 = Bu
97 R^1 = Oct; R^2 = H (8β–O)
98 R^1 = Hex; R^2 = H (8β–O)
99 R^1 = Ang; R^2 = Sen
100 R^1 = Ang; R^2 = Mebu
101 R^1, R^2 = Sen
102 R^1 = Sen; R^2 = Mebu
103 R^1 = Oct; R^2 = Mebu
104 R^1 = Meoct; R^2 = Mebu
105 R^1 = Meoct; R^2 = Mebu
107 R^1 = Mehept; R^2 = Mebu

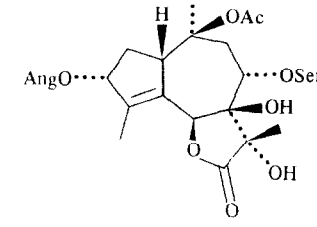


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Table 1. Species of the Umbelliferae containing sesquiterpene lactones

Species (synonym)	Tribe*	Sesquiterpene lactone (synonym)	Formula	Reference†
Ferula badchysi Korov. [49] (*F. oopoda* Aitch.)	Peuc.	Badkhysidin	**48**‡	50, 21
		Badkhysin	**38**‡	51, 21
		Dehydrooopodin	**50**	52, 37
Ferula diversivittata Regel et Schmalh. [49] (*F. suaveolens* Aitch. et Hemsl. or *F. sintenisii* Wollf)	Peuc.	Malafil	**25**	53, 54, 21
		2-Oxo-8α,11α-diangeloyloxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (4-angeloyloxypruteninone-10, talasin A)	**23**	53, 54, 21
Ferula gigantea B. Fedtsch [49] (*Ferula gigas* K.-Pol.)	Peuc.	Fegvolide	**34**	26, 21
		Ferugolide	**29**	25, 21
		Giferolide	**28**	25, 21
		Gigantolide	**30**	25, 21
		Malafil	**25**	25, 21
		Malafilin	**26**	25, 21
		Malafilinin	**27**	25, 21
		2-Oxo-8α,11α-diangeloyloxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (4-angeloyloxypruteninone-10, talasin A)	**23**	25, 21
Ferula grigoriewii B. Fedtsch. [49]	Peuc.	Grilactone	**16**	55, 16, 17
Ferula litwinoviana K.-Pol. [49]	Peuc.	Malafil	**25**	56, 21
		Malafilin	**26**	56, 21
		2-Oxo-8α,1α-diangeloyloxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (4-angeloyloxypruteninone-(10), talasin A)	**23**	56, 21
Ferula malacophylla M. Pimenov et J. Baranova [57]	Peuc.	Malafil	**25**	24, 21
		Malafilidin	**72**	58
		Malafilin	**26**	24, 21
		Malafilinin	**27**	59, 21
		2-Oxo-8α,11α-diangeloyloxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (4-angeloyloxypruteninone-10, talasin A)	**23**	24, 21
Ferula olgae Regel et Schmalh. [49]	Peuc.	Oferin	**32**	23, 21
		Olgin	**31**	23, 21
		Olgoferin	**33**	23, 21
		2-Oxo-8α-angeloyloxy-11α-acetoxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (4-acetoxypruteninone-10, laferin)	**20**	23, 21
		2-Oxo-8α,11α-diangeloyloxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (4-angeloyloxypruteninone-10, talasin A)	**23**	23, 21
		2-Oxo-8α-angeloyloxy-11α-isobutyryloxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (talasin B)	**24**	23, 21
Ferula oopoda (Boiss. et Buhsc) Boiss. [49]	Peuc.	Badkhysidin	**48**‡	50, 37
		Badkhysin	**38**‡	51, 21
		Badkhysinin	**49**	60, 37
		Dehydrooopodin	**50**	61, 37
		Feropodin	**51**‡	62, 37

Table 1. (*Continued*)

Species (synonym)	Tribe*	Sesquiterpene lactone (synonym)	Formula	Reference†
		Ferulidin	**37**‡	63, 21
		Ferulin	**73**‡	64, 65
		Grilactone	**16**	66, 16, 17
		Oopodin	**52**‡	67, 37
		Oxylactone	**53**‡	68, 37
		Semopodin	**74**§	69
Ferula penninervis Regel et Schmalh. [49]	Peuc.	Fegolide	**75**§	70
		Ferolide	**76**§	71
		Grilactone	**16**	72, 16, 17
Ferula varia (Schrenck) Trautv. [57] (*F. shair* Borzcz.)	Peuc.	2-Oxo-8α-angeloyloxy-11α-acetoxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (4-acetoxypruteninone-10, laferin)	**20**	73, 21
		Shairidin	**77**	73, 18
Guillonea scabra (Cav.) Cosson [74] (*Laserpitium scabrum* Cav.)	Las.	Badkhysin	**38**‡	75, 21
		8-Desangeloylshairidin	**17**	18, 19
		Guillonein	**18**	19, 20
		Malafilinin	**27**	75, 21
		Shairidin	**77**	18
Laser trilobum (L.) Borkh. [74] (*Siler trilobum* (L.) Crantz or *Laserpitium trilobum* L.)	Las.	2β-Angeloyloxy-8α-(2′-methyl)butyryloxy-10β-acetoxy-11α-hydroxyslov-3-enolide	**78**	1, 3
		2β-Angeloyloxy-8α-(2′-methyl)butyryloxy-10β,11α-diacetoxyslov-3-enolide (Archangelolide)	**79**	1, 3
		8-Deacetoxylaserolide	**2**	1, 3
		10β-Hydroxy-11α-angeloyloxyslov-3-enolide	**80**	1, 3
		Isolaserolide	**61**	28, 2, 1
		Isolasolide	**47**	1, 3
		Isotrilobolide	—	28
		Laserolide	**1**	28, 2, 1
		Lasolide	**46**	28, 1, 37
		γ-Lactone	—	76
		8α-(2′-Methyl)butyryloxy-10β,11α-diacetoxyslov-3-enolide	**81**	1, 3
		Trilobolide	**39**	77, 28, 1
		(Silerin)		34, 35
Laserpitium archangelica Wulf. [74]	Las.	2β-Angeloyloxy-8α-(2′-methyl)butyryloxy-10β,11α-diacetoxyslov-3-enolide (Archangelolide)	**79**	15, 1
Laserpitium gallicum L. [74]	Las.	Gallicolide	**3**	4
Laserpitium krapfii Crantz subsp. *krapfii* [75] (*L. marginatum* Waldst. et Kit. or *L. alpinum* Waldst. et Kit.)	Las.	8α-Angeloyloxy-10β-acetoxy-1βH,5βH,6αH,7αH,11αH-guaian-6,12-olide	**12**	78, 13, 12
		Guaianolide	**82**‖	78
Laserpitium prutenicum L. [74] (*L. selinoides* Crantz)	Las.	2-Oxo-8α-angeloyloxy-11α-acetoxy-5βH,6αH,7αH-guai-3,10(14)-dien-6,12-olide (4-acetoxyisopruteninone-10)	**35**	22, 21
		2-Oxo-8α-angeloyloxy-11α-acetoxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-		

		olide (4-acetoxypruteninone-10, laferin)	**20**	22, 21
		2-Oxo-8α,11α-diangeloyloxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (4-angeloyloxypruteninone-10, talasin A)	**23**	22, 21
		11α-Angeloyloxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (prutenin)	**36**	22, 21
Laserpitium siler L. subsp. *garganicum* [74]	Las.	8α-Angeloyloxy-10β,11α-diacetoxyslov-3-enolide (acetylisomontanolide)	**11**	79, 10
		8α-Angeloyloxy-10β-hydroxy-11α-acetoxyslov-3-enolide (isomontanolide)	**83**	79, 10
		8α,11α-Diangeloyloxy-10β-acetoxyslov-3-enolide	**84**	79
		8α,11α-Diangeloyloxy-10β-hydroxyslov-3-enolide (gradolide, tarolide)	**85**	79, 14
		Isosilerolide	**44**	79, 36, 37
Laserpitium siler L. subsp. *siler* [74]	Las.	8α-Angeloyloxy-10β,11α-diacetoxyslov-3-enolide (acetylisomontanolide)	**11**	80, 10
		8α-Angeloyloxy-10β-hydroxy-11α-acetoxyslov-3-enolide (isomontanolide)	**83**	80, 10
		8α,11α-Diangeloyloxy-10β-hydroxyslov-3-enolide (gradolide, tarolide)	**84**	81, 14
		8α,10β-Dihydroxy-11α-acetoxyslov-3-enolide	**86**	11
		4β,10β-Dihydroxy-8α-angeloyloxy-11α-acetoxyslov-2-enolide	**87**	11
		2α-Hydroxy-8α-angeloyloxy-10β,11α-diacetoxyslov-3-enolide	**88**	11
		4β-Hydroxy-8α-angeloyloxy-10β,11α-diacetoxyslov-2-enolide	**89**	11
		8α-Hydroxy-10β,11α-diacetoxyslov-3-enolide	**90**	11
		8α-Isobutyryloxy-10β,11α-diacetoxyslov-3-enolide (polhovolide)	**91**	14
		8α-Isobutyryloxy-10β-hydroxy-11α-acetoxyslov-3-enolide	**92**	11
		Isosilerolide	**44**	11, 36, 37
		γ-Lactone	—	81
		8α-(2'-Methyl)butyryloxy-10β-hydroxy-11α-acetoxyslov-3-enolide	**93**	11
		8α-Senecioyloxy-10β-hydroxy-11α-acetoxyslov-3-enolide (montanolide)	**94**	82, 10
		Silerolide	**45**	82, 37
		Trilobolide	**39**	11, 1, 34, 35
Melanoselinum decipiens (Schrader et Wendl. Hoffm. [74] (*Thapsia decipiens* (Schrader et Wendl.) Hooker f.)	Las.	Decipienin A	**54**	40, 37
		Decipienin B	**55**	40, 37
		Decipienin C	**71**	41
		Decipienin D	**56**	41, 37
		Decipienin E	**57**	41, 37
		Decipienin F	**58**	41, 37
		Decipienin G	**59**	42, 37
		Decipienin H	**60**	42, 37
Smyrnium connatum Boiss. et Kotschy [83]	Smyr.	Istanbulin C	**65**	45
Smyrnium apiifolium Willd. (*S. creticum* Miller or *S. aeolicum* Cand.)	Smyr.	Istanbulin D	**66**	46
		Istanbulin E	**67**	46
Smyrnium olusatrum L. [74] (*S. vulgare* S. F. Gray)	Smyr.	Istanbulin A	**68**	44, 47
		Istanbulin B	**69**	44, 47
Smyrnium rotundifolium Miller [74]	Smyr.	1β,10α-Epoxy-4-methoxyglechomanolide	**7**	9
		1β,10α-Epoxy-4-methoxy-8-hydroxyglechomanolide	**6**	9
Talasia transiliensis (Herd.) Korov. [49] (*Peucedanum transiliense* Herd.)	Peuc.	2-Oxo-8α,11α-diangeloyloxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (talasin A)	**23**	84, 85, 21
		2-Oxo-8α-angeloyloxy-11α-isobutyryloxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (talasin B)	**24**	84, 85, 21

Table 1. (*Continued*)

Species (synonym)	Tribe*	Sesquiterpene lactone (synonym)	Formula	Reference†
Thapsia garganica L. [74] (*T. decussata* Lag.)	Las.	Thapsigargin	**40**	31, 35
		Thapsigargicin	**41**	31, 35
		Thapsivillosin I	**95**	32
		Thapsivillosin J	**96**	32
		Triester 1	**97** ¶	86
		Triester 2	**98** ¶	86
Thapsia maxima Miller [74]	Las.	Thapsivillosin A	**99**	31, 32
		Thapsivillosin B	**100**	31, 32
		Thapsivillosin H	**101**	32
Thapsia transtagana Brot. [83]	Las.	Thapsitranstagin	**102**	31, 32
Thapsia villosa L. [74]	Las.	Thapsigargin	**40**	31, 32
		Thapsivillosin A	**99**	31, 32
		Thapsivillosin B	**100**	31, 32
		Thapsivillosin C	**103**	31, 32
		Thapsivillosin D	**104**	31, 32
		Thapsivillosin E	**105**	31, 32
		Thapsivillosin F	**106**	31, 32
		Thapsivillosin G	**107**	32
		Trilobolide	**39**	31, 1, 34, 35

*According to ref. [48]; Las. = Laserpitieae; Peuc. = Peucedaneae; Smyr. = Smyrnieae.

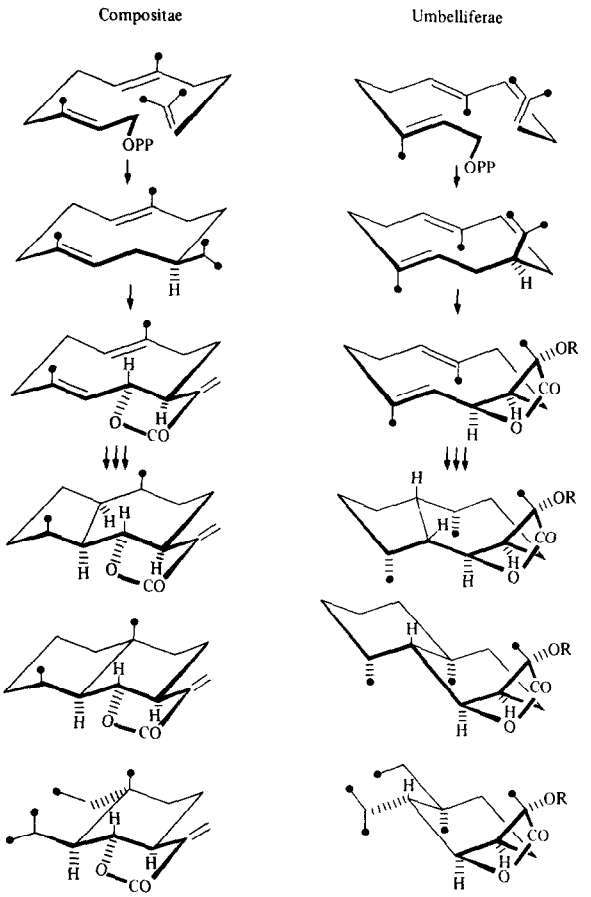
†First reference(s): The first described identification of the compound in the mentioned species. Last reference(s): The last published structure.

‡The configuration of the C-11 methyl group cannot be unequivocally assigned from the data available.

§Stereostructure completed by authors (M.H and M.B.).

‖The structure highly improbable.

¶The configuration on C-1, C-2, C-3 and C-10 changed by authors (M.H. and M.B.).



Scheme 2

5βH,6αH,7αH,10α Me-eleman-6,12-olide (**62**) with the 7*S*-configuration [1, 2].

Eremophilanolides

Eremophilanolides are represented in the family by istanbulins A [44], B [44], C [45], D [46] and E [46] (**63–67**), which occur in the genus *Smyrnium* (tribe Smyrnieae). A study of the stereostructures of istanbulins A and B indicated that their relative and absolute configurations could be expressed by formulae **68** and **69** [47]. These two lactones are the first representatives of the stereostructural type of eremophilanolide, characterized by the basic skeleton, 4*R*,5*S*,10*R*-eremophilan-8,12-olide (**70**) [47]. This type of eremophilanolide is probably structurally related to the furodiene **8** and the germacranolides **6** and **7**, which were isolated from *Smyrnium rotundifolium* [9]. As with the istanbulins, compounds **6–8** also have the γ-lactone group with the double bond between C-7 and C-11 closed at C-8.

Pseudoguaianolides

A single pseudoguaianolide has been described so far, i.e. decipienin C (**71**) in *Melanoselinum decipienes* [41]. The stereostructure of this natural compound contains a *cis*-annellated γ-lactone ring with a seven-membered homocycle, but the relative configurations of the chiral centres at C-1 and C-5 have not yet been determined [41].

All umbellifer species in which sesquiterpene lactones have been described so far, are listed in Table 1, together with the names of the lactones identified.

DISCUSSION

The newly proven structures of sesquiterpene lactones isolated from members of the Umbelliferae, especially their relative and absolute configurations, indicates that all skeletal types determined so far (germacranolides, guaianolides, eudesmanolides, eremophilanolides and elemanolide) have a different stereostructure from the analogous skeletal types of sesquiterpene lactones obtained from the species of the Compositae. Therefore the possibility must be considered that the conformation of the *trans, trans*-farnesyl diphosphate precursor in the great majority of the species of Compositae (in which the 'usual' types of sesquiterpene lactones are synthesized) is different from that which gives rise to the sesquiterpene lactones of the Umbelliferae. The biogenetic steps leading to the sesquiterpene lactones in these two plant families form two parallel series and proceed very probably in both families by similar reactions, as indicated in Scheme 2.

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