THE STRUCTURE OF 2-OXO-8α-ANGELOYLOXY-11α-ACETOXY-5βH,6αH,7αH-GUAI-1(10),3-DIEN-6,12-OLIDE, A SESQUITERPENIC LACTONE FROM *Laserpitium prutenicum* L. REVISION OF THE STEREOSTRUCTURES OF NATIVE 2-OXOGUAI-1(10),3-DIEN-6,12-OLIDES FROM THE SPECIES OF THE *Umbelliferae* FAMILY*

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On the basis of an analysis of its NMR spectra and X-ray analysis the stereostructure of the so-called 4-acetoxypruteninone-(10) (laferin) has been corrected to that of formula *I*. The stereostructures of almost all so far described native 2-oxoguai-1(10),3-dien-6,12-olides isolated from the species of *Umbelliferae* have been corrected on the basis of ^{1}H NMR parameters.

In connection with a systematic study of sesquiterpenic lactones of the species of the *Umbelliferae* family we investigated the species *Laserpitium prutenicum* L. (*Laserpitieae* tribe). This plant material was analyzed by Bohlmann and Zdero[1] a number of years ago. Of the four sesquiterpenic lactones described by them we now investigated lactone *I* which these authors called 4-acetoxypruteninone-(10) in accordance with the different numbering of the guaiane skeleton used at that time, and proposed[1] for it the structure *Ia*. Later, this lactone was obtained under the name laferin from *Ferula olgae* REGEL. et SCHMALH. (*Umbelliferae* family, *Peucedaneae* tribe), and its originally proposed structure was corrected[2] to *Ib*. From the point of view of components – sesquiterpenic lactones – lactone *I* represents a connection between the *Laserpitieae* and *Peucedaneae* tribe (for example the genera *Laserpitium* and *Ferula*, respectively), as do some further sesquiterpenic lactones, as for example shairidin (*II*), isolated from *Ferula varia* (SCHRENK) TRAUTV. (*Peucedaneae*)[3] and *Guillonea scabra* (CAV.) COSSON (*Laserpitieae*)[4], or malafilinin (*III*), obtained from *F. mallacophyla* M. PIMENOV et J. BARANOVA[5], and also from *G. scabra*[6].

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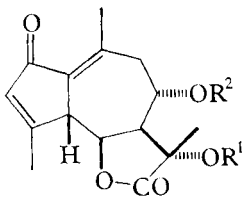
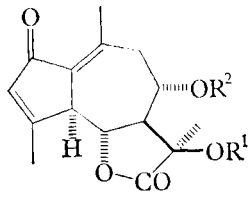
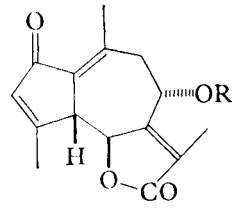
In the species of the *Laserpitieae* tribe guaianolides of predominantly slov-3-enolide type have been found so far, *i.e.* 1βH,5βH,6αH,7αH-guai-3-en-6,12-olide with 7(*R*) configuration[7] (*IV*), while in the species of the *Peucedaneae* tribe they were guaianolides of predominantly 2-oxoguai-1(10),3-dien-6,12-olide[7] (*V*) type. The stereostructures of the guaianolides of the mentioned type *V* from the species of *Umbelliferae* described so far and derived by means of X-ray structural analysis, *i.e.* grilactone[8] (*VI*), desangeloylshairidin[9] (*VII*), and guillonein[10] (*VIII*), indicated that the stereostructures of the guaianolides of type *V* described so far, from the species *Umbelliferae*, for which originally the structures based on 2-oxo-5αH,6βH,7αH-guai-1(10),3-dien-6,12-olide[7] (*IX*) were proposed, will not be correct. We supposed that the study of the structure of lactone *I*, especially by means of ^{1}H NMR spectroscopy and X-ray structural analysis would confirm the structure of this substance assumed by us, based on 2-oxo-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide[7] (*X*), and bring further evidence for the solution of the stereostructures of guaianolides from the species of *Umbelliferae*.



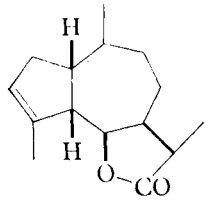
I: R^1 = Ac; R^2 = Ang
III: R^1 = Ac; R^2 = Bzl
XXX: R^1, R^2 = Ang
XXXII: R^1 = Ang; R^2 = Ver
XXXIII: R^1 = Sen; R^2 = Ans
XXXIV: R^1 = Sen; R^2 = Bzl
XXXV: R^1 = Ac; R^2 = Ans
XXXVI: R^1 = Sen; R^2 = Ver
XXXVII: R^1 = Ac; R^2 = Ver
XXXVIII: R^1 = i But; R^2 = Mac
XXXIX: R^1 = Ac; R^2 = Mac
XL: R^1, R^2 = Mac
XLI: R^1 = i But; R^2 = Ang



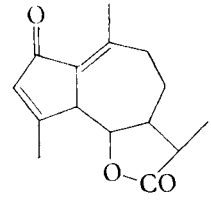
Ia: R^1 = Ang; R^2 = Ac
Ib: R^1 = Ac; R^2 = Ang



II: R = Ang
VII: R = H



IV



V

The results of X-ray structural analysis of lactone *I* show (Fig. 1) that the configuration at the ring junction is such that H(5), O(6), and C(11) are all above the approximate plane of the seven-membered ring (*i.e.* they are all β) and hence that the configuration is 5βH,6αH, and 7αH. Moreover, since the acetoxy group is at C(11) and the angeloyloxy group is at C(8), and both are α, the structure of the studied lactone is that depicted in *I*. The molecule should presumably be renamed 2-oxo-

-8α-angeloyloxy-11α-acetoxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide. Hence the structures *Ia* and *Ib*, initially assigned[1,2] and subsequently cited in the authoritative reviews by Fisher and coworkers[11] and by Seaman[12], are not correct. The structural analysis demonstrates that the ring junction configuration in this compound is analogous to that in the slovanolides[13] and in grilactone[8]. The atomic positional parameters, principal bond lenghts and angles are listed in Tables I–III.

The seven-membered substituted cycloheptene ring adopts a flattened chair conformation, the approximate mirror plane passing through C(10) and the midpoint of the C(6)–C(7) bond. Thus, the flattening is such that the atoms C(5), C(1), C(10), C(9), and C(8) are approximately co-planar (maximum deviation 0·073 (6) Å) while atoms C(6) and C(7) are both above this plane (1·264 (6) and 1·067 (6) Å, respectively).

The cyclopentenone ring is approximately planar, with no atom deviating by more than 0·020 (6) Å from the least-squares plane. A similar result was observed by Ruban and coworkers[14] in the structure of lactucin (*XI*), which also contains a keto

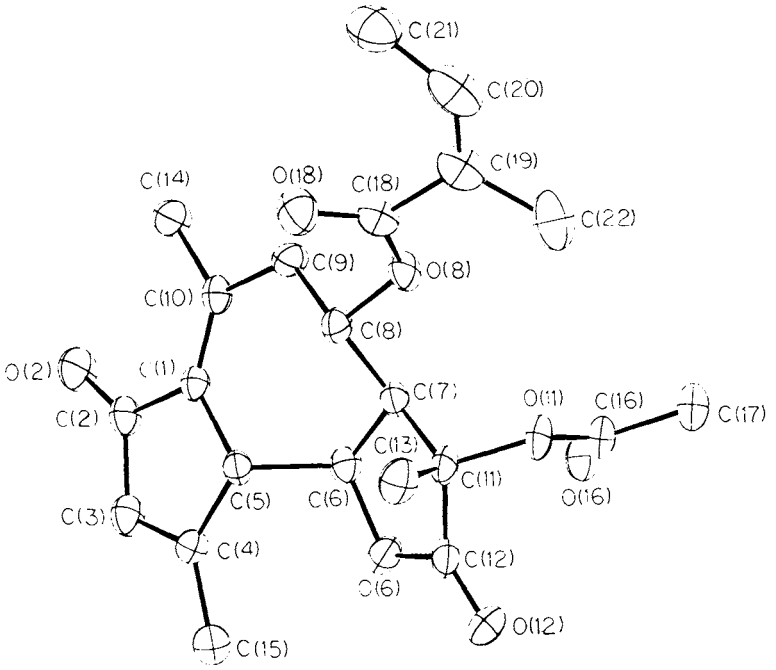
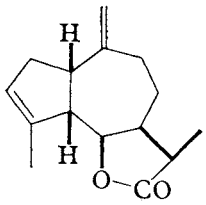
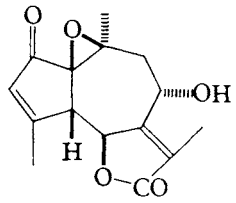


FIG. 1

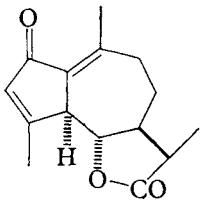
View of one molecule of lactone *I*. Thermal ellipsoids are drawn at the 47% probability level; hydrogen atoms are omitted for clarity



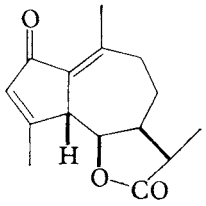
VI



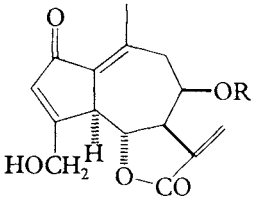
VIII



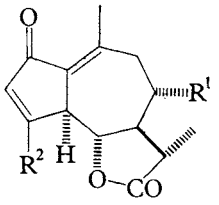
IX



X



XI: R = H
XIII: R = Phac-OH



XII: R^1 = OAc; R^2 = CH_3
XIV: R^1 = H; R^2 = CH_3
XV: R^1 = OH; R^2 = CH_2OH
XXV: R^1 = OAc; R^2 = CHO
XXVI: R^1 = H; R^2 = CH_2OAc

group at C(2) and double bonds at C(1)=C(10) and C(3)=C(4); the average magnitude of the endocyclic torsion angles in the cyclopentenone moiety in the present case is 2·3°, while in lactucin[14] (*XI*) it is only 0·7°. As is common[8,15,16] in *cis*-fused γ-lactones, the lactone ring is also fairly flat; in the present structure the maximum torsion angle in the lactone ring is 17·7°, which suggests that this ring is flatter here than in the other slovanolide analogues[8,15,16]. The torsion angles in the molecule are collected in Table IV.

^{1}H and ^{13}C NMR spectra of lactone *I* (data in Table V) are fully consistent with the structure determined by X-ray analysis. The ^{13}C NMR spectrum indicated the presence of 15 carbons in the guaianolide skeleton and 7 signals which were assigned to an acetate and angelate group on the basis of known data for ester groups[17,18]. Of the skeletal carbons the conjugated and the lactone carbonyl could be easily assigned to the signals at δ 194·97 and 173·27. The signals of four olefinic carbons (δ 169·12; 145·15; 136·13, and 129·05) were assigned to carbons C(4), C(10), C(3), and C(1) on the basis of multiplicity (only C(3) at δ 136·13 carries a hydrogen) and a comparison with the ^{13}C NMR data of cyclopentenone[19,20]. The signals at δ 78·43, 77·93, and 67·02 were assigned to sp^3 carbon atoms carrying oxygen, *i.e.* C(6), C(11), and C(8), similarly as the signals at δ 48·00, 47·31, and 43·97 were assigned to carbon

C(5), C(7), and C(9), mainly on the basis of comparison with the ^{13}C NMR data of structurally similar compounds. The assignment of the methyl signals C(13), C(14), and C(15) which occur within a narrow range of δ values, between 20·0 and 20·8, is only tentative. Very important information was obtained from the undecoupled ^{13}C NMR spectrum, where the acetate could be classified[21] as tertiary and localised at C(11) on the basis of the signal of acetate carbonyl (δ 169·91, quartet, J = 3·5 Hz). Hence, the angelate must be in position C(8). In the ^{1}H NMR spectrum

TABLE I

Atomic positional parameters for 2-Oxo-8α-angeloyloxy-11α-acetoxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (*I*)

Atom	*X*	*Y*	*Z*
O(2)	0·7228(4)	0·0769(2)	0·9253(4)
O(6)	0·5773(3)	−0·2338(2)	1·1309(4)
O(8)	0·9444(3)	−0·2639(2)	1·1915(4)
O(11)	0·7587(4)	−0·3894(2)	1·2178(4)
O(12)	0·5322(3)	−0·3437(3)	1·2469(5)
O(16)	0·6812(4)	−0·4021(3)	1·0272(5)
O(18)	1·0466(4)	−0·1833(3)	1·3149(5)
C(1)	0·7504(5)	−0·0496(3)	1·0506(5)
C(2)	0·6903(5)	0·0232(3)	0·9964(6)
C(3)	0·5816(5)	0·0150(4)	1·0435(6)
C(4)	0·5683(5)	−0·0536(3)	1·1130(6)
C(5)	0·6733(5)	−0·0990(3)	1·1283(6)
C(6)	0·6719(5)	−0·1920(4)	1·0851(6)
C(7)	0·7684(5)	−0·2445(3)	1·1275(6)
C(8)	0·8672(4)	−0·1978(4)	1·1700(6)
C(9)	0·9145(5)	−0·1404(4)	1·0690(6)
C(10)	0·8526(5)	−0·0662(3)	1·0228(6)
C(11)	0·7207(5)	−0·3038(3)	1·2277(6)
C(12)	0·6005(5)	−0·3004(4)	1·2034(6)
C(13)	0·7378(6)	−0·2811(4)	1·3643(6)
C(14)	0·9188(6)	−0·0132(4)	0·9375(7)
C(15)	0·4666(5)	−0·0794(4)	1·1731(7)
C(16)	0·7321(6)	−0·4313(4)	1·1108(8)
C(17)	0·7784(7)	−0·5174(4)	1·1195(11)
C(18)	1·0288(5)	−0·2502(4)	1·2628(6)
C(19)	1·0984(5)	−0·3276(5)	1·2696(7)
C(20)	1·1962(7)	−0·3240(5)	1·2791(8)
C(21)	1·2671(6)	−0·2506(5)	1·2802(8)
C(22)	1·0378(7)	−0·4106(4)	1·2589(8)

all hydrogens were structurally assigned and their spin–spin interactions were determined (Table V). Since the configurations on carbons C(5), C(6), C(7), and C(8) are known from X-ray analysis, the coupling constants measured can be used for the determination of the conformation of lactone *I* in solution. The high values of $J_{5,6}$ and $J_{7,8}$ (11·4 and 11·2, respectively) indicate a *trans* arrangement of the hydrogens H(5), H(6) or H(7), H(8), with dihedral angles close to 180°. Only the slightly lower value $J_{6,7}$ = 9·9 Hz requires a dihedral angle ≈0° for *cis*-oriented hydrogens H(6), H(7). The distinctly different values of the constants $J_{8,9}$ and $J_{8,9'}$ (3·4 and 10·9 Hz) indicate a *gauche* and *anti* arrangement of hydrogens in the fragment $-C(8)H-C(9)H_2$ unambigously. The very high observed value of the geminal interaction $J_{9,9'}$ = 19·2 Hz is evidently a consequence of a hyperconjugation contribution ΔJ of the vicinal double bond C(10)=C(1). It is known[22,23] that ΔJ depends on the orientation of the C—H bonds with respect to the π-electrons of the C=C bond and that it is maximum ($\Delta J \approx 4$ Hz) when the C—H bonds make an angle of 30° with the π-electrons. This situation takes place just in the case of lactone *I* in the conformation determined by X-ray analysis in the crystal. Since this conformation also fulfils all the above discussed geometric relations of hydrogens, derived from $J_{H,H}$ values, it may be concluded that the preferred conformation of lactone *I* in solution is in agreement with the spatial arrangement (Fig. 1) found in crystal.

TABLE II
Bond lengths (Å) in lactone *I*

Atoms	Distance	Atoms	Distance
C(1), C(2)	1·501(5)	C(10), C(14)	1·491(5)
C(1), C(5)	1·495(5)	C(11), C(12)	1·527(6)
C(1), C(10)	1·339(5)	C(11), C(13)	1·512(6)
C(2), C(3)	1·455(6)	C(11), O(11)	1·452(5)
C(2), O(2)	1·214(4)	C(12), O(6)	1·347(5)
C(3), C(4)	1·332(5)	C(12), O(12)	1·192(5)
C(4), C(5)	1·510(5)	C(16), C(17)	1·495(7)
C(4), C(15)	1·482(6)	C(16), O(11)	1·361(7)
C(5), C(6)	1·555(5)	C(16), O(16)	1·189(6)
C(6), C(7)	1·538(5)	C(18), C(19)	1·515(6)
C(6), O(6)	1·443(5)	C(18), O(8)	1·317(5)
C(7), C(8)	1·513(5)	C(18), O(18)	1·224(5)
C(7), C(11)	1·544(5)	C(19), C(20)	1·228(7)
C(8), C(9)	1·530(5)	C(19), C(22)	1·531(7)
C(8), O(8)	1·449(4)	C(20,) C(21)	1·470(8)
C(9), C(10)	1·499(5)		

TABLE III
Bond angles (deg) in lactone *I*

Atoms	Angle
C(2), C(1), C(5)	107·4(3)
C(2), C(1), C(10)	123·1(4)
C(5), C(1), C(10)	129·4(3)
C(1), C(2), C(3)	105·4(4)
C(1), C(2), O(2)	128·3(4)
C(3), C(2), O(2)	126·3(4)
C(2), C(3), C(4)	112·5(4)
C(3), C(4), C(5)	110·3(3)
C(3), C(4), C(15)	125·1(4)
C(5), C(4), C(15)	124·5(3)
C(1), C(5), C(4)	104·4(3)
C(1), C(5), C(6)	110·4(3)
C(4), C(5), C(6)	114·7(3)
C(5), C(6), C(7)	115·2(3)
C(5), C(6), O(6)	110·6(3)
C(7), C(6), O(6)	107·0(3)
C(6), C(7), C(8)	117·4(3)
C(6), C(7), C(11)	103·5(3)
C(8), C(7), C(11)	114·3(3)
C(7), C(8), C(9)	113·7(3)
C(7), C(8), O(8)	103·5(3)
C(9), C(8), O(8)	106·8(3)
C(8), C(9), C(10)	120·3(3)
C(1), C(10), C(9)	125·2(4)
C(1), C(10), C(14)	123·5(3)
C(9), C(10), C(14)	111·2(3)
C(7), C(11), C(12)	104·0(4)
C(7), C(11), C(13)	117·4(3)
C(7), C(11), O(11)	113·7(3)
C(12), C(11), C(13)	107·0(4)
C(12), C(11), O(11)	110·1(3)
C(13), C(11), O(11)	104·4(3)
C(11), C(12), O(6)	109·7(4)
C(11), C(12), O(12)	128·3(4)
O(6), C(12), O(12)	121·7(4)
C(17), C(16), O(11)	107·8(6)
C(17), C(16), O(16)	127·9(7)
O(11), C(16), O(16)	124·3(5)
C(19), C(18), O(8)	110·6(4)
C(19), C(18), O(18)	125·9(4)
O(8), C(18), O(18)	123·5(4)

TABLE III
(*Continued*)

Atoms	Angle
C(18), C(19), C(20)	122·5(6)
C(18), C(19), C(22)	114·8(4)
C(20), C(19), C(22)	122·7(6)
C(19), C(20), C(21)	129·7(6)
C(6), O(6), C(12)	112·4(3)
C(8), O(8), C(18)	120·2(3)
C(11), O(11), C(16)	116·3(4)

The earlier erroneous conclusions[1,2] made from the NMR data of lactone *I* and a grave suspicion concerning similar mistakes for a series of further substances led us to an attempt at critical evaluation of the situation and the possibilities of discriminating *trans*- and *cis*-lactones of type *IX* and *X*. An analysis of models shows (Fig. 2) that *trans*-lactones of type *IX* can assume two types of conformation, *A* and *B* (Fig. 2), analogous to the conformations found[10] for guillonein (*VIII*) in crystal (type *A*) and in solution (type *B*). The situation in *cis*-lactones is similar, where two conformational types, *C* and *D* (Fig. 2) can be found, of which type *C* represents the average state of two similar limit forms *C(a)* and *C(b)*, which corresponds to the conformation found in this paper for lactone *I*. Type *D* seems unlikely in view of the unfavourable steric interactions of 1,3-diaxial hydrogens H(5), H(9) with C(11) and may be also C(11)-methyl. In Fig. 2 the values of dihedral angles of $\Phi_{H,H}$ hydrogens in positions 5 to 9 are also presented, as well as the approximate values of the $J_{H,H}$ constants corresponding to these angles on the basis of the described relationship $J_{H,H} = f(\Phi)$ (ref.[24]). It is evident from the figure that the value $J_{5,6}$ will be approximately the same for *cis*- and *trans*-lactones in all conformational types *A* to *D*. Similarly, in $J_{6,7}$ very similar values (≥ 10 Hz) may be expected for *trans*-lactones (types *A*, *B*) and *cis*-lactones in the conformation of type *C*. The limit forms *C(a)* and *C(b)* could have slighly lower values, and type *D* distinctly lower values. However the occurence of the latter type is not very probable. Since Fig. 2 shows even for constants $J_{7,8}$ and $J_{8,9}$ that analogous values as in *cis*-lactone with conformation of *C*-type can be found at least in one of the possible conformations (*A*, *B*) of the *trans*-lactone, it is evident that the utilization of vicinal $J_{H,H}$ only for the differentiation between *trans* and *cis*-lactones of type *IX* and *X* is very problematic. Therefore we focussed our attention on the finding of further possible NMR criteria for both groups of lactones of types *IX* and *X*. The available ^{1}H NMR data for these substances indicated distinct differences in chemical shifts of hydrogens H(6) the

TABLE IV
Torsion angles (deg) in lactone *I*

Atom 1	Atom 2	Atom 3	Atom 4	Angle
C(10)	C(1)	C(2)	C(3)	176·2
C(5)	C(1)	C(2)	C(3)	0·3
C(10)	C(1)	C(2)	O(2)	— 1·8
C(5)	C(1)	C(2)	O(2)	—177·7
C(1)	C(2)	C(3)	C(4)	— 2·5
O(2)	C(2)	C(3)	C(4)	175·5
C(2)	C(3)	C(4)	C(15)	—179·6
C(2)	C(3)	C(4)	C(5)	3·7
C(3)	C(4)	C(5)	C(1)	— 3·3
C(3)	C(4)	C(5)	C(6)	—124·2
C(15)	C(4)	C(5)	C(1)	180·0
C(15)	C(4)	C(5)	C(6)	59·0
C(4)	C(5)	C(1)	C(2)	1·6
C(4)	C(5)	C(1)	C(10)	—173·9
C(6)	C(5)	C(1)	C(2)	125·4
C(6)	C(5)	C(1)	C(10)	— 50·2
C(1)	C(5)	C(6)	C(7)	76·0
C(4)	C(5)	C(6)	C(7)	—166·4
C(1)	C(5)	C(6)	O(6)	—162·5
C(4)	C(5)	C(6)	O(6)	— 45·0
C(5)	C(6)	C(7)	C(8)	— 17·9
C(5)	C(6)	C(7)	C(11)	109·1
O(6)	C(6)	C(7)	C(8)	—141·3
O(6)	C(6)	C(7)	C(11)	— 14·3
C(6)	C(7)	C(8)	C(9)	— 59·4
C(6)	C(7)	C(8)	O(8)	—174·9
C(11)	C(7)	C(8)	C(9)	179·1
C(11)	C(7)	C(8)	O(8)	63·6
C(7)	C(8)	C(9)	C(10)	65·2
O(8)	C(8)	C(9)	C(10)	178·6
C(8)	C(9)	C(10)	C(1)	— 9·0
C(8)	C(9)	C(10)	C(14)	172·7
C(9)	C(10)	C(1)	C(5)	— 1·7
C(14)	C(10)	C(1)	C(5)	176·4
C(9)	C(10)	C(1)	C(2)	—176·7
C(14)	C(10)	C(1)	C(2)	1·5
C(6)	C(7)	C(11)	C(12)	17·7
C(6)	C(7)	C(11)	C(13)	—100·3
C(6)	C(7)	C(11)	O(11)	137·4
C(8)	C(7)	C(11)	C(12)	146·6
C(8)	C(7)	C(11)	C(13)	28·6

TABLE IV
(*Continued*)

Atom 1	Atom 2	Atom 3	Atom 4	Angle
C(8)	C(7)	C(11)	O(11)	− 93·7
C(7)	C(11)	C(12)	O(6)	− 16·0
C(7)	C(11)	C(12)	O(12)	169·7
C(13)	C(11)	C(12)	O(6)	109·0
C(13)	C(11)	C(12)	O(12)	− 65·3
O(11)	C(11)	C(12)	O(6)	−138·2
O(11)	C(11)	C(12)	O(12)	47·6
C(11)	C(12)	O(6)	C(6)	7·2
O(12)	C(12)	O(6)	C(6)	−178·1
C(12)	O(6)	C(6)	C(7)	4·8
C(12)	O(6)	C(6)	C(5)	−121·3
C(7)	C(11)	O(11)	C(16)	− 64·1
C(12)	C(11)	O(11)	C(16)	52·1
C(13)	C(11)	O(11)	C(16)	166·7
C(11)	O(11)	C(16)	O(16)	0·3
C(11)	O(11)	C(16)	C(17)	−179·9
C(7)	C(8)	O(8)	C(18)	−160·3
C(9)	C(8)	O(8)	C(18)	79·4
C(8)	O(8)	C(18)	C(19)	−179·1
C(8)	O(8)	C(18)	O(18)	0·7
O(8)	C(18)	C(19)	C(20)	147·2
O(18)	C(18)	C(19)	C(20)	− 32·6
C(18)	C(19)	C(20)	C(21)	− 3·1
C(22)	C(19)	C(20)	C(21)	174·6

values of which occur in two different ranges, δ 3·2 – 3·9 or 4·5 – 4·9. At the same time H(6) should not be affected more distinctly by substitution effects, because structural changes take place on carbons C(8), C(11) or C(15), while the neighbouring C(5) and C(7) remain without change. Hence, it may be concluded that there is a dependence between the chemical shift of H(6) and the type of annellation of the lactone cycle. Of the two compounds *I* and *XI*, the structures of which were demonstrated by X-ray analysis, lactucin (*XI*) with the *trans*-annellated lactone and $\delta_{H(6)} = 3{\cdot}65$ belongs to the first group and lactone *I* with the *cis*-annellated lactone and $\delta_{H(6)} = 4{\cdot}66$ to the second one. A further striking difference between the NMR parameters of compounds *XI* and *I* is in the value of the geminal coupling constant $J_{9,9'}$ (13·8 and 19·2 Hz, respectively). A detailed analysis of data showed that in all cases with an indicated $J_{9,9'}$ value the low absolute value of this constant (13 to 14 Hz) is accompanied by low $\delta_{H(6)}$ values (3·2 – 3·6), and high $J_{9,9'}$ values (18 to

19·5 Hz) accompany higher $\delta_{H(6)}$ values (4·5–4·9). This indicates the possibility of differentiating *trans*- and *cis*-lactones of type *IX* and *X* on the basis of $\delta_{H(6)}$ and $J_{9,9'}$. The distinct downfield shift of H(6) in the case of *cis*-lactones *X* (in contrast to *trans*-lactones *IX*) is probably a consequence of the van der Waals effect[25] which has its origin in the steric interaction of *cis*-oriented hydrogens H(6) and H(7). This interaction does not occur in *trans*-lactones. A similar effect should be also detectable

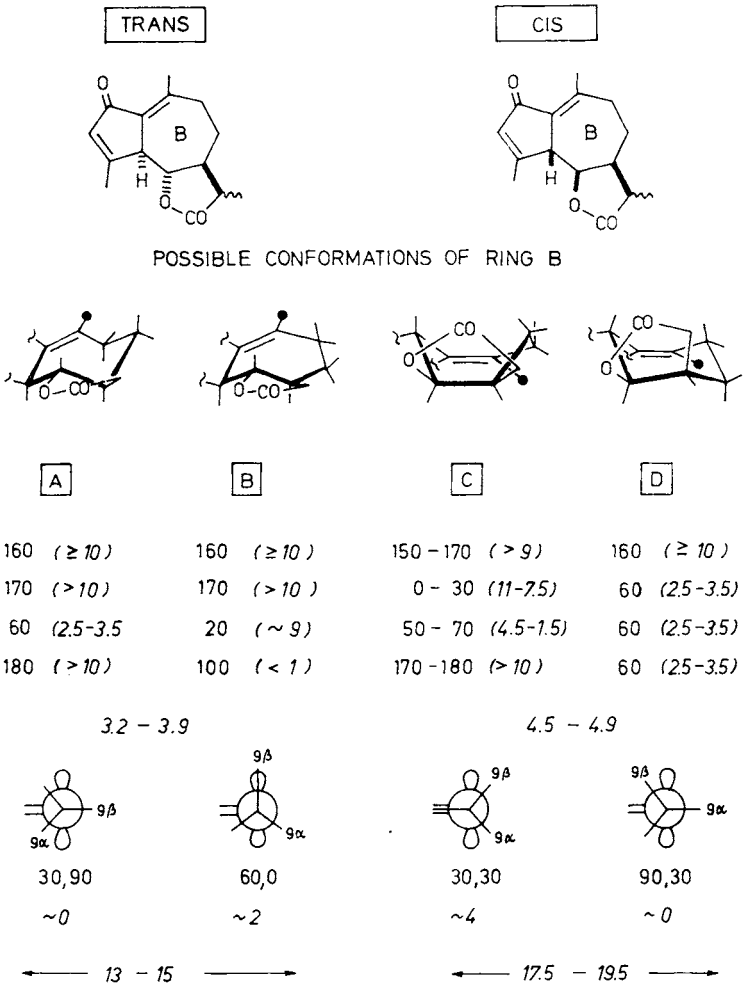


FIG. 2

Conformational and ^{1}H NMR characteristics of *trans*- and *cis*-2-oxoguai-1(10)3-dien-6,12-olides

on hydrogen H(7). However, the shift of H(7) is distinctly affected by the substitution at C(8) and C(11) and it is thus not generally utilisable for the differentiation of *cis*- and *trans*-lactones. As for the $J_{9,9'}$ value its dependence on the orientation to the neighbouring double bond C(10)=C(1) may be expected. As shown in Fig. 2, in *cis*-lactones in the most probable conformation *C* there exist optimum conditions for a maximal hyperconjugation contribution ($\Delta J \geqq 4$ Hz) of the π-orbitals of the double bond, and thus also for the observation of high absolute $J_{9,9'}$ values. In *trans*-lactones *IX* in conformation *A* the contribution ΔJ is minimum (≈ 0), and it should not exceed ≈ 2 Hz even in conformation *B*. Hence it is evident that the criteria summarized in Fig. 2 have a logical explanation.

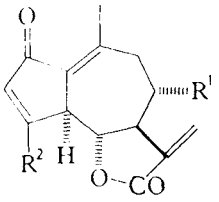
The ^{1}H NMR data of the seven-membered ring hydrogens in so far described *trans*-lactones of type *IX*, with the structures *XI*–*XXIX*, which are consistent with the above mentioned NMR criteria, are surveyed in Table VI. Distinctly different

TABLE V

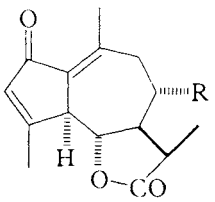
Proton and carbon-13 NMR parameters of lactone *I* in deuteriochloroform

Proton	δ_H	($J_{H,H}$)	Carbon	δ_C
H(3)	6·21 p	($J_{3,15} = 1{\cdot}4$; $J_{3,5} = 1{\cdot}4$)	C(1)	129·05
H(5)	3·58 bd	($J_{5,6} = 11{\cdot}4$; $J_{5,3} = 1{\cdot}4$;	C(2)	194·97
		$J_{5,9} = 1{\cdot}1$; $J_{5,9'} = 1{\cdot}4$)	C(3)	136·13
H(6)	4·66 dd	($J_{6,5} = 11{\cdot}4$; $J_{6,7} = 9{\cdot}9$)	C(4)	169·12
H(7)	3·57 dd	($J_{7,6} = 9{\cdot}9$; $J_{7,8} = 11{\cdot}2$)	C(5)	48·00
H(8)	5·59 dt	($J_{8,7} = 11{\cdot}2$; $J_{8,9} = 3{\cdot}4$;	C(6)	78·43
		$J_{8,9'} = 10{\cdot}9$)	C(7)	47·31
H(9)	2·91 bdd	($J_{9,9'} = 19{\cdot}2$; $J_{9,8} = 3{\cdot}4$;	C(8)	67·02
		$J_{9,5} = 1{\cdot}1$; $J_{9,14} \neq 0$)	C(9)	43·97
H(9′)	2·49 bdd	($J_{9',9} = 19{\cdot}2$; $J_{9',8} = 10{\cdot}9$;	C(10)	145·15
		$J_{9',5} = 1{\cdot}4$; $J_{9',14} \neq 0$)	C(11)	77·93
H(13)	1·60 s	—	C(12)	173·27
H(14)	2·25 bs	—	C(13)	20·00[a]
H(15)	2·25 bs	—	C(14)	20·56[a]
OAc	2·10 s	—	C(15)	20·29[a]
OAng H(3′)	6·23 qq	($J_{3',4'} = 7{\cdot}3$; $J_{3',5'} = 1{\cdot}5$)	Ester groups	
H(4′)	2·05 dq	($J_{4',3'} = 7{\cdot}3$; $J_{4',5'} = 1{\cdot}5$)	OAc C=O	169·91
H(5′)	1·92 p	($J_{5',4'} = J_{5',3'} = 1{\cdot}5$)	CH_3	20·81[a]
			OAng C(1′)	166·29
			C(2′)	126·60
			C(3′)	141·27
			C(4′)	15·93
			C(5′)	20·29[a]

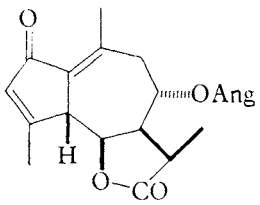
[a] Assignment of signals can be interchanged.



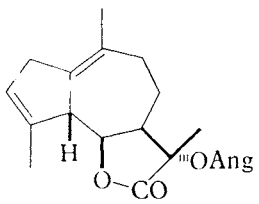
XVI: R^1 = H; R^2 = CH_3
XVII: R^1 = OH; R^2 = CH_3
XVIII: R^1 = OAc; R^2 = CH_3
XIX: R^1 = OAc; R^2 = CH_2OH
XX: R^1 = (*A*); R^2 = CH_2OH
XXI: R^1 = (*B*); R^2 = CH_2OH
XXII: R^1 = OAc; R^2 = CHO
XXIII: R^1 = OMac; R^2 = CHO
XXIV: R^1 = (*C*); R^2 = CHO



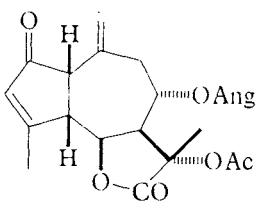
XXVII: R = H
XXVIII: R = OH
XXIX: R = OAc



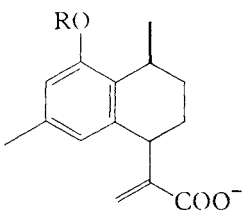
XXXI



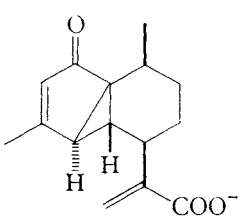
XLII



XLIII



(*A*), R = H
(*B*), R = Ac



(*C*)

Ang = $COC(CH_3)=CH.CH_3$; Bzl = COC_6H_5; Ver = $COC_6H_3(OCH_3)_2(3,4)$; Ac = $COCH_3$; Sen = $COCH=C(CH_3)_2$; Ans = $COC_6H_4(OCH_3)(4)$; Mac = $COC(CH_3)=CH_2$; i But = = $COCH(CH_3)_2$; Phac-OH = $COCH_2C_6H_4OH(4)$

TABLE VI.

Proton NMR parameters of seven-membered ring in *trans*-lactones

Compound	H(5) ($J_{5,6}$)	H(6) ($J_{6,7}$)	H(7) ($J_{7,8}$)	H(8) ($J_{8,9}$; $J_{8,9'}$)	H(9) H(9') ($J_{9,9'}$)	Ref.
Matricarin (*XII*)	3·40 (10·2)	3·72 (9·8)	2·32 (10·1)	4·84 (10·8; 2·1)	2·72 2·39 (13·7)	32
Lactucopicrin[a] (*XIII*)	3·5—3·9 ([b])	3·5—3·9 ([b])	3·33 ([b])	5·00 (10; 2·5)	2·73 2·46 (12·5)	33
Desacetoxymatricarin (*XIV*)	3·35 (10·5)	3·54 (9—10)	[b]	[b]	[b] [b]	34
11β,13-Dihydrolactucin (*XV*)	3·57 (10)	3·65 (10)	2·13 (10)	3·75 (11; 1)	2·71 2·39 (14)	35
XXVI	3·58 (10)	3·81 (10)	2·00 (*b*)	1·87 (*b*)	2·45 2·35 (*b*)	36
XXV	4·31 (10)	3·65 (10)	2·50 (10)	4·88 (11; 2)	2·50 2·81 (13·5)	37
Achilin (*XXVII*)	3·40 (10)	3·84 (9)	[b]	[b]	[b] [b]	38
Grossmizin (*XXVIII*)	3·40 (10)	3·86 (10)	[b] (10)	3·74 ([b]; [b])	[b] [b]	39
8-Acetoxyachilin (*XXIX*)	3·41 (10)	3·90 (10)	[b] (10)	4·76 ([b]; [b])	[b] [b]	39
Dehydroleucodin (*XVI*)	3·60 (10)	3·60 (10)	2·85 (10; 3)	1·40; [b] (12; 2; 3; 5)	2·20 [b] (13)	40
XVII	3·70 (10)	3·27 (10)	3·22 (10)	3·98 (10; 2·5)	[b] [b]	41
11,13-Dehydromatricarin (*XVIII*)	3·52 (10)	3·72 (10)	3·27 (10)	4·92 (10; 2)	2·73 2·47 (13)	41
XIX	3·31 (*b*)	3·31 (10·5)	3·26 (10·5)	4·93 (10·5; 2·2)	2·50 2·74 (13·5)	37
XX	3·67 (*b*)	3·67 (10·5)	3·20 (10·5)	4·99 (10·5; 2)	2·75 2·45 (13·5)	37
XXI	3·67 (*b*)	3·67 (10·5)	3·20 (10·5)	4·99 (10·5; 2)	2·76 2·56 (13·5)	37
XXII	4·11 (10)	3·65[c] (10)	3·37 (10)	4·95 (10; 2·5)	2·58 2·81 (13)	37
XXIII	4·12 (10)	3·67 (10)	3·45 (10)	5·01 (10; 2·5)	2·62 2·87 (13)	37
XXIV	4·13 (10)	3·67 (10)	[b] (10)	5·05 (10; 2·5)	2·87 2·58 (13·5)	37
Lactucin (*XI*)	3·65 (10)	3·60 (10)	3·21 (9·9)	3·99 (9·9; [b])	[b] [b] (13·8)	39

TABLE VII

Proton NMR parameters of seven-membered ring in *cis*-lactones

Compound	H(5) ($J_{5,6}$)	H(6) ($J_{6,7}$)	H(7) ($J_{7,8}$)	H(8) ($J_{8,9}$; $J_{8,9'}$)	H(9) H(9') ($J_{9,9'}$)	Ref.
Lactone *I*	3·58 (11·4)	4·66 (9·9)	3·57 (11·2)	5·59 (3·4; 10·9)	2·91 2·49 (19·2)	[a]
Angeloyloxy-pruteninone (*XXX*)	3·61 (11·4)	4·72 (9·9)	3·63 (11·4)	5·65 (3·5; 10·7)	2·90 2·52 (19·1)	[a]
Fegvolide (*XXXII*)	3·66 (10·2)	4·76 (10·0)	3·73 (11)	5·78 (4; 11)	2·96 2·56 (18)	28
Ferugolide (*XXXIII*)	3·70 (10·2)	4·81 (10·0)	3·77 (11·0)	5·81 (3·5; 11·0)	3·14 2·61 (19·5)	29
Giferolide (*XXXIV*)	3·69 (10·2)	4·80 (10·0)	3·78 (11·0)	5·80 (3·5; 11·0)	3·08 2·60 (19·5)	29
Gigantolide (*XXXV*)	3·61 (10·2)	4·72 (10·0)	3·72 (11·0)	5·79 (3·5; 11·0)	3·04 2·56 (19·5)	29
Malafil (*XXXVI*)	3·63 (11·0)	4·72 (10·0)	3·67 (10·3)	5·73 (3·9; 10·3)	3·04 2·56 (18·1)	29, 30
Malafilin (*XXXVII*)	3·63 (11·0)	4·72 (10·0)	3·67 (10·3)	5·73 (3·9; 10·3)	3·02 2·56 (18·1)	29, 30
Malafilinin (*III*)	3·65 (10·2)	4·73 (10)	3·72 (11)	5·76 (3·5; 11)	3·04 2·59 (19·5)	5, 29
Oferin (*XXXVIII*)	[b] (11·8)	4·61 (10)	[b] (11)	5·50 (2; 11)	[b]	2
Olgin (*XXXIX*)	[b] (11·8)	4·61 (10)	[b] (11)	5·49 (2; 11)	[b]	2
Olgoferin (*XL*)	[b] (11·8)	4·70 (10)	[b] (11)	5·55 (2; 11)	[b]	2
Talasin A[c] (*XXX*)	3·60 (10·2)	4·73 (10·0)	3·65 (11·0)	5·66 (3·5; 11·0)	2·91 2·48 (19·5)	5, 29, 31
Talasin B[d] (*XLI*)	[b] (11·8)	3·90[e] (10)	[b] (11)	5·20 (2; 11)	[b]	2
Badkhyzin (*XXXI*)	3·70 (10)	4·55 (7·5)	[b] (10)	5·55 (4; 10)	[b]	26, 27

[a] NMR parameters from this paper; [b] the values of parameters are not given in literature; [c] apparently identical with angeloyloxypruteninone (*XXX*); [d] data from $C_6^2H_6$ solution; [e] very probably erroneous value — it should be corrected to approximately 4·7, similarly as it was done in the case of talasin A (refs[2,29,31]).

←

[a] Data from pentadeuteriopyridine solution; [b] the values of parameters are not given in literature; [c] the evidently wrong value 2·65 (ref.[37]) was corrected to 3·65.

values for $\delta_{H(6)}$ or $J_{9,9'}$ are observed, however, in all guaianolides of type *V* from *Umbelliferae* described so far, the stereostructures of which were formulated the same as before for lactone *I*, in the sense of *trans*-lactones of type *IX*. They are angeloyloxypruteninone[1]*, badkhyzin[26,27], fegvolide[28], ferugolide[29], gigantolide[29], giferolide[29], malafil[29,30], malafilin[29,30], malafilinin[5,30], oferin[2], olgin[2], olgoferin[2], talasin A[2,29,31]*, and talasin B[2]. On the basis of the above discussed arguments we consider that it is necessary to correct their structures to *cis*-lactones with correct structures: angeloyloxypruteninone (*XXX*), badkhyzin (*XXXI*), fegvolide (*XXXII*), ferugolide (*XXXIII*), giferolide (*XXXIV*), gigantolide (*XXXV*), malafil (*XXXVI*), malafilin (*XXXVII*), malafilinin (*III*), oferin (*XXXVIII*), olgin (*XXXIX*), olgoferin (*XL*), talasin A (*XXX*)* and talasin B (*XLI*). Therefore their ^{1}H NMR data are given among *cis*-lactones in Table VII. As regards prutenin and acetoxyisopruteninone[1] we propose a correction of their structures in the sense of formula *XLII* for prutenin and *XLIII* for acetoxyisopruteninone on the basis of $\delta_{H(6)}$ (4·60 and 4·74, respectively).

Finally it may be stated that all the so far isolated and described native guaianolides from *Umbelliferae* are structurally related and that all can be derived from the basic type, 1βH,5βH,6αH,7αH-guaian-6,12-olide (*IV*). This type of guaianolides (ref.[26]) has so far only been found in guaianolides from the species of the *Umbelliferae* family, of which it seems typical, in contrast to the guaianolides from the *Compositae* family for which the basic 1αH,5αH,6βH,7αH-guaian-6,12-olide skeleton seems more typical.

EXPERIMENTAL

The melting point was determined on a Kofler block and it was not corrected. For column chromatography silica gel according to Pitra and Štěrba (30—60 mμ, deactivated by addition of 11% of water) was used, while silica gel G Merck according to Stahl was used for thin layer chromatography. The IR spectrum was measured in chloroform on a Perkin–Elmer PE 580 instrument. The mass spectrum was measured on an AEI MS 902 spectrometer. The NMR spectra were measured on a FT-NMR spectrometer Varian XL-200 (^{1}H on 200 MHz; ^{13}C on 50·3 MHz) in deuteriochloroform with tetramethylsilane as internal standard. The circular dichroism was measured on a Roussel–Jouan CD 185 dichrographe, in methanol.

2-Oxo-8α-angeloyloxy-11α-acetoxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (*I*)

The ground, dried roots (8·5 kg) of *Laserpitium prutenicum* L., collected in Poland in 1973 were extracted exhaustively with light petroleum at room temperature. After distilling off of the solvent the extract weighed 48 g. One part of it (33 g) was chromatographed on a silica gel column (1 200 g) with light petroleum–ether mixture with increasing concentration of the more polar solvent. Repeated column chromatography with 20% ether in light petroleum gave 2-oxo-8α-angeloyloxy-11α-acetoxy-5βH,6αH,7αH-guai-1(10),3-dien-6,12-olide (*I*; 142 mg), m.p. 142 to

* Talasin A[2,29,31] is evidently identical with angeloyloxypruteninone[1] as evident from the comparison of their ^{1}H NMR data (Table VII).

144 °C. IR spectrum (cm^{-1}): 1 793 (γ-lactone), 1 739, 1 232 (acetate), 1 704 (α,β-unsaturated ester), 1 688 (α,β-unsaturated ketone), 1 615, 1 637 (double bond). Mass spectrum (*m/z*): 402 (M), 342 (M−60), 302 (M−100), 242 (M−60−100), 83 ($C_4H_7CO^+$), 55 ($C_4H_7^+$). CD spectrum (nm, $\Delta\varepsilon$): 345, −0·4; 295, ±0; 279, −0·4.

X-Ray Structural Analysis of *I*

Crystal data: $C_{22}H_{26}O_7$, orthorhombic, $P2_12_12_1$, $a = 12{\cdot}510(5)$, $b = 15{\cdot}976(7)$, $c = 10{\cdot}629(2)$ Å, $U = 2\,124(2)$ Å^3, $Z = 4$, $D_m = 1{\cdot}24(3)$, $D_c = 1{\cdot}258$ g cm^{-3}, $T = 295$ K.

Data collection: A crystal of dimensions 1·6 × 1·1 × 0·7 mm was used for data collection in Chapel Hill on an Enraf-Nonius CAD 4 diffractometer equipped with a molybdenum tube ($\lambda K_\alpha = 0{\cdot}7107$ Å) and a graphite monochromator. Cell constants were obtained by a least squares refinement of the positions of 25 reflections with $22° < 2\theta$ (Mo) $< 32°$. 2 754 independent intensities were gathered in a ω-2θ scan mode in the region $2° < 2\theta$ (Mo) $< 55°$; there was very little observable diffracted intensity at value of 2θ (Mo) $> 55°$. The data were corrected for backgrounds and for Lorentz-polarization effects, but not for absorption, and assigned estimated standard deviations using the method of Ibers and coworkers[42] with $p = 0{\cdot}025$. Of the 2 754 independent data, only 1 279 reflections had $I > 2\sigma(I)$, and only these data were used in the subsequent structure refinement.

Solution and refinement of the structure: The structure was solved by direct methods[43] and refined by full-matrix least-squares techniques. All refinements were carried out on *F*, the function minimised being $\sum w(|Fo| - |Fc|)^2$, where the weights *w* are defined as $4Fo^2/\sigma^2(Fo^2)$. The hydrogen atoms attached to carbon atoms were placed in calculated positions assuming C—H distances of 0·95 Å, and these positions were not refined; all other atoms were refined anisotropically. The final values of the agreement factors $R_1 = \sum||Fo| - |Fc||/\sum|Fo|$ and $R_2 = [\sum w(|Fo| - |Fc|)^2/\sum w|Fo|^2]^{1/2}$, were 0·069 and 0·067, respectively, and the error in an observation of unit weight was 2·6. In the final least-squares cycle no parameter experienced a shift of more then 0·02 σ-, which indicates convergence. A final difference Fourier map was featureless, with no peak higher than 0·13 e Å^{-3}. The final positional parameters, along with their standard deviations as estimated from the inverse matrix, are collected in Table I. Tables of anisotropic thermal parameters and observed and calculated structure amplitudes are available on request*. The absolute configuration of the molecule cannot be independently determined on the basis of the present crystallographic experiment, but the positions in Table I and elswhere were assigned on the assumption of the established configuration at C(7).

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