Phytochemistry, Vol 24, No 5, pp 1009–1015, 1985
Printed in Great Britain

0031-9422/85 $3 00+0 00

DIMERIC GUAIANOLIDES FROM *ARTEMISIA SIEVERSIANA*

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(*Revised received* 10 *August* 1984)

Key Word Index—*Artemisia sieversiana, A frigida*, Compositae, sesquiterpene lactones, guaianolides, dimeric guaianolides

Abstract—The aerial parts of *Artemisia sieversiana* afforded in addition to known compounds five new guaianolides and four dimeric guaianolides, three of them closely related to absinthin and one derived from estafiatin as a monomer The structures were elucidated by extensive NMR studies, which allowed the assignment of the 14 chiral centres *Artemisia frigida* afforded several known compounds and one new guaianolide, 8-desoxy-cumambrin B, the most likely precursor of many guaianolides

INTRODUCTION

From the large genus *Artemisia* (Compositae, tribe Anthemideae) already many species have been studied chemically Characteristic for this genus are the large variety of sesquiterpene lactones [1, 2], the acetylenic compounds [3], coumarin derivatives [4] and phenylpropane derivatives, especially sesamin-like compounds [5] We now have reinvestigated two species from Mongolia, *Artemisia sieversiana* and *A frigida*, which both gave sesquiterpene lactones as well as several known acetylenes The results will be discussed in this paper

RESULTS AND DISCUSSION

The aerial parts of *Artemisia frigida* Willd, which has been studied previously [6–11], afforded the *E/Z*-isomeric 5- and 6-ring spiroketalenol ether [3], 1-phenylhexa-2,4-diyne [3], hanphyllin [12], 11,13-dehydrodesacetyl matricarin [13], tanaparthin α-peroxide [14] and 8-desoxycumambrin B (**11**), its structure clearly following from the molecular formula $C_{15}H_{20}O_3$ and the ^1H NMR spectrum (Table 1) Spin decoupling allowed the assignment of nearly all signals, which further led to a complete sequence, clearly leading to the proposed structure The stereochemistry followed from the couplings observed and by comparison with the spectra of similar lactones with known configurations

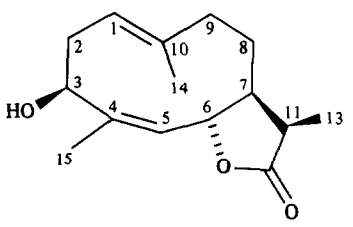
The extract of the aerial parts of *Artemisia sieversiana* Willd, which has been studied previously [1, 5, 15–17] contained a very complex mixture Repeated thin layer chromatography and HPLC finally gave in addition to widespread compounds (see Experimental) the lignans sesamin, e,a-ashantin, e,e-sesartemin, e,a-, e,e- and a,a-yangambin, which have been isolated from the roots of this species [5, 6], large amounts of absinthin (**6**) [18], ludartin [19], anabsinthin [20] as well as the germacranolide **1**, the guaianolides **3**, **4** and **5**, three dimeric guaianolides related to absinthin (**7**–**9**), the further dimer **10** related to estafiatin and the neryl derivative **12**

The structure of **1**, molecular formula $C_{15}H_{22}O_3$, followed from the ^1H NMR (Table 1) and the ^{13}C NMR spectral data (see Experimental) The presence of a heliangolide could be deduced from the typical small coupling $J_{6,7}$ in the ^1H NMR spectrum at elevated temperature, where all signals could be assigned by spin decoupling The stereochemistry as well as the conformation followed from the NOEs which have been determined by NOE difference spectroscopy (see Experimental) The results showed that a conformer was present with H-15 below and H-14 above the plane The clear NOE between H-15 and H-3 indicated a 3β-hydroxy group

The structure of **3** could be deduced from the ^1H NMR spectrum (Table 1) which was in part close to those of similar lactones Again all signals could be assigned by spin decoupling The stereochemistry at C-1, C-2, C-5, C-6, C-7 and C-11 followed from the couplings observed

The ^1H NMR spectral data of **4** (Table 1) were close to those of estafiatin However, the 13-H exomethylene signals were replaced by a double quartet at δ2 65 and a methyl doublet at δ1 13 Again all data agreed with the presence of a 11β-methyl group

The ^1H NMR spectrum of **5** (Table 1) showed that again an epoxide was present (doublets at δ3 83 and 3 67) Inspection of a model indicated that the couplings observed agreed only with the proposed stereochemistry The configuration at C-11 was deduced again from the characteristic NMR data, which also showed that we were dealing with a derivative of dehydrocostuslactone Most likely **1** was the common precursor for **3**–**5** as well as for **2**, the monomer of the dimeric guaianolide absinthin which, however, so far has not been isolated Probably this diene is very reactive and therefore only can be seen in Diels–Alder-adducts like absinthin The structure and the configuration of the latter has been studied for a long time and finally was elucidated by high field ^1H NMR spectroscopy [18] We have confirmed again the stereochemistry by extensive NOE difference spectroscopy and spin decoupling The ^1H NMR spectrum of **7** (Table 2) was very similar to that of **6** However, clear differences were visible in the chemical shift of two signals, which by spin



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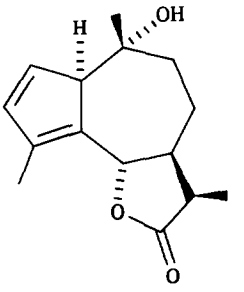

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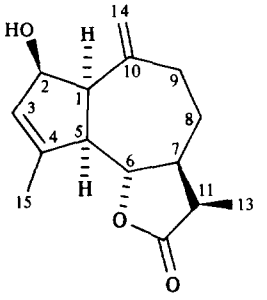

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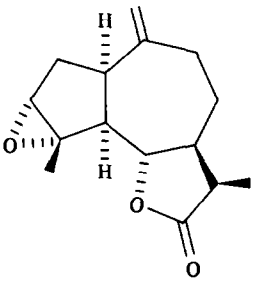

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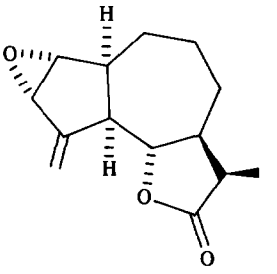

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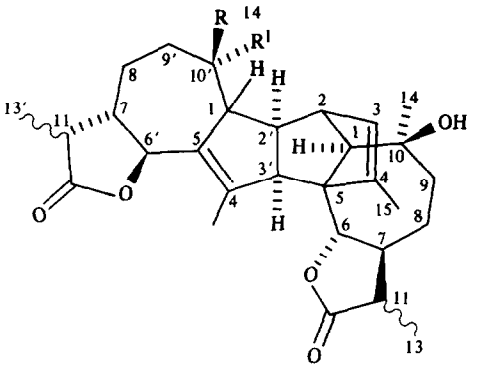
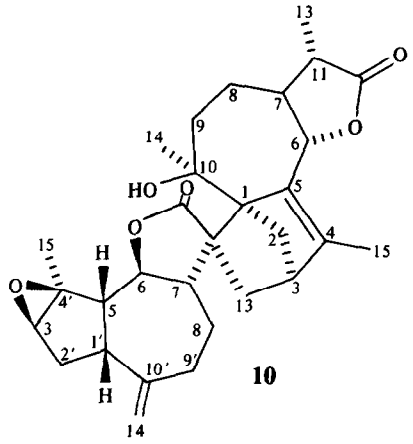
Table 1 ^{1}H NMR spectral data of **1**, **3**–**5** and **11** (400 MHz, $CDCl_3$, TMS as internal standard)

	1 (60°)	3	4	5	11
H-1	5 14 *br t*	2 88 *dd*	2 87 *ddd*	3 05 *br d*	2 55 *ddd*
H-2	2 66 *ddd* 2 20 *m*	4 81 *br s*	2 14 *ddd* 1 78 *ddd*	3 83 *br d*	2 35 *br d* 2 28 *m*
H-3	4 45 *dd*	5 68 *br s*	3 36 *br s*	3 67 *d*	5 47 *br s*
H-5	5 37 *br d*	3 07 *br t*	2 35 *dd*	2 69 *br d*	2 78 *br t*
H-6	5 69 *dd*	4 06 *t*	4 04 *t*	4 08 *t*	4 23 *dd*
H-7	2 16 *dddd*	2 40 *dddd*	2 40 *dddd*	2 44 *dddd*	3 17 *dddd*
H-8α	1 66 *br ddd*	1 93 *dddd*	1 84 *dddd*	1 95 *dddd*	2 25 *dddd*
H-8β	1 45 *dddd*	1 42 *dddd*	1 43 *dddd*	1 37 *dddd*	1 46 *dddd*
H-9α	2 02 *ddd*	2 04 *ddd*	2 06 *ddd*	2 03 *ddd*	1 98 *ddd*
H-9β	2 37 *br d*	2 51 *ddd*	2 31 *ddd*	2 58 *ddd*	1 70 *ddd*
H-11	2 87 *dq*	2 67 *dq*	2 65 *dq*	2 70 *dq*	—
H-13	1 20 *d*	1 16 *d*	1 13 *d*	1 18 *d*	6 17 *d* 5 44 *d*
H-14 H-14′	1 76 *br s*	4 90 *br s* 4 84 *br s*	4 85 *br s* 4 83 *br s*	4 92 *br s* 4 65 *br s*	1 19 *s*
H-15	1 74 *br s*	1 90 *d*	1 58 *s*	5 52 *d* 5 44 *d*	1 87 *br s*
OH		1 51 *d*			

J (Hz) Compounds **1** 1, 2 = 1, 2′ = 8, 2, 2′ = 14, 2, 3 = 2′, 3 = 3 5, 5, 6 = 11, 6, 7 = 2, 7, 8α = 3 5, 7, 8β = 12, 7, 11 = 9, 8α, 8β = 14, 8α, 9α = 3 5, 8α, 9β = 8, 8β, 9α = 12, 8β, 9β = 3, 9α, 9β = 14, 11, 13 = 7, compounds **3**–**5** 5, 6 = 6, 7 = 10; 7, 8α = 5, 7, 8β = 10; 7, 11 = 8, 8α, 8β = 13, 8α, 9α = 5, 8α, 9β = 7 5, 8β, 9α = 12, 8β, 9β = 5, 9α, 9β = 13 5, 11, 13 = 7, compound **3** 1, 2 = 3 5, 1, 5 = 8, 2, 3 = 3, 15 ~ 1, compound **4** 1, 2 = 7 5, 1, 2′ = 11, 1, 5 = 8, 2, 2′ = 14, 2′, 3 = 1, compound **5** 1, 2 ~ 0 5, 1, 5 = 9, 2, 3 = 2 5, 5, 15 = 5, 15′ = 2 5, compound **11** 1, 2 = 8, 1, 2′ = 9, 1, 5 = 8, 2, 2′ = 18, 5, 6 = 10, 6, 7 = 9 5, 7, 8α = 6, 7, 8β = 11, 7, 13 = 3 5, 7, 13′ = 3, 8α, 8β = 14, 8α, 9α = 6, 8α, 9β = 5, 8β, 9α = 9, 8β, 9β = 5



	R	R^1	11	11′
6*	Me	OH	βH	αH
7	Me	OH	αH	αH
8	OH	Me	βH	βH
9	OH	Me	αH	βH



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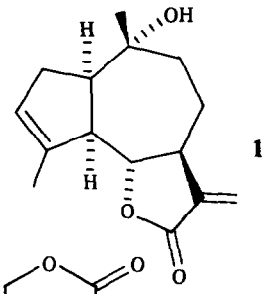

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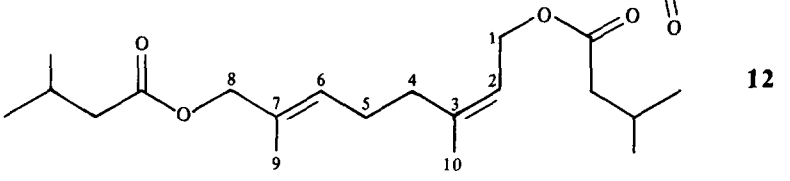

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* α and β at C-11′ as followed from the formulae (no inverse absolute configuration)

decoupling could be assigned to H-7 and H-11 An important point for the assignment of all signals was the fact that the H-6′ doublet was broadened due to allylic coupling, while the H-6 signal here and also in the spectra of **8**–**10** was a sharp doublet The coupling $J_{7,11}$ was 8 Hz indicating a 11β-methyl group This was supported by the ^{13}C NMR data While again most signals had the same chemical shifts as those of **6**, the shifts of the signals assigned to C-7, C-8, C-11 and C-13 clearly differed Inspection of a model showed that especially the observed upfield shift of the C-8 signal in the spectrum of **7** was in agreement with the expected effects Having the ^{13}C shifts of **6** and **7** at hand a few previous assignments [18] were changed (Table 3) Again extensive NOE difference spectroscopy fully supported the proposed configuration at all chiral centres (Table 4) Thus a clear NOE between H-1 and H-2′ indicated the *endo* mode of the cyclo addition and the NOEs between H-2, H-14 and H-14′ allowed the assignment of the configurations at C-10 and C-10′ Furthermore NOEs were useful for the assignment of the sequences to overcome blocks of quaternary carbons

The ^1H NMR spectrum of **8** (Table 2) again was similar

Table 2 ^{1}H NMR spectral data of **6–10** (400 MHz, $CDCl_3$, TMS as internal standard)

	6	**7**	**8**	**9**	**10** (C_6D_6)*	$CDCl_3$
H-1	1 98 *br s*	2 00 *br s*	1 98 *br s*	2 05 *br s*	—	—
H-2	2 84 *br dd*	2 84 *br dd*	2 91 *br dd*	2 93 *br dd*	2 48 *dd* 1 03 *dd*	2 28 *dd*
H-3	5 55 *br s*	5 55 *br s*	5 59 *br s*	5 61 *br s*	2 32 *br s*	2 55 *br s*
H-6	4 72 *d*	4 85 *d*	4 73 *d*	4 91 *d*	4 62 *br d*	4 74 *br d*
H-7	1 80 *m*	2 40 *dddd*	1 80 *m*	2 43 *dddd*	1 35 *m*	
H-11	2 18 *dq*	2 67 *dq*	2 24 *dq*	2 71 *dq*	1 87 *dq*	
H-13	1 23 *d*	1 22 *d*	1 26 *d*	1 26 *d*	1 07 *d*	1 21 *d*
H-14	1 17 *s*	1 16 *s*	1 16 *s*	1 19 *s*	1 27 *s*	1 30 *s*
H-15	1 77 *d*	1 77 *br s*	1 75 *d*	1 78 *d*	1 94 *d*	1 91 *br s*
H-1′	2 28 *br s*	2 27 *br s*	2 37 *br s*	2 38 *br s*	3 04 *br ddd*	2 91 *br ddd*
H-2′	2 81 *ddd*	2 81 *ddd*	2 84 *ddd*	2 86 *ddd*	1 83 *dd* 1 35 *m*	
H-3′	3 19 *br d*	3 23 *br d*	3 18 *br d*	3 25 *br d*	3 03 *br s*	3 35 *br s*
H-6′	4 59 *br d*	4 58 *br d*	4 74 *br d*	4 76 *br d*	3 29 *dd*	3 85 *dd*
H-7′	1 64 *m*	1 70 *m*	2 30 *dddd*	2 31 *dddd*	3 16 *dddd*	3 28 *dddd*
H-11′	2 23 *dq*	2 18 *dq*	2 60 *dq*	2 62 *dq*	—	—
H-13′	1 19 *d*	1 19 *d*	1 15 *d*	1 18 *d*	1 57 *br dd* 2 04 *dd*	
H-14′	1 29 *s*	1 29 *s*	0 87 *s*	0 88 *s*	4 83 *br d* 4 78 *br d*	4 83 *br d* 4 69 *br d*
H-15′	1 94 *br s*	1 93 *br s*	1 89 *br s*	1 92 *br s*	1 75 *s*	1 57 *s*
10-OH	2 15 *d*	2 15 *d*	2 22 *br s*	2 20 *br s*		

*H-5′ 2 55 *dd*, H-8$_1$′ 1 35 *m*, H-8$_2$′ 0 86 *br ddd*, H-9$_1$′ 1 99 *ddd*, H-9$_2$′ 1 57 *ddd*, *J* (Hz) Compounds **6–9** 1,2 = 1, 2,3 = 2 5, 2,2′ = 4, 3,15 = 1 5, 6,7 = 10, 11,13 = 7, 1′,2′ = 4, 2′,3′ = 8, 6′,7′ = 11, 11′,13′ = 7, 9α,OH = 2, (compound **7** 7,11 = 8, 7′,11′ = 12, compound **8** 7,11 = 12, 7′,11′ = 8, compound **9** 7,11 = 7′,11′ = 8), compound **10** 2$_1$,2$_2$ = 9, 2$_1$,3 = 1 5, 2$_2$,3 = 2$_2$,13$_2$ = 2, 6,7 = 11, 6,15 = 1 5, 7,11 = 12, 11,13 = 7, 1′,2$_1$ = 7, 1′,2$_2$ = 10, 1′,5′ = 8 5, 2$_1$′,2$_2$′ = 14, 5′,6′ = 11, 6′,7′ = 8 5, 7′,8$_1$′ = 5, 7′,8$_2$′ = 12, 8$_1$′,8$_2$′ = 13, 8$_1$′,9$_1$′ = 2, 8$_1$′,9$_2$′ = 3, 8$_2$′,9$_1$′ = 9, 8$_2$′,9$_2$′ = 3, 9$_1$′,9$_2$ = 13 5, 13$_1$′,13$_2$′ = 12, 14$_1$′,14$_2$′ = 2 5

to that of **6** However, in this case more differences were visible While the signals of H-1–H-15 in **8**, which could be assigned by spin decoupling, agreed with those of **6**, the signals of H-1′, H-6′, H-15′ and especially those of H-7′, H-11′ and H-14′ differed from those of **6** Accordingly, the stereochemistry of **8** was altered in the left part of the molecule The changed configuration at C-11′ led to a smaller coupling $J_{7,11}$ As in the case of **7** this caused a clear upfield shift of C-8′ in the ^{13}C NMR spectrum of **8** Also the shifts of C-7′, C-11′ and C-13′ were clearly influenced Thus an 11′α-methyl group was present in **8** The clear upfield shift of the H-14′ signal in the ^{1}H NMR spectrum of **8**, obviously due to the shielding effect of the $\Delta^{4'}$ double bond, indicated a changed configuration also at C-10′ NOE difference spectroscopy (Table 4) confirmed this assumption and also from the ^{13}C NMR shift of C-14′ the presence of an axial methyl could be deduced The chemical shift of C-1–C-15, however, were close to those of **6** As also the ^{1}H NMR signals of H-1–H-15 were nearly identical with those of **6**, the stereochemistry of the right hand moiety of the dimer therefore was the same in **6** and **8**

The ^{1}H NMR spectrum of **9** (Table 2) showed even more differences to that of **6** Spin decoupling allowed the assignment of nearly all signals The chemical shift of H-11 as well as the coupling $J_{7,11}$ indicated a 11β-methyl group The same is true for H-11′, thus indicating an 11′α-methyl too The chemical shift of H-14′ further indicated that the configuration at C-10′ most likely was the same as in **8** Again NOE difference spectroscopy (Table 4) confirmed these assignments and also the ^{13}C NMR data (Table 3) agreed with the proposed structure Accordingly, to explain the formation of **6–9** the original presence of the following monomers had to be assumed **5**, 11-epi-**5** and 10,11-epi-**5**, It is remarkable that absinthin (**6**), which is the main component, required the formation of **2**, a guaianolide with a C-11α-methyl, while all the monomeric lactones, which were isolated from the species, had a 11β-methyl group In all dimers (**6–9**) the OH protons showed a coupling with H-9α, indicating a fixed position, which could be explained, if a hydrogen bond with the 3,4-double bond was assumed

The structure of **10**, which showed molecular formula $C_{30}H_{38}O_6$, and thus differing from **6–9** by two less hydrogens, could be deduced again from the ^{1}H NMR spectrum (Table 2) While some signals were similar to those of **6** most were clearly different One of the olefinic methyls of **6** obviously was replaced by an exocyclic double bond as followed from the downfield broadened doublets at δ4 83 and 4 78 Spin decoupling and NOE difference spectroscopy allowed the assignment of nearly all signals leading to sequences which only could be combined to the proposed structure The changed situation in **10** also followed from the H-6′ signal, which now was a double doublet, and from the broadened singlet at δ3 03 which sharpened on irradiation of H-2′ signals

Table 3 ^{13}C NMR spectral data of **6–10** ($CDCl_3$)

	6	7	8	9	10
C-1	71 4*d*	71 5*d*	71 3*d*	71 3*d*	71 2*s*
C-2	45 7*d*	45 6*d*	45 3*d*	45 4*d*	45 6*t*
C-3	122 1*d*	122 1*d*	122 4*d*	122 3*d*	45 7*d*
C-4	148 5*s*	148 4*s*	148 1*s*	148 2*s*	135 4*s*
C-5	64 2*s*	64 4*s*	64 2*s*	64 5*s*	147 4*s*
C-6	82 7*d*	82 7*d*	82 9*d*	82 8*d*	83 7*d*
C-7	46 7*d*	39 9*d*	49 6*d*	40 0*d*	46 8*d*
C-8	27 5*t*	23 7*t*	27 5*t*	23 8*t*	28 1*t*
C-9	42 5*t*	42 3*t*	42 5*t*	42 4*t*	42 7*t*
C-10	71 9*s*	71 8*s*	72 0*s*	71 9*s*	76 4*s*
C-11	42 0*d*	40 5*d*	42 1*d*	40 7*d*	42 2*d*
C-12	178 4*s*	178 8*s*	178 6*s*	179 7*s*	178 6*s*
C-13	13 1*q*	11 0*q*	13 0*q*	11 0*q*	12 5*q*
C-14	32 3*q*	32 2*q*	32 3*q*	32 2*q*	32 1*q*
C-15	13 7*q*	13 7*q*	13 7*q*	13 8*q*	14 2*q*
C-1′	57 1*d*	57 1*d*	58 4*d*	58 4*d*	42 2*d*
C-2′	46 5*d*	46 7*d*	47 2*d*	47 2*d*	24 3*t*
C-3′	58 9*d*	58 9*d*	59 1*d*	59 1*d*	64 0*d*
C-4′	134 9*s*	135 0*s*	135 2*s*	135 3*s*	66 3*s*
C-5′	147 5*s*	147 6*s*	145 6*s*	145 7*s*	50 7*d*
C-6′	81 4*d*	81 4*d*	80 4*d*	80 4*d*	81 4*d*
C-7′	49 4*d*	49 4*d*	44 0*d*	44 0*d*	54 6*d*
C-8′	23 6*t*	23 6*t*	22 4*t*	22 5*t*	28 9*t*
C-9′	43 7*t*	43 7*t*	45 3*t*	45 2*t*	33 1*t*
C-10′	74 1*s*	74 1*s*	75 7*s*	75 7*s*	143 1*s*
C-11′	42 3*d*	42 3*d*	40 1*d*	40 1*d*	54 5*s*
C-12′	178 8*s*	179 9*s*	179 7*s*	180 0*s*	183 3*s*
C-13′	12 2*q*	12 2*q*	9 2*q*	9 2*q*	38 5*t*
C-14′	29 4*q*	29 4*q*	22 7*q*	22 7*q*	113 5*t*
C-15′	18 3*q*	18 4*q*	17 9*q*	18 0*q*	18 4*q*

Several signals of the left hand moiety were nearly identical with those of estafiatin The absence of the exomethylene H-13 signals indicated where the cyclo addition had taken place as a pair of double doublets obviously had to be assigned to the H-13′ protons This was supported by spin decoupling and some clear NOEs (see Experimental) which further allowed the assignment of the whole stereochemistry at the various chiral centres As followed from the downfield shift and the broadening of the H-6 signal in the right hand moiety of the molecule a 4,5-double bond was present, thus indicating that **10** was not formed from the same monomer as **6** The stereochemistry at C-1, C-3 and C-11′ followed from the corresponding NOEs if models were inspected A clear NOE between 10-OH and H-14 and H-5′ indicated a hydrogen bond with the lactone oxygen of the left part of the molecule A clear NOE between H-6 and H-7′ was important for relative configuration at these centres and showed that again from the possible eight different possibilities one of the four *endo* modes of cycloaddition had taken place The ^{13}C NMR data (Table 3) also agreed with the proposed structure **10** we have named artisieversin

The structure of **12** easily could be deduced from the ^1H NMR spectrum (see Experimental) which, of course, was close to that of other neryl derivatives The relative position of the 8-isovaleroyloxy group followed from the chemical shift of H-6 and H-9

The chemistry of *A sieversiana* agrees with a placement in the *Absinthium* group [21] Further investigation, however, may show whether these dimeric lactones are more widespread

EXPERIMENTAL

The air dried aerial parts were extracted with MeOH–Et_2O–petrol, 1 1 1, at room temp and worked-up in usual fashion [22] The column chromatography of the extract of *Artemisia frigida* (200 g, aerial parts, collected in the Mongolian Peoples Republic, Töw-Aimak, Kerulen valley, 30 km NE of Mungen-Mort, August 1983, voucher deposited in the Institute of Plant Biochemistry at Halle, GDR) gave fractions as follows 1 (petrol), 2 (Et_2O–petrol, 1 9), 3 (Et_2O–petrol, 1 3 and 1 1) and 4 (Et_2O and Et_2O–MeOH, 9 1) TLC and GC/MS of fraction 1 showed the presence of phenyl-hexa-2,4-diyne, germacrene D, α and β-farnesene, caryophyllene and α and γ-curcumene TLC of fraction 2 (Et_2O–petrol, 1 9) gave 17 mg 6*E*-6 ring-, 16 mg 6*Z*-6 ring-, 10 mg 6*E*-5 ring and 4 mg 6*Z*-5 ring-spiroketal enol ether [3] TLC of fractions 3 and 4 (Et_2O–petrol, 3 1) afforded 12 mg hanphyllin, 10 mg **11** (R_f 0 55), 3 mg 11,13-dehydrodesacetylmatricarin and 3 mg tanaparthin-α-peroxide

Table 4 NOEs with 7–10*

Irrad of	7 NOE	Irrad of	8 NOE	Irrad of	9 NOE	Irrad of	10 NOE
H-1	H-7, H-2′, H-3′	H-1	H-2, H-2′, H-3′	H-1	H-2′, H-3′	H-1′	H-5′, H-14$_1$′
H-1′	H-3	H-2	H-1, H-1′, H-3, H-14	H-1′	H-3	H-5′	H-1′
H-2′	H-1, H-14′	H-1′	H-3	H-2′	H-1	H-6	H-7′
H-3	H-2, H-15, H-1′	H-2′	H-1, H-3′, H-14′	H-3′	H-1	H-7′	H-5′, H-6
H-3′	H-1	H-3	H-2, H-1′, OH	H-14	H-2	H-8′	H-6′, H-13′
H-6	H-15	H-3′	H-1, H-1′, H-15	H-14′	H-2′, H-6′	H-14	H-2
H-7	H-1, H-11, H-3′	10-OH	H-3, H-6, H-14			H-14$_1$′	H-1′
H-14	H-2	H-14′	H-2′, H-6′			H-15	H-3
H-14′	H-2′,					H-15′	H-3′, H-5′, H-6′
H-15	H-6					10-OH	H-5′, H-14
H-15′	H-3′, H-6′						
10-OH	H-3, H-6						

*400 MHz, $CDCl_3$, homonuclear NOE difference multiple experiments A, one control B (Bruker aspect 2000 pulse programme) D1 = 0 02 s, D2 = 2 s, DP = 40 L, 500 cycles with 16 scans

The extract of the aerial parts of *Artemisia sieversiana* (2 kg, collected in the Mongolian Peoples Republic, Bulgan-Aimak, 30 km E of Chutang, July 1983, voucher deposited in the Institute of Plant Biochemistry at Halle, GDR), gave the following crude CC fractions. 1 (petrol and Et_2O–petrol, 1 9, 0 72 g), 2 (Et_2O–petrol, 1 3, 2 3 g), 3 (Et_2O–petrol, 1 1, 2 6 g), 4 (Et_2O, 2.3 g), 5 (Et_2O–MeOH, 9 1, 20 0 g) and 6 (Et_2O–MeOH, 3 1, 1 1 g) from which only a definite part was separated further TLC (petrol) of 160 mg of fraction 1 gave 25 mg germacrene D and 14 mg α-curcumene TLC of 100 mg of fraction 2 (Et_2O–petrol, 1 4) gave 7 mg neryl isovalerate and 10 mg **12** (R_f 0 30) TLC of 100 mg of fraction 3 (Et_2O–petrol, 3 7) afforded further 10 mg **12** TLC of 200 mg of fraction 4 (C_6H_6–CH_2Cl_2–Et_2O, 2 2 1) gave 1 5 mg **12** and 25 mg sesamin Repeated CC of fraction 5 gave the following fractions 5/1 (Et_2O–petrol, 1 1, 0 6 g), 5/2 (Et_2O–petrol, 11 9, 2 23 g), 5/3 (Et_2O–petrol, 3 2, 2 26 g), 5/4 (Et_2O–petrol, 3 11, 4 4 g), 5/5 (Et_2O, 3 88 g), 5/6 (Et_2O–MeOH, 20 1, 4 0 g) and 5/7 (Et_2O–MeOH, 20 1, 1 4 g) TLC of 5/1 (Et_2O–petrol, 1 1) gave 360 mg **12** and 60 mg e,a-ashantin TLC of 200 mg of 5/2 (Et_2O) gave three bands (5/2/1–5/2/3). HPLC of 5/2/1 (RP 8, MeOH–H_2O, 3 2, *ca* 100 bar, flow rate 3 ml/min) afforded 1 mg **4** (R_t 9 0 min), 0 5 mg ludartin (R_t 9 5 min) and 26 mg **1** (R_t 11 min) TLC (Et_2O) of 5/2/2 gave 21 mg **1** and 35 mg e,a-ashantin and TLC (Et_2O) of 5/2/3 afforded 9 mg e,e-sesartemin TLC of 400 mg of 5/3 (C_6H_6–CH_2Cl_2–Et_2O, 1 1 1) gave three bands (5/3/1–5/3/3) TLC (Et_2O) of 5/3/1 gave 10 mg e,a-ashantin and a mixture, which on HPLC (MeOH–H_2O, 7 3, conditions s.a.) gave 1 mg **5** (R_t 5 5 min) and 33 mg e,a-ashantin (R_t 7 5 min). TLC of 5/3/2 (Et_2O) gave 41 mg e,a-ashantin, 55 mg e,e-sesartemin and 6 5 mg **10** (R_f 0 3). 5/3/3 contained 125 mg **1** TLC of 300 mg of 5/4 (Et_2O, two developments) gave five bands (5/4/1–5/4/5) TLC of 5/4/1 (C_6H_6–CH_2Cl_2–Et_2O, 1 1 1) gave 5 mg e,a-ashantin, 10 mg **1** and 4 5 mg **10**, 5/4/2 contained 43 mg e,e-sesartemin, 5/4/3 on repeated TLC (Et_2O) gave 12 mg e,a-yangambin, 9 mg e,e-sesartemin and 1 3 mg **3** (R_f 0 25) 5/4/4 contained further 13 mg **3** and 5/4/5 contained 17 mg a,a-yangambin 5/5 contained a mixture of e,a-, e,e- and a,a-yangambin (*ca* 2 1 6) and 5/6 contained 2.4 g **6** TLC of 400 mg of 5/7 (Et_2O–MeOH, 50 1, two developments) gave four bands (5/7/1–5/7/4) 5/7/1 afforded 5 mg a,a-yangambin, 5/7/2 7 mg **6**, 5/7/3 9 mg **6** and 4 5 mg **8** and 5/7/4 was a mixture, which by HPLC (MeOH–H_2O, 1 1, condition as above) afforded 5 5 mg anabsinthin (R_t 5 7 min), 7 mg **9** (R_t 7 5 min), 19 5 mg **8** (R_t 8 5 min), 10 mg **7** (R_t 10 min) and 2 5 mg **6** TLC of 200 mg of fraction 6 (Et_2O–MeOH, 20 1) gave 1 mg **3**, 9 mg a,a-yangambin, 40 mg **6** and 10 mg of a mixture of **7**–**9** Known compounds were identified by comparing the 400 MHz ^1H NMR spectra with those of authentic material or by rigorous structure elucidation using all spectroscopic methods and by comparison with data from the literature Though the lactones were homogeneous by ^1H NMR and TLC in different solvent mixtures and by HPLC they could not be induced to crystallize

11α,13-*Dihydro-4-Z-hanphyllin* (**1**) Colourless oil, IR $\nu_{max}^{CHCl_3}$ cm^{-1} 3600 (OH), 1760 (γ-lactone), MS *m/z* (rel int) 250 157 $[M]^+$ (36) (calc for $C_{15}H_{22}O_3$ 250 157), 232 $[M-H_2O]^+$ (12), 177 (22), 159 (38), 123 (46), 95 (96), 81 (62), 67 (58), 55 (100), ^{13}C NMR ($CDCl_3$, C-1–C-15) 121 6 *d*, 31 9 *t*, 76 7 *d*, 140 1 *s*, 126 1 *d*, 81 4 *d*, 45 2 *d*, 24 8 *t*, 40 2 *t*, 137 9 *s*, 36 7 *d*, 179 6 *s*, 10 9 *q*, 17 5 *q*, 23 3 *q*, NOE between H-1 and H-7, H-3 and H-15, H-11 and H-5, H-14 and H-6, H-15 and H-3, H-5, H-6

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{-20 \quad -21 \quad -24 \quad -47} \; (c\ 0\,29,\ CHCl_3)$$

2β-*Hydroxy*-8-*desoxy*-11α,13-*dihydrorupicolin B* (**3**) Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1} 3600 (OH), 1780 (γ-lactone); MS *m/z* (rel int) 248 141 $[M]^+$ (2) (calc for $C_{15}H_{20}O_3$ 248 141), 233 $[M-Me]^+$ (4), 230 $[M-H_2O]^+$ (8), 166 (74), 93 (100),

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+148 \quad +152 \quad +174 \quad +311} \; (c\ 0\,21,\ CHCl_3)$$

11α,13-*Dihydroestafiatin* (**4**) Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1} 1780 (γ-lactone), MS *m/z* (rel int) 248 141 $[M]^+$ (17) (calc for $C_{15}H_{20}O_3$ 248 141), 233 $[M-Me]^+$ (63), 230 $[M-H_2O]^+$ (9), 220 $[M-CO]^+$ (6), 205 $[233-CO]^+$ (7), 97 (100),

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+94 \quad +110 \quad +120 \quad +204} \; (c\ 0\,05,\ CHCl_3)$$

2α,3α-*Epoxy*-11α,13-*dihydro-dehydrocostuslactone* (**5**) Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1} 1780 (γ-lactone), MS *m/z* (rel int) 246 126 $[M]^+$ (31) (calc for $C_{15}H_{18}O_3$ 246 126), 218 $[M-CO]^+$ (17), 95 (93), 55 (100)

11-*Epiabsinthin* (**7**) Colourless, viscous oil, IR $\nu_{max}^{CCl_4}$ cm^{-1} 3560 (OH), 1785 (γ-lactone), MS *m/z* (rel int): 496 282 $[M]^+$ (3) (calc for $C_{30}H_{40}O_6$ 396 282), 248 $[C_{15}H_{20}O_3$, RDA$]^+$ (100), 233 $[248-Me]^+$ (24), 230 $[248-H_2O]^+$ (81), 215 $[230-Me]^+$ (12), 205 $[233-CO]^+$ (41),

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+159 \quad +165 \quad +188 \quad +315} \; (c\ 0\,34,\ CHCl_3)$$

10′,11′-*Epiabsinthin* (**8**) Colourless, viscous oil, IR $\nu_{max}^{CCl_4}$ cm^{-1} 3620, 3340 (OH), 1770 (γ-lactone), MS *m/z* (rel int) 496 282 $[M]^+$ (4) (calc for $C_{30}H_{40}O_6$ 496 282), 478 $[M-H_2O]^+$ (1), 248 $[C_{15}H_{20}O_3$, RDA$]^+$ (100), 233 $[248-Me]^+$ (27), 230 $[248-H_2O]^+$ (58), 215 $[230-Me]^+$ (91), 205 $[233-CO]^+$ (41),

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+107 \quad +113 \quad +127 \quad +216} \; (c\ 0\,62,\ CHCl_3)$$

11,10′,11′-*Epiabsinthin* (**9**) Colourless, viscous oil, IR $\nu_{max}^{CCl_4}$ cm^{-1} 3620 (OH), 1780 (γ-lactone), MS *m/z* (rel int) 496 282 $[M]^+$ (1 5) (calc for $C_{30}H_{40}O_6$ 496 282), 478 $[M-H_2O]^+$ (0 5), 248 $[C_{15}H_{20}O_3$, RDA$]^+$ (91), 233 $[248-Me]^+$ (27), 230 $[248-H_2O]^+$ (100), 215 $[230-Me]^+$ (94), 205 $[233-CO]^+$ (51),

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\,nm}{+46 \quad +51 \quad +57 \quad +94} \; (c\ 0\,35,\ CHCl_3)$$

Artesieversin (**10**) Colourless, viscous oil, IR $\nu_{max}^{CCl_4}$ cm^{-1} 3620, 3460 (OH), 1780 (γ-lactone), MS *m/z* (rel int) 494 $[M]^+$ (0 1), 476 256 $[M-H_2O]^+$ (3 5) (calc for $C_{30}H_{36}O_5$ 476 256), 248 $[C_{15}H_{20}O_3$, RDA$]^+$ (75), 233 $[248-Me]^+$ (24), 231 $[C_{15}H_{19}O_2]^+$ (78), 230 $[248-H_2O]^+$ (100), 215 $[230-Me]^+$ (62), 205 $[233-CO]^+$ (63), 97 (99)

8-*Desoxycumambrin B* (**11**) Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1} 3600 (OH), 1775 (γ-lactone), MS *m/z* (rel int) 248 141 $[M]^+$ (8) (calc for $C_{15}H_{20}O_3$ 248 141), 230 $[M-H_2O]^+$ (100), 215 $[230-Me]^+$ (17), 187 $[215-CO]^+$ (17), 173 (90), 107 (94), 55 (98)

8-*Isovaleryloxy-nerylisovalerate* (**12**) Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1} 1735 (CO_2R), MS *m/z* (rel int) 338 246 $[M]^+$ (0 5) (calc for $C_{20}H_{34}O_4$ 338 246), 237 $[M-OCOR]^+$ (4 3), 236 $[M-RCO_2H]^+$ (1 5), 134 $[236-RCO_2H]^+$ (100), 119 $[134-Me]^+$ (52), 85 $[RCO]^+$ (14), 57 $[85-CO]^+$ (98), ^1H NMR ($CDCl_3$) 4 55 *br d* (H-1), 5 36 *br t* (H-2), 2 15 m (H-4, H-5), 5 44 *br t* (H-6), 4 44 *br s* (H-8), 1 76 *br s* (H-9), 1 64 *br s* (H-10), 2 21 *d* (H-2′), 2 11 *tqq* (H-3′), 0 94 *d* and 0 92 *d* (H-4′, H-5′), (*J* [Hz] 1,2 = 5, 6 = 2′, 3′ = 3′, 4′ = 3′, 5′ = 7)

Acknowledgements—We thank the Deutsche Forschungsgemeinschaft for financial support and Dr W Hilbig, University of Halle, for determination of the plant material

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