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SESQUITERPENE LACTONES AND OTHER CONSTITUENTS FROM *EREMANTHUS SEIDELII, E. GOYAZENSIS* AND *VANILLOSMOPSIS ERYTHROPAPPA*

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Key Word *Index-Eremanthus seidelii; Eremanthus goyozensis, Vanillosmopsis erythropappa*;Compositae; Vernonieae; sesquiterpene lactones; 3,10-epoxygermacranolides; 4,5-dihydroeremantholides; X-ray analysis.

Abstract-Extraction of the aerial parts of ***Eremanthus seidelii*** and reinvestigation of ***E. goyazensis*** gave four new 4,5-dihydrofuranoheliangolides and two new 4,5-dihydroeremantholides as well as some known sesquiterpene lactones. X-Ray analysis of one of the 4,5-dihydroeremantholides showed that the new lactones from ***E. seidelii*** and ***E. goyazensis*** differ in ***C-4*** stereochemistry from isomers previously isolated from ***Eremanthus*** and related species. Criteria based on NMR spectroscopy for distinguishing between the two series are given. The C-4 stereochemistry of zexbrevin is discussed and the tentative conclusion is reached that in the earlier correlation between tagitinin A and zexbrevin C-4 epimerization took place at the oxidation stage. Reinvestigation of ***Vanillosmopsis erythropappa*** wood resulted in isolation of several lactones not previously reported from this species.

INTRODUCTION

Extracts of various *Eremanthus* species (Compositae, tribe Vernonieae) possess schistosomicidal properties [1–3]. The active constituent in the heartwood oil of ***E. elaeagnus is*** the guaianolide eremanthin **(1)** [1,3,4] which is also found in the schistosomicidal wood oil of *Vanillosmopsis* ***erythropappa*** [1, 4, 5], in the aerial parts of other members of subtribe Lychnophorinae [6-143 and in a few ***Vernonia*** species [15,16]. The herbaceous parts of ***E. goyazensis*** yield the schistosomicidal and cytotoxic heliangolide goyazensolide **(4s)** [17,18] which is closely related to the cytotoxic lactones eremantholides A, B and C (**5a–c**) from the wood of ***E. elaeagnus*** [19,20]. Analogues of goyazensolide and the eremantholides have since been reported from other Lychnophorinae [6–14, 21–27].

In order to secure more eremanthin and goyazensolide for further evaluation as schistosomicides we have extracted collections from Minas Gerais State, Brazil, of ***E. goyazensis*** and what was initially thought to be. *E.* ***elaeagnus*** but what on closer study turned out to be the recently described E. ***seidelii*** MacLeish and Schumacher [28].‡ Unlike ***E. elaeagnus*** the aerial parts of ***E. seidelii*** did not furnish eremanthin, but gave the new sesquiterpene lactones **2a–d, 3a** and 3d as well as the flavone isorhamnetin (6). Substances isolated from the aerial parts of ***E. goyazensis*** were, in addition to goyazensolide **(4a)** and its 11,13-dihydro derivative, the sesquiterpene lactones **2a–c, 3a, 3b, 5c** (eremantholide C) [20], **5d** [9, 27] and isorhamnetin. Finally, extraction of ***Vanillosmopsis erythropappa*** wood with ethyl acetate after preliminary extraction with hexane to remove the wood oil which contains eremanthin and other sesquiterpene lactones [1, 4, 8, 29] gave goyazensolide **(4a)**, 15-deoxygoyazensolide **(4b)** [18, 30], lychnopholide **(4c)** [12], costunolide (7) and bisabolol(8). Compounds **4b**, 7 and 8 have been isolated previously from other parts of ***V. erythropappa*** [1, 29–31].

RESULTS AND DISCUSSION

We begin by considering lactones **2a–d** whose mass, ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) showed that they were 1-oxo-3,10-epoxy-8-acyloxygermacra-2,11(13)-dien-6,12-olides differing from each other only in the nature of the acyloxy group on C-8. Extensive decoupling in the usual way which will not be detailed here established the sequence C-4 through C-9 and the attachment of the α,β-unsaturated lactone ring to C-7. Closure of the lactone to C-6 was assumed on the basis of the relative shifts of H-6 and H-8 and by analogy with lactone constituents of other ***Eremanthus*** species. The nature of the various acyloxy groups was also evident from the spectroscopic evidence; interestingly acetylation of **2c** furnished not the expected **2d**, but the isomeric monoacetate 2e as demonstrated by the ^{1}H NMR shifts on addition of trichloroacetylisocyanate (TAI) (Table 1).

As to stereochemistry, a-orientation of the various acyloxy substituents at C-8 could be deduced from both the chemical shift of H-8 near 64.4 and the coupling constants involving H-7, H-8 and H-9a,b ($J_{7,8} \sim 3$, $J_{8,9a}$

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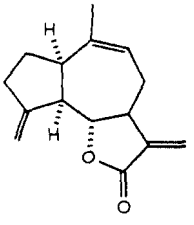
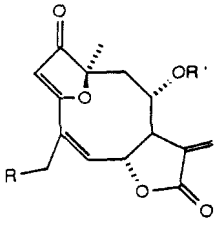
‡According to these authors, ***E. seidelii*** is restricted to the cerrado surrounding the Furnas reservoir in southwestern Minais Gerais where our material was collected. It is closely related to ***E. elaeagnus*** but distinguishable by the number of heads per capitulescence., pappus colour, leaf shape and flowering period.

= 12, $J_{8,9b}$ ~2 Hz); for comparison ^1H and ^{13}C NMR spectra of isomer **10a** (zexbrevin) with a B-orientated C-8 substituent (H-8's near 65.3, $J_{7,8}$'s ~ 1, $J_{8,9a}$'s ~ 5, $J_{8,9b}$ 5- 2-3 Hz) are included in Tables 1 and 2 (for further discussion of zexbrevin stereochemistry and its implications see below). Consequently **2a** was 4,5-dihydro-15-desoxygoyazensolide (**2a** or **9a**).

Formulae of two lactones obtained as a mixture from *Eremanthus bicolor* and originally allotted structures **2a** and **2f** [7], and of the corresponding angelate from *Piptolepis ericoides* presumed to be **2g** [8], have recently been altered to **9a**, **9b** and **9c** as a result of NOE experiments on related compounds [32]. 'H NMR data for these substances taken from the literature are included

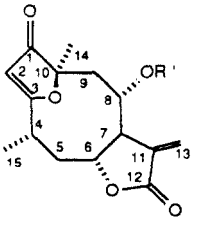




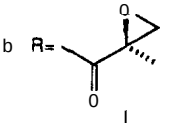
4 a R=OH, R'=MeAcr

b R=H, R'=MeAcr

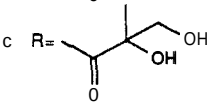
c R=H, R'=Ang



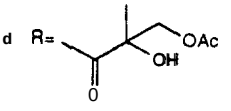
2 a R=MeAcr



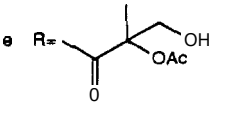
b R=



c R=



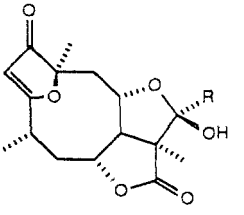
d R=



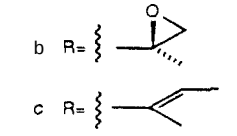
e R=

f R=Tigl

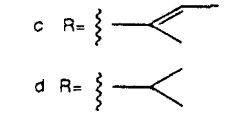
g R=Ang



3 a R=

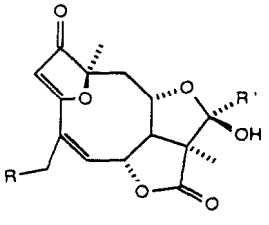


b R=



c R=

d R=



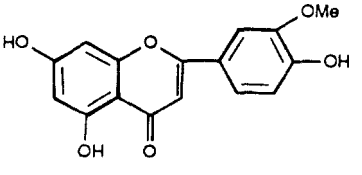
5 a R=H, R'=

b R=H, R'=

c R=H, R'=

d R=OH, R'=

e R=H, R'=



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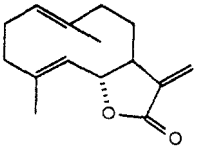

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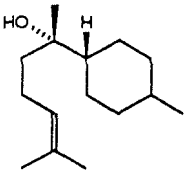

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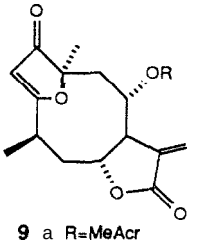
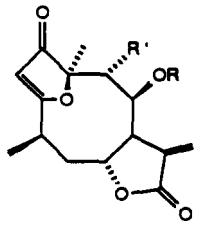


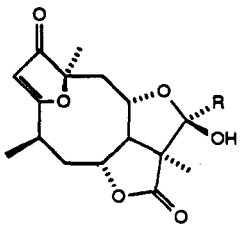
9 a R=MeAcr

b R=Tigl

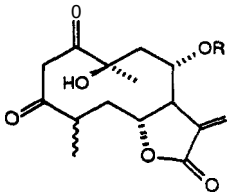
c R=Ang



10a R=MeAcr, R ' =H
b R=Tigl, R ' =H
c R=Ang, R ' =H
d R=MeAcr, R '=OAc



11a R=
b R=
c R=



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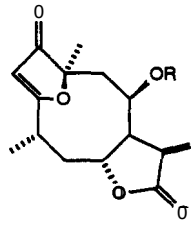
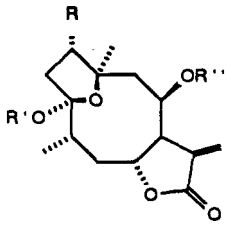


13a R=MeAcr
b R=Ang



14a R, R'=OH, R''=iBu
b R, R'=H, R''=iBu
C R=H, R'=Et, R''=iBu
d R, R'=OH, R''=i-Val

in Table 1; comparison with the spectra of our four compounds from *E.* seidelii and E. ***goyazensis*** reveals subtle differences in the chemical shifts of **H-5**$\alpha\beta$ and **H-15** and in the coupling constants involving H-5a and **H-5**β (which are essentially inverted) and the presence (in the previously reported lactones) or absence in the new lactones of allylic coupling between H-2 and H-4. Hence the two series differ in stereochemistry at C-4. While models of both **2a–d** and 9a-e can be twisted to accommodate an H-2, H-4 dihedral angle requisite for allylic coupling between these two protons [33],* the observed strong enhancement of the H-2 signal (12.5%) on irradiation of the frequency of H-4 in our compounds seemed to argue in favour of formulas **2a-d.**

In a quite similar way it was shown that our **lactones 3a, b** whose ^{1}**H** and ^{13}**C** NMR spectra are listed in Tables 3 and 4 were 4,5-dihydro derivatives of eremantholide C **(5c)** and its so far unknown **18,19-epoxide 5e.** Three such lactones originally formulated as **3a, 3c** and 3d [7] and later [32] revised to **lla-c** have been isolated from *E.* bicolor. For comparison the ^{1}**H** NMR spectrum of one of these, the presumed **11a,** is also listed in Table 3 and shows that the same spectral differences noted above between the 4,5-dihydro lactones from *E.* seidelii and *E.* goyazensis, on the one hand, and from ***E. bicolor*** on the other also exist for the **4,5-dihydroeremantholides.** Consequently if the lactones from ***E. bicolor*** are indeed **lla-c,** those from *E.* ***seidelii*** and ***E. goyazensis*** should be **3a, b.**

To resolve once and for all the uncertainties **which have** plagued the assignment of C-4 stereochemistry in this series of compounds an X-ray analysis of **3b** was undertaken. Crystal data are given in the Experimental section. Figure **1** is a stereoscopic view of the molecule which shows that the C-4 methyl group of **3b,** and hence that of the other compounds from ***E. seidelii*** and ***E. goyazensis,*** is alpha orientated, i.e. that the C-4 stereochemistry is **4*S*** since the absolute configuration corresponds to the relative configuration shown in the formulas. Conversely in the compounds from ***E. bicobr*** and ***P. ericoides*** the C-4 methyl group is beta oriented and C-4 is 4R. Tables 5 and 6 list bond lengths and bond angles (the lists of final atomic and final anisotropic thermal parameters are deposited at the Cambridge Crystallographic Data Center).

In the crystal of **3b** the conformation of the I-membered ring embodying the **3,10-oxygen** bridge is not

*A dihedral angle close to 90" required for maximum allylic coupling [33] is more easily achieved in models with H-4 alpha than in models with H-4 **beta,** although the presence of allylic coupling was originally invoked [7] as an argument in favour of formulas **2a, f** for compounds now known to possess structures **9a, b.**

Table 1. ^1H NMR spectra of compounds

H	**2a** ($CDCl_3$)	2a (C_6D_6)*	**2b** ($CDCl_3$)	**2b** (C_6D_6)*	**2c**‡ ($CDCl_3$)	**2c** (C_6D_6)*	**2d** ($CDCl_3$)§	2d (C_6D_6)*
2	5.68 *s*	5.09 *s*	*5.68 s*	5.30 *s*	5.70 *s*	5.91 *s*	*5.68 s*	*5.68 s*
4	3.14 *ddq* (10, *6.5, 6.5)*	2.01 *ddq* (11, *7, 7)*	3.18 *ddq* *(10.5, 7, 7)*	2.35 *ddq*	3.29 *ddq* (11, *7,* 7)	3.41 (obsc.)	*3.25 ddq* (11, 7, 7)	*3.06 ddq* *(10.5, 7.5, 7)*
5α	*1.94 ddd* *(13.5.* 11. 10.5)	*1.27 ddd*	*1.91 ddd* *(14,* 11, *10.5)*	*1.31 ddd*	*1.89 ddd* *(14,* 11, 10.5)	1.36 *ddd*	*1.88 ddd* *(13,* 11, *10.5)*	*1.35 ddd*
5β	2.45 *dd* *(13.5, 7)*	*1.86 dd*	*2.43 dd* (14, *7)*	*1.96 dd*	2.46 *dd* *(13.5, 7)*	*2.27 dd*	*2.45 br dd* *(13.5, 7)*	2.16 *hrdd* *(13.5, 7.5)*
6	*4.52 dd* (11, *5)*	*4.37 dd*	*4.47 dd* *(10.5, 4.5)*	*4.35 dd*	*4.50* dd (10.5, 4.5)	*4.60 dd*	*4.50* dd (11, 5)	*4.53* dd
7	*3.37 m*	*2.89 m*	*3.40 dddd* *(5, 3, 2.5, 2.5)*	*2.92 m*	3.43 *m*	*2.94 m*	3.40 *m*	2.95 *m*
8	*4.39 ddd* (12, *3, 1.5)*	*4.46 ddd*	*4.33 ddd* *(11.5, 2.5, 2.5)*	*4.40 ddd*	4.39 ddd (12, 3, 2)	*4.49 ddd*	4.33 ddd (12, 3. 1.5)	4.41 *ddd*
9α	*2.47* dd (13.5, 12)	*1.86 dd*	*2.44* dd (14, 11.5)	*1.84 dd*	2.43 dd (13, 12.5)	1.80 dd	2.42 dd (13, 11.5)	*1.88 dd*
9β	2.32 *dd* (14, *2)*	*2.16* dd	2.29 dd (14, 2)	*2.14* dd	2.30 dd (13.5. 2)	2.10 *dd*	2.21 *dd* (13, 1.5)	*2.02* dd
13a	6.21 *d* (3)	6.27 *d*	6.29 *d* (3)	6.23 *d*	6.31 *d* (3)	*6.24 d* (3)	6.29 *d* (3)	6.25 *d*
13b	5.45 *d* *(2.5)*	5.05 *d*	5.47 *d* (2.5)	5.04 *d*	5.49 *d* (2.5)	*4.97 d*	5.48 *d* *(2.5)*	5.05 *d*
14†	*1.50 s*	1.14s	1.45 *s*	1.16 *s*	1.48 *s*	*1.29 s*	1.47 *s*	1.23 *s*
15†	1.34 *d* (6.5)	0.71 *d* *(7)*	1.32 d (7)	1.16 *s*	1.32 *d* (7)	*0.87 d*	1.32 *d* (7)	0.84 *d*
3'a	6.00 *br d* *(1.5)*	*5.87 br d*	2.39 *d* (6)	2.41 *d*	3.62 *d* (11.5)	*3.46 d*	4.22 *d* (11.5)	4.28 *d*
3'b	*5.52 dq* (1.5)	*5.07* (obsc.)	2.69 *d* *(6)*	2.04 *d*	3.50 *d* (12)	*3.41 d*	3.97 (11.5)	4.13 *d*
4†	*1.83 br d* *(1.5)*	1.63 *br d*	1.48 *s*	1.13 *s*	1.34 *s*	1.10s	1.27 *s*	1.10 *s*
OH	—						4.20 *br*	4.27 *br*
Act	—						2.07 *s*	1.97 *s*

*All signals broadened.

†Intensity three protons.

‡ No change on addition of TAI except for H-3'a 4.11 *d*, H-3'b 3.76 *d*, H-4' 1.61 *s* NH 8.60 *s*, 10.3 *br*

§No change on addition of TAI except for H-3'a 4.50 *d*, H-3'b 4.29 *d*, H-4' 1.57 *s*, NH 8.5s.

significantly different from that found for other 3,10-epoxy-4,5-dihydroheliangolides [34–37]. If the conformation of **3b** and its congeners in solution approximates the conformation in the solid state, the coupling constants, the pronounced NOE between H-2 and H-4 and the absence of allylic coupling between H-2 and H-4 are all accounted for. It is interesting that biosynthesis of these substances-whether it involves biocyclization of precursors such as 12 or enzymatic reduction of precursors of type 4 or 5 seems to produce different C-4 stereochemistry in *E. seidelii* and *goyazensis*, on the one hand, and *E. bicolor* and *P. ericoides* on the other, although the possibility of epimerization at C-4, the γ-position of an a&unsaturated ketone, possibly via a hemiketal-ketal equilibrium such as **2** ⟶ **12** ⟶ **9** during the extraction and isolation process cannot be totally dismissed.

In this connection it seems appropriate to comment on the confusion in the literature concerning the C-4 stereochemistry of zexbrevin (**10a**) and its ester analogues **10b–d**.* Zexbrevin was originally isolated from *Zexmenia brevifolia* [40] and was subsequently also found in *Calea zacatechichi* together with its tiglate analogue **10b** [41] and in *Viguiera gregii* [42]. Its initially proposed stereochemistry **2a** [40] was revised to **13a** as a result of correlations involving the conversion of tagitinin A (**14a**) to tetrahydrozexbrevin and to tirotundin (tagitinin D, **14b**) [43, 44]. The stereochemistry assigned to tirotundin was based on an X-ray analysis of its ethyl ether **14c** [34] and formed the cornerstone of this complex set of interrelationships.

* Because of the confusion, Gao. Wang and Mabry [38] failed to recognize that their ladibranolide **10c** from *Viguiera latibracteata* was in fact identical with trichomoriolide from *Trichogoniopsis morii* [39] which was originally assigned structure **13c** in accordance with the then accepted formula for rexbrevin.

2a-2e and **9a-9c** (270 MHz)

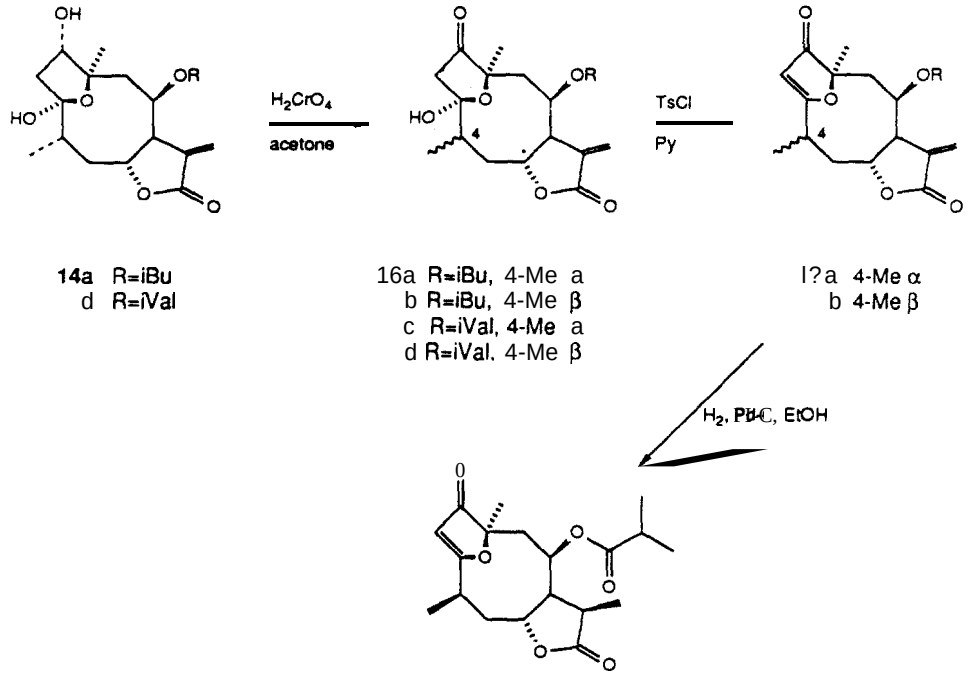
2e ($CDCl_3$)	**2e** (C_6D_6)*		**9a,b** ‖ ($CDCl_3$)		**9c***¶ ($CDCl_3$)	**10a**** ($CDCl_3$)	**16b** ($CDCl_3$)	**16b** (C_6D_6 + 3 drops DMSO-d_6)
5.70 *s*	5.00 *s*	5.70 d (1.5)		5.69 d	5.69 br *s*	5.56 *br*	2.88 d (18.5) 2.63 *d* (18.5)	2.80 *d* 2.53 d
3.17 ddq (11, 7, 7)	2.03 ddq		3.06 *br* dd (7, 7, 1.5)		3.05 *br dq* (7, 7)	3.05 *br dq* (1, 7, 7)	2.04 ddq (7)	1.52 *dd*
1.91 ddd (13, 11, 10.5)	1.26 ddd		2.11 *brd* *(14, 1.5)*		2.11 brd (14)	2.06 *br d* (15)	1.95 *br d* (14)	1.83 *brd*
2.43 dd (13.5, 7)	1.81 *dd*		*2.49 ddd* *(14, 7, 11)*		2.50 ddd (14, 7, 11)	2.61 ddd (15, 7, 8.5)	2.23 ddd (14, 11, 9)	2.45 *ddd*
4.42 dd (11, 5)	*4.20* dd	*4.34 ddd* (11, 5, 1.5)		4.33 ddd	4.36 ddd (11, 5?)	4.48 dd (8.5, 5)	4.54 ddd (11, 6 ~ 1.5)	4.41 ddd
3.46 m	2.95 *m*		3.36 *ddd* *(5.4, 3.5, 3)*		3.35 m (5, 4, 3.3, 3)	3.30 *br* ddd (5, 3, 2.7)	4.09 dddd (6, 3, 3, 3)	4.15 *ddd*
4.40 ddd (12, 3, 1.5)	4.42 ddd	*4.50 ddd* (10, *4, 2)*		4.51 brdd	4.53 ddd (10, 4, 2)	5.17 *dd* (5, 2.5)	5.61 ddd (11.5, 4.5, 3.3)	5.64 *ddd*
2.39 dd (13, 5, 12)	1.83 *dd*	*2.35* dd (13.5, 10)		2.34 *dd*	*2.34* dd (13, 10)	2.71 dd (16, 5)	1.70 dd (14, 11.5)	1.55 *dd*
2.24 dd (13.5, 2)	*2.09* dd		2.48 dd (13.5, 2)		2.46 *dd* (13, 2)	2.25 dd (16, 2.5)	1.97 dd (14, 4.5)	1.96 *dd*
6.34 *d* (3)	6.24 *d*	6.19 *d* (3.5)		6.16 *d*	6.19 *d* (3.3)	6.36 d (3)	6.30 *d* (3)	6.22 *d*
5.52 *d* *(2.5)*	4.99 d	5.46 d (3)		5.43 *d*	5.42 *d* (3)	5.70 *d* (2.7)	5.58 *d* (3)	5.25 *d*
1.48 *s*	1.15 *s*	1.49 *s*		1.48 *s*	1.48 *s*	1.42 *s*	1.78 *s*	1.41 *s*
1.33 d (7)	0.68 *d*		1.42 d (7)		1.43 *d* (7)	1.39 d (7)	1.56 *d* (7)	0.96 *d*
3.99 *d* (11.5)	3.99 *d*					5.99 *br d* (1.5)	1.05 *d*† (7)	0.98 *d*† (7)
3.65 *d* (11.5)	3.44 *d*					5.60 *dq* (1.5, 1.5)		
1.52 *s*	1.40 *s*					1.87 *brd* *(1.5)*	1.07 d (3)	0.97 *d* (7)
							3.79 *s*	3.40 s
2.05 *s*	1.63 *s*						2.43 *sept* (7)-H-2	2.26 *sept* (7)-H-2

‖ Taken from ref. [7].
¶ Taken from ref. [8].
**At 200 MHz, taken from ref. [42].

Somewhat later isolation from a *Calea* species and subsequent X-ray analysis of a **lactone 10d** which had 'NMR properties reminiscent of a **9α-acetoxyzexbrevin**' led Fischer and coworkers [35, 45] to reformulate **zexbrevin** as **10a**,† while in essentially contemporaneous articles on the photochemistry of tetrahydrozexbrevin [46] based largely on X-ray analyses of tetrahydrozexbrevin [37] and phototetrahydrozexbrevin A [47] formulas of these compounds were consistently represented as containing an a-orientated C-4 methyl **group.**‡ Only careful study of Fig. 1 and 2 of ref. [37], the latter representing a stereoscopic view of the conformation and packing of tetrahydrozexbrevin, and Fig. 1 of ref. [47] reveals that the C-4 methyl groups of tetrahydrozexbrevin and phototetrahydrozexbrevin A are in fact β-orientated and that tetrahydrozexbrevin is actually represented by formula 15 (Scheme 1) in accordance with the proposal of the Fischer group. Indeed, the **^{1}H NMR** spectrum of zexbrevin (Table 1) exhibits the features now known to be diagnostic for B-orientation of the C-4

†As is evident from the previous discussion NMR evidence was, at the time, in the absence of information about spectral properties of C-4 diastereomers, not sufficient to distinguish between a-and /I-orientation of the C-4 methyl group. In retrospect the presence of **allylic** coupling between H-2 and H-4 evidenced by broadening of the H-2 signal which is exhibited by **zexbrevin** as well as by **9a–c, 10b–d** and **lla-c,** but not by **2a–e** and **3a, b** can be seen as being diagnostic of /I-orientation of the C-4 methyl group in zexbrevin.

‡In fact ref. [37] is misleadingly entitled '(4βH,6βH,11αH)-3β,10β-epoxy-8β-isobutyryloxy-1-oxogermacr-2-en-6,12-olide (tetrahydrozexbrevin), $C_{19}H_{26}O_6$, A Sesquiterpene Lactone'.



14a R=iBu
d R=iVal

16a R=iBu, 4-Me a
b R=iBu, 4-Me β
c R=iVal, 4-Me a
d R=iVal, 4-Me β

17a 4-Me α
b 4-Me β

15

Scheme 1.

Table 2. ^{13}C NMR spectra of compounds **2a–e** ($CDCl_3$, 67.89 MHz)*

C	2a	2b	2c	2d	2e	10a‡
1	204.95 *s*	204.68 *s*	205.50 *s*	204.57 *s*	204.97 s	205.18 *s*
2	105.52 *d*	105.61 ***d***	106.37 ***d***	105.74 *d*	105.78 ***d***	102.05 *s*
3	192.57 *s*	192.44 *s*	192.43 *s*	192.32 *s*	192.10 *s*	192.13 *s*
4	33.56 ***d***	33.55 *d*†	33.00 ***d***	33.29 ***d***	33.49 *d*†	31.37 *d*
5	42.35 *t*	42.34 *t* t	42.22 *t*	42.30 *t*	42.30 *t*	40.96 *t*
6	82.14 *t*	82.05 *d t*	81.99 ***d***	82.07 *d*	82.13 ***d***	74.41 *d*
7	54.36 ***d***	54.16 *d*†	53.75 *d*	53.94 ***d***	53.78 *d*	51.61 *d*
8	71.93 ***d***	75.21 *d*†	73.52 ***d***	73.31 *d*	12.74 *d*	74.41 *d*
9	45.23 *t*	45.11 *t*†	45.21 t	45.22 t	45.17 *t*†	43.10 *t*
10	89.84 *s*	89.78 *s*	89.59 *s*	89.67 *s*	89.61 *s*	88.29 *s*
11	133.93 *s*	133.59 *s*	133.15 *s*	132.92 *s*	132.77 *s*	139.53 *s*
12	168.72 *s*	168.33 *s*	168.77 *s*	168.42 *s*	168.65 *s*	168.54 *s*
13	124.07 *t*†	124.24 *t*†	125.60 *t*	124.92 *t*	125.12 *t*	123.05 *t*
14	21.07 *q*†	21.06 *q*	21.21 *q*	21.09 *q*	20.91 *q*	22.74 *q*
15	18.46 *q*†	18.44 *q*†	18.16 *q*	18.36 *q*	18.56 *q*	16.04 *q*
1'	166.74 s	170.27 *s*	173.50 *s*	174.05 *s*	174.65 *s*	166.12 *s*
2	135.61 *s*	53.52 *s*	74.30 *s*	73.40 *s*	78.77 *s*	135.82 *s*
3'	126.10 *t*†	52.51 t	50.88 *t*	68.85 *t*	46.74 *t*†	126.70 t
4'	17.87 *q*	17.23 *q*	22.82 *q*	20.49 *q*	21.65 *q*†	18.05 *q*
AC				170.62 *s*	171.06 *s*	
				22.04 *q*	20.65 *q*†	

*Multiplicities established by DEPT pulse sequence.
† Assignment by single frequency heteronuclear decoupling.
‡Taken from ref. [41].

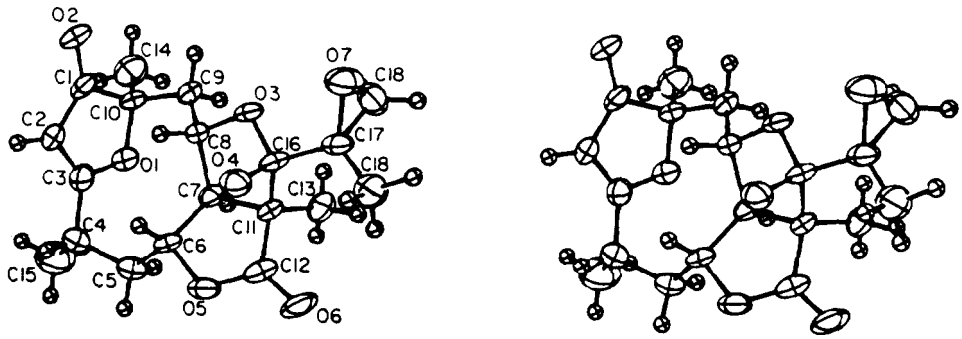


Fig. 1. Stereoscopic view of compound **36**.

Table 3. ^{1}H NMR spectra of compounds **3a, b** and **11a** ($CDCl_3$, 270 MHz)

H	3a	3a*	3b	3b*	11af
2	5.57 *s*	5.29 *s*	5.59 *s*	5.87 *s*	5.61 *brs*
4	3.12 *ddq* (11, 7, 7)	2.50 *ddq* (obsc)	3.13 *ddq* (11, 7, 7)	3.04 *ddq*	(1.5) 3.00 *br dq* (7, 7, 1.5, 1.5)
5α	1.86 ddd (13, 11, 10.5)	1.55 *ddd*	1.86 *ddd* (13, 11, 10.5)	1.55 *ddd*	2.15 *br d* (14, 1.5)
5β	2.47 *br dd* (13, 7)	2.14 *br dd*	2.49 *ddd* (13, 7)	2.40 *dd*	2.44 *dd* (14, 11, 7)
6	4.27 *dd* (11, 7)	4.18 *dd*	4.28 dd (13.5, 7)	4.41 dd	4.24 *dd* (11, 6.5)
7	2.53 dd (7, 4.5)	2.26 *dd*	2.57 *dd* (7, 4.5)	2.26 dd (7, 5)	2.57 *dd* (6.5,5)
8	3.99 ddd (12, 4.5, 2)	4.01 *ddd*	3.98 *ddd* (12, 5, 2)	4.05 ddd	3.98 *ddd* (12, 5, 2)
9a	1.96 *dd* (13, 12)	1.70 *dd*	1.90 *dd* (13, 12)	1.68 dd	2.46 *dd* (13.5, 2)
9β	2.44 dd (13, 2)	2.50 dd	2.38 dd (13, 2)	2.61 dd	2.01 dd (13.5, 12)
13†	1.20 *s*	1.13 *s*	1.37 *s*	1.08 *s*	1.22 *s*
14†	1.43 *s*	1.15 *s*	1.48 *s*	1.39 *s*	1.45 *s*
15†	1.31 *d* (7)	0.86 *d*	1.31 *d* (7)	1.08 *s*	1.38 *d* (7)
18a	5.30 *br s*	3.43 *br s*	3.12 *d* (6)	2.98 *d* (6)	5.23 *br s*
18b	5.05 *t* (1)	5.05 *br s*	2.71 *d* (6)	2.38 *d* (6)	5.07 *br s*
19†	1.90 *br s*	2.89 *br s*	1.57 *s*	1.78 *s*	1.90 *br s*
OH	2.75 *s*	4.05 *br*	3.31 *s*		1.71 *s*

*In C_6D_6 solution. All signals broadened.
†Intensity 3 protons.
‡Taken from ref. [7].

methyl group (allylic coupling between H-2 and H-4, relative shifts of H-5α and H-5β and their coupling constants).

Stereochemistry **15** for tetrahydrozexbrevin implies that during stage 1 or 2 of the three stage conversion of tagitinin A to tetrahydrozexbrevin (Scheme 1) [43] the asymmetric centre at C-4 was inverted or that tagitinin A also possesses a /?-orientated C-4 methyl group. In the latter case C-4 epimerization, presumably by equilibration through a hemiacetal–γ-ketol equilibrium, must have taken place during the conversion [43] of tagitinin A to tirotundin **14b** and its ethyl ether **14c**.

Indirect but persuasive evidence has been adduced recently [48, 49] in favour of our original formulation of tagitinin A as **14a so** that epimerization during the conversion of **14a** to **15a** (Scheme 1) seemed a *priori* more likely to account for the C-4 stereochemistry of zexbrevin than a change in the C-4 configuration of tagitinin A. Superposition of the signals of H-2b, H-4 and H-5a, b in the ^{1}H NMR spectrum of tagitinin A interfered with accu-

Table 4. ^{13}C NMR spectra of compounds **3a**, b (CDCI,, 67.89 MHz)*

C	3a	3b
1	205.81 *s*	205.75 *s*
2	105.09 ***d***	105.10 ***d***
3	192.58 *s*	192.47 *s*
4	33.41 ***d***	33.18 ***dt***
5	43.98*t*	43.63 *t* t
6	81.54 ***d***	81.55 ***dt***
7	66.40 ***d***	67.11 *d*†
8	76.90 ***d***	76.49 ***d t***
9	42.26 *t*	42.18 *t*†
10	90.38 *s*	90.25 *s*
11	60.21 *s*	60.04 *s*‡
12	175.81 *s*	174.97 s
13	22.59*q*	21.32 ***qt***
14	21.04*q*	20.94 *q*†
15	18.93 *q*‡	18.48 *q*
16	106.43 *s*	104.94 *s*
17	142.25 *s*	58.39 *s*‡
18	115.78 *t*	53.64 *t*†
19	18.46 *q*‡	17.33 ***qt***

Multiplicities established by DEPT pulse sequence.

†Assignment by single frequency heteronuclear decoupling.

‡Assignments interchangeable within column.

Table 5. ^{13}C NMR spectra of compounds **4b**, **c** ($CDCl_3$, 67.89 MHz)*

C	4b	**4c**
1	***204.65 s***	204.71 s
2	***104.65 d***	104.69 dt
3	***186.78 s***	186.83 s
4	***130.42 s***‡	130.44 *s*‡
5	***135.09 d***	135.12 ***d***
6	***81.46 d***	81.61 dt
7	***51.19 d***	51.23 dt
8	***73.40 d***	73.00 ***d***†
9	***43.81 t***	44.04 *t*†
10	***89.55 s***	89.64 *s*
11	***133.62 s***‡	133.84 *s*‡
12	***168.66 s***	168.02 *s*
13	***124.30 t***	124.10 *t*
14	***20.62 q***	20.65 *q* t
15	***20.25 q***	20.22 *q*†
1'	***166.69 s***	167.00 *s*
2	***135.58 s***	126.51 *s*
3'	***126.28 t***	140.54 ***d***
4	17.92 *q*	19.93 *q*
5'		15.64 *q*

*Multiplicities established by DEPT pulse sequence.

†Assignment by single frequency heteronuclear decoupling.

‡ Assignments interchangeable within column

rate determination of the relevant coupling constants; however reexamination of a small sample of dehydrotagitinin A **(16a** or **16b)** remaining from our earlier work [43] on a modern NMR spectrometer resulted in the frequencies and coupling constants listed in Table 1. It is seen that the coupling constants involving H-4, H-5 and H-6 essentially duplicate those found in zexbrevin **(10a)** rather than those found in the C-4 epimers **2a-e.. Consequently** we believe that dehydrotagitinin A is best described by formula **16b** and that epimerization of **16a** to the more stable [49] 4β-methyl isomer **16b** is at present the most plausible explanation for the correlations involving zexbrevin, tagitinin A and tirotundin. The analogous conversion **[SO]** of viguilenin **(14d)** to dehydroviguilenin **(16d)** presumably follows the same course since the 'H and ^{13}C NMR spectra of **14a** and **14d on** the one hand and **16b** and **16d** are superimposable except for the signals of the differing side chains.

EXPERIMENTAL

Plant material. Aerial parts of ***Eremanthus seidelii*** MacLeish and Schumacher were collected by W. V. in October 1985 in Furnas near Capitolio, Minas Gerais State. Aerial parts of ***Eremanthus goyazensis*** Sch.-Bip. were collected by W.V. in Furnas in May 1985. ***Vanillosmopsis erythropappa*** Sch.-Bip. wood was collected at the same location: vouchers are kept in the FCF de Ribeirao Preto.

Extraction and isolation of constituents. Aerial parts, mainly leaves, of ***E. seidelii (2.95*** kg) were pulverized and extracted with EtOAc ***to give*** 122 g of crude extract which was dissolved in MeOH–H_2O (19: 1). The soln was extracted with hexane: the MeOH–H_2O layer was concd at red. pres. and the residue extracted with EtOAc. Evapn of the extract at red. pres. gave 68 g of residue which was chromatographed over 400g silica gel, 200 ml fractions being eluted as follows: F1–10 (hexane), 11-48 (hexane–EtOAc 99: I), 49–60 (hexane–EtOAc 49: 1), 61-72 (hexane–EtOAc 24: 1), 73-87 (hexane–EtOAc 47: 3), 88-95 (hexane–EtOAc 93:7), 96–120 (hexane-EtOAc 9: 1), 121–137 (hexane–EtOAc 17:3), 138-159 (hexane–EtOAc 4: 1), 160–190 (hexane–EtOAc 3:2), 224–235 (hexane–EtOAc 1: 1), 236–250 (hexane–EtOAc 2: 3), 256–265 (hexane–EtOAc 3: 7), 266–280 (EtOAc), 281-300 (EtOH).

Recrystallization of fr. 95-98 from hexane–EtOAc (4: 1) gave 640 mg of **2a**, mp 174-176". Recrystallization of fr 104–111 from hexane–EtOAc (7: 3) gave 1.8 g of (**3a**) mp 228–232°, Frs 128-144 on recrystallization from hexane–EtOAc gave 1.0 g of **3b**, mp 225". Recrystallization offrs 145-155 from EtOH gave 110 mg of isorhamnetin (**6**), identified (^{1}H NMR, MS) by comparison with an authentic sample. A 231 mg portion of frs 156161 (6.0 g) on purification by TLC (hexane–EtOAc 7: 3, twice) afforded 160 mg of 2d and 60 mg of a 4: 1 mixture of **2c** and **2b**, which was separated by acetylation of the mixture and prep. TLC (*vide infra*).

Aerial parts of *E. goyazensis* (3.2 kg) were pulverized and extracted with EtOAc to give 200 g of crude extract which was dissolved in MeOH–H_2O (195: 5). The soln was extracted with hexane; the MeOH–H_2O layer was concd at red. pres. and the residue extracted with EtOAc. Evapn of the extract gave 80 g of residue which was chromatographed over 400 g silica gel, 400 ml

Table 6. Bond lengths (A) in 3b with standard deviations in parentheses.

Distances	Bond length (A)
Cl-C2	1.409 (9)
Cl–C10	1.522 (9)
C2–C3	1.340 (9)
C3–O1	1.343 (9)
C3–C4	1.503 (9)
C4–C5	1.522 (10)
C4–C15	1.538 (7)
C5–C6	1.453 (7)
C6–O5	1.543 (7)
C6–C7	1.542 (7)
C7–C8	1.532 (7)
C7–C11	1.447 (7)
C8–O3	1.495 (7)
C8–C9	1.527 (7)
C9–C10	1.445 (7)
Clo-01	1.522 (7)
C10–C1	1.511 (7)
C11–C12	1.530 (8)
C11–C16	1.564 (7)
C12–C13	1.530 (7)
C12–O5	1.336 (7)
C12–O6	1.217 (7)
C16–O3	1.408 (7)
C16–O4	1.395 (7)
C16–C17	1.510 (7)
C17–O7	1.442 (7)
C17–C19	1.447 (9)
C17–C18	1.463 (8)
C18–O7	1.432 (8)

Table 7. Bond angles (°) in **3b** with standard deviations in parentheses

Atoms			Angles (deg)
c3	01	Cl0	108.4 (7)
C8	03	Cl6	107.9 (7)
02	Cl	Cl0	121.6 (9)
02	Cl	c2	130.2 (9)
Cl0	Cl	c2	108.1 (9)
c3	c2	Cl	106.2 (9)
C6	C5	C12	112.2 (10)
01	c3	c4	113.2 (9)
01	c3	c2	115.0 (9)
c4	c3	c2	131.7 (9)
c3	c4	C5	111.5 (7)
c3	c4	Cl5	110.8 (7)
C5	c4	C15	111.1 (7)
C4	C5	C6	115.3 (7)
05	C6	C5	107.9 (7)
05	C6	C7	105.2 (7)
C5	C6	C7	115.9 (7)
C6	C7	C8	116.7 (7)
C6	C7	Cl 1	105.4 (7)
C8	C7	Cl 1	105.9 (7)
03	C8	C7	104.6 (7)
03	C8	C9	107.5 (7)
C7	C8	C9	116.9 (7)
C8	C9	Cl0	113.6 (7)
01	Cl0	c9	106.8 (7)
01	Cl0	Cl	102.0 (7)
01	Cl0	C14	110.1 (7)
c9	C10	C l	109.6 (7)
c9	Cl0	C14	114.5 (7)
Cl	C l 0	C14	113.0 (7)
c7	Cl1	Cl2	103.3 (8)
c7	C l 1	C13	113.4 (7)
c7	Cl1	Cl6	100.8 (7)
C12	C11	C13	111.6 (7)
Cl2	Cl1	Cl6	113.1 (7)
013	C11	Cl6	113.7 (7)
05	Cl2	06	121.4 (7)
05	Cl2	Cl1	111.8 (7)
06	Cl2	Cl1	126.7 (7)
03	Cl6	04	110.9 (7)
03	C l 6	C11	103.2 (7)
03	Cl6	Cl7	108.8 (7)
04	Cl6	Cl1	105.3 (7)
04	Cl6	Cl7	111.7 (7)
C11	C16	C17	116.6 (7)
Cl6	Cl7	07	114.3 (7)
C16	C17	C19	116.0 (7)
C16	C17	C18	119.2 (7)
07	C17	C19	114.0 (7)
07	Cl7	Cl8	59.1 (8)
Cl9	Cl7	Cl8	120.8 (9)
C17	07	Cl8	61.2 (8)
Cl7	Cl8	07	59.7 (8)

fractions being eluted as follows: Frs l-7 (hexane), 8:13 (hexane–EtOAc 99: 1), 14-24 (hexane–EtOAc 19: 1), 2547 (hexane–EtOAc 9: 1), 48-69 (hexane–EtOAc 17:3), 70–86 (EtOAc 4: 1), 87-100 (hexane–EtOAc 3:1), 101-112 (hexane-EtOAc 7: 3), 113-127 (hexane–EtOAc 3: 2), 128–140 (hexane–EtOAc 2: 3), 141-156 (hexane–EtOAc 1:4), 157-168 (EtOAc), 169-173 (EtOAc–EtOH 1:1), 174181 (EtOH).

Frs 60-85 were combined and recrystallized (hexane–EtOAc 7: 3) to give 300 mg of eremantholide C (**5c**), mp 232" lit mp 229-230" [20], identical in all respects with an authentic sample. Frs 86–100 were combined and recrystallized (hexane–EtOAc 4: 1) to give 191 mg of 2a. Frs 111 and 112 were combined and recrystallized from hexane–EtOAc (7:3) to give 60mg of **3b**, 143-144". Frs 113-120 (combined wt 5 g) were mixtures of goyazensolide (**4a**) [17,18] and **5d** [9]. Frs 121–132 were combined and washed with a little $CHCl_3$. The $CHCl_3$-insoluble material (1.4 g) was slightly impure **2c**. The $CHCl_3$ soluble material (2.0 g) was rechromatographed over silica gel, elution with hexane–EtOAc containing increasing amounts of EtOAc. This initially afforded 149 mg of a mixture containing **3b**, **2b** and **2c**; the more polar eluates were essentially pure **5d**.

Frs 128–140 (1.12 g) were combined and rechromatographed over 20 g of silica gel inactivated with 10% H_2O. The hexane–EtOAc (7:3) eluate was purified to give in order of increasing polarity **3b**, **2c** and **2b**. Frs 141-156 (1.0 g) were also combined and rechromatographed over 20 g silica gel. Elution with hexane–EtOAc mixtures of increasing polarity afforded, in order,25 mg of isorhamnetin and 220 mg of a mixture which was separated by HPLC (Lichnisorb RP-18, 5 μm, solvent MeOH–H_2O 7: 3, flow rate 0.5 ml/min) into goyazensolide (**4a**) and its 11β (H), 13-dihydro derivative (**4d**). Frs 157-168 (4 g) were also combined. Rechromatography of the material over silica gel

(eluent hexane–EtOAc 2:3) failed to separate the constituents which were identified as **3a**, **4a** and **5d**.

Powdered wood of ***Vanillosmopsis erythropappa (9.8*** kg) was extracted with hexane. The constituents of the hexane extract or wood oil have been reported [1, 4, 8, 29]. Further extraction of the wood with EtOAc and evapn of the extract afforded 240 g of material which was chromatographed over 400g silica gel, 200 ml fractions being collected as follows: frs l-10 (hexane), 1 l-20 (hexane–EtOAc 9: 1), 21–60 (hexane–EtOAc) 61-80 (hexane–EtOAc 4: 1), 81-110 (hexane–EtOAc 7:3), 111-125 (hexane–EtOAc 3:2), 126–140 (hexane–EtOAc 1: 1), 141-160 (hexane–EtOAc 2:3), 161-170 (hexane–EtOAc 1:4), 171-190 (EtOAc) and 191-200 (EtOH). Fr. 5 contained 135 mg of bisabolol. Recrystallization of frs 90–105 (3.0 g) from hexane–EtOAc (7:3) gave 1.4 g of lychnopholide (**4c**), mp 125–128°, lit mp 128" [12] (for correction of structure see [8]). Fr. 115 (0.8 g) after purification by prep. TLC afforded costunolide and a very small amount of **4b**. **Combination** of frs 120–130 (1.0 g) and chromatography over silica gel followed by prep. TLC (CH_2Cl_2–EtOAc 3: 2) gave additional **4b**. The previously unreported ^{13}C NMR spectra of 4b and **4c** are listed in Table 5.

(4S,6R,7S,8S,10R)-1-*Oxo*-3,10-*epoxy*-8-*methacryloxygermacra*-2,11(13)-*dien*-6,12-*olide* (**2a**). M p 174–176°; (hexane–EtOAc 4: 1); IR ν_{max} cm-': 1765, 1710, 1695, 1593; MS EI ***m/z*** (rel int.): 346 [M]' (36.5), 277 (11.0), 260 (10.5) 249 (5.0), 232 (25.8) 217 (6.4), 190 (7.7). 165 (5.2), 137 (6.6), 125 (67.5), 69 (100); MS CI ***m/z:*** **347** $[M+1]^+$ (100). ^1H and ^{13}C NMR spectra are listed in Tables 1 and 2.

(4S,6R,7S,8S,10R)-1-*Oxo*-3,10-*epoxy*-8-(2,3-*epoxypropanoyloxy*)-*germacra*-2,11(13)-*diene*-6,12-*olide* (**2b**). Mp 143-144" (dec) (hexane–EtOAc 7:3); IR ν_{max} cm-': 1770, 1740, 1710, 1605; MS EI m/z (rel. int.): 362 [M]' (11.2), 277 (1.2), 260 (14.9) 232 (28.7) 125 (100), 57 (27); MS CI ***m/z:*** 363 $[M+1]^+$ (100), 261 (3.4); ^1H and ^{13}C NMR spectra are listed in Tables 1 and 2.

(4S,6R,7S,8S,10R)-1-*Oxo*-3,10-*epoxy*-8-(2,3-*dihydroxypropanoyloxy*)-*germacra*-2,11(13)-*dien*-6,12-*olide* (**2c**). Mp 175-177" (EtOAc–hexane 7:3); IR ν_{max} cm^{-1}: 3400, 1770, 1740, 1695, 1600; MS El m/z (rel. int.): 380 [M]' (0.06), 362 (1.8), 349 (6.5), 277 (1.6), 261 (10.6), 260 (17.3), 232 (32.1), 181 (13.6) 149 (14.5) 125 (100); MS CI ***m/z:*** 381 $[M+1]^+$ (3.7), 363 (20.9) 261 (5.6). 'Hand ^{13}C NMR spectra are listed in Tables 1 and 2.

Acetylation of 30 mg of the mixture of **2b** and **2c** from *E. seidelii* (Ac_2O–pyridine, overnight) and purification of the crude product by prep. TLC (CH_2Cl_2–Et_2O 17: 3) gave 13 mg of 2e and 5 mg of **2b**. Compound **2e** was a gum; IR ν_{max} cm^{-1} 3480, 1760, 1745, 1705, 1600; MS EI ***m/z*** (rel. int.): 362 $[M-C_2H_4O_2]^+$ (0.5), 349 (2.9), 277 (3.4) 278 (10.3), 261 (6.4), 260 (16.5), 232 (63.6) 190 (20.4), 181 (10.2), 163 (44.5) 149 (15.8) 135 (62.9), 125 (100), 117 (3.6), 112 (3.6), 99 (5.7); MS CI m/z (rel. int.): 423 $[M+1]^+$ (0.5), 407 (6.5), 363 (5.7), 347 (18.2), 263 (29.8), 181 (16.8), 101 (13.7). 85 (7.2). ^1H and ^{13}C NMR spectra are listed in Tables 1 and 2.

(4S,6R,7S,8S,10R)-*Oxo*-3,10-*epoxy*-8-(3-*acetoxy*-2-*hydroxypropanoyloxy*)-*germacra*-2,11(13)-*diene*-6,12-*olide* (**2d**). Colourless gum; IR ν_{max} cm^{-1}: 3440, 1765, 1740, 1700, 1600; MS EI ***m/z*** (rel. int.): 422 $[M]^+$ (2.9), 362 (14.4). 349 (14.7), 332 (2.6), 306 (23.7) 278 (20.1), 277 (2.2), 262 (38.1), 261 (15.9), 260 (20.3), 232 (48), 190 (15.6), 181 (23.5), 165 (6.5) 143 (19.2), 138 (11.9), 125 (100), 117 (26.8), 112 (17.2), 99 (46.3); MS CI ***m/z*** (rel. int.): 423 $[M+1]^+$ (100), 401 (5.7), 360 (20.1), 347 (7.6), 279 (20.9), 263 (471), 261 (12.4), 189 (5.4), 163 (26.6). 145 (10.7), 117 (12.6), 107 (14.1). ^1H and ^{13}C NMR spectra are listed in Tables 1 and 2.

(4S,6R,7S,8S,10R,11S,16R)-4,5-*Dihydroeremantholide C* (3a). Mp 2288232" (hexane–EtOAc 7:3); IR ν_{max} cm-': 3360, 1766, 1694, 1589, 1215; MS EI *m/z* (rel. int.): 348 [M]' (6), 331 (61), 330 (S), 279 (2), 236 (5.3), 168 (15.4), 136 (28.8), 125 (100), 69 (93.7); MS CI m/z (rel. int.): 349 $[M+1]^+$ (46.6). 332 (18.9), 331 (100); CD curve (MeOH) $[\theta]_{308}$ + 2240, $[\theta]_{276}$ 0, $[\theta]_{260}$ − 964, $[\theta]_{234}$ 0, $[\theta]_{205}$ 0 (last reading). 'H and ^{13}C NMR spectra are listed in Tables 3 and 4.

(4S,6R,7S,8S,10R,11S,16R,17R)-4,5-*Dihydro*-17,18-*epoxyeremantholide C* (3b). Mp 225" (hexane–EtOAc); IR ν_{max} cm-i: 3355, 1754, 1686, 1592, 1245; MS EI ***m/z*** (rel. int.): 364 $[M]^+$ (4.1), 347 (3.2), 346 (0.9), 307 (4.5), 236 (5.5), 125 (100), 85 (3.9), 69 (30.9); MS CI ***m/z:*** 365 $[M+1]^+$ (100), 347 (33.7); CD curve (MeOH) $[\theta]_{310}$ + 2230, $[\theta]_{276}$ 0, $[\theta]_{258}$ − 784. $[\theta]_{239}$ 0, $[\theta]_{205}$ 0 (last reading). ^1H and ^{13}C NMR spectra are listed in Tables 3 and 4.

X-Ray *analysis of* **3b**. Single crystals of **3b**, prepared by slow evapn of a 1: 1 soln of hexane–EtOAc, were monoclinic, space group $P2_1$ with $a = 7.110(3)$, $b = 10.304(7)$, $c = 12.984(8)$ A, β 74.96(7)° and d_{calcd} = 1.32 g/cm^3 for Z = 2 ($C_{19}H_{24}O_7$, M_r = 364.4). The intensity data were measured on a CAD4 Enraf Nonius diffractometer (Mo radiation. monochromated, θ–2θ scans). The size of the crystal used for data collection was *ca* 0.3 × 0.3 × 0.3 mm". No absorption correction was necessary (μ = 0.94). A total of 1864 reflections were measured for $2\theta \leq 50$ of which 1572 were considered to be observed. The structure was solved by direct methods using MULTAN 78 [51] and refined by full-matrix least squares methods. In the final refinement anisotropic thermal parameters were used for non-hydrogen atoms. Methyl hydrogen atoms were located from a difference Fourier map; the remaining hydrogen atom parameters were calculated assuming idealized geometry. Hydrogen atoms ***were*** included in the structure factor calculations, but their parameters were not refined. The final discrepancy indices were R = 6.9 and R_w = 7.4 for the 1522 observed reflections. The final difference Fourier map was essentially featureless with no peak greater than 0.3 e/Å^3.

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