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NEW GERMACRANOLIDES FROM *LIATRIS* SPECIES*

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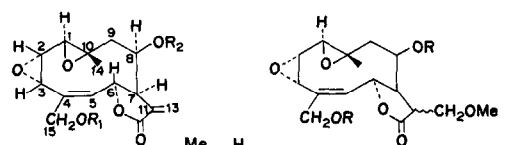
Key Word Index—*Liatris elegans*; *L. secunda*; *L. punctata*; Compositae; germacranolides; eleganin; liscundin; liscunditrin; liatripunctin; cytotoxic sesquiterpene lactones.

Abstract—Three closely related *cis*-Δ^4-diepoxygermacranolides were isolated from two *Liatris* species. Structures of eleganin from *L. elegans* (Walt.) Michx, and liscundin and liscunditrin from *L. secunda* (Ell.) Small. were established by NMR spectrometry, chemical transformations and correlation with punctaliatrin previously isolated from *L. punctata* Hook. Reinvestigation of the latter species yielded another germacranolide liatripunctin whose structure is reported.

INTRODUCTION

In an earlier communication [1] we reported the isolation of two new linear polyoxygenated diterpenes from a chloroform extract of *Liatris elegans* (Walt.) Michx. A minor constituent was a new cytotoxic sesquiterpene lactone, eleganin, whose structure has now been elucidated as (**1a**). The structure of two new closely related lactones (**1c**) and (**1e**) from *Liatris secunda* (Ell.) Small is also reported as is the structure of a new germacranolide liatripunctin (**6**) which was obtained on reinvestigation of *Liatris punctata* Hook [2, 3].



(**1a**) R_1 = H, R_2 = –C(=O)–C(Me)=CH–CH_2OAc

(**1b**) R_1 = Ac, R_2 as above

(**1c**) R_1 = H, R_2 = –C(=O)–C(Me)=CH–Me

(**1d**) R_1 = Ac, R_2 as above

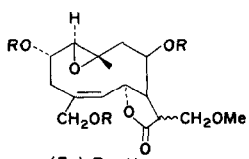
(**1e**) R_1 = H, R_2 = –C(=O)–C(CH_2OAc)=CH–Me

(**1f**) R_1 = Ac, R_2 as above

(**1g**) R_1 = H, R_2 = –C(=O)–epoxide

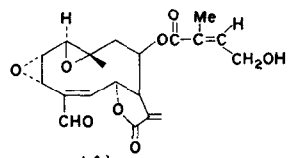
(**2a**) R = H

(**2b**) R = Ac



(**3a**) R = H

(**3b**) R = Ac



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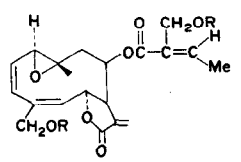
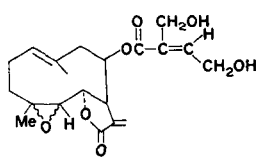


(**5a**) R = H

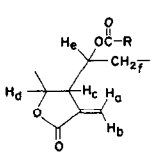
(**5b**) R = Ac



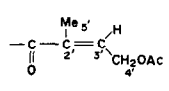
(**6**)

RESULTS AND DISCUSSION

Eleganin (**1a**), $C_{22}H_{26}O_9$ (MS and elemental analysis), mp 142–143°, $[\alpha]_D^{22}$ – 108°, was a conjugated γ-lactone (IR bands at 1760 and 1650 cm^{-1}, strong UV end absorption). The NMR spectrum (Table 1) exhibited the typical doublets of H_a and H_b in partial structure **7** at 6·37 and 5·83 ppm.



(**7**)



(**8**)

* Part 7 in a series "Constituents of *Liatris* species. For part 6, see Herz, W., Poplawski, J. and Sharma, R. P. *J. Org. Chem.* (1975) **40**, 199.

Table 1. NMR spectra of

Compound	H-1	H-2	H-3	H-5	H-6	H-7	H-8
1a†	2·55*d* (8·5)	3·13*dd* (8·5, 4)	3·69*dbr* (4)	5·57*dbr* (11·5)	5·44*dbr* (11·5)	2·96*m*‡	5·17*m*
1b¶	2·53*d* (8·5)	3·14*dd* (8·5, 4)	3·71*dbr* (4)	5·49*br*§	5·49*br*§	2·90*m*	5·20*m*
2a**	††	††	††	5·88*dbr* (11·5)	5·11*dbr* (11·5)	*	3·82*m*‡‡
2b§§	2·54*d* (8·5)	3·14*dd* (8·5, 4)	3·47*dbr* (4)	6·00*dd* (11·5, 1·5)	5·32*dd* (11·5, 2)	2·45*m*	5·13*m*
3a**	††	††	††	5·77*dbr* (11·5)	5·17*dbr* (11·5)	††	††
3b§§	2·92*d* (8·5)	4·80*dd* (4, 8·5)	††	5·94*dd* (11·5, 1·5)	5·29*dd* (11·5, 2)	2·46*m*	5·14*m*
4	2·44*d* (8·5)	3·15*dd* (8·5, 4)	3·86*dbr* (4)	6·33*dd* (11·5, 1)	5·63*dd* (11·5, 1·5)	3·03*m*	5·26*m*
6§§	5·52*m*	††	††	2·70*d* (10·2)	4·48*dd* (10·2, 9)	3·94*m* (9, 4·2, 3·6, 3·3)	5·72*m* (8, 8, 4·2)

* Run at 90 MHz in $CDCl_3$ solution except where indicated, using TMS as internal standard. Values are δ in ppm. Figures in parentheses are line separations or coupling constants in Hz.

† Spectra of (1c), (1e) and (1g) were essentially identical except for C-8 ester. In (1c), H-3′ 6·14*m*; H-4′ 1·98*m*; H-5′ 1·84*m*. In (1e), H-3′ 6·49*d*(7); H-4 2·04*d*(7); H-5′ 4·60; 2·00(Ac). In (1g), H-3′ 6·14*m*; H-3′ 3·00; H-4′ 1·23*d*(6); H-5′ 1·68*br*.

‡ $J_{7,8} \sim 1$ Hz in this and related compounds.

§ Two protons, center of AB system.

‖ Three protons.

Irradiation experiments involving H_a and H_b established the identity of a narrowly split multiplet at 2·96 ppm as that due to H_c. Irradiation at the frequency of H_c sharpened a broad doublet at 5·44 ppm (J 11·5 Hz) and converted a multiplet at 5·17 ppm to a doublet of doublets (J 4, 2 Hz). Thus H_d and H_e are at 5·44 or 5·17 ppm respectively or the reverse. If it is assumed that H_d is the proton under the lactone oxygen, then H_e could be assigned tentatively to a proton on carbon carrying one of the two ester functions whose presence was indicated by the IR spectrum (bands at 1735 and 1720 cm^{-1}). One of these was obviously an acetate (NMR signal at 2·06), the other a five carbon acyl group on the basis of the molecular formula if eleganin were a sesquiterpene lactone.

Since the low resolution MS displayed diagnostically important peaks at 277 (M-157), 259 (M-157-18) and 99 (base peak), the inference was drawn that the ester side chain (**8**) previously found in graminiliatrin [1] was also present in eleganin. This conclusion was corroborated by the NMR spectrum which revealed the presence of a vinyl multiplet at 6·07 ppm (H-3′) coupled to the two proton multiplet (4·97 ppm) of H-4′ and the vinyl multiplet of H-5′.

Irradiation at 5·17 ppm (tentatively the frequency of H_e) affected the H_c multiplet and collapsed two well separated doublets of doublets at 2·79 and 1·44 ppm to doublets (J 15 Hz). Conversely, irradiation at the frequency of each of these affected the 5·17 ppm multiplet and collapsed the other into a doublet, thus demonstrating that H_e was adjacent to a methylene group [H_f of (**7**)]. It was further shown that a broad

eleganin and derivatives*

H-9	H-13	H-14‖	H-15	H-3′	H-4′	H-5′‖	Others
2·79*dd* (15, 4) 1·44*d* (15, 2)	6·37*d* (1·75) 5·38 (1·75)	1·57*s*	4·25*s*§	6·07*m*	4·97*m*	1·88*m*	2·06(Ac)‖
2·83*dd* (15, 4) 1·42*dd* (15, 2)	6·42*d* (1·75) 5·85*d* (1·75)	1·59*s*	4·73*s*§	6·11*m*	5·0*m*	1·9*m*	2·11*s*, 2·08*s*(Ac)‖
††	3·60*m*	1·59*s*	4·02*s*§	—	—	—	3·27*s*(OMe)‖
2·70*dd* (15, 4) 1·32*dd* (15, 2)	3·66*m*§	1·62*s*	4·71*s*§	—	—	—	3·40*s*(OMe)‖ 2·13*s*, 2·13*s*(Ac)‖
††	3·58*m*§	1·47*s*	4·02*s*§	—	—	—	3·28*s*(OMe)‖
2·77*dd* (15, 4) 1·25*dd* (15, 2)	3·67*m*§	1·55*s*	4·65*s*§	—	—	—	3·39*s*(OMe)‖ 2·12*s*, 2·11*s*(Ac)‖
2·85*dd* (15, 4) 1·44*dd* (15, 2)	6·52*d* (1·75) 5·93*d* (1·75)	1·56*s*	9·60*s*	6·11*m*	5·02*m*	1·93*m*	2·07*s*(Ac)‖
2·36*dd* (15, 8) 1·88*d* (15, 8)	6·25*d* (3·6) 5·42*d* (3·3)	1·92*m*	1·30*s*	6·81*t* (6)	4·4*d*‖‖ (6)	4·33*s*§	

¶ Spectra of (**1d**) and (**1f**) were essentially identical except for C-8 ester. In (**1d**), H-3′ 6·14*m*; H-4′ 2·0*m*‖; H-5′ 1·87*m*§; 2·11(*Ac*)‖. *In* **1f**, H-3′ 6·55*q*(7); H-4′ 2·10*d*(7)‖; H-5′ 4·72§.

** Run in DMSO-d_6.

†† Superimposed or obscured signal.

‡‡ Sharpens on D_2O exchange.

§§ Run at 270 MHz.

‖‖ Two protons.

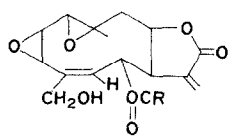
doublet at 3·69 ppm was coupled (J 4 Hz) to a doublet of doublets at 3·14 ppm which in turn was coupled (J 8·5 Hz) to a sharp doublet at 2·55 ppm. The broadening of the signal at 3·69 ppm could be traced to a small coupling with another proton at 5·57 ppm. The appearance of the signals at 5·57 and 5·44 ppm suggested that they constituted an AB system, but because of the similarity in chemical shift it was not possible to demonstrate conclusively that they were coupled to each other.

Decoupling also showed that a two proton multiplet at 4·25 ppm (presumably due to $-CH_2OH$ as it was shifted downfield to 4·73 ppm in the NMR spectrum of the acetate **1b**) was allylically or homoallylically coupled to the proton at 5·57 ppm. Lastly, the NMR spectrum displayed a methyl singlet at 1·57 ppm ($CH_3-\dot{C}-O$). As the IR spectrum of acetate (**1b**) did not exhibit an –OH frequency, it was assumed that the remaining two oxygen atoms were represented by epoxide or ether linkages.

The above data could be explained by formula (**1a**) if H_d corresponds to the NMR signal of 5·44 ppm, or by formula **9**, if H_d corresponds to the signal at 5·17 ppm. Proof for the presence of part structure $-CH=\dot{C}-CH_2OH$ in both formulas was adduced by MnO_2 oxidation which resulted in formation of an α,β-unsaturated aldehyde **4**. In the NMR spectrum of this substance the signal formerly at 5·57 ppm had shifted to 6·33 ppm (vinyl proton β to aldehyde carbonyl), thus demonstrating that it was associated with a vinylic proton, and its coupling to a resonance at 5·63 ppm, formerly the signal at 5·44 ppm [H-6 in (**1a**), H-8 in C], could be clearly discerned.

The latter observation made formula (**1a**) much more likely than formula (**9**).

Structures (**1a**) or (**9**) were also accommodated by the ^{13}C-NMR spectrum. Comparison of the noise-decoupled with the off-resonance ^{13}C-NMR spectrum of eleganin revealed the presence of three carbonyl singlets (170·6, 169·1, 165·2), three tertiary vinylic carbons (singlets at 136·4, 125·7 and 125·7), three secondary vinylic carbons (doublets at 141 and 124·5), one primary olefinic carbon (triplet at 125·7 ppm), two primary carbons attached to oxygen (triplets at 63·5 and 62·7), five secondary carbons (doublets at 79·9, 74·7, 61·5, 55·1 and 51·6) and one tertiary carbon of this type (singlet at 56·7) in addition to two carbon signals at 49·1*d* and 42·2*t* and the expected three methyl quartets at 20·7, 19·7 and 19·3 ppm*.



(**9**)

The possibility of lactone ring closure to C-8 as in **9** was rejected on the following grounds. Hydrolysis of **1a** with K_2CO_3–MeOH gave (**2a**) by loss of the ester side chain and addition of the elements of methanol to the α,β-unsaturated lactone function as indicated by the NMR spectrum (Table 1), elemental analysis and MS. The NMR spectrum also revealed the now well-separated components of the AB system provisionally assigned to H-5 and H-6 at 5·11 and 5·88 ppm, respectively. These frequencies were too low to be assigned to the newly-generated =CH–OH signal which was found at 3·82 ppm and was identified by its paramagnetic shift to 5·13 ppm on acetylation of (**2a**) to (**2b**). Since the hydrolysis was carried out under very mild conditions and since the multiplicity of the proton formerly under the ester function had not changed, the possibility of lactone rearrangement during the hydrolysis was ruled out. Hence the assumption that H_e of partial formula (**7**) was associated with the 5·17 ppm signal and H_d with the 5·44 ppm signal of eleganin was shown to be correct and the lactone ring of eleganin was closed to C-6.

Further proof for the correctness of formula (**1a**) was provided by the separation and appearance of the signals at 5·32 and 6·00 ppm in the 270 MHz spectrum of (**2b**) which permitted the demonstration, by double irradiation, that they were spin-coupled to each other and could be identified with H-5 and H-6. Furthermore, irradiation at 5·13 ppm (H-8) converted a doublet of doublets at 2·70 and 1·32 ppm (H-9) to doublets (J 15 Hz) and affected a signal at 2·45 ppm (H–C–H-7). The diamagnetic shift of H-7 accompanying the conversion of (**1b**) to (**2b**) was in agreement with its transformation from an allylic to a non-allylic position as required by the formulae.

Hydrogenation of (**2a**) afforded a triol (**3a**) obviously generated by hydrogenolysis of an allylic carbon–oxygen bond. Acetylation gave the triacetate (**3b**) and the spectral changes accompanying this transformation were consonant with the proposed formula. Decoupling experiments on (**3b**) demonstrated that the newly generated hydroxyl group was at C-2. Irradiation at 4·86 ppm collapsed the one-proton doublet at 2·92 ppm (H-1) to a singlet and caused some changes in the allylic methylene region of the spectrum.

Before giving the final proof for the structure of (**1a**), we would like to discuss liscundin (**1c**) and liscunditrin (**1e**), two lactones which were isolated from the chloroform extract of *Liatris secunda* in the form of gums. NMR and MS (see footnote of Table 1, and Experimental) showed that these substances differed from eleganin only in the nature of the ester side chain, (**1c**) containing an angeloyl function and (**1e**) the acetylsarracinoyl moiety. Starting material was recovered on treatment of (**1c**) or (**1e**) with K_2CO_3–MeOH at room temp. for 30 min. Higher temperatures or prolonged reaction times resulted in a complex mixture of products. However the use of sodium methoxide in methanol gave (**2a**) in good yield from (**1c**) and (**1e**), thus proving the above-mentioned relationship.

Final proof for the structures of (**1a**), (**1c**) and (**1e**) came from the following correlation. Acetylation of punctaliatrin (**5a**) of known structure and

* Assignment of a number of these frequencies to specific carbon atoms is easily possible on the basis of predicted chemical shifts [4] and published information [5, 6], but resolution of several ambiguities (such as distinction between the frequencies of C-6 and C-8 and those of C-1, C-2 and C-3) would have required single frequency decoupling experiments which were not carried out.

stereochemistry [2, 7] followed by peracid oxidation gave a mixture of products from which a substance identical in all respects with (**1e**) could be isolated. Hence the lactones from *L. elegans* and *L. secunda* have a *cis*-4,5 double bond and the stereochemistry at C-1, C-6, C-7, C-8 and C-10 is the same as that of punctaliatrin.

The remaining question as to the stereochemistry of the 2,3-epoxide was answered as follows. In (**1a**)–(**1g**), the magnitude of $J_{1,2}$ (8·5 Hz) indicates that H-1 and H-2 are *trans*, not *cis*. Hence H-2 should be β and the 2,3-epoxide ring α. This conclusion was supported by the values of $J_{2,3\alpha}$ and $J_{2,3\beta}$ in (**3b**) (4 Hz each) which are satisfied by a model in which the acetoxy group on C-2 is α-, not β-oriented.

We draw attention to the small values of $J_{7,13}$ in (**1a**)–(**1g**) characteristic of germacranolides which contain a *trans*-fused lactone ring closed to C-6 and incorporate a *cis*-4,5 double bond [8] and to the positive Cotton effect of (**1a**) at 240 nm (at somewhat shorter wavelength than normal, possibly due to superposition of the unsaturated ester and lactone chromophores) whose sign, like those of some other α-methylene-γ-lactones in which the carbon–oxygen bond function is allylic [9–12] violates the empirical rule that *trans*-fused lactones closed to C-6 exhibit a negative, *cis*-fused lactones closed to C-6 a positive Cotton effect [13]. That the abnormality is not necessarily characteristic of all *cis*-Δ^4-germacranolides whose lactone ring is closed to C-6 has been discussed [11]. On the other hand, *trans*-Δ^4-germacranolides whose lactone ring is closed to C-6 seem to follow the rule [13].

Extraction of a new collection of *L. punctata*, which was undertaken to secure additional quantities of punctaliatrin for biological tests, resulted in isolation of only one homogeneous but noncrystalline fraction, $C_{20}H_{24}O_7$, $[\alpha]_D^{22} - 75°$, which was different from punctaliatrin. Double irradiation experiments (Table 1) permitted deduction of the gross structural formula as **6**. Even at 270 MHz, signals of H-2 and H-3 were superimposed in the methylene region, but were identified because irradiation at the frequency of H-1 (5·52 ppm) which also allylically coupled to the protons of the C-10 methyl group effected some changes. The absence of an NOE between H-1 and H-14 demonstrated that the new substance, liatripunctin, had a *trans*-1,10 double bond. The magnitude of $J_{5,6}$ (10·2 Hz) required a rather large angle between H-5 and H-6 such as would be obtained by epoxidation of a *cis*-4,5 double bond. The magnitude of $J_{6,7}$ further indicated a *trans*, rather than a *cis*-lactone ring fusion. Hence if the C-7 side-chain were β and equatorial as is usual, the absolute stereochemistry of liatripunctin is H-6β and H-7α. The CD curve of liatripunctin exhibited a negative Cotton effect at 257 nm. This might be cited as an additional argument in favor of the thesis that liatripunctin is a *trans*-fused lactone; however, such an argument would be suspect for the following reason. While 4,5-epoxides of *trans,trans*-$\Delta^{1(10)}$-*trans*-C-6 fused germacradienolides appear to follow the rule (compare the CD curves of costunolide and parthenolide [13]), 4,5-epoxides of *cis,trans*-$\Delta^{1(10),4}$-*trans*-C-6 fused germacradienolides do not (compare uvedalin with enhydrin and maculatin [11]) and there is no information on 4,5-epoxides of *trans,cis*-$\Delta^{1(10),4}$-germacradienolides, a class to which liatripunctin very likely belongs.

Inspection of the (rather flexible) models suggests that the value of $J_{7,8}$ is more in keeping with a β-oriented ester function at C-8, especially since, as has already been indicated, liatripunctin appears to be derived from a *cis*-Δ^4-germacranolide precursor probably related to **1a**, **1c**, **1e**, punctaliatrin [2] and provincialin [8]. Consequently we suggest (**6**) as a tentative structure for liatripunction, with the epoxide oxygen atom either above or below the plane of the ring. In the former orientation, H-7 and the epoxide oxygen are far apart, in the latter they are reasonably close. This may account for the deshielding of H-7 whose signal appears at an unusually low frequency.

EXPERIMENTAL

Experimental details have been specified previously [14].

Eleganin (**1a**). Chromatography of a *Liatris elegans* (*Walt*). Michx. extract has been described [1]. Fractions 12–18 (C_6H_6–$CHCl_3$, 5:1) gave solid material which was recrystallized from EtOAc, yield of **1a** 3·0 g, mp 142–143°, $[\alpha]_D^{22} - 108°$ (c6), CD curve $[\theta]_{240} + 3960$, IR: ν_{max} cm^{-1} 3400 (–OH), 1760 (γ-lactone), 1735 (acetate), 1720 (conjugated ester), 1650 (conjugated double bond), 1250, 1030, 980, 920, MS: *m/e* 434 (M+), 392 (M-42), 374 (M-60), 277 (M-157), 259 (M-157-18), 99 (base peak). (Calc for $C_{22}H_{26}O_9$: C, 60·82; H, 6·03; O, 33·14. Found: C, 60·80; H, 6·01; O, 33·07%).

Acetylation of 0·1 g (**1a**) with C_5H_5N–Ac_2O and purification of the crude product by preparative TLC furnished 0·095 g of noncrystalline (**1b**), IR: ν_{max} cm^{-1} 1770, 1750, 1730, 1650,

1240, 1040, 980 and 920. (Calc for $C_{24}H_{28}O_{10}$: C, 60·50; H, 9·92; O, 33·48. Found: C, 60·39; H, 5·77; O, 33·63%).

Extraction of Liatris secunda. Extraction of 1·8 kg *Liatris secunda* (Ell.) Small (for source see Ref. [3]) in the usual fashion [15] gave 12 g crude gum which was chromatographed over 500 g silicic acid (Mallinckrodt 100 mesh), 200 ml fractions were collected, 1–10 (C_6H_6), 11–20 (C_6H_6–$CHCl_3$, 10:1), 21–30 (C_6H_6–$CHCl_3$, 5:1), 31–40 (C_6H_6–$CHCl_3$, 1:1), 41–50 (C_6H_6–$CHCl_3$, 1:5), 51–60 (C_6H_6–$CHCl_3$, 1:10), 61–70 ($CHCl_3$), 71–80 ($CHCl_3$–MeOH, 20:1), 81–90 ($CHCl_3$–MeOH, 10:1).

Fractions 11–19 gave 2 g noncrystalline (**1c**) which was further purified by preparative TLC on Sil gel (C_6H_6–EtOAc, 1:2) to yield 1·2 g of a homogeneous gum, $[\alpha]_D^{22}$ −75° (c2), strong end absorption, ϵ_{212} = 14400, IR: $\nu_{max}cm^{-1}$ 3400, 1760, 1720, 1640, 1220, 1090, 955, 920 and 840, MS: *m/e* 376 (M+), 358 (M–H_2O), 259 (M–H_2O–$C_5H_7O_2$), 83 (base peak). (Calc for $C_{20}H_{24}O_7$: C, 63·82; H, 6·40; O, 29·70. Found: C, 63·45; H, 6·24; O, 29·80%). Acetylation of (**1c**) with C_5H_5N–Ac_2O and purification of the product by preparative-TLC gave (**1d**) as a gum, IR: $\nu_{max}cm^{-1}$ 1760, 1720, 1640, 1250, 1150, 1040.

Fractions 21–30 gave one major spot and were combined (1·5 g). Preparative-TLC on Si gel (C_6H_6–EtOAc, 1:3) gave (**1e**) as an amorphous solid, mp 161°, $[\alpha]_D^{22}$ −5·0° (c1), IR: $\nu_{max}cm^{-1}$ 3400, 1765, 1730, 1650, 1240, 1030, 980 and 920, MS: *m/e* 434 (M+), 392 (M-42), 374 (M-60, *m* at 322·3), 277 (M-15), 259 (M-157-18). (Calc for $C_{22}H_{26}O_9$: C, 60·82; H, 6·03; O, 33·14. Found: C, 60·62; H, 5·56; O, 33·72%). The acetate (**1f**) was a gum, IR: $\nu_{max}cm^{-1}$ 1760, 1740, 1730, 1650, 1240, 1120, 1040.

Oxidation of eleganin to **4**. A soln of 0·2 g (**1a**) in 10 ml $CHCl_3$ was stirred with excess active MnO_2 for 12 hr and filtered. The oxidant was washed with hot $CHCl_3$. The combined filtrate and washings were washed, dried and evaporated. The residue crystallized on trituration with EtOAc to yield (**4**) (0·15 g), mp 160°, $[\alpha]_D^{22}$ −98° (c4), IR: $\nu_{max}cm^{-1}$ 1760, 1740, 1720, 1650, 1250, 1130, 840, UV: λ_{max} 215 (ϵ = 18000). (Calc for $C_{22}H_{24}O_9$: C, 61·11; H, 5·59; O, 33·30. Found: C, 61·10; H, 5·46; O, 33·31%).

Conversion of (**1a**) *to* (**2a**). A soln of 0·2 g (**1a**) in 10 ml dry MeOH was mixed with 0·4 g K_2CO_3 in 1 ml H_2O and allowed to stand (N_2 atmosphere), the reaction being monitored by TLC. All starting material had disappeared within 1 hr. The mixture was diluted with H_2O and extracted with EtOAc. The washed and dried extract was evaporated, the residue was purified by preparative-TLC on Si gel ($CHCl_3$–MeOH, 9:1) and recrystallized from EtOAc to yield **2a** (0·06 g), mp 210°, $[\alpha]_D^{22}$ −18·4° (c1·08), IR: $\nu_{max}cm^{-1}$ 1740, 1050, 980, 910, MS: *m/e* 327 (M+), 308 (M-18), 295 (M-CH_2OH), 277 (M-18-CH_2OH). (Calc for $C_{16}H_{22}O_7$: C, 58·59; H, 6·79; O, 34·32. Found: C, 59·01; H, 6·73; O, 34·53%).

The acetate **2b** (0·035 g from 0·040 g of starting material) was recrystallized from EtOAc and had mp 137°, $[\alpha]_D^{22}$ −25° (c1), IR: $\nu_{max}cm^{-1}$ 1750, 1735, 1240, 1030, 980, 920, MS: *m/e* 410 (M+), 379 (M-CH_2OH), 350 (M-$C_2H_5O_2$), 319 (M-CH_2OH-$C_2H_4O_2$), 290 (M-2$C_2H_4O_2$). (Calc for $C_{20}H_{26}O_9$: C, 58·53; H, 6·39; O, 35·08. Found: C, 58·99; H, 6·40; O, 35·00%).

Conversion of (**1c**) *and* (**1e**) *to* (**2a**). A soln of 0·2 g (**1c**) in 15 ml dry MeOH containing 0·1 g NaOMe was stirred (N_2 atmosphere) until all starting material had disappeared (30 min). The mixture was acidified with dil. HOAc diluted with H_2O and extracted with EtOAc. The usual workup and purification by preparative-TLC furnished 0·06 g (**2a**) identical with material obtained from **1a**, and converted to **2b**, identical with authentic material. In the same manner 0·2 g (**1f**) was converted to 0·05 g (**2a**) and the latter characterized as (**2b**), both samples identical with material from (**1a**).

Hydrogenolysis of (**2a**). A soln of 0·05 g (**2a**) in 15 ml EtOAc was hydrogenated at atm pres with 0·04 g 5% Pd–C. The filtered soln was evaporated and the residue purified by preparative-TLC ($CHCl_3$–MeOH, 9:1) and recrystallized from EtOAc to yield (**3a**) (0·03 g), mp 160°, IR: $\nu_{max}cm^{-1}$ 1740, 1230, 1020. Acetylation of the product in the usual fashion gave 0·028 g (**3b**) which was recrystallized from MeOH, mp 230°, $[\alpha]_D^{22}$ +250° (c 0·1), MS: *m/e* 454 (M+), 439 (M-15), 412 (M-42), 411 (M-43), 394 (M-60), 381 (M-42-31), 352 (M-60-42), 334 (M-2 × 60), 299 (M-2 × 60-42), 274 (M-3 × 60). (Calcd for $C_{22}H_{30}O_{10}$: C, 58·14; H, 6·65; O, 35·20. Found: C, 58·62; H, 6·60; O, 34·93%).

Epoxidation of (**1c**). Treatment of (**1a**) with *m*-chloroperbenzoic acid resulted in recovery of starting material. Treatment of 0·05 g (**1c**) in 5 ml dry $CHCl_3$ with 0·05 g of the peracid by stirring at room temp for 24 hr, dilution with $CHCl_3$ followed by the usual workup gave, after evaporation of solvent, a solid residue (**1g**) which was recrystallized from EtOAc to yield (0·04 g), mp 175°, IR: $\nu_{max}cm^{-1}$ 1760, 1250, 1090, 985, 920. (Calc for $C_{20}H_{24}O_8$: C, 61·22; H, 6·16; O, 32·62. Found: C, 61·59; H, 6·31; O, 32·49%).

Conversion of punctaliatrin (**5a**) *to* (**1f**). The diacetate (**5b**) was prepared from 0·02 g (**4a**) as described [2]. Oxidation of 0·02 g (**5b**) in 3 ml $CHCl_3$ with 0·04 g *m*-chloroperbenzoic acid at room temp. by stirring for 3 hr gave a complex mixture (TLC analysis) which was separated by TLC on Si gel $PF_{254-366}$ (C_6H_6–EtOAc, 1:1). The band having the same R_f as (**1f**) was eluted with $CHCl_3$; evaporation of the solvent gave a gum (12 mg) which was identical with (**1f**) in mixture TLC, IR and NMR spectrum.

Isolation of liatripunctin (**6**). Above ground parts of *Liatris punctata* Hook., collected by Dr. N. C. Henderson near Ottawa, Kansas in early September 1972. wt 10·1 kg, was extracted with $CHCl_3$ in the usual fashion. The crude gum (40 g), was chromatographed over 1 kg silicic acid. Successive elution with C_6H_6, C_6H_6–$CHCl_3$, $CHCl_3$ and then $CHCl_3$–MeOH gave mixtures. Only the $CHCl_3$ eluate gave a homogeneous fraction as a gum, (3·0 g), which was rechromatographed over Sil gel (EtOAc–C_6H_6, 3:1) and then purified by preparative-TLC to give **6** as a single spot (1·5 g), $[\alpha]_D^{22}$ −41·7° (c1·2), CD curve $[\theta]_{257}$ −1109, UV: strong end absorption, ϵ_{210} = 15000, IR: $\nu_{max}cm^{-1}$ 3400, 1750, 1700, 1650, 1620, 1250, 1120, 1140, 1020. (Calc for $C_{20}H_{26}O_7$: C, 63·48; H, 6·93; O, 29·60. Found: C, 63·30, H, 7·09; O, 29·91%).

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