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SESQUITERPENE LACTONES OF *EUPATORIUM ANOMALUM* AND *EUPATORIUM MOHRII**

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Key Word Index—*Eupatorium anomalum*; *Eupatorium mohrii*; Compositae; guaianolides; germacranolides; heliangolides; sesquiterpene lactones.

Abstract—Several new guaianolides and the previously known heliangolide eurecurvin have been isolated from *Eupatorium anomalum*. *Eupatorium mohrii* also yielded three of the new guaianolides together with eurecurvin and a new germacradienolide. The implications of these findings are discussed.

INTRODUCTION

As part of our continuing study [1–5] of *Eupatorium* species *sensu stricto* which elaborate a number of sesquiterpene lactones with cytotoxic and antitumor activity [1, 6–8], we have examined the two hybrid biotypes *E. anomalum* Nash and *E. mohrii* Greene. This has resulted in the isolation of a number of sesquiterpene lactones whose occurrence may reflect the putative parentage of the two species [9]. *E. anomalum* consists of rare diploids, some triploids and most often tetraploids based on X = 10 which reflect hybridization between *E. rotundifolium* and *E. recurvans*. *E. mohrii* which consists of diploids, mainly triploids and seldom tetraploids reflects hybridization between the same two species with a backcross to *E. recurvans*. We have reported earlier [10] on the flavanol glycosides of *E. mohrii* which was then referred to as a collection of '*E. recurvans*' Small, a naturally occurring hybrid of *E. recurvans* and *E. rotundifolium*.

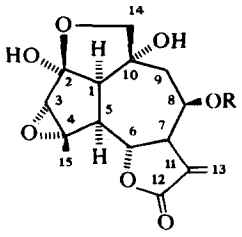
RESULTS AND DISCUSSION

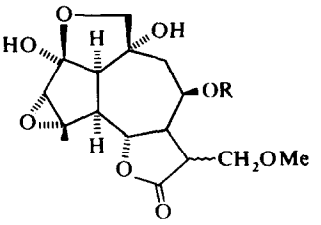
Three apparently homogeneous lactone fractions from *E. anomalum* were inseparable mixtures of **1a**, **4a**, and **6a** with smaller amounts of the isomeric esters **1b**, **4b** and **6b**, respectively. This was not immediately obvious from the ^{1}H NMR spectra although eventual detailed analysis of the 270 MHz spectra (Table 1) and comparison with pure **1a** and **4a** isolated subsequently from *E. mohrii* showed the relatively weak signals of the isovalerate superimposed on the more prominent signals of the α-methylbutrate ester side chain. In fact single crystals representing the **1a**, **1b** mixture were used successfully for an X-ray analysis [11] at which time disorder in the ester side chain gave a clue to the presence of two very similar ester moieties [12]. The ^{13}C NMR spectra (Table 2), while originally confusing, were decisive, each spectrum containing an 'extra' carbonyl singlet, an 'extra' doublet, an 'extra' triplet and two 'extra' superimposed quartets, all at frequencies characteristic of an isovaleryl residue.

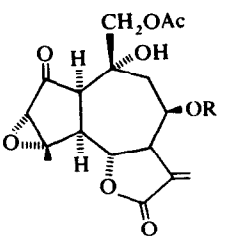
Lactone mixture **1a**, **1b**, $C_{20}H_{26}O_8$, mp 152–153° (pure **1a**, mp 158–159°), was a dihydric alcohol (IR, NMR) whose hydroxyl groups were tertiary (NMR). Nevertheless, acetylation afforded a monoacetate **3a**, **3b** whose spectroscopic properties indicated that conversion of a hemiacetal to a ketoacetate of the type shown in the formulae had taken place. If so, the new keto group was in a five-membered ring (IR spectrum) and we were probably dealing with a guaianolide. An attempt to hydrolyse the ester functions under mild conditions [1] only led to the methanol addition products **2a**, **2b**.

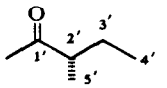
The above chemical evidence and extensive spin-decoupling experiments on **1a**, **1b** and their transforma-

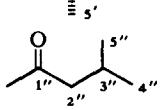
* Supported in part by a grant (CA-13121) from the U.S. Public Health Service through the National Cancer Institute.







1a R =  (α-methylbutyrate)

1b R =  (isovalerate)

2a R = α-methylbutyrate
2b R = isovalerate

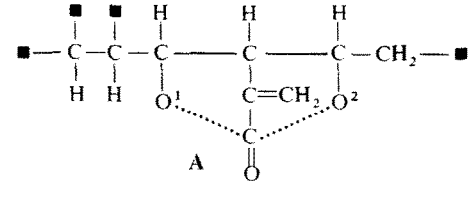
3a R = α-methylbutyrate
3b R = isovalerate

Table 1. ^{1}H NMR spectra of the sesquiterpene lactones from *Eupatorium* sp*

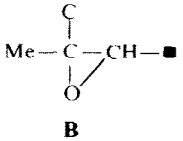
Compound	H-1	H-2	H-3	H-5	H-6	H-7	H-8	H-9	H-13	H-14	H-15†	Misc.‡
1a	2.63*d* (10)§	—	3.50	2.90*dd* (10)§	4.49*dd* (12, 9)	3.06*m* (9, 3.5, 3, 3)	5.69*m*	2.33*m*‖	6.32*d* (3.5) 5.55*d* (3)	4.32*d*§ (12) 4.10*d*§ (12)	1.64	2.4*m* (H-2′), 1.46*m* 1.6*m* (H-3′), 0.89*t* (7, H-4′)†, 1.10*d* (7, H-5′)†
2a	2.59*d* (10)§	—	3.44	2.70*t* (12)§	4.40*dd* (12, 9)	2.77*m*	5.35*m*	2.59*m* 2.32*m*	3.72*dd* (11, 3)§ 3.36*dd* (11, 2)§	4.35*d* (10.5)§ 4.09*d* (10.5)§	1.58	" 2.45*m* (H-11) 3.36 (OMe)†
3a	3.35*d* (8)§	—	3.27	3.03*dd* (10, 8)§	4.23*dd* (12, 10)	4.09*m*	5.58*m*	2.39*m*	6.28*d* (3.5) 5.46*d* (3)	4.31§**	1.79	" 2.11 (Ac)†¶
4a	2.13*dd* (4.5, 7.5)§	4.35*dbr* (4.5)	3.26*br*	2.52*dd* (10.5, 7.5)§	4.73*dd* (10.5, 9)	3.97*m* (9, 4, 3.5, 3)	5.55*dt* (4, 8)	2.40*m* 1.6*m*	6.25*d* (5) 5.41*d* (3)	1.41†	1.68	"
4c	2.25*dd* (4.5, 7)§	5.17*dbr* (4.5)	3.21	2.47*dd* (12, 7)	4.51*dd* (12, 9)	3.88*m* (9, 4, 3.5, 3)	5.46*dt* (4, 9)	2.3*m* 1.9*m*	6.12*d* (3.5) 5.30*d* (3)	1.55	1.96	"
5a	2.12*dd* (4.5, 7)	4.31*dbr* (4.5)	3.21	2.46*dd* (12, 8)	4.61*dd* (12, 9)	3.4*m*	5.23*dt* (4, 9)	2.36*m*	3.62*dd* (10, 4) 3.55*dd* (10, 3)	1.38	1.62	" 2.77*m* (4, 3, 12, H-11) 3.32 (OMe)†
6a	1.75*dd* (4.5, 7.5)	4.45*dbr* (4.5)	3.27	2.26*dd* (11, 7.5)	4.78*dd* (11, 8.5)	3.09*m* (8.5, 4, 3, 3)	5.39*dt* (4, 8)	2.93*dd* (14, 8) 1.88*d* (14, 8)	6.26*d* (3) 5.46*d* (3)	2.59	1.60	"
8a	5.12*m*	2.50*m*†† 2.40*m*	4.34*dd* (10, 6)	4.72*dbr* (9.5, 1.5)	5.12*dd* (9.5, 8.5)	2.96*m*	5.90*dbr* (2.8, ~1)	4.28*d* (2.8)	6.36*d* (3) 5.73*d* (3)	1.59*br*	1.82*d* (1.5)	"
8b	5.27*m*	2.64*m*†† 2.42*m*	5.27*m*	4.87*dbr* (10, 1.5)	5.08*dd* (10, 8.5)	3.03*m*	6.02*dbr* (2.8, ~1)	5.34*d* (2.8)	6.37*d* (3) 5.73*d* (3)	1.65*br*	1.83*d* (1.5)	" 2.07, 2.16 (Ac)†

* Run in $CDCl_3$ at 270 MHz. Unmarked signals are singlets. Values in parentheses are coupling constants.
† Intensity three protons.
‡ Signals of isovalerate component in mixtures near 2.1*m* (H-2″), 2*m* (H-3″), 0.94*d*, 0.91*d* (H-4″, H-5″).
§ A or B component of AB system.
‖ Intensity two protons.
¶ Signals of α-methylbutyryl side chain approximately the same as in **1a**.
** Center of AB system.
†† $J_{2a,2b}$ = 13 Hz.

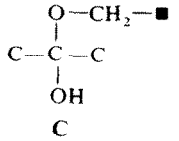
tion products indicated the presence of partial structure **A**, where the lactone ring was closed to either O^1 or O^2 and the ester side chain was attached to the other. Partial structures **B** and **C**, with the hemiacetal carbon of the latter probably included in a five-membered ring, also had to be accommodated in a tetracyclic (including the lactone) structure.



A



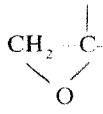
B



C

Because our interpretation of the data was confused by what was then thought to be contradictory evidence from ^{13}C NMR spectroscopy, single crystals of **1a**, **1b** mixture were examined by X-ray crystallography [11]. This led to the structure and relative stereochemistry shown in formula **1**. We deduce that this also represents the absolute stereochemistry because of an empirical rule [13] relating the sign of the n,π^*-Cotton effect of an α,β-unsaturated lactone to the direction of ring closure which generally applies to guaianolides. The somewhat anomalous CD curve of **1a**, which exhibited a weak negative Cotton effect near 270 nm instead of the usual minimum (or maximum) near 250 nm characteristic of an α,β-unsaturated lactone, may indicate that in MeOH the hemiacetal is in equilibrium with the hydroxyketone (for an analogous situation in a very similar compound see ref. [14]), since **4a** (*vide infra*) exhibited the expected strongly negative Cotton effect at somewhat lower wavelength. The absolute stereochemistry at C-2′ was assumed to be the same as that of other α-methylbutyrates from *Eupatorium* species [4].

Two non-crystalline lactone fractions, $C_{20}H_{28}O_7$ and $C_{20}H_{26}O_7$, were **4a**, **4b** and **6a**, **6b**, respectively, **4a** being subsequently isolated in pure form from *E. mohrii*. The structural assignments were based on the replacement

(group in **4a**, **4b** by  in **6a**, **6b**, on the trans-

formation of **4a**, **4b** to **4c**, **4d** and **5a**, **5b**, spin-decoupling experiments (Table 1) which established the sequence C-2, C-1, C-5, C-6, C-7, C-8, C-9 in all compounds and the close correspondence in chemical shifts (^{1}H NMR and ^{13}C NMR spectra) and coupling constants (^{1}H NMR) between **6a**, **6b** and graminiliatrin (**6c**) of established structure [14, 15]. The ^{13}C NMR spectrum of the last-named compound is listed in Table 2 for comparison;

Table 2. ^{13}C NMR spectra of the guaianolides and germacradienolide of *Eupatorium* sp.*

	1a†	4a‡	6a†	6c‡	8a†
C-1	58.02*d*	51.83*d*	49.11	49.39*d*	123.58*d*§
C-2	114.23	72.34*d*	73.05*d*	72.86*d*	34.58*t*
C-3	64.63*d*	64.01*d*	64.50*d*	64.56*d*	74.93*d*
C-4	65.97	65.91	65.89	65.79	144.00
C-5	51.26*d*§	49.68*d*	50.39*d*	50.09*d*	129.40*d*§
C-6	75.36*d*	77.82*d*	76.70*d*	77.22*d*	74.93*d*
C-7	49.81*d*§	47.36*d*	48.13*d*	48.13*d*	50.47*d*
C-8	65.78*d*	67.00*d*	65.47	67.90*d*	80.55*d*
C-9	38.62*t*	39.87*t*	37.18	36.20*t*	77.74*d*
C-10	81.88	72.75	54.56	55.65	137.33
C-11	134.03	134.96	133.85	134.26	135.61
C-12	168.16	170.01	172.30	169.42	169.45
C-13	122.21*t*	121.34*t*	123.62	122.71*t*	122.40*t*
C-14	80.49*t*	33.31*q*	53.39*t*	56.41*t*	12.24*q*
C-15	19.01*q*	19.17*q*	18.36*q*	19.70*q*§	13.59*q*
C-1′	175.35	176.46	175.98	171.08	176.88
C-2′	41.37*d*	41.05*d*	40.88*d*	128.40	41.51*d*
C-3′	26.61*t*	26.61*t*	26.47*t*	138.56*d*	26.56*t*
C-4′	11.60*q*	11.55*q*	11.43*q*	62.98*t*	11.58*q*
C-5′	16.83*q*	16.77*q*	16.67*q*	18.31*q*§	17.05*q*
C-1″	171.65	172.79	172.38	165.80	
C-2″	43.44*t*	43.34*t*	43.15*t*	20.79*q*	
C-3″	25.66*d*	25.58*d*	25.53*d*		
C-4″, C-5″	22.31*q*	22.36*q*	22.20*q*		

* Run in $CDCl_3$ at 67.9 MHz. Unmarked signals are singlets.
† Assignments made by analogy and not verified by single frequency off-resonance decoupling.
‡ Assignment of multiplets made by single frequency off-resonance decoupling except where indicated.
§ Assignments may be interchanged.

assignment of all multiplets in **4a** and **6c** was confirmed by single frequency off-resonance decoupling.

Eurecurvin (**7b**), previously found in *E. recurvans* [4], was isolated from *E. anomalum* as well as from *E. mohrii*; the latter species also yielded the known [4] eurecurvin analog **7a** as well as a non-crystalline germacradienolide **8a** (or **8c**) further characterized as the diacetate **8b** (or **8d**). Partial structures **D** and **E** which together account for all fifteen skeletal carbon atoms were established by spin-decoupling experiments (Table 1), the methyl group on C-4 being allylically coupled to H-5 and *trans* to it (absence of NOE), as was the methyl group on C-10 to H-1. Since the protons on the two carbons carrying hydroxyl groups were not coupled, combination of **D** and **E** was possible in one way only to give a substance with gross structure **8a**.

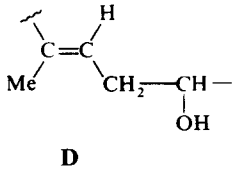
That **8a** was not a heliangolide but a *trans,trans*-germacradienolide was also shown by the magnitude of $J_{7,13}$ [16]; in such compounds the —CH(O—C(O)—)— signal at lower field is associated with the proton on the carbon carrying the ester side chain. Consequently, the α-methylbutyrate ester was attached to C-8 and the lactone ring was closed to C-6. The magnitudes of $J_{5,6}$, $J_{6,7}$ and $J_{7,8}$ (10, 8.5 and ~1 Hz) required that the lactone ring was *trans*-fused, a conclusion supported by the negative Cotton effect in the 250 nm region, and that H-8 was *cis* to H-7. Similarly, the values for $J_{2,3}$ (10 and 6 Hz) were consonant only with β-orientation of the hydroxyl group on C-3.

The remaining problem was the configuration at C-9. The observed value for $J_{8,9}$ (2.8 Hz) was intermediate between the values expected for $J_{8\alpha,9\alpha}$ (dihedral angle from Dreiding models ~85°) and $J_{8\alpha,9\beta}$ (dihedral angle ~35°). The literature lists few measurements of $J_{8,9}$ for *trans,trans*-germacradienolides (or their 4,5-epoxides) with authenticated stereochemistry; similarity to the data recorded for the herbolides (β-hydroxyl or ester on C-9, $J_{8\alpha,9\alpha}$ = 3, $J_{8\beta,9\alpha}$ = 10 Hz [17, 18]) eupatoriopicrin, eupatolide and cupassopin (β-hydroxyl or ester on C-8, $J_{8\alpha,9\alpha}$ = 1.2, $J_{8\alpha,9\beta}$ = 5 Hz) [1, 19–22] suggests that the C-8 hydroxyl of our lactone was β-orientated as in **8a**. However, for reasons that are not immediately obvious, formula **8e**, with the C-8 hydroxyl α, has recently [8] been assigned to a minor lactone from '*E. rotundifolium* ssp. *ovatum*' (*vide infra*) which, to judge on the basis of the recorded chemical shifts and coupling constants, is the angeloyl analog of our lactone from *E. mohrii*.

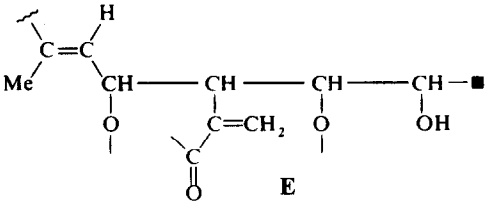
Lactone **1** may represent an intermediate stage in the *in vivo* conversion of compounds like **6** and their 3,4-deoxy analogs which are found in some *Liatris* species [14, 15] and in *Eupatorium rotundifolium* (in the latter an extra hydroxyl group is generally attached to C-1) [8, 23] to a type of dilactone so far found only in *E. perfoliatum* [2]; in fact oxidation of **6c** afforded a hemiacetal of type **1** [14]. The similarity in lactone content between *E. anomalum* and *E. mohrii* is striking; that these lactones are either identical with, or very closely related to, the lactones found in the putative parents of these hybrid biotypes could be taken to support the relationship posited on other grounds [9].

Because our results on *E. mohrii* differed drastically from those reported by Bohlmann *et al.* [8], who isolated several lactones identical with or similar to the lactones we found in *E. hyssopifolium* L. [1]*, we have examined

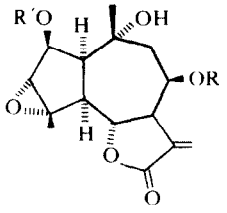
* Re-examination of the vouchers of *E. hyssopifolium* used for the work described in ref. [1] indicate that our material was diploid and can be referred to *E. lecheaefolium* Greene [24]. The very similar results reported by Bohlmann *et al.* for their *E. hyssopifolium* L. and their '*E. mohrii*' (= *E. hyssopifolium* L., Johnson 4938 and 4942, not King 4938 and 4942 as given in ref. [8], both annotated by Professor R. K. Godfrey) were probably derived from triploid material.



D

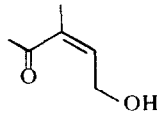


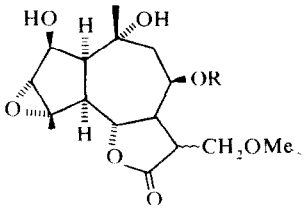
E



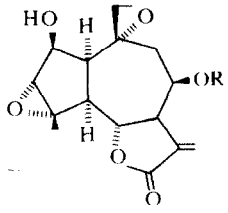
4a R = α-methylbutyrate, R′ = H
4b R = isovalerate, R′ = H
4c R = α-methylbutyrate, R′ = Ac
4d R = isovalerate, R′ = Ac

4e R =



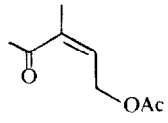


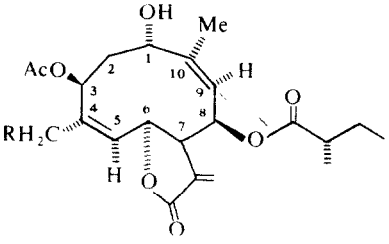
5a R = α-methylbutyrate
5b R = isovalerate



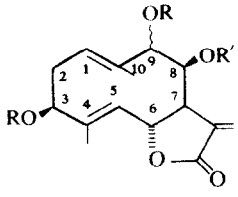
6a R = α-methylbutyrate
6b R = isovalerate

6c R =





7a R = H
7b R = OH



8a H-8α, R = H, R′ = α-methylbutyrate
8b H-8α, R = Ac, R′ = α-methylbutyrate
8c H-8β, R = H, R′ = α-methylbutyrate
8d H-8β, R = Ac, R′ = α-methylbutyrate
8e H-8β, R = H, R′ = Ang

voucher specimens of the collections extracted by the German authors. This revealed that '*E. mohrii*' of Bohlmann *et al.* actually was *E. hyssopifolium* L. and resolved the apparent discrepancy. Their collection of *E. rotundifolium* L. ssp. *ovatum* (Bigel.) Montgom. and Fairbr. can be referred to *E.* ap. *cordigerum* Fern.*

EXPERIMENTAL

Extraction of Eupatorium anomalum. Aerial parts of *E. anomalum* Nash (14.4 kg) collected by Dr. R. K. Godfrey on 24 July 1968 along the Lighthouse Road, St. Marks Wildlife Refuge, Wakulla Co., Fla. (Godfrey voucher #67072 on deposit in herbarium of Florida State University), were extracted in the usual fashion [26]. The crude extract (32.5 g) was chromatographed over 1.1 kg Si gel (Mallinckrodt, 100 mesh); the following fractions (1 l. each) were collected; 1–9 (C_6H_6), 10–14 (C_6H_6–$CHCl_3$, 9:1), 15–18 (C_6H_6–$CHCl_3$, 4:1), 19–22 (C_6H_6–$CHCl_3$, 7:3), 23–28 (C_6H_6–$CHCl_3$, 1:1), 29–38 (C_6H_6–$CHCl_3$, 1:3), 39–42 ($CHCl_3$, 43–57 ($CHCl_3$–MeOH, 49:1), 58–66 ($CHCl_3$–MeOH, 19:1), 67–75 ($CHCl_3$–MeOH, 8:2), 76 (MeOH). The eluates were monitored by TLC.

Purification of fractions 39 and 40 by PLC (EtOAc–$CHCl_3$, 1:1) furnished 0.20 g of a gum which exhibited IR bands ($CHCl_3$) at 1760, 1725, 1715 and 1650 cm^{-1} and was a mixture of α-methylbutyrate and isovalerate esters **6a** and **6b** (^1H NMR and ^{13}C NMR spectra). The elementary analysis for carbon remained unsatisfactory. (Calc. for $C_{20}H_{26}O_7$: C, 63.48; H, 7.05; O, 29.60; MW, 378.1678. Found: C, 61.00; H, 6.79; O, 29.89%; MW (MS), 378.1678 (very weak)). Other significant peaks in the high resolution MS appeared at *m/e* (rel. int.) 360 ($C_{20}H_{24}O_6$, 1.3), 276 ($C_{15}H_{16}O_5$, 2.5), 256 ($C_{15}H_{14}O_4$, 6.6), 85 (C_5H_9O, 37).

PLC of fraction 52 (EtOAc–$CHCl_3$, 1:1) yielded 0.44 g of a gum which had IR bands ($CHCl_3$) at 3580, 1760 and 1720 cm^{-1} and was a mixture of α-methylbutyrate and isovalerate esters **4a** and **4b** (^1H NMR and ^{13}C NMR spectra). (Calc. for $C_{20}H_{28}O_7$: C, 63.16; H, 7.42; O, 29.44; MW, 380. Found: C, 62.82; H, 7.46; O, 29.89%; MW (MS), 380 (very weak)). In the high resolution MS the first peak corresponded to the loss of 2 H_2O (calc. for $C_{20}H_{24}O_5$; 344.1623. Found: 344.1599 (1.3%)). Other significant peaks were at *m/e* (rel. int.) 279 ($C_{15}H_{19}O_5$, 0.5), 278 ($C_{15}H_{18}O_5$, 0.5), 260 ($C_{15}H_{16}O_4$, 4.7), 242 ($C_{15}H_{14}O_3$, 5.1), 85 (C_5H_9O, 65.1).

PLC of fraction 53 (EtOAc–$CHCl_3$, 1:1) gave 3.0 g of colorless crystalline material which had mp 152–153°. IR ν_{max}^{KBr} cm^{-1}: 3500, 1780, 1735 and 1670; $\nu_{max}^{CHCl_3}$ cm^{-1}: 3560, 3500, 1770, 1730, 1660. Single crystals of this material (from MeOH) were used for X-ray analysis but subsequent detailed examination of the ^1H NMR and ^{13}C NMR spectra showed it to be an approximately 4:1 mixture of α-methylbutyrate and isovalerate esters **1a** and **1b**. (Calc. for $C_{20}H_{26}O_8$: C, 60.90; H, 6.64; O, 32.45; MW, 394.1627. Found: C, 60.82; H, 6.95; O, 32.85%; MW (MS) 394.1630 (2.8%)). Other significant peaks in the high resolution MS occurred at *m/e* (rel. int.) 310 ($C_{15}H_{18}O_7$, 2.7), 309 ($C_{15}H_{17}O_7$, 3.9), 292 ($C_{15}H_{16}O_6$, 14.4), 274 ($C_{15}H_{14}O_5$, 11.7), 85 (C_5H_9O, 44.6).

PLC of fractions 58 and 59 (EtOAc–C_6H_6, 1:1) gave eurecurvin (**7b**) as a solid, mp 185–186°, identical in all respects with material previously [4] isolated from *E. recurvans*.

Reactions of **1**. (a) Acetylation of 0.15 g of the mixture of **1a** and **1b** with Py–Ac_2O followed by the usual work-up and purification by PLC resulted in 45 mg of a mixture of unidentified products containing no acetyl function (NMR spectrum) and 75 mg of a gummy mixture of **3c** and **3d** which had IR

* Johnson 4940, not King 4940 as given in ref. [7], is *E.* ap. *cordigerum* Fern., putatively *E. perfoliatum* L. (diploid, pollen parent) × *E. rotundifolium* (triploid, female parent [9], as annotated by Professor R. K. Godfrey). According to Drs. Sullivan [9] and Godfrey, Montgomery and Fairbrothers' [25] concept of ssp. *ovatum* is comprised of *E. rotundifolium* of various derivations.

$\nu_{max}^{CHCl_3}$ cm^{-1}: 1765, 1740 and 1730; significant peaks in the low resolution MS at *m/e* 436 (M^+), 418 ($M^+ - H_2O$), 394 ($M^+ - C_2H_2O$), 376 ($M^+ - C_2H_4O_2$), 334 ($M^+ - C_5H_{10}O_2$), 292 ($M^+ - C_2H_2O - C_5H_{10}O_2$), 274 ($M^+ - C_2H_6O_2 - C_5H_{10}O_2$) and 85 ($C_5H_9O$, base peak). (b) A soln of 0.1 g of the mixture of **1a** and **1b** in 10 ml dry MeOH was stirred (N_2 atm) with 80 mg NaOMe for 40 min at room temp. The gummy product mixture of **2a** and **2b** was purified by PLC (EtOAc–$CHCl_3$, 1:1); low resolution MS peaks at *m/e* 426 (M^+), 408 ($M^+ - H_2O$), 395 (M^+ – Me)), 390 ($M^+ - 2H_3O$), 342 ($M^+ - C_5H_8O$), 324 ($M^+ - C_5H_{10}O_2$), 306 ($M^+ - C_5H_{10}O_2 - H_2O$), 293 (395 $- C_5H_{10}O_2$). (c) A soln of 0.20 g **1a** and **1b** mixture in 100 ml EtOAc containing 0.31 g 10% Pd–$BaSO_4$ was hydrogenated at atmos. pres. for 6 hr. The NMR spectrum of the gummy product after purification by PLC (EtOAc–$CHCl_3$, 1:1), indicated the presence of a mixture of starting material and 11,13-dihydro derivatives in approximately 3:1 ratio.

Reactions of **4**. (a) Acetylation of 52 mg of the mixture of **4a** and **4b** with 1 ml Ac_2O and 0.5 ml Py, and PLC of the crude product (EtOAc–$CHCl_3$, 1:1) gave a mixture of **4c** and **4d**; MS, 422 (M^+). (b) A soln of 0.12 g **4a** and **4b** mixture in 12 ml dry MeOH (N_2 atm) was stirred with 0.12 g NaOMe at room temp. for 6 hr. The resulting mixture of **5a** and **5b** was purified by PLC; MS, 412 (M^+).

Extraction of Eupatorium mohrii. Aerial parts of *E. mohrii* Greene (14 kg) collected by Dr. R. K. Godfrey on 4 August 1968 along route 67 4 miles north of Carabelle, Franklin County, Florida (Godfrey voucher #67977 on deposit in herbarium of Florida State University) were extracted with $CHCl_3$ and worked up in the usual fashion. The crude gum was taken up in a small amount of $CHCl_3$ and deposited 16.7 g of solid material after standing for several years, which was a mixture of **7b** and **7a** (approximate ratio 9:1). Eurecurvin (**7b**) could be obtained in pure form by repeated recrystallization of the mixture from MeOH–EtOAc. Isolation of **7a**, identical in all respects with material previously [4] isolated from *E. recurvans*, was achieved by PLC of the mixture ($CHCl_3$–MeOH, 9:1). Evapn of the filtrate gave 225 g of a crude gum, a portion of which (150 g) was absorbed on 200 g Si gel and chromatographed over 1.2 kg of Si gel. The following fractions (0.5 l. each) were collected: 1–11 (C_6H_6), 12–23 (C_6H_6–$CHCl_3$, 1:1), 24–34 ($CHCl_3$), 35–41 ($CHCl_3$–MeOH, 49:1), 42–45 ($CHCl_3$–MeOH, 19:1) and 46–48 ($CHCl_3$–MeOH, 9:1). Fractions 31–33 (10.1 g) which showed identical TLC patterns and contained one major component were combined and rechromatographed. This yielded 4.36 g **4a** as a colorless gum in the $CHCl_3$-MeOH (49:1) eluates, $[\alpha]_D$ $-56.9°$ (*c* 0.0305, $CHCl_3$); CD curve $[\theta]_{250}$ −1540 (min), $[\theta]_{235}$ −1360 (max), $[\theta]$ −16800 (min), $[\theta]_{206}$ −12000 (last reading).

Fractions 38–40 (12 g) containing a mixture of **7b** and **1a** were combined. Recrystallization from MeOH–EtOAc afforded 3.18 g **7b**; pure **1a**, mp 158–159°, $[\alpha]_D$ +3.21° (*c* 0.005, $CHCl_3$), was obtained from the mother liquors by PLC ($CHCl_3$–MeOH, 9:1, 2 developments) and recrystallization from $CHCl_3$–hexane. The CD curve for pure **1a** had $[\theta]_{270}$ −320 (min), $[\theta]_{228}$ 3470 (max), $[\theta]_{226}$ 3420 (last reading). Fraction 43 (7.4 g) contained one major (**8a**) and several minor constituents. Isolation of pure **8a** posed considerable difficulties, but was eventually achieved by PLC (EtOAc–hexane, 6 developments). The non-crystalline material had IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3580, 3440, 1755, 1730, 1655, 1240, 1140, 1050, 975, 905, 870 and 820; UV λ_{max}^{MeOH} nm: 212 (ε 10000); $[\alpha]_D$ +50.3° (*c* 0.025, $CHCl_3$); CD curve $[\theta]_{260}$ −4400 (min), $[\theta]_{216}$ 75100 (max), $[\theta]_{212}$ 65300 (last reading). (Calc. for $C_{20}H_{28}O_6$; MW, 364.18857. Found: MW (MS), 364.18857). A soln of 50 mg **8a** in 0.5 ml dry Py and 1 ml Ac_2O was kept at room temp. for 2 days, diluted with H_2O and extracted with $CHCl_3$. Evapn of the washed and dried extract and purification by PLC ($CHCl_3$–MeOH, 19:1) gave **8b** (or **8d**) as a viscous oil, whose NMR spectrum is reported in Table 1.

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