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SESQUITERPENE LACTONES FROM *HELIANTHUS GROSSESERRATUS**

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Key Word Index—*Helianthus grosseserratus*; Compositae; Heliantheae; sesquiterpene lactones; eudesmanolides; heliangolides; desacetylovatifolin; *ent*-kaurenic acids; ciliaric acid; flavones; hispidulin; pectolinarigenin.

Abstract—The isolation is reported of six new sesquiterpene lactones based on the eudesmanolide, *trans, trans*-germacradienolide and heliangolide skeletons from *Helianthus grosseserratus* Martens. The diterpenes grandifloric, 17-hydroxy-*ent*-isokaur-15-enic and ciliaric acids and the flavones hispidulin and pectolinarigenin were also found.

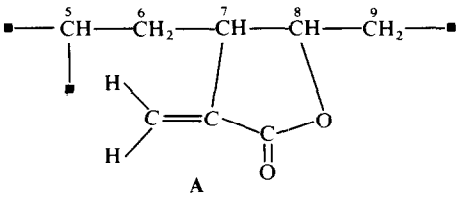
INTRODUCTION

In continuation of our earlier work on *Helianthus* species [1], we have investigated the constituents of *Helianthus grosseserratus* Martens [2] and hereby report isolation of a number of new sesquiterpene lactones as well as three previously known diterpene acids and the flavones hispidulin (**1a**) and pectolinarigenin (**1b**).

RESULTS AND DISCUSSION

The diterpenes were grandifloric acid (**2a**), previously isolated in the form of the acetate **2b** [3, 4], 17-hydroxy-*ent*-isokaur-15-enoic acid **3a**, previously isolated in the form of its acetate **3b** [5] and ciliaric acid (**4a**), previously found only in *Helianthus ciliaris* DC [6].

One group of three new sesquiterpene lactones **5a**, **5b** and **6a** was related to the alantolide ivasperin (**7**) [5]. Analysis of the 270 MHz ^{1}H NMR spectra of **5a** and **5b** (Table 1) and spin-decoupling established the presence of partial structures **A**–**C** (R = H and Ac, respectively, numbering as in final formula, ■ indicates carbon carrying no hydrogen) which together accounted for all carbon, hydrogen and oxygen atoms of the empirical formulas and for the ^{13}C NMR spectra (Table 2). Partial structure **B** was further supported by the demonstration of allylic coupling involving H-3 and H-15 and was confirmed by oxidation of **5b** (Jones reagent) to an α, β-unsaturated ketone **6b**. The latter, whose ketone group was included in a 6-membered or larger ring (IR frequency at 1670 cm^{-1}, carbonyl singlet near 198 ppm. cf. carbonyl signal of pinnatifidin **6c** [8]), was also obtained by acetylation of the third lactone **6a**.



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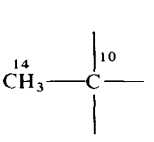

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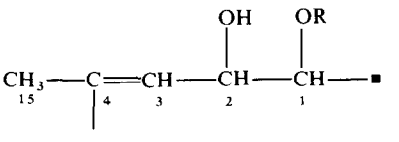


B (R = H, Ac)

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

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

	5a	5b	6a	6b	7	9a	10a	10b	12
H-1	3.44 *br* (1, 0.5)	4.63 *br*	3.44 *br* (0.5)	4.92 *br*	3.09 *d* (9.5)	—	—	—	5.04 *ddbr* (12, 5, 1)
H-2	3.98 *br* (2.5, 1)	3.92 *br*	—	—	3.54 *dtbr* (5, 9.5)	5.68	5.80	5.77	¶
H-3	5.51 *dqd* (2.5, 1, 0.5)	5.52 *dqd*	5.85 *dd* (1, 0.5)	5.93 *qd*	2.61 *dd* (12, 5) 2.05 *dd* (12, 9.5)	—	—	—	¶
H-5	2.22 *ddbr* (12, 3)	2.24 *ddbr*	2.76 *ddbbr*	2.70 *ddbr*	1.85 *ddt* (13.5, 3, 15)	6.20 *dt* (4.5, 1.5)	4.79 *dt* (9, 1.5)	5.72 *dt* (9, 2)	4.86 *dq* (10, 1.5)
H-6a	1.99 *ddd* (13, 6.5, 3)	2.00 *ddd*	2.10 *ddd*	2.20 *ddd*	1.78 *ddd* (13.5, 6.5, 3)	5.37 *dt* (4.5, 1)	4.31 *dd* (9, 5.5)	4.38 *dd*	5.13 *dd* (11.5, 10)
H-6b	1.34 *dt* (13, 12)	1.34 *dt*	1.38 *dt*	1.45 *dt*	1.40 *t* (13.5)				
H-7	3.02 *dtbr* (12, 6.5, 1)	3.03 *dtbr*	3.07 *dtbr*	3.12 *dtbr*	2.95 *dt* (13.5, 6.5)	3.72 *dddd* (4.5, 3.3, 3, 1.5)	3.64 *ddt* (5.5, 3.5, 3)	3.57 *ddt*	2.79 *dddd* (11.5, 4, 3.5, 3)
H-8	4.62 *dt* (2, 6.5)	4.58 *dt*	4.62 *dt*	4.60 *dt*	4.55 *dt* (2, 6.5)	5.23 *ddd* (6, 3, 1.5)	5.18 *ddd* (5.5, 3, 2)	5.13 *ddd*	4.48 *ddd* (6, 4, 2.5)
H-9a	2.17 *dd* (15, 6.5)	2.13 *dd*	2.37 *dd*	1.81 *dd*	2.61 *dd* (15, 2)	2.49 *dd* (14, 6)	2.62 *dd* (15, 5.5)	2.52 *dd*	2.87 *dd* (15, 6)
H-9b	1.93 *dd* (15, 2)	1.99 *dd*	1.94 *dd*	2.10 *dd*	1.48 *dd* (15, 6.5)	2.37 *dd* (14, 3)	2.23 *dd* (15, 2)	2.14 *dd*	2.47 *dd* (15, 2.5)
H-13a	6.14 *br* (1)	6.14 *br*	6.18 *br*	6.20 *br*	6.14 *d* (1)	6.35 *d* (3.3)	6.35 *d* (3.5)	6.29 *d* (3)	6.33 *d* (3.5)
H-13b	5.77 *br* (1)	5.64 *br*	5.65 *br*	5.67 *br*	5.61 *d* (1)	5.70 *d* (3)	5.73 *d* (d)	5.82 *d* (2)	5.62 (3)
H-14	1.00†	1.08†	0.91†	1.09†	0.78†	1.49†	1.43†	1.38†	4.12 *dbr* (13) 3.80 *dbr* (13)
H-15	1.72 *br*† (1)	1.72 *br*†	1.91 *br*†	2.00†	4.90 *br* (2) 4.59 *br* (1.5)	4.39 *br*‡	6.13 *br* (1.5) 5.93 *br* (1.5)	5.82 *d* (2) 5.77 *d* (2)	1.86 *d*† (1.5)
Misc.		2.08 (Ac)		2.13 (Ac)		§	§	2.14† (Ac)	‖

* Run at 270 MHz in $CDCl_3$. Unmarked signals are singlets. Frequencies in ppm downfield from TMS as internal standard. Coupling constants (in parentheses) in Hz are not given if they correspond to those in preceding column.

† Intensity three protons.

‡ Intensity two protons.

§ Isovaleroyl side chain, 2.12 *d* (6.5, H-2′)‡, 1.97 *m* (H-3′), 0.90 *d* (7)† and 0.88 *d*† (7, H-4′ and H-5′)†.

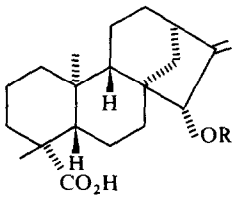
‖ Isovaleroyl side chain 1.95 *m* (H-2′ and H-3′), 0.79 *d* (7) and 0.77 *d* (7, H-4′ and H-5′)†.

¶ In four proton multiplet near 2.3 ppm.

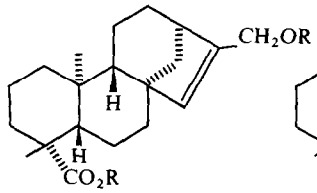
These facts and the observation that H-15 was weakly coupled to H-5 required that **A**, **B** and **C** be combined to give the gross structures shown in the formulas. Regarding the stereochemistry, the magnitudes of $J_{5,6}$ (12 and 3 Hz), $J_{7,8}$ (6.5 Hz) and $J_{7,13}$ (1 Hz) indicated the presence of a *cis*-fused lactone ring closed to C-8 of a eudesmane system, as is apparent by comparison with the high resolution NMR spectra of ivasperin (**7**, Table 1), granilin [8] and other alantolides. On the other hand the coupling constants involving H-1 and H-2 ($J_{1,2} = 1$ as compared with 9.5 Hz for **7**, 3 and 2 for granilin) and long range coupling involving H-1 and H-3 (*W*-coupling) showed that the two hydroxyl groups of **5a** and **5b** were both axial. This presumably also holds for the hydroxyl group of **6a** although the possibility that epimerization to the more stable equatorial configuration at C-1 might have occurred cannot be excluded completely.

An attempt to prepare an acetonide from **5a** (acetone, H_2SO_4) resulted in facile dehydration-*cum*-rearrangement to the aromatic lactone **8**. The same substance was formed, albeit more slowly, on treatment of ivasperin with sulfuric acid. Rearrangements of this type in the santonin series are well known.

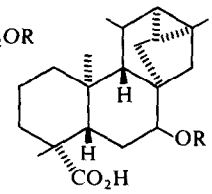
Two closely-related furenone heliangolides **9a** and **10a** were also isolated. The former is an ester analog of budlein A (**9b**) from *Viguiera buddleiaeformis* [9] and lactones



2a R = H
2b R = Ac



3a R, R′ = H
3b R = H, R′ = Ac
3c R = Me, R′ = H



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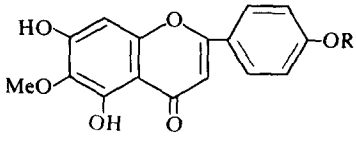
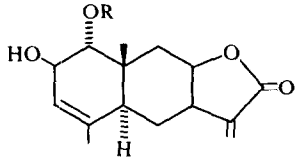
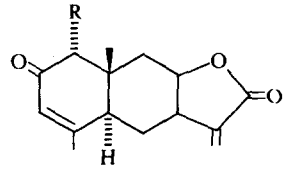
4b R = Ac



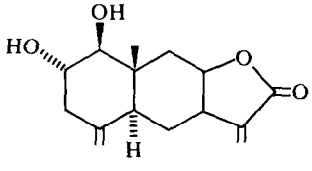
1a R = H
1b R = Me



5a R = H
5b R = Ac



6a R = OH
6b R = OAc
6c R = H



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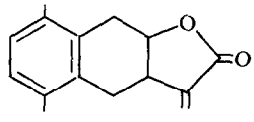

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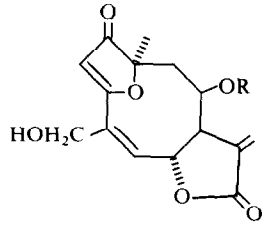
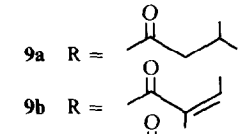
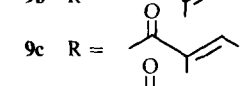


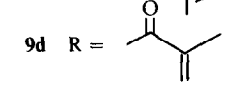


9a R =

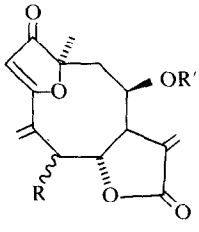
9b R =

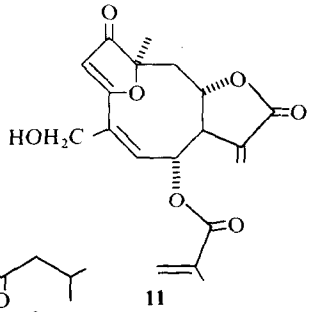


9c R =



9d R =





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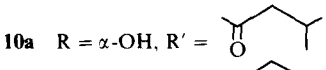
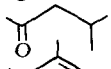
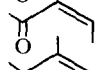


10a R = α-OH, R′ =



10b R = α-OAc, R′ =



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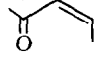

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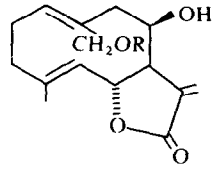

12a R = H
12b R = Ac

Table 2. ^{13}C NMR spectra of the sesquiterpene lactones from *H. grosseserratus**

Carbon	5a†	5b	6a	9a	10a†	12
1	78.05 *d*	79.25 *d*‡	77.76 *d*‡	205.78	204.69	134.07 *d*‡
2	71.46	67.68 *d*‡	197.86	104.73 *d*	104.92 *d*	25.95 *t*
3	124.00 *d*	121.96 *d*	124.32 *d*	182.98	184.34	39.66 *t*
4	135.53	136.37	162.51	138.45	141.52§	142.27
5	36.98 *d*	37.37 *d*‡	38.47 *d*‡	133.39 *d*	73.85 *d*‡	126.91 *d*‡
6	27.40 *t*	27.04 *t*	25.94 *t*	75.42 *d*	79.96 *d*‡	75.33 *d*
7	41.03 *d*	40.56 *d*‡	40.41 *d*‡	48.04 *d*	49.37 *d*‡	53.70 *d*
8	77.64 *d*	76.99 *d*‡	76.69 *d*‡	74.19 *d*	75.12 *d*‡	70.22 *d*
9	35.54 *t*	34.75 *t*	33.60 *t*	41.98 *t*§	42.61 ¶	44.54 *t*
10	35.24	33.50	38.56	87.68	86.00	138.39
11	143.07	141.71	141.40	136.18	140.79§	135.35
12	170.39	170.50§	170.23	168.83	168.57	170.69
13	119.56 *t*	120.52 *t*	120.91 *t*	124.00 *t*	122.20 *t*‖	120.84 *t*
14	18.33 *q*	17.56 *q*	17.01 *q*	21.02 *q*	22.09 *q*	60.30 *t*
15	21.18 *q*	21.05 *q*	22.00 *q*	61.93 *t*	119.68 *t*‖	17.19 *q*
1′		170.23§		171.38	171.35	
2′		21.05 *q*		42.67 *t*§	43.43 ¶	
3′				25.24 *d*	25.30 *d*	
4′				22.23 *q*	22.20 *q*	
5′				22.09 *q*	22.20 *q*	

* Run at 67.9 MHz in $CDCl_3$ unless specified otherwise. Unmarked signals are singlets.
† Run in C_5D_5N.
‡ Assignment by single frequency off-resonance decoupling.
§, ‖, ¶ Assignments possibly interchangeable.

9c, **d** from *Calea zacatechichi* [10].* Structure and stereochemistry were established by spin decoupling in the usual way; coupling constants and chemical shifts in the ^1H and ^{13}C NMR spectra closely resemble those of **9c** and **9d** [10]. An allylic rearrangement of **9a** can be invoked as the genesis of **10a** whose structure is evident on comparing its ^1H and ^{13}C NMR spectra with those of **9a**; its stereochemistry at C-5, C-6, C-7 and C-8 was again based on the observed coupling constants (Table 1). However, while such an allylic rearrangement was observed *in vitro* on acetylation of goyazensolide (**11**) with Ac_2O–Py [11], acetylation of **9a** under identical conditions gave a complex mixture in which **10b**, prepared unequivocally from **10a**, was at best a minor component. A similar observation has been made in the case of budlein A [9] although earlier [12] it was reported that acetylation of a mixture of lactones containing budlein A from *Viguiera angustifolia* permitted isolation of an acetate to which formula **10c** was ascribed. However, since H-5 of this substance is described [12] as a singlet and H-6 only as a doublet ($J = 5$ Hz), whereas in **10b**, H-5 is strongly coupled to H-6 (9 Hz) and allylically coupled to H-15, the presumed **10c** may actually be the C-6 epimer **10d**.

A sixth new lactone was the desacetyl derivative **12a** of ovatifolin (**12b**) [13, 14]. That this substance was not a heliangolide derivative but a *trans, trans*-1(10),4,5-germacradienolide with the assigned stereochemistry was clear from the values of $J_{7,13}$, the absence of significant NOE involving H-5 and H-15 and the close correspondence of chemical shifts, (both in the ^1H and ^{13}C NMR spectra) and coupling constants with those of closely related compounds. That the acetoxy group was on C-14 and not on C-15 could be demonstrated by spin-decoupling which showed that H-5, identified by its coupling to H-6 in the usual way, was allylically coupled to the protons of a vinyl methyl group (H-15), whereas the doublet of doublets of H-1 was additionally broadened by allylic coupling to the protons of $-CH_2OAc$.

H. grosseserratus exhibits a somewhat greater diversity of sesquiterpene lactone types than other previously-studied lactone-containing *Helianthus* species [1]. All of these belong to sections *Ciliares*, *Divaricati* and *Viguieropsis* as categorized by Heisler [2, 15] but further studies are needed to determine whether lactones are characteristic of these sections and if so, what type.

* To eliminate continuing confusion about how to indicate the correct stereochemistry of these and related heliangolide derivatives, we redraw earlier formulae in accordance with previously recommended rules [Roger, D., Moss, G. P. and Neidle, I. (1972) *J. Chem. Soc. Chem. Commun.* 142] so that re-entrant angles at tetrahedral ring carbon atoms are shown only when this corresponds to reality. For 3, 10 ethers this results in a change at C-3 (from vertex to re-entrant) and for heliangolides in general, in a change at C-6 (from re-entrant to vertex). In compounds of type **10** a substituent which was wedged on formerly re-entrant C-6 now becomes dotted and vice versa.

EXPERIMENTAL

Isolation of Helianthus grosseserratus *constituents.* Above ground parts (10 kg) of *H. grosseserratus* Martens, (collected by Drs N. C. Henderson and G. D. Anderson on Sept. 20, 1975 along Interstate 35 about 2 miles east of the Baldwin exit, Franklin Co. Kansas, Henderson and Anderson voucher 75-104 on deposit in herbarium of University of Missouri-Kansas City) was extracted with $CHCl_3$ and worked up in the usual fashion [16]. The crude

gum (60 g) was adsorbed on 70 g Si gel (Mallinckrodt 100 mesh) and chromatographed over 0.7 kg Si gel packed in toluene–$CHCl_3$ (1:1), 500 ml fractions being collected and monitored by TLC as follows: 1–5 ($CHCl_3$–toluene, 1:1), 6–10 ($CHCl_3$), 11–16 ($CHCl_3$–MeOH 99:1), 17–21 ($CHCl_3$–MeOH, 97:3), 22–26 ($CHCl_3$–MeOH, 19:1), 27–31 ($CHCl_3$–MeOH, 9:1).

Fractions 1–5 contained waxy material. TLC of fractions 6–8 showed the presence of two carboxylic acids which were converted to acetates and separated by prep. TLC. The faster moving acetate (10 mg) crystallized from MeOH as colourless plates, mp 174°, and was identified as acetylgrandifloric acid, mp 173–174° [4], by IR, NMR and mass spectrometry. The slower moving acetate **3b** (10 mg) had mp 140–142° from $CHCl_3$–hexane; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500 (*br*), 1730, 1705 and 1250; ^1H NMR: δ 5.42 (*br*, H-15), 4.62 (center of AB system, H-17), 2.53 (*m*), 1.23 (3H, *s*, H-18), and 0.97 (3H, *s*, H-20), MS *m/e*: 360 (M^+), 345,318,300 (base peak) and 285. This substance has previously been reported only in the form of its methyl ester [5]. Fractions 9 and 10 contained one major constituent which was recrystallized from $CHCl_3$ (200 mg), mp 290°. Acetylation of 60 mg gave an acetate (60 mg), mp 196°. Identification of this material as ciliaric acid (**4a**) [6] will be described in connection with other work.

Fractions 11–16 contained two compounds which were separated by prep. TLC (EtOAc–hexane, 3:2, double development). The upper band gave a colourless gum (**5b**) which could not be induced to crystallize, yield 60 mg; $[\alpha]_D$ +65.7° ($CHCl_3$, *c* 0.16): IR ν_{max}^{neat} cm^{-1}: 3450, 1760, 1740, 1665, 1270 and 1250; MS *m/e*: 360 (M^+, weak), 291, 288, 264, 246, 231, 185, 159, 135 and 95. (Calc. for $C_{17}H_{22}O_5$: MW, 306. 1467. Found: MW (MS), 306.1469). Jones oxidation of 20 mg of **5b** gave 15 mg of ketoacetate **6b**, mp 199–200°, IR ν_{max}^{KBr} cm^{-1}: 1760, 1740, 1670, 1615, 1265 and 1210; CD curve (MeOH) $[\theta]_{314}$ 4600, $[\theta]_{225}$ 20000 (sh), $[\theta]_{210}$ 24300 (last reading).

The lower band gave a substance (**6a**) which was recrystallized from EtOAc–hexane, mp 175–176°, yield 160 mg, $[\alpha]_D$ +350° (*c* 0.03), $CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 3400, 1770, 1670, 1625 and 1270; CD curve (MeOH) $[\theta]_{325}$ 2100, $[\theta]_{265}$ − 1300, $[\theta]_{212}$ 33 300 (last reading). (Calc. for $C_{15}H_{18}O_4$: MW, 262.1204; Found: MW (MS), 262.1213, 3%). Other significant peaks in the high resolution MS were at *m/e* (rel. int.): 244 ($C_{15}H_{16}O_3$, 5.5), 234 ($C_{14}H_{18}O_3$, 0.9), 233 ($C_{14}H_{17}O_3$, 3.3), 219 ($C_{13}H_{15}O_3$, 1.1), 216 ($C_{14}H_{16}O_2$, 2.9), 210 ($C_{13}H_{13}O_2$, 3.1), 178 ($C_{10}H_{10}O_3$, 3.7), 173 ($C_{12}H_{13}O$, 3.6), 135 ($C_9H_{11}O$, 6.6) 95 (C_6H_7O, 100). Acetylation of **6a** gave **6b** identical with material obtained by oxidation of **5b**.

Fractions 17–21 contained two coloured substances which were separated by prep. TLC ($CHCl_3$–MeOH, 9:1). The upper band on crystallization from $CHCl_3$–MeOH gave 50 mg of pectolinarigenin, mp 253–255° by direct comparison with authentic material. The lower band on recrystallization from $CHCl_3$–hexane furnished 100 mg of hispidulin, mp 290°, identified by comparison with authentic material.

Fractions 22–26 were combined. Prep. TLC (EtOAc–hexane, 3:2, double development) gave two substances. The upper band contained 200 mg of **5a**, mp 222–224° from $CHCl_3$–hexane, $[\alpha]_D$ +154° (*c* 0.43, MeOH); IR ν_{max}^{KBr} cm^{-1}: 3400, 3250, 1755, 1665 and 1270. (Calc. for $C_{15}H_{20}O_4$: MW, 264.1361. Found: MW (MS), 264.1361, 4.8%). Other significant peaks in the high resolution MS were at *m/e* (rel. int.): 249 ($C_{14}H_{17}O_4$, 2.3), 246 ($C_{15}H_{18}O_3$, 16.4), 244 ($C_{15}H_{16}O_3$, 3), 228 ($C_{15}H_{16}O_2$, 8.1), 218 ($C_{14}H_{18}O_2$, 7.8), 217 ($C_{14}H_{17}O_2$, 6.6), 213 ($C_{14}H_{13}O_2$, 5.8), 203 ($C_{13}H_{15}O_2$, 8.5), 193 ($C_{15}H_{13}$, 3.8), 180 ($C_{10}H_{12}O_3$, 14), 162 ($C_{10}H_{10}O_2$, 22.3), 157 ($C_{12}H_{13}$, 12.8), 145 ($C_{11}H_{13}$, 13.3), 143 ($C_{11}H_{11}$, 17.4), 135 ($C_9H_{11}O$, 23.1), 131 ($C_{10}H_{11}$, 17.7) 122 ($C_8H_{10}O$, 18.4), 119 (C_9H_{11}, 33.9), 117 (C_9H_9, 19.4), 107 (C_8H_{11}, 21.8), 105 (C_8H_9, 33.4), 97 (C_6H_7O, 100) and 95 (C_6H_7O, 49.1).

The lower band was crystallized from EtOAc–hexane to give 150 mg of **12**, mp 154–155°, $[\alpha]_D$ − 220° (*c* 0.2, MeOH); IR ν_{max}^{KBr} cm^{-1}: 3490, 3390, 1750, 1660, 1315, 880 and 840. The substance exhibited a weak molecular ion at *m/e* 264 ($C_{15}H_{20}O_4$); other stronger significant ions were at *m/e* 262, 246, 228, 213, 143, 115 and 91.

Fractions 27–31 contained two substances which were separated by prep. TLC (EtOAc–hexane, 3:2, double development). The material in the upper band (**9a**) was a gum which could not be induced to crystallize, yield 550 mg, $[\alpha]_D$ −60° (*c* 0.32, $CHCl_3$); IR ν_{max}^{film} cm^{-1}: 3450, 1770, 1745, 1710, 1660 and 1590; MS *m/e*: 376 (M^+, weak), 288, 273, 270, 255, 230 and 121. (Calc. for $C_{20}H_{24}O_7$: MW; 376.1522. Found: MW (MS), 376.1519). Substance **10a** (0.30 g) was a glass, IR ν_{max}^{KBr} cm^{-1}: 3400, 1750 (Strong), 1650, (sh), 1260, 1250 and 1170. (Calc. for $C_{20}H_{24}O_7$: MW, 376. 1521. Found: MW (MS), 376.1501, 1.6%). Other significants peaks occurred at *m/e* (rel. int.): 293 ($C_{15}H_{17}O_6$, 1.9), 292 ($C_{15}H_{16}O_6$, 3.2), 275 ($C_{15}H_{15}O_5$, 1.7), 274 ($C_{15}H_{14}O_5$, 4.8), 246 ($C_{14}H_{14}O_4$, 8.6), 245 ($C_{14}H_{13}O_4$, 2.1), 231 ($C_{13}H_{11}O_4$, 5.4), 229 ($C_{14}H_{13}O_3$, 3.6), 228 ($C_{14}H_{12}O_3$, 8), 203 ($C_{12}H_{11}O_3$, 9.5), 187 ($C_{12}H_{11}O_2$, 4.5), 186 ($C_{12}H_{10}O_2$, 17.5) and 152 ($C_8H_8O_3$, 100). Acetylation of 20 mg of **10a** and purification by prep. TLC gave 15 mg of **10b** which was a gum; IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1775, 1710, 1600, 1260 and 1240; the ^1H NMR spectrum is given in Table 1.

Rearrangements of **5a** *and* **7**. Compound **5a** was recovered quantitatively when a soln in dry Me_2CO was stirred with dry $CuSO_4$ for 12 hr at room temp. Stirring 50 mg of **5a** in 5 ml dry Me_2CO and 0.1 ml conc. H_2SO_4 for 2 hr caused complete disappearance of starting material. The soln was diluted with H_2O, neutralized and extracted with Et_2O. Concentration of the dried Et_2O extract afforded 30 mg of **8**, mp 116°, IR ν_{max}^{KBr} cm^{-1}: 1750, 1660, 1490, 1410, 1270, 1150, 1070, 1005, 870, 825 and 820; ^1H NMR: δ 6.93 (2H, H-2 and H-3), 6.22 (*d*, *J* = 3 Hz and 5.68 *d*, *J* = 2.5 Hz, H-13), 5.02 (*dt*, *J* = 9, 5.5 Hz, H-8), 3.42 (*m*, H-7), 3.07 (*dd*, *J* = 15, 5.5 Hz, H-9a), 2.68 (*complex*, H-6a, 6b and 9b), 2.27 (3H) and 2.23 (3H, aromatic methyls); MS *m/e*: 228 (M^+), 213, 210, 183, 156 and 132. Conversion of ivasperin (50 mg) to **8** (25 mg) required stirring for 6 hr to complete disappearance of starting material.

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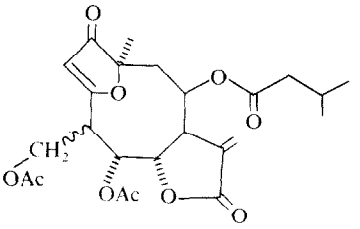
NOTE ADDED IN PROOF

Since acceptance of this manuscript we have succeeded in acetylating **9a** (Ac_2O–Py, 50 hr, 0°) and have shown that budlein A acetate is **10d**. The products from 0.35 g of **9a** were separated by TLC (EtOAc–hexane, 1:1). The material from the upper band clearly differed from **10b** and was therefore the C-5 epimer. NMR signals at 6.43 *d* (3) and 5.75 *d* (3, H-13), 6.12 *br* and 5.90 *br* (H-15), 5.73 (H-2), 5.90 *br* (H-5), 5.22 *m* (H-8), 4.54 *d* (5, H-6)), 4.15 *m* (H-7), 2.53 *dd* (15,5) and 2.28 *dd* (15, 2, H-9), 2.09 (Ac) superimposed on multiplets of H-2′ and H-3′, 1.51 (H-14), 1.00 *d* (7) and 0.98 *d* (7, H-4′ and H-5′). (Calc. for $C_{22}H_{26}O_7$: MW, 402. Found: MW (MS), 402). The spectrum parallels that of budlein A acetate except for the nature of the esterifying group, hence budlein A acetate is **10d**.

The material from the lower band, wt 0.17 g, was the diacetate **13**, NMR signals at 6.34 *d* (3) and 5.75 *d* (3.5, H-13), 5.63 (H-2), 5.20 *br* (H-5), 5.09 *tbr* (4, H-8), 4.85 *d* (4, H-6), 4.65 *dd* (12, 6) and 4.43 *dd* (12, 5, H-15), 3.95 *ddd* (4, 3.5, 3, H-7), 2.59 *dd* (16, 4.5) and 2.30 *dd* (16, 2, H-9), 2.15 and 2.12 (Ac) superimposed on multiplets of H- , H-2′ and H-3′, 1.42 (H-14), 0.91 *d* (7) and 0.90 *d* (7, H-4′ and H-5). (Calc. for $C_{24}H_{30}O_9$: MW, 420. Found: MW (MS), 420).



13