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FURANOHELIANGOLIDES AND OTHER COMPOUNDS FROM *CALEA HYMENOLEPIS**

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Key Word Index—*Calea hymenolepis*; Compositae; sesquiterpene lactones; furanoheliangolides; *p*-hydroxyacetophenone derivatives; Diels–Alder adducts.

Abstract—*Calea hymenolepis* afforded in addition to known compounds two new furanoheliangolides, one being a Diels–Alder adduct with myrcene, a *p*-hydroxyacetophenone derivative and two dimeric ones, again being formal Diels–Alder adducts. The structures were elucidated by highfield ^1H NMR spectroscopy.

INTRODUCTION

From the large genus *Calea* (tribe Heliantheae, subtribe Neurolininae) mainly furanoheliangolides and their precursors have been isolated as characteristic compounds [1–6]. Furthermore, several prenylated *p*-hydroxyacetophenones are widespread [3–5, 7]. We have now investigated *Calea hymenolepis* Baker.

RESULTS AND DISCUSSION

The roots of *C. hymenolepis* afforded bicyclogermacrene, *β*-sesquiphellandrene, the benzofuranes **1** [3], **2** [3] and **3** [3], **11** and two further acetophenone derivatives, the dimeric compounds **8** and **9**. The structure of **8** followed from the molecular formula ($C_{28}H_{28}O_6$), the mass spectral fragmentation pattern and the ^1H NMR spectrum (Table 1), which showed signals of two acetyl, one olefinic and one tertiary methyl group. Furthermore, two methoxy signals and two sets of signals of unsymmetric trisubstituted benzene derivatives were present. Spin decoupling, the observed chemical shifts and comparison of the signals with those of **1** led to the proposed structure. The unusual upfield shift of the signal of the methylenol ether was probably due to the shielding effect of the second aromatic ring, which was in agreement with a model. Therefore compound **8** was the formal Diels–Alder product of **1** formed by endo-addition. However, compound **1**, on heating at 100° gave no adduct. Accordingly **8** was not an artefact. The ^1H NMR spectrum of **9** was in part very similar to that of **8**. However, the molecular formula ($C_{28}H_{28}O_8$) already indicated that **9** may be the formal Diels–Alder adduct of **1** and **5**. Accordingly, the chemical shifts of the aromatic protons were different, but in part very similar to those of **4**. The chemical shift of H-4′ was unusual and a conformation has to be assumed, where this proton was deshielded by the carbomethoxy group. Compounds **8** and **9** have been named caleahymenone A and B respectively. Furthermore, the acetate **6** was obtained and its structure followed from the ^1H NMR spectrum (see Experimental), which was similar to that of compound **1**.

Table 1. ^1H NMR spectral data of compounds **7**–**9** (400 MHz, $CDCl_3$, TMS as internal standard)

	7		**8**	**9**
H-3	7.52 *d*	H-4	8.16 *d*	8.54 *d*
H-5	7.23 *dd*	H-6	7.93 *dd*	8.09 *dd*
H-6	6.84 *d*	H-7	7.55 *d*	7.53 *dd*
H-7	5.89 *q*	H-9	2.63 *s*	2.64 *s*
H-8	1.57 *d*	H-11	2.36 *ddd* 2.21 *ddd*	2.20 *m*
H-9	6.93 *d*	H-11′	2.14 *br d* 1.87 *ddd*	2.05 *m*
H-10	6.87 *d*	H-12	1.64 *s*	1.66 *s*
H-12	5.13 *br s*	H-4′	8.12 *d*	8.50 *d*
H-12′	5.07 *br s*	H-6′	7.88 *dd*	7.95 *dd*
H-13	2.01 *br s*	H-7′	7.38 *d*	7.04 *d*
OMe	3.84 *s*	H-9′	2.57 *s*	2.60 *s*
OSen	5.73 *qq*	H-12′	1.97 *s*	1.95 *s*
	2.17 *d*	OMe	3.49 *s*	3.84 *s*
	1.90 *d*		3.36 *s*	3.34 *s*

J (Hz): Compound **7**: 3, 5 = 2; 5, 6 = 8.5; 7, 8 = 6.5; 9, 10 = 16; OSen: 2′, 4′ = 2′, 5′ = 1; compounds **8** and **9**: 4, 6 = 4′, 6′ = 2; 6, 7 = 6′, 7′ = 8.5; compound **8**: $11_1, 11_2 = 15$; $11_1, 11'_1 = 3$; $11_1, 11'_2 = 6$; $11_2, 11'_1 = 2$; $11_2, 11'_2 = 12$; $11'_1, 11'_2 = 13$.

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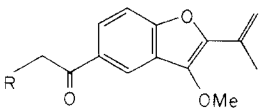
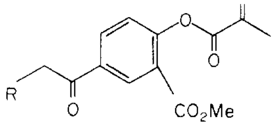
*Part 441 in the series "Naturally Occurring Terpene Derivatives". For Part 440 see Bohlmann, F., Jakupovic, J., Schuster, A., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21** (in press).



1 R = H
2 R = OAc
3 R = OH



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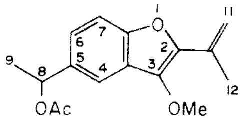
5 R = H



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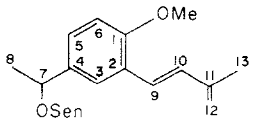

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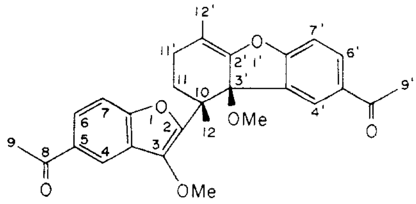

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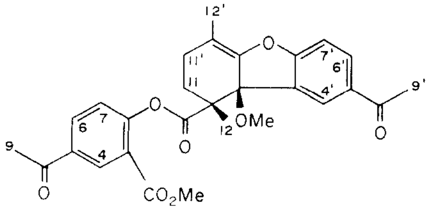

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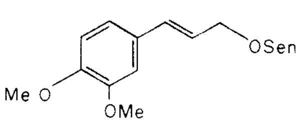

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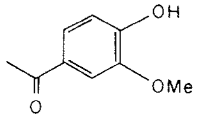

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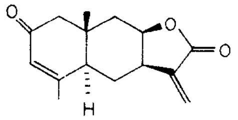

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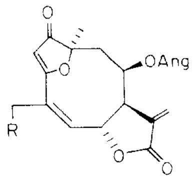
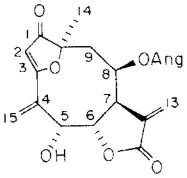
* Numbering as in 1.

The aerial parts afforded germacrene D, bicyclogermacrene, sitosterol, stigmasterol, **1**, **2** [3], **4** [3], **10**, pinnatifidin (**12**) [8], the senecioate **7**, the furanoheliangolides **13** [4] and **14** [1], the heliangolide **16** [9] and two further sesquiterpene lactones, **15**, the isomer of **14** and the furanoheliangolide myrcene adduct **17**. The structure of **7** clearly followed from the ^{1}H NMR spectrum (Table 1), which was similar to those of similar compounds. We have named compound **7** calepin senecioate. The structure of **15** followed from the ^{1}H NMR spectral data (Table 2), which were similar to those of a corresponding isovalerate from a *Helian-*



13 R = H
14 R = OH



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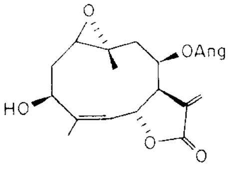

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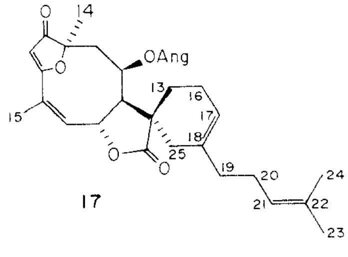

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Table 2. ^{1}H NMR spectral data of compounds **15** and **17** (400 MHz, $CDCl_3$, TMS as internal standard)

	15	**17**
H-2	5.77 *s*	5.67 *s*
H-5	4.72 *ddd*	6.26 *dt*
H-6	4.27 *dd*	5.41 *br dd*
H-7	3.69 *dddd*	3.05 *dd*
H-8	5.18 *ddd*	5.30 *ddd*
H-9	2.67 *dd*	2.51 *dd*
H-9′	2.27 *dd*	2.32 *dd*
H-13	6.42 *d*	1.95 *m*
H-13′	5.74 *d*	
H-14	1.48 *s*	1.44 *s*
H-15	6.12 *d* 5.92 *d*	4.43 *br s*
OCOR	6.11 *qq*	
	1.93 *dq*	
	1.76 *dq*	
H-16, H-19, H-20, H-25	—	2.04 *m*
H-21	—	5.12 *br t*
H-23	—	1.70 *br s*
H-24	—	1.63 *br s*
OCOR	—	6.12 *qq*
	—	1.98 *dq*
	—	1.80 *dq*

J (Hz): Compound **15**: 5,6 = 9; 5, 15 = 1.5; 6, 7 = 5.5; 7, 8 ~ 3; 7, 13 = 3.5; 7, 13′ = 3; 8, 9 = 5; 8, 9′ = 2.5; 9, 9′ = 15; compound **17**: 5, 6 = 4.5; 5, 15 = 1.5; 6, 7 = 4; 7, 8 = 1.5; 8, 9 = 5; 8, 9′ = 2; 9, 9′ = 15; 20, 21 = 6.

thus species [10]. The nature of the ester group followed from the typical signals. Compound **15** was therefore deduced to be isoatripliciolide angelate. The ^{1}H NMR spectrum of **17** (Table 2) and the molecular formula $C_{30}H_{38}O_7$ indicated a sesquiterpene lactone which was linked with a monoterpene residue. The absence of the typical signals of exomethylene protons showed that the terpene unit was linked with the lactone at C-13. Spin decoupling showed that H-7 was a double doublet at δ 3.05, which was coupled with signals at 5.41 and 5.30. The former was further coupled with a double triplet at δ 6.26, which itself showed allylic coupling with a broad singlet at 4.43. The signal at δ 5.30 was coupled with the double doublet at δ 2.51 and 2.32, obviously those of H-9. Together with the singlets at δ 5.67 and 1.44 (3H) the presence of a furanoheliangolide was indicated. Irradiation of a broadened triplet at δ 5.12 sharpened the signals of two olefinic methyl groups and altered a broad multiplet at 2.04 (8H). Though these signals could not separated, their allylic nature was obvious. All data therefore agreed with structure **17**, a formal Diels–Alder adduct of **13** and myrcene, which we have named caleamyrcenolide.

So far no lactones of type **17** have been reported. However, a furanoheliangolide linked with a pinene is known in another *Calea* species [4] and compounds **1**–**5** have been isolated previously only from a *Calea* species.

EXPERIMENTAL

The air-dried plant material (voucher RMK 8874, deposited in the U.S. National Herbarium, Washington) was extracted with Et_2O–petrol (1:2) and the resulting extracts were separated by CC (Si gel) and repeated TLC (Si gel). Known compounds were identified by comparing the ^{1}H NMR spectra with those of authentic material. The roots (40 g) afforded 10 mg bicyclogermacrene, 10 mg β-sesquiphellandrene, 10 mg **1**, 40 mg **2**, 10 mg **3**, 5 mg **6** (Et_2O–petrol, 1:3), 5 mg **8** (Et_2O–petrol, 1:3), 1 mg **9** (Et_2O–petrol, 1:3) and 5 mg **11**, while the aerial parts (200 g) gave 100 mg germacrene D, 100 mg bicyclogermacrene, 50 mg sitosterol, 50 mg stigmasterol, 20 mg lupeol, 20 mg **1**, 30 mg **2**, 20 mg **4**, 150 mg **7** (Et_2O–petrol, 1:10), 50 mg **10**, 6 mg **12**, 5 mg **13**, 20 mg **14**, 5 mg **15** (C_6H_6–CH_2Cl_2–Et_2O, 5:5:1), 10 mg **16** and 1 mg **17** (C_6H_6–CH_2Cl_2–Et_2O, 5:5:1).

8-O-*Dihydrocaleteucrin acetate* (**6**). Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 1745, 1250 (OAc), 1630 (C=C); MS *m/z* (rel. int.): 274.121 $[M]^+$ (100) ($C_{16}H_{18}O_4$), 259 $[M-Me]^+$ (21), 232 $[M-\text{ketene}]^+$ (14), 215 $[M-OAc]^+$ (49), 199 $[259-HOAc]^+$ (19); ^{1}H NMR ($CDCl_3$): 7.58 (*d*, *J* = 1.5 Hz, H-4), 7.29 (*dd*, *J* = 8.5, 1.5 Hz, H-6), 7.36 (*d*, *J* = 8.5 Hz, H-7), 5.98 (*q*, *J* = 6.5 Hz, H-8), 1.59 (*d*, *J* = 6.5 Hz, H-9), 5.69 (*br s*, H-11), 5.13 (*dq*, *J* = 1, 1 Hz, H-11), 2.21 (*br s*, H-12), 4.01 (*s*, OMe), 2.08 (*s*, OAc).

Calelepin senecioate (**7**). Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 1725, 1660 ($C=CCO_2R$), 1610, 980 (*trans* CH=CH–), 900 ($C=CH_2$); MS *m/z* (rel. int.): 300.173 $[M]^+$ (21) ($C_{19}H_{24}O_3$), 201 $[M-OCOR]^+$ (51), 200 $[M-RCO_2H]^+$ (55), 185 $[200-Me]^+$ (100), 83 $[C_4H_7CO]^+$ (82), 55 $[83-CO]^+$ (51).

Caleahymenone A (**8**). Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 1690 (PhCO); MS *m/z* (rel. int.): 460.189 $[M]^+$ (100) ($C_{28}H_{28}O_6$), 445 $[M-Me]^+$ (80), 428 $[M-MeOH]^+$ (6), 413 $[445-MeOH]^+$ (12), 239 $[428-C_{11}H_9O_3]^+$ (58), 230 $[C_{14}H_{14}O_3]^+$ (21) (RDA), 215 $[230-Me]^+$ (18).

Caleahymenone B (**9**). Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 1690 (PhCO, CO_2R); MS *m/z* (rel. int.): 492.178 $[M]^+$ (24) ($C_{28}H_{28}O_8$), 477 $[M-Me]^+$ (6), 461 $[M-OMe]^+$ (7), 271 $[M-C_{11}H_9O_5]^+$ (62), 239 $[271-MeOH]^+$ (100), 230 $[C_{14}H_{14}O_3]^+$ (38) (RDA), 215 $[230-Me]^+$ (10).

Isoatripliciolide angelate (**15**). Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 3600 (OH), 1790 (γ-lactone), 1725 ($C=CCO_2R$, C=O), MS *m/z* (rel. int.): 374.137 $[M]^+$ (2) ($C_{20}H_{22}O_7$), 83 $[C_4H_7CO]^+$ (100), 55 $[83-CO]^+$ (95).

$$[\alpha]^{\lambda}_{24^\circ} = \frac{589 \quad 578 \quad 546 \quad 436\,\text{nm}}{-10 \quad -16 \quad -18 \quad -29} \; (\mathrm{CHCl_3};\ c = 0.1).$$

Caleamyrcenolide (**17**). Colourless gum, IR $\nu_{\max}^{\mathrm{CCl_4}}$ cm^{-1}: 1790 (γ-lactone), 1730 ($C=CCO_2R$); MS *m/z* (rel. int.): 510.262 $[M]^+$ (3) ($C_{30}H_{38}O_7$), 492 $[M-H_2O]^+$ (0.5), 410 $[M-AngOH]^+$ (3), 392 $[410-H_2O]^+$ (1), 256 $[492-C_{10}H_{16}]^+$ (3) (RDA), 83 $[C_4H_7CO]^+$ (100), 69 $[C_5H_9]^+$ (50), 55 $[83-CO]^+$ (82).

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REFERENCES

1. Herz, W. and Kumar, N. (1980) *Phytochemistry* **19**, 593.
2. Ferreira, Z. S., Roque, N. F., Gottlieb, O. R., Oliveira, F. and Gottlieb, H. E. (1980) *Phytochemistry* **19**, 1481.
3. Bohlmann, F., Zdero, C., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 1643.
4. Bohlmann, F., Fritz, U., King, R. M. and Robinson, H. (1981) *Phytochemistry* **20**, 743.
5. Bohlmann, F., Bapuji, M., King, R. M. and Robinson, H. (1982) *Phytochemistry* **21**, 421.

6. Quijano, L., Romo de Vivar, A. R. and Rios, T. (1979) *Phytochemistry* **18**, 1745.
7. Lousenco, T. O., Risue, G. A. and Roque, N. F. (1981) *Phytochemistry* **20**, 773.
8. Herz, W., Mitra, R. B., Rabindran, K. and Viswanathan, N. (1962) *J. Org. Chem.* **27**, 4041.
9. Martinez, J. R., Ayamante, B. I. S., Nunez-Alarcon, J. A. and Romo de Vivar, A. R. (1979) *Phytochemistry* **18**, 1527.
10. Herz, W. and Kumar, N. (1981) *Phytochemistry* **20**, 99.