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DIMERIC CHROMENES AND MIXED DIMERS OF A CHROMENE WITH EUPARIN FROM *ENCELIA CANESCENS*

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Key Word Index—*Encelia canescens*; Compositae; *p*-hydroxyacetophenone derivatives; dimeric chromenes; mixed dimers of a chromene and euparin; tremetone derivative; chromene derivative.

Abstract—The investigation of *Encelia canescens* afforded, in addition to several known compounds, four new dimeric *p*-hydroxyacetophenone derivatives, two epimeric chromene dimers and two epimeric mixed dimers of euparin and encecalin. Furthermore, derivatives of tremetone and of encecalin were present. The structures were elucidated hy high field ^{1}H NMR spectroscopy.

INTRODUCTION

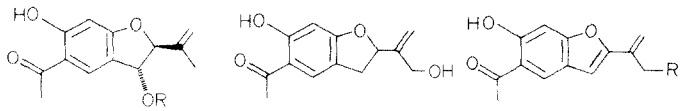
The genus *Encelia* (Compositae, tribe Heliantheae) is placed in the large subtribe Ecliptinae [1]. So far three species have been studied chemically. While two species afforded eudesmanolides [2, 3], another contained euparin and the chromene derivative encecalin [4]. A hybrid of the latter species gave both a chromene derivative and an eudesmanolide [5]. We now have investigated *Encelia canescens* Lam. The results will be discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts of *Encelia canescens* collected in Peru, afforded α- and β-farnesene, germacrene D, caryophyllene, α- and β-bergamotene, γ- and *ar*-curcumene, sesquiphellandrene, bisabolene and its endoperoxide [6], tridecapentainene, taraxasteryl acetate, the toxol derivatives **1** [7], **2** and **3** [8], euparin (**4**) and its 12-hydroxy derivative **5** [9], the chromene derivatives **6** [10], **7** [10], **8** [11], **9** [12], **10** [13], **11** and **12** [13] and mixture of dimeric chromene derivatives, the epimers **13** and **14**. By far the major components were **3**, **5**, **6** and **10**. The roots afforded **1**, **4**, **6**, **9**, **10** and the two further dimeric euparin derivatives **15** and **16**. The structure of **2** could be deduced readily from the ^{1}H NMR spectrum (see Experimental) though it was not completely free from **1**. The difference in the ester residue followed from the typical ^{1}H NMR signals. Also the structure of **11** could be deduced from the ^{1}H NMR spectrum (see Experimental) which was close to that of **10**. The additional methoxy signal and a slight change in the chemical shift of the H-9 signal clearly indicated the presence of the *O*-methyl ether of **10**.

The diastereomers **13** and **14** could be separated by repeated TLC. The molecular formula was $C_{28}H_{34}O_5$ for both. In the mass spectrum a significant fragment, *m/z* 233, was formed by splitting of the diphenyl ether linkage. The base peak, *m/z* 201, was the result of elimination of methanol from the fragment, *m/z* 233. Also the counterpart of the latter, *m/z* 217, was visible. There were small differences in the ^{1}H NMR spectra (Table 1) of **13** and **14**. In particular, the H-9 signal was shifted more downfield in the meso compound **14** when compared with the shift of H-9 in the spectrum of **13**. The latter was optically active while **14** was inactive. Accordingly the ^{1}H NMR signals were identical for both parts of the dimer **14**. However, also in the spectrum of **13** no differences were visible for the corresponding signals of the protons of the two parts of the dimer. Thus the optical rotation of **13** could only be explained by differences in the relative stereochemistry at C-9 and C-9′. The ^{1}H NMR data were close to those of **11**. Compound **13** we have named encecanescin.

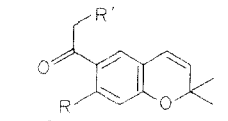
The diastereomers **15** and **16** could be separated only by reversed phase HPLC. The molecular formula for both was $C_{27}H_{30}O_6$ and the base peak this time was formed by elimination of a methyl group followed by loss of water. A further intense fragment, *m/z* 217, was formed by splitting the C-11–C-9′ linkage. The ^{1}H NMR spectra (Table 2) of **15** and **16** showed that they were formed by a combination of two different components. The ^{1}H NMR spectral data of one moiety were close to those of euparin (**4**), except for the signals of the isopropenyl group, while those of the second moiety were close to those of **10**; only the H-9 signal was missing and the methyl doublet was replaced by a singlet at δ 1.54 and 1.52, respectively. The signals of the isopropenyl group in the first moiety were replaced by those of a monosubstituted isopropyl group. Thus a linkage between C-11 and C-9′ was the only possible one. This leads to a compound with two asymmetric centers. Accordingly two diastereomers were possible. Compound **15** showed a very small optical rotation while that of **16** was zero even at different wavelengths. The ^{1}H NMR signals of **15** and **16**, which could all be assigned by spin decoupling, again differed slightly. Inspection of models showed that these differences could be explained if a conformation was preferred in which the methyls at C-10 and C-9′ were as far away from each other as possible. If this is true **16** would be in a conformation where the aromatic parts come close together thus explaining the observed shielding effects (H-3, H-11′). Compound **15** we have named encecanescol.



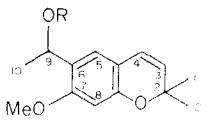
1 R = Ang
2 R = iVal

3

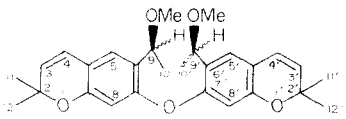
4 R = H
5 R = OH



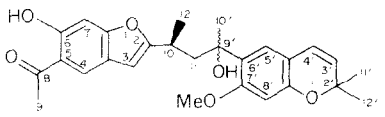
	6	**7**	**8**	**9**
R	H	OH	OMe	OH
R'	H	H	H	OH



10 R = H
11 R = Me
12 R = Ang



13 9'-α-Me
14 9'-β-Me



15 9'-α-Me
16 9'-β-Me

Table 1. ^{1}H NMR spectral data of compounds **13** and **14** (400 MHz, $CDCl_3$, TMS as internal standard)

	13	**14**
H-3	5.47 *d*	5.41 *d*
H-4	6.32 *d*	6.21 *d*
H-5	7.10 *s*	6.99 *s*
H-8	6.31 *s*	6.25 *s*
H-9	4.59 *q*	4.81 *q*
H-10	1.32 *d*	1.38 *d*
H-11	1.42 *s*	1.41 *s*
H-12	1.46 *s*	1.42 *s*
OMe	3.67 *s*	3.68 *s*

J (Hz): 3, 4 = 9; 9, 10 = 6.

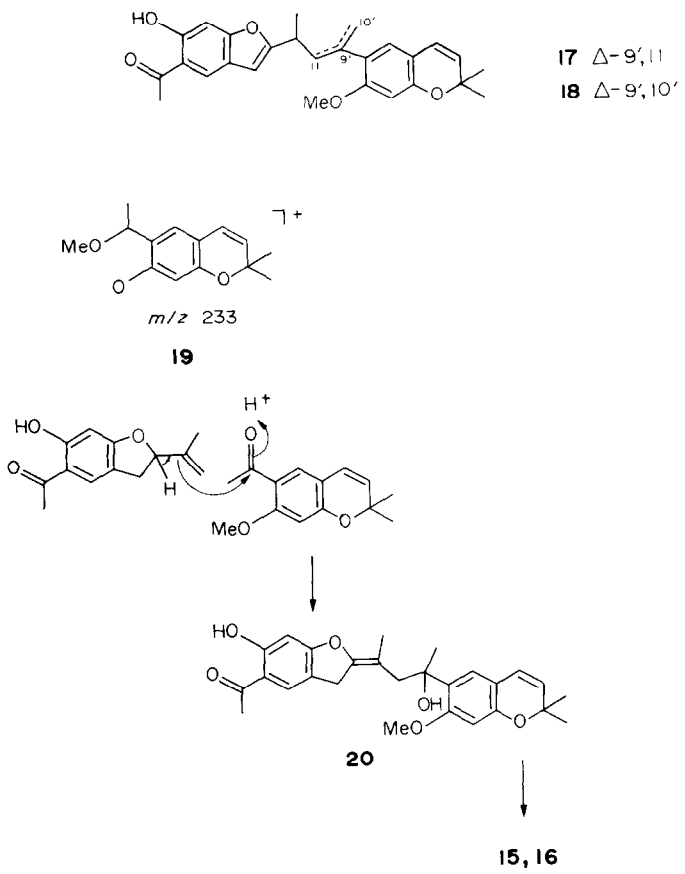
Elimination of water led to **18** which was partly isomerized to **17** when heated with *p*-toluenesulfonic acid in benzene. Also these compounds showed no optical rotation. The formation of **15** and **16** could be explained as the result of a proton-catalysed addition of 6-hydroxytremetone to encecalin (**8**) leading to **20** which on isomerization could lead to **15** and **16** (see Scheme 1). This would explain the presence of two dimers.

The chemistry of this *Encelia* species showed similarities to that of *E. californica* [4], although in this latter case only two compounds were identified. Furthermore, a

Table 2. ^{1}H NMR spectral data of compounds **15**–**18** (400 MHz, $CDCl_3$, TMS as internal standard)

	15	**16**	**17**	**18**
H-3	6.44 *d*	6.16 *d*	6.44 *d*	6.72 *br s*
H-4	7.86 *s*	7.72 *s*	7.85 *s*	7.91 *s*
H-7	6.96 *d*	6.79 *d*	6.95 *d*	6.98 *br s*
H-9	2.69 *s*	2.65 *s*	2.66 *s*	2.70 *s*
H-10	3.10 *ddq*	3.35 *ddq*	4.16 *dq*	3.40 *ddq*
H-11$_1$	2.17 *dd*	2.07 *dd*	6.42 *dd*	2.37 *dd*
H-11$_2$	2.27 *dd*	2.39 *dd*		2.77 *dd*
H-12	1.08 *d*	1.23 *d*	1.36 *d*	1.25 *d*
H-3'	5.42 *d*	5.28 *d*	5.45 *d*	5.46 *d*
H-4'	6.18 *d*	6.02 *d*	6.28 *d*	6.29 *d*
H-5'	6.71 *s*	6.60 *s*	6.88 *s*	6.81 *s*
H-8'	6.26 *s*	6.03 *s*	6.35 *s*	6.39 *s*
H-10'	1.54 *s*	1.52 *s*	2.02 *d*	5.13 *br s* 5.81 *br s*
H-11'	1.39 *s*	1.11 *s*	1.41 *s*	1.44 *s*
H-12'	1.37 *s*	1.29 *s*	1.42 *s*	
OMe	3.73 *s*	3.77 *s*	3.80 *s*	3.81 *s*
OH	2.82 *br s*	3.31 *br s*	—	—

J (Hz): 3', 4' = 10; 10, 12 = 7; 11$_1$, 11$_2$ = 14; compound **15**: 3, 7 = 1; 10, 11$_1$ = 5; 10, 11$_2$ = 8; compound **16**: 3, 7 = 1; 10, 11$_1$ = 4.5; 10, 11$_2$ = 10.2; compound **17**: 10, 11 = 9; 10', 11 = 1; compound **18**: 10, 11$_1$ = 5; 10, 11$_2$ = 9.



Scheme 1.

clear relationship to *Flourensia* is obvious from the constituents isolated so far. Also botanically these two genera are the most closely related in a somewhat diverse subtribe. The chemistry of this subtribe also is not very uniform.

EXPERIMENTAL

The air-dried plant material, collected in Jan. 1982 in Peru (vouchers RMK 8993, 9009 and 9010) were extracted with Et_2O–petrol (1:2) and the resulting extracts were separated by CC (Si gel) and further by repeated TLC (Si gel). Known compounds were identified by comparing the high field ^{1}H NMR spectra with those of authentic material. The aerial parts (630 g) gave a fraction of 80 mg of sesquiterpene hydrocarbons containing β-bisabolene (main), germacrene D, caryophyllene, α- and β-farnesene, α- and β-bergamotene, sesquiphellandrene, *ar*- and γ-curcumene, 15 mg tridecapentainene, 3 mg bisabolene endoperoxide, 20 mg taraxasteryl acetate, 5 mg **1**, 5 mg **2** (Et_2O–petrol, 1:1), 2.5 g **3**, 100 mg **4**, 1 g **5**, 1 g **6**, 50 mg **7**, 50 mg **8**, 10 mg **9**, 1 g **10**, 5 mg **11** (Et_2O–petrol, 1:3), 20 mg **12**, 15 mg **13** and 7 mg **14**. The roots (100 g) gave 5 mg **1**, 7 mg **4**, 10 mg **6**, 5 mg **9**, 10 mg **10** and 15 mg **15/16** (Et_2O–petrol, 3:1) which were separated by HPLC (MeOH–H_2O, 8:2). Compounds **14–16** most likely were crystalline. Due to the small amounts, however, no crystals were obtained.

6-Hydroxy-3α-isovaleryloxytremetone (**2**). Colourless gum, ^{1}H NMR ($CDCl_3$, 400 MHz): 5.09 *br d* (H-2), 6.00 *d* (H-3), 7.82 *s* (H-4), 6.44 *s* (H-7), 2.56 *s* (H-9), 4.97 *br s* and 4.95 *br s* (H-11), 1.73 *br s* (H-12), 2.23 *d*, 2.13 *m*, 0.93 *d* (*i* Val) [*J* (Hz): 2,3 = 2; OiVal: 2', 3' = 3', 4 = 1', 5' = 7].

2,2-Dimethyl-6-(1-methoxyethyl)-7-methoxychromene (**11**). Colourless gum, ^{1}H NMR ($CDCl_3$, 400 MHz): 6.30 *d* (H-3), 5.46 *d* (H-4), 6.97 *s* (H-5), 6.36 *s* (H-8), 4.66 *q* (H-9), 1.36 *d* (H-10), 1.43 *s* (H-11, H-12), 3.78 *s* and 3.25 *s* (OMe); [*J* (Hz): 3, 4 = 10; 9, 10 = 6].

Encecanescin (**13**). Colourless crystals, mp 162–163°; MS *m/z* (rel. int.): 450.240 $[M]^+$ (9) ($C_{28}H_{34}O_5$), 435 $[M-Me]^+$ (12), 233 $[\mathbf{19}]^+$ (78), 217 $[M-233]^+$ (48), 201 $[233-MeOH]^+$ (100).

$$[\alpha]_{24}^{\lambda,\circ} = \frac{589 \quad 578 \quad 546 \quad 436 \quad 365\,nm}{-113 \quad -119 \quad -136 \quad -246 \quad -422}$$

($CHCl_3$; *c* 0.35).

9-epi-encecanescin (**14**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1645, 1629, 1565, 1500, 1290, 1210, 1150; MS *m/z* (rel. int.): 450.240 $[M]^+$ (8), 435 (9), 217 (31), 201 (100). $[\alpha]_D = \pm 0°$ (at 578, 546, 436 and 365 nm).

Encecanescol (**15**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3480 (OH), 3600–2600, 1640 (*o*-hydroxyphenyl ketone), 1615 (C=C); MS *m/z* (rel. int.): 450.204 $[M]^+$ (10) ($C_{27}H_{30}O_6$), 435 $[M-Me]^+$ (28), 432 $[M-H_2O]^+$ (14), 417 $[432-Me]^+$ (29), 217 $[C_{13}H_{13}O_3]^+$ (78), 201 (100). $[\alpha]_D$ *ca* −3°. 5 mg **15** in 4 ml C_6H_6 was heated with 5 mg *p*-toluenesulfonic acid for 5 min at 55°. TLC (Et_2O–petrol, 1:1) afforded 3 mg **18** and 1 mg **17**. When the mixture was heated for 30 min at 55° 1 mg 18 and 3 mg 17 were obtained. ^{1}H NMR spectra see Table 2. $[\alpha]_D$ *ca* 0°.

9'-*Epi-encecansescol* (**16**). Colourless gum; MS *m/z* (rel. int.): 450.204 $[M]^+$ (32), 435 $[M-Me]^+$ (100), 432 $[M-H_2O]^+$ (24), 417 $[432-Me]^+$ (32), 217 (95), 201 (64), $[\alpha]_D = \pm 0°$.

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REFERENCES

1. Robinson, H. (1981) *Smithson. Contrib. Botany* **51**, 48.
2. Geissman, T. A. and Mukherjee, R. (1968) *J. Org. Chem.* **33**, 656.
3. Sims, J. J. and Bergmann, K. A. (1972) *Phytochemistry* **11**, 444.
4. Bjeldanes, L. and Geissman, T. A. (1969) *Phytochemistry* **8**, 1293.
5. Bjeldanes, L. and Geissman, T. A. (1971) *Phytochemistry* **10**, 1079.
6. Bohlmann, F., Jakupovic, J. and Zdero, C. (1978) *Phytochemistry* **17**, 2034.
7. Bohlmann, F. and Zdero, C. (1971) *Chem. Ber.* **104**, 964.
8. Bohlmann, F. and Zdero, C. (1978) *Phytochemistry* **17**, 1161.
9. Bohlmann, F., Dutta, L. N., Dorner, W., King, R. M. and Robinson, H. (1979) *Phytochemistry* **18**, 673.
10. Bohlmann, F. and Grenz, M. (1970) *Chem. Ber.* **103**, 90.
11. Bjeldanes, L. and Geissman, T. A. (1969) *Phytochemistry* **8**, 1293.
12. Bohlmann, F. and Jakupovic, J. (1978) *Phytochemistry* **17**, 1677.
13. Bohlmann, F. and Grenz, M. (1977) *Chem. Ber.* **110**, 295.