2. Nakao, M. and Shibue, C. (1924) *Yakugaku Zasshi* **44**, 913.
3. Paniker, P. M. B., Rao, B. S. and Simonsen, J. L. (1926) *J. Indian Inst. Sci.* **9A**, 133.
4. Bohlmann, F., Zeisberg, R. and Klein, E. (1975) *Org. Magn. Reson.* **7**, 426.
5. Burns, W. D. P., Carson, M. S., Cocker, W. and Shannon, P. V. R. (1968) *J. Chem. Soc.* (*C*) 3073.

*Phytochemistry*, Vol. 26, No. 12, pp. 3351–3353, 1987.
Printed in Great Britain.

0031–9422/87 $3.00 + 0.00


# A DIMER OF *d*-PINOCARVONE FROM *CEDRONELLA CANARIENSIS*

MARÍA C. CARREIRAS, BENJAMÍN RODRÍGUEZ,* ROSARIO E. LÓPEZ-GARCÍA† and ROSA M. RABANAL†

Instituto de Química Orgánica, CSIC, Juan de la Cierva 3, 28006 Madrid, Spain; †Departamento de Farmacología, Facultad de Farmacia, La Laguna, Tenerife, Spain

(*Received* 18 *March* 1987)

**Key Word Index**—*Cedronella canariensis*; Labiatae; terpenes, *d*-pinocarvone, dimer of *d*-pinocarvone; cedronellone; ursolic acid.

**Abstract**—From the aerial parts of *Cedronella canariensis* a dimer of *d*-pinocarvone, cedronellone, has been isolated, together with large amounts of *d*-pinocarvone and ursolic acid. The structure of cedronellone was established by chemical and spectroscopic means.

## INTRODUCTION

*Cedronella canariensis* Webb. & Berth. (Labiatae) is a plant endemic to the Canary and Madeira Islands [1], the chemical study of which has not been previously carried out. From the aerial parts of this species we have isolated large amounts of the monoterpene *d*-pinocarvone (**1**, 0.74% on dry plant) [2] and ursolic acid (1.42%), besides minor quantities of a dimer of *d*-pinocarvone (**2**, cedronellone, 0.1%) not previously described as synthetic or natural product.

## RESULTS AND DISCUSSION

Cedronellone (**2**) had a molecular formula $C_{20}H_{28}O_2$ and its IR spectrum showed ketone (1728 $cm^{-1}$) and enol-ether (1690 $cm^{-1}$, strong) absorptions. The $^1H$ and $^{13}C$ NMR spectra of compound **2** revealed four methyl groups (C-Me singlets at $\delta$1.38, 1.25, 0.90 and 0.79, and carbon atom resonances at $\delta$27.33, 25.95, 22.13 and 20.54, all quartets in the spectrum recorded under SFORD conditions), a ketone function ($\delta$208.53, *s*), a fully substituted enol-ether grouping (no signals of olefinic protons, carbon atom resonances at $\delta$142.46, *s*, and 112.26, *s*), a fully substituted carbon atom bearing an oxygen atom ($\delta$80.33, *s*), six methylene and four methine groupings and, finally, two quaternary carbon atoms (see Experimental).

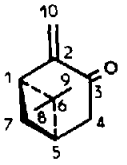
Distillation of cedronellone (**2**) under vacuum quantitatively yielded *d*-pinocarvone (**1**) [2], thus establishing that compound **2** was a dimer of this monoterpenoid.

The *R* stereochemistry of the C-2′ centre of cedronellone (**2**) was established as follows. Reduction of compound **2** with sodium borohydride gave a mixture of two epimeric alcohols (**3** and **4**), one of which (**3**) was an extremely unstable substance which was quantitatively transformed into another compound (**5**) in the extraction process of the reaction (see Experimental). The structure of the derivative **5** was in agreement with its spectroscopic data [IR: no hydroxyl absorption; $^{13}C$ NMR: carbons bearing oxygen atoms at $\delta$105.92, *s* (C-3), 81.66, *s* (C-2′) and 75.38, *d* (C-3′), see also Experimental]. On the other hand, application of the Horeau's method [3] to the alcohol **4** established as *R* the absolute configuration of its hydroxyl function.

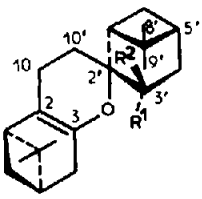
All the above facts were only compatible with a 2′*R* configuration of cedronellone (**2**), since the 3′*S*-hydroxy derivative (**3**), which possesses a *cis* relationship between the hydroxyl group and the ethereal oxygen atom, was transformed into the tetrahydropyran **5**. In compound **4**, with a 3′*R* configuration in a *d*-pinocarvone hydrocarbon skeleton, its hydroxyl group is *trans* with respect to the ethereal oxygen atom, thus excluding the possibility of the formation of a tetrahydropyran derivative.

It is reasonable to assume that cedronellone (**2**) can be formed from *d*-pinocarvone (**1**) by a hetero-Diels–Alder reaction. This assumption was also in agreement with a 2′*R* configuration for compound **2**, since it is known [4]

*Author to whom correspondence should be addressed.



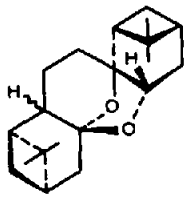
1



2 $R^1, R^2 = O$

3 $R^1 = OH$, $R^2 = H$

4 $R^1 = H$, $R^2 = OH$



5

that this reaction follows Alder's rule of maximum accumulation of unsaturated centres. Thus, the 2'*R* dimer of *d*-pinocarvone should be favoured over the 2'*S* isomer.

Cedronellone (2) is a stereoisomer of aritasone [5, 6], a dimer of *l*-pinocarvone previously isolated from *Chenopodium ambrosioides*. To our knowledge, this is the first report of *d*-pinocarvone (1) from a species belonging to the family Labiatae.

## EXPERIMENTAL

Mps are uncorr. Plant materials were collected in June 1986 in the Madeira Island and voucher specimens were deposited in the Herbarium of the 'Instituto Superior de Agronomia', Lisbon (Portugal).

*Extraction and isolation of the compounds.* Dried and finely powdered *Cedronella canariensis* aerial parts (3.1 kg) were extracted with $Me_2CO$ (15 l) at room temp. for a week. The extract (126 g) was chromatographed on a silica gel column (Merck, No. 7734, deactivated with 15% $H_2O$, 1.5 kg). Elution with *n*-hexane–EtOAc (19:1) successively yielded cedronellone (2, 3.1 g) and *d*-pinocarvone (1, 23 g). Further elution with $CHCl_3$–MeOH (4:1) gave ursolic acid (44 g), identified by the physical (mp, $[\alpha]_D$) and spectroscopic (IR, $^1H$ and $^{13}C$ NMR, MS) data of its methyl ester derivative and by comparison (mmp, TLC) with an authentic sample.

*Cedronellone* (2). Mp 106–107° (MeOH); $[\alpha]_D^{20} + 79.3°$ ($CHCl_3$; *c* 0.916); CD nm ($\Delta\varepsilon$): 255 (−0.52), 280 (0), 315 (+2.06), 322.5 (+2.20), 333 (+1.90), 385 (0) (MeOH; *c* 0.076); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 3000, 2980, 2940, 2840, 1728, 1690, 1470, 1375, 1160, 1150, 1060, 1030, 980, 940, 870, 840, 720; UV $\lambda_{max}^{EtOH}$ nm (log $\varepsilon$): 220 (3.48), 280 (2.06); $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 2.70–1.65 (16 H, methylene and methine protons), C-Me singlets at 1.38 (3 H), 1.25 (3 H), 0.90 (3 H) and 0.79 (3 H); $^{13}C$ NMR (50.3 MHz, $CDCl_3$) (assignments based on ref. [7]) $\delta$ (carbon number): 43.89 *d* (1)*, 112.26 *s* (2), 142.46 *s* (3), 32.89 *t* (4)†, 40.45 *d* (5), 40.14 *s* (6), 32.32 *t* (7)†, 27.33 *q* (8), 22.13 *q* (9), 21.70 *t* (10), 44.94 *d* (1')*, 80.33 *s* (2'), 208.53 *s* (3'), 43.24 *t* (4'), 37.93 d (5'), 38.93 *s* (6'), 26.96 *t* (7'), 25.95 *q* (8'), 20.54 *q* (9'), 26.96 *t* (10') (*† these assignments may be reversed); EIMS (70 eV, direct inlet) *m/z* (rel. int.): 300 $[M]^+$ (31), 285 (2), 257 (9), 231 (13), 203 (12), 151 (53), 150 (27), 149 (25), 135 (41), 121 (40), 107 (100), 91 (38), 81 (52), 69 (43), 53 (70), 41 (72). (Found: C, 79.92; H, 9.67. $C_{20}H_{28}O_2$ requires: C, 79.95; H, 9.39%.)

*Vacuum distillation of cedronellone* (2) *to give* d*-pinocarvone* (1). Compound 2 (300 mg) was distilled under vacuum (0.7 mm Hg). The distillate was *d*-pinocarvone (1): thick oil; $[\alpha]_D^{21} + 67.9°$ ($CHCl_3$; *c* 0.109) [2]; IR $\nu_{max}^{NaCl}$ $cm^{-1}$: 2935, 1710, 1630, 1465, 1370, 1330, 1285, 1120, 1060, 1030, 925 [8]; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 5.98 (1H, *d*, *J* = 1.6 Hz, *syn* H-10), 5.02 (1H, *d*, *J* = 1.6 Hz, *anti* H-10), 2.78 (1H, *t*, *J* = 6 Hz, H-1), 2.76–2.65 (2H, complex signal, H-4$\alpha$ and H-7$\alpha$), 2.53 (1H, *dd*, $J_1$ = 19.5 Hz, $J_2$ = 3.2 Hz, H-4$\beta$), 2.21 (1H, seven lines, H-5), 1.37 (3H, *s*, Me-8), 1.31 (1H, *d*, *J* = 10.5 Hz, H-7$\beta$), 0.82 (3H, *s*, Me-9) (identical with the spectrum of pinocarvone [9]); EIMS (70 eV, direct inlet) *m/z* (rel. int.): 150 $[M]^+$ (17), 135 (27), 108 (56), 107 (46), 91 (29), 81 (91), 79 (70), 69 (48), 53 (100), 41 (69). $C_{10}H_{14}O$: *M*, 150. Identical in all respects with *d*-pinocarvone [2, 8–10].

$NaBH_4$ *reduction of* 2*: compounds* 4 *and* 5. Compound 2 (600 mg) in MeOH–dioxane (1:1) soln (50 ml) was treated with an excess of $NaBH_4$ at room temp. for 10 min. The reaction was controlled by TLC showing two spots corresponding to compounds 3 and 4, both more polar than the starting material (2). After work-up in the usual manner, TLC revealed the presence of two compounds, one of which (5) was less polar than cedronellone (2), whereas the other one was the most polar compound detected in the reduction reaction (substance 4). This mixture was chromatographed (silica gel column, *n*-hexane–EtOAc 9:1 as eluent) to give compounds 4 (200 mg) and 5 (320 mg).

*Compound* 4. Thick oil; IR $\nu_{max}^{NaCl}$ $cm^{-1}$: 3450, 2920, 2840, 1685, 1470, 1370, 1230, 1160, 1065, 1030, 835; $^1H$ NMR (90 MHz, $CDCl_3$): $\delta$ 4.23 (1H, *dd*, $J_1$ = 10.2 Hz, $J_2$ = 6.9 Hz, H-3'), C-Me singlets at 1.20 (6H), 0.94 (3H) and 0.77 (3H); EIMS (70 eV, direct inlet) *m/z* (rel. int.): 302 $[M]^+$ (4), 287 (1), 284 (21), 153 (11), 151 (12), 149 (14), 107 (100), 91 (50), 69 (43), 41 (37). $C_{20}H_{30}O_2$: *M*, 302.

*Compound* 5. Mp 70–72° (MeOH); $[\alpha]_D^{19} - 10.4°$ ($CHCl_3$; *c* 0.383); IR $\nu_{max}^{KBr}$ $cm^{-1}$: 2980, 2920, 2865, 1450, 1390, 1365, 1065, 1040, 970, 900; $^1H$ NMR (300 MHz, $CDCl_3$): $\delta$ 4.00 (1H, *dd*, $J_1$ = 9.0 Hz, $J_2$ = 2.4 Hz, H-3'), C-Me singlets at 1.29 (3H), 1.21 (3H), 1.08 (3H) and 0.86 (3H); $^{13}C$ NMR (50.3 MHz, $CDCl_3$) (assignments based on ref. [7]) $\delta$ (carbon number): 44.25 *d* (1), 47.57 *d* (2), 105.92 *s* (3), 38.45 *t* (4), 39.49 *d* (5), 38.14 *s* (6), 33.14 *t* (7), 26.85 *q* (8), 21.80 *q* (9), 22.23 *t* (10), 50.85 *d* (1'), 81.66 *s* (2'), 75.38 *d* (3'), 36.67 *t* (4'), 40.82 *d* (5'), 37.82 *s* (6'), 30.97 *t* (7'), 27.57 *q* (8'), 23.76 *q* (9'), 25.84 *t* (10'); EIMS (70 eV, direct inlet) *m/z* (rel. int.): 302 $[M]^+$ (2), 287 (0.2), 242 (3), 199 (6), 173 (8), 160 (11), 133 (28), 108 (100), 93 (33), 91 (38), 79 (12), 69 (34), 55 (19), 41 (39). (Found: C, 79.31; H, 10.18. $C_{20}H_{30}O_2$ requires: C, 79.42, H, 10.00%.)

*Application of the Horeau's method to compound* 4. This was performed in the usual manner [3]. Compound 4 (0.114 mmol) and (±)-$\alpha$-phenylbutyric anhydride (0.498 mmol) in pyridine (2 ml) solution 16 hr at room temp.: $\alpha_1 = -0.540$, $\alpha_2 = -0.615$; $\alpha_1 - 1.1\alpha_2 = +0.136$. Configuration 3'*R*.

*Acknowledgements*—We thank Prof. J. do Amaral Franco, Instituto Superior de Agronomia, Lisbon, for the botanical classification of the plant material. This work was supported by the 'Comisión Asesora de Investigación Científica y Técnica', Madrid.

## REFERENCES

1. Bramwell, D. and Bramwell, Z. I. (1974) *Wild Flowers of the Canary Islands* p. 194. Stanley Thornes, London.

2. Glasby, J. S. (1982) *Encyclopaedia of the Terpenoids* Vol. 2. Wiley, New York.
3. Horeau, A. and Nouaille, A. (1971) *Tetrahedron Letters* 1939.
4. Colonge, J. and Descotes, G. (1967) *α,β-Unsaturated Carbonyl Compounds as Dienes*, in *Organic Chemistry, a series of Monographs* (Blomquist, A. T. ed.) Vol. 8, p. 217. Academic Press, New York.
5. Takemoto, T. and Nakajima, T. (1957) *J. Pharm. Soc. Jpn* 77, 1157.
6. Nakajima, T. (1962) *J. Pharm. Soc. Jpn* 82, 1278.
7. Coxon, J. M., Hydes, G. J. and Steel, P. J. (1984) *J. Chem. Soc. Perkin Trans.* II 1351.
8. Russell, G. F. and Olson, K. V. (1972) *J. Food Sci.* 37, 405.
9. Abraham, R. J., Cooper, M. A., Indyk, H., Sieverns, T. M. and Whittaker, D. (1973) *Org. Magn Reson.* 5, 373.
10. Jefford, C. W., Boschung, A. F., Moriarty, R. M., Rimbault, C. G. and Laffer, M. H. (1973) *Helv. Chim. Acta* 56, 2649.

*Phytochemistry*, Vol. 26, No. 12, pp. 3353–3354, 1987.
Printed in Great Britain.

0031–9422/87 $3.00 + 0.00
Pergamon Journals Ltd.

# ERANTHEMOSIDE, A NEW IRIDOID GLUCOSIDE FROM *ERANTHEMUM PULCHELLUM* (ACANTHACEAE)

HENRIK FISCHER W. JENSEN, SØREN ROSENDAL JENSEN and BENT JUHL NIELSEN

Department of Organic Chemistry, The Technical University of Denmark, Bygn. 201, DK-2800 Lyngby, Denmark

(*Received* 10 *March* 1987)

**Key Word Index**—*Eranthemum pulchellum*; Acanthaceae; iridoid glucoside; eranthemoside; betaine.

**Abstract**—A new iridoid glucoside, eranthemoside, has been isolated from *Eranthemum pulchellum* (Acanthaceae). The structure was established solely by spectroscopic means. The quaternary amino acid betaine was also isolated.

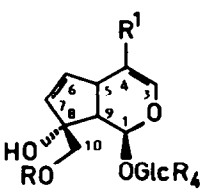
## INTRODUCTION

Iridoid glucosides are commonly encountered in the Scrophulariaceae and related families, their presence being considered as a valuable systematic character [1]. In the Acanthaceae, however, iridoids do not appear to be commonly occurring except in seeds [1]. Only a few reports of these compounds in whole plants have been published [1–4]. During a search for iridoid glucosides in a number of species within Acanthaceae we encountered a new iridoid glucoside in *Eranthemum pulchellum* Andrews ( = *E. nervosum*, (Vahl) R. Br.), the structure elucidation of which is reported here.

## RESULTS AND DISCUSSION

An $^1$H NMR spectrum of the crude aqueous extract of twigs of *E. pulchellum* showed several signals in the interval between 5 and 6 ppm indicating the presence of an iridoid glucoside. In addition a very intense signal could be seen at *ca* 3.2 ppm. Reversed phase chromatography of the extract gave two fractions. The most polar fraction contained the compound with the NMR signal at $\delta$3.2. Silica gel chromatography (see Experimental) provided betaine.

The second fraction contained a new iridoid glucoside **1** which we have named eranthemoside. The $^1$H NMR spectrum showed five signals in the interval $\delta$5–6.5 ppm with a pattern suggesting a monotropein-like structure, though without the carboxyl group at C-4. In a decoupling experiment irradiation at $\delta$3.3 (H-5, partially overlapping with the sugar protons) changed four of the low field signals, of which one pair then could be ascribed to H-3 and H-4 (6.20 and 5.13 ppm, respectively). The remaining signals, including a singlet at $\delta$3.68 (10-$CH_2OH$) suggested the structure **1**. The $^{13}$C NMR spectrum (see Table 1) contained 15 signals of which six could be ascribed to a $\beta$-glucopyranosyl moiety while the remaining signals were in accord with the structure **1**. Assuming the usual stereochemistry for iridoid glucosides at C-1, C-5 and C-9, the configuration at the remaining centre, C-8, could be determined by comparison with the spectra of galioside (**3**) and its 8-epimer, gardenoside. Thus the shift values arising from the cyclopentane carbon atoms (C-5–C-9) were almost coincident in the spectra of **1** and **3**, while




**1** R = R$^1$ = H

**2** R = Ac; R$^1$ = H

**3** R = H; R$^1$ = COOMe