COUMARINS AND FERULOL ESTERS FROM CACHRYS SICULA

MANUEL GRANDE, MARÍA T. AGUADO*, BALBINO MANCHEÑO* and FRANCISCO PIERA*

Departamento de Química Orgánica, Facultad de Química, 37008 Salamanca, Spain; *Departamento de Química Orgánica, Facultad de Ciencias, Apartado 99, 03080 Alicante, Spain

(Revised received 4 June 1985)

Key Word Index—Cachrys sicula; Umbelliferae; furocoumarins; (−)-sprengelianin; ferulol esters.

Abstract—(−)-Sprengelianin, (−)-prantschimgin and other minor coumarins were isolated from the roots and/or the umbels of Cachrys sicula. The roots also afforded the monoterpenic hydroxyaldehyde ferulol esterified to angelic, tiglic and senecioic acids. The (−)-enantiomer of sprengelianin (2′S) had not been reported previously. The coumarins saxalin and pabulenol and the aromatic aldehyde 2,3,4-trimethylbenzaldehyde were also identified but these substances are presumably artefacts.

INTRODUCTION

Cachrys sicula L. (= Hippomarathrum pterocaenum (DC) Boiss.) is a plant endemic to the South-western Mediterranean region [1] which causes skin irritation and blistering as some of us could verify after collecting the plant material. Coumarins are commonly abundant within the species of the tribe Smyrneae [2] and presumably these substances are responsible for the injurious action of the plant. Apart from the fungicide, antibiotic and other biological actions [3], some coumarins and psoralens in particular, can act as skin irritants for which contact of the coumarin with the humid (sweaty) skin and irradiation with UV light are essential. The contact photodermatitis produced has been attributed to the photocycloaddition between a molecule of furocoumarin and one or two pyrimidine bases of epidermal DNA [4].

In previous studies on the chemical constituents of C. sicula the isolation of N,N′-o-toluylethylenediamine [5], bergapten, isoimperatorin and isopimpinellin [6] has been reported.

RESULTS AND DISCUSSION

The benzene extract from the umbels of C. sicula (9% dry wt) was firstly chromatographed on a dry silica gel column and pure components were isolated after recrystallization or chromatography. The following coumarins were identified by spectroscopic means (1H NMR, IR, UV and EI mass spectrometry) and by comparison of their physical constants with those described in the literature: isoimperatorin (1) [7], imperatorin (2) [7], bergapten (3) [7], xanthotoxin (4) [8], isopimpinellin (5) [8], tert-O-methylheraclenol (6) [9], (−)-prantschimgin (10) [7], (−)-sprengelianin (11) and ulopteral (13) [10].

The benzene extracts from the roots (5% dry wt) afforded after chromatography, the furocoumarins imperatorin (2), saxalin (7) [9], pabulenol (8) [11], oxyypeucedanin (9) [7], (−)-prantschimgin (10) and (−)-sprengelianin (11).

Only the racemic sprengelianin was previously described [12]. Alkaline hydrolysis of the laevorotatory sprengelianin isolated from C. sicula gave (+)-marmesin (12) for which the absolute configuration was known [13] and consequently, we assigned the absolute 2′S configuration to the natural (−)-sprengelianin. The most abundant coumarins in both umbels and the roots are (−)-prantschimgin and (−)-sprengelianin.

Earlier fractions of the main chromatography of the root extract afforded an aromatic aldehyde which was identified as 2,3,4-trimethylbenzaldehyde (15) according to IR and 1H NMR data [14]. As the crude extract showed an aldehyde signal at 89.55 clearly different from that shown by 15 (δ10.25), it was concluded that a chemical
of 9 can be opened in the presence of HCl to give after substitution or elimination, 7 and 8, respectively. The chloroocoumarin saxalin, reported as a natural product from other sources, could be, in some cases, also an artefact.

Triacylglycerols were also isolated from both benzene extracts. After hydrolysis and esterification with diazomethane the fatty acid methyl esters were analysed by GC. Oleic acid (umbels, 71%; roots, 44%) was the most abundant component.

**EXPERIMENTAL**

*General.* Mps are uncorr. $^1$H NMR were measured at 60 MHz in CDCl$_3$ using TMS as int. standard. MS were measured on a quadrupole mass spectrometer, 70 eV, direct inlet probe. Analytical TLC separations were carried out using Merck silica gel-60 plates, 0.25 mm. Fluorescence, H$_2$SO$_4$-MeOH (1:3) or 5% EtOH-phosphomolybdic acid with heating for 5 min at 120°C were used for spot visualization. Fluorescence of coumarins was observed under 365 nm UV light. Prep. TLC separations were carried out on Merck silica gel 60F$_{254}$ plates, 20 x 20 cm, 0.75 mm, UV-visualization and EtOAc as extraction solvent. CC was performed on Merck silica gel-60, 0.063-0.2 mm.

Plant material was collected in July near Torrevieja, Alicante; and identified by Dr. A. Escarré, Department of Biology, University of Alicante.

*Extraction and isolation.* (a) Aerial parts. Air-dried and powdered immature umbels, collected after flowering (1710 g) were extracted with CH$_2$Cl$_2$ (Soxhlet). The extract was concd in vacuo giving 164 g, (9.4%) of dried plant. Crude extract (7.98 g) was chromatographed on a dry silica gel column (120 cm, 259 g) using C$_6$H$_6$-EtOAc (7: 3) as eluent. The column was cut into 20 fractions. Fractions 6-7 of this chromatography (1.54 g) crystallized from Et$_2$O to give pure 1 (420 mg). The mother liquor was concd to dryness (1.12 g) and subjected to CC on silica gel (20 g) using C$_6$H$_6$-EtOAc (7: 3) as eluent to give triacylglycerols (0.73 g) which were saponified and esterified with CH$_3$N$_2$. The Me esters were analysed by GC (20% DEGS-chromosorb W AW-DMS 80-100, 2 m x 2 mm; 190°C) The main components were identified as the Me esters of oleic (71%), linoleic (23%) palmitic (6.5%) and myristic acids (0.1%). Fractions 8-10 (0.45 g) afforded after crystallization from EtOAc-MeOH pure 2 (162 mg). Recrystallizations of fraction 11 (0.76 g) from hexane-EtOAc gave pure 3 (70 mg), and fractions 12-14 (2.66 g) from C$_6$H$_6$-EtOAc gave pure 4 (150 mg). The mother liquor of this last fraction was concd to dryness and recrystallized from hexane-EtOAc allowing the isolation of pure 5 (7 mg). Fractions 15-18 (1.03 g) consisted mainly of a 1:1 mixture of 10 and 11, identified in the extract from the roots. Fractions 19-20 of the main chromatography (0.74 g) after washing with 4% NaOH, left a residue (0.27 g) which was fractionated by silica gel CC (10 g) using mixtures of C$_6$H$_6$-EtOAc as eluent. Prep. TLC allowed the isolation of 6 (7 mg) and 13 (6 mg).

(b) Roots. Air-dried and cut roots (320 g) were extracted with C$_6$H$_6$ at room temp. The extract was concd in vacuo giving 15 g (4.7%). The crude extract, crystallized from C$_6$H$_6$, gave 4 g of a mixture containing mainly 10 and 11 in a 11:9 ratio as deduced from $^1$H NMR. The mother liquor concd to dryness (11 g) was chromatographed on a dry silica gel column (96 cm, 120 g) using CH$_2$Cl$_2$ as eluent (300 ml). The column was cut into 17 fractions. Fraction 3 (0.269 g) of the main chromatography was washed with 5% NaHCO$_3$, and the neutral part (0.153 g) subjected to CC on silica gel (20 g) using mixtures of hexane-EtOAc as eluent to give 15 (78 mg). Fractions 4-5 (1.113 g) crystallized from Et$_2$O gave 2 (400 mg). The mother liquor concd to dryness (0.39 g) was
Constituents of Cachrys  

507

and Dr. J. M. Hernández, Universidad de Salamanca (Spain), for

MS measurements and Dr. A. Escarré, University of Alicante, for

identification of plant material.

REFERENCES


2. González, A. G., Cardona, R. J., López, M., Medina, J. M. and
70, 109.


4. Dall'Acqua, T., Vedaldi, D., Guiotto, A., Rodighiero, P.,
Chem. 24, 406.


and Rodríguez, F. (1977) An. Quim. 73, 1188.


Chim. Fr. 208.

Letters 5463.


17. Kubeck, K. H. and Ullmann, I. (1973) Phytochemistry 20,
828.

1453.


25, 344.

25, 995.


1769.

Ber. 106, 1047.


chromatographed on silica gel (20 g) with hexane–EtOAc mix-
tures as eluent. Prep. TLC of fractions 4–5 of the chromatogra-
phy (0.124 g), eluted with C4H10–EtOAc (6:4) as eluent (20 ml/mill) yielded 20 fractions. Prep. TLC of fraction 7 (57 mg), C4H10–EtOAc as eluent, gave 7 (50 mg). Prep. TLC of fraction 6 (77 mg) from LCC,

hexane–EtOAc (3:7) as eluent, gave 8 (70 mg). The acidic fraction

of 12 and 13 was esterified with CH2N2 and analyzed by GC as

above. The most abundant Me esters were those of okic (44%),

and Dr. J. M. Hernández, Universidad de Salamanca (Spain), for

identification of plant material.

REFERENCES


2. González, A. G., Cardona, R. J., López, M., Medina, J. M. and
70, 109.


4. Dall’Acqua, T., Vedaldi, D., Guiotto, A., Rodighiero, P.,
Chem. 24, 406.


and Rodríguez, F. (1977) An. Quim. 73, 1188.


Chim. Fr. 208.

Letters 5463.


17. Kubeck, K. H. and Ullmann, I. (1973) Phytochemistry 20,
828.

1453.


25, 344.

25, 995.


1769.

Ber. 108, 2822.