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CULARINE ALKALOIDS FROM *CERATOCAPNOS HETEROCARPA*

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Key Word Index—*Ceratocapnos heterocarpa*; Fumariaceae; cularine alkaloids; norsarcocapnine; cularidine; oxocompostelline; oxosarcocapnine.

Abstract—The new cularine alkaloid (+)-norsarcocapnine has been isolated from *Ceratocapnos heterocarpa*, together with (+)-cularidine, oxocompostelline and oxosarcocapnine.

INTRODUCTION

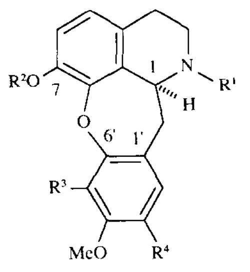
In an earlier paper [1] we reported the presence of (−)-caseamine, an unusual 1,2-substituted protoberberine alkaloid, from *Ceratocapnos heterocarpa* Durieu (Fumariaceae). Further investigation of this plant resulted in the isolation of four cularine alkaloids, the novel (+)-norsarcocapnine (**1**), (+)-cularidine (**2**), oxocompostelline (**3**) and oxosarcocapnine (**4**). This is the first report on the co-occurrence of cularines and 1,2-substituted protoberberine alkaloids in a plant, giving some support for their suggested biosynthetic relationship [2].

RESULTS AND DISCUSSION

The methanolic extract of *C. heterocarpa* was subjected to acid/base treatment to afford the alkaloid fraction, that was chromatographed over silica gel to give compounds **1**–**4**. Compound **1** was obtained as pale yellowish crystals and analysed for $C_{19}H_{21}NO_4$. The ^{1}H NMR spectrum showed the presence of one proton as a doublet of doublets at δ4.42 ($J = 11.4$ and 3.9 Hz), three methoxy groups at δ3.96, 3.83 and 3.78, four aromatic protons and the absence of a methyl group on the nitrogen, and indicated a *nor*-cularine skeleton. As expected, five aromatic carbon atoms bonded to oxygen were observed in the ^{13}C NMR spectrum of **1**. Substituents were located at positions 7,4′ and 5′ as deduced from the two AB spin systems, δ6.8 and 6.73 ($J = 8.4$ Hz) and δ6.74 and 6.55 ($J = 8.6$ Hz) observed for the aromatic protons. The coincidence of the base peak and the molecular ion in the mass spectrum was also in agreement with the absence of a methoxy group at position-3′. The 2D-COSY spectrum showed the coupling between the doublet at δ6.8 (H-5) and the benzylic protons at C-4 (δ2.67), as well as the *ortho*-relationship between the doublet at δ6.73 (H-6) and the methoxy group at C-7. In an analogous way were assigned the doublets at δ6.74 and 6.55 as H-2′ and H-3′ respectively as well as the methoxyl at C-4′ (δ3.78). Its positive optical rotation indicates the *S* configuration at C-1, as occurs with all cularines known so far [3]. From these data, we conclude that **1** is (+)-norsarcocapnine. Synthetic (±)-norsarcocapnine has been partially described as the reduction product of oxosarcocapnine (**4**) [4], or more recently as an intermediate in the total synthesis of (±)-norsarcocapnidine [5].

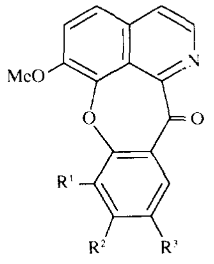
The major cularine component was the phenolic base (+)-cularidine (**2**) previously described in *Dicentra cucullaria* [6], *Corydalis claviculata* [7] and *Sarcocapnos crassifolia* [5]. Its structure was confirmed by comparison with an authentic sample. Complementary spectroscopic data for (+)-cularidine (**2**) is given in the Experimental.

The yellow band eluted from the column was a mixture of the oxocularines, which were separated and readily



1 $R^1 = H$ $R^2 = Me$ $R^3 = OMe$ $R^4 = H$

2 $R^1 = Me$ $R^2 = H$ $R^3 = H$ $R^4 = OMe$



3 $R^1 = H$ $R^2 + R^3 = O{-}CH_2{-}O$

4 $R^1 = OMe$ $R^2 = OMe$ $R^3 = H$

identified from its UV, MS and NMR spectra as oxocompostelline (**3**) and oxosarcocapnine (**4**).

EXPERIMENTAL

General. Mps: uncorr. Optical rotations were recorded at 18–20° using a 1 dm cell. ^{1}H and ^{13}C NMR spectra were obtained at 200 and 50.3 MHz, respectively. EIMS spectra, direct inlet, 70 eV. TLC were performed on silica gel 60 F 254 plates. CC was carried on silica gel 60 (70–230 mesh).

Plant material. The plant material used in this work was collected in April and May 1986 in Moron de la Frontera (Sevilla, Spain), and was identified by Prof. Baltasar Cabezudo, Department of Vegetal Biology, University of Málaga, Spain. A voucher specimen is on deposit in its Herbarium.

Isolation of cularine alkaloids. The air-dried and powdered plant (3.0 kg) was extracted with hot MeOH. Acid–base fractionation of the extract gave a crude alkaloid fraction (33.7 g), that was dissolved in $CHCl_3$–MeOH, and the $CHCl_3$–MeOH soluble part (27.2 g) was separated by silica gel CC with the solvent systems: CH_2Cl_2, CH_2Cl_2–EtOAc, EtOAc, EtOAc–MeOH and MeOH. Further purification by prep. TLC and crystallization afforded the cularine alkaloids which were by order of increasing polarity on TLC: oxosarcocapnine (**4**) (5 mg), oxocompostelline (**3**) (3 mg), (+)-cularidine (**2**) (800 mg) and (+)-norsarcocapnine (**1**) (290 mg), giving the following physical and spectroscopic properties:

(+)-*Norsarcocapnine* (**1**). Pale yellowish crystals. Mp 110°; $[\alpha]_D + 165°$ (MeOH; *c* 0.06); UV λ_{max} nm (log ε) in MeOH: 206 (4.68), 228 sh (4.26), 280 (3.61); IR ν_{max} cm^{-1}: 3450; ^{1}H NMR ($CDCl_3$): δ6.80 (1H, *d*, $J = 8.4$ Hz, H-5), 6.74 (1H, *d*, $J = 8.6$ Hz, H-2′), 6.73 (1H, *d*, $J = 8.4$ Hz, H-6), 6.55 (1H, *d*, $J = 8.6$ Hz, H-3′), 4.42 (1H, *dd*, $J = 11.4$ and 3.9 Hz, H-1), 3.96 (3H, *s*, OMe on C-5′), 3.83 (3H, *s*, OMe on C-7), 3.78 (3H, *s*, OMe on C-4′), 3.25 (1H, *dd*, $J = 11.4$ and 14.9 Hz, H-$\alpha\beta$), 3.10 (2H, *m*, H-3), 3.05 (1H, *dd*, $J = 3.9$ and 14.9 Hz, H-$\alpha\alpha$), 2.67 (2H, *t*, $J = 6.1$ Hz, H-4); ^{13}C NMR ($CDCl_3$): δ152.18 (C-7), 149.80, 149.58 (C-6′, C-4′), 144.35 (C-8), 141.09 (C-5′), 132.25 (C-8a), 127.75 (C-4a), 124.42 (C-5, C-2′), 122.48 (C-1′), 111.43 (C-6), (107.96 (C-3′), 61.30 (OMe on C-5′), 56.35, 56.24 (2 OMe), 51.02 (C-1), 40.46 (C-3), 38.06 (C-α), 28.23 (C-4). EIMS *m/z* (rel. int.): 327 $[M]^+$ (found: 327.1468; $C_{19}H_{21}NO_4$ requires: 327.14705) (100), 312 (51.6), 294 (49), 162 (68).

(+)-*Cularidine* (**2**). Colourless crystals. Mp 148° (MeOH), (lit. [8] mp 156°); $[\alpha]_D + 275°$ (MeOH; *c* 0.5), (ref. [8] $[\alpha]_D + 292°$ ($CHCl_3$; *c* 0.99)); MS and ^{1}H NMR spectra were identical with ref. [9]. ^{1}H NMR ($CDCl_3$): δ6.79 (2H, *s*, H-5, H-6), 6.68 (1H, *s*, H-5′), 6.52 (1H, *s*, H-2′), 4.22 (1H, *dd*, $J = 3.7$ and 11.4 Hz, H-1), 3.85 (3H, *s*, OMe on C-4′), 3.80 (3H, *s*, OMe on C-3′), 3.18 (1H, *dd*, $J = 3.7$ and 15.8 Hz, H-$\alpha\alpha$), 3.02 (1H, *dd*, $J = 11.4$ and 15.8 Hz, H-$\alpha\beta$), 3.09–2.96 (4H, *m*, aliphatic CH_2), 2.54 (3H, *s*, NMe); ^{13}C NMR ($CDCl_3$): δ148.14, 148.03 (C-6′, C-7′), 145.45, 145.30, 142.52 (C-3′, C-8, C-4′), 131.02 (C-8a), 125.94 (C-4a), 124.91 (C-5), 118.50 (C-1′), 114.36 (C-2′), 113.67 (C-6), 104.52 (C-5′), 57.74 (C-1), 56.39, 56.17 (2 × OMe), 48.45 (C-3), 42.11 (NMe), 36.29 (C-α), 26.11 (C-4).

Oxocompostelline (**3**). Yellow crystals. Mp 250° (EtOH), (lit. [10] mp 259°); spectroscopic data identical with ref. [10].

Oxosarcocapnine (**4**). Yellow crystals. Mp 194° (EtOH), (lit. [4] mp 202–203°); spectroscopic data identical with ref. [4].

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