NEW CURARINE-RELATED ALKALOIDS FROM SARCOCAPNOS BAETICA
SUBSP. INTEGRIFOLIA

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Abstract - We report the isolation of four new curarine-related alkaloids from Sarcocapnos baetica
(Boiss. & Reuter) Nyman subsp. integrifolia (Boiss.) Cuatrec. (+)-4-hydroxysarcocapnine (1), 3,4-
dioxosarcocapnine (2), (+)-sarcocapnine N-oxide (3) and (+)-N-methylcurarine (4).

In this paper, we describe the isolation, from aerial parts of Sarcocapnos baetica (Boiss. & Reuter) Nyman subsp. integrifolia (Boiss.) Cuatrec., of four new compounds belonging or biogenetically related to these groups: (+)-4-hydroxysarcocapnine (1), 3,4-dioxosarcocapnine (2), (+)-sarcocapnine N-oxide (3) and (+)-N-methylcurarine (4).

(+)-4-Hydroxysarcocapnine was isolated as an amorphous solid, [α]D +157.0° (c: 0.13, CHCl3). Its uv spectrum showed absorptions at λmax (EtOH)(log ε nm) 218sh (3.49), 235(3.65), 272sh (3.33) and 280 (3.34), and suffered bathochromic shift in basic media to λmax (EtOH/NaOH)(log ε nm) 218sh (3.57), 236 (3.59), 250sh (3.69) and 288(3.73). Its molecular formula, C19H21N05, was established by high resolution ms (calcld: 343.1413, found: 343.1412(100)); important fragments were observed at m/z(%) 328[M-15]++(40), 300[M-43]++(14), 190(24) and 174(25). The pmr (250 MHz, CDC3, δ)(Figure 1) exhibited the characteristic curarine ABX system of C1 and Cα protons at δ 4.36, 3.51 and 2.82 (J1-αδ= 4.2, J1-αβ = 11.6 and Jαα-αβ= 16.6 Hz); in addition, the presence of signals due to two methoxy groups, one N-methyl group and two pairs of ortho coupled aromatic protons clearly suggested a phenolic isocurarine structure. An aliphatic hydroxy group was located at C4 on the basis of the observation of a second ABX system at δ 4.60 (broad signal, 1H, H4), 3.03( dd, J4-3β = 4.2 and J3α-3β = 11.6 Hz, 1H, H3β) and 2.83(dd, J4.3β= 2.1 and J3α.3β=11.6 Hz, 1H, H3α). Structure 1 of (+)-4-hydroxysarcocapnine was definitively confirmed by an noe difference study (Figure 1). Syn stereochemistry for this alkaloid was established by simply comparing its H1 chemical shift (δ 4.36) with that of the parent curarine, (+)-sarcocapnine (δ 4.60).1

3,4-Dioxosarcocapnine (2) is a very minor component of S. baetica subsp. integrifolia. It was isolated as an orange, optically inactive, amorphous solid. Its uv spectrum, which showed bands at λmax(EtOH)(log ε nm) 240(3.18), 325(3.02) and 430(2.73) and suffered change upon addition of base to λmax (EtOH/NaOH)(log ε nm) 240(3.21), 335(3.00) and 450(2.65), is
characteristic of a highly conjugated phenolic system. Its pmr (CDCl₃, 250MHz, δ)(Figure 1) suggested a phenolic 3,4-
dioxisacapnidine structure, exhibiting signals due to five aromatic protons, two methoxy groups and one highly deshielded N-
methyl group; no more signals were observed in the aliphatic region of the spectrum. In addition to the molecular ion at
m/z(%): 353.0895 (calcd: 353.0894) (53), which established the molecular formula C₈₉H₁₂₅N₂O₁₆, the mass spectrum also
showed significant peaks at m/z (%): 325[M-28]⁺(42) and 310 [M-43]⁺(100) due to correlative losses of carbonyl and methyl
fragments. The structure of 3,4-dioxosacapnidine (2) was finally confirmed by a pmr nOe difference study (Figure 1).
In view of the evidence previously reported for the biogenetic transformation of 4-hydroxyaporphines into 4,5-
dioxaaporphines, 3,4-dioxocarulines can be considered as probably derived biogenetically from 4-hydroxycarulines by further
oxidation. The co-occurrence of 4-hydroxyisocarulines and their related 3,4-dioxocarulines in Sarcocapnos enneaphylla 1,2
and S. basica subsp. integrifolia supports this hypothesis.

(+)-Sarcocapnidine N-oxide (3) was isolated as a white, optically active [α]D +430° (c: 0.20, MeOH) amorphous powder. Its
phenolic nature was deduced from a bathochromic shift observed in its u.v. spectrum on addition of base: λ max(EtOH)(log ε)
217 sh(3.35), 240(3.65) and 281(3.60) nm, λ max(log ε)(EtOH/NaOH) 221 sh(3.40), 246(3.71), 283(3.69) and 294 sh(3.66)
nm. Its molecular formula, C₁₀₉H₁₂₂N₂O₁₆, was established by high resolution ms, which showed the molecular ion at m/z(%)
343.1411 (calcd: 343.1413). In addition, the mass spectrum showed characteristic fragments of an N-oxide at m/z(%)
327[M-16]⁺(16), 284[M-59]⁺(100) and 58(CH₂=NMMeOH)⁺ (58). The pmr (CDCl₃, 250MHz, δ)(Figure 1) was also very
significant, exhibiting signals due to four aromatic protons, which appear as two pairs of doublets, two methoxy groups and a
highly deshielded N-methyl group (δ 3.13). It also showed the characteristic ABX caruline system at downfield δ 4.64, 3.93
and 3.52 (J₁-αα=3.6, J₁-αβ=10.5 and Jαα-αβ=13.5 Hz). All the pmr assignments and the location of the phenolic group at
C₅' were confirmed by nOe (Figure 1) and decoupling experiments. Structure 3 of (+)-sacapnidine N-oxide was finally
confirmed by direct comparison (tlc and pmr) with a synthetic mixture of the two diastereomeric sacapnidine N-oxides. 7

From S. basica subsp. integrifolia, two amorphous solids were isolated which had a very similar pmr and ms but different Rf
values (in neutral Al₂O₃, 95%CH₂Cl₂-5%MeOH). Given that their spectral data suggested a quaternary caruline salt structure,
we considered the possibility of the different Rf values being due to two different anions. This was confirmed by the
transformation of both salts into the iodide when treated with KI. 8 The spectroscopic data given are those of the quaternary
caruline iodide, which was obtained as an optically active [α]D +200° (c: 0.42, MeOH), amorphous solid. Its u.v. spectra in
neutral, acidic and basic media were characteristic of a non-phenolic caruline-type compound, with λ max(EtOH)(log ε)nm
235(3.20) and 285(3.20). The molecular formula, C₂₁H₂₇N₂O₄, was established by high resolution ms, which showed a very
small molecular ion at m/z(%): 356.1851 (calcd: 356.1854)(1.3) and characteristic fragments at m/z(%): 355 [M-1]⁺(5.6),
341[M-15]⁺(34), 326 [M-30]⁺(100) and 58(CH₂=NMMe₂)⁺ (62). The pmr spectrum (250MHz, CDCl₃, δ)(Figure 1) showed
signals due to four aromatic protons, which appear as a pair of doublets and two singlets; a very highly deshielded ABX
caruline system, due to H₁ and H₂ζ protons, centred at δ 5.28, 3.80 and 3.47 (J₁-αα=3.5, J₁-αβ=12.6, and Jαα-αβ=15.1 Hz); three methoxy groups, and two highly deshielded N-methyl groups. These data suggested the structure of (+)-
caruline methiodide (4) for this compound, which proved to be identical (tlc, pmr, ms) to caruline methiodide obtained by N-
methylation (MeI, MeOH) of (+)-caruline. All assignments of its pmr spectrum data were based on nOe (Figure 1) and
decoupling experiments.
(+) Sarcosapnidine N-oxide (3) and (+)-cularine methiodide (4) have previously been described as synthetic compounds which have been used as intermediates in the partial synthesis of norsecosarcosapnidine (5) and secocularine (6) (Figure 2) respectively. Alkaloids 5 and 6 may therefore be derived biogenetically from 3 and 4, respectively, by means of "in vivo" degradation. It is noteworthy, however, that although we have isolated from Sarcoscapnos baetica subsp. integrifolia the first examples of a cularine N-oxide and a quaternary cularine salt, no secocularine or norsecocularine-type alkaloids have been isolated from the plant. This fact led us to consider that the latter compounds could not be formed during the extraction and manipulation of their respective proposed precursors.4,7

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