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ALKALOIDS FROM *SARCOCAPNOS ENNEAPHYLLA*

EMILIA TOJO, DOMINGO DOMINGUEZ and LUIS CASTEDO

Departamento de Química Orgánica de la Facultad de Química y Sección de Alcaloides del CSIC, Santiago de Compostela, Spain

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Key Word Index—*Sarcocapnos enneaphylla*; Fumariaceae; alkaloid content; isoquinoline alkaloids; cularines.

Abstract—Chemical investigation of *Sarcocapnos enneaphylla* resulted in the isolation of 35 alkaloids, 27 of which were identified as known isoquinoline alkaloids. The remainder were found to be a new aporphinoid, *N*-methylsecoglaucine, a new morphinandienone, (+)-*O*-methylpallidine *N*-oxide and six new cularines, (+)-enneaphylline, (+)-sarcophylline, (+)-4-hydroxysarcocapnine, aristoyagonine, secosarcocapnine and norsecosarcocapnine. Their structures were elucidated by spectroscopic and chemical methods.

INTRODUCTION

The genus *Sarcocapnos* (Fumariaceae) has been shown to be a rich source of isoquinoline alkaloids, most of them with a cularine skeleton [1]. In continuance of our chemical research on the alkaloids of Spanish Fumariaceae, an intensive study of *S. enneaphylla* was carried out. The plant is a caespitose, perennial herb typical of the Meridional Iberic System mountains [2]. Previous work from our laboratory of this plant [3] resulted in the isolation of the first natural cancentrine-type [4] cularines, (+)-sarcocapnine (**4**) [5], oxosarcocapnine (**7**) [5], oxosarcophylline (**8**) [6], oxosarcocapnidine (**9**) [7] and yagonine (**11**) [6], together with the new clasical cularines (+)-celtine (**2**) [8], (+)-celtisine (**3**) [8] and oxocompostelline (**6**) [9], the new example of a ribasine alkaloid, (+)-ribasidine (**17**) [10] and 11 known alkaloids, cularicine, cularidine [11], glaucine, *O*-methylatherolyne [12], dihydrosanguinarine, norsanguinarine, oxisanguinarine, sanguinarine, chelidonine, chelamine [13] and protopine [14]. A re-examination of the components of *S. enneaphylla* has now led us to the isolation of another six new cancentrine-type cularines, a new aporphinoid and a new morphinandienone.

RESULTS AND DISCUSSION

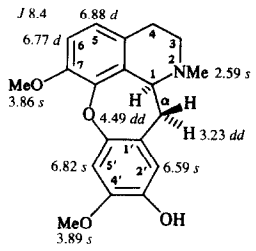
Extraction and separation of alkaloids were performed by the usual procedures as described in the Experimental. Thirty-five different isoquinolines were isolated, 27 of them being identified as the known alkaloids (+)-celtine (**2**) [8], (+)-celtisine (**3**) [8], (+)-sarcocapnine (**4**) [5], (+)-sarcocapnidine [7], (+)-cularine, (+)-cularicine, (+)-cularidine [11], oxocompostelline (**6**) [9], oxosarcocapnine (**7**) [5], (+)-oxosarcophylline (**8**) [6], oxosarcocapnidine (**9**) [7], yagonine (**11**) [6], secocularine [15], (+)-glaucine, (+)-isocoridine, *O*-methylatheroline, corunnine, pontevedrine, dehydroglaucine [12], (+)-chelidonine, (+)-chelamine, (+)-8-hydroxymethyldihydrosanguinarine [13], protopine [14], (−)-scoulerine [16], (+)-ribasine [17], (+)-ribasidine (**17**) [10] and (+)-*O*-methylpallidine [18, 19]. Their structures were established spectroscopically and by direct comparison with authentic samples.

The remaining eight compounds were identified as six new cularines, a new aporphinoid and a new morphinandienone. They were named as (+)-enneaphylline (**1**), (+)-sarcophylline (**5**), (+)-4-hydroxysarcocapnine (**10**), aristoyagonine (**12**), secosarcocapnine (**13**), norsecosarcocapnine (**14**), *N*-methylsecoglaucine (**15**) and (+)-*O*-methylpallidine *N*-oxide (**16**). Their structures were elucidated by spectroscopic analysis and confirmed by chemical transformations and partial or total synthesis.

(+)-Enneaphylline (**1**), $C_{19}H_{21}NO_4$, was obtained as prisms, mp 205–207° (EtOH). The bathochromic shift of its UV spectrum in basic media together with the broad IR signal at 3440 cm^{-1} revealed its phenolic nature. The ^1H NMR suggested a cularine-type structure. The mass spectrum with its base peak at *m/z* 327 $[M]^+$, showed the hydroxyl group to be located at C-3′ [1], which was also supported by NOEDS experiments (Experimental). Structure **1** for enneaphylline was finally confirmed by comparison with the synthetic product obtained from crassifoline by phenolic oxidative coupling [20, 21].

(+)-Sarcophylline (**5**), $C_{19}H_{21}NO_4$, was isolated as an amorphous powder. The bathochromic shift of its UV spectrum in basic media together with the broad IR signal at 3400 cm^{-1} revealed its phenolic nature. The isocularine skeleton was deduced from its ^1H NMR spectrum which exhibited two methoxyl singlets and two aromatic AB quartets; all assignments were supported by NOEDS experiments (Experimental). Confirmation of structure **5** for sarcophylline was obtained by its conversion into sarcocapnine (**4**) after methylation with diazomethane [20].

(+)-4-Hydroxysarcocapnine (**10**), $C_{20}H_{23}NO_5$, was shown to be the first known isocularine alkaloid bearing a hydroxyl group at C-4. The IR spectrum in CCl_4 exhibited a broad band at 3511 cm^{-1}, which did not change upon dilution and was therefore attributed to an intramolecularly hydrogen bonded hydroxyl. Its ^1H NMR was very significant, showing two doublets of doublets for H-1 (δ4.17, $J_{1\text{-}\alpha\alpha}=2.9$, $J_{1\text{-}\alpha\beta}=11.3$ Hz) and H-4 (δ4.58, $J_{4\text{-}3\alpha}=2.3$, $J_{4\text{-}3\beta}=3.9$ Hz). All assignments



$J_{1\text{-}\alpha\alpha}$3.7, $J_{1\text{-}\alpha\beta}$12.0, $J_{\alpha\alpha\text{-}\alpha\beta}$16.0

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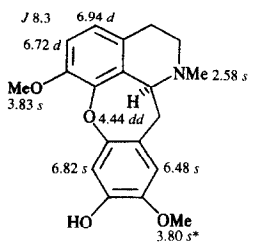

$J_{1\text{-}\alpha\alpha}$4.2, $J_{1\text{-}\alpha\beta}$11.3

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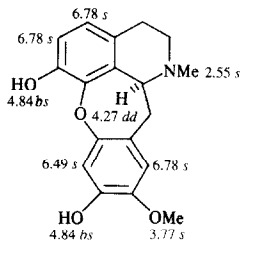

$J_{1\text{-}\alpha\alpha}$4.7, $J_{1\text{-}\alpha\beta}$10.4

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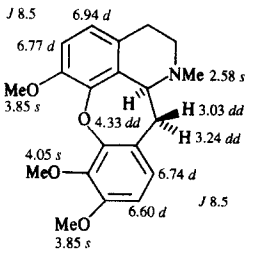

$J_{1\text{-}\alpha\alpha}$3.4, $J_{1\text{-}\alpha\beta}$11.8, $J_{\alpha\alpha\text{-}\alpha\beta}$16.0

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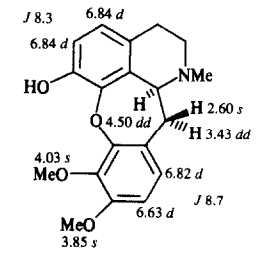

$J_{1\text{-}\alpha\alpha}$4.3, $J_{1\text{-}\alpha\beta}$12.0, $J_{\alpha\alpha\text{-}\alpha\beta}$16.2

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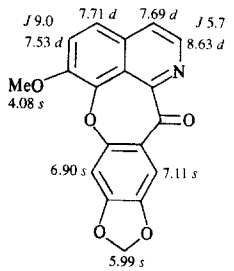

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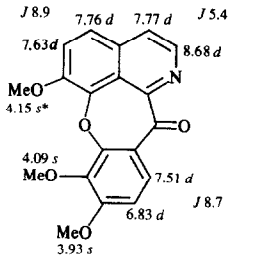

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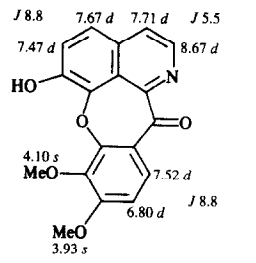

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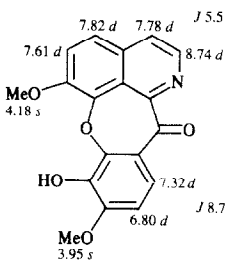

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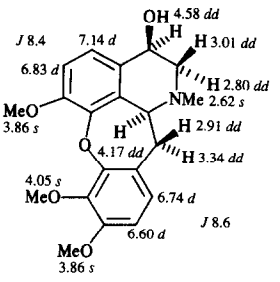
were based on decoupling and NOEDS experiments (Experimental). Configuration at C-4 was confirmed by total synthesis of both epimers by means of the oxidation of a suitable precursor at the benzylic position [22, 23].

Aristoyagonine (**12**), $C_{19}H_{17}NO_5$, was obtained as yellow needles. Its UV spectrum showed absorptions at 220, 230, 250, 296, 330 (sh) and 410 nm and the IR spectrum dispalyed bands at 1700 and 1680 cm^{-1}. ^1H NMR and NOEDS experiments suggested an aristo-isocularine-type structure. This assignment was also supported by the ^{13}C NMR and mass spectra (Experimental). Structure **12** for aristoyagonine was finally confirmed by comparison with synthetic material obtained from yagonine (**11**) [6, 23].

The secocularine nature of secosarcocapnine (**13**) and norsecosarcocapnine (**14**) was deduced on the bases of the ^1H NMR spectra. Characteristic signals in the aliphatic region suggested the presence of a $CH_2CH_2NMe_2$ side chain in compound **13** and CH_2CH_2NHMe in compound **14**. NOEDS experiments confirmed all assignments. This interpretation was supported by the presence of base peaks in the mass spectra at *m/z* 58 ($[CH_2=NMe_2]^+$) and 44 ($[CH_2=NHMe]^+$), respectively. The structure of secosarcocapnine (**13**) was confirmed by direct comparison with the synthetic product obtained by Hoffmann degradation of sarcocapnine methiodide [24]. Structure **14** for norsecosarcocapnine was confirmed by partial synthesis from the parent sarcocapnine (**4**) by means of Cope elimination of its *N*-oxide [25] and by transformation into secosarcocapnine (**13**) via *N*-methylation.

N-Methylsecoglaucine* (**15**), $C_{22}H_{27}NO_4$, was isolated as an amorphous powder. Its UV spectrum showed a highly conjugated system with maxima at 269, 285 (sh), 322, 349 and 367 nm. The ^1H NMR spectrum displayed five aromatic protons, three as singlets and two as an AB system. Characteristic signals in the aliphatic region suggested the presence of a $CH_2CH_2NMe_2$ side chain. This was supported by the base peak observed in the mass spectrum at *m/z* 58 ($[CH_2=NMe_2]^+$). Further proof for structure **15** came from direct comparison (TLC R_f, IR, ^1H NMR and mass spectrum with synthetic material obtained by Hoffmann degradation of glaucine meth-

*This alkaloid was simultaneously isolated in our Laboratories from *Platycapnos spicata*. Blanco, O., Castedo, L., Cid, M. M., Seijas, J. A. and Villaverde, M. C.



$J_{4\text{-}3\alpha}$2.3, $J_{4\text{-}3\beta}$3.9, $J_{3\alpha\text{-}3\beta}$11.6
$J_{1\text{-}\alpha\alpha}$2.9, $J_{1\text{-}\alpha\beta}$11.3, $J_{\alpha\alpha\text{-}\alpha\beta}$16.1

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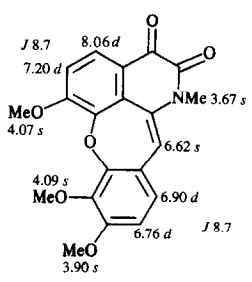

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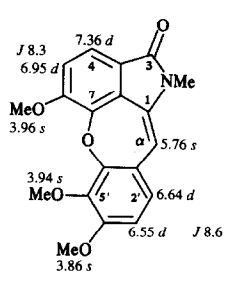

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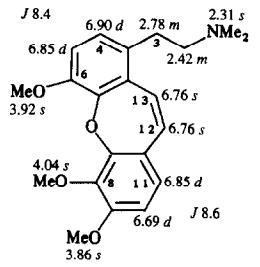

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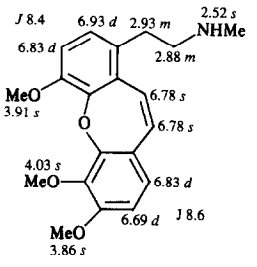

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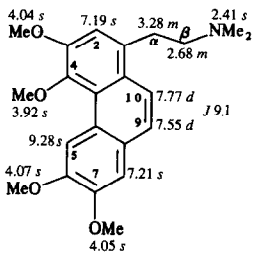

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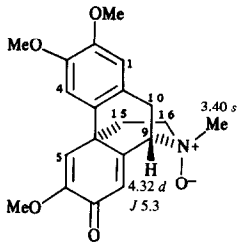

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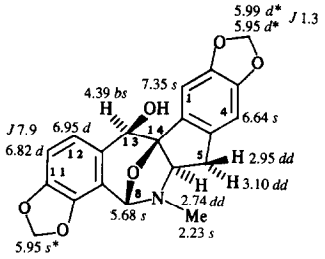

$J_{6,5\alpha}$8.0, $J_{6,5\beta}$3.1, $J_{5\alpha,5\beta}$16.0

17

*Chemical shifts with identical superscripts are interchangeable.

iodide [26]. ^{1}H NMR assignments, shown around **15**, were confirmed by NOEDS experiments (Experimental).

(+)-*O*-Methylpallidine *N*-oxide (**16**), $C_{20}H_{23}NO_5$, was obtained as an amorphous substance. Its UV spectrum (240, 286 nm) and IR spectrum (1670, 1640, 1620 cm^{-1}) were reminiscent of a morphinandienone [27]. The aromatic region of the ^{1}H NMR spectrum exhibited four one-proton singlets at δ6.87, 6.62, 6.52 and 6.38, as well as three singlets at δ3.91, 3.87 and 3.82 for three methoxyl groups, a pattern very close to that of *O*-methylpallidine. In addition, the H-9 doublet centred at δ4.32 (J = 5.3 Hz), and the downfield chemical shift of the *N*-methyl singlet (δ3.40) suggested the presence of an *N*-oxide functionality. This assumption was supported by the mass spectrum which showed the $[M]^+$ at *m/z* 357 and other significant peaks at *m/z* 341 $[M-16]^+$, 298 (40) and 284 (100). Further proof for structure **16** was obtained from ^{13}C NMR which was very close to that of *O*-methylpallidine [28], the only difference lying in the signals of groups bound to *N* (Me, C-9 and C-16) which appear on the *N*-oxide at *ca* 15 ppm lower field. Similar differences were observed for the ^{13}C NMR thebaine and its *N*-oxide [29]. Structure **16** for *O*-methylpallidine *N*-oxide was finally confirmed by comparison with synthetic material obtained by treatment of (+)-*O*-methylpallidine (**16**) with *m*-chloroperbenzoic acid [30].

EXPERIMENTAL

General. Mps: uncorr. MS were recorded at 70 eV, HRMS at the Midwest Center for Mass Spectrometry (University of Nebraska, U.S.A). Both ^{1}H NMR were recorded in $CDCl_3$ at 250 and 80 MHz with TMS as int. standard; all data are summarized on the corresponding structure. Coupling constants are in Hz. CC was carried out on Merck silica gel and Woelm N (grade IV) neutral alumina. TLC was performed on Merck GF-254 type 60 silica gel and neutral alumina plates with the following solvent systems: C_6H_6–EtOAc–Et_2NH (7:2:1), EtOAc–$CHCl_3$–EtOH (1:1:1), CH_2Cl_2–MeOH (49:1), (19:1) and (9:1), hexane–C_6H_6 (1:1), hexane–Et_2O (1:1), (2:1) and (3:1). Alkaloids were detected by UV and after spraying with Dragendorff's reagent or I_2 vapour.

Plant material. Sarcocapnos enneaphylla (L.) DC. was collected in June 1982 in Cuenca, Spain. A voucher specimen is deposited in the Herbarium of the Department of Botany, Faculty of Pharmacy, University of Santiago de Compostela, Spain.

Extraction of alkaloids. Ground, air-dried whole plant (10 kg) was exhaustively extracted with MeOH. The MeOH extract was concd to small vol. and kept cold to leave a resinous ppt. The extract was filtered and concd to a viscous residue that was dissolved in 5% HCl. The acid soln was washed with Et_2O, made alkaline by addition of 20% NaOH and extracted with CH_2Cl_2. The organic extract was dried (Na_2SO_4) and evapd to give 80 g of an oily residue (Ext. A) which was chromatographed over 2 kg of silica gel using a CH_2Cl_2–MeOH stepwise gradient to afford 38 frs. Each was purified by prep. TLC or fractionally crystallized to give 35 alkaloids, which were by order of increasing polarity on TLC: dehydroglaucine (0.230 g), yagonine (**11**) (0.100 g), aristoyagonine (**12**) (0.070 g), oxosarcocapnine (**7**) (0.310 g), oxosarcophylline (**8**) (0.250 g), (+)-chelidonine (3.00 g), (+)-ribasine (0.200 g), (+)-ribasidine (**17**) (0.050 g), (+)-sarcophylline (**5**) (0.030 g), (+)-sarcocapnine (**4**) (10.5 g), (+)-sarcocapnidine (0.070 g), (+)-cularine (0.150 g), (+)-4-hydroxysarcocapnine (**10**) (0.350 g), (+)-chelamine (0.500 g), (+)-glaucine (0.300 g), (+)-isocoridine (0.150 g), (+)-enneaphylline (**1**) (0.050 g), *O*-methylatheroline (0.215 g), corunnine (0.060 g), (+)-*O*-methylpallidine (0.125 g), pontevedrine (0.080 g), secosarcocapnine (**13**) (0.165 g), secocularine (0.030 g), *N*-methylsecoglaucine (0.045 g) (**15**), (+)-8-hydroxymethyldihydrosanguinarine (0.030 g), protopine (4.00 g), (−)-scoulerine (0.020 g), norsecosarcocapnine (**14**) (0.055 g) and (+)-*O*-methylpallidine *N*-oxide (**16**) (0.030 g). The alkaline aq. extracts remaining were extracted with CH_2Cl_2 at pH 7 after successive additions of HCl and NH_4Cl. The organic extracts were dried (Na_2SO_4) and evapd to give 21 g of an oily residue (Ext. B) which was chromatographed over neutral alumina using a C_6H_6–CH_2Cl_2–MeOH stepwise gradient to afford 23 frs. TLC showed the presence of some cularines previously isolated from the plant: cularidine, cularicine [11], celtine (**2**) [8], celtisine (**3**) [8], oxocompostelline (**6**) [9] and oxosarcocapnidine (**9**) [7]. All known alkaloids were identified by comparison of their physical and spectroscopic data with those of authentic samples previously isolated in our laboratories or with those reported in the literature.

(+)-*Enneaphylline* (**1**). Prisms, mp 205–207° (EtOH). $[\alpha]_D$ +256° (EtOH; *c* 0.8). UV λ_{max}^{EtOH} (log ε) nm: 226 (4.04), 284 (3.85); $\lambda_{max}^{EtOH-NaOH}$ (log ε) nm: 223 (4.33), 284 (3.66), 303 (3.71). IR ν_{max}^{KBr} cm^{-1}: 3440 (OH). EIMS *m/z* (rel. int.): 327 $[M]^+$ (100), 312 $[M-Me]^+$ (64), 174 (39). Molecular formula $C_{19}H_{21}NO_4$ $[M]^+$ (c: 327.1470; HRMS f: 327.1465). Significant ^1H NMR NOEDS are: MeOC-7 to H-6, 5%; H-2′ to H-αα, 4%; MeOC-4′ to H-5′, 6%.

(+)-*Celtine* (**2**). Mp 94–96° (EtOH). $[\alpha]_D$ +181° (MeOH; *c* 0.08). UV λ_{max}^{EtOH} (log ε) nm: 216 (4.11), 228 (3.95) (sh), 282 (3.58); $\lambda_{max}^{EtOH-NaOH}$ (log ε) nm: 216 (4.59), 298 (3.60). IR ν_{max}^{KBr} cm^{-1}: 3350, 1510, 1280. EIMS *m/z* (rel. int.): 327 $[M]^+$ (45), 312 (100), 284 (9), 253 (8), 174 (10). Molecular formula $C_{19}H_{21}NO_4$ $[M]^+$ (c: 327.1470; HRMS f: 327.1483).

(+)-*Celtisine* (**3**). Mp 158–160° (EtOH). $[\alpha]_D$ +212° (MeOH; *c* 0.025). UV λ_{max}^{MeOH} (log ε) nm: 225 (4.10), 283 (3.85); $\lambda_{max}^{EtOH-NaOH}$ (log ε) nm: 225 (4.50), 294 (3.91). IR ν_{max}^{KBr} cm^{-1}: 3400, 1510, 1305. EIMS *m/z* (rel. int.): 313 $[M]^+$ (54), 298 (100), 296 (12), 270 (9), 161 (5). Molecular formula $C_{18}H_{19}NO_4$ $[M]^+$ (c: 313.1314; HRMS f: 313.1328).

(+)-*Sarcocapnine* (**4**). Crystallized as its hydrochloride, mp 210–212° (EtOH–Et_2O). $[\alpha]_D$ +210° (EtOH; *c* 0.29). UV λ_{max}^{EtOH} (log ε) nm: 232 (4.12), 283 (3.14). EIMS *m/z* (rel. int.): 341 $[M]^+$ (100), 326 (58), 298 (21), 176 (85), 174 (60). Anal. calc. for $C_{20}H_{23}NO_4$: C, 63.58; H, 6.36; N: 3.71. Found; C, 63.67; H, 6.63; N, 3.52.

(+)-*Sarcophylline* (**5**). Amorphous powder. $[\alpha]_D$ +200° ($CHCl_3$: *c* 1.65). UV λ_{max}^{EtOH} (log ε) nm: 219 (4.01), 282 (3.86); $\lambda_{max}^{EtOH-NaOH}$ (log ε) nm: 222 (4.10), 285 (3.36), 293 (3.40). IR ν_{max}^{KBr} cm^{-1}: 3400 (OH). EIMS *m/z* (rel. int.): 327 $[M]^+$ (100), 312 (56), 294 (53), 162 (66). Molecular formula $C_{19}H_{21}NO_4$ $[M]^+$ (c: 327.1470; HRMS f: 327.1470). Significant ^1H NMR NOEDS are: H-3′ to MeOC-4′, 10%; MeOC-4′ to H-3′, 5%.

O-*Methylation of sarcophylline* (**5**). A MeOH soln of sarcophylline (**5**) was left overnight with excess CH_2N_2 in dry Et_2O. Air was then bubbled to eliminate excess reagent and solvent removed under red. pres. R_f values, ^1H NMR and MS of the resulting product were identical with those of natural sarcocapnine (**4**).

Oxocompostelline (**6**). $C_{18}H_{11}NO_5$, yellow crystals, mp 259–260° (EtOH). UV λ_{max}^{EtOH} (log ε) nm: 208 (4.67), 254 (4.41), 292 (sh), 397 (3.61); $\lambda_{max}^{EtOH-HCl}$ (log ε) nm: 208 (4.67), 261 (4.34), 4.10 (3.47), 4.60 (3.23). IR ν_{max}^{KBr} cm^{-1}: 1670. EIMS *m/z* (rel. int.): 321 $[M]^+$ (72), 306 (5), 293 (5), 278 (100).

Oxosarcocapnine (**7**). Yellow crystals, mp 200–201° (EtOH). UV λ_{max}^{EtOH} (log ε) nm: 254 (4.19), 330 (3.16), 400 (3.53); $\lambda_{max}^{EtOH-HCl}$ nm: 266, 398, 462. IR ν_{max}^{KBr} cm^{-1}: 3000. EIMS *m/z* (rel. int.): 337 $[M]^+$ (100), 309 (12), 306 (20), 294 (62), 279 (10), 251 (12), 236 (20), 208 (7), 189 (9). Anal. calc. for $C_{19}H_{15}NO_5$: C, 67.41; H, 4.30; N, 3.92. Found: C, 67.66; H, 4.45; N, 4.15.

Oxosarcophylline (**8**). Yellow needles, mp 170–171° (EtOH). UV λ_{max}^{EtOH} (log ε) nm: 218 (4.48), 252 (4.27), 330 (3.54), 396 (3.61); λ_{max}^{EtOH} (log ε) nm: 218 (4.48), 260 (4.24), 395 (3.53), 470 (3.25); $\lambda_{max}^{EtOH-NaOH}$ (log ε) nm: 218 (4.37), 280 (4.25), 310 (3.90) (sh), 510 (3.52). IR ν_{max}^{KBr} cm^{-1}: 1670, 3400, EIMS *m/z* (rel. int.): 323 $[M]^+$ (100), 306 (34), 295 (27), 292 (31), 280 (17), 272 (17), 237 (28), 209 (17), 181 (12), 153 (28). Molecular formula $C_{18}H_{13}NO_5$ $[M]^+$ (c: 323.0794; HRMS f: 323.0798).

Oxosarcocapnidine (**9**). Yellow crystals, mp 231–232° (MeOH). UV λ_{max}^{EtOH} (log ε) nm: 252 (4.26), 342 (3.34), 396 (3.59); $\lambda_{max}^{EtOH-NaOH}$ (log ε) nm: 243 (4.26), 340 (3.34), 400 (3.57); $\lambda_{max}^{EtOH-HCl}$ (log ε) nm: 217 (4.28), 265 (4.05), 458 (3.55). IR ν_{max}^{KBr} cm^{-1}: 3400, 1670. EIMS *m/z* (rel. int.): 323 $[M]^+$ (100), 308 (8), 306 (14), 295 (13), 280 (50), 265 (11), 237 (16), 209 (11). Molecular formula $C_{18}H_{13}NO_5$ $[M]^+$ (c: 323.0790; HRMS f: 323.0807).

(+)-4-*Hydroxysarcocapnine* (**10**). Prisms, mp 145–146° (EtOH). $[\alpha]_D$ +314° ($CHCl_3$; *c* 0.11). UV λ_{max}^{EtOH} (log ε) nm: 218 (4.26), 230 (4.09) (sh), 282 (3.46). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3511 (no change upon dilution). ^{13}C NMR (62.83 MHz, $CDCl_3$): δ151.99 (*s*), 151.05 (*s*), 148.47 (*s*), 143.37 (*s*), 140.40 (*s*), 133.42 (*s*), 128.79 (*s*), 125.06 (*d*), 124.90 (*d*), 120.69 (*s*), 111.12 (*d*), 107.20 (*d*), 66.17 (*d*), 61.07 (*q*), 58.60 (*d*), 57.40 (*t*), 56.05 (*q*), 55.96 (*q*), 43.12 (*q*, NMe), 37.40 (*t*, C-α). EIMS *m/z* (rel. int.): 357 $[M]^+$ (86), 342 (49), 324 (49), 314 (26), 192 (100), 190 (43). Anal. calc. for $C_{20}H_{23}NO_5$: C, 67.00; H, 6.40; N, 3.90. Found: C, 67.39; H, 6.51; N, 3.90. Significant ^1H NMR NOEDS are: H-1 to H-3α, 2%; H-1 to NMe, 6%; H-1 to H-αα, 3%; H-αα to H-1, 7%; H-αα to H-2′, 9%; H-αα to NMe, 6%; H-4 to H-3α, 4%, H-4 to H-3β, 3%; H-4 to H-5, 9%.

Yagonine (**11**). Red needles, mp 226–227° (EtOH). UV λ_{max}^{EtOH} nm: 217, 254, 340, 435. IR ν_{max}^{KBr} cm^{-1}: 1680, 1590. ^{13}C NMR (62.83 MHz, $CDCl_3$) δ: 175.24 (*s*, CO), 156.96 (*s*, CO), 156.76 (*s*), 155.33 (*s*), 149.30 (*s*), 141.98 (*s*), 141.33 (*s*), 133.48 (*s*), 130.03 (*s*), 122.29 (*s*), 121.82 (*s*), 126.83 (*d*), 124.26 (*d*), 118.59 (*d*), 113.94 (*d*), 108.95 (*d*), 61.61 (*q*), 56.47 (*q*), 56.22 (*q*), 32.92 (*q*, NMe). EIMS *m/z* (rel. int.): 367 $[M]^+$ (20), 366 (100), 338 (55), 323 (57), 308 (13), 280 (25). Molecular formula $C_{20}H_{17}NO_6$ $[M]^+$ (C: 367.1056; HRMS f: 367.1061).

Aristoyagonine (**12**). Yellow needles, mp 165–166° (MeOH). UV λ_{max}^{EtOH} nm: 220, 230, 250, 296, 330 (sh), 410. IR ν_{max}^{KBr} cm^{-1}:

1700, 1680. EIMS *m/z* (rel. int.): 339 $[M]^+$ (100), 324 (30), 309 (7), 296 (10), 281 (17), 253 (12), 238 (27). Molecular formula $C_{19}H_{17}NO_5$ $[M]^+$ (c: 339.1107; HRMS f: 339.1107). ^{13}C NMR (62.83 MHz, $CDCl_3$): δ166.13 (*s*, CO), 154.94 (*s*), 152.14 (*s*), 148.05 (*s*), 141.87 (*s*), 141.48 (*s*), 135.42 (*s*), 127.79 (*s*), 125.82 (*s*), 122.03 (*s*), 121.62 (*s*), 118.80 (*s*), 115.03 (*s*), 108.21 (*s*), 107.94 (*s*), 61.19 (*q*), 56.70 (*q*), 56.07 (*q*), 25.49 (*q*, NMe). Significant ^1H NMR NOEDS are: H-4 to H-5, 6%; H-5 to H-4, 4%; H-5 to MeOC-6, 5%; H-α to H-2', 8%; H-2' to H-α, 6%; H-α to NMe, 6%; NMe to H-α, 2%; H-3' to MeOC-4', 7%; MeOC-4' to H-3', 3%.

Secosarcocapnine (**13**). Crystallized as its hydrochloride, mp 186–188° (EtOH–Et_2O). UV λ_{max}^{EtOH} (log ε): 206 (4.1), 219 (3.9), 246 (3.7), 312 (3.7). IR ν_{max}^{KBr} cm^{-1}: 3000–2650, 1595, 1480, 1275, 1095. EIMS *m/z* (rel. int.): 355 $[M]^+$ (4), 298 (1), 165 (2), 152 (2), 139 (2), 58 (100). Molecular formula $C_{21}H_{25}NO_4$ $[M]^+$ (c: 355.1784; HRMS f: 355.1795). Significant ^1H NMR NOEDS are: H-3 to H-4, 5%; MeOC-6 to H-5, 5%; MeOC-9 to H-10, 6%; H-10 to MeOC-9, 11% H-12, 13 to H-11, 4%; H-12, 13 to H-3, 6%; H-12, 13 to H-2, 2%.

Preparation of secosarcocapnine (**13**). A mixt. of sarcocapnine (**4**) (0.100 g, 0.29 mmol), MeI (4 ml) and MeOH (5 ml) was stirred at room temp. for 36 hr. After removal of solvent, sarcocapnine methiodide was dissolved in EtOH (5 ml) and EtONa (500 mg Na in 10 ml EtOH) was added. The reaction mixt. was refluxed for 4 hr. Solvent was removed, the residue dil. with H_2O (20 ml) and extracted with CH_2Cl_2 (3 × 15 ml). Prep. TLC purification gave **13** in 70% yield, which was identical (R_f, ^1H NMR, MS) to the natural product.

Norsecosarcocapnine (**14**). Amorphous powder. UV λ_{max}^{EtOH} (log ε) nm: 222 (3.6), 244 (3.5), 310 (3.6). IR ν_{max}^{film} cm^{-1}: 3400, 3000–2800, 1600, 1480, 1275, 1090. EIMS *m/z* (rel. int.): 341 $[M]^+$ (5), 298 (22), 165 (2), 152 (2), 149 (3), 139 (2), 44 (100). Molecular formula $C_{20}H_{23}NO_4$ $[M]^+$ (c: 341.1627; HRMS f: 341.1626). Significant ^1H NMR NOEDS are: H-2 to H-12, 13, 2%; H-3 to H-12, 13, 5%; H-3 to H-4, 4%; MeOC-6 to H-5, 3%; MeOC-9 to H-10, 4%; H-10 to MeOC-9, 7%.

N-*Methylation of norsecosarcocapnine* (**14**). To a soln of **14** (0.010 g, 0.03 mmol) in MeOH (2 ml) was added 1 ml of HCHO (26%) and the mixt. heated to 45–50° for 30 min. After cooling, excess $NaBH_4$ was added and the reaction mixt. stirred at room temp. for 1.5 hr. Solvent was removed, the residue washed with H_2O (3 × 5 ml) and extracted with CH_2Cl_2 (3 × 10 ml). The dried extracts (Na_2SO_4) were concd and purified by prep. TLC, giving secosarcocapnine (**13**).

N-*Methylsecoglaucine* (**15**). Amorphous powder. UV λ_{max}^{MeOH} (log ε) nm: 269 (4.41), 2.85 (3.90) (sh), 322 (3.67), 349 (2.56) and 367 (2.54). IR ν_{max}^{KBr} cm^{-1}: 3000–2750, 1585, 1515, 1470, 1265, 1240, 1110. EIMS *m/z* (rel. int.): 369 $[M]^+$ (66), 311 (17), 279 (13), 149 (20), 58 $[CH_2{=}NMe_2]^+$ (100). Molecular formula $C_{22}H_{27}NO_4$ $[M]^+$ (c: 369.1940; HRMS f: 369.1942). Significant ^1H NMR NOEDS are: H-2 to MeOC-3, 10%; H-α to H-2, 5%; H-α to NMe, 3%; H-α to H-10, 9%; H-10 to H-α, 7%; H-β to NMe, 5%; H-β to H-10, 3%; MeOC-4 to H-5, 2%; MeOC-6 to H-5, 7%, H-8 to MeOC-7, 11%; H-8 to H-9, 13%.

(+)-O-*Methylpallidine* N-*oxide* (**16**). Amorphous compound. $[\alpha]_D$ +20° ($CHCl_3$; *c* 2.1). UV λ_{max} (log ε) nm: 240 (4.47), 2.86 (3.99). IR ν_{max}^{film} cm^{-1}: 1670, 1640, 1620. ^{13}C NMR (62.83 MHz, $CDCl_3$): δ179.9 (*s*, CO), 155.3, 152.0, 149.2, 149.1 (C-6, C-2, C-3, C-14), 130.4 (C-12), 126.9 (C-11), 123.8 (C-8), 116.7 (C-5), 116.5 (C-4), 109.1 (C-1), 76.1 (C-9), 60.1 (C-16), 57.7, 56.3, 56.0 (3 × OMe), 55.2 (NMe), 40.4, 36.7 (C-13, C-15), 35.6 (C-10). EIMS *m/z* (rel. int.): 357 $[M]^+$ (10), 341 $[M-16]^+$ (13), 298 (40), 284 (100). Molecular formula $C_{20}H_{23}NO_5$ $[M]^+$ (c: 357.1576; HRMS f: 357.1587).

(+)-*Ribasidine* (**17**). Needles, mp 230° ($CHCl_3$). $[\alpha]_D$ +120° (EtOH; *c* 0.04). UV λ_{max}^{EtOH} (log ε) nm: 211 (4.48), 235 (3.98) (sh), 291 (3.98); $\lambda_{max}^{EtOH-HCl}$ (log ε) nm: 242 (3.93). IR ν_{max}^{KBr} cm^{-1}: 3580, 3050–2860, 1485, 1255, 1030. ^{13}C NMR (20 MHz, $CDCl_3$–CD_3OD): δ149.69 (*s*), 147.17 (*s*), 146.86 (*s*), 143.89 (*s*) 137.77 (*s*), 132.02 (*s*) 129.48 (*s*), 123.60 (*d*), 113.75 (*s*), 108.86 (*d*), 107.48 (*d*), 105.25 (*d*), 101.63 (*t*), 101.44 (*t*), 95.98 (*s*), 89.24 (*d*) 71.64 (*d*), 66.88 (*d*), 36.04 (*t*), 35.04 (*q*, NMe). EIMS *m/z* (rel. int.): 367 $[M]^+$ (31), 366 (11), 204 (5), 192 (100), 188 (38), 176 (34), 163 (11), 149 (7), 146 (6). Molecular formula $C_{20}H_{17}NO_6$ $[M]^+$ (c: 367.1056; HRMS f: 367.1056).

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