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CANCENTRINE-TYPE CULARINE ALKALOIDS:SARCOCAPNINE AND OXOSARCOCAPNINE[1].

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Summary.The first two cancentrine-type cularines, namely sarcocapnine and oxosarcocapnine were isolated from Sarcocapnos enneaphylla (D.C.). Their structure has been proposed on chemical and spectroscopic data.

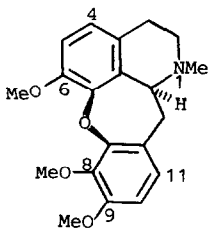
Cularine alkaloids which occur exclusively in Fumariaceae plants possess an isoquinoline skeleton[2]. They are assumed to arise through a direct oxidative coupling of a 7,8,3',4'-tetraoxygenated tetrahydrobenzylisoquinoline instead of emerging from the intermediacy of a procularine undergoing a dienone-phenol rearrengement[3]. The four members of this group which have been characterized so far all possess oxygenated functions at C_6, C_9 and C_{10}. Only the cularine moiety of the cularine- morphine dimers (cancentrine and derivatives) has got substituents at C_6, C_8 and C_9[2]. Recently as a consequence of the synthetic efforts towards the cularines it has been shown that this latter substitution pattern is provided by a biogenetic-type approach to the synthesis of cularines[4].

As a continuation to our work on the isoquinoline alkaloid group we should like to report our study on the alkaloid content of a Spanish Fumariaceae, namely Sarcocapnos enneaphylla(D.C.), which had been collected in the Guadalajara province. This led to the isolation of the first two natural cancentrine-type[5] cularines, namely sarcocapnine 1 and oxosarcocapnine 2. Together with these two new compounds we have also isolated the known isoquinolines:protopine, chelidonine, sanguinarine, dihydrosanguinarine, norsanguinarine, oxosanguinarine and glaucine.

Sarcocapnine 1 crystallized as hydrochloride from ethanol/ether, mp 213-15°, showing $[\alpha]_D^{25}$ = +218 (EtOH, c=0.3 g/l). Its UV spectrum in neutral, acidic and basic media was characteristic of a non-phenolic isoquinoline showing λ_{max}(EtOH)(log ε), 232(4.12) and 283(3.14) nm. Furthermore the IR spectrum of 1 did not exhibit any absorption band due to OH or carbonyl groups. The mass spectrum of 1 confirmed its molecular formula $C_{20}H_{23}O_4N$ obtained by elemental analysis, showing m/e (%) at, 341 (M^+, 100), 326(66), 298(40). Most significant of all, the pmr (80Mz,$CDCl_3$,δ) of 1 exhibited an NMe group at 2.54 (s, 3H), three CH_2 groups at 2.60-3.50 (m,6H), three methoxyls at 4.02 (s, 3H) and 3.82 (s, 6H), a methine proton centred at 4.30 as a pair of doublets (J=10.7 Hz, J'=3.7 Hz, H_{12a}) and four aromatic protons as two AB quartets at δ_A=6.76 and δ_B=6.56, J_{AB}=8.5 Hz and $\delta_{A'}$=6.85, $\delta_{B'}$=6.76 ppm, $J_{A'B'}$=8.6 Hz. All these data suggested a cularine skeleton having an "isocularine" pattern of substitution. A literatura search showed that (±)sarcocapnine 1 had been synthesized by Kametani et al.[4]. Its published data are in accordance with those of natural sarcocapnine 1[6]. The absolute stereochemistry of sarcocapnine 1 was established as that shown in Fig.I through the CD spectra of its hydrochloride which displayed identical Cotton effect to that of (+)cularine hydrochloride[7].

On the other hand, oxosarcocapnine 2 was obtained as yellow crystals from ethanol, mp 202-3°C, $[\alpha]_D^{25}$ =0. Its molecular formula, $C_{19}H_{15}O_5N$ was established by elemental analysis and confirmed by

mass spectrometry which showed m/e (%), 337 (M^+, 100), 294(60). Its UV spectrum exhibited λ_{max} (EtOH) (log ε) 254 (4.19), 330(3.16) and 400(3.53) nm, which on addition of acid suffered a



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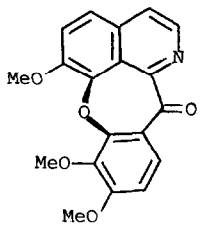

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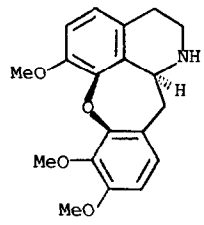

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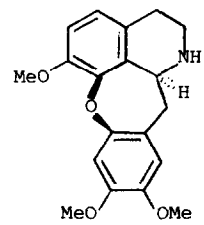

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Fig I

bathochromic shift, λ_{max} (EtOH + HCl), 266, 398 and 462 nm. The IR (KBr) of oxosarcocapnine 2 displayed a band at 1675 cm^{-1} (conjugated CO), while no signals were apparent at frequencies higher than 3000 cm^{-1}. The pmr ($CDCl_3$ + TFAA-d_1, δ) of 2 showed three methoxyls as singlets at 3.97, 4.03 and 4.23, while the aromatic zone exhibited an AB quartet at δ_A= 7.67, δ_B= 6.88, J_{AB}= 8.8Hz, a two hydrogen singlet at 8.09 and a second quartet at δ_A= 8.44, δ_B= 8.67 ppm, J_{AB}= 6.1 Hz. All these data are consistent with structure 2 for oxosarcocapnine. Further proof for this structure was obtained by Zn/HCl/AcOH reduction of 2 which yielded norsarcocapnine 3[8], a product well differentiated with the isomeric cularimine 4. N-methylation (1. HCHO/EtOH;2. $NaBH_4$) of 3 yielded 1 identified as (±)sarcocapnine. A short partial synthesis of oxosarcocapnine 2 was carried out by oxidation of 1 with Fremy's salt in pyridine-water[9] which produced 2 in 50% yield. Its identity with natural oxosarcocapnine was proved by direct comparison (IR, NMR, tlc).

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5. This nomenclature was first used by T.Kametani et al. (see reference 4).
6. Unfortunately, Prof.Kametani was unable to provide us with an authentic sample of (±)sarcocapnine.
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8. Spectral data of 3: UV (EtOH) λ_{max}229 (sh), 274, 283, 295;MS, m/e (%) 327 (M^+, 100), 312(32), 294 (20), 162(47), 86(34), 84(56);pmr($CDCl_3$, δ), 2.69-3.13(m, 6H, 3xCH_2), 3.81, 3.85, 3.98(3xOMe), 4.42 (dd, J= 4.4Hz and J'= 10.5Hz, 1H, H_{12a}),6.77(2H,s,H_4,H_5), 6.57 and 6.73ppm(2H,AB q,J=7.7,H_{10}, H_{11}).
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