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NEW OXIDIZED ISOCULARINE ALKALOIDS FROM SARCOCAPNOS PLANTS

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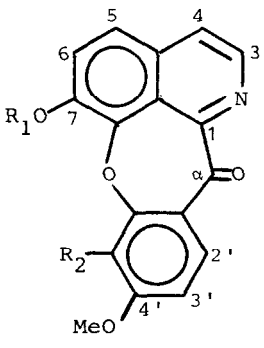
Abstract: Structures 1a , 3 and 6 were deduced for the new oxoisocularine alkaloids, oxosarcophylline, yagonine and aristoyagonine, respectively, on the basis of spectroscopic studies and synthesis.

The *Fumariaceae* plants are a rich source of cularine alkaloids[1]. Our current studies on the chemical components of plants of the genus *Sarcocapnos*, have led us to the isolation of three new cularines, namely oxosarcophylline 1a, yagonine 3 and aristoyagonine 6, the last two being the first dioxocularine and N-methylated aristocularine, respectively.

Oxosarcophylline 1a(from *S. Enneaphylla* (L.)DC and *S. Crassifolia* (L.)DC) was obtained as yellow needles, mp 170-171ºC(EtOH). Its UV spectrum was very similar to that of oxosarcocapnine 1b[2], showing absorptions at λ_{max}(EtOH) (log ε):218(4.48), 252(4.27), 330(3.54) and 396(3.61) nm, which on addition of acid suffered a bathochromic shift, λ_{max}(EtOH+HCl)(log ε):218(4.48), 260(4.24), 395(3.53) and 470(3.25) nm. Its phenolic nature was deduced from a strong bathochromic shift observed on addition of base, λ_{max}(EtOH+NaOH)(log ε):218 (4.37), 280(4.25), 310(sh, 3.90) and 510(3.52) nm. Its IR spectrum (KBr) displayed bands at 3400(OH) and 1670 cm^{-1}(conjugated carbonyl). The molecular formula $C_{18}H_{13}NO_5$ was established by high resolution MS, which showed the molecular ion at m/e(%):323.0798(100)(calculated:323.0794) and fragments were also observed at m/e 306(34), 295(27), 292(31) and 280(17). The isocularine skeleton was deduced from its PMR spectrum(250MHz,$CDCl_3$,δ),which exhibited two methoxyl singlets and three aromatic AB quartets.The substitution pattern of oxosarcophylline 1a was firmely established by O-methylation with diazomethane, which gave a product identical to authentic oxosarcocapnine 1b. The phenolic group was located at the C_7 position by comparison of the mass spectrum of oxosarcophylline (which exhibits a low peak at M^+-43) with those of the other oxocularines which possess a methoxy group at C_7[2,3]. This was confirmed by NOEDS[4] experiments as shown in Fig.I[9].

Yagonine 3(from *S.Enneaphylla*) was obtained as red needles,mp 226-227ºC (EtOH). Its UV spectrum showed a highly conjugated system, with absorptions at λ_{max}(EtOH):217,254,340 and 435 nm. Its IR spectrum (KBr) displayed a broad absorption band at 1680 cm^{-1}(C=O), and no signals were apparent at frequencies higher than 3000 cm^{-1}. Its ^{13}CNMR spectrum (62.83 MHz,$CDCl_3$,δ) showed the presence of two carbonyl groups, with signals at 175.24 and 156.96, nine



1a, R_1=H; R_2=OMe
1b, R_1=Me; R_2=OMe

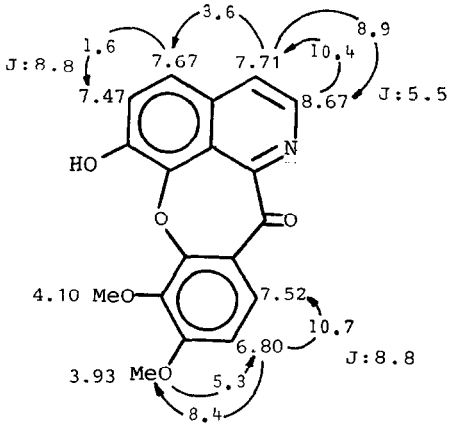


Fig.I(1a)

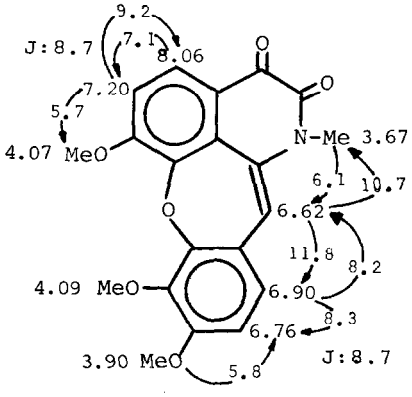


Fig.II(3)

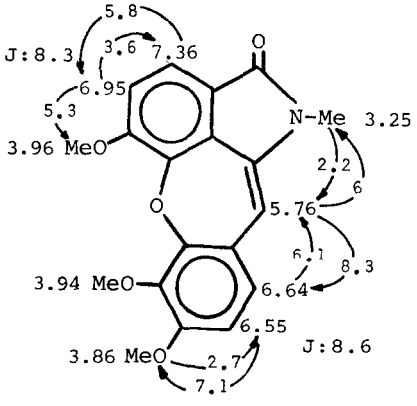
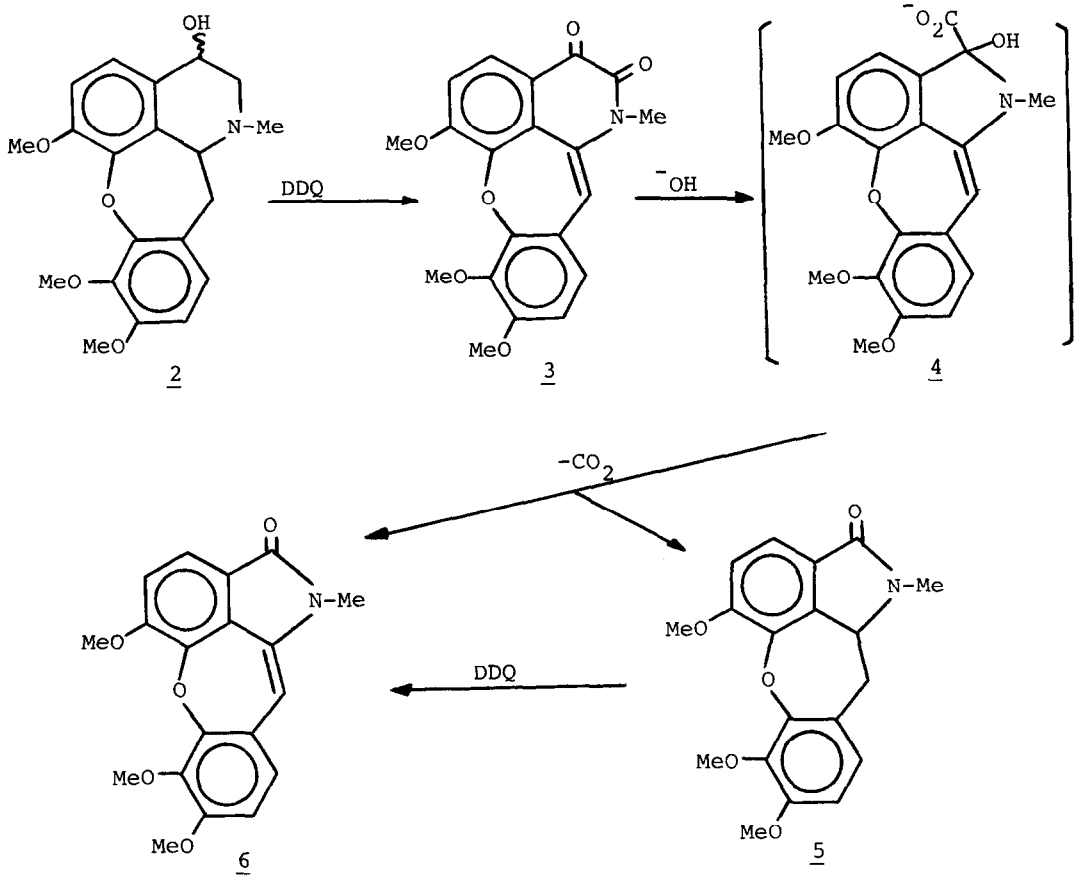


Fig.III(6)

quaternary sp^2 carbons (156.76, 155.33, 149.30, 141.98, 141.33, 133.48, 130.03, 122.29 and 121.82), five sp^2 carbons bound to hydrogen (126.83, 124.26, 118.59, 113.94 and 108.95), three methoxyl groups (61.61, 56.47 and 56.22) and one N-methyl group (32.92). The PMR spectrum, with NOEDS(Fig.II), was consistent with the 3,4-dioxocularine structure 3. Its molecular formula $C_{20}H_{17}NO_6$ was confirmed by a high resolution MS which exhibited the molecular ion at m/e(%):367.1061(20)(calculated 367.1056)and fragments were also observed at m/e 366(100), 338(55), 323(57), 308(13) and 280(25). Structure 3 for yagonine was finally confirmed by comparison with synthetic material, which has been obtained by a method previously reported for the preparation of dioxoaporphines[5]. Thus DDQ oxidation (deoxygenated benzene/80°C/2 hrs) of a mixture of the two 4-hydroxysarcocapnine epimers 2[6] afforded yagonine 3 in 41% yield after column chromatography.



2 3 4 5 6

Aristoyagonine 6, (from *S. tnneaphylla*), was obtained as yellow needles, mp 165-166ºC(MeOH). Its UV spectrum showed absorptions at λ_{max}(EtOH):220, 230, 250, 296, 330(sh) and 410 nm (no change upon addition of acid or base was observed). The IR spectrum (KBr) displayed bands at 1700 and 1680 cm^{-1}. Its molecular formula $C_{19}H_{17}NO_5$ was confirmed by a high resolution MS, which exhibited the molecular ion at m/e(%):339.1107(M^+,100)(calculated:339.1107) and fragments were also observed at m/e 324(30), 309(7), 296(10), 281(17), 253(12) and 238(27). Its PMR data (250 MHz,$CDCl_3$,δ) and NOEDS experiments (Fig.III) suggested the aristoisocularine-type structure 6. The ^{13}CNMR spectrum (62.83 MHz,$CDCl_3$,δ) confirmed the presence of a carbonyl group (166.13), fourteen sp^2 carbons (154.94, 152.14, 148.05, 141.87, 141.48, 135.42, 127.79, 125.82, 122.03, 121.62, 118.80, 115.03, 108.21 and 107.94), three methoxyl groups (61.19, 56.70 and 56.07) and one N-Me group (25.49). In order to confirm the structure of aristoyagonine 6, we have carried out its synthesis from yagonine 3, by means of a benzilic acid type rearrangment, which has previously been observed to occur easily in the dioxoaporphine alkaloids[5]. However, treatment of a methanolic suspension of yagonine 3 with a large excess of barium hydroxide for four hours at room temperature, gave only a very low yield (7%) of aristoyagonine 6, together with colorless

compound 5[7] (56%). 5 can be assumed to arise from the decarboxylation of the benzilic acid rearranged intermediate 4, which has been isolated in the alkaline treatment of analogous systems[8]. Contrary to what is known in the dioxoaporphines, the oxydized derivative 6 is in our case a minor product in this process. Another noteworthy difference is that no replacement of any methoxyl group was observed when the rearrangment of 3 was carried out with ethanolic sodium hydroxide at room temperature.

Compound 5 was oxidized with DDQ (refluxing benzene, 24 hrs), giving aristoyagonine 6 in quantitative yield, which was identical to the natural compound.

The dioxocularines and aristocularines are probably biogenetically derived from 4-hydroxycularines by further oxidation.

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REFERENCES AND NOTES

1.- For previous work see:
a) J.M.Boente, L.Castedo, D.Domínguez, A.Fariña, A.R. de Lera and M.C. Villaverde, Tet. Lett., 889 (1984).
b) J.M.Boente, L.Castedo, A.R. de Lera, J.M.Saá, R.Suau and M.C.Vidal, Tet. Lett., 1829 (1984).

2.- M.J.Campello, L.Castedo, J.M.Saá, R.Suau and M.C.Vidal,Tet.Lett.,239(1982).

3.- J.M.Boente, L.Castedo, A.R. de Lera, J.M.Saá, R.Suau and M.C.Vidal, Tet. Lett., 24, 2295 (1983).

4.- L.D.Hall and J.K.M.Sanders, J. Am. Chem. Soc., 102, 5703 (1980).

5.- L.Castedo, R.Suau and A.Mouriño, Tet. Lett., 501 (1976).

6.- L.Castedo, D.Domínguez, A.R. de Lera and E.Tojo, Tet. Lett., submitted for publication.

7.- 5 Crystallized from MeOH (mp 162-164ºC) and analysed for $C_{19}H_{19}NO_5$; UV λ_{max}(EtOH):222, 265 and 296(sh) nm; IR(KBr):1680 cm^{-1}; MS: m/e(%): 341(M^+,100), 326(28), 310(44), 189(28), 176(26) and 167(36); PMR(250 MHz, $CDCl_3$,δ):3.17(s,3H,-NMe). 3.89(s,3H,-OMe), 4.00(s,3H,-OMe), 4.03(s,3H, -OMe), 4.52, 3.39 and 2.86(ABX,H_1,$H_{\alpha\alpha}$ and $H_{\alpha\beta}$ respectively, $J_{1-\alpha\alpha}$=2.7, $J_{1-\alpha\beta}$=11.3, $J_{\alpha\alpha-\alpha\beta}$=13.6), 6.67 and 6.89(ABq, J=8.6,H_3, and H_2,) and 7.05 and 7.52(ABq, J=8.1,H_6 and H_5).

8.- P.A.S.Smith and R.O.Kan, J. Am. Chem. Soc., 83, 2580 (1961).

9.- Arrows in Figs. I-III have the following meaning:
irradiated proton——% enhancement——►observed proton.

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