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STRUCTURE AND STEREOCHEMISTRY OF CORYTENSINE, A NEW PHTHALIDEISOQUINOLINE ALKALOID FROM <u>CORYDALIS OCHOTENSIS</u>

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<u>Abstract</u>- A new phthalideisoquinoline alkaloid, corytensine, has been isolated from <u>Corydalis</u> <u>ochotensis</u> <u>Turcz</u>., and its structure and stereochemistry have been established as <u>(1)</u> from spectral data and a single crystal X-ray analysis.

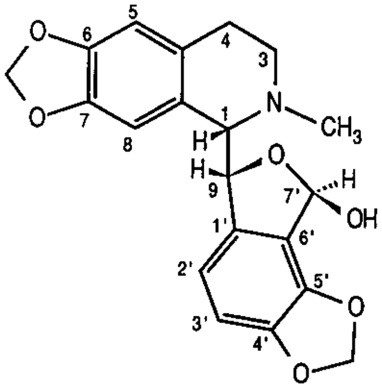
In previous paper[1], we reported the isolation and structural elucidation of several new alkaloids from <u>Corydalis ochotensis Turcz</u>. We now describe the structural elucidation of a further new phthalideisoquinoline alkaloid, corytensine, isolated from the whole herb of the same plant which was collected at Nan-Tou, Taiwan.

Corytensine (<u>1</u>) was isolated as colorless prisms[2], mp 215-215.5 °C (Me_2CO), $[\alpha]_D^{25}+168^o$ (c =0.5, $CHCl_3$). Elemental analysis established the molecular formula as $C_{20}H_{19}NO_6$. An absorption band at 239 nm (logϵ 3.91) and a characteristic tetrahydroisoquinoline band at 290 nm (end absorption) in the uv spectrum of <u>1</u> were very similar to those of (+)-egenine (<u>2</u>)[3](With undefined stereochemistry at C-7') and (-)-narcotinehemiacetal (<u>3</u>)[4]. The ir spectrum of <u>1</u> showed a hydroxy absorption at 3400 cm^{-1}. Salient features of its ^1H-nmr (400 MHz, $CDCl_3$) spectrum were the presence of an N-methyl singlet at δ 1.96 (3H), four mutually coupled resonance at δ 2.47 (1H,dt, J=15.5 and 3.0 Hz, H-4eq), 2.54 (1H, ddd, J=13.0, 10.5, and 3.0 Hz, H-3ax), 3.00 (1H, dt, J=10.5 and 3.0 Hz, H-3eq), and 3.20 (1H, ddd, J=15.5, 13.0, and 3.0 Hz, H-4ax). Two one-proton benzylic signals for H-1 and H-9 appeared as singlets at δ 3.68 and 5.29 thereby indicating a dihedral angle of <u>ca</u>. 90° between these atoms. Signals for two methylenedioxy groups occurred at δ 5.90 and 5.94 (each 1H, d, J=1.7 Hz), and 6.04 and 6.08 (each 1H, d, J=1.5 Hz). An AB quartet at δ 6.83 and 6.85 (J=8 Hz) was assigned to two ortho-related aromatic ring protons (H-2' and H-3'). Other one-proton singlets which appeared at δ 6.25, 6.60 and 6.71 were attributed to H-7', H-5, and H-8, respectively. A singlet at δ 6.25 in the ^{1}H-nmr spectrum and a carbon resonance at δ 97.7 in the ^{13}C-nmr spectrum indicated the presence of a hemiacetal system. The EI mass spectrum lacked a molecular ion peak but contained instead of several small peaks at m/z 370 $(M+1)^+$, 368 $(M-1)^+$, and 352 $(M-17)^+$; the base peak, which occurred at m/z 190, was due to the familiar benylic cleavage of phthalideisoquinolines. The foregoing spectral data led to the assignment of structure **1** to corytensine.

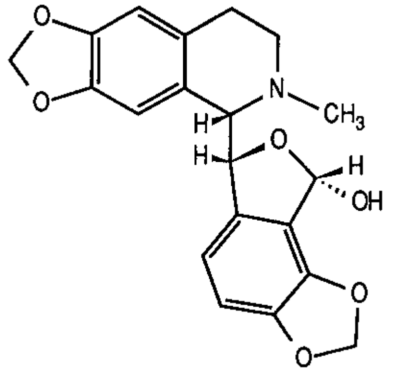
The complete structure and relative stereochemistry of corytensine were defined unequivocally by nOe studies (Table 1) and a single-crystal X-ray analysis. Crystal data: $C_{20}H_{19}NO_6$ **(1)**, M = 369.38, orthorhombic, space group $P2_12_12_1$, a = 12.936(2) Å, c = 7.649(1) Å, U = 1684.1 Å^3, $D_{calcd.}$ = 1.457 g cm^{-3}, μ (Cu-Kα radiation, = 1.5418 Å) = 8.6 cm^{-1}. One octant of intensity data (1737 reflections) was recorded from a crystal of dimensions ca. 0.40 x 0.40 x 0.60 mm mounted on an Enraf-Nonius CAD-4 diffractometer (Cu-Kα radiation, incident-beam graphite monochromator; ω-2θ scans, $\theta_{max.}$ =67°). The data were corrected for the usual Lorentz and polarization effects. The crystal structure was solved by direct methods.[5] Initial non-hydrogen atom positions were obtained from an

Table 1. ^{1}H-Nmr Chemical Shift (δ) and NOE Data for Corytensine (1)

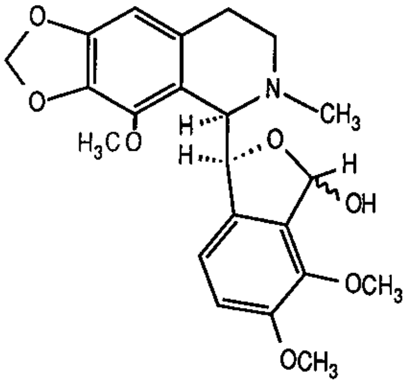
Proton irradiated	Proton observed	% Area increase
N-Me (1.96)	H-1 (3.68)	8.8
	H-3ax (2.54)	4.5
	H-3eq (3.00)	4.5
H-1 (3.68)	H-9 (5.29)	4.2
	H-8 (6.71)	5.8
	N-Me (1.96)	5.6
	H-2' (6.83)	2.8
H-9 (5.29)	H-1 (3.68)	3.4
	H-8 (6.71)	7.1
	H-2' (6.83)	2.9
H-7' (6.25)	no nOe	



1



2



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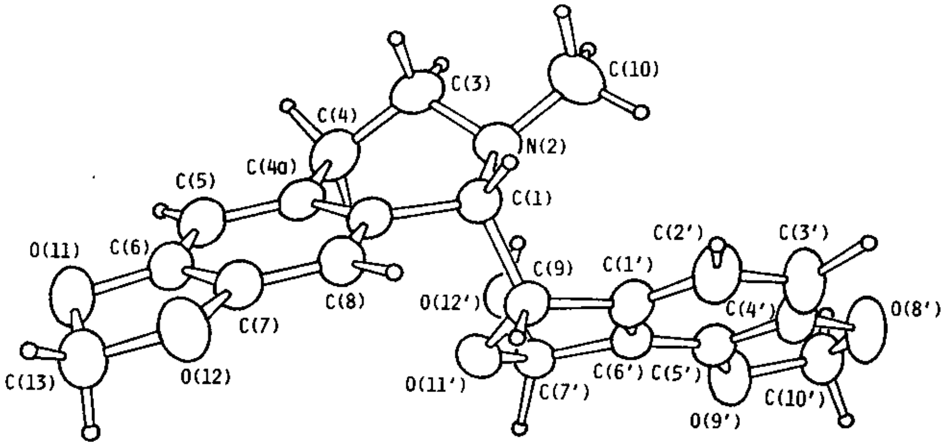

Figure 1. Structure and solid-state conformation of corytensine (1); small circles denote hydrogen atoms.

E-map. Hydrogen atoms were all located in a difference Fourier synthesis evaluated following several rounds of full-matrix least-squares adjustment of nonçhydrogen atom positional and anisotropic temperature factor parameters. With the inclusion of hydrogen atom positional and isotropic thermal parameters as variables in the final least-squares iterations, the refinement converged at $R = 0.035$, $R_w = 0.053$)[6] over 1684 reflections with $I > 3.0\sigma(I)$. A view of the solid-state conformation is presented in Figure 1.

Corytensine (1) is the C-7' epimer of (+)-egenine (2). Accordingly, the results of the present study now allow the complete relative stereochemistry of the latter to be defined as shown. Moreover, assuming that their absolute configuration at C-1 is S as in all classical phthalideisoquinolines exhibiting a positive specific rotation,[7] the absolute stereochemistries of both 1 and 2 must also be as represented.

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REFERENCES AND NOTES

1. Part VIII in the series "Studies on the Alkaloids of Formosan Corydalis Species". For part VII, see T.-S. Wu, S.-C. Huang, S.-T. Lu, and Y.-C. Wu, J. Chinese Chem. Soc., **34**, 157 (1987), and references cited therein.
2. The yield of 1 is 0.001% from the whole herb. ir$\nu^{KBr}_{max.}$ cm^{-1}: 3400, 1505, 1490, 1475; HRMS: Calcd for $C_{20}H_{19}NO_6$ 368.1132 $(M-1)^+$, Found, 368.1124; Calcd for $C_{20}H_{20}NO_6$ 370.1290 $(M+1)^+$, Found, 370.1308; Anal. Calcd for $C_{20}H_{19}NO_6$: C, 65.03; H, 5.19; N, 3.79. Found: C, 64.74; H, 5.17; N, 3.70; EIMS m/z: 370 $(M+1)^+$, 368, 352, 190(100%), 188, 178, 175, 162, 149, 132; CIMS m/z: 370$(M+1)^+$, 192, 190(100%), 179, 163; ^{13}C-nmr ($CDCl_3$, 25 MHz): δ 148.2(s), 146.3(s), 146.1(s), 141.6(s), 135.2 (s), 130.5(s), 128.6(s), 124.1(s), 113.8(s), 108.9(d), 108.1(d), 106.8(d), 101.8(t), 100.8(t), 97.7(d), 89.7(d), 68.5(d), 53.8(t), 46.7(q), 29.2(t); CD $\Delta\varepsilon$(nm)(MeOH): +0.254(302), +0.169(297), +0.505(283), +0.169(257), +3.56(231.5), +0(221), -5.17(213).
3. B. Gozler, T. Gozler, and M. Shamma, Tetrahedron, **39**, 577 (1983).
4. G. Sariyar and M. Shamma, Phytochemistry, **25**, 2403 (1986).
5. Crystallographic calculations *were performed on* PDP11/44 and MIcroVAX II computers by use of the Enraf-Nonius Structure Determination Package incorporating the direct methods program MULTAN11/82.
6. $R = \sum||F_0| - |F_c||/\sum|F_0|$; $R_w = [\sum w(|F_c| - |F_c|)^2/\sum w|F_0|^2]^{1/2}$
7. For a listing of spectral data for phthalideisoquinoline alkaloids, see G. Blaskó, D. J. Gula, and M. Shamma, J. Nat. Prod., **45**, 105 (1982).

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