New Papaveraceae Alkaloids Including an 7,8-Oxygenated Isoquinoline, the Postulated Precursor of the Cularine Alkaloids

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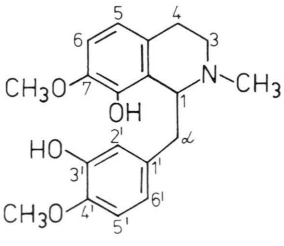
The first 7,8,3′,4′-oxygenated benzylisoquinoline, the probable precursor of the cularine alkaloids, has been isolated together with 2 new cularines and 10 other alkaloids from *Corydalis claviculata.*

Cularine alkaloids occur only in the Fumariaceae family [1]. The "classical" cularines are oxygenated at C_7, $C_{3'}$ and $C_{4'}$. Recently two cancentrine-type alkaloids with oxygen functions at C_7, $C_{4'}$ and $C_{5'}$ have been described [2]. The biogenesis of both types can be explained by direct oxydative coupling of the 7,8,3′,4′-substituted benzylisoquinoline (**1**) [3, 4], an isomer of reticuline.

In the course of biogenetic studies we isolated this base **1**, together with **2**, a cancentrine-type cularine, and O-methylcularicine (**3**) from *Corydalis claviculata* DC. (Fumariaceae). Additionally to these three new compounds, cularine, cularidine, cularicine, stylopine and protopine, already described by Manske [5], as well as (+)-reticuline, (−)-scoulerine, (−)-cheilanthifoline, (+)-thaliporphine and cularimine were isolated.

Base **1** was obtained as an oil (λ_{max} 280 nm), $[\alpha]_D = +37.6°$ ($c = 0.1$; EtOH). Addition of NaOH caused a bathochromic shift of the UV-spectrum, indicating the presence of phenolic hydroxyl groups; acetylation established two. The mass spectrum exhibited a benzylisoquinoline alkaloid. The base peak $m/e = 192$ (100%; $C_{11}H_{14}NO_2$, c.192.1024; f.192.1014) is due to the isoquinoline part with one hydroxyl and one methoxy group. The peak $m/e = 137$ (8%; $C_8H_9O_2$, c.137.0602; f.137.0601) represents the benzyl moiety substituted in the same manner. This corresponds to a molecular formula $C_{19}H_{23}NO_4$. The ^{1}H-NMR spectrum (300 MHz, $CDCl_3$) showed one NCH_3 ($\delta = 2.37$) and two OCH_3 functions ($\delta = 3.85$, 3.89). Six aliphatic protons appear as a multiplet ($\delta = 2.44-3.39$). The pair of doublets ($\delta = 4.12$; J = 3.7 Hz/9.1 Hz) is due to the proton at C_1. The signals at $\delta = 6.75$, 6.78 and 6.92 represent the ABX-spin system of the 3′,4′-oxygenated benzyl part. The AB system ($\delta = 6.61$ and 6.73; J = 8.3 Hz) reveals the 7,8-substitution pattern of the isoquinoline. The positions of the methoxy groups were determined by NOE experiments. Enhancement of the signals corresponding to H_6 ($\delta = 6.73$) and $H_{5'}$ ($\delta = 6.75$) assign positions 7 and 4′ to the OCH_3 functions, placing the hydroxyl groups in 8 and 3′. These data are in agreement with the spectra of synthetic racemate **1** [4, 6]. This is the first 7,8,3′,4′-oxygenated benzylisoquinoline isolated from a natural source.

Base **2** crystallized from methanol as colourless needles, mp. 118 °C, $[\alpha]_D = +268°$ ($c = 0.1$; EtOH), $C_{19}H_{21}NO_4$ (M^+, 100%; c.327.1470; f.327.1470). The structure was established by MS and NMR including NOE experiments as the cularine **2** and was confirmed by spectral comparison with synthetic racemate **2** [4]. This is the first cularine with the substitution pattern at C_7, $C_{4'}$ and $C_{5'}$ isolated from a Corydalis species.



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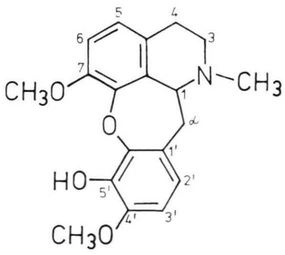

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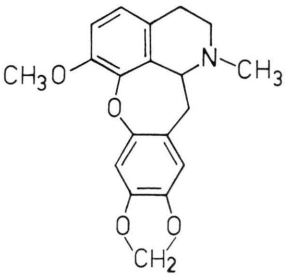

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O-methylcularicine (**3**), $[\alpha]_D = +283°$ ($c = 0.1$; EtOH), was analyzed for $C_{19}H_{19}NO_4$ (M^+, 100%; c.325.1314; f.325.1320). The structure **3** proposed by the spectral data was confirmed by direct comparison with **3** prepared by methylation of cularicine with diazomethane.

Acknowledgement

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Note added in proof (July 12th, 1983): The alkaloids **1** and **2** had also been recently isolated from *Sarcocapnos crassifolia:* J. M. Boente *et al.*, Tetrahedron Lett. **24,** 2303 (1983).