

## 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*.

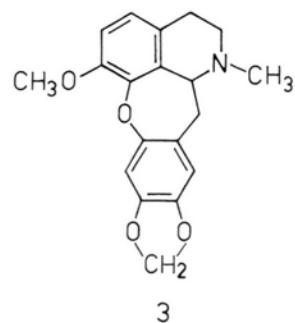
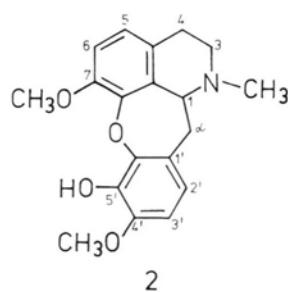
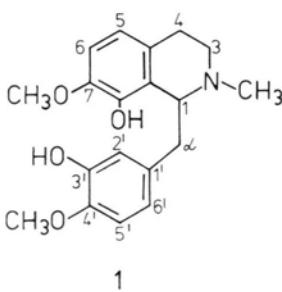
Cularine alkaloids occur only in the Fumariaceae family [1]. The “classical” cularines are oxygenated at C<sub>7</sub>, C<sub>3'</sub> and C<sub>4'</sub>. Recently two cancentrine-type alkaloids with oxygen functions at C<sub>7</sub>, C<sub>4'</sub> and C<sub>5'</sub> have been described [2]. The biogenesis 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 ( $\lambda_{\text{max}}$  280 nm),  $[\alpha]_D = +37.6^\circ$  ( $c = 0.1$ ; 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<sub>11</sub>H<sub>14</sub>NO<sub>2</sub>, 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<sub>8</sub>H<sub>9</sub>O<sub>2</sub>, c.137.0602; f.137.0601) represents the benzyl moiety substituted in the same manner. This corresponds to a molecular formula C<sub>19</sub>H<sub>23</sub>NO<sub>4</sub>. The <sup>1</sup>H-NMR spectrum (300 MHz, CDCl<sub>3</sub>) showed one NCH<sub>3</sub> ( $\delta = 2.37$ ) and two OCH<sub>3</sub> 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<sub>1</sub>. 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<sub>6</sub> ( $\delta = 6.73$ ) and H<sub>5'</sub> ( $\delta = 6.75$ ) assign positions 7 and 4' to the OCH<sub>3</sub> 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,  $[\alpha]_D = +268^\circ$  ( $c = 0.1$ ; EtOH), C<sub>19</sub>H<sub>21</sub>NO<sub>4</sub> (M<sup>+</sup>, 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<sub>7</sub>, C<sub>4'</sub> and C<sub>5'</sub> isolated from a *Corydalis* species.



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O-methylcularicine (**3**),  $[\alpha]_D = +283^\circ$  ( $c = 0.1$ ; 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.

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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).