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# THE BIOSYNTHESIS OF CULARINE

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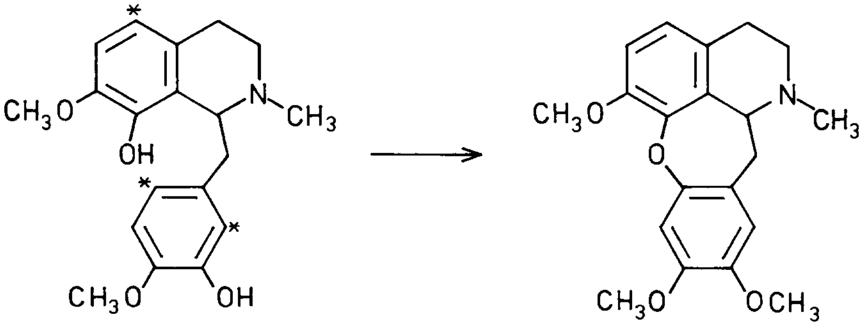
Summary: The incorporation of the 7,8-oxygenated benzylisoquinoline 1 into cularine (2) is demonstrated.

The cularine alkaloids are assumed to arise by direct oxydative coupling of a 7,8,3',4'-substituted benzylisoquinoline.[1,2] This postulated precursor has recently been isolated independently by Boente et al.[3] from *Sarcocapnos crassifolia* DC and by us[4] from *Corydalis claviculata* DC (both Fumariaceae). We now wish to report the incorporation of 1 into cularine (2).



1 2

The benzylisoquinoline 1, isolated from *Corydalis claviculata*, was tritium labelled by heating with tritium water. This method is known to exchange hydrogen in ortho and para positions to the phenolic hydroxyl groups[5] (marked with an asterisk in structure 1). The labile tritium was removed and the sample purified by column chromatography on silica gel. The labelled positions were furthermore proved by bromination. Thus, the tribromo derivative (1, Br in marked positions) showed a 99.7% loss of the original activity.

The labelled alkaloid 1 with a total activity of 5.0 mCi (specific activity 3.1 mCi/mg) was applied to flowering Corydalis claviculata plants by root uptake.[6] After feeding for ten days work up of the dried plants yielded 31.6 mg of nonphenolic alkaloids with a total activity of 18.7 μCi and 56.2 mg of phenolic bases with the activity of 170 μCi. The latter were not further investigated. Thin layer chromatography of the nonphenolic alkaloid extract in different solvent systems showed after staining with iodine vapors three major spots corresponding to stylopine (ca. 5%), protopine (ca. 40%) and cularine (ca. 50%). The radioactivity was located almost completely (>95%) in the cularine spot as determined by analytical thin layer radiochromatography.

To 6.3 mg of the nonphenolic alkaloids (corresponding to about 3.2 mg of cularine base) 12.3 mg of nonlabelled cularine as oxalate were added and crystallized to a constant specific activity of 0.21 μCi/mg calculated as cularine base. This corresponds to a $^{3}H$-retention of 0.32%. Considering the fact that one tritium is lost during the biosynthesis this figure represents a minimum incorporation rate.
The isolation of 1 and its incorporation into 2 clearly demonstrates the role of this benzylisoquinoline as the precursor of cularine alkaloids.

None of the isolated stylopine and protopine showed any radioactivity. These two alkaloids may be formed from (+)-reticuline as demonstrated for Papaver somniferum and Chelidonium majus.[7] (+)-Reticuline is also present in Corydalis claviculata[4].

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