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

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Z. Naturforsch. 38c, 670–671 (1983); received May 14, 1983

Papaveraceae, Cularines, Benzylisoquinolines

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 C7, C3’- and C4’. Recently two cancentrine-type alkaloids with oxygen functions at C7, C4’- and C5’ have been described [2]. The biogenesis of both types can be explained by direct oxidative 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, (+)-thali­porphine and cularimine were isolated.

Base 1 was obtained as an oil (λmax 280 nm), [α]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%; C19H20NO4, m/z = 192.1024; f. 192.1014) is due to the isoquinoline part with one hydroxyl and one methoxy group. The peak m/e = 137 (8%; C11H11NO2, c.137.0602; f.137.0601) represents the benzyl moiety substituted in the same manner. This corresponds to a molecular formula C19H20NO4. The 1H-NMR spectrum (300 MHz, CDCl3) showed one NCH3 (δ = 2.37) and two OCH3 functions (δ = 3.85, 3.89). Six aliphatic protons appear as a multiplet (δ = 2.44 – 3.39). The pair of doublets (δ = 4.12; J = 3.7 Hz/9.1 Hz) is due to the proton at C1. The signals at δ = 6.75, 6.78 and 6.92 represent the ABX-spin system of the 3’,4’-oxygenated benzyl part. The AB system (δ = 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 H6 (δ = 6.73) and H5’ (δ = 6.75) assign positions 7 and 4’ to the OCH3 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, [α]D = +268° (c = 0.1; EtOH), C19H20NO4 (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 C7, C4’ and C5’ isolated from a Corydalis species.
O-methylcularicine (3), \([\alpha]_D = +283^\circ\) (c = 0.1; EtOH), was analyzed for \(C_{19}H_{18}NO_4\) (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.


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).

Acknowledgement

We are grateful to Dr. V. Wray for NOE measurements and to Prof. T. Kametani for copies of IR and \(^1\)H-NMR spectra.