

THREE NEW ISOQUINOLINE ALKALOIDS FROM CORYDALIS CLAVICULATA (L.) DC.

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Abstract- We describe the isolation from Corydalis claviculata (L.) DC. and the structure determination of the three new alkaloids dioxocularine 1, norsecocularine 2 and viguine 3.

Recent studies carried out in our laboratories on the alkaloids of plants of the genera Sarcocapnos and Corydalis (Fumariaceae) have led to the isolation of the first members of two new groups of cularine-related alkaloids, the 3,4-dioxocularines¹ and the secocularines². Now we wish to describe the isolation from Corydalis claviculata (L.) DC. of a new member of each group, namely dioxocularine 1 and norsecocularine 2. In addition we have also isolated from the same source a non-phenolic N-benzyltetrahydroisoquinoline alkaloid, viguine 3.

Dioxocularine 1 is a very minor component of C. Claviculata (L.) DC. being obtained as red crystals, mp 212-214°C (EtOH). Its PMR spectrum (250 MHz, CDCl₃, δ) (Figure I) suggested a 3,4-dioxocularine structure exhibiting the presence of five aromatic protons, three methoxyl groups and one highly deshielded N-methyl group; no signals were observed in the aliphatic part of the spectrum. Also very useful for establishing the structure of this compound was the CMR spectrum (62.83 MHz, CDCl₃, δ), which revealed the presence of two carbonyl groups (singlets at 175.31 and 156.90), nine quaternary sp² carbons (singlets at 156.86, 151.36, 148.93, 146.86, 141.40, 134.34, 129.58, 121.89 and 119.96), five methine sp² carbons (doublets at 126.72, 118.12, 113.92, 111.62 and 105.24), three methoxy groups (quartets at 56.65, 56.38 and 56.29) and an N-methyl group (quartet at 32.83). Moreover the UV spectrum, which remained unchanged upon addition of acid and base, showed bands at λ_{max}^{EtOH} (log ε): 224 (4.40), 260 (4.15), 304 (3.96), 340 (4.06) and 452 (3.75) nm characteristic of the highly conjugated system of a 3,4-dioxocularine, and the IR spectrum (KBr) exhibited strong absorption at 1680 cm⁻¹ due to a conjugated carbonyl group. Further proof was obtained from the mass spectrum; in addition to the molecular ion at m/z 367 (100) which confirmed the molecular formula C₂₀H₁₇NO₆ deduced by elemental analysis, it showed significant peaks due to correlative losses of carbonyl and methyl fragments at m/z 339 (31), 324 (38), 296 (34), 281 (14), 266 (6), 238 (17) and 210 (14). Finally, structure 1 for dioxocularine was confirmed by a PMR nOe difference study (Figure I) and by direct comparison with synthetic material³.

Norsecocularine 2, obtained as white crystals, mp 203-205°C (benzene), is also a minor component in the plant. Its molecular formula, C₂₀H₂₃NO₄, was established by high resolution MS which showed the molecular ion at 341.1625 (calculated 341.1627).

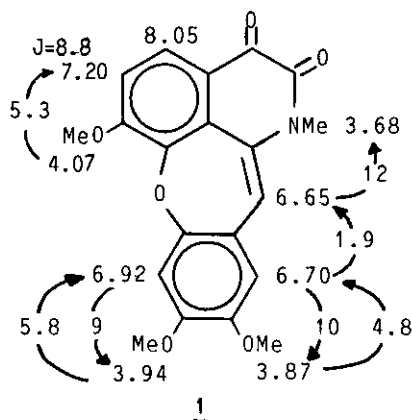


Figure I

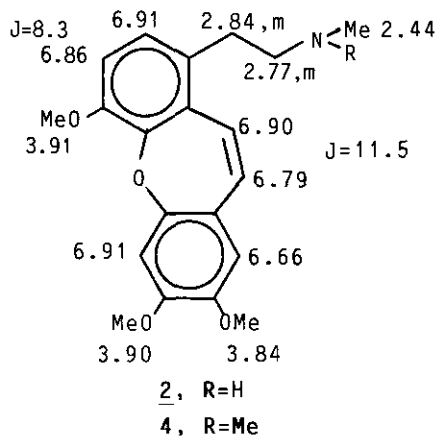


Figure II (PMR data for 2)

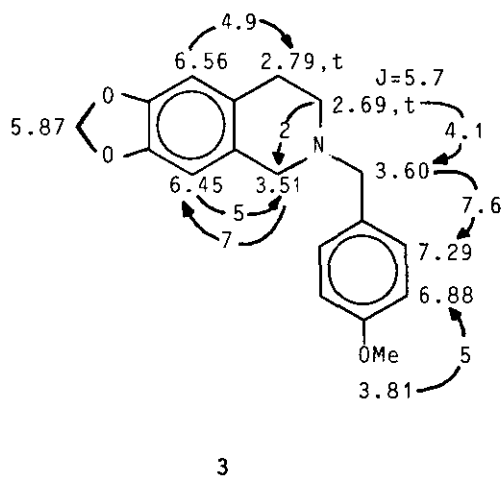
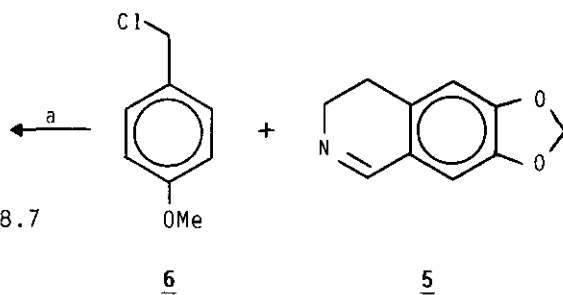


Figure III



a. CHCl_3 , reflux; NaBH_4 , MeOH, 72%

The UV spectrum, characteristic of a secocubane structure², showed absorption bands at $\lambda_{\text{max}}^{\text{EtOH}}$ ($\log \epsilon$): 220 (4.23), 296 sh (3.68) and 316 (3.76) nm and no change with acid or base. In spite of its non-phenolic nature, the IR spectrum exhibited absorption at 3400 cm^{-1} , revealing the presence of an -NH group. Its PMR spectrum (250 MHz, CDCl_3 , δ) (Figure II) showed the characteristic aromatic part of a secocubane with two ABq, one of them with a very large coupling constant, and two one-proton singlets. In addition, signals in the aliphatic part suggested that the molecule possessed a $-\text{CH}_2\text{CH}_2\text{NHMe}$, which was also supported by the

presence of a base peak in the mass spectrum at m/z 44 ($\text{CH}_2=\text{NHMe}^+$). Other signals were observed at m/z 341 (M^+ , 1), 298 (4), 297 (2), 165 (3), 152 (4), 139 (4), 115 (2). Structure 2 for this compound was confirmed by its transformation into secocularine 4 (which has been isolated in our laboratory from Sarcocapnos crassifolia (L.) DC.²) via N-methylation with H-COH/ NaBH_4 . Comparison of the PMR data of the two compounds allowed us to assign all of its resonances as shown in Figure II.

The third alkaloid, viguine 3, was isolated as white crystals, mp 63-64°C (benzene/hexane). Its molecular formula, $\text{C}_{18}\text{H}_{19}\text{NO}_3$, was established by elemental analysis of its hydrochloride (mp 232-233°C, EtOH) and confirmed by MS, which showed the molecular ion at m/z 297 (23) with other significant peaks at 176 (23), 148 (63) and 121 (100). The UV spectrum showed absorption bands at $\lambda_{\text{max}}^{\text{EtOH}}$: 224 and 294 nm and no change was observed upon addition of acid or base. The most significant signals of its PMR spectrum (250 MHz, CDCl_3 , δ) (Figure III) were a pair of doublets due to a para-disubstituted benzene ring and, in the aliphatic part, two singlets for two isolated methylene groups and two triplets for a $-\text{CH}_2\text{CH}_2-$ system, which strongly suggested an N-benzyltetrahydroisoquinoline skeleton for this compound. Further proof for structure 3 came from a PMR nOe difference study and direct comparison with synthetic material, which was easily obtained by coupling of 6,7-methylenedioxy-3,4-dihydroisoquinoline⁴ (norhydrastinine) 5 and 4-methoxybenzylchloride⁵ 6, followed by treatment with NaBH_4 .

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