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Aconcaguine: An Isoquinoline-derived Alkaloid from *Berberis actinacantha*

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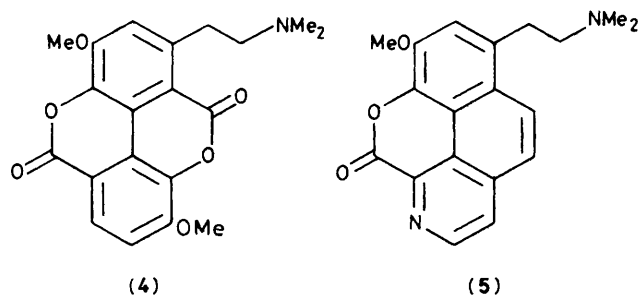
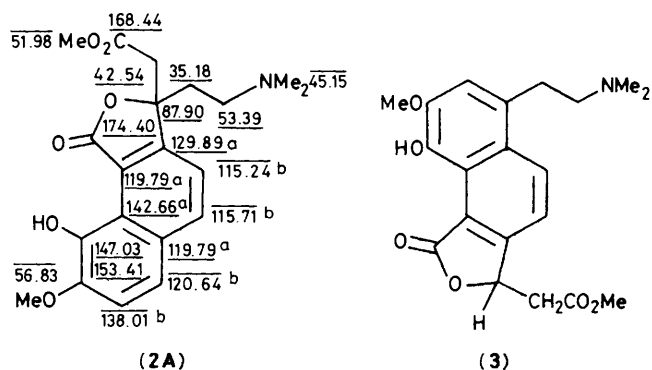
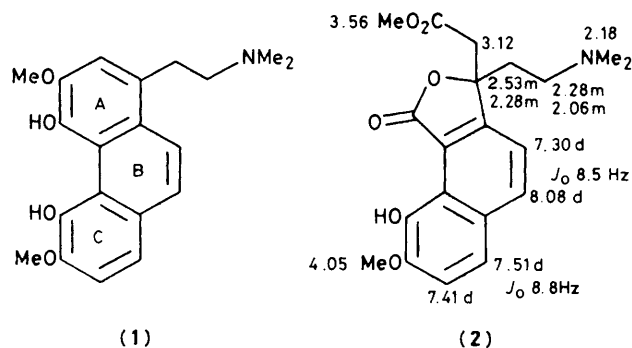
Chilean *Berberis actinacantha* Mart. ex Schult. (Berberidaceae) has yielded the novel alkaloid (+)-aconcaguine (**2**) which is probably derived from intradiol oxidative cleavage of ring A of magnoflorinemethine (**1**).

We have obtained from Chilean *Berberis actinacantha* Mart. ex Schult. (Berberidaceae), which had previously supplied chiloenamine (**3**),¹ the novel yellow amorphous base (\pm)-aconcaguine (**2**). The molecular composition of aconcaguine, C₂₀H₂₃NO₆, makes it structurally isomeric with (**3**). Furthermore, the i.r. spectrum of (**2**) in the carbonyl region, ν_{\max} (CHCl₃) 1715 and 1745 cm⁻¹, was essentially superimposable on that of chiloenamine (**3**) while the complex u.v. spectrum indicated a highly conjugated system, and was also very similar to that for chiloenamine (**3**).[†]

The 360 MHz n.m.r. spectrum of aconcaguine in CDCl₃ is outlined around structure (**2**). The two pairs of aromatic doublets at δ 7.30 and 8.08, and at δ 7.41 and 7.51, pointed to a tetrasubstituted naphthalene skeleton. The dimethylamino moiety could be inferred from the 6-proton singlet at δ 2.18. Two *O*-methyl singlets were also in evidence, one due to a methyl ester at δ 3.56, and the other at lower field (δ 4.05) due to an aromatic OMe group.

The positions of the substituents around the naphthalene nucleus were confirmed by a detailed n.m.r. nuclear Overhauser enhancement (n.O.e.) difference study.² In particular, the two side chains must be proximate since irradiation of the methylene multiplet at δ 2.53 resulted in a 1.9% enhancement of the singlet at δ 3.12 due to the methylene protons adjacent to the ester carbonyl group.[†]

The ¹³C n.m.r. spectrum of aconcaguine (**2**) was also obtained, and the carbon multiplicities were determined by the gated spin echo (GASPE) technique.³ Signals appearing above an arbitrary line arise from quaternary and methylene carbon atoms and are shown in structure (**2A**) with the chemical shift values underlined. On the other hand, signals



[†] Aconcaguine (**2**): λ_{\max} (MeOH) 215, 267, 322, 335, and 384 nm (log ϵ 4.45, 4.42, 3.66, 3.64, and 3.68); m/z 373 (M^+ ; 6%), 342 (0.5), 315 (0.1), 301 (0.5), 300 (0.1), 242 (0.5), 227 (1), 213 (0.8), and 58 (100); n.O.e. values δ 2.53 \rightarrow 3.12 (1.9%), 3.12 \rightarrow 7.30 (6.1%), 7.30 \rightarrow 8.08 (14.6%), 8.08 \rightarrow 7.30 (14.1%), 8.08 \rightarrow 7.51 (18.4%), 7.51 \rightarrow 8.08 (19.4%), 4.05 \rightarrow 7.41 (24.7%), and 7.41 \rightarrow 4.05 (13.6%). 5 mg of (**2**) were obtained from 25 kg of dried twigs of *B. actinacantha* collected on Cerro Lo Curro, in Santiago, Chile. The quaternary aporphine (+)-magnoflorine is also abundantly present in the plant.

that are found below the arbitrary line are due to methine and methyl carbon atoms and are indicated with a bar over them. Chemical shifts with identical superscripts are interchangeable.

An important feature of the mass spectrum of aconcaguine (**2**) is that the molecular ion, m/z 373 (6%), is appreciably stronger than in chiloenamine (**3**), since loss of the CH_2NMe_2 moiety from the molecular ion of aconcaguine is not as favoured a process.

Aconcaguine (**2**) should be compared with the above-mentioned chiloenamine (**3**),¹ with the well known taspine (**4**),⁴ and with the recently described santiagonamine (**5**),⁵ all of which are found among members of the Berberidaceae. These four alkaloids appear to be derived biogenetically from 1,2,10,11-tetraoxygenated aporphines. More specifically, aconcaguine (**2**) is probably the product of catechol dioxyge-

nase intradiol cleavage of ring A of magnoflorinemethine (**1**), followed by lactonization.⁶

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