ILICIFOLINE : NEW BERBINE DIMER ALKALOID FROM *BERBERIS ILICIFOLIA*

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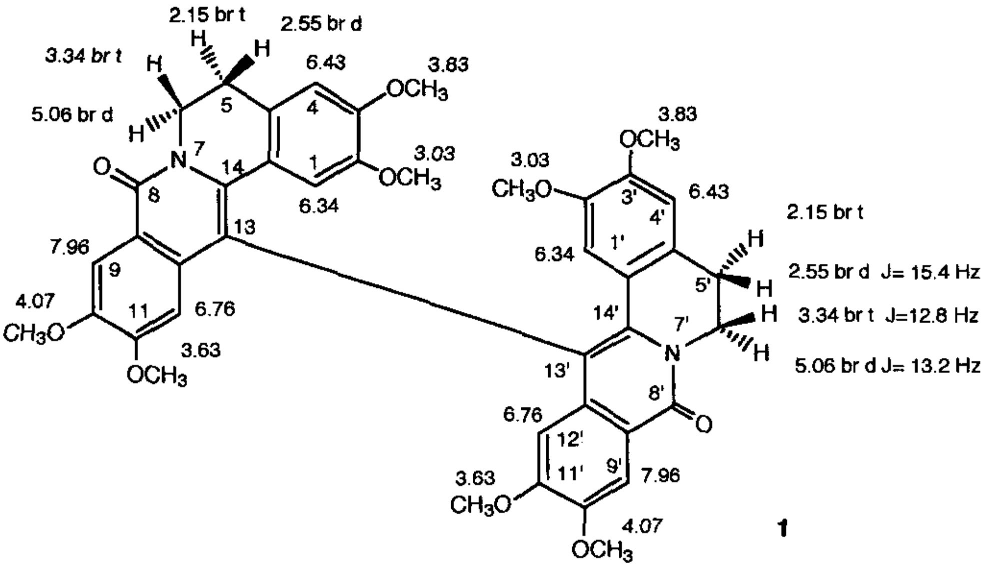
Abstract - From *Berberis ilicifolia*, a new dimer is described, but this alkaloid is related to a bisberbine. *It is the first dimer of this type in Berberis.*

As part of a continuing study of the alkaloids of Chilean *Berberis*[1,2] we have investigated the content of *Berberis liicifolia* Forst (Berberidaceae), a Pataganian specie that grows at the southern part of Chile. One fraction obtained by eluting the alkaloids through a column of silica gel using 5% MeOH in $CHCl_3$ was subjected to tlc. From this fraction crystallized on MeOH the yellow compound (**1**) (50 mg), mp 260°C that corresponds to a berbine dimer of 8-oxopseudopalmatine[3] (**2**), $[\alpha]_D$ 0° (0.2 MeOH); λ max *(MeOH) 233, 260, 334 nm (log ε 2.31, 2.27, 2.12)*; HREIms, for $C_{42}H_{40}N_2O_{10}$ (M^+, 100), calcd 732.7342, fd 732.7267; EIms (rel. int. %), m/z 732 (M^+, 100), 718 (11), 717 (21), 702 (3), 366 (14), 351 (6), CIms, m/z 732.0.

The 360 MHz ^1H-nmr spectrum in $CDCl_3$, as summarized around structure (**1**) is close to that for 8-oxopseudopalmatine (**2**). The main difference lies in the chemical shift of the C-2-OCH_3 and C-2'-OCH_3 at δ 3.03 for ilicifoline (**1**) and δ 3.95 for 8-oxopseudopalmatine (**2**); while a two-proton aromatic singlet at C-1 and C-1' is found at δ 6.34 meaning that the C-2-OCH_3, C-2'-OCH_3, H-1 and H-1' are affected for the aromatic ring D and D', because their proximity with those hydrogens.



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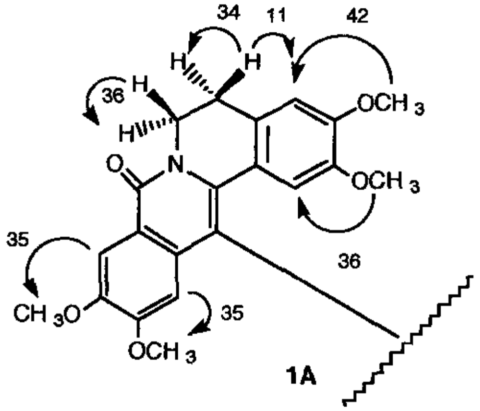
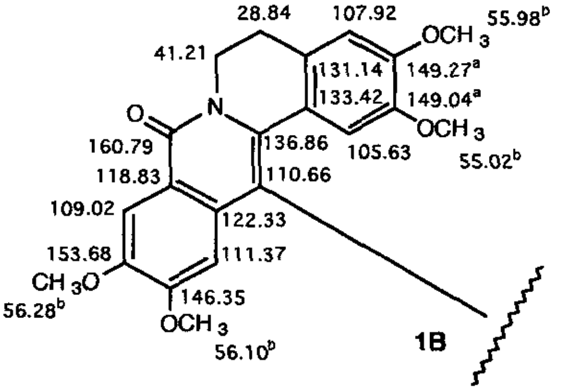
The nmr chemical shift assignments were confirmed by a detailed nmr nOeds study (**1A**). Significant nmr nOe's are H-1 to 2-OCH_3 or 2'-OCH_3 to H-1' 36%; H-1 to H-12' or H-12 to H-1', 9%; H-4 to 3-OCH_3 or 3'-OCH_3 to H-4', 42%; H-4 to H-5β or H-4' to H-5'β, 11%; H-5α to H-5β or H-5'α to H-5'β, 34%; H-6β to H-6α or H-6'β to H-6'α 36%; H-9 to 10-OCH_3 or H-9' to 10'-OCH_3 35%; 11-OCH_3 to H-12 or 11'-OCH_3 to H-12' 35%.

The 125 MHz ^{13}C-nmr spectrum of ilicifoline (**1**), as summarized around (**1B**), was also obtained, and the carbon multiplicities were determined by the gated spin echo (GASPE) technique.[4] Chemical shifts with identical superscrips are interchangeable.

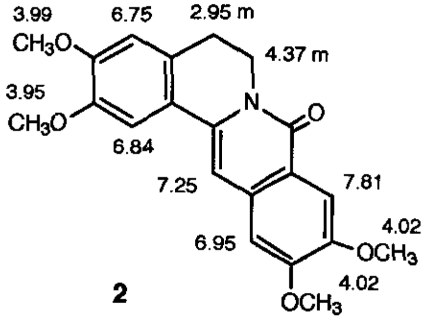
Previous to the isolation of ilicifoline (**1**) from *Berberis ilicifolia* a related dimeric alkaloid was obtained from *Jatrorriza palmata*.[5] This compound corresponds to a dimeric protoberberine alkaloid and was named bisjatrorrhizine (**3**).[4] Ilicifoline could be formed by a coupling of two units of 8-oxopseudopalmatine (**2**) while bisjatrorrhizine (**3**) specifically would involve an *orho* oxidative coupling of the phenolic group of jatrorrhizine.



1A



1B



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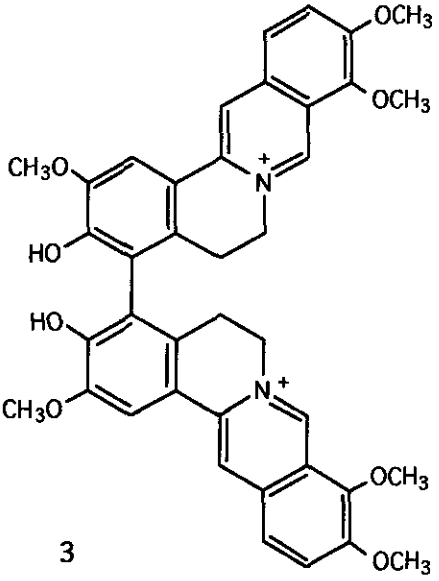

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EXPERIMENTAL

Berberis ilicifolia Forst (dried roots, 20 kg) was gathered in Fuerte Bulnes, 40 km from Punta Arenas in Chile. The plant was air dried and powdered. The plant material was extracted with methanol (40 l) at room temperature for three days. The dried methanolic extract was treated with 5% HCl (5 l). Following basification with NH_4OH, the alkaloids were then separated on silica gel columns (1.5 kg), elution being with $CHCl_3$ (5 l) and increasing percentage of MeOH (20% MeOH in $CHCl_3$). Final purification of the alkaloids (10 g) was on column using tlc silica gel Merck. From one of these fractions eluted with 5% MeOH in $CHCl_3$ crystallized a yellow berbine dimer (200 mg) (mp 260°C). From MeOH, known alkaloids were also present : berberine (300 mg), palmatine (54 mg), jatrorhizine (40 mg), (+)-chitraline (16 mg), (+)-pakistanine (145 mg), and (-)-sinoacutine (182 mg).

ACKNOWLEDGMENTS

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