(-)-JABOROMAGELLONINE: NEW WITHANOLIDE FROM SEEDS OF JABOROSA MAGELLANICA

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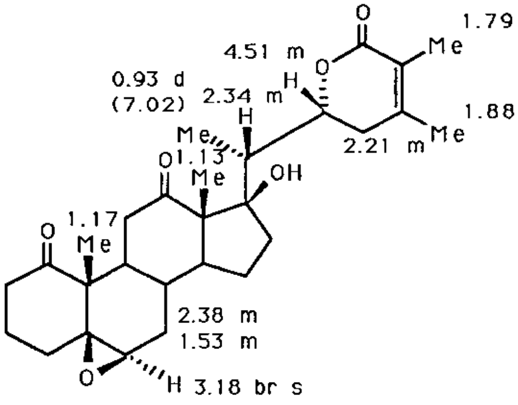
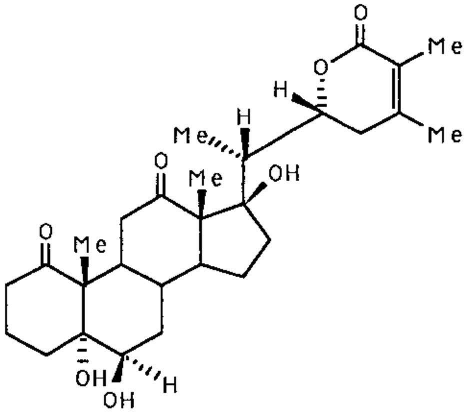
Abstract. - From seeds of *Jaborosa magellanica* (Griseb.) Dusén (Solanaceae), a new withanolide was isolated and studied by nmr and mass spectroscopy.

Jaborosa magellanica (Griseb.) Dusén, is a Chilean Patagonia plant used as a folk medicine. In the course of an investigation of the constituents of this plant, collected along the northern shores of the Strait of Magellan, we were able to isolate a new δ-lactone withanolide presents in the seeds of *J. magellanica*. Previous works in *J. magellanica* allowed us to isolate a series of withanolides, some of which had the presence of δ-lactone and other the γ-lactone ring.[1~4] All of our δ-lactones have in common a 12-oxo and a 17β-hydroxyl functions in their skeletons. Our actual compound (-)-jaboromagellonine (1) is a new example of a δ-lactone with that characteristic pattern. The 12-oxo-withanolides rarely occurred in nature, and only three examples are known, one in *Nicandra physaloides*[5] and two in *Datura quercifolia*.[6~7]



1



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The methanol extract of seeds of J. magellanica was subjected to column chromatography fractionation, producing mixtures of high amount of steroids. Tlc and crystallization gave the new δ-lactone withanolide, we named (−)-jaboromagellonine (1).

The ^{1}H nmr and ^{13}C nmr spectra allowed the assignments of the δ-lactone, indicating that it consists of a 1,12-dioxo-5β,6β-epoxy-17β-hydroxywithanolide. Its ^{1}H nmr spectrum in $CDCl_3$ presented a broad singlet at δ 3.18, which was assigned to H-6, suggesting a 1-oxo-5β,6β-epoxywithanolide. The presence of two methyl signals at δ 1.79 and δ 1.88 is well correlated with an α,β-unsaturated lactone bearing methyl groups at positions C-24 and C-25. The other methyl groups are located at δ 1.13 (H-18), δ 1.17 (H-19), and δ 0.93 d (H-21, J= 7.02 Hz). The doublet at δ 0.93 assigned to H-21 indicated the absence of a hydroxyl group at C-20, and the complex signal at δ 4.51 is characteristic for H-22. The ^{1}H nmr spectrum of (−)-jaboromagellonine (1) is similar to (+)-jaboromagellone (2), a previous δ-lactone withanolide isolated from the aerial part of J. magellanica.[1] The proton nmr spectrum of 1 in pyridine-d_5 produced a changed for H-22 (Δ δ=0.75), and H-18 (Δ δ=0.13), indicating that all of those hydrogens are located at the same side of the molecule. Hydrogens H-22 and H-18 are in a 1,3-diaxial relationship with the alcoholic function at C-17.[8]

This is the same pattern observed for (+)-jaboromagellone (2).[1] (−)-Jaboromagellonine (1) showed a cd spectrum with a maximun at 240 nm indicative of the C-22 R configuration.[9~11] The high resolution mass spectrum of (−)-jaboromagellonine (1) includes a molecular ion at m/z 470.2614 corresponding to the molecular formula, $C_{28}H_{38}O_6$ (calcd 470.2668). A base peak at m/z 125.0617 ($C_7H_9O_2$, calcd 125.0602) was due to the cleavage of ring E along C-20 (22) linkage. A large peak at m/z 153.0901 ($C_9H_{13}O_2$, calcd 153.0915) arisen from cleavage between C-17(20), is characteristic of the δ-lactone withanolides.[1]

(+)-Jaboromagellone (2) may very well arise biogenetically from the (−)-jaboromagellonine (1) through opening of the oxirane ring with formation of a trans -glycol.

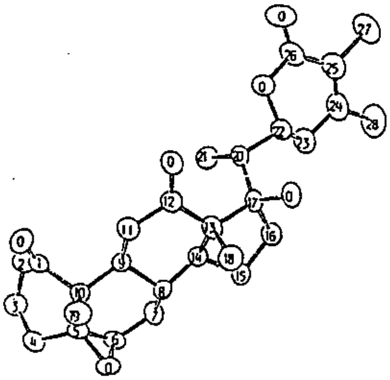

Figure 1. Perspective drawing of (−)-jaboromagellonine (1).

Both compounds were found before in aerial part and now in the seeds of *J*. *magellanica*. An X-ray analysis was carried out on 1 (Figure 1), by Dr. M. Parvez of the Department of Chemistry, The Pennsylvania State University. The configuration indicated in 1, derives from the fact that naturally occurring steroidal derivatives generally incorporate a C(19) methyl groups which lies above the mean plane of the molecule. According to the X-ray analysis the 5,6-epoxide is in the same side that C(19) does it in 1. This work will be described in full in a separate paper.

EXPERIMENTAL

The seeds of *J*. *magellanica* were collected in southern part of Chile, in Punta Arenas. The plant was identified by professor Edmundo Pisano, Instituto de la Patagonia, Universidad de Magallanes and its specimen has been deposited in the Area of Botany, Universidad de Magallanes.

The cold MeOH (30 l, three days) extract of the seeds (15 kg) of *J*. *magellanica* was evaporated under vacuum to afford a syrup. This was loaded on a silica gel column (1.0 kg). Elution was with $CHCl_3$ and $CHCl_3$-MeOH mixtures of increasing polarity. The fraction obtained using $CHCl_3$-MeOH (97:3) weighed 2.4 g. This fraction was subjected to repeated prep. Tlc on silica gel, using the same system $CHCl_3$-MeOH (97:3) to afford white solid compound 1 (100mg), mp 216 ^{0}C (MeOH), $[\alpha]_D = -21.2^0$ (c=4.10 MeOH), cd (c=0.11, MeOH), $\Delta\varepsilon$ (nm) 0(320), -2.29 (290), +4.7 (255), uv λ_{max} (MeOH) (nm) : 231 nm (logε 4.5), ir υ_{max} (KBr)(cm^{-1}) : 3400, and 1705-1695, ^{1}H-nmr (270 MHz, C_5D_5N): δ 1.04 (3H, d, J= 7.15 Hz, H-21),1.26 (3H, s, H-18), 1.33 (3H, s, H-19), 1.60 (3H, s, H-27), 1.75 (3H, s, H-28), 3.23 (1H, br s, H-6), 5.26 (1H, m, H-22), ^{13}C-nmr (90 MHz, $CDCl_3$) : 214.11 (C-12), 212.28 (C-1), 165.51 (C-26), 148.88 (C-24), 121.84 (C-25), 82.90 (C-17), 76.49 (C-22), 64.56 (C-5), 60.08 (C-6), 57.93 (C-13), 52.16 (C-10), 45.44 (C-14), 44.21 (C-9), 41.11 (C-20), 37.43 (C-11), 34.55 (C-4), 34.55 (C-16), 33.93 (C-23), 31.51 (C-7), 30.28 (C-2), 28.39 (C-8), 22.05 (C-15), 20.42 (C-28), 18.68 (C-18), 17.80 (C-3), 12.92 (C-21), 12.45 (C-19), 12.35 (C-27). HREIms, m/z (rel int %): 470.2614 (M^+, calcd for $C_{28}H_{38}O_6$ 470.2668) (2), 317.1751 (calcd for $C_{19}H_{25}O_4$ 317.1752) (29), 261.1489 (calcd for $C_{16}H_{21}O_3$ 261.1490)(6), 177.0955 (calcd for $C_{11}H_{13}O_2$ 177.0915) (8), 153.0901 ($C_9H_{13}O_2$, calcd 153.0915) (26), 138.0667 (calcd for $C_8H_{10}O_2$ 138.0680) (2), 125.0617 (calcd for $C_7H_9O_2$, 125.0602) (100).

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