Total NMR Assignment of Furanditerpene Derivatives from *Pterodon Polygalaeiflorus* Benth.

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**Abstract**: *Pterodon polygalaeiflorus* Benth, popularly known as “Sucupira-branca”, is a well-known tree in the central region of Brazil. The seeds of this tree are used in folk medicine as anti-rheumatic, anti-inflammatory and analgesic preparations. From the hexane extract of its fruits, 6α,7β-dihydroxyvouacapan-17β-oic acid (ADV), a furanditerpene that presents anti-inflammatory, analgesic, and plant growth regulatory activities was isolated. ADV (1) and some derivatives have previously been studied to obtain some clues about chemical structure-biological activity relationship. Some ADV esters containing an OH group at C-6 have already been obtained. Both hydroxyl and carbonyl groups can receive hydrogen bonds, while the hydroxyl group can also donate a hydrogen bond. With the aim of mapping the biological receptor, the replacement of the OH group at C-6 of ADV by a carbonyl group was made. Therefore, the 6-oxo-voucapan-7α,17β-lactone (3) derivative was prepared. Here we described the NMR studies of four ester derivatives obtained from (3), which were as follows: methyl 6-oxo-7α-hydroxyvouacapan-17β-oate (4), ethyl 6-oxo-7β-hydroxyvouacapan-17β-oate (5), propyl 6-oxo-7α-hydroxyvouacapan-17β-oate (6), 2-methoxy-ethyl 6-oxo-7α-hydroxyvouacapan-17β-oate (7). Their resonances were unequivocally assigned by the use of 1D (1H and 13C NMR, DEPT-135, NOE difference), and 2D (COSY, HMQC, HMBC) NMR techniques.

The seeds of *Pterodon polygalaeiflorus* Benth, popularly known as “Sucupira-branca” are used in folk medicine as anti-rheumatic, anti-inflammatory and analgesic preparations. From the hexane extract of its fruits it was isolated the 6α,7β-dihydroxyvouacapan-17β-oic acid (ADV, 1, Figure 1), a furanditerpene that presents anti-inflammatory, analgesic, and plant growth regulatory activities. To obtain some information with respect to the chemical structure-biological activity relationship, ADV, as well as its lactone (6α-hydroxyvouacapan-7β,17β-lactone, HVL, 2, Figure 1) and some of their ester and amide derivatives were previously studied. The NH, OH, and CO groups are able to receive hydrogen bonds, while the NH and OH groups can also donate a hydrogen to hydrogen bonds.

To map the receptor structure, the replacement of the OH group at C-6 of the ADV lactone derivative, HVL (2) by a carbonyl group was undertaken. The total NMR characterization of four esters (4-7) derived from the POL (3, Figure 1) is described herein.

The total NMR assignment of the esters 4-7 is discussed below. The synthesis of these compounds has already been reported. The 1D and 2D NMR techniques of 1H, 13C, DEPT-135, NOE difference; COSY, HMQC, and HMBC were used.
1H and 13C NMR spectra were recorded on a Bruker AVANCE DRX 400 spectrometer, in CDCl3. Chemical shifts are reported in parts per million (δ units), relative to TMS as internal standard, and scalar coupling constants (J) are reported in hertz. Pulse conditions were as follows: for 1H NMR spectra - dwell time (DW) 149.600 µs, acquisition time (AQ) 3.985 s, number of transients (NS) 16, recycle delay (RD) 1.000 s; for 13C NMR spectra – DW 31.400 µs, AQ 2.058 s, NS 1024, RD 2.000 s, decoupling multiple resonance method Waltz-16; for COSYGR – DW 125.000 µs, AQ 0.116 s, NS 1, DS 8, RD 2.000 s, data points (TD) 1024 (F2) and 256 (F1); HMQC – DW 54.400 µs, AQ 0.058, NS 16, RD 2.000 s, TD 1024 (F2) and 512 (F1); HMBC – DW 54.400 µs, AQ 0.223 s, NS 32, RD 2.000, delay for long range coupling (D6) 0.070 s, TD 2048 (F2) and 512 (F1).

Figure 1 shows the synthetic route to obtain the esters 4-7. The synthesis accomplishment was verified by the appearance of the hydroxyl group hydrogen resonance around δ 3.6 in the 1H NMR spectra of all the esters. Other pieces of evidence for the obtention of the esters are provided by the 1H and 13C resonances due to the R groups shown in Figure 1 from 4 to 7.

The HMQC contour map was useful to attribute resonance signals to non-magnetically equivalent gem hydrogens, since they resonate at different chemical shifts. To illustrate, an expansion of ester 6 13C NMR spectrum is shown in Figure 2, where C-11 and C-22 present the same δC 22.0.

![Figure 1. Synthetic route of C-6 ceto ester derivatives (4-7) of ADV.](image)

![Figure 2. Partial 13C NMR spectrum of ester 6 in CDCl3 at 100 MHz.](image)
Since both signals are due to CH$_2$, they were also overlapped in DEPT-135. Therefore, they were assigned from the HMQC analysis (upper right side of Figure 2) by the correlations of $\delta_C$ 22.0 with H-11ax ($\delta$ 2.50), H-11eq ($\delta$ 2.75), and H-22 ($\delta$ 1.70). The HMBC contour maps were useful for the assignment of non-hydrogenated carbon signals and also for distinguishing the CH$_3$-20 ($\delta_H$ 0.91; $\delta_C$ 15.1) from both CH$_3$-18 ($\delta_H$ 0.97; $\delta_C$ 32.5) and CH$_3$-19 ($\delta_H$ 1.32; $\delta_C$ 22.2) signals. Thus, H-20 correlates via $^3$J with both C-1 ($\delta_C$ 38.6) and C-9 ($\delta_C$ 48.1) signals, and via $^2$J with C-10 ($\delta$ 42.8). The NOE difference experiment distinguished between CH$_3$-18 and CH$_3$-19 signals. NMR techniques confirmed the synthesis and the structures of the esters.

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**References**