

## Total NMR Assignment of Furanditerpene Derivatives from *Pterodon Polygalaeflorus* Benth.

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**Abstract:** *Pterodon polygalaeflorus* 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, 6 $\alpha$ ,7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -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-vouacapan-7 $\alpha$ ,17 $\beta$ -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-7 $\alpha$ -hydroxyvouacapan-17 $\beta$ -oate (**4**), ethyl 6-oxo-7 $\beta$ -hydroxyvouacapan-17 $\beta$ -oate (**5**), propyl 6-oxo-7 $\alpha$ -hydroxyvouacapan-17 $\beta$ -oate (**6**), 2-methoxy-ethyl 6-oxo-7 $\alpha$ -hydroxyvouacapan-17 $\beta$ -oate (**7**). Their resonances were unequivocally assigned by the use of 1D ( $^1\text{H}$  and  $^{13}\text{C}$  NMR, DEPT-135, NOE difference), and 2D (COSY, HMQC, HMBC) NMR techniques.

The seeds of *Pterodon polygalaeflorus* Benth, popularly known as “Sucupira-branca” are used in folk medicine as anti-rheumatic, anti-inflammatory and analgesic preparations.<sup>1</sup> From the hexane extract of its fruits it was isolated the 6 $\alpha$ ,7 $\beta$ -dihydroxyvouacapan-17 $\beta$ -oic acid (ADV, **1**, Figure 1)<sup>2</sup>, a furanditerpene that presents anti-inflammatory, analgesic, and plant growth regulatory activities.<sup>2,3</sup>

To obtain some information with respect to the chemical structure-biological activity relationship, ADV, as well as its lactone (6 $\alpha$ -hydroxyvouacapan-7 $\beta$ ,17 $\beta$ -lactone, HVL, **2**, Figure 1) and some of their ester and amide derivatives were previously studied.<sup>4</sup> 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.

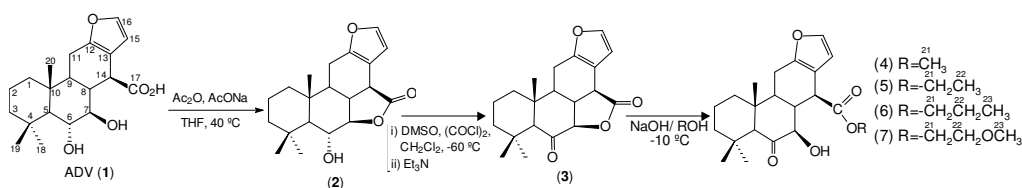
The total NMR assignment of the esters **4-7** is discussed below. The synthesis of these compounds has already been reported.<sup>5</sup> The 1D and 2D NMR techniques of  $^1\text{H}$ ,  $^{13}\text{C}$ , DEPT-135, NOE difference; COSY, HMQC, and HMBC were used.

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$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker AVANCE DRX 400 spectrometer, in  $\text{CDCl}_3$ . Chemical shifts are reported in parts per million ( $\delta$  units), relative to TMS as internal standard, and scalar coupling constants ( $J$ ) are reported in hertz. Pulse conditions were as follows: for  $^1\text{H}$  NMR spectra - dwell time (DW) 149.600  $\mu\text{s}$ , acquisition time (AQ) 3.985 s, number of transients (NS) 16, recycle delay (RD) 1.000 s; for  $^{13}\text{C}$  NMR spectra – DW 31.400  $\mu\text{s}$ , AQ 2.058 s, NS 1024, RD 2.000 s, decoupling multiple resonance method Waltz-16; for COSYGR – DW 125.000  $\mu\text{s}$ , AQ 0.116 s, NS 1, DS 8, RD 2.000 s, data points (TD) 1024 (F2) and 256 (F1); HMQC – DW 54.400

$\mu\text{s}$ , AQ 0.058, NS 16, RD 2.000 s, TD 1024 (F2) and 512 (F1); HMBC – DW 54.400  $\mu\text{s}$ , AQ 0.223 s, NS 32, RD 2.000, delay for long range coupling (D6) 0.070 s, TD 2048 (F2) and 512 (F1).

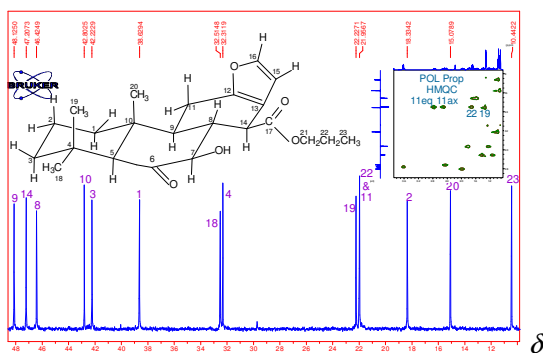
Figure 1 shows the synthetic route to obtain the esters **4-7**. The synthesis accomplishment was verified by the appearance of the hydroxyl group hydrogen resonance around  $\delta$  3.6 in the  $^1\text{H}$  NMR spectra of all the esters. Other pieces of evidence for the obtention of the esters are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



**Figure 1.** Synthetic route of C-6 keto ester derivatives (**4-7**) of ADV.<sup>6,7</sup>

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**  $^{13}\text{C}$  NMR spectrum is shown in Figure 2, where C-11 and C-22 present the same  $\delta_{\text{C}}$  22.0.



**Figure 2.** Partial  $^{13}\text{C}$  NMR spectrum of ester **6** in  $\text{CDCl}_3$  at 100 MHz.

Since both signals are due to CH<sub>2</sub>, 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<sub>3</sub>-20 ( $\delta_H$  0.91;  $\delta_C$  15.1) from both CH<sub>3</sub>-18 ( $\delta_H$  0.97;  $\delta_C$  32.5) and CH<sub>3</sub>-19 ( $\delta_H$  1.32;  $\delta_C$  22.2) signals. Thus, H-20 correlates via  $^3J$  with both C-1 ( $\delta_C$  38.6) and C-9 ( $\delta_C$  48.1) signals, and via  $^2J$  with C-10 ( $\delta$  42.8). The NOE difference experiment distinguished between CH<sub>3</sub>-18 and CH<sub>3</sub>-19 signals. NMR techniques confirmed the synthesis and the structures of the esters.

### Acknowledgements

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