

# CLERODANE DERIVATIVE: BIPRODUCTS OF GRANGIA MADERASPATNA

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## KEYWORDS INDEX

Grangea maderaspatana; Compositae; diterpines; clerodane derivatives; Nor-diterpine; seco-clerodanes.

## ABSTRACT

The aerial parts of Grangea maderaspatana afforded in addition to compounds isolated previously two new ones, three clerodane derivatives, a nor-clerodane, a seco-clerodane and nor-seco-clerodane. The structure was elucidated by NMR spectroscopic methods.

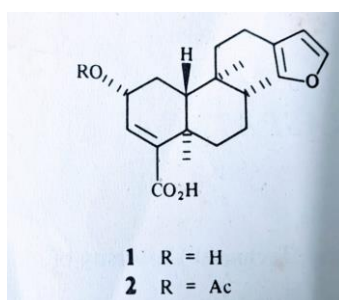
## INTRODUCTION

*Grangea maderaspatana* is a small herb of family compositae. Its leaves are used as stomach ache, ear ache<sup>1</sup>, anti-spasmodic, antiseptic and andodyne fomentations. Investigation of aerial parts of the plant afforded two new diterpenoids including two clerodane derivatives, a nor-clerodane, a seco-clerodane in addition to several known compounds. The results are discussed in this paper.

## RESULT AND DISCUSSION

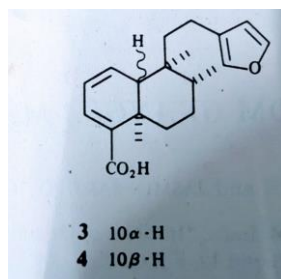
The extract of aerial part of Grangea maderaspatana afforded in addition to compound isolated previously<sup>[2,3]</sup> phytol, lupeol, p- hydroxybenzoic acid, the phenyl alanine derivative, the diterpenes hardwickiic acid and strictic acid.

The structure of **2a** was deduced from its proton NMR spectrum [Table 1], which was close to that of the corresponding alcohol **1a**<sup>[2]</sup>.



As expected, the H-2 signal was shifted downfield  $\delta$  5.42, ddd and acetoxy methyl singlet  $\delta$ 2.08 was present.

The proton NMR spectrum of **3a** [Table 1] was close to that of **4a** [2,4]. However, several signals were slightly different. Spin decoupling allowed the assignment of nearly all signals and by NOE difference spectroscopy the configuration at all chiral centres could be determined. Clear effects between H-19 and H-10(10%), H-17 and H-10(6%), H-20 and H-17 (5%), H-10 (12%) and H-2(7%) required a cis- relationship of H-10, H-17, H-19, and H-20.



The molecular formula of **2a** and its methyl ester indicated that this diterpene differed from the known 2-disoxy derivative of 1 by one additional oxygen. The proton NMR spectrum [Table 1] indicated that **2a** was the corresponding 15,16-butenolide. Accordingly, the signal of the furane protons were replaced by a triplet at  $\delta$  7.09 and a two-proton quartet at  $\delta$  4.76 while the remaining signals were nearly identical with those of the corresponding furan derivative.

In addition to the above compounds, we also found some compounds like:

- ➔ (-) Hardwickiic Acid; C<sub>20</sub>S<sub>28</sub>O<sub>3</sub>. It is classified as colourless solid, m.p. 143-44<sup>0</sup>. It belongs to clerodane group of diterpenoids having  $\beta$ -substituted furane ring.
- ➔ Strictic Acid; C<sub>20</sub>H<sub>26</sub>O<sub>3</sub> was obtained as colourless needles, m.p. 160<sup>0</sup> having seco-clerodane skeleton.
- ➔ Nidoresedic Acid; C<sub>20</sub>H<sub>26</sub>O<sub>3</sub> classified as colourless gum<sup>3</sup>. It belongs to clerodane group of diterpenoid.
- ➔ Nor-Strictic Acid; C<sub>17</sub>H<sub>24</sub>O<sub>4</sub> isolated as its dimethyl ester and found as nor-seco-diterpene.

## EXPERIMENTAL

The air-dried aerial part (1 kg) was extracted with Et<sub>2</sub>O-petrol-MeOH (1:1:1) at room temperature for 24 hours. Evaporation of the solvent at reduced pressure furnished a green semi-solid mass which was dissolved in 200 ml MeOH and left overnight in the refrigerator. After filtration, the filtrate was concd and chromatographed over silica gel and gave following fraction:

Fraction 1 was a complex mixture of diterpene acids. Therefore, it was subjected to methylation with CH<sub>2</sub>N<sub>2</sub> & separated by HPLC giving 21mg of **2a** Rt12.4 minutes.

- ➔ 2 $\alpha$ - Acetoxyhardwickiic Acid (**2**). Isolated as its methyl ester. **2a**

Colourless gum; IR  $\nu_{\max}^{\text{CCl}_4}$  cm<sup>-1</sup>: 1760, 1730, (OAc), 1715 (C=C—CO<sub>2</sub>R); MS  $m/z$  (rel. int.): 388.224 [M]<sup>+</sup> (12) (calc. for C<sub>23</sub>H<sub>32</sub>O<sub>5</sub>: 388.224), 346[M- ketene]<sup>+</sup> (12), 345 [M-MeCO]<sup>+</sup> (22), 328 [M-AcOH] (4), 314 [345-OMe]<sup>+</sup> (8), 313 [345-MeOH]<sup>+</sup> (9), 299 [314-Me]<sup>+</sup> (6), 95 (34), 81 (38) and 61 (100); [ $\alpha$ ]<sub>D</sub> -1.1<sup>0</sup> (CHCl<sub>3</sub>; c 2.07)

→ 10-epi-Nidorededic acid (3). Isolated as its methyl ester **3a**

Colourless gum; IR  $\nu_{\max}^{\text{CCl}_4}$   $\text{cm}^{-1}$ : 1700 (C=C—C=C—CO<sub>2</sub>R); MS  $m/z$  (rel. int.): 328.203 [M]<sup>+</sup> (8) (calc. for C<sub>21</sub>H<sub>28</sub>O<sub>3</sub>: 328.203), 313 [328-Me]<sup>+</sup> (8), 297 [M-OMe]<sup>+</sup> (4), 285 [313-CO]<sup>+</sup> (10), 151 (98) and 81 (100);  $[\alpha]_{\text{D}} -66.1^\circ$  (CHCl<sub>3</sub>; c 1.0)

Table 1: <sup>1</sup>H NMR spectral data of compounds **2a**, **3a** . (CDCl<sub>3</sub>, 400Mz, TMS as internal Standard)

H	<b>2a</b> *	<b>3a</b>
1	+	6.01 <i>br dd</i>
2	5.42 <i>ddd</i>	6.18 <i>br dd</i>
3	6.42 <i>br d</i>	6.64 <i>br d</i>
10	+	2.15 <i>br d</i>
14	6.30 <i>br s</i>	6.20 <i>br s</i>
15	7.34 <i>dd</i>	7.31 <i>dd</i>
16	7.23 <i>br s</i>	7.13 <i>br s</i>
17	0.86 <i>d</i>	1.02 <i>d</i>
19	1.35 <i>s</i>	1.17 <i>s</i>
20	0.78 <i>s</i>	0.92 <i>s</i>
OMe	3,.70 <i>s</i>	3.72 <i>s</i>

+: Unassigned multiplets.

\*: OAc: 2.08 *s*

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