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# A clerodane derivative from *Grangea maderaspatana*

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**Abstract**

A new clerodane, 15-hydroxy-16-*oxo*-15,16H-hardwickiic acid (15-hydroxycleroda-3,13-dien-15,16-olide-18-oic acid) has been isolated from the aerial parts of *Grangea maderaspatana*, besides the known clerodane diterpenes. © 1999 Elsevier Science Ltd. All rights reserved.

*Keywords: Grangea maderaspatana*; Compositae; Diterpenes; 15-Hydroxy-16-*oxo*-15,16H-hardwickiic acid

## 1. Introduction

*Grangea* is a small genus of herbs and distributed in tropical and sub-tropical parts of the Africa and Asia. *G. maderaspatana* is a common weed usually grown in sandy lands and waste places. Previously steroidal constituents (Iyer & Iyer, 1978), hardwickiic acid, the corresponding 1,2-dehydro-derivative, acetylenic compounds (Pandey et al., 1984), eight new clerodane diterpenes including five clerodane, a *nor* clerodane, a *seco*-clerodane and a *nor*-*seco*-clerodane derivatives along with auranamide (Singh, Jain & Jakupovic, 1988; Singh & Jain, 1990), grangolide and eudesmanolides (Rojatkar, Chiplunkar & Nagasampagi, 1994) have been reported from various parts of this species. Further investigation of its aerial parts afforded a new *trans*-clerodane, named as 15-hydroxy-16-*oxo*-15,16H-hardwickiic acid (**1**) in addition to previously reported compounds.

## 2. Results and discussion

The compound (**1**) was isolated as colourless gum and purified as its methyl ester. Its structure was established mainly by high field $^1$H-NMR and high resolution mass spectrometry. Its molecular formula $C_{21}H_{30}O_5$ was followed from accurate mass measurements of peak at *m/z* 344.198 $[M\text{-}H_2O]^+$ corresponding to molecular composition $C_{21}H_{28}O_4$. IR spectrum exhibited the presence of, α,β-unsaturated-γ-lactone (1770 $cm^{-1}$), α,β-unsaturated ester (1715 $cm^{-1}$) and hydroxyl group (3300 $cm^{-1}$). The $^1$H-NMR spectrum, when recorded in $CDCl_3$, was very close to that of hardwickiic acid except for lack of the usual furanic proton absorption and the addition of two broad singlets at $\delta$ 6.76 ($J$ = 1.5, 1.5 Hz) and 5.75 ($J$ = 1.5, 1.5 Hz) which could correspond to H-14 and H-15, respectively, in the C-13/C-16 α,β-unsaturated lactone. It was further confirmed from the $^{13}$C chemical shifts of C-13 (135.0), C-14 (143.5), C-15 (99.5) and C-16 (174.0) carbons that we are dealing with a hydroxy-lactone moiety with β-alkyl substituent. The sequence of protons was determined by spin decoupling experiments. A double doublet at $\delta$ 6.60 of H-3 was coupled to H-2α at $\delta$ 2.30 and H-2β at $\delta$ 2.28 each of which was in turn coupled to H-1α at $\delta$ 1.71 and H-1β at $\delta$ 1.53. The nature of the lactone group in the side chain followed from the chemical shift of H-14 at $\delta$ 6.76 which was coupled vicinally to H-15 at $\delta$ 5.75 and allylically to H-12α, β at $\delta$ 2.17 and 2.07, respectively. The chemical shifts of H-17, H-19 and H-20 at $\delta$ 0.82, 1.27 and 0.77 showed that we are dealing with an A/B ring *trans* fused clerodane. Furthermore, the H-17 signal was doubled. Accordingly the epimeric 15-hydroxy de-

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Table 1
$^1H$ and $^{13}C$NMR spectra of compound **1b**

| H (400 MHz) | | C (100 MHz) | |
|---|---|---|---|
| 1 | 1.71 *ddbr* (12, 7, 1) | 1 | 18.0 |
| 1′ | 1.53 *ddd* (12, 11, 5) | 2 | 27.5 |
| 2 | 2.30 *m* | 3 | 139.0 |
| 2′ | 2.28 *m* | 4 | 143.0 |
| 3 | 6.60 *dd* (4, 3) | 5 | 39.0 |
| 6 | 2.32 *m* | 6 | 37.7 |
| 6′ | 1.15 *tbr* (12, 3) | 7 | 28.0 |
| 7 | 1.40–150 *m* | 8 | 37.0 |
| 7′ | 140–150 *m* | 9 | 39.5 |
| 8β | 1.63 *dq* (11, 7) | 10 | 47.0 |
| 10β | 1.38 *dd* (12, 1) | 11 | 36.0 |
| 11 | 1.67 *tbr* (13) | 12 | 20.0 |
| 11′ | 1.50 *tbr* (13) | 13 | 135.0 |
| 12 | 2.17 *tbr* (13) | 14 | 143.5 |
| 12′ | 2.07 *tbr* (13) | 15 | 99.5 |
| 14 | 6.76 *dt* (1.5, 1.5) | 16 | 174.0 |
| 15 | 5.75 *dt* (1.5, 1.5) | 17 | 11.0 |
| 17 | 0.82 *d*, (0.81 d)[a](7) | 18 | 170.0 |
| 19 | 1.27 *s* | 19 | 21.0 |
| 20 | 0.77 *s* | 20 | 19.0 |
| OMe | 3.68 *s* | OMe | 51.0 |

[a] Values of epimer.

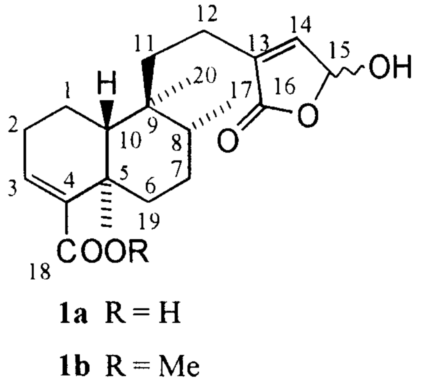
rivatives of (**1**) were present which could not be separated. Earlier the isolation of corresponding epimeric 15-methoxy derivatives (**2**) from this species (Singh et al., 1988) further ascertained the presence of β-butenolide and proposed structure for (**1**) . The detailed assignments of various $^1H$- and $^{13}C$- signals are depicted in Table 1.

## 3. Experimental

IR spectra were measured in $CCl_4$/Nujol and $^1H$- and $^{13}C$-NMR spectra were recorded in $CDCl_3$. Optical rotations were measured in $CHCl_3$ and HPLC were performed using MeOH-$H_2O$ mixture in various proportions. Prep TLC performed on TLC glass plates silica gel $60F_{254}$ precoated layer thickness 0.5 mm. The plant material were obtained from M/S United Chemicals and Allied Products, Calcutta and specimen deposited at RUBL Herbaruim, Jaipur.

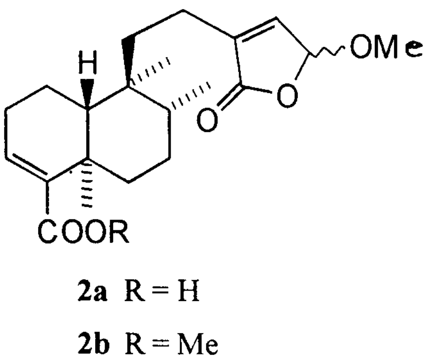
### 3.1. Extraction and isolation

The air-dried aerial parts (2 kg) of *G. maderaspatana* were extracted with $Et_2O$–petrol–MeOH (1 : 1 : 1) at room temperature for 24 h. Evaporation of the solvent under vacuo furnished a greenish semisolid mass which was defatted by dissolving in MeOH (250 ml) and left over night in the refrigerator. Filtered, precipitate was rejected and the filtrate was concentrated and column chromatographed over silica gel (60–120 mesh) and following fractions were collected. Fraction-1 (petrol), fraction-2 (petrol–$Et_2O$, 3 : 1), fraction-3 (petrol–$Et_2O$, 1 : 1) and fraction-4 ($Et_2O$). Fraction-1 gave α-humulene (40 mg). Fraction-2 was a yellow oil and separated on TLC ($C_6H_6$-$CH_2Cl_2$, 1 : 1) affording 200 mg of phytol, 10 mg of 3-hydroxy-8-acetoxy-pentadeca-1,9,14-trien-4,6-diyne, 40 mg of lupeol and 400 mg mixture of diterpene acids, which on subsequent methylation with ethereal solution of $CH_2N_2$ and HPLC separation (MeOH–$H_2O$, 9 : 1) over RP 18 (analytical column) gave 30 mg of methyl 10-epinidoresedoate ($R_t$ 11.8 min), 100 mg of methyl strictiate ($R_t$ 12.7 min), 170 mg mixture of methyl esters of centipedic and nidoresedic acids ($R_t$ 15.0 min) and 100 mg of methyl ester of hardwickiic acid ($R_t$ 16.6 min). Fraction-3 on TLC ($C_6H_6$–$CH_2Cl_2$–$Et_2O$, 4.5 : 4.5 : 1) yielded 6 mg of 3,8-dihydroxy pentadeca-1,9,14-trien-4,6-diyne, 14 mg of *p*-hydroxybenzoic acid and 150 mg complex mixture of diterpene lactones. The latter was treated with $CH_2N_2$ and subsequent HPLC (MeOH–$H_2O$, 9 : 1) gave methyl esters of 15-methoxy-16-*oxo*-15,16H-strictic acid (20 mg, $R_t$ 6.6 min), 15-methoxy-16-*oxo*-15,16H-hardwickiic acid (**2b**) (30 mg, $R_t$ 7.0 min), 15-methoxy-16-*oxo*-nidoresedic acid (16 mg, $R_t$ 7.2 min), *nor*-strictic acid (24 mg, $R_t$ 7.9 min), *nor*-hardwickiic acid (10 mg, $R_t$ 9.4 min) and 2α-acetoxy hardwickiic



**1a** R = H

**1b** R = Me



**2a** R = H

**2b** R = Me

acid (40 mg, $R_t$ 12.4 min). Fraction-4 was a yellow solid mass and separated on TLC ($C_6H_6$–$CH_2Cl_2$–$Et_2O$, 1 : 1 : 1) after treatment with diazomethane affording methyl esters of 16-*oxo*-15,16H-hardwickiic acid (12 mg, $R_f$ 0.30), 16-*oxo*-15,16H-strictic acid (20 mg, $R_f$ 0.28), auranamide (14 mg, $R_f$ 0.25) and compound (**1b**) (30 mg, $R_f$ 0.20).

### *3.2. 15-Hydroxy-16-oxo-15,16H-hardwickiic acid (15–Hydroxycleroda-3,13-dien-15,16-olide-18-oic acid) (**1a**)*

Colourless gum, isolated as its methyl ester, $C_{21}H_{30}O_5$, $[\alpha]_D^{25}$-31° ($CHCl_3$, c 0.20); IR $\nu_{max}$ $CCl_4$ $cm^{-1}$: 3300 (OH), 1770 (γ-lactone), 1715 (C=C–COOR); MS *m/z* (rel. int.): 344.198 $[M\text{-}H_2O]^+$ (25) (calc for $C_{21}H_{28}O_4$: 344.198), 329 $[344\text{-}Me]^+$ (15), 297 $[329\text{-}MeOH]^+$ (10); $^1H$- and $^{13}C$-NMR ($CDCl_3$), Table 1.

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