

NEO-CLERODANE DITERPENOIDS FROM *BACCHARIS MACRAEI*

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Abstract—From the aerial parts of *Baccharis macraei* two new clerodane diterpenes, bacchasmacranone and 2 β -hydroxybacchasmacranone, were isolated besides the known hardwickiic and hauriwaic acids. The structures of the new compounds were elucidated by spectroscopic methods.

INTRODUCTION

So far, ca 15% of the known *Baccharis* species have been chemically examined. Diterpenes with the beyerane, kaurene and clerodane types of carbon skeletons have been isolated, the latter being the most abundant and of varied structural diversity. A number of aromatic compounds have also been reported in the genus [1–3]. This paper describes the isolation and characterization of four clerodane derivatives present in *Baccharis macraei*, a shrub that grows in the littoral zone of central Chile [4].

Two of the terpenoids were identified as (–)-hardwickiic acid (**1**) and (–)-hauriwaic acid (**4**). The other two compounds, for which we propose the names bacchasmacranone (**2**) and 2 β -hydroxy-bacchasmacranone (**3a**), are new.

RESULTS AND DISCUSSION

The dichloromethane extract of the aerial parts of *B. macraei* was subjected to column chromatography on silica gel, using increasing proportions of ethyl acetate in petrol ether to afford (–)-hardwickiic acid (**1**) [5],

bacchasmacranone (**2**), 2 β -hydroxy-bacchasmacranone (**3a**) and (–)-hauriwaic acid (**4**) [6].

Compound **2**, analysed for C₂₀H₂₄O₄ by both mass spectral ([M]⁺ at *m/z* 328) and ¹³C NMR methods. The nature of a β -monosubstituted furan-clerodane diterpene was evident from the ¹H NMR spectrum of **2** (Table 1), which showed signals for two α -furan protons at δ 7.40 and 7.28 and one β -furan proton at δ 6.30, a secondary and a tertiary methyl group at δ 1.02 and 0.64 respectively, and also typical absorptions for an α,β -unsaturated-18,19-clerodanolide (δ 6.89, *dd*, H-3; 3.94, *dd*, H-19; 4.03, *d*, H-19'; IR: 1770 cm⁻¹) [7, 8]. The remaining oxygen atom in the molecule was part of a carbonyl function because the IR spectrum showed an absorption band at 1710 cm⁻¹. The location of this function at C-7 was deduced from the ¹³C NMR spectrum of compound **2** (Table 2) which showed the expected deshielding effects on C-6 and C-8 and also a pronounced γ -effect on the equatorial C-8 methyl group, in a similar fashion as found in eremone [9]. The assignments of the remaining signals in the ¹³C NMR spectrum of **2** were made on the basis of the observed multiplicities (APT), empirical shift rules [10] and comparison with reported ¹³C NMR spectral data of similar derivatives [7, 8, 11]. The observed values are completely in accord with structure **2** and bacchasmacranone corresponded thus to 7-oxo-hauriwaic acid lactone.

The IR spectrum of compound **3a**, C₂₀H₂₄O₅ ([M]⁺ 344), indicated the presence of a furan ring, an olefinic double bond, a lactone, a ketone and hydroxyl groups (see Experimental). Acetylation of **3a** gave a crystalline monoacetate **3b**, the IR spectrum of which showed no hydroxyl absorption. The ¹H NMR spectrum of **3b** was very informative, since most signals were well resolved and readily assigned after analysis of the contour plot of the two dimensional homonuclear ¹H–¹H chemical shift correlation diagram. Thus, the following assignments for the ring A protons could be made, which are in agreement with structure **3b**. The signal at δ 5.46 (shifted to δ 4.63 in **3a**) was assigned to the equatorial H-2. This signal was coupled to the olefinic H-3 at δ 6.85 (*J* = 7.4 Hz) and also with the protons of a methylene group at δ 2.09 and 1.51, assigned to H-1 β and H-1 α , respectively. The latter is further coupled to a doublet (*J* = 13.9 Hz) at δ 2.97 (H-10). These assignments are in agreement with those

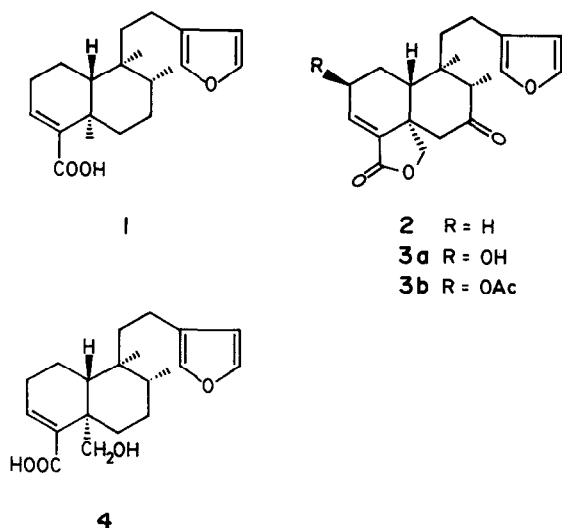


Table 1. ^1H NMR spectral data of compounds **2**, **3a**, and **3b** (250 MHz, CDCl_3 , TMS as int. standard)

H	2	3a	3b*
1 α	1.24 dddd (12.5, 12.5, 12.5, 4.0) [†]	1.40 ddd (3.1, 13.8)	1.51 ddd (2.1, 13.9)
1 β	1.87 m	1.99 d(br) (13.8)	2.09 d(br) (14.0)
2 α		4.63 dt (2.9, 6.4)	5.46 dt (2.4, 7.4)
3	6.89 dd (2.2, 7.4)	6.82 d (6.4)	6.85 d (7.4)
6 α	2.38 d(br) (12.5)	2.47 dd (2.1, 12.3)	2.48 d(br) (12.5)
6 β	2.73 d (12.5)	2.73 d (12.3)	2.73 d (12.5)
8 β	2.69 q (6.6)	2.76 q (6.6)	2.76 q (6.7)
10	2.40 d(br) (13.0)	3.13 d(br) (13.8)	2.97 d(br) (13.9)
14	6.30 s(br)	6.29 s(br)	6.26 s(br)
15	7.40 t (1.6)	7.37 t (1.5)	7.38 t (1.6)
16	7.28 s	7.26 s	7.24 s
17	1.02 d (6.6)	1.03 d (6.6)	1.05 d (6.7)
19	3.94 dd (2.2, 8.2)	3.91 dd (2.1, 8.3)	3.94 dd (2.0, 8.3)
19'	4.03 d (8.2)	4.03 d (8.3)	4.00 d (8.3)
20	0.64 s	0.64 s	0.64 s
Ac			2.10 s

* Two multiplets for 2H each at δ 2.48 and 1.72 should correspond to the H-11 and H-12 protons.[†] J in Hz.Table 2. ^{13}C NMR spectral data of compounds **2** and **3b** (62.5 MHz, CDCl_3 , TMS as int. standard)

C	2	3b
1	20.3	25.4
2	27.3	65.8
3	136.1	129.9
4	138.5	141.7
5	47.8	47.8
6	50.6	50.0
7	209.6	208.6
8	51.5	51.5
9	43.8	43.0
10	48.1	40.2
11	38.0	38.2
12	18.6	18.2
13	124.0	123.9
14	110.7	110.5
15	143.1	143.2
16	137.2	138.5
17	7.7	7.7
18	168.0	169.7
19	71.2	70.1
20	18.9	18.9
MeCO		167.8
MeCo		20.7

reported for teugin and articuline, diterpenoids with the same A ring as compound **3b** [12, 13]. The remaining signals in the ^1H NMR spectrum of **3a** and **3b** were very similar to those exhibited by bacchasmacranone (**2**) (Table 1). The ^{13}C NMR spectrum of **3b** confirmed all the above results, including the β -axial disposition of the acetoxyl group at C-2 (cf. C-10 in **2**) and also defined the relative configuration of 2 β -acetyl-bacchasmacranone as shown in the formulae.

The neo-clerodane absolute configuration [14] of 2 β -hydroxybacchasmacranone was established by application of the Horeau method [15] which defined as *S* the absolute configuration of its C-2 axial alcohol (see Experimental).

EXPERIMENTAL

Mps: uncorr; ^1H NMR: 60 or 250 MHz in CDCl_3 with TMS as int. standard; ^{13}C NMR: 62.5 MHz, CDCl_3 with TMS as int. standard. Assignments of ^{13}C NMR chemical shifts were made with the aid of APT at 62.5 MHz. IR: film on NaCl or KBr pellets; MS: direct inlet. 70 eV.

Baccharis macraei Hook et Arn., collected in Concón, Viña del Mar, Chile, in May 1985, was identified by Dr. Otto Zoellner, (Universidad Católica de Valparaíso). A voucher specimen is deposited at Universidad Federico Santa María.

The aerial parts of *B. macraei* (500 g) were extracted at room temp. with CH_2Cl_2 for 12 hr, affording 40 g of a clear syrup. This crude material (10 g) was chromatographed on a silica gel column (400 g) and eluted with mixtures of petrol and EtOAc of increasing polarity. Fractions of 100 ml were taken and combined based upon TLC monitoring, yielding the following compounds in order of elution: (–)-hardwickiic acid (**1**, 60 mg), a mixture of oleanolic acid and bacchasmacranone (**2**), 2 β -hydroxybacchasmacranone (**3a**, 180 mg) and (–)-hautriwaic acid (**4**, 40 mg). The mixture of oleanolic acid and **2** (330 mg), after treatment with CH_3N_2 , was rechromatographed on a silica gel column (40 g) and eluted with petrol–EtOAc (3:1), yielding oleanolic acid methyl ester (60 mg) and **2** (205 mg).

Bacchasmacranone (**2**). Mp 126–127° (*n*-hexane–EtOAc); $[\alpha]_D^{25} -176.4^\circ$ (CHCl_3 ; *c* 0.62). IR $\nu_{\text{max}}^{\text{KBr}} \text{cm}^{-1}$: 3120, 2980–2860, 1770, 1710, 1660, 1470, 1280, 1200, 1160, 1025, 880; UV $\lambda_{\text{max}}^{\text{EtOH}} \text{nm}$: 209 (ϵ 12 331); ^1H and ^{13}C NMR: Tables 1 and 2. MS m/z (rel. int.): 328 $[\text{M}]^+$ (26), 233 $[\text{M} - \text{C}_6\text{H}_7\text{O}]^+$ (100), 135 (28), 121 (20), 95 $[\text{C}_6\text{H}_7\text{O}]^+$ (59), 91 (42), 82 (20), 81 $[\text{C}_5\text{H}_5\text{O}]^+$ (98), 55 (20), 53 (35).

2 β -Hydroxybacchasmacranone (**3a**). Mp 198–199° (petrol–EtOAc); $[\alpha]_D^{25} -220.0^\circ$ (CHCl_3 –MeOH; *c* 0.60). IR $\nu_{\text{max}}^{\text{KBr}} \text{cm}^{-1}$:

3440, 3120, 2980, 2860, 1780, 1700, 1650, 1480, 1280, 1200, 1170, 880, 810. UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm: 240 (ϵ 15 334); $^1\text{H NMR}$: Table 1. MS m/z (rel. int.): 344 [M] $^+$ (8), 284 [$\text{M} - \text{C}_2\text{H}_4\text{O}_2$] $^+$ (82), 249 [$\text{M} - \text{C}_6\text{H}_7\text{O}$] $^+$ (20), 231 [$\text{M} - \text{C}_6\text{H}_7\text{O} - \text{H}_2\text{O}$] $^+$ (23), 152 (28), 137 (65), 95 [$\text{C}_6\text{H}_7\text{O}$] $^+$ (62), 81 [$\text{C}_5\text{H}_5\text{O}$] $^+$ (100), 69 (40), 55 (83), 53 (40).

2 β -Hydroxybacchasmacranone acetate (3b). Compound **3a** (100 mg) was treated with Ac_2O (3.0 ml) and pyridine (0.5 ml) at room temp. for 24 hr. After addition of EtOH, the reaction mixture was evapd to dryness and the white solid residue was washed with EtOH, filtered and pure 2 β -hydroxybacchasmacranone acetate (**3b**, 80 mg) was obtained as colourless crystals, mp 163–164 $^\circ$ (CHCl_3 –EtOH). $[\alpha]_{\text{D}}^{25} - 277.4^\circ$ (CHCl_3 ; c 1.004). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3120, 2980–2880, 1780, 1745, 1710, 1595, 1240, 1220, 1040, 890; ^1H and $^{13}\text{C NMR}$: Tables 1 and 2. MS m/z (rel. int.): 386 [M] $^+$ (14.3), 326 [$\text{M} - \text{HOAc}$] $^+$ (12.5), 291 [$\text{M} - \text{C}_6\text{H}_7\text{O}$] $^+$ (10.7), 231 [$326 - \text{C}_6\text{H}_7\text{O}$] $^+$ (100), 95 ($\text{C}_6\text{H}_7\text{O}$] $^+$ (53.6), 81 [$\text{C}_5\text{H}_5\text{O}$] $^+$ (75.0), 43 (67.9).

Application of Horeau method [15] to compound 3a. A mixture of (\pm)- α -phenylbutyric anhydride (2.1 mmol) and compound **3a** (1.05 mmol) in pyridine (2 ml) was kept at room temp. for 18 hr; usual work up gave 95% yield of ester and α -phenylbutyric acid, $[\alpha]_{\text{D}}^{25} = +9.2$. Optical yield 28.6%.

Hardwickiic and hautriwaic acids were identified by comparison of their physical (mp, $[\alpha]_{\text{D}}^{25}$) and spectroscopic ($^1\text{H NMR}$ and MS) properties with those reported in the literature [5,6 and references cited therein].

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