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NEO-CLERODANE DITERPENOIDS FROM *BACCHARIS INCARUM*

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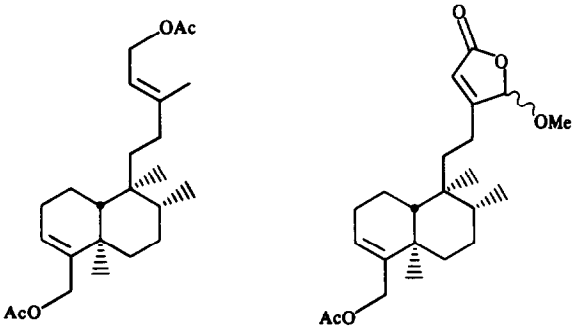
Key Word Index—*Baccharis incarum*; Compositae; Astereae; diterpenes; clerodanes.

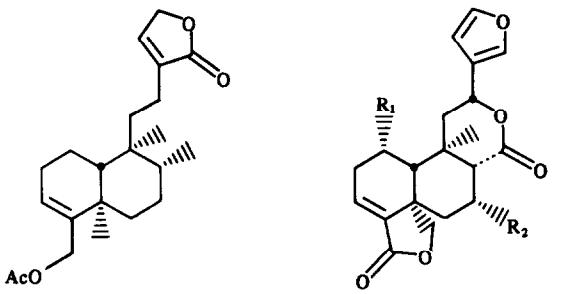
Abstract—Five new neo-clerodane diterpenoids were isolated from *Baccharis incarum*. Their structures were established by spectroscopic methods.

INTRODUCTION

In a preceding paper [1] we reported the isolation and structural elucidation of a number of neo-clerodane diterpenoids from *B. incarum* Wedd. A re-investigation of this species using a modified isolation procedure afforded in addition to known compounds, five new clerodane diterpenes: the kolavane derivative **1**, the clerodane lactones **2** and **3**, 7α-hydroxybacchotricuneatin A (**4**) and 1α-acetylbacchotricuneatin A (**5**). Their structures were determined by spectroscopic methods.



1 **2**



3

4 R_1 = H R_2 = OH
5 R_1 = OAc R_2 = H

RESULTS AND DISCUSSION

The ^{1}H NMR spectrum of **1** exhibited typical signals for a bicyclic clerodane carbon skeleton (Table 1): two tertiary, one secondary and one vinyl methyl groups, the latter long-range coupled to an olefinic proton at δ5.37, which was in turn coupled to an acetoxyl methylene group. The *trans*-clerodane configuration of **1** was deduced from the absorptions at δ1.06, assigned to the α-axial C-5 methyl group. In related *cis*-clerodanes, the C-18 acetoxyl substituent deshields this methyl group by 0.15 ppm [1, 2]. The chemical shifts of the C-9 and C-8 methyl groups are also in agreement with the relative configuration shown in **1** [3]. The *E*-configuration of the 13,14-double bond was suggested by comparison of the H-14 and H-16 absorptions with those of similar kolavane derivatives [4].

The IR spectra of compounds **2** and **3** showed absorptions due to α,β-unsaturated γ-lactones (1750 cm^{-1}) and ester functions (1730 cm^{-1}). Their ^{1}H NMR spectra (Table 1) also displayed similar signals of nearly identical chemical shifts assigned to acetoxyl methylene groups, two tertiary and one secondary methyl groups and one olefinic proton. The nature of their side chains followed from the corresponding ^{1}H NMR signals which were in agreement with a β-substituted γ-butenolide in **2** and an α-substituted γ-butenolide in **3**. An extra methoxyl signal in the ^{1}H NMR spectrum of **2** indicated that this compound was a mixture of C-16 epimers. The relative configurations depicted in **2** and **3** were based on the same arguments as discussed above.

Compound **4**, $C_{20}H_{22}O_6$, showed absorptions in the IR spectrum assigned to a δ-lactone (1740 cm^{-1}), another lactone group, probably an α,β-unsaturated γ-lactone (1755 cm^{-1}), double bonds (3120, 1650, 870 cm^{-1}) and a hydroxyl group (3550 cm^{-1}). Its ^{1}H NMR spectrum showed the presence of a β-substituted furan ring, only one tertiary methyl group and the absence of the signal typical of the secondary methyl group at C-8 present in the usual clerodane diterpenes of *Baccharis*. These facts suggested a structure related to bacchotricuneatin A (**4**, $R_1 = R_2 = H$), a compound originally isolated from *B. tricuneata* [5]. Placement of the extra hydroxyl group of **4** at C-7 and its axial orientation was indicated by the couplings of H-7 ($W_{1/2}$ = 7 Hz), the narrow doublet (3.0 Hz) at δ2.67 assigned to H-8 and the strong deshielding effect exerted on the *exo* H-19 methylene proton (δ5.34) as compared to the *endo* H-19 (δ3.93) which also showed the expected *W* coupling [3] with H-6β. The corresponding values for the *exo* and *endo* H-19 in

Table 1. ^{1}H NMR data of compounds 1–5 (60 MHz for 1 and 250 MHz for 2–5, $CDCl_3$, TMS as internal standard)*

H	1	2	3	4†	5‡
3	5.62 *m* ($W_{1/2}$ = 8 Hz)	5.52 *m* ($W_{1/2}$ = 7.5 Hz)	5.53 *m* ($W_{1/2}$ = 6.0 Hz)	6.73 *dd* (7.3, 2.1)	6.57 *dd* (6.6, 1.9)
14	5.37 *t* (*br*) (7.0)	5.67 *s* (*br*)	7.07 *s* (*br*)	6.44 *s* (*br*)	6.39 *d* (1.0)
15	4.60 *d* (7.0)		4.73 *s* (*br*)	7.48 *s* (*br*)	7.44 *s* (*br*)
16	1.72 *s* (*br*)	6.71 *s* (*br*)		7.45 *s* (*br*)	7.41 *t* (1.5)
17	0.80 *d* (6.0)	0.76 *d* (5.2)	0.78 *d* (6.1)		
18	4.56 *s* (*br*)	4.44 *s* (*br*)	4.47 *s* (*br*)		
19				5.34 *d* (7.5)	4.45 *dd* (7.7, 1.9)
	1.06 *s*	1.0 *s*	1.02 *s*		
19′				3.93 *dd* (7.5, 2.2)	4.33 *d* (7.7)
20	0.76 *s*	0.69 *s*	0.71 *s*	1.14 *s*	0.89 *s*
Ac	2.06 *s*	2.00 *s*	2.02 *s*		2.02 *s*
OMe		3.50 *s*			
		3.51 *s*			

*Values in parentheses are coupling constants in Hz.

†1.41 *m* (H-6β); 2.53 *dd* (14.4, 2.2, H-6α); 2.67 *d* (3.0, H-8); 4.67 *m* ($W_{1/2}$ = 7 Hz, H-7β); 5.39 *dd* (10.2, 7.4, H-12).

‡2.63 *dd* (11.9, 3.9, H-8); 5.38 *dd* (10.4, 6.3, H-12); 5.46 *m* ($W_{1/2}$ = 8.3 Hz, H-1β).

bacchotricuneatin A are δ4.22 and 3.99, respectively. This effect, due to the 1,3-diaxial interaction caused by the 7α-hydroxyl group, was also reflected in the downfield shift (0.30 ppm) of H-20 in **4** when compared to that of bacchotricuneatin A. The remaining signals in the ^{1}H NMR spectrum, including the couplings were very similar to those of bacchotriacuneatin A. Accordingly, the stereochemistry of 7α-hydroxybacchotricuneatin A (**4**) was the same.

The spectroscopic data of compound **5** were very similar to those of **4** and its structure and stereochemistry was easily deduced from the ^{1}H NMR spectra. Again, placement of an axial acetyl group at C-1 induced a downfield shift of the *endo* H-19. Further evidence for the proposed stereochemistry was obtained by examination of the ^{13}C NMR spectrum of **5** (see Experimental) which showed, after comparison with that of bacchotricuneatin A [5], the expected downfield shifts for C-1, C-2 and C-10 and an upfield shift of 6.3 ppm for C-3. Thus, compound **5** corresponded to 1α-acetylbacchotricuneatin A (the 1α-hydroxyl derivative of **5** was recently reported for the first time from *Liatris spicata* [6]).

The absolute configuration of compounds **1**–**5** was not established but it very probably corresponds to that shown in the formulae in keeping with the neo-clerodane [7] configuration exhibited by all the clerodane diterpenoids isolated so far from *Baccharis* whose absolute configuration has been rigorously established [5, 8–12].

EXPERIMENTAL

Isolation procedure. Dried and ground plant material [1] (2.5 kg) was percolated at room temp. with MeOH for 36 hr. The MeOH extract (500 g) was first partitioned between $CHCl_3$ and MeOH–H_2O (1:9), then the $CHCl_3$, solubles were partitioned between petrol and MeOH–H_2O (9:1) to give 60 g of aq. MeOH solubles. This extract was fractionated by flash-CC on silica gel eluted with mixtures of increasing polarity of petrol and EtOAc. Compounds **1**–**5** were isolated after repeated chromatography (silica gel) of suitable fractions.

Compound **1**. 85 mg. Oil. $[\alpha]_D^{25} = -31.4°$ ($CHCl_3$; *c* 0.83). IR ν_{max}^{film} cm^{-1}: 1720, 1670, 1240. EIMS *m/z* (rel. int.): 331 [M − AcO]$^+$ (4), 316 [331 − Me]$^+$ (2), 274 (12), 256 (13), 201 (20), 187 (60), 159 (58), 119 (81), 105 (100).

Compound **2**. 282 mg. Oil. $[\alpha]_D^{25} = -152.2°$ ($CHCl_3$; *c* 0.84). IR ν_{max}^{film} cm^{-1}: 1750, 1730, 1660, 1230. EIMS *m/z* (rel. int.): 330 [M − AcOH]$^+$ (18), 272 (23), 204 (23), 189 (80), 187 (100), 175 (25), 159 (60), 119 (90), 105 (75).

Compound **3**. 185 mg. Oil. $[\alpha]_D^{25} = -22.8°$ ($CHCl_3$; *c* 0.55). IR ν_{max}^{film} cm^{-1}: 1745, 1720, 1660, 1230. EIMS *m/z* (rel. int.): 300 [M − AcOH]$^+$ (4), 285 [300 − Me]$^+$ (7), 205 (10), 203 (25), 189 (40), 134 (38), 121 (100), 105 (55).

7α-Hydroxybacchotricuneatin A (**4**). 72 mg. Mp 242–243° (Me_2CO). $[\alpha]_D^{25} = -154.6°$ ($CHCl_3$; *c* 0.24). IR ν_{max}^{KBr} cm^{-1}: 3550, 3120, 1755, 1740, 1650, 870. EIMS *m/z* (rel. int.): 358 [M]$^+$ (5), 340 [M − H_2O]$^+$ (5), 328 (45), 312 (15), 190 (24), 121 (100), 95 (41), 94 (40), 81 (24).

1α-Acetylbacchotricuneatin A (**5**). 40 mg. Mp 203–205° (Et_2O). $[\alpha]_D^{25} = -121.3°$ ($CHCl_3$; *c* 0.40). IR ν_{max}^{KBr} cm^{-1}: 1750, 1730, 1720, 1660, 1240. EIMS *m/z* (rel. int.): 400 [M]$^+$ (8), 342 (7), 283 (7), 279 (8), 263 (22), 239 (8), 205 (20), 149 (50), 117 (100), 116 (95), 95 (23), 94 (17), 82 (50), 81 (18). ^{13}C NMR (62.9 MHz, $CDCl_3$, TMS as internal standard): δ173.1 (*s*, C-17), 170.1 (*s*, Ac), 168.5 (*s*, C-18), 144.2 (*d*, C-15), 137.0 (*s*, C-4), 129.9 (*d*, C-3), 124.4 (*s*, C-13), 108.6 (*d*, C-14), 72.6 (*t*, C-19), 70.1 (*d*, C-12), 66.0 (*d*, C-1), 54.6 (*d*, C-8), 48.5 (*d*, C-10), 44.7 (*s*, C-5), 42.7 (*t*, C-11), 37.2 (*s*, C-9), 34.3 (*t*,

C-2), 33.3 (*t*, C-6), 21.5 (*q*, C-20), 21.5 (*q*, Ac), 19.6 (*t*, C-7).

Bacchalineol [13] and its malonate half-ester and *O*-methyl ester derivatives were also isolated from *B. incarum*. Their identities were confirmed by comparison of their spectroscopic data with that of the literature [13].

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