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NEO-CLERODANE DITERPENOIDS FROM *BACCHARIS RHOMBOIDALIS*

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Key Word Index—*Baccharis rhomboidalis*; Compositae; Astereae; diterpenes; clerodanes; ^{13}C NMR.

Abstract—Three new neo-clerodane diterpenoids were isolated together with other known clerodanes from *Baccharis rhomboidalis*. Their structures were established by spectroscopic methods.

INTRODUCTION

As a continuation of our chemical investigations of the genus *Baccharis* [1], we have studied *B. rhomboidalis* Remy from Central Chile. Besides compounds **1** and **5** [2] already isolated from other *Baccharis* species, a new neo-clerodane dilactone (**7**) and three other new clerodane diterpenoids **3**, **4** and **6** were found. The new compounds were characterized by spectroscopic methods and some chemical transformations.

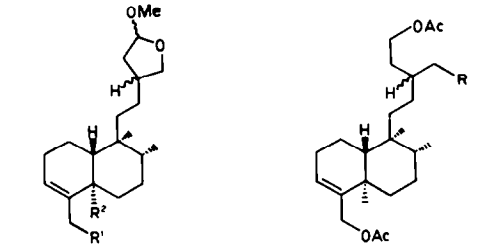
RESULTS AND DISCUSSION

Compounds **1**–**4** were shown to correspond to inseparable mixtures of epimeric cyclic acetals. Compound **3** differed in its ^{1}H NMR spectrum from that of **1** by the replacement of the tertiary methyl group by a hydroxymethylene group (Table 1). Acetylation of **3** afforded a diacetate, identical in all respects to the natural product **4** also isolated in this work. Comparison of the ^{13}C NMR spectra of compounds **1** and **3** (Table 2) indicated C-19 as the site of the additional hydroxyl group in **3** and also confirmed the relative configuration shown in the formulae [1, 3].

Compound **6** was shown to correspond to a clerodane-type diterpene possessing three primary acetoxyl groups, one trisubstituted double bond, two tertiary methyl groups and one secondary methyl group. Again, comparison of the ^{13}C NMR spectra of compound **6** with that of **5** (Table 2), also isolated from *B. rhomboidalis*, showed that the acetyl groups were located at C-15, C-16 and C-18.

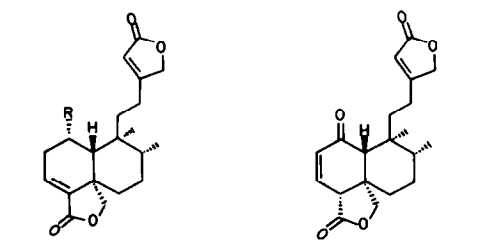
The combined UV and IR data of compound **7**, $C_{20}H_{26}O_5$, indicated the presence of α,β unsaturated-γ-lactone and hydroxyl groups. Compound **7** was readily acetylated and then oxidized to a ketone which exhibited new IR bands at 1718 and 1680 cm^{-1}, respectively. The ^{1}H NMR spectrum of **7**, showed a one-proton multiplet at δ4.20 (shifted to δ5.40 in the acetylated derivative), a narrowly split triplet at δ6.0 which showed long-range coupling to a 2H doublet, which was characteristic of a proton on the α-carbon of a β-substituted butenolide ring [4]. It also showed signals assigned to an olefinic proton at δ6.50, a tertiary and a secondary methyl group at δ0.90 and 0.82, respectively and an AB-system at δ4.62 and 4.43. Mild oxidation of **7** afforded an α,β-unsaturated ketone (see Experimental) which showed in its ^{1}H NMR spectrum a new set of signals at δ6.12 and 6.50 (*dd*, 10 and 3.0 Hz) coupled to a triplet at δ3.15, together with the concomitant disappearance of the methine and olefinic protons at δ4.20 and 6.50, respectively. These findings were in agreement with the position of the secondary hydroxyl at C-1 in **7** and isomerization of the 3,4-double bond in the newly formed α,β-unsaturated ketone as shown in **9**. The axial α-orientation of the 1-hydroxyl group in **7** (and of the 1-acetoxyl group in **8**) was suggested by the narrow multiplet ($W_{1/2}$ = 7.6) assigned to the equatorial proton at C-1 in these compounds.

The stereochemistry of compound **7** and of its deriva-



	1	2	3	4
R'	OH	OAc	OH	OAc
R²	Me	Me	CH_2OH	CH_2OAc

	5	6
R	H	OAc



	7	8
R	OH	OAc

9

Table 1. ^{1}H NMR data of compounds 3–9 [60 MHz (4 and 7), 100 MHz (8) or 250 MHz (3, 6 and 9), $CDCl_3$, TMS as int. standard]

H	3	4	6	7*	8	9†
1				4.20 m‡ ($W_{1/2}$ = 7.6)	5.40 m‡ ($W_{1/2}$ = 7.8)	
3	5.69 *t* (3.6)	5.73 *s* (*br*)	5.53 *t* (3.0)	6.50 *t* (4.0)	6.60 *dd* (6.0, 4.0)	6.50 *dd* (10.0, 3.1)
14				6.0 *m** ($W_{1/2}$ = 4.0)	5.90 *m*‡ ($W_{1/2}$ = 4.0)	5.80 *t* (1.5)
15	4.98 *t* (2.8)* 4.95 *d* (5.1)	5.07 *d* (5.0)	4.07 *t* (6.6)			
16	3,43 *t* (7.9) 3.37 *t* (7.9)	3.97 *t* (8) 3.35 *t* (8)	3.96 *d* (4.7)	4.90 *d* (2.0)	4.82 *d* (2.0)	4.68 *s* (*br*)
16′	3.90 *t* (7.9) 3.40 *t* (7.9)					
17	0.78 *d* (6.1)	0.79 *d* (6.0)	0.74 *d* (5.6)	0.82 *d* (5.0)	0.89 *d* (5.0)	0.85 *d* (5.9)
18			4.42 *d* (12.8)			
	4.37 *s* (*br*)	4.59 *s* (*br*)				
18′			4.45 *d* (12.8)			
19	4.17 *d* (11.4)	4.48 *d* (11)		4.62 *d* (4.0)	4.50 *dd* (8.0, 1.0)	4.35 *d* (9.5)
			1.01 *s*			
19′	3.80 *d* (11.4)	4.07 *d* (11)		4.43 *d* (4.0)	4.38 *d* (8.0)	4.06 *d* (*br*) (9.5)
20	0.72 *s*	0.74 *s*	0.67 *s*	0.90 *s*	0.78 *s*	0.90 *s*
OMe	3.02 *s* 3.30 *s*	3.30 *s* 3.33 *s*				
Ac		2.02 *s*	2.01 *s* (6H)			
					2.09 *s*	
		2.04 *s*	2.02 *s* (3H)			

*In DMSO-d_6.
†6.12*dd* (10.0, 2.8), H-2; 3.15 *t* (3.0), H-4 and 2.62 *s*, H-10.
‡Values in parentheses are coupling constants in Hz and half-band width of multiplets in Hz.

Table 2. ^{13}C NMR data of compounds 1–9 [20.1 MHz (1, 3, 5, 6) or 62.5 MHz (8, 9), $CDCl_3$, TMS as int. standard]*

C	1	3	5	6	8	9
1	18.2	17.1	17.1	17.8	65.4	197.2
2	26.5†	26.7†	26.4†	26.5†	34.1	132.6
3	121.1	129.0	125.8	125.8	128.9	137.6
4	147.5	145.0	142.6	142.5	137.1	52.3*
5	37.5	39.1	37.6	37.6	44.6	43.9
6	37.0	30.9	35.9	35.9	32.6	33.8
7	26.2†	26.3†	27.7†	26.9†	27.3	26.5
8	36.1	36.2	35.9	35.9	37.3	37.2
9	38.4	38.5	38.3	38.4	38.9	38.2
10	46.1	46.1	45.8	45.9	48.6	53.0*
11	37.2	37.0	35.3	34.9	35.2	35.6
12	27.2	27.1	29.4	23.7	21.6	23.0
13	37.6	37.3	30.3	31.7	169.6	170.1
14	39.2	42.8	35.2	29.2	114.9	115.5
15	105.5 105.0	105.5 105.0	62.8	62.4	173.3	170.2
16	72.0 71.7	72.3 71.7	19.5	66.0	72.6	72.1
17	15.9	15.7	15.7	15.8	17.7	16.3
18	62.3	64.0	64.8	64.8	168.5	173.3
19	21.2	64.6	70.8	70.8	72.6	73.0
20	18.2	18.7	18.2	18.3	14.8	14.9
OMe	54.8 54.3	54.7 54.3	—	—	—	—
MeCO	—	—	20.9	20.9	20.9	—
MeCO	—	—	168.9	170.8	169.5	—

*Multiplicity were obtained with proton-flip method (APT).
†Interchangeable.

tives was ascertained from the combined evidence of their ^1H and ^{13}C NMR spectra in comparison with the data of a large group of related clerodanes [5, 6]. Thus, the chemical shifts of the tertiary and secondary methyl groups at C-9 and C-8 respectively were in agreement with the data of compounds having both of these substituents as alpha on a *trans*-clerodane skeleton [7]. The W coupling exhibited by the α H-19 in **8** and **9** confirmed the α-axial configuration of the C-19 methylene group in agreement with *trans* clerodanes having an axial methyl group at C-5 and an axial H-6 [8].

The neo-clerodane absolute configuration [9] of compound **7** was established by application of the Horeau method [10] which defined as *S* the absolute configuration of its C-1 axial alcohol (see Experimental). The absolute configuration of compounds **3** and **6** was not established, but it very probably corresponds to that shown in the formulae since all the clerodane terpenoids isolated from *Baccharis* so far have the neo-clerodane configuration.

EXPERIMENTAL

Plant material. Leaves and top parts of *Baccharis rhomboidalis* Remy were collected in Cajón del Maipo, Santiago, in December. Voucher specimens are kept at the Herbarium (M.M.), Facultad de Ciencias, Universidad de Chile.

Isolation procedure. Dried and ground plant material (3.2 kg) was percolated at room temp. with petrol (60–80°) (3 × 15 l.), then with 95% EtOH (3 × 15 l.) for 48 hr. The EtOH extract (400 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 110 g aq. MeOH solubles. This extract was fractionated by flash-CC on silica gel eluted with mixtures of increasing polarity of petrol and EtOAc. Compounds **1–8** were isolated after repeated chromatography (silica gel) of suitable fractions and further purified by preparation of the acetylated derivatives.

Compound **3**. 120 mg, mp 129–133° (Me_2CO). IR ν_{max}^{KBr} cm^{-1}: 3200, 3000–2900, 1490, 1220, 1040; ^1H NMR: Table 1; ^{13}C NMR: Table 2; MS *m/z* (rel. int.): 334 $[M-H_2O]^+$(14), 321 $[M-CH_2O]^+$(9), 303 (2.4), 289 (9), 273 (8.7), 272 (37), 271 (33), 263 (10), 227 (10), 189 (6), 187 (9), 175 (40), 174 (21), 173 (100), 147 (32), 145 (67).

Compound **4**. Oil (640 mg). IR ν_{max}^{film} cm^{-1}: 1720, 1240; ^1H NMR: Table 1; MS *m/z* (rel. int.): 376 $[M-AcOH]^+$ (4.2), 304 (5.4), 271 (100), 189 (22.2), 187 (41.3), 173 (40.5).

Compound **6**. Oil (502 mg). IR ν_{max}^{film} cm^{-1}: 2950, 1740, 1670, 1240, 1220; ^1H NMR: Table 1; ^{13}C NMR: Table 2; MS *m/z* (rel. int.): 390 $[M-AcOH]^+$(6.3), 375 (1.5), 315 (1.5), 255 (21), 189 (91), 120 (54), 119 (75), 109 (55), 107 (54), 106 (39), 105 (100).

Compound **7**. 307 mg, mp 234–235° (MeOH). $[\alpha]_D^{25}$ −60.5 ($CHCl_3$–MeOH, 4:1; *c* 0.18). IR ν_{max}^{KBr} cm^{-1}: 3485, 3120, 2970, 1755, 1730, 1670, 1645; UV λ_{max} 216 nm (16090); MS *m/z* (rel. int.): 328.1600 $[C_{20}H_{24}O_4, M-H_2O]$ (7.9), 316.1609 $[C_{19}H_{24}O_4, M-CH_2O]$ (42.2), 298.1600 $[C_{19}H_{22}O_3]$ (12.3), 287.1303 $[C_{17}H_{19}O_4]$ (100), 231.1369 $[C_{15}H_{19}O_2]$ (45.8), 205.1242 $[C_{13}H_{17}O_2]$ (60.6), 173.1133 $[C_9H_{17}O_3]$ (40.4), 159.1165 $[C_{12}H_{15}]$ (85.2); ^1H NMR: Table 1.

Compound **8**. Acetylation of **7** (Ac_2O–pyridine) gave **8**, mp 225° ($CHCl_3$–hexane). IR ν_{max}^{KBr} cm^{-1}: 2950, 1755, 1738, 1718, 1620, 1240; ^1H NMR: Table 1; ^{13}C NMR: Table 2.

Compound **9**. Compound **8** (100 mg) was oxidized with pyridinium dichromate (2 g) in 6 ml DMF at 0° for 3 hr. Usual work-up gave **9** (60 mg) mp 219° (EtOH). UV λ_{max} 230 nm (6130); IR ν_{max}^{KBr} cm^{-1}: 3100, 2970, 1770, 1730, 1685, 1630, 1010; ^1H NMR: Table 1; ^{13}C NMR: Table 2; MS *m/z* (rel. int.): 344.1596 $[C_{20}H_{24}O_5]$ (11), 313 (7), 235 (18), 234 $[M-C_6H_6O_2]$ (100), 233 (28), 189 (14), 161 (12), 112 (22), 111 (83), 107 (28).

Compounds **1**, **2** and **5** were identified by comparison of their spectral characteristics with those reported in the lit [2]. The hitherto unreported ^{13}C NMR data of compounds **1** and **5** are listed in Table 2.

Application of Horeau method [10] *to compound* **7**. A mixture of (±)-α-phenylbutyric anhydride (0.49 mmol) and compound **7** (0.23 mmol) in C_5H_5N (2 ml) was kept at room temp. for 18 hr: usual work-up gave 117 mg α-phenylbutyric acid, $[\alpha]_D = -7.0$ and 96 mg of ester. Optical yield 24%.

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