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ENT-LABDANES FROM *BACCHARIS STERNBERGIANA*

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Key Word Index—*Baccharis sternbergiana*; *B. tricuneata*; Compositae; diterpenes; *ent*-labdane derivatives; 12-acetoxytremetone.

Abstract—The aerial parts of *Baccharis sternbergiana* afforded six new *ent*-labdane derivatives, while those of a *Baccharis tricuneata* subspecies gave 12-acetoxytremetone.

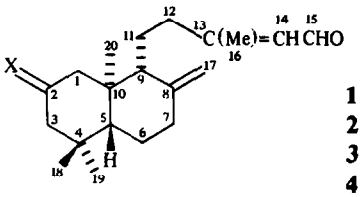
From the large genus *Baccharis* (tribe Astereae), already several species have been studied chemically and some groups have become apparent. We have now investigated the aerial parts of *Baccharis sternbergiana* Steud. In addition to germacrene D, caryophyllene, δ-cadinene, β-curcumene, phytol, taraxasterol, friedelinol, lupeol and its Δ^{12}-isomer, stigmasterol, naringenin 7-*O*-methyl ether and its 7,4′-*O*-dimethyl ether, several diterpenes, the *ent*-labdanes **1**–**6**, were isolated. Oxidation of **1** and **2** afforded the ketones **3** and **4**, respectively. Compound **3** had earlier been prepared by oxidation of *ent*-2β-hydroxymanool [1]. Clearly the keto aldehyde **4** differed from **3** only in the stereochemistry of the 13,14-double bond. As could be deduced from the ^{1}H NMR spectrum (Table 1), **3** was an *ent*-labdane with an *E*-configurated double bond, and, accordingly, **4** was the *Z*-isomer (H-16: δ2.15 *d* and 1.96 *d*, respectively). The structures of **1** and **2** could easily be deduced, therefore, from the H-2 signal. As all couplings were small, an axial hydroxyl group was present. The signals of H-14, H-15 and H-16 showed that again **1** and **2** only differed in the configuration of the side-chain double bond.

The structures of **5** and **6** also followed clearly from the ^{1}H NMR spectrum (Table 1), especially when compared with those of closely related diterpenes. Obviously **5** had a 2α-hydroxy group while in **6** this position was occupied by a keto group. The nature of the side chain followed from the methyl doublet and the multiplet of a methylol group. Mild acetylation of **5** gave the monoacetate **7**. While the signal of H-2 was unchanged, that of H-15 was shifted downfield, indicating that only the primary hydroxyl group was acetylated. The aerial parts of a subspecies of *B. tricuneata* HBK from Peru gave, in addition to known compounds, 12-acetoxytremetone (**8**), as followed from the ^{1}H NMR spectrum.

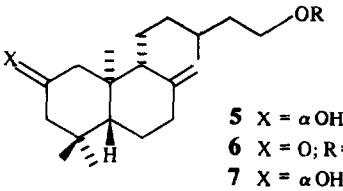
The chemistry of *Baccharis sternbergiana* is, in part, similar to that of *B. oxydonta* [1]. Clerodanes are much more widespread in this genus [1–10] but naringenin and its derivatives are frequent [1, 2, 4, 10] in those *Baccharis* species which often also contain baccharis oxide and 2,4-dihydroxyacetophenone derivatives [1, 2, 4]. Many additional constituents have been reported from this large genus with more than 400 species, and further investigations are necessary to obtain a clear picture on the chemotaxonomy.

EXPERIMENTAL

The air-dried aerial parts, collected in Peru, were extracted with Et_2O–petrol, 1:2 (12 hr room temp.), and the resulting extract was worked up in the usual fashion. Known compounds were identified by comparing the 400 MHz ^{1}H NMR spectra with those of authentic material. CC fractions (100 ml) of the



1 X = αOH, H; 13–*E*
2 X = αOH, H; 13–*Z*
3 X = O; 13*E*
4 X = O; 13*Z*



5 X = αOH, H; R = H
6 X = O; R = H
7 X = αOH, H; R = Ac

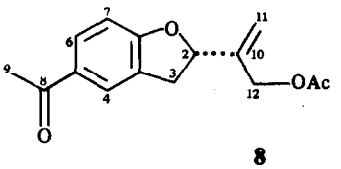


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Table 1. ^{1}H NMR spectral data of compounds 1–7 (400 MHz, $CDCl_3$, TMS as internal standard)

	1	2	3	4	5	6	7*
H-1			2.18 *dd*	2.17 *dd*		2.16 *dd*	
H-1′			2.33 *br d*	2.33 *br d*		2.33 *br d*	
H-2	4.16 *dddd*	4.17 *dddd*	—	—	4.15 *m*	—	4.14 *m*
H-3			2.40 *dd*	2.39 *dd*		2.43 *dd*	
H-3′				2.15 *br d*		2.20 *br d*	
H-7	2.41 *ddd*	2.40 *ddd*	2.47 *ddd*	2.47 *ddd*	2.40 *ddd*	2.45 *ddd*	2.41 *ddd*
H-12	2.35 *m*	2.50 *ddd*	2.35 *m*	2.51 *m*			
H-12′		2.64 *ddd*		2.67 *ddd*			
H-14	5.88 *dd*	5.89 *dd*	5.84 *dd*	5.91 *br d*			
H-15	9.99 *d*	9.83 *d*	9.99 *d*	9.81 *d*	3.68 *m*	3.67 *m*	4.21 *m*
H-16	2.18 *d*	1.98 *d*	2.15 *d*	1.96 *br s*	0.91 *d*	0.90 *d*	0.97 *d*
H-17	4.90 *br s*	4.93 *d*	4.94 *br s*	4.99 *br s*	4.85 *br s*	4.89 *br s*	4.88 *br s*
H-17′	4.51 *br s*	4.57 *d*	4.56 *br s*	4.62 *br s*	4.52 *br s*	4.56 *br s*	4.56 *br s*
H-18	0.99 *s*	0.98 *s*	1.05 *s*	1.05 *s*	1.00 *s*	1.05 *s*	1.05 *s*
H-19	0.91 *s*	0.90 *s*	0.70 *s*	0.70 *s*	0.92 *s*	0.69 *s*	0.97 *s*
H-20	0.92 *s*	0.92 *s*	0.84 *s*	0.83 *s*	0.92 *s*	0.84 *s*	0.98 *s*
OAc	—	—	—	—	—	—	2.06 *s*

*C_6D_6, H-15 4.19 and 4.14 (*dt*, J = 10, 6 Hz).

J (Hz): compounds **1** and **2**: 1, 2 = 1′, 2 = 2, 3 = 2, 3′ = 4; 6, 7 = 6′, 7 ~ 3; 7, 7′ = 13; 11, 12 = 11, 12′ = 11′, 12 = 11′, 12′ ~ 13; 14, 15 = 8; 14, 16 = 1.5; compounds **3** and **4**: 1, 1′ = 2, 2′ = 13; 1, 3 = 2; 6, 7 = 6′, 7 ~ 3; 7, 7′ = 13; 11, 12 ~ 8; 12, 12′ = 13; 14, 15 = 8; 14, 16 = 1.5; compounds **5** and **7**: 6, 7 = 6′, 7 ~ 3; 7, 7′ = 13; 13, 16 = 7; compound **6**: 1, 1′ = 2, 2′ = 13; 1, 3 = 2; 13, 16 = 7.

extract of *B. sternbergiana* (400 g, voucher RMK 9088) were as follows: 1 (petrol), 2 (Et_2O–petrol, 1 : 10), 3 (Et_2O–petrol, 1 : 3), 4 (Et_2O–petrol, 1 : 1), 5 (Et_2O) and 6 (Et_2O–MeOH, 10 : 1). TLC of fraction 1 (silica gel, $AgNO_3$-coated, petrol) gave 50 mg germacrene D, 20 mg caryophyllene, 10 mg β-curcumene and 20 mg δ-cadinene. Combined fractions 3 and 4 on repeated TLC (always SiO_2 PF 254; Et_2O–petrol, 1 : 1, several developments; detection by UV at 255 nm) afforded 8.5 mg **4** (R_f 0.63), 4 mg **3** (R_f 0.60), 5 mg naringenin 7,4′-*O*-dimethyl ether, 3 mg naringenin 7-*O*-methyl ether, 3 mg phytol, 30 mg taraxasterol, 5 mg lupeol and its Δ^{12}-isomer (2 : 1), 10 mg friedelinol and 2 mg stigmasterol. TLC of fraction 5 (Et_2O–petrol, 3 : 1 and C_6H_6–CH_2Cl_2–Et_2O, 2 : 2 : 1) gave 11 mg **2** (R_f 0.55), 11 mg **1** (R_f 0.52), 3 mg **6** (R_f 0.42) and 0.5 mg **5** (R_f 0.30).

The extract of *B. tricuneata* (330 g, voucher RMK 9005) gave CC fractions (100 ml) as follows: 1 (petrol), 2 (Et_2O–petrol, 1 : 10 and 1 : 3) and fraction 3 (Et_2O–petrol, 1 : 1 and Et_2O). TLC of fraction 1 (silica gel, $AgNO_3$-coated, petrol) gave 30 mg germacrene D, 2 mg α-humulene and 5 mg bicyclogermacrene. TLC of fraction 2 (SiO_2 PF 254; Et_2O–petrol, 1 : 3) gave 200 mg **8** (R_f 0.35), and TLC of fraction 3 (Et_2O–petrol, 1 : 1) afforded 50 mg *epi*-friedelinol, 50 mg 3,5-*bis*-[3,3-dimethylallyl]-*p*-hydroxyacetophenone, 1.5 g 3,5-*bis*-[3,3-dimethylallyl]-coumaric acid and 1 g sakuranetin. Compounds **1**–**8** were homogeneous by TLC in different solvent mixtures and showed no impurities in the 400 MHz ^{1}H NMR spectra, but could not be induced to crystallize.

Ent-2α-*hydroxylabda*-8(17),14E-*dien*-15-*al* (**1**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 2740, 1680, 1645 (C=CCHO), 3080, 900 (C=CH_2); MS *m/z* (rel. int.): 304.240 $[M]^+$ (5) ($C_{20}H_{32}O_2$), 289 $[M-Me]^+$ (10), 286 $[M-H_2O]^+$ (5), 203 $[286-OCHC=C(Me)CH_2]^+$ (17), 84 $[C_4H_7CHO$, McLafferty$]^+$ (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-20 \quad -20 \quad -26 \quad -42} \ (CHCl_3;\ c\ 0.5).$$

11 mg **1** in 1 ml CH_2Cl_2 was stirred for 1 hr with 10 mg pyridine chlorochromate. Usual work-up afforded 6 mg **3**, identical to the natural ketone.

Ent-2α-*hydroxylabda*-8(17),14Z-*dien*-15-*al* (**2**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3620 (OH), 2740, 1690, 1645 (C=CCHO), 3090, 895 (C=CH_2); MS *m/z* (rel. int.): 304.240 $[M]^+$ (6) ($C_{20}H_{32}O_2$), 289 $[M-Me]^+$ (10), 286 $[M-H_2O]^+$ (14), 203 (20), 84 (100). Oxidation with pyridine chlorochromate (see above) gave **4**, identical to the natural compound.

Ent-2-*oxo*-*labda*-8(17),14E-*dien*-15-*al* (**3**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2720, 2680, 1640 (C=CCHO), 1710 (C=O), 3090, 900 (C=CH_2); MS *m/z* (rel. int.): 302.225 $[M]^+$ (6) ($C_{20}H_{30}O_2$), 287 $[M-Me]^+$ (27), 258 $[287-CHO]^+$ (16), 219 $[M-OCHCH=C(Me)CH_2]^+$ (31), 84 (51), 55 (100).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-20 \quad -20 \quad -25 \quad -52} \ (CHCl_3;\ c\ 0.4).$$

Ent-2-*oxolabda*-8(17),14Z-*dien*-15-*al* (**4**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 2720, 2680, 1640 (C=CCHO), 1710 (C=O), 3080, 900 (C=CH_2); MS *m/z* (rel. int.): 302.225 $[M]^+$ (7) ($C_{20}H_{30}O_2$), 287 $[M-Me]^+$ (24), 258 $[287-CHO]^+$ (18), 219 $[M-C_5H_7O]^+$ (31), 84 (58), 55 (100).

Ent-2α,15-*dihydroxylabda*-8(17)-*ene* (**5**), which was purified as its acetate (**7**) (Ac_2O, 70°), colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1745 (OAc); MS *m/z* (rel. int.): 350 $[M]^+$ (1) ($C_{22}H_{38}O_3$), 332 $[M-H_2O]^+$ (18), 317 $[332-Me]^+$ (10), 135 $[C_{10}H_{15}]^+$ (100).

Ent-2-*oxolabda*-8(17)-*en*-15-*ol* (**6**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1710 (C=O), 3080, 900 (C=CH_2); MS *m/z* (rel. int.): 306.256 $[M]^+$ (11) ($C_{20}H_{34}O_2$), 291 $[M-Me]^+$ (31), 151 (100), 81 (84), 55 (96).

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-24 \quad -24 \quad -29 \quad -59} \ (CHCl_3;\ c\ 0.3).$$

12-*Acetoxytremetone* (**8**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1750 (OAc), 1680, 1610 (PhCO); MS *m/z* (rel. int.): 260.105 $[M]^+$ (12) ($C_{15}H_{16}O_4$), 200 $[M-HOAc]^+$ (100), 185 $[200-Me]^+$ (36), 160 $[M-CH_2{=}CHCH_2OAc]^+$ (51), 145 $[160-Me]^+$ (95); ^1H NMR ($CDCl_3$): 5.38 (*br t*, H-2), 3.45 and 3.17 (*br dd*, H-3), 7.82 (*br s*, H-4), 7.81 (*br d*, H-6), 6.81 (*d*, H-7), 2.54 (*s*, H-9), 5.35 and 5.28 (*br s*, H-11), 5.10 and 5.03 (*br d*, H-12), 2.01 (*s*, OAc). [*J* (Hz): 2, 3 = 8; 3, 3′ = 14; 6, 7 = 8; 12, 12′ = 12.]

$$[\alpha]_{24°}^{\lambda} = \frac{589 \quad 578 \quad 546 \quad 436\ nm}{-59 \quad -61 \quad -73 \quad -125}\ (CHCl_3;\ c\ 1.5).$$

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