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DITERPENOIDS FROM *BACCHARIS TOLA*

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Key Word Index—*Baccharis tola*; Compositae; new diterpenes; *ent*-beyerenol; epoxylabdene.

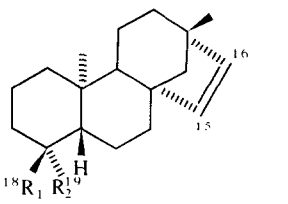
Abstract—Erythroxylol-A, oleanolic acid, erythroxylol-A oxide, scopolatine, 4-hydroxy-3-methoxyacetophenone and two new diterpenes, *ent*-beyer-14-en-18-ol and 19-hydroxy-13-epimanoyl oxide, were isolated from *B. tola*.

INTRODUCTION

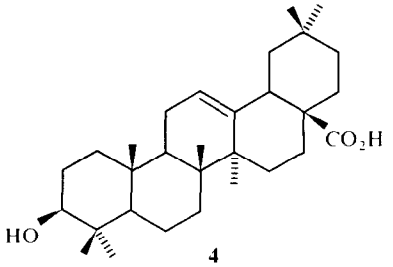
Less than 5% of the known *Baccharis* species have been chemically examined. Besides flavones, triterpenes, sesquiterpenes and diterpenes of the clerodano type have been isolated [1]. In this communication we report the isolation and characterization of five terpenoids in *B. tola*. Three of the terpenoids were identified as erythroxylol-A (**1**) [2], oleanolic acid (**4**) and erythroxylol-A-14,15-oxide (**5**) [3]. The other two diterpenes, *ent*-beyer-15-en-18-ol (**2**) and 19-hydroxy-13-epimanoyl oxide (**6**), are new. Scopolatine (**9**) and 4-hydroxy-3-methoxyacetophenone (**10**), were also isolated.

RESULTS AND DISCUSSION

From the petrol–ether extract of *B. tola*, five terpenes were isolated by Si gel CC and repeated PLC (Si gel). The spectral data of the least polar compound, **1**, $C_{20}H_{32}O$ (M^+ 288), suggested that **1** was *ent*-beyer-15-en-19-ol, (erythroxylol-A) which was confirmed by comparison of the physical properties of **1** and of its derivatives with those reported in ref. [2]. The spectral properties of the second compound, **2**, $C_{20}H_{32}O$ (M^+ 288), were very similar to those of **1**. The ^1H NMR spectrum showed a two-proton AB quartet centred at δ 3.10 (J = 11 Hz), assigned to a primary hydroxyl group and a two-proton AB quartet centred at δ 5.50 (J = 6 Hz), corresponding to a *cis*-disubstituted olefin. Three methyl singlets were also evident at δ 0.70, 0.73 and 0.96. Compound **2** was converted to (+)-hibaene (**3**) by $LiAlH_4$ reduction of its tosylate, thus demostrating that **2** also belongs to the *ent*-beyerene series and only differed from **1** in the position of the CH_2OH group. On the basis of the ^1H NMR, it can be inferred that **2** is epimeric at C-4, since the oxymethylene signals occupy different field positions in the two isomers [4, 5]. The stereochemistry at C-4 was confirmed by comparison of the ^{13}C NMR spectra of both compounds with that of the parent compound **3** [6]. The introduction of the hydroxyl



	1	2	3
R_1	Me	CH_2OH	Me
R_2	CH_2OH	Me	Me



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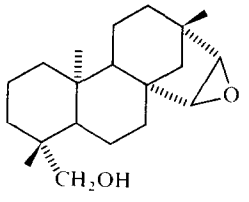

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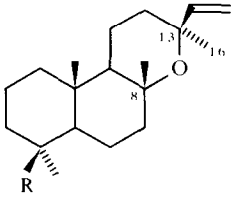
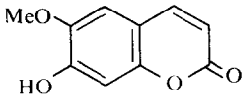


	6	7	8
R	CH_2OH	CH_2OAc	Me



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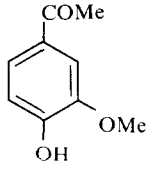

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Table 1. ^{13}C NMR data (ppm) of compounds **1**–**3**, **7** and **8***

Carbon No.	1	2	3	7	8
1	39.2	38.8	39.3	39.5	38.9
2	18.3	18.0	18.7	18.6	18.4
3	35.7	35.4	42.2	36.8	41.9
4	38.5	37.6	33.3	37.4	32.5
5	56.8	49.1	56.1	57.3	55.5
6	20.1	19.9	20.3	20.4	19.8
7	37.3	37.0	37.4	43.8	42.6
8	49.0	48.6	49.1	75.6	74.9
9	53.0	52.8	53.0	58.8	56.2
10	37.3	37.1	37.4	36.8	36.7
11	20.3	20.3	20.5	16.4	15.2
12	33.2	33.2	33.7	35.3	35.5
13	43.6	43.6	43.6	73.2	73.0
14	61.2	61.2	61.3	148.4	147.8
15	135.0	135.0	135.2	109.5	110.0
16	136.5	136.0	136.1	33.2	28.4
17	24.9	24.9	25.0	24.1	25.4
18	27.0	72.3	33.8	27.5	32.5
19	65.5	17.7	22.0	66.6	21.3
20	15.6	15.6	15.1	16.4	16.6

* Recorded in $CDCl_3$ except **7** which was run in C_6D_6. Assignments were made by comparing chemical shifts to published data and confirmed by off-resonance partially decoupled spectra (data for **3** and **8** are reproduced from refs. [6] and [9], respectively).

either at C-19 (**1**) or C-18 (**2**) produced the same γ-effect (-6.7 ppm) on C-3 and also nearly the same β-effect on C-4 ($+4.5$ ppm). The γ-effect on C-5, however, is quite different in both isomers: -7.0 ppm in **2** (CH_2OH equatorial) and 0 ppm in **1**, a result to be expected since the axial CH_2OH group cannot interact with H-5. From these spectral data and chemical transformation, **2** was confirmed to be *ent*-beyer-15-en-18-ol.

The MS of the next compound ($C_{30}H_{48}O_3$, M^+ 456) suggested it was oleanolic acid (**4**). Its identity was confirmed by methylation of **4** and direct comparison with an authentic sample (IR, mp, mmp). The spectroscopic data of the fourth compound showed it to be *ent*-beyer-15,16-epoxy-an-19-ol (**5**), erythroxylol-A epoxide [3].

The fifth compound, **6**, $C_{20}H_{34}O_2$ (M^+ 306), gave a typical ^1H NMR spectrum for an 8,13-epoxylabd-14-ene (manoyl oxide) skeleton with a primary hydroxyl group: three one-proton quartets at δ 6.02, 4.90 and 4.80, characteristic of a vinyl group; the oxymethylene group displayed two doublets at 3.68 and 3.45 (J = 10 Hz). The spectrum also showed two methyl singlets at 1.20 and 1.13 and two more at 0.97 and 0.73. Compound **6** is, accordingly, an isomer of jhanol (18-hydroxy-manoyl oxide), whose oxymethylene protons appear at δ 3.47 and 3.15, thus suggesting an axial CH_2OH group in **6** [7]. Also, close inspection of the methyl signals in the spectra of both compounds and comparison with those of 13-epimanoyl oxide and other related compounds [8], suggested that **6** and jhanol are also epimeric at C-13. These observations were fully confirmed by comparison of the ^{13}C NMR spectra of **6** and **7** with that of manoyl oxide (**8**) and other related diterpenes [7, 9]. The diamagnetic shift undergone by C-3 (5.4) and C-18 (5.9), together with the paramagnetic one at C-4 (4.2 ppm) and the nearly null γ-effect on C-5 (as compared with a 6.0 ppm upfield shift in jhanol), clearly indicate the introduction of the hydroxyl group at C-19 in **6**. C-16, on the other hand, resonated at 33.2 ppm (28.8 in jhanol), a downfield shift consonant with its equatorial disposition [10]. Therefore, on the basis of these data, **6** is shown to be 19-hydroxy-13-epimanoyl oxide. However, the absolute configuration has not been established and it may be enantiomeric to the structure shown.

From the EtOH extract of *B. tola*, it was only possible to isolate scopolatine (**9**) and 4-hydroxy-3-methoxyacetophenone (**10**) [11].

EXPERIMENTAL

^1H NMR and ^{13}C NMR spectra were recorded at 60 and 20.0 MHz respectively ($CDCl_3$ soln and TMS as int. standard). Mps (uncorr.) were determined on a Kofler hot stage apparatus. Analytical TLC and PLC were run on Si gel 60-GF_{254} and Si gel 60 (70–230 mesh) was used for CC. MS were recorded by direct inlet with 70 eV ionization.

Isolation of the diterpenes. Air-dried *B. tola* (3.5 kg), collected at El Tatio (Antofagasta, Chile) in December, was first extracted with Et_2O–petrol (1:2) and the resulting extract was chromatographed on a Si gel column. The mixture of products was further separated by dry column chromatography and/or PLC. The EtOH extract was treated in a similar manner.

Erythroxylol-A (**1**) (1.5 g). Mp 119°, $[\alpha]_D$ + 42.6° (lit. 119–120°, $[\alpha]_D$ + 39° [2]). *O*-Acetylester, mp 73°, $[\alpha]_D$ 32.1 (lit. 72–73°, $[\alpha]_D$ 34° [2]). Toluene-*p*-sulphonate ester, mp 102° (lit. 106° [2]). MS *m/e* (rel. int.): 288.2451 (M^+, calc. for $C_{20}H_{32}O$: 288.2445, 100%), 257 (85), 148 (72), 133 (50), 123 (76), 122 (48), 121 (48), 119 (68), 109 (35), 105 (100).

Ent-*beyer*-15-*en*-18-*ol* (**2**) (0.9 g). Mp 112° (hexane), $[\alpha]_D$ 29.7° ($CHCl_3$); IR ν_{max}^{KBr} cm^{-1}: 3200, 3000–2800, 1040, 980. ^1H NMR: δ 0.71 (3H, *s*), 0.73 (3H, *s*), 0.96 (1H, *s*), 2.93 (1H, *d*, *J*

= 11 Hz), 3.26 (1 H, *d*, *J* = 11 Hz), 5.35 (1 H, *d*, *J* = 6 Hz), 5.60 (1 H, *d*, *J* = 6 Hz). MS *m/e* (rel. int.): 288.2452 (M^+, calc. for $C_{20}H_{32}O$: 288.2445, 86), 257 (98), 229 (74), 161 (69), 148 (43), 135 (80), 134 (76), 133 (67), 105 (100).

(+)-*Hibaene* (**3**) *from* **2**. A soln of **2** (54 mg) and toluene-*p*-sulphonyl chloride (200 mg) in dry Py (2 ml) was set aside at 20° for 60 hr. Work-up gave the toluene-*p*-sulfonate ester, mp 114° (MeOH), $[\alpha]_D$ + 0.78°. This compound was treated with $LiAlH_4$ (50 mg) in refluxing dry dioxane for 48 hr. After work-up and chromatography of the residue over alumina gave, on elution with petrol–ether, (+)-hibaene, (**3**), mp 30°, $[\alpha]_D^{25}$ + 32° (lit. 30–33°, $[\alpha]_D$ 33° [2]).

Oleanolic acid (**4**). Compound **4** (120 mg) was isolated as a solid, mp 308° (lit. 310° [4]). MS *m/e* (rel. int.): 456 (M^+, 7%), 256 (39), 248 (100), 204 (24), 203 (93). Methyl ester, mp 192° (lit. 198° [11]).

Ent-*beyer*-15,16-*epoxy*-*an*-19-*ol* (**5**). Isolated as solid (80 mg), mp 115° (MeOH) (lit. 115–116.5° [3]). ^{1}H NMR: δ 0.90 (3 H, *s*), 0.98 (3 H, *s*), 1.01 (3 H, *s*), 3.0 (1 H, *d*, *J* = 3 Hz), 3.3 (1 H, *d*, *J* = 3 Hz), 3.43 (1 H, *d*, *J* = 11 Hz), 3.76 (1 H, *d*, *J* = 11 Hz). MS *m/e* (rel. int.): 304 (M^+, 80%), 273 (28), 255 (38), 245 (31), 149 (31), 147 (24), 135 (50), 123 (38), 121 (45), 107 (33), 105 (29), 95 (33), 32 (100).

19-*Hydroxy*-13-*epimanoyl oxide* (**6**). Compound **6** (180 mg), was isolated as a solid, mp 109° (hexane). IR ν_{max}^{KBr} cm^{-1}: 3300, 3050–2900, 1640, 1480. ^{1}H NMR: δ 0.73 (3 H, *s*), 0.97 (3 H, *s*), 1.13 (3 H, *s*), 1.20 (3 H, *s*), 3.45 (1 H, *d*, *J* = 10 Hz), 3.68 (1 H, *d*, *J* = 10 Hz), 4.8 (1 H, *q*, *J* = 11, 2 Hz), 4.9 (1 H, *q*, *J* = 17.5, 2 Hz), 6.02 (1 H, *q*, *J* = 17.5, 11 Hz). MS *m/e* (rel. int.): 306 (M^+, 17), 291 (100), 273 (72), 254 (40), 235 (40), 208 (33), 205 (71), 177 (57), 135 (48), 121 (48), 109 (60), 105 (37).

19-*Acetoxy*-13-*epimanoyl oxide* (**7**). Acetylation of 60 mg **6** in 1 ml Py and 1 ml Ac_2O for 24 hr followed by the usual work-up, gave **7** as an oil. IR ν_{max}^{film} cm^{-1}: 3050–2850, 1740, 1240. ^{1}H NMR: δ 0.73 (3 H, *s*), 0.95 (3 H, *s*), 1.10 (3 H, *s*), 1.20 (3 H, *s*), 2.03 (3 H, *s*), 3.86 (1 H, *d*, *J* = 11 Hz), 4.16 (1 H, *d*, *J* = 11 Hz), 4.8 (1 H, *q*, *J* = 11, 2 Hz), 4.9 (1 H, *q*, *J* = 17.5, 2 Hz), 6.02 (1 H, *q*, *J* = 17.5, 11 Hz). MS *m/e* (rel. int.): 348 (M^+, 5), 333 (100), 273 (25), 256 (79), 250 (25), 190 (43), 177 (41), 135 (65).

6-*Methoxy*-7-*hydroxycoumarine* (*scopolatine*) (**9**). Compound **9** (9.8 g) was isolated as a solid, mp 203° (lit. 204° [11]). ^{1}H NMR: δ 3.9 (3 H, *s*), 6.2 (1 H, *d*, *J* = 9 Hz), 6.8 (1 H, *s*), 7.0 (1 H, *s*), 7.7 (1 H, *d*, *J* = 9 Hz). MS *m/e* (rel. int.): 192 (M^+, 100%), 177 (70), 164 (36), 149 (49), 121 (36).

4-*Hydroxy*-3-*methoxyacetophenone* (**10**) (110 mg). Mp 115° (lit 116° [11]). IR ν_{max}^{KBr} cm^{-1}: 3280, 1655, 1580. ^{1}H NMR: δ 2.5 (3 H, *s*), 6.3 (1 H, *s*), 6.9 (1 H, *d*, *J* = 10 Hz), 7.4–7.6 (2 H, *m*). MS *m/e* (rel. int.): 167 (M^+, 55%), 151 (100), 123 (25), 108 (6), 80 (3).

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