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DITERPENOIDS FROM *BACCHARIS TOLA*

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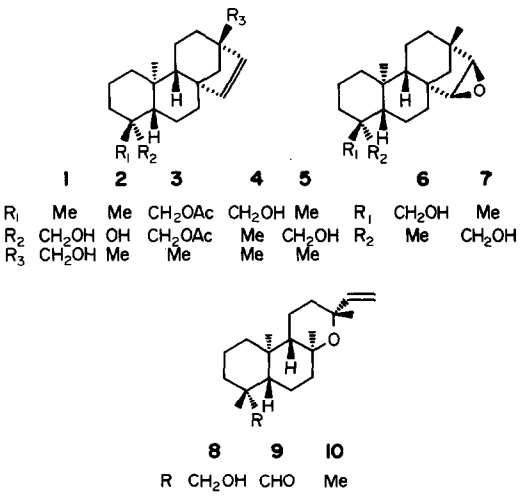
Key Word Index—*Baccharis tola*; Compositae; diterpenes; *ent*-beyerenols.

Abstract—*ent*-4α-Hydroxy-19-norbeyer-15-ene, *ent*-beyer-15-en-17,19-diol, apigenin and two new diterpenes, *ent*-beyer-15-en-18,19-diol and 15β,16β-epoxide-*ent*-beyeran-18-ol were isolated from *Baccharis tola*.

INTRODUCTION

In a previous paper [1] the characterization of *ent*-beyer-15-en-18-ol and 19-hydroxy-13-epimanoyl oxide, as well as the identification of other known *ent*-beyerene-type diterpenoids from the petrol–ether extract of *Baccharis tola* was described. Further examination of the eluates from the chromatography of this extract resulted in the isolation of four additional terpenoids. Two of these terpenoids were identified as *ent*-beyer-15-en-17,19-ol (**1**) and *ent*-4α-hydroxy-19-norbeyer-15-ene (**2**). The other two terpenoids, *ent*-beyer-15-en-18,19-diol (**3**) and 15β,16β-epoxide-*ent*-beyeran-18-ol (**6**) are new. Apigenin was also isolated. The absolute configuration shown in structure **8** for 19-hydroxyepimanoyl oxide and previously reported in ref. [1], was established by its conversion by Huang–Minlon reduction to epimanoyl oxide (**10**).



RESULTS AND DISCUSSION

The spectral properties of **1**, $C_{20}H_{32}O_2$ (M^+ at m/z 304), showed it to be *ent*-beyer-15-en-17,19-diol (erythroxydiol-A) isolated previously from *Erythroxylum monogynum* [2]. Further confirmation of its identity was obtained by comparison of its ^{13}C NMR spectrum with that of other related diterpenoids (Table 1). The spectral properties of **2** suggested a monohydroxylated norhibaene derivative. Its identification followed comparison of its physical properties with those reported for *ent*-4α-hydroxy-19-norbeyer-15-ene, also isolated from *E. monogynum* [3].

Compound **3**, characterized as its diacetate, $C_{24}H_{36}O_4$ (M^+ at m/z 388), gave a typical ^1H NMR spectrum for a beyerene skeleton with two primary acetoxyl groups. The spectrum showed a two proton AB system at δ 5.40 (J = 6 Hz) and 5.60 (J = 6 Hz) corresponding to a *cis*-disubstituted olefin, two three-proton singlets at 0.84 and 1.04 and two two-proton AB systems at 3.76 (J = 12 Hz) and 4.01 (J = 12 Hz), and 3.93 (J = 11 Hz) and 4.30 (J = 11 Hz). The oxymethylene groups were tentatively assigned to C-18 and C-19, respectively, by comparison of

Table 1. ^{13}C NMR data of compounds **1**,**3**,**6** and **7**

Carbon No.	1	3*	6*	7*
1	38.9	38.6	38.9	39.3
2	19.6	17.6	17.7	18.1
3	36.2	30.9	35.6	35.2
4	38.9	40.1	38.7	38.9
5	55.9	50.8	50.4	56.5
6	20.1	20.4	19.7	20.8
7	37.2	37.4	37.5	37.4
8	48.4	48.6	44.1	44.2
9	53.1	53.0	55.7	55.6
10	36.9	37.1	36.5	36.9
11	20.8	20.9	20.7	20.5
12	28.0	33.1	32.8	33.4
13	47.7	43.6	35.8	36.3
14	56.7	61.0	46.7	46.7
15	136.4	134.7	60.6	59.9
16	131.8	136.7	56.4	56.7
17	69.6	24.8	21.5	21.4
18	27.4	69.6	72.9	27.5
19	67.0	64.6	17.6	67.0
20	15.7	15.7	16.2	16.2
Me–CO	—	171.0	170.9	171.1
Me–CO	—	20.4	19.2	19.3

The spectra were obtained in $CDCl_3$ solutions. The δ values are in ppm downfield from TMS.

*Spectra obtained with the acetylated compounds.

their chemical shifts with those of **4** and **5** [1] and other similar diterpenoids of known stereochemistry. These assignments were fully confirmed by the ^{13}C NMR spectrum of **3**. Thus, placement of both CH_2OAc groups at C-4 resulted in pronounced γ-effects on C-3 ($\Delta\delta - 11.1$) and β-effects on C-4 ($\Delta\delta + 7.0$) (values related to the unsubstituted compound) [1]. The signal for C-5 showed nearly the same shielding effects ($\Delta\delta - 5.2$) as observed in **4**. C-18 and C-19 exhibited mutual shielding effects when compared to the corresponding values in **4** and **5** while C-20 and C-17, the other likely sites of substitution, maintained the same chemical shifts as in **4** and **5**. Therefore, on the basis of these data, **3** is shown to be *ent*-beyer-15-en-18,19-diol. The absolute configuration of **3** was not determined, however, we choose the *ent*-configuration as all the diterpenoids isolated so far from *Baccharis tola* belong to this series.

The spectral properties of **6**, characterized as its acetate, $C_{22}H_{34}O_3$ (M^+ at m/z 346) were very similar to those of **7** [1]. These compounds are epimeric at C-4, as was clearly shown by their ^{13}C NMR spectra. The equatorial (C-18) or axial (C-19) disposition of the CH_2OAc group is readily determined by the presence or absence, respectively, of a shielding effect on C-5. It is also of interest to note in the ^{13}C NMR spectra of these compounds the pronounced shielding effect exerted by the 15,16-epoxide on C-14 ($\Delta\delta - 15$). This γ-syn effect of the oxirane ring, which is well documented in other related bicyclic systems [4–6], coupled to the fact that the C-14 signal appears as a double doublet instead of a triplet in the SFORD spectrum of **6** and **7** [7, 8], indicates a β-orientation of the epoxide ring in these compounds. On the other hand, oxidation of **4**, of known absolute configuration, with *m*-chloroperbenzoic acid, gave a product identical in all respects to the natural product. Compound **6** corresponds, therefore, to 15β,16β-epoxide-*ent*-beyeran-18-ol.

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.

ent-*Beyer*-15-*en*-17,19-*diol* (**1**) (310 *mg*). Mp 179°, $[\alpha]_D + 59.2°$ ($CHCl_3$) (lit. 179–181°, $[\alpha]_D + 60°$ [1]). ^1H NMR: δ 0.76 (3H, *s*), 1.00 (3H, *s*), 3.41 (1H, *d*, J = 10 Hz), 3.77 (1H, *d*, J = 10 Hz), 5.56 (1H, *d*, J = 6 Hz), 5.80 (1H, *d*, J = 6 Hz). MS m/z (rel. int.): 304 $[M]^+$ (8), 273 (8), 150 (30), 136 (43), 126 (86), 106 (100). *O*-Diacetylester, mp 55–56°, $[\alpha]_D + 32°$ (lit. 56–58° [2]). IR ν_{max}^{KBr} cm^{-1}: 2950, 2850, 1720, 1360, 1240, 1020. ^1H NMR: δ 0.82 (3H, *s*), 0.98 (3H, *s*), 2.02 (6H, *s*), 3.77 (1H, *d*, J = 11 Hz), 4.24 (1H, *d*, J = 11 Hz), 5.54 (1H, *d*, J = 6 Hz), 5.76 (1H, *d*, J = 6 Hz). MS m/z (rel. int.): 388 $[M]^+$ (8), 387 (50), 386 (100), 327 (28), 313 (33), 266 (43), 253 (62), 225 (38), 190 (29), 157 (57), 130 (71), 118 (67).

ent-4α-*Hydroxy*-19-*norbeyer*-15-*ene* (**2**). Colourless oil, (40 mg). $[\alpha]_D + 23.6°$ ($CHCl_3$) (lit. $[\alpha]_D + 25°$ [3]). ^1H NMR: δ 0.90 (3H, *s*), 0.99 (3H, *s*), 1.16 (1H, *s*), 5.44 (1H, *d*, J = 6 Hz), 5.74 (1H, *d*, J = 6 Hz). MS m/z (rel. int.): 274.092 $[M]^+$ (calc. for $C_{19}H_{30}O$: 274.092) (80), 256.140 (38), 245.083 (23), 241.050 (21), 189.067 (40), 161.001 (48), 147.016 (40), 135.100 (97), 122.070 (54), 107.100 (45), 106.096 (57), 93.066 (100), 81.035 (51), 43.088 (80).

ent-*Beyer*-15-*en*-18,19-*diol* (**3**). Colourless oil, characterized as its diacetate (82 mg), $[\alpha]_D + 85°$ ($CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 2900, 1740, 1440, 1370, 1240. ^1H NMR: δ 0.84 (3H, *s*), 1.04 (3H, *s*), 2.05 (6H, *s*), 3.76 (1H, *d*, J = 12 Hz), 3.93 (1H, *d*, J = 11 Hz), 4.01 (1H, *d*, J = 12 Hz), 4.30 (1H, *d*, J = 11 Hz), 5.40 (1H, *d*, J = 6 Hz), 5.60 (1H, *d*, J = 6 Hz). MS m/z (rel. int.): 388 $[M]^+$ (85), 328 (30), 315 (17), 268 (41), 255 (32), 148 (30), 147 (35), 145 (36), 135 (88), 134 (68), 133 (61), 122 (63), 121 (53), 119 (61), 109 (27), 107 (56), 106 (65), 105 (100).

15β,16β-*Epoxide*-ent-*beyeran*-18-*ol* (**6**) (67 *mg*). Mp 101°, $[\alpha]_D + 42.5°$ ($CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 3450, 2850, 1450, 1380, 1040. ^1H NMR: δ 0.80 (3H, *s*), 1.00 (3H, *s*), 1.04 (3H, *s*), 2.82 (1H, *d*, J = 4 Hz), 2.92 (1H, *d*, J = 11 Hz), 3.26 (1H, *d*, J = 4 Hz), 3.33 (1H, *d*, J = 11 Hz). MS m/z (rel. int.): 304 $[M]^+$ (2), 274 (8), 255 (9), 245 (12), 231 (10), 203 (13), 173 (61), 135 (100). *O*-Acetylester (95 mg), mp 88°, $[\alpha]_D - 15.9°$ ($CHCl_3$). IR ν_{max}^{KBr} cm^{-1}: 2950, 1730, 1440, 1380, 1240. ^1H NMR: δ 0.87 (3H, *s*), 1.00 (6H, *s*), 2.02 (3H, *s*), 2.84 (1H, *d*, J = 4 Hz), 3.22 (1H, *d*, J = 4 Hz), 3.54 (1H, *d*, J = 11 Hz), 3.84 (1H, *d*, J = 11 Hz). MS m/z (rel. int.): 346 $[M]^+$ (46), 286 (7), 273 (25), 255 (42), 173 (43), 149 (42), 147 (33), 145 (28), 135 (100), 121 (67), 107 (66), 105 (58), 97 (37), 95 (66), 93 (68).

Oxidation of 19-*hydroxy*-13-*epimanoyl oxide*. Compound **8**, 600 mg, was oxidized with pyridinium chlorochromate in dry CH_2Cl_2 following the procedure reported in ref. [9] giving 13-epimanoyl oxide-19-ol (**9**) (580 mg). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3005, 1720. ^1H NMR (90 MHz): δ 0.63 (3H, *s*), 1.02 (3H, *s*), 1.16 (3H, *s*) 1.26 (3H, *s*) 4.94 (1H, *dd*, J = 9.5, 1.8 Hz), 4.97 (1H, *dd*, J = 16.5, 1.8 Hz), 6.03 (1H, *dd*, J = 16.5, 9.5 Hz), 9.86 (1H, *s*). MS m/z (rel. int.): 304 $[M]^+$ (1), 289 (14), 271 (3), 261 (6), 244 (4), 243 (18), 207 (8), 206 (29), 205 (9), 201 (12), 124 (100).

Huang–Minlon reduction of 13-*epimanoyl oxide*-19-*al*. Compound **9** (540 mg), was reduced by the same procedure as described in ref. [9]. Work-up gave *ent*-13-epimanoyl oxide (**10**) (80 mg). Mp 98°, $[\alpha]_D - 36.8°$ (EtOH) (lit. 99°, $[\alpha]_D - 37°$ [10]). IR ν_{max}^{KBr} cm^{-1}: 2950, 1440, 1360, 1080. ^1H NMR (90 MHz): δ 0.74 (3H, *s*), 0.80 (3H, *s*), 0.88 (3H, *s*), 1.15 (3H, *s*), 1.24 (3H, *s*), 4.92 (1H, *dd*, J = 9.5, 1.8 Hz), 4.98 (1H, *dd*, J = 16.5, 1.8 Hz), 6.04 (1H, *dd*, J = 16.5, 9.5 Hz). MS m/z (rel. int.): 290 $[M]^+$ (2), 275 (20), 257 (55), 246 (9), 192 (52), 191 (36), 138 (100).

5-*Hydroxy*-7,4′-*dimethoxiflavone* (*apigenin*) (85 *mg*). Mp 168° (lit. 168° [11]). IR ν_{max}^{KBr} cm^{-1}: 3400, 2850, 1620, 1500, 1440. ^1H NMR: δ 3.88 (6H, *s*), 6.37 (1H, *d*, J = 3 Hz), 6.48 (1H, *d*, J = 3 Hz), 6.56 (1H, *s*), 7.03 (2H, *d*, J = 10 Hz), 7.50 (2H, *d*, J = 10 Hz). MS m/z (rel. int.): 298 $[M]^+$ (21), 269 (8), 255 (7), 167 (8), 139 (22), 133 (24), 118 (29), 96 (100).

Oxidation of ent-*beyer*-15-*en*-18-*ol*. Compound **4** (150 mg) was oxidized with *m*-chloroperbenzoic acid in dry $CHCl_3$ following the procedure described in ref. [9]. Work-up gave 15β,16β-epoxide-*ent*-beyeran-18-ol (**6**) (157 mg). Mp 102°. IR ν_{max}^{KBr} cm^{-1}: 3440, 2850, 1440, 1380. ^1H NMR: δ 0.80 (3H, *s*), 1.00 (3H, *s*), 1.03 (3H, *s*), 2.81 (1H, *d*, J = 4 Hz), 2.92 (1H, *d*, J = 11 Hz), 3.25 (1H, *d*, J = 4 Hz), 3.33 (1H, *d*, J = 11 Hz). MS m/z (rel. int.): 304 $[M]^+$ (3), 135 (100).

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