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EUDESMANE SESQUITERPENES FROM *ARTEMISIA ERIOPODA*

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Key Word Index—*Artemisia eriopoda*; Compositae; sesquiterpenes; eudesmane.

Abstract—Three new and one known eudesmane diol were isolated from *Artemisia eriopoda*. The structures were elucidated by spectroscopic methods. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

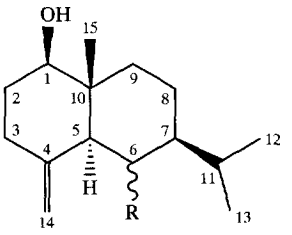
In South China, *Artemisia eriopoda* Bunge has been used in folk medicine in place of the traditional Chinese herb *A. annua* which has been used as an antimalarial drug in China for centuries. The species of *A. eriopoda* investigated chemically in a previous work [1] were reported to contain no sesquiterpenes, although *A. annua* is rich in sesquiterpenes [2, 3]. We have re-examined the aerial parts of *A. eriopoda* and obtained four eudesmane sesquiterpenes (**1–4**).

RESULTS AND DISCUSSION

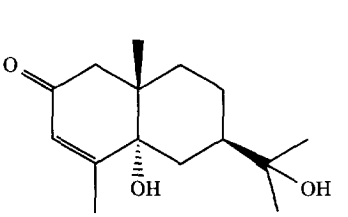
The extract from the aerial parts of *A. eriopoda* on CC over silica gel yielded three new eudesmane diols: 1β,6β-dihydroxy-4(14)-eudesmene (**2**), 5α-hydroxy-isopterocarpolone (**3**) and 1-oxo-cryptomeridiol (**4**); along with known compounds: 1β,6α-dihydroxy-4(14)-eudesmene (**1**) [4–6], α-amyrin [1, 7], β-sitosterol[1, 8], scopoletin [9, 10], esculetin [9] and sitosteryl β-D-glucoside [8].

Compound **2** gave rise to a mass spectrum which was nearly identical with that of **1**, indicating that both compounds have the same gross structure. The ^{1}H NMR spectrum was also similar to that of compound **1**, except for the 6β-hydroxy group. H-6 appeared as a triplet at δ 3.67, and the smaller coupling constant (J = 4.5 Hz) supported the equatorial positioning of this proton. This difference from **1** is the consequence of the interaction of an equatorial proton with the neighboring two axial protons (H-5 and H-7). This feature of the 6β-hydroxy group was also confirmed by the lowfield shift (comparison with **1**) of Me-15 (+ 0.35 ppm, from δ 0.71 to 1.06) due to a 1,3-diaxial interaction [11] between the 6β-hydroxy group and the 10β-methyl group. Therefore, the structure of **2** was determined as 1β,6β-dihydroxy-4(14)-eudesmene.

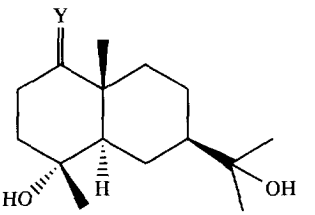
Compound **3** showed a clear $[M + 1]^+$ peak at m/z 253. It was assigned the molecular formula $C_{15}H_{24}O_3$ by EI-mass spectrum and the ^{13}C and ^{1}H NMR data. The IR spectrum contained bands at 3453 and 3420 cm^{-1} for hydroxyls, and at 1710, 1655 and 839 cm^{-1} for an α,β-unsaturated ketone. This feature was also estimated by a UV maximum at $\lambda_{max}^{CHCl_3}$ nm (log ε) 245 (3.261). The ^{1}H NMR (400 MHz, $CDCl_3$) spectrum had signals for an angular methyl (δ 0.99, *s*,



1 R = α-OH
2 R = β-OH



3



4 y = O
4a y = H, β-OH

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3H) and the gem-dimethyl of a hydroxy isopropyl group (δ 1.09 and 1.25, *s*, each 3H) similar to those seen in the ^{1}H NMR spectrum of isopterocarpolone [12]. The C-4 vinylic methyl appeared as a broad singlet at δ 2.00 (*brs*, 3H) and δ 5.81 (*brs*, 1H) was assigned to the C-3 olefinic proton. These signals suggested the incorporation of an α,β-unsaturated ketone system as in a –C=O–CH=C–Me grouping. This was also confirmed by the two doublets at δ 2.08 and 2.75 (J = 17.0 Hz) in an AB system of the methylene group α to the CO group which was assigned to the two protons at C-1. By comparison of the ^{13}C NMR spectral data (Table 1) of **3** with that of β-eudesmol [13], the second tertiary hydroxy group was assigned to the quarternary C-5 (δ 76.04). The stereochemistry of **3** including the tertiary OH group at C-5 was confirmed by the CD spectrum by application of the octant rule [14] and by comparison with reference substances [15, 16]. The proposed *trans*-decalin system for **3** exhibited a negative Cotton effect with a fine structure for the n-π^* transition ($[\theta]_{330}$ −310) and the $\pi-\pi^*$ transition of the α,β-unsaturated ketone ($[\theta]_{256}$ −13 400) in the CD. The CD curve was similar to that of α-rotunol [16]. Based on these data and on biogenetic considerations, compound **3** was shown to be 5α-hydroxyisopterocarpolone.

Compound **4** gave rise to a $[M]^+$ peak at *m/z* 254, and this together with the ^{13}C and ^{1}H NMR data indicated the molecular formula to be $C_{15}H_{26}O_3$. The IR spectrum contained bands at 3442 and 3396 cm^{-1} for hydroxyls and at, 1698 cm^{-1} for a ketone. The ^{1}H NMR (400 MHz, acetone-d_6) spectrum contained signals for an angular methyl (δ 1.27, 3H, *s*, Me-15), the gem-dimethyl of a hydroxy isopropyl group (δ 1.19 and 1.20, *s*, each 3H, Me-12 and Me-13) (the presence of a tertiary hydroxyl in the isopropyl group was also confirmed by the fragment at *m/z* 59 in the mass spectrum), and a singlet methyl at C-4 (δ 1.10, 3H, *s*, Me-14). The ^{13}C NMR spectral data (Table 1) showed that the quarternary C-4 was oxygenated (δ 73.74), therefore the second tertiary hydroxy group was assigned to C-4. Comparison of these signals along with those of the C-2 protons at δ 2.58 (1H, *ddd*, J = 15.7, 10.3, 6.3 Hz, H-2β) and 2.15 (1H, *ddd*, J = 15.7, 6.3, 5.1 Hz, H-2α) and the C-3 protons at δ 2.25 (2H, *m*) with the ^{1}H NMR spectral data of corymbolone [17, 18], suggested presence of the system O=C–CH_2–CH_2–C–OH (–Me). Then the ketone was assigned at C-1, this was also deduced by the low field shift of the quarternary C-10 at δ 46.56. Reduction of **4** with $NaBH_4$ produced **4a**. A comparison of the ^{1}H NMR data of **4a** with **4** showed the highfield shift of Me-14 and Me-15 of **4a** at δ 1.04 (−0.06 ppm, from δ 1.10 to δ 1.04) and 0.89 (−0.38 ppm, from δ 1.27 to δ 0.89), respectively. Finally, the configuration at C-4 of **4** was determined by NOED. Clear effects were observed between H-2β and H-15 (6%) as well as between H-2β and H-14 (5%) on irradiating H-2β (δ 2.58), which required a 4β-methyl configuration. On comparison with cryptomeridiol [19], the structure of **4** was established to be 1-oxo-cryptomeridiol.

Table 1. ^{13}C NMR spectral data of compounds **1**, **3** and **4** (100.6 MHz, δ ppm)*

C	1†	3†	4‡
1	78.99	42.25	215.61
2	35.06§	199.01	41.06
3	31.88§	125.43	35.90§
4	146.21	167.04	73.74
5	55.85	76.04	47.79
6	66.98	34.32§	22.09
7	49.29	47.01	42.49
8	18.12	22.71	21.55
9	36.25§	35.02§	33.64§
10	41.86	40.12	46.56
11	25.96	72.59	70.72
12	16.15	25.49	23.40
13	21.06	28.58	29.92
14	107.77	22.71	29.70
15	11.56	18.84	29.00

*Status of each carbon confirmed through DEPT experiment.

†Measured in $CDCl_3$.

‡Measured in acetone-d_6.

§Assignments may be interchangeable within the same column.

EXPERIMENTAL

General. Mps: uncorr.; MS: 70 ev, direct inlet.

Plant material, extraction and isolation. The air-dried aerial parts of *A. eriopoda* (2.7 kg) were collected in September 1991 from Luqu county, Gansu province of P. R. China, and identified by Prof. Guo-Lang Zhang, Department of Biology, Lanzhou University. The pulverized, air-dried plants material was extracted twice for 48 hr with petrol–MeOH–Et_2O (1:1:1) at room temp. After evapn under red. pres., the residue was refluxed with *ca* 250 ml MeOH until the solid was entirely dissolved. The soln was cooled to room temp. and kept at −10° for 24 hr, and then filtered. The filtrate was evapd under red. pres. to give a black residue (18 g). The residue was chromatographed on a silica gel column (ϕ 36 mm) (silica gel 200–300 mesh, 200 g) with solvents of increasing polarity in the order petrol, petrol–EtOAc, EtOAc, EtOAc–MeOH, and MeOH. Frs eluted with petrol–EtOAc (15:1) (following elution with 1500 ml of this solvent) afforded compound **2** (10 mg) which was purified by CC and by prep. TLC (petrol–EtOAc 12:1, ×3, R_f 0.35). Frs eluted with petrol–EtOAc (8:1) gave α-amyrin (12 mg), β-sitosterol (70 mg), scopoletin (60 mg) and esculetin (25 mg), which were purified by CC and by recrystallization. Frs eluted with petrol–EtOAc (6:1–2:1) afforded a sesquiterpene mixt. (1.1 g). This mixt. was subjected to silica gel CC with petrol–Me_2CO (5:1). Evapn of solvent from the CC frs (100 ml each) combined according to TLC monitoring yielded 18 frs. Compound **1** (15 mg) was obtained from fr. 4 and was purified with CC and by prep. TLC (petrol–Me_2CO

6:1, ×4, R_f 0.45). Compounds **3** (20 mg) and **4** (25 mg) were obtained from fr. 15 and purified by the above same procedure. Sitosteryl β-D-glucoside (55 mg) was obtained from the fractions eluted with EtOAc and purified by recrystallization.

1β,6α-Dihydroxy-4(14)-eudesmene (**1**). Oil, $[\alpha]_D^{20}$ +47.5° (Me_2CO; *c* 0.2). EI-MS *m/z* (rel. int.): 238 $[M]^+$ (5), 220 $[M-H_2O]^+$ (60), 205(2), 202(8), 177(50), IR (film) $\nu_{max}^{CHCl_3}$ cm^{-1}: 3398 (–OH), 2930, 2869, 1459, 1373 (*brs*), 1061, 1002; ^1H NMR ($CDCl_3$, 400 MHz): δ 5.03 (1H, *brs*, H-14), 4.75 (1H, *brs*, H-14′), 3.72 (1H, *t*, *J* = 9.9 Hz, H-6β), 3.44 (1H, *dd*, *J* = 4.7, 11.5 Hz; H-1α), 0.97 and 0.88 (each 3H, *d*, *J* = 7.2 Hz, Me-12 and Me-13), 0.71 (3H, *s*, Me-15); ^{13}C NMR: Table 1.

1β,6β-Dihydroxy-4(14)-eudesmene (**2**). Oil, $[\alpha]_D^{20}$ +54° (Me_2CO; *c* 0.05). EI-MS *m/z* (rel. int.): 238 $[M]^+$ (4), 220 $[M-H_2O]^+$ (37), 203 (9), 177 (28); ^1H NMR ($CDCl_3$, 400 MHz): δ 1.06 (3H, *s*, Me-15), 0.91 and 0.98 (each 3H, *d*, *J* = 7 Hz, Me-12 and Me-13), 3.67 (1H, *t*, *J* = 4.5 Hz, H-6 α), 3.50 (1H, *dd*, *J* = 4.1, 10.8 Hz; H-1α) 4.65 (1H, *brs*, H-14), 4.84 (1H, *brs*, H-14′).

5α-Hydroxyisopterocarpolone (**3**). Oil, $[\alpha]_D^{20}$ +39° (MeOH; *c* 0.5), CD (MeOH): $[\theta]_{330}$ −310 (*c* 0.2), $[\theta]_{256}$ −13 400 (*c* 0.01). IR (film) $\nu_{max}^{CHCl_3}$ cm^{-1}: 3453 (–OH), 3420 (–OH), 1710, 1655, 839 (α,β-unsaturated ketone); UV $\lambda_{max}^{CHCl_3}$ nm (log ε): 245 (3.261); EI-MS *m/z* (rel. int.): 253 $[M+1]^+$ (35), 252 $[M]^+$ (17), 234 $[M-H_2O]^+$ (5), 217 (8), 194 (70), 179 (15), 139 (100), 59 (72); ^1H NMR ($CDCl_3$, 400 MHz): δ 0.99 (3H, *s*, Me − 15), 1.09 (3H, *s*, Me − 12), 1.25 (3H, *s*, Me − 13), 2.00 (3H, *brs*, Me − 14), 2.08 (1H, *d*, *J* = 17.0 Hz, H-1β), 2.75 (1H, *d*, *J* = 17.0 Hz, H-1α), 3.10 (2H, *brs*, 20H), 5.81 (1H, *brs*, H-3); ^{13}C NMR: Table 1.

1-Oxo-isocryptomeridiol (**4**). Needles, m.p. 119–120°, $[\alpha]_D^{20}$ −56° (MeOH; *c* 0.1). IR ν_{max}^{KBr} cm^{-1}: 3442 (–OH), 3396 (–OH), 1698 (6-membered ring ketone), 2969, 2944, 2865, 1465, 1375, 1072; EI-MS *m/z* (rel. int.): 254 $[M]^+$ (2), 236 $[M-H_2O]^+$ (6), 218 $[M-2H_2O]^+$ (18), 203 (12), 178 (62), 163 (41), 148 (75), 59 (71), 43 (100); ^1H NMR (acetone − d_6, 400 MHz): δ 1.10 (3H, *s*, Me-14), 1.27 (3H, *s*, Me-15), 1.19 (3H, *s*, Me-12), 1.20 (3H, *s*, Me-13), 2.15 (1H, *ddd*, *J* = 15.7, 6.3, 5.1 Hz, H-2α), 2.25 (2H, *m*, H-3), 2.58 (1H, *ddd*, *J* = 15.7, 10.3, 6.3 Hz, H-2β), 1.80 (2H, *m*, H-6), 1.95 (2H, *m*, H-9), 1.61 (2H, *m*, H-8); ^{13}C NMR: Table 1.

Reduction of 1-*oxo-cryptomeridiol* (**4**). To 9.7 mg of **4** dissolved in dry EtOH (15 ml), an excess of $NaBH_4$ (dissolved in 20 ml dry EtOH) was added in several portions and the mixt. was stirred at −20° for 2.5 hr and then worked-up as usual to give an oily residue of **4a** · **4a** (8.3 mg) was purified by prep. TLC (petrol–Me_2CO 1:1, ×3, R_f 0.25). 1β-hydroxycryptomeridiol (**4a**): oil, $[\alpha]_D^{20}$ +105° (MeOH: *c* 0.02). IR (film) $\nu_{max}^{CHCl_3}$ cm^{-1}: 3381 (*br*) (–OH), 2964, 2931, 2861, 1462, 1381, 1050; ^1H NMR (400 MHz, acetone-d_6): δ 0.89 (3H, *s*, Me-15), 1.04 (3H, *s*, Me-14), 1.19 (3H, *s*, Me-12), 1.20 (3H, *s*, Me-13), 3.20 (1H, *dd*, *J* = 5.0, 9.5 Hz, H-1α).

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