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EUDESMANE ALCOHOLS FROM *JASONIA GLUTINOSA*

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Key Word Index —*Jasonia glutinosa*; Compositae; sesquiterpenoids; eudesmane derivatives.

Abstract—Three new sesquiterpene alcohols have been isolated from *Jasonia glutinosa*. Their structures were elucidated by spectroscopic methods and chemical correlations as (−)-[11*R*]-4α,14-epoxyeudesm-11,12-diol, (−)-[11*R*]-eudesm-4(14)-en-5β,11,12-triol and (+)-[11*R*]-eudesm-4(14)-en-5α,11,12-triol and they are called α-epoxy kudtdiol, 5-*epi*-kudtriol and kudtriol respectively.

INTRODUCTION

In a previous paper we reported the structural determination of kudtdiol (**1**), the major sesquiterpenic component of *J. glutinosa* (family Compositae; tribe Inuleae), as (+)-[11*R*]-eudesm-4(14)-en-11,12-diol [1]. The same structure had previously been proposed to sesquibenhidiol, a substance isolated from *Chamaecyparis formosensis* [2], but the physical constants reported (mp 123°, $[\alpha]_D$ − 38°) differed from those found for kudtdiol (mp 90°, $[\alpha]_D$ + 72.9°). Recently, Bohlmann [3] isolated from another species of Compositae, *Flourensia heterolepsis* (Heliantheae), an oily product ($[\alpha]_D$ + 50.4°) whose spectroscopic properties corresponded to those of kudtiol. In addition other sesquiterpenic acids with a eudesmane skeleton were isolated.

In this report we describe the structures of three new sesquiterpene alcohols with eudesmane and 5-*epi*-eudesmane skeletons, which we isolated from *Jasonia glutinosa*.

RESULTS AND DISCUSSION

The neutral fraction of the benzene extract from the aerial parts of *J. glutinosa*, after dry column chromatography, mostly yielded kudtdiol (**1**). From a more polar fraction of the chromatography, α-epoxykudtdiol (**2**), 5-*epi*-kudtriol (**3**) and kudtriol (**4**) were isolated.

α-*Epoxy-kudtdiol* (**2**)

The IR spectrum of **2** showed absorptions of hydroxyl and oxiranic groups (3400, 3020, 1260, 1040, 935, 920 cm^{-1}). The ^1H NMR spectrum had signals of a quaternary methyl (δ 0.80 *s*), a methyl geminal with a tertiary hydroxyl (1.06, *s*), an oxiranic methylene (2.48 and 2.72, AB, J = 5 Hz) and two geminal protons of a primary hydroxyl group (3.35 and 3.47, AB, J = 11 Hz). On acetylation (Ac_2O-pyridine room temp.), a hydroxyacetate **5** (IR bands at 3460, 1740 cm^{-1}) was obtained, whose ^1H NMR spectrum had the acetate methyl signal at δ 2.10 and the methylene protons geminal with the acetate group absorbing at 4.01. These data, compared with those of kudtdiol, allow us to propose structure **2**.

On the other hand, since the major product of the epoxidation of **1** with *m*-chloroperbenzoic acid has been shown to be spectroscopically identical with the natural product **2**, and since it has been established that the homoallylic axial methyl group at C-10 preferentially induces an α-attack of the epoxidizing agent [4], the configuration of the epoxyl group must be that depicted in **2**. Furthermore the C-10 methyl resonances in the triol **6**, obtained on $LiAlH_4$ reduction of **2**, and in the triol **7**, obtained from kudtdiol acetate **8**, confirm the proposed structure.

5-epi-*Kudtriol* (**3**) *and kudtriol* (**4**)

Both substances had very similar chromatographic and spectroscopic properties. The less polar product **3** had M^+ at *m/e* 254 ($C_{15}H_{26}O_3$) and IR absorptions for hydroxyl groups and exocyclic unsaturation. Its ^1H NMR spectrum showed signals for a quaternary methyl (δ 0.99, *s*), a methyl geminal with a tertiary hydroxyl (1.13, *s*), two geminal protons of a primary hydroxyl (3.35 and 3.55, AB, J = 11 *Hz*) and an olefinic exocyclic methylene (4.90, *br s*). Compound **3** on acetylation gave the dihydroxymonoacetate **9**, whose ^1H NMR spectrum had an acetate singlet at 2.05, and the AB methylene signals at 3.35 and 3.55 of **3** changed to a singlet at 3.99.

Substance **4** also had M^+ at *m/e* 254 ($C_{15}H_{26}O_3$) and major differences in the IR and ^1H NMR spectra from those of substance **3** were the C—O absorption band at 1040 cm^{-1} and the resonances of the C-10 methyl group (δ 0.83) and the vinylidene group (4.65 and 4.76). Compound **4** on acetylation also gave a dihydroxymonoacetate **10**, similar to **9** except for the ^1H NMR signals of the same groups.

These data suggest, for both substances, a structure like that of kudtdiol (**1**), with an additional tertiary hydroxyl located at C-5 or C-7. The observed effects on the C-10 methyl and C-14 proton resonances, compared with those of kudtdiol (**1**), allow us to propose the structure eudesm-4(14)-en-5,11,12-triol for these substances. The stereochemistry at C-5 for both triols was assigned by comparison of the relative deshielding of the C-10 methyl and the $C{=}CH_2$ resonances in **3**, which must have the C-5

hydroxyl group in the β disposition. Consequently, **4** has the opposite configuration.

The confirmation of the proposed structures **3** and **4** was achieved by partial synthesis from kudtdiol acetate (**8**), which after treatment with H_2SO_4–HOAc–H_2O gave compounds **11** (33%), **12** (6%), unreacted **8** (44%), **1** (3%), **13** (5%) and **14** (9%). The saponification of **11**, followed by sensitized photoxidation [5] of **15** and $NaBH_4$ reduction led to the isolation of synthetic **3** and **4**, in agreement with the results obtained with similar substances [6]. Both compounds were identical to the natural **3** and **4** in R_f and spectral properties.

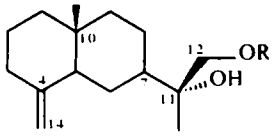
The isopropylidenic ketal **16**, easily obtained from **4**, showed a pyridine-induced shift ($\Delta^{CDCl_3}_{pyridine} = -0.06$ ppm) for the C-10 methyl group which agrees with a dihedral angle of $\theta \simeq 180°$ with respect to the C-5 hydroxyl [7]. When ketalization of **3** was attempted a complex reaction mixture was obtained, which could be explained by possible multiple interactions between the three hydroxyl groups in the conformation **17**.

EXPERIMENTAL

Optical rotations were measured in $CHCl_3$ soln. IR spectra in film form or $CHCl_3$ soln. ^{1}H NMR (60 MHz) in $CDCl_3$ with int. TMS, chemical shifts are in δ, MS (70 eV) values are in *m/e* units (% relative abundance). TLC, PLC and CC separations were performed on Si gel G, Si gel $HF_{313+263}$ and Si gel 60 (Merck).

Extraction and isolation. Jasonia glutinosa was collected in Algara (Guadalajara, Spain) September 1976. The air-dried plant (4.897 kg) was extracted with refluxing C_6H_6 for 12 hr, yielding 151.4 g. Dewaxing with MeOH gave waxes (66.7 g) and the remaining product, on treatment with urea in MeOH (saturated soln), produced 19.7 g of linear products. The dewaxed material in Et_2O soln was extracted with 10% NaOH to yield 35.5 g of neutral fraction and 19.3 g of acid fraction. The neutral fraction by dry CC yields 17.1 g of **1** and 2.57 g of a mixture which by CC on Si gel and Ag^+–Si gel (20%) yielded 300 mg of **1**, 72 mg of **2**, 119 mg of **3** and 95 mg of **4**.

Kudtdiol (**1**). Mp 90° (CH_2Cl_2–hexane) $[\alpha]_D$ + 72.9° (*c* 2.15). IR ν_{max} cm^{-1}: 3390, 3060, 1640, 1045, 880. ^{1}H NMR: δ 0.69 (3 H,



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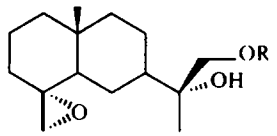

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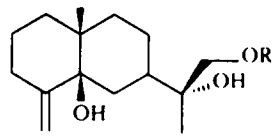

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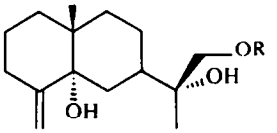

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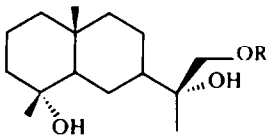

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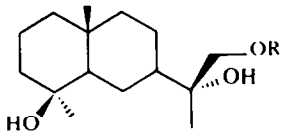

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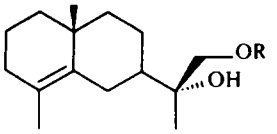

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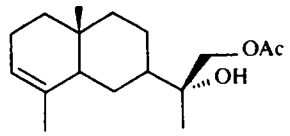

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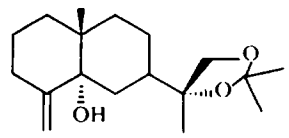

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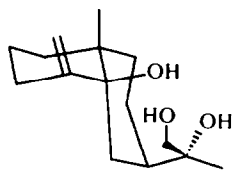

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s, Me–C-10), 1.11 (3 H, *s*, Me–C-11), 3.38 and 3.52 (2 H, AB, J = 11 Hz, H-12), 4.42 (1 H, *br s*, H-14), 4.69 (1 H, *br s*, H-14). MS *m/e* (rel. int.): M^+ 238 (6), 223 (2), 220 (2), 207 (100), 189 (77), 164 (19), 149 (47).

Kudtdiol monoacetate (**8**). 374 mg of **1**, on acetylation (room temp.) gave 421 mg of **8**. $[\alpha]_D$ + 63.2° (*c* 2.09). IR ν_{max} cm^{-1}: 3460, 3060, 1740, 1640, 1235, 1040, 880. ^1H NMR: δ 0.69 (3H, *s*, Me–C-10), 1.14 (3 H, *s*, Me–C-11), 2.06 (3 H, *s*, –OAc), 4.01 (2 H, *s*, H-12), 4.43 (1 H, *br s*, H-14), 4.67 (1 H, *br s*, H-14). MS *m/e* (rel. int.): M^+ 280 (2), 262 (1), 220 (2), 207 (15), 202 (11), 189 (19), 163 (6), 117 (100).

α-Epoxykudtdiol (**2**). $[\alpha]_D$ − 6.05° (*c* 0.90). IR ν_{max} cm^{-1}: 3400, 3020, 1105, 1040. ^1H NMR: δ 0.80 (3 H, *s*, Me–C-10), 1.06 (3 H, *s*, Me–C-11), 2.48 and 2.72 (2 H, AB, J = 5 Hz, H-14), 3.35 and 3.47 (2 H, AB, J = 11 Hz, H-12).

α-Epoxykudtdiol monoacetate (**5**). Acetylation of **2** (23 mg) gave **5** (25 mg). $[\alpha]_D$ − 3.20° (*c* 0.62). IR ν_{max} cm^{-1}: 3460, 3020, 1740, 1235, 1035. ^1H NMR: δ 0.86 (3 H, *s*, Me–C-10), 1.14 (3 H, *s*, Me–C-11), 2.10 (3 H, *s*, –OAc), 2.50 and 2.74 (2 H, AB, J = 5 Hz, H-14), 3.92 and 4.10 (2 H, AB, J = 12 Hz, H-12).

Synthesis of α-epoxykudtdiol. Treatment of **1** (208 mg) with *m*-chloroperbenzoic acid in CH_2Cl_2 soln, followed by PLC (Et_2O) afforded α-epoxykudtdiol (94 mg) identical with the natural product **2**.

Reduction of α-epoxykudtdiol. Compound **2** (55 mg) by $LiAlH_4$ reduction gave (−)-[11*R*]-eudesm-4α,11,12-triol **6**. $[\alpha]_D$ − 6.9° (*c* 1.01). IR ν_{max} cm^{-1}: 3350, 1170, 1095, 1050, 905. ^1H NMR: 0.86 (3 H, *s*, Me–C-10), 1.10 (6 H, *s*, Me–C-11 and Me–C-4), 3.39 and 3.53 (2 H, AB, J = 10 Hz, H-12). *Monoacetate* **14**. Mp 100° (CH_2Cl_2–hexane). $[\alpha]_D$ − 4.1° (*c* 2.03). IR (soln) ν_{max} cm^{-1}: 3580, 1730, 1235, 1030, 900. ^1H NMR: δ 0.86 (3 H, *s*, Me–C-10), 1.12 (3 H, *s*, Me–C-4), 1.17 (3 H, *s*, Me–C-11), 2.10 (3 H, *s*, –OAc), 4.02 (2 *H*, *s*, H-12).

5-epi-*Kudtriol* (**3**). $C_{15}H_{26}O_3$, $[\alpha]_D$ − 10.4° (*c* 0.79). IR (soln) ν_{max} cm^{-1}: 3570, 3400, 3060, 1635, 1200, 1020, 900. ^1H NMR: δ 0.99 (3 H, *s*, Me–C-10), 1.13 (3 H, *s*, Me–C-11), 3.35 and 3.55 (2 H, AB, J = 11 Hz, H-12), 4.90 (2 H, *br s*, H-14). MS *m/e* (rel. int.): M^+ 254 (6), 236 (18), 223 (13), 221 (25), 218 (10), 205 (74), 203 (13), 187 (65), 162 (58), 147 (100).

5-epi-*Kudtriol monoacetate* (**9**). Acetylation of **3** (30 mg) gave **9** (28 mg). $[\alpha]_D$ − 8.2° (*c* 0.37). IR ν_{max} cm^{-1}: 3440, 3060, 1730, 1640, 1240, 1030, 900. ^1H NMR: δ 0.99 (3 H, *s*, Me–C-10), 1.16 (3 H, *s*, Me–C-11), 2.05 (3 H, *s*, –OAc), 3.99 (2 H, *s*, H-12), 4.89 (2 H, *br s*, H-14).

Kudtriol (**4**). $C_{15}H_{26}O_3$, $[\alpha]_D$ + 76.5° (*c* 1.03). IR (soln) ν_{max} cm^{-1}: 3570, 3400, 3060, 1640, 1205, 1095, 1040, 900. ^1H NMR: δ 0.83 (3 H, *s*, Me–C-10), 1.06 (3 H, *s*, Me–C-11), 3.40 and 3.56 (2 H, AB, J = 12 Hz, H-12), 4.65 (1 H, *br s*, H-14), 4.76 (1 H, *br s*, H-14). MS *m/e* (rel. int.): M^+ 254 (1), 236 (2), 223 (1), 222 (2), 221 (1), 218 (1), 205 (7), 203 (2), 187 (4), 162 (10), 147 (17), 83 (100).

Kudtriol monoacetate (**10**). Acetylation of **4** (35 mg) gave **10** (37 mg). $[\alpha]_D$ + 56.7° (*c* 0.59). IR (soln) ν_{max} cm^{-1}: 3580, 3420, 3060, 1730, 1640, 1240, 1040, 905. ^1H NMR: δ 0.84 (3 H, *s*, Me–C-10), 1.14 (3 H, *s*, Me–C-11), 2.07 (3 H, *s*, –OAc), 4.01 (2 H, *s*, H-12), 4.65 (1 H, *br s*, H-14), 4.76 (1 H, *br s*, H-14).

Synthesis of 5-epi-*kudtriol* (**3**) *and kudtriol* (**4**). *Isomerization of kudtdiol monoacetate* (**8**). To HOAc soln of **8** (1.825 g in 1.86 ml) were added H_2SO_4 (1.16 ml) and H_2O (4.6 ml). After 1.75 hr, 1.820 g of the reaction mixture were recovered which on Ag^+–Si gel (20%) CC afforded several products. (+)-[11*R*]-*Eudesm-4-en-11,12-diol monoacetate* (**11**), (532 mg, hexane–EtOAc, 20:1) $[\alpha]_D$ + 97.8° (*c* 1.32). ^1H NMR (CCl_4): δ 1.01 (3 H, *s*, Me–C-10), 1.10 (3 H, *s*, Me–C-11), 1.59 (3 H, *s*, Me–C-4), 2.04 (3 H, *s*, –OAc), 3.94 (2 H, *s*, H-12). The saponification of **11** gave **15**, mp 115° (hexane–CH_2Cl_2), $[\alpha]_D$ + 94.4° (*c* 0.96). IR (soln) ν_{max} cm^{-1}: 3540, 3400, 1090, 1030. ^1H NMR: δ 1.01 (3 H, *s*, Me–C-10), 1.12 (3 H, *s*, Me–C-11), 1.59 (3 H, *s*, Me–C-4), 3.40 and 3.60 (2 H, AB, J = 11 Hz, H-12). (+)-[11*R*]-*Eudesm-3-en-11,12-diol monoacetate* (**12**), (100 mg, hexane–EtOAc, 20:1) $[\alpha]_D$ + 17.4° (*c* 2.15). IR (soln) ν_{max} cm^{-1}: 3570, 3010, 1735, 1650, 1230, 1035, 905, 840. ^1H NMR: δ 0.75 (3 H, *s*, Me–C-10), 1.13 (3 H, *s*, Me–C-11), 1.58 (3 H, *s*, Me–C-4), 2.06 (3 H, *s*, –OAc), 4.30 (2 H, *s*, H-12); 5.30 (1 H, *m*, H-3). *Kudtdiol monoacetate* (**8**), (712 mg, hexane–EtOAC, 9:1). (+)-[11*R*]-*Eudesm-4,11,12-triol monoacetate* (**13**), (78 mg, hexane–EtOAc, 9:1). $[\alpha]_D$ + 8.8° (*c* 2.13). IR ν_{max} cm^{-1}: 3460, 1725, 1240, 1040. ^1H NMR: δ 1.01 (3 H, *s*, Me–C-10), 1.15 (6 H, *s*, Me C-11 and Me–C-4), 2.07 (3 H, *s*, –OAc), 4.03 (2 H, *s*, H-12). The saponification of **13** gave **7**. $[\alpha]_D$ + 10.0° (*c* 0.65). IR (soln) ν_{max} cm^{-1}: 3580, 3400, 1085, 1030. ^1H NMR: δ 1.01 (3 H, *s*, Me–C-10), 1.14 (3 H, *s*, Me–C-11), 1.17 (3 H, *s*, Me–C-4), 3.43 and 3.61 (2 H, AB, J = 10 Hz, H-12). *Kudtdiol* (**1**), (49 mg, hexane–EtOAc, 1:1). (−)-(11*R*)-*Eudesm-4,11,12-triol monoacetate* (**6**), (143 mg, hexane–EtOAc, 1:1).

Photoxidation of (+)-[11*R*]-*eudesm-4-en-11,12-diol* (**15**). Compound **15** (160 mg) by oxidation (Rose Bengale as sensitizer) in *iso*-PrOH, followed by $NaBH_4$ reduction and CC on Ag^+–Si gel (20%) afford **3** (27 mg) and **4** (36 mg).

5α-Hydroxyeudesm-4(14)-en-11,12-iso-propylidene ketal (**16**). Kudtriol (**4**) (47 mg) was reacted with 0.8 ml of $Me_2C(OMe)_2$ and TsOH in Me_2CO; after PLC (hexane–Et_2O, 1:1) 25 mg of **16** were isolated, mp 155° (hexane–CH_2Cl_2). IR (KBr) ν_{max} cm^{-1}: 3460, 3080, 1640, 1235, 1195, 1095, 1045, 890. ^1H NMR: δ 0.85 (3 H, *s*, Me–C-10), 1.24 (3 H, *s*, Me–C-11), 1.35 (3 H, *s*, Me–C-1), 1.41 (3 H, *s*, Me–C-1), 3.64 and 3.92 (2 H, AB, J = 8 Hz, H-12), 4.69 (1 H, *br s*, H-14), 4.79 (1 H, *br s*, H-14).

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