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EUDESMANOLIDES AND EPOXYCUAUTHEMONES FROM *PLUCHEA QUITOC*

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Key Word Index—*Pluchea quitoc*; Compositae; eudesmanolides; epoxycuauthemones.

Abstract—Three new eudesman-8,12-olides named 3β-angeloyloxy-4β-acetoxy-eudesm-7(11)-en-8α,12-olide; 3β-angeloyloxy-4β-acetoxy-8β-hydroxy-eudesm-7(11)-en-8α,12-olide and 3β-angeloyloxy-4α,8β-dihydroxy-eudesm-7(11)-en-8α,12-olide and three new epoxycuauthemones, 3β-angeloyloxy-7β,11-epoxy-4α-hydroxyeudesman-8-one; 4β-acetoxy-3β-angeloyloxy-7α,11-epoxyeudesman-8-one and 3β-angeloyloxy-7α,11-epoxy-4α-hydroxy-5,6-dehydroeudesman-8-one, together with the furofuran lignan pinoresinol were obtained from the hexane extract and from the chloroform-soluble portion of the ethanolic extract of the aerial parts of *Pluchea quitoc*. Their structures were deduced by spectroscopic studies, including 2D-shift correlation experiments.

INTRODUCTION

In the course of our research on the aerial parts of *Pluchea quitoc*, we have previously reported on the isolation and structure of sesquiterpenes derived from cuauthemone and other known compounds [1, 2]. In the present communication, we describe the isolation and structural elucidation of three new eudesman-8,12-olides (**1**–**3**), three new epoxycuauthemones (**4**–**6**), together with the known furofuran lignan pinoresinol (**7**) [3], from the hexane extract and $CHCl_3$-soluble portion of the ethanolic extract of the aerial parts of *P. quitoc*.

RESULTS AND DISCUSSION

Fractions of the hexane extract of the aerial parts of *P. quitoc*, after chromatographic separation, yielded the sesquiterpenes **1**, **2**, **4**–**6**. The eudesmanolide **3** and pinoresinol (**7**) were isolated from the $CHCl_3$-soluble fraction of the ethanolic extract using similar techniques. The structures of the sesquiterpenes were deduced from their ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) with the aid of spin-decoupling experiments and ^{1}H-^{1}H and ^{13}C-^{1}H COSY spectra. The nature of the ester group at C-3 for compounds **1**–**6** was determined to be an angelate moiety from the characteristic ^{1}H and ^{13}C NMR signals. The location of the angelate group at C-3 and the configuration at this chiral centre, β with respect to the angelate, was deduced from the coupling constants of the H-3 signals on the ^{1}H NMR spectra (Table 1). In compounds **1**, **2** and **5** the presence of a second ester group, an acetate, was evident from the NMR signals and its location was proposed on the basis of the deshielding effect on H-3 caused by this group when it is linked to C-4 [4]. The stereochemistry at C-4 compounds **1**, **2** and **5** was proposed from the chemical shifts of C-4 and C-15 when compared with those of the known compounds **8** (δ_C 87.4 and 16.7) [1] and **9** (δ_C 83.4 and 19.3) [5], indicating the same configuration as in compound **8**, that is β (equatorial) with respect to the acetoxy group. The stereochemistry at C-4 in compounds **3** and **4** was proposed to be α with respect to the hydroxy group from the chemical shift of Me-15 in the ^{1}H NMR spectrum, since it is known that when the hydroxy group is β the methyl hydrogens of Me-15 resonate at a higher field [6]; and also, in the case of compound **3**, from the downfield shift of the signal of H-6α caused by the 4α-hydroxy group [4].

Compound **1** showed the presence in the ^{1}H NMR spectrum of a double-double doublet at δ_H 4.79 (12.5, 6.2 and 0.7 Hz) attributed to H-8. The coupling constants of H-8 permitted us to propose the stereochemistry at C-8 with the lactone-ring α (equatorial). Double irradiation of H-8 collapsed the signal attributed to H-9β to a doublet ($J = 12.5$ Hz) an also modified the signal of H-9α, in accordance to the proposed stereochemistry at C-8. To confirm the chemical shift of H-9α, whose signal was partially

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Table 1. ^{1}H NMR spectral data of compounds **1**–**6** (300 MHz)

H	**1**	**2**	**3**	**4**	**4** (in C_6D_6)	**5**	**6**
3α	5.81 *dd* (11.7; 5.2)	5.79 *dd* (11.9; 5.4)	4.71 *dd* (11.8; 5.0)	4.84 *dd* (11.6; 4.6)	4.80 *dd* (12.1; 4.6)	5.87 *dd* (10.7; 5.0)	4.93 *dd* (11.5; 4.9)
5α	2.78 *dd* (13.5; 3.3)	2.81 *dd* (12.6; 2.4)	1.40 *dd* (13.1; 2.8)	2.15[#]	1.57 *dd* (13.6; 2.9)	3.29 *dd* (12.5; 5.3)	—
6	—	—	—	—	—	—	6.00 *s*
6α	2.69 *dd* (13.5; 3.3)	2.59 *dd* (12.6; 2.4)	3.05 *dd* (13.1; 2.8)	2.24 *dd* (12.1; 1.5)	2.18 *dd* (13.6; 2.9)	1.84 *dd* (14.8; 5.3)	—
6β	2.30 *t* (13.5)	2.34 *t* (12.6)	2.32 *tq* (13.1; 1.3)	2.01[#]	1.85 *t* (13.6)	2.18[#]	—
8β	4.79 *ddd* (12.5; 6.2; 0.7)	—	—	—	—	—	—
9α	1.13 *t* (12.5)	1.55 *d* (12.8)	1.49 *d* (13.6)	2.11[#]	1.61 *bd* (13.1)	2.57 *d* (15.3)	2.72 *d* (12.0)
9β	2.22 *dd* (12.5; 6.2)	2.20 *d* (12.8)	2.21 *d* (13.6)	2.36 *d* (13.5)	2.06 *d* (13.1)	2.18[#]	2.42 *d* (12.0)
12	—	—	—	1.20 *s*	1.10 *s*	1.32 *s*	1.31 *s*
13	1.78 *bs*	1.76 *bs*	1.84 *d* (1.3)	1.47 *s*	1.27 *s*	1.41 *s*	1.44 *s*
14	1.12 *s*	1.21 *s*	1.21 *s*	1.04 *s*	0.56 *s*	1.05 *s*	1.26 *s*
15	1.39 *s*	1.37 *s*	1.24 *s*	1.21 *s*	0.86 *s*	1.40 *s*	1.49 *s*
3′	6.08 *qq* (7.2; 1.4)	6.06 *qq* (7.3; 1.4)	6.14 *qq* (7.2; 1.5)	6.14 *qq* (7.2; 1.4)	5.72 *qq* (7.2; 1.4)	6.06 *qq* (7.2; 1.4)	6.15 *qq* (7.1; 1.1)
4′	1.98 *dq* (7.2; 1.4)	1.97 *dq* (7.3; 1.4)	2.00 *dq* (7.2; 1.5)	2.01 *dq* (7.2; 1.4)	1.97 *dq* (7.2; 1.4)	1.97 *dq* (7.2; 1.4)	2.02 *dq* (7.1; 1.1)
5′	1.90 *dq* (1.4; 1.4)	1.89 *dq* (1.4; 1.4)	1.92 *dq* (1.5; 1.5)	1.92 *dq* (1.4; 1.4)	1.84 *dq* (1.4; 1.4)	1.89 *dq* (1.4; 1.4)	1.94 *dq* (1.1; 1.1)
4-AcO	1.97 *s*	1.96 *s*	—	—	—	1.91 *s*	—
4-OH	—	—	4.12 *bs**	2.45 *bs**	—	2.20 *bs**	—
7-OH	—	3.65 *bs**	3.88 *bs**	—	—	—	—

Solution in $CDCl_3$ referenced to $CHCl_3$ at δ 7.26 ppm. Coupling constant J, Hz in parentheses.
* Signal changes with D_2O.
[#] Overlapping signals, determined by ^{1}H-^{1}H and ^{13}C-^{1}H COSY spectral data.

overlapped by the Me-14 signal, irradiation at δ 1.13 (H-9α and Me-14) collapsed the signals at δ_H 2.22 (H-9β) and at 4.79 (H-8) to a doublet (J = 6.2 Hz) and to a double doublet (J = 6.2 and 0.7 Hz), respectively. The ^{1}H-^{1}H COSY spectrum of compound **1** showed cross-correlation of H-8 with both H-9 and with Me-13 (long-range coupling).

Compounds **2** and **3**, unlike compound **1**, did not show in their ^{1}H NMR spectra signals associated with H-8. The ^{13}C NMR and DEPT spectra of **2** and **3** showed non-protonated carbon signals attributed to C-8 at a lower field when compared with compound **1**, suggestive of the presence of a hydroxyl group on C-8. The stereochemistry at C-8 for **2** and **3**, was proposed on the basis of the diaxial deshielding effect of the hydroxy group at C-8 on Me-14 observed in the ^{1}H NMR spectra (δ_H 1.21 for **2** and **3**, and 1.12 for **1**). In the ^{1}H NMR and ^{1}H-^{1}H COSY spectra of compound **3** coupling of H-6β was observed with H-6α, H-5α and with Me-13; cross-correlation of H-9α with Me-14 was also noted (W-coupling). Double irradiation experiments with compound **3** were used to confirm the assignments of the signals in the ^{1}H NMR spectrum: irradiation of H-6α collapsed the H-5α signal to a doublet (J = 13.1 Hz) and the signal of H-6β changed from a triple quartet to a double quartet (J = 13.1 and 1.3 Hz); irradiation of the H-9β signal (δ_H 2.21) modified the H-9α signal to a broad singlet.

The ^{13}C NMR spectrum of compound **4** showed a signal of a ketonic carbonyl group (δ_H 205.5), together with four signals of carbons linked to oxygen attributed to C-3, C-4 and two other ones, that were most likely to form an epoxy group at C-7 and C-11. The stereochemistry of the epoxy group was assigned by comparing the chemical shifts of Me-12 and Me-13 with those of compound **11** (δ_H 1.24 and 1.48) and **12** (δ_H 1.35 and 1.44) [7], and also by comparing the chemical shifts of C-7 and C-11 with those of compound **11** (δ_C 70.2 and 63.1) [7]. This indicated that the epoxy group should be β, as in **11**. The ^{1}H-^{1}H NMR spectrum of **4** in $CDCl_3$ showed cross correlation of H-9α with Me-14. Since some of the signals in the ^{1}H NMR spectrum in $CDCl_3$ overlapped, the spectrum was also taken in deuteriobenzene making it possible to confirm the assignments of H-5α, H-6 and H-9 by double irradiation.

The ^{13}C NMR spectrum of compound **5** also showed signals of a ketonic carbonyl group and a

Table 2. ^{13}C NMR spectral data of compounds **1**–**6** (75.4 MHz)

C	1	2	3	4	5	6
1	37.3 *t*	37.9 *t*	38.4 *t*	38.2 *t*	38.1 *t*	37.9 *t*
2	25.1 *t*	25.2 *t*	25.0 *t*	25.5 *t*	25.6 *t*	25.3 *t*
3	73.6 *d*	73.4 *d*	81.2 *d*	81.0 *d*	74.0 *d*	79.1 *d*
4	86.9 *s*	87.3 *s*	74.1 *s*	73.8 *s*	85.5 *s*	75.2 *s*
5	47.5 *d*	49.0 *d*	55.8 *d*	52.0 *d*	44.4 *d*	156.2 *s*
6	22.6 *t*	22.7 *t*	21.0 *t*	26.2 *t*	26.4 *t*	121.3 *d*
7	160.3 *s*	159.4 *s*	160.6 *s*	70.1 *s*	67.2 *s**	66.9 *s*
8	77.4 *d*	102.9 *s*	102.6 *s*	205.5 *s*	206.0 *s*	203.2 *s*
9	50.2 *t*	54.0 *t*	53.8 *t*	59.4 *t*	57.8 *t*	57.8 *t*
10	35.8 *s*	35.8 *s*	34.9 *s*	38.4 *s*	37.9 *s*	41.3 *s*
11	120.8 *s*	122.6 *s*	122.0 *s*	63.7 *s*	65.7 *s**	66.6 *s*
12	174.2 *s*	172.9 *s*	171.2 *s*	19.7 *q*	20.8 *q*	19.3 *q*
13	8.0 *q*	8.0 *q*	8.2 *q*	19.4 *q*	21.0 *q*	20.6 *q*
14	19.2 *q*	19.8 *q*	19.3 *q*	18.9 *q*	20.0 *q*	26.7 *q*
15	16.8 *q*	17.2 *q*	18.1 *q*	18.0 *q*	16.9 *q*	24.7 *q*
1′	166.8 *s*	167.9 *s*	168.3 *s*	168.4 *s*	166.8 *s*	168.1 *s*
2′	127.9 *s*	127.8 *s*	127.6 *s*	127.7 *s*	127.9 *s*	127.7 *s*
3′	137.9 *d*	138.0 *d*	139.0 *d*	139.0 *d*	137.8 *d*	139.0 *d*
4′	15.7 *q*	15.8 *q*	15.9 *q*	15.9 *q*	15.7 *q*	15.9 *q*
5′	20.6 *q*	20.6 *q*	20.6 *q*	20.6 *q*	20.6 *q*	20.6 *q*
4-$CH_3\underline{C}O$	170.2 *s*	170.2 *s*	—	—	170.0 *s*	—
4-$\underline{C}H_3CO$	22.5 *q*	22.7 *q*	—	—	22.5 *q*	—

Solution in $CDCl_3$ referenced to $CHCl_3$ at δ 77.23 ppm. Multiplicities of the carbons were determined by DEPT experiments. Assignments were confirmed by ^{13}C-^1H COSY spectral data.

* Interchangeable signals.

7,11-epoxy group. The stereochemistry of the epoxy group was assigned as in the case of **4**; the chemical shifts of C-7 and C-11 showed significant differences when compared to those of **11**, which suggested this group was α, as in **12**. A deshielding effect on H-9α attributed to the α-epoxy group was observed. Double irradiation experiments were used to confirm the assignments of H-5α, H-6 and H-9. Cross correlation of H-9α with Me-14 was observed in the ^1H-^1H NMR spectrum. In the ^1H NMR spectra of compounds **4** and **5**, the signals of H-6α were at a higher field (δ 0.78 and 0.81, respectively) when compared with compounds **10** (δ_H 3.02) and **8** (δ_H 2.65) [1], the related olefins. On the other hand, the signals of H-6β of compounds **4** and **5** showed little difference (δ 0.18 and 0.09, respectively) when compared with those of compounds **10** (δ_H 2.19) and **8** (δ_H 2.27), respectively. Since the ^1H NMR spectral data of compound **10** were not fully assigned in the original reference [8], the chemical shifts differences were calculated using the data of compound **10** isolated from *Pluchea quitoc* [1] and unpublished work. The absence of a H-5α signal in the ^1H NMR spectrum of compound **6** indicated the presence of a trisubstituted double bond between C-5 and C-6. This double bond caused similar deshielding effects in the signals of Me-14 and Me-15 in both the ^1H and ^{13}C NMR spectra (Tables 1 and 2) when compared with those observed for compound **4**. These experimental data suggested the same orientation for these methyl groups with respect to the double bond, leading us to propose a β-orientation for the Me-15 attached to C-4 in **6**. The presence of an epoxy group and its stereochemistry (α) was suggested using the same arguments as for compounds **4** and **5**. Me-14 showed cross correlation with H-9α in the ^1H-^1H NMR spectrum, confirming its assignment.

EXPERIMENTAL

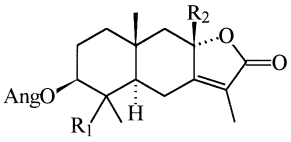
General

Mps: uncorr; IR: $CHCl_3$; ^1H and ^{13}C NMR: 300 and 75.4 MHz, respectively; EIMS: VG.AUTO SPEC-300; TLC: Silica gel 60 H (Merck 7736); CC: Silica gel (Merck 7734).

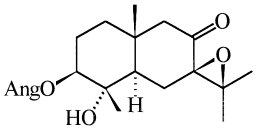
For *plant material* and *extraction* with hexane see Ref. [1] and for *partition* with $CHCl_3$ of the EtOH extract see Ref. [2].

Isolation

The fractions of the hexane extract eluted with mixts of hexane-EtOAc (9:1) from a chromatographic column afforded compounds **4** (6 mg), which was purified by CC with mixts of hexane–CH_2Cl_2–MeOH (100:100:5.2), and **5** (5 mg), which was purified by CC with mixts of hexane–CH_2Cl_2–MeOH (100:100:3.8). Compound **6** (5 mg) was obtained from the former column eluted with hexane–EtOAc (17:3) and purified by CC with mixts of hexane–CH_2Cl_2–MeOH



1 $R_1 = \beta OAc$; $R_2 = H$
2 $R_1 = \beta OAc$; $R_2 = OH$
3 $R_1 = \alpha OH$; $R_2 = OH$



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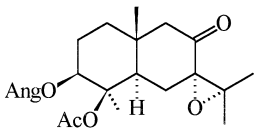

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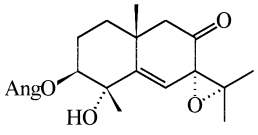

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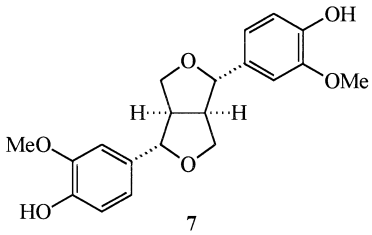

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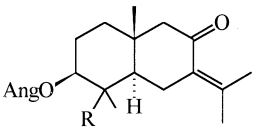
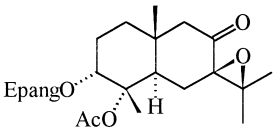


8 R = βOAc
9 R = αOAc
10 R = αOH



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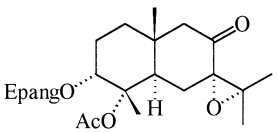

12

(100:100:5.2). The fr. of the hexane extract eluted with mixts of hexane–EtOAc (4:1) afforded compounds **1** (20 mg) and **2** (6 mg) which were purified by CC with mixts of hexane–Me_2CO (19:1 and 9:1, respectively). Compound **1** was recrystallized from hexane–EtOAc (17:3). The frs of the $CHCl_3$-soluble portion of the ethanolic extract eluted with mixts of $CHCl_3$–EtOAc (3:1) from a chromatographic column yielded compounds **3** (6 mg) and **7** (3 mg) purified by CC with mixts of hexane–CH_2Cl_2–MeOH (100:100:3) and hexane–EtOAc (13:6), respectively.

3*β-Angeloyloxy*-4*β-acetoxy-eudesm*-7(11)-*en*-8α,12-*olide* (**1**). Colourless solid, mp 148–150°. $[\alpha]_D^{25}$ −91.1° ($CHCl_3$, *c* 0.09). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1756, 1735 (CO, CO_2R); ^1H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 390 $[M]^+$ (0), 330 $[M-AcOH]^+$ (9), 231 $[M-AcOH-AngO]^+$ (20), 230 $[M-AcOH-AngOH]^+$ (68), 215 $[230-Me]^+$ (23), 91 $[C_7H_7]^+$ (31), 83 $[C_4H_7CO]^+$ (100).

3*β-Angeloyloxy*-4*β-acetoxy*-8*β-hydroxy-eudesm*-7(11)-*en*-8α,12-*olide* (**2**). Oil. $[\alpha]_D^{25}$ −11.9° ($CHCl_3$, *c* 0.08). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3346 (OH), 1734 (CO, CO_2R); ^1H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 406 $[M]^+$ (5), 246 $[M-AcOH-AngOH]^+$ (19), 228 $[246-H_2O]^+$ (83), 213 $[246-H_2O-Me]^+$ (100), 91 $[C_7H_7]^+$ (98), 83 $[C_4H_7CO]^+$ (98).

3*β-Angeloyloxy*-4α,8*β-dihydroxy-eudesm*-7(11)-*en*-8α,12-*olide* (**3**). Oil. $[\alpha]_D^{25}$ −34.5° ($CHCl_3$, *c* 0.11). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3386 (OH), 1737, 1704 (CO, CO_2R); ^1H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 364 $[M]^+$ (0), 346 $[M-H_2O]^+$ (3), 281 $[M-C_4H_7CO]^+$ (5), 246 $[M-H_2O-AngOH]^+$ (4), 231 $[246-Me]^+$ (7), 228 $[246-H_2O]^+$ (7), 213 $[246-H_2O-Me]^+$ (7), 91 $[C_7H_7]^+$ (12), 83 $[C_4H_7CO]^+$ (100).

3*β-Angeloyloxy*-7*β*-11-*epoxy*-4α-*hydroxyeudesman*-8-*one* (**4**). Colourless oil. $[\alpha]_D^{25}$ +59.0° ($CDCl_3$, *c* 0.1). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3453 (OH), 1715 (CO, CO_2R), 1236 and 1152 (C—O); ^1H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 350 $[M]^+$ (93), 335 $[M-Me]^+$ (46), 332 $[M-H_2O]^+$ (52), 314 $[332-H_2O]^+$ (44), 250 $[M-AngOH]^+$ (29), 214 $[250-2H_2O]^+$ (19), 105 $[C_8H_9]^+$ (29), 91 $[C_7H_7]^+$ (26), 83 $[C_4H_7CO]^+$ (100).

4*β-Acetoxy*-3*β-angeloyloxy*-7α,11-*epoxyeudesman*-8-*one* (**5**). Colourless oil. $[\alpha]_D^{25}$ +79.0° ($CDCl_3$, *c* 0.1). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 1727 (CO, CO_2R), 1241 and 1154

(C—O); ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 392 $[M]^+$ (0), 332 $[M-AcOH]^+$ (6), 232 $[M-AcOH-AngOH]^+$ (12), 214 $[232-H_2O]^+$ (20), 105 $[C_8H_9]^+$ (39), 91 $[C_7H_7]^+$ (29), 83 $[C_4H_7CO]^+$ (100).

3*β*-*Angeloyloxy*-7α,11-*epoxy*-4α-*hydroxy*-5,6-*dehydroeudesman*-8-*one* (**6**). Colourless oil, $[\alpha]_D^{25}$ +88.6° ($CDCl_3$, *c* 0.07). IR $\nu_{max}^{CHCl_3}$ cm^{-1}: 3420 (OH), 1721 (CO, CO_2R), 1232 and 1155 (C—O); ^{1}H NMR: Table 1; ^{13}C NMR: Table 2; EIMS *m/z* (rel. int.): 348 $[M]^+$ (10), 330 $[M-H_2O]^+$ (27), 312 $[330-H_2O]^+$ (9), 230 $[330-AngOH]^+$ (19), 83 $[C_4H_7CO]^+$ (100).

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