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EUDESMANE DERIVATIVES FROM *PLUCHEA QUITOC*

GISELLE M. S. P. GUILHON and ADOLFO H. MÜLLER*

Departamento de Química, Centro de Ciências Exatas e Naturais, Universidade Federal do Pará, Campus Universitário, 66075-900 Belém, PA, Brazil

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Key Word Index—*Pluchea quitoc*; Compositae; sesquiterpenes; eudesmane derivatives.

Abstract—Four new eudesmane derivatives have been isolated from the hexane extract of the aerial parts of *Pluchea quitoc*. Their structures were deduced from spectroscopic studies, including 2D-shift correlation and DEPT NMR experiments. Stigmasterol, β-amyrin, taraxasterol, pseudo-taraxasterol, together with two known eudesmane derivatives were also obtained. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Pluchea quitoc DC (Compositae, tribe Inuleae) is a medicinal plant, like some other plants belonging to this genus [1–4]. It has been used as an expectorant, carminative, digestive and anti-rheumatic in the north and central-west of Brazil [5]. No work on its chemical constituents has been reported so far.

As a result of this work, stigmasterol, β-amyrin, taraxasterol, pseudo-taraxasterol and six eudesmane derivatives like cuauthemone (**1–6**) have been isolated from the hexane extract of the aerial parts of *P. quitoc*. Compound **2** was reported from *P. symphytifolia* [6] and **5** from *P. suaveolens* [7]. Compound **1** was first reported from *P. suaveolens* [7], but its structure was revised for **2** [6], and like **3**, **4** and **6**, seems to be new from natural sources.

RESULTS AND DISCUSSION

The less polar fractions of the hexane extract of *P. quitoc* afforded stigmasterol and a mixture of β-amyrin, taraxasterol and, as a minor constituent, pseudo-taraxasterol. These terpenoids were identified by comparison of their ^{13}C NMR spectral data with those reported in the literature [8, 9].

The more polar fractions of the hexane extract after exhaustive chromatographic separation yielded the eudesmane derivatives **1–6**. The structure of these compounds were deduced from their ^{1}H and ^{13}C NMR spectral data (Tables 1 and 2) with the aid of ^{1}H-^{1}H and ^{13}C-^{1}H COSY spectra. The multiplicity of the carbons were determined by DEPT NMR experiments. The nature of the ester group at C-3, an angelate moiety for all compounds, was determined from the characteristic ^{1}H and ^{13}C NMR signals. The configuration at C-3, was β for all compounds with respect to the ester group and was deduced from the coupling constants of the H-3 signals on the ^{1}H NMR spectra.

The ^{1}H NMR spectra of compounds **1** and **2** were very similar except for the singlet signals of the protons associated to the hydroxy and hydroperoxide groups. In the former there were two signals attributed to protons of hydroxy groups, one at δ_H 2.77 and the other at δ_H 4.34, the latter probably being related to the carbonyl at C-8. The spectrum of **2** showed a signal of a hydroxylic proton at δ_H 3.28, but instead of the resonance of the hydroxylic proton at a lower field (δ_H 4.34) there was a signal at δ_H 8.77 that suggested the presence of a hydroperoxide group, whose location at C-11 was supported by the chemical shift of the olefinic proton H-6, Me-12 and Me-13, shifted slightly to a lower field when compared to **1** [10]. These observations permitted us to localize the hydroxy and hydroperoxide groups in **2** and to assign the signals of the hydroxylic protons in **1**. The ^{13}C NMR spectra of **1** and **2** showed significant differences; the carbon signals of Me-12 and Me-13 of compound **1** were at a lower field when compared to **2** (δ_C 29.2 and 28.9 for **1**; δ_C 25.0 and 24.4 for **2**) and the signal of C-11 was shifted 11.5 ppm upfield (δ_C 71.9 for **1** and δ_C 83.4 for **2**). These data of ^{13}C NMR presented good accordance when compared to those of compounds with a similar side chain with a hydroxy or a hydroperoxide group, which showed a chemical shift difference of 11.4 ppm for the carbons bearing these groups (δ_C 71.0 for OH and δ_C 82.4 for OOH) and *ca* 6 p.p.m. difference for the methyl groups attached to the carbon linked to OH (δ_C 30.2 and 30.1) or OOH (δ_C 24.5 and 24.6) [11]. On

Based in part on the doctoral thesis that will be presented by G.M.S.P.G. to the Universidade Federal do Pará, PA, Brazil.

*Author to whom correspondence should be addressed.

Table 1. ^{1}H NMR spectral data of compounds **1–4** and **6** (300 HMz)

Number	**1**	**2**	**3**	**4**	**6**
3α	4.84 *dd* (11.5; 4.9)	4.87 *dd* (11.5; 4.9)	6.00 *dd* (11.3; 5.6)	5.93 *dd* (11.4; 5.1)	5.86 *dd* (11.8; 5.2)
5α	2.58 *d* (2.0)	2.65 *d* (2.0)	4.02 *d* (2.2)	3.16 *dd* (13.2; 4.4)	2.71 *dd* (12.9; 2.0)
6α	—	—	—	2.65 *dd* (15.4; 4.1)	2.51 *dd* (13.9; 2.5)
6	7.05 *d* (2.0)	7.22 *d* (2.0)	6.83 *d* (2.2)	—	—
6β	—	—	—	2.27 *m*	2.07 *bt* (13.9)
9α	2.27 *d* (15.8)	2.29 *s*	2.30 *d* (15.8)	2.20 *d* (14.9)	1.56 *d* (12.3)
9β	2.33 *d* (15.8)	2.29 *s*	2.37 *d* (15.8)	2.26 *d* (14.9)	1.71 *d* (12.3)
12α	—	—	—	—	4.03 *dd* (16.3; 1.9)
12	1.42 *s*	1.45 *s*	1.40 *s*	1.96 *d* (1.5)	—
12β	—	—	—	—	4.65 *dd* (16.3; 0.8)
13	1.44 *s*	1.48 *s*	1.42 *s*	1.77 *d* (1.1)	1.59 *s*
14	0.96 *s*	0.95 *s*	0.97 *s*	0.95 *s*	1.21 *s*
15	1.21 *s*	1.23 *s*	1.34 *s*	1.38 *s*	1.32 *s*
3′	6.14 *qq* (7.2; 1.4)	6.13 *qq* (7.2; 1.4)	6.08 *qq* (7.3; 1.4)	6.05 *qq* (7.2; 1.5)	6.05 *qq* (7.1; 0.7)
4′	2.00 *dq* (7.2; 1.4)	2.00 *dq* (7.2; 1.4)	1.98 *dq* (7.3; 1.4)	1.96 *dq* (7.2; 1.5)	1.97 *bd* (7.1)
5′	1.91 *dq* (1.4; 1.4)	1.90 *dq* (1.4; 1.4)	1.90 *dq* (1.4; 1.4)	1.89 *dq* (1.5; 1.5)	1.89 *bs*
4-AcO	—	—	1.98 s	1.94 s	1.96 s
4-OH*	2.77 bs	3.28 bs	—	—	—
8-OH*	—	—	—	—	3.13 bs
11-OH*	4.34 bs	—	4.12 bs	—	—
11-OOH*	—	8.77 bs	—	—	—

Solution in $CDCl_3$ referenced to $CHCl_3$ at δ 7.26 ppm. Coupling constant *J*, Hz in parentheses. ^{1}H–^{1}H COSY spectra were used to recognise the spin–spin interactions.

*Signals change with D_2O.

the other hand, the ^{13}C NMR data for C-11, Me-12 and Me-13 of the epimer of **2** at C-4 [10] and those of odonticin, differed from **2** only by the nature of the ester group at C-3 [12], both isolated from *P. arguta*, are not in total accordance to these observations. The stereochemistry at C-4 in **1**, the same as **2**, was established by the chemical shift of the olefinic proton H-6 at δ_H 7.05 and the chemical shift of Me-15 at δ_H 1.21, because it is known that when the hydroxyl at C-4 is β-oriented the chemical shifts of the olefinic proton H-6 and Me-15 are shifted slightly upfield [10, 13].

The structure of compound **3** was deduced by comparison of its spectral data to those of its epimer at C-4 (**7**), isolated from *P. suaveolens* [7], and to those of **9**, isolated from *Epaltes brasiliensis* and different from **3** only by the nature of the ester group at C-3 [13]. Again, the signals of the olefinic proton H-6 and Me-15 in the ^{1}H NMR spectrum played an important role determining the stereochemistry at C-4.

The ^{1}H NMR data of compound **4** were similar to those of **8**, isolated from *P. suaveolens* [7] and from *Epaltes divericata* [14], but the signal of H-5α (δ_H 3.16) in **4** was at a lower field than H-6α (δ_H 2.65), as confirmed by ^{13}C-^{1}H COSY spectrum, whereas in **8** the signal of H-6α was at δ_H 3.19 and the signal of H-5α was not assigned. The ^{13}C NMR data of **4** compared to **8** [14] showed significant differences for the signals of C-4 (3.9 p.p.m. downfield) and C-15 (1.6 p.p.m. upfield). These observations lead us to propose that **4** must be the epimer at C-4 of **8**.

The ^{1}H NMR spectrum of compound **6** indicated resonances at δ_H 4.03 (*dd*, J = 16.3/1.9 Hz), and δ_H 4.65 (*dd*, J = 16.3/0.8 Hz) attributed to the geminal protons attached to C-12 of the dihydrofuran ring, which showed ^5J long-range coupling only with H-6β, and not with H-6α (^5J) or with the methyl group (^4J) attached to C-11, as observed by spin decoupling experiments. These resonances showed strong correlation only with the signal of the carbon at δ_C 72.9 (*t*, C-12) in the ^{13}C-^{1}H COSY spectrum, thus confirming the geminal position for these protons. The signal of

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

Number	1	2	3	4	5	6
1	37.0 *t*	37.0 *t*	36.5 *t*	37.7 *t*	38.3 *t*	38.5 *t*
2	25.4 *t*	25.5 *t*	25.6 *t*	25.8 *t*	25.5 *t*	25.4 *t*
3	81.0 *d*	81.0 *d*	72.9 *d*	74.0 *d*	81.3 *d*	73.8 *d*
4	73.3 *s*	73.6 *s*	85.7 *s*	87.4 *s*	74.4 *s*	87.6 *s*
5	54.1 *d*	54.2 *d*	48.6 *d*	44.9 *d*	51.1 *d*	47.5 *d*
6	141.7 *d*	143.4 *d*	140.1 *d*	25.6 *t*	25.5 *t*	20.9 *t*
7	144.6 *s*	142.3 *s*	145.1 *s*	129.9 *s*	130.3 *s*	129.5 *s*
8	200.8 *s*	197.8 *s*	200.3 *s*	201.8 *s*	202.1 *s*	97.1 *s*
9	57.5 *t*	57.8 *t*	57.6 *t*	59.9 *t*	59.8 *t*	49.7 *t*
10	39.0 *s*	39.0 *s*	40.0 *s*	36.9 *s*	36.4 *s*	35.6 *s*
11	71.9 *s*	83.4 *s*	71.7 *s*	144.5 *s*	144.8 *s*	125.1 *s*
12	29.2 *q*	25.0 *q*	28.9 *q*	23.3 *q*	23.4 *q*	72.9 *t*
13	28.9 *q*	24.4 *q*	29.1 *q*	22.5 *q*	22.7 *q*	13.3 *q*
14	18.1 *q*	18.1 *q*	18.5 *q*	19.4 *q*	18.9 *q*	19.7 *q*
15	19.5 *q*	19.4 *q*	18.7 *q*	16.7 *q*	17.5 *q*	17.0 *q*
1′	168.4 *s*	168.4 *s*	167.0 *s*	167.0 *s*	168.3 *s*	167.0 *s*
2′	127.6 *s*	127.7 *s*	127.8 *s*	128.0 *s*	127.9 *s*	128.1 *s*
3′	139.2 *d*	139.2 *d*	138.1 *d*	137.7 *d*	138.5 *d*	137.6 *d*
4′	15.9 *q*	15.9 *q*	15.7 *q*	15.7 *q*	15.8 *q*	15.7 *q*
5′	20.6 *q*	20.6 *q*	20.6 *q*	20.6 *q*	20.6 *q*	20.6 *q*
4-$\underline{C}H_3CO$	—	—	22.8 *q*	22.7 *q*	—	22.7 *q*
4-$CH_3\underline{C}O$	—	—	170.7 *s*	170.3 *s*	—	170.2 *s*

Solution in $CDCl_3$ referenced to $CHCl_3$ at δ 77.23 ppm. Multiplicity of the carbons were determined by DEPT experiments. All assignments were confirmed by ^1H–^1H and ^{13}C–^1H COSY experiments.

Me-14 (δ_H 1.21) was probably affected by the deshielding effect of $\beta(ax)$-OH at C-8, as in compound **10** (δ_H 1.25) isolated from *P. rosea* [15]. The ^{13}C NMR spectrum of **6** showed no carbonyl signal associated to C-8 and instead, there were two signals of carbon linked to oxygen, one at δ_C 97.1 (*s*) and the other at δ_C 72.9 (*t*), in agreement with the proposal of a hemicetalic carbon (C-8) and a CH_2O moiety (C-12), respectively. The ^{13}C-^1H COSY spectrum of **6** also showed that the signal of H-5α (δ_H 2.71) was at a lower field than H-6α (δ_H 2.51), as observed in compound **4**. This argument, together with the similarity of the ^{13}C NMR data of C-4 and C-15 when compared to those of **4**, allowed us to propose a β-orientation for the acetate group attached to C-4 in **6**.

EXPERIMENTAL

IR spectra were recorded in $CHCl_3$. ^1H and ^{13}C NMR spectra were recorded at 300 and 75.4 MHz, respectively, in $CDCl_3$ on a Varian GEMINI 300 instrument. EIMS were obtained by direct probe insertion at 70 eV. Silica gel 60 H (Merck 7736) and silica gel (Merck 7734), respectively, for TLC and CC were used.

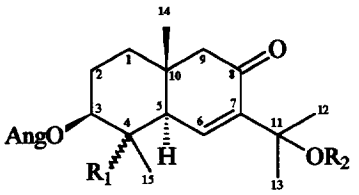
Plant material. Pluchea quitoc DC was collected at Peixe-Boi, State of Pará, Brazil, in September 1994, and identified by the botanist Dr. João Ubiratan Santos from Museu Paraense Emilio Goeldi (Belém-PA, Brazil) where a voucher specimen has been deposited.

Extraction and isolation. The aerial parts of *P. quitoc* (7 kg) were air dried and extracted with hexane at room temp. Part of the crude hexane extract (20 g) was subjected to chromatography on a silica gel column and eluted with solvents of increasing polarity in the order, hexane, hexane-EtOAc, EtOAc and MeOH. The triterpenoid fractions were obtained from 5–10% EtOAc in hexane, yielding 127 mg of a mixt of β-amyrin, taraxasterol and pseudo-taraxasterol and 229 mg of stigmasterol. The fractions of sesquiterpenic compounds were obtained from 10–20% EtOAc in hexane and were subjected to repeated CC on silica gel with mixtures of 1–10% Me_2CO in hexane to give **4** (35 mg), **6** (5 mg), **3** (20 mg), **5** (154 mg), **1** (18 mg) and **2** (25 mg).

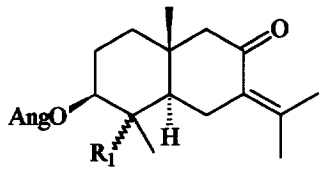
3β-*Angeloyloxy*-4α,11-*dihydroxy*-6,7-*dehydroeudesman*-8-*one* (**1**). Oil. $[\alpha]_D$ +20.65° ($CHCl_3$; *c* 0.09). IR ν_{max} cm^{-1}: 3410 (OH), 1708, 1237 (CO_2R), 1660 (C=CCO). ^1H NMR: see Table 1. ^{13}C NMR: see Table 2. EIMS *m/z* (rel. int.): 335 $[M-Me]^+$ (93), 332 $[M-H_2O]^+$ (16), 235 $[335-AngOH]^+$ (27), 217 $[235-H_2O]^+$ (24), 189 $[217-CO]^+$ (38), 83 $[C_4H_7CO]^+$ (100), 69 $[C_3H_5CO]^+$ (56).

4β-*Acetoxy*-3β-*angeloyloxy*-11-*hydroxy*-6,7-*dehydroeudesman*-8-*one* (**3**). Oil. $[\alpha]_D$ +40.62° ($CHCl_3$; *c* 0.06). IR ν_{max} cm^{-1}: 3500 (OH), 1728, 1241 (CO_2R), 1665 (C=CCO). ^1H NMR: see Table 1. ^{13}C NMR: see Table 2. EIMS *m/z* (rel. int.): 392 $[M]^+$ (10), 332 $[M-AcOH]^+$ (20), 317 $[333-Me]^+$ (46), 314 $[332-H_2O]^+$ (11), 232 $[332-AngOH]^+$ (55), 217 $[317-AngOH]^+$ (42), 189 $[217-CO]^+$ (41), 83 $[C_4H_7CO]^+$ (100), 69 $[C_3H_5CO]^+$ (51).

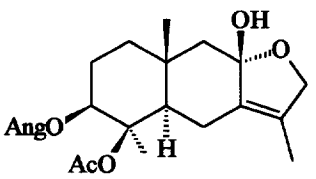
4β-*Acetoxy*-3β-*angeloyloxy*-7,11-*dehydroeudesman*-8-*one* (**4**). Oil. $[\alpha]_D$ +30.19° ($CHCl_3$; *c* 0.11). IR



1 $R_1 = \alpha OH$ $R_2 = H$
2 $R_1 = \alpha OH$ $R_2 = OH$
3 $R_1 = \beta OAc$ $R_2 = H$
7 $R_1 = \alpha OAc$ $R_2 = H$



4 $R_1 = \beta OAc$
5 $R_1 = \alpha OH$
8 $R_1 = \alpha OAc$



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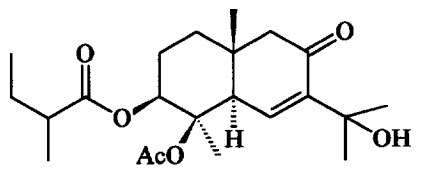

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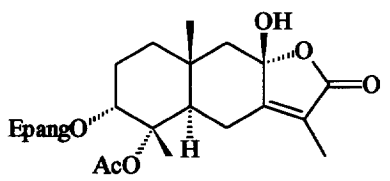

10

ν_{max} cm^{-1}: 1732, 1244 (CO_2R), 1684 (C=CCO). ^1H NMR: see Table 1. ^{13}C NMR: see Table 2. EIMS *m/z* (rel. int.): 348 $[M - CO]^+$ (11), 333 $[348 - Me]^+$ (6), 316 $[M - AcOH]^+$ (5), 233 $[333 - AngOH]^+$ (29), 216 $[316 - AngOH]^+$ (16), 201 $[216 - Me]^+$ (25), 83 $[C_4H_7CO]^+$ (100), 69 $[C_3H_5CO]^+$ (55).

4β-*Acetoxy*-3β-*angeloyloxy*-8β-*hydroxy*-8α-*oxy*-8αO.12C-7,11-*dehydroeudesmane* (**6**). Amorphous. $[\alpha]_D$ +114.28° ($CHCl_3$; *c* 0.01). IR ν_{max} cm^{-1}: 3458 (OH), 1721, 1706, 1247 (CO_2R). ^1H NMR: see Table 1. ^{13}C NMR: see Table 2. EIMS *m/z* (rel. int.): 392 $[M]^+$ (2), 391 $[M - H]^+$ (9), 390 $[M - H_2]^+$ (27), 332 $[M - AcOH]^+$ (12), 331 $[391 - AcOH]^+$ (28), 330 $[390 - AcOH]^+$ (70), 314 $[332 - H_2O]^+$ (19), 302 $[330 - CO]^+$ (40), 232 $[332 - AngOH]^+$ (20), 231 $[331 - AngOH]^+$ (28), 230 $[330 - AngOH]^+$ (35), 215 $[232 - OH]^+$ (37), 202 $[302 - AngOH]^+$ (69), 83 $[C_4H_7CO]^+$ (100), 69 $[C_3H_5CO]^+$ (51).

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