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EUDESMANE DERIVATIVES FROM *LAGGERA CRISPATA* AND *PLUCHEA CAROLONESIS*

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Key Word Index—*Laggera crispata*; *Pluchea carolonesis*; Asteraceae; sesquiterpenes; eudesmane derivatives.

Abstract—Investigation of the aerial parts of *Laggera crispata* and *Pluchea carolonesis* afforded in addition to several known compounds, three new eudesmane derivatives, 3β,4α-dihydroxy-7-epi-eudesm-11(13)-ene, 3α-(2′,3′-dihydroxy-2′-methylbutanoyl)-4,11-dihydoxy-6,7-dehydroeudesman-8-one and 3α-(3′-chloro-2′-hydroxy-2′-methylbutanoyl)cuauhtemone. The structures were elucidated by spectroscopic methods

INTRODUCTION

The Plucheeae (Family Asteraceae) is a small tribe of 28 genera and approximately 220 species. They are common in South and Central America, but many species are found also in Africa, tropical Asia, and Australia [1]. Among this tribe, we have investigated the chemical constituents of two species, *Laggera crispata* Vahl Hepper and Wood and *Pluchea carolonesis* (Jacq.) G. Donl. From about 17 species of the genus *Laggera*, only *L. aurita*, *L. alata* and, recently, *L. pterodonta* have been chemically investigated. Thymol derivatives, laggerol, bisabolene derivatives as well as several eudesmane derivatives were isolated [2–4]. On the other hand, the extracts of some species of the genus *Pluchea* are used in folk medicine and the ethnomedical properties of different species of that genus [5–7] prompted us to re-investigate *Pluchea carolonesis*. The previous chemical investigations of some *Pluchea* species have shown also that eudesmane derivatives such as pluchenes are characteristic [8–12]. Additionally, eudsmanoic acids, eudesmanolides and sulphated flavonoids have been reported [13–16]. In this paper, we report the isolation and structural elucidation of three new sesquiterpenes with eudesmane type from *L. crispata* and *P. carolonesis*.

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RESULTS AND DISCUSSION

The methylene chloride-methanol (1:1) extract of the aerial parts of *Laggera crispata* afforded the new sesquiterpene **1**, the known compound 3α-angeloyloxy-4α,11-dihydroxy-eudesm-6-en-8-one **2** [17, 18] and the two methyl esters of palmitic acid and oleic acid.

The EI-mass spectrum of compound **1** showed a molecular ion peak at *m/z* 238 corresponding to the molecular formula $C_{15}H_{26}O_2$, followed by elimination of a molecule of water and methyl group at *m/z* 220 and 205, respectively. The ^1H and ^{13}C NMR spectra (Tables 1 and 2) showed that **1** had an eudesm-11,13-ene skeleton with a 3,4-diol. Two tertiary methyl singlet signals appeared at δ 0.92 and 1.04 and were assigned to H-14 and H-15, respectively. The olefinic methyl H-12 was established from the downfield signal (3H) which appeared at δ 1.73 as a doublet (J = 1.5 Hz) and showed allylic coupling in the ^1H-^1H COSY spectrum to the exomethylene proton signals at δ 4.84 and 4.90. These exomethylene protons which correlated with a carbon signal at δ 111.0 (*t*) in the 2D ^1H-^{13}C COSY spectrum, were indicative of a $\Delta^{11,13}$ double bond. The presence of a secondary hydroxyl group at C-3 was deduced from a signal which appeared at δ 3.41 as a doublet of doublets (J = 11, 5 Hz) and which showed coupling with H-2α at δ 1.49 and H-2β at δ 1.71 in the ^1H-^1H COSY spectrum.

Table 1. ^{1}H NMR spectral data of compounds **1** and **1a**. (400 MHz, $CDCl_3$, δ-values)

H	1	1a
2α,2β	1.49 *m*, 1.71 *m*	*
3	3.41 *dd*, *J* = 11, 5 Hz	4.71 *dd*, *J* = 11, 4 Hz
5	1.28 *dd*, *J* = 13, 3 Hz	*
6α	2.03 *ddd*, *J* = 14, 6, 3 Hz	*
6β	1.27 *ddd*, *J* = 14, 13, 3 Hz	*
7	2.41 *br s*	2.45 *br s*
8α,8β	1.81 *m*, 1.69 *m*	*
12	1.73 *d*, *J* = 1.5 Hz	1.75 *d*, *J* = 1.5 Hz
13	4.84 *br s*	4.86 *br s*
13′	4.90 *br d*, *J* = 1.5 Hz	4.93 *br s*
14	0.92 *s*	0.99 *s*
15	1.04 *s*	1.12 *s*
OAc	-	2.19 *s*

*Overlapping signals.

Furthermore, acetylation of **1** gave the monoacetate derivative **1a** in which H-3 was shifted more downfield and resonated at δ 4.7 *dd* (J = 10, 4 Hz). The stereochemistry of the chiral center at C-3 was deduced from the coupling constants ($J_{2\alpha,3}$ = 11 and $J_{2\beta,3}$ = 5 Hz) that clearly indicated a 3β-OH [19, 20]. This was supported by the NOE's observed between H-3, H-2α and H-5α, while no effects were observed between H-3, H-14 and/or H-15, while the configuration of 4α-OH was established from the clear NOE's between H-14 and H-15 with H-6β. The broad singlet at δ 2.41 (H-7) was in agreement with 7-epi configuration [21] which was supported by the clear NOE's observed between H-7, H-6β and H-8β. The other protons were established by 2D ^{1}H and ^{1}H-^{13}C COSY experiments. Finally, the structure of **1** was proved by 2D-hetero long range coupling HMBC experiments (Table 3). The structure of the known compound **2** was deduced by comparison of its ^{1}H NMR and EI-mass spectral data with those in the literature [17, 18].

The aerial parts of *P. carolonesis* gave two new eudesmane derivatives, namely, 3α-(2′,3′-dihydroxy-2′-methylbutanoyl)4,11-dihydroxy-6,7-dehydroeudesman-8-one **3** and 3α-(3′-chloro-2′-hydroxy-2′-methylbutanoyl)cuauhtemone **4**, in addition to the eight known compounds, cuauhtemone **5** [8], 3α-angeloyl cuauhtemone **6** [8], 3α-(2′,3′-epoxy-2′-methylbutanoyl)cuauhtemone **7** [8], 4-acetoxy-3α-(2′,3′-epoxy-2-methylbutanoyl) cuauhtemone **8** [9], 3α-(2′,3′-epoxy-2′-methylbutanoyl)-4α,11-dihydroxy-6,7-dehydroeudesman-8-one **9** [22], 4α-acetoxy-3α-(2′,3′-epoxy-2-methylbutanoyl)-11-hydroxy-6,7-dehydroeudesman-8-one **10** [22], 3α-(3′-chloro-2′-hydroxy-2′-methylbutanoyl)-4α,11-dihydroxy-6,7-dehydroeudesman-8-one **11** [22], 4α-acetoxy-3α-(3′-chloro-2′-hydroxy-2′-methylbutanoyl)-11-hydroxy-6,7-dehydroeudesman-8-one **12** [22]. Recently, we have confirmed the absolute configuration of **8** by X-ray analysis [23].

Table 2. ^{13}C NMR spectral data of compounds (**1**–**2**). (100 M Hz, $CDCl_3$, δ-values)

C	1*	1a*†	Multiplicity§
1	39.5	39.2	*t*
2	27.4	25.8	*t*
3	79.7	82.1	*d*
4	75.8	74.5	*s*
5	47.1	48.3	*d*
6	22.5	22.1	*t*
7	38.8	38.8	*d*
8	23.4	23.1	*t*
9	40.1	40.2	*t*
10	35.2	35.2	*s*
11	146.7	146.8	*s*
12	22.8	22.7	*q*
13	111.0	111.5	*t*
14	18.7	18.9	*q*
15	16.2	17.5	*q*

* Assignments were confirmed by ^{1}H-^{13}C COSY
† 3-OAc: 172.0 and 21.4
‡ 3-OTig: 166.8, 127.4, 139.1, 20.1 and 15.6
§ Deduced from DEPT experiments.

Table 3. Long-range hetero cosy (HMBC) spectral data of compound **1**

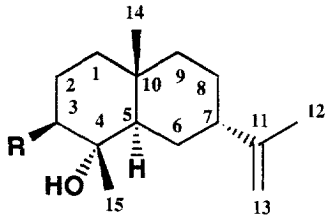
C	H
C-1	H-2, H-5, H-14
C-3	H-2, H-5, H-6, H-15
C-4	H-2, H-3, H-5, H-6, H-15
C-5	H-6, H-7, H-14, H-15
C-7	H-5, H-9, H-12, H-13, H-13′
C-8	H-6, H-9
C-9	H-5, H-8, H-14
C-10	H-1, H-9, H-5, H-6, H-14
C-11	H-6, H-12, H-13, H-13′
C-12	H-13, H-13′
C-14	H-1, H-5, H-9
C-15	H-3, H-5

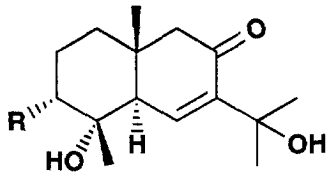
The structure of compound **3** was deduced by comparison of the ^{1}H NMR spectrum with those of **9**–**12** [22, 23]. The characteristic H-6 was detected as a doublet at δ 7.02, H-3 as a triplet at δ 5.02, H-3′ as a quartet at δ 4.00 and H-5′ as a doublet at δ 2.82. Furthermore, the HRCI-mass spectrum exhibited a peak at *m/z* 385.2211 (calc. 385.2226, $C_{20}H_{32}O_7$), followed by loss of a molecule of water at *m/z* 367.2103 (calc. 367.2120, $C_{20}H_{31}O_6$). A close compound to **3** has been reported from *Pluchea arguta* [24].

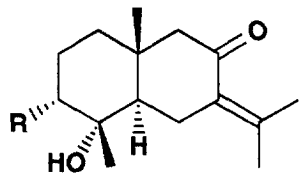
Similarly, the structure of compound **4** could be easily established by comparison of its ^{1}H NMR data with those of **7** [8]. The dowinfield shift of H-3′ at δ 4.28 suggested that the side chain at C-3 was 3′-chloro-2′-hydroxy-2′-methylbutanoyl, instead of 2′,3′-epoxy-2′-methylbutanoyl in **7**. This was supported by the HRCI-mass spectrum which showed a molecular ion peak at *m/z* 387.1916 (calc. 387.1938, $C_{20}H_{31}O_5Cl$), with an isotopic peak at *m/z* 389.1970, (calc. 389.1945, $_{20}H_{32}O_5Cl^{37}$). The other signals were identical with compound **7**.

EXPERIMENTAL

The aerial parts (150 g) of *L. crispata* were collected in Ethiopia, Addis Ababa, in December 1990

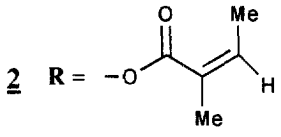




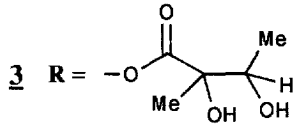


1 R = OH

1a R = OAc

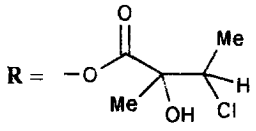


2 R =



3 R =

4



R =

(voucher 92/17, identified by Dr. C. Jeffrey, Kew Garden, London) and extracted with CH_2Cl_2–MeOH (1:1) for 24 hr. The solvent was removed under red. pres. to obtain 7 g of a gummy material. The extract was separated by flash column, silica gel, using *n*-hexane, increasing the degree of polarity by addition of CH_2Cl_2. Separation of the *n*-hexane–Et_2O (75:25) fraction by Sephadex LH-20, solvent *n*-hexane–CH_2Cl_2–MeOH (5:3:0.5) gave 15 mg of **7** and the *n*-hexane–Et_2O (1:1) fraction gave 38 mg of **1**.

3β,4α-Dihydroxy-7-epi-eudesm-11(13)-ene (**1**)

Colourless oil; IR: $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400. EIMS (direct inlet) 70 eV, *m/z* (rel. int.): 238 $[M]^+$ (9), 220 $[M-H_2O]^+$ (14), 205 $[220\text{-}CH_3]^+$ (10), 179 $[220\text{-}C_3H_5]^+$, 163 (12), 138 (40), 123 (32), 107 (19), 71 (33), 43 (100).

Acetylation of (**1**)

About 15 mg of **1** were acetylated using 5 ml Ac_2O in pyridine and left for 24 hr at room temp. The excess of the Ac_2O was decomposed by addition of water and the organic layer was extracted with $CHCl_3$. After evaporation under red. pres. the resultant derivatives were subjected to prep. TLC (silica gel, petrol–ether 1:1) to give 11 mg of **1a**.

3β-Acetoxy,4α-hydroxy-7-epi-eudesm-11(13)-ene (**1a**)

Colourless oil; IR: $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (OH), 1745 (C=O) positive ion FAB-MS (direct inlet) *m/z* (rel. int.): 281 $[M+H]^+$ (10), 263 $[M-H_2O+H]^+$ (55), 203 $[263\text{-AcOH}]^+$ (100), 161 (28), 117 (35), 95 (63), 59 (66). For ^1H and ^{13}C NMR data (see Tables 1 and 2).

The aerial parts of *P. carolonesis* were collected in Haiti Island in March 1990, a voucher specimen was deposited in the Herbarium of Department de Quimica, University de National Pedro Henriquez, Santo Domingo, Dominican. The air-dried aerial parts were extracted with CH_2Cl_2–MeOH (1:1) and the extract was separated as reported previously [24]. The first fraction, *n*-hexane–Et_2O (3:1), was subjected to Sephadex LH-20 column, solvent *n*-hexane–CH_2Cl_2–MeOH (5:3:0.5) to give 40 mg of **8**, 6 mg of **10** and 6 mg of **12**. The second fraction, *n*-hexane–Et_2O (2:1), gave 4 mg of **6**, 7 mg of **7** and 2 mg of **9**. The third fraction, *n*-hexane–Et_2O (1:1), gave 12 mg of **5**, 2 mg of **4**, 4 mg of **11** and 1.5 mg of **3**.

3α-(2′,3′-Dihydroxy-2′-methylbutanoyl)4,11-dihydoxy-6,7-dehydroeudesman-8-one (**3**)

Colourless gum; IR: $\nu_{max}^{CHCl_3}$ cm^{-1}: 3500–3400 (OH), 1730 (C=O, ester), 1670 (C=O, α,β-unsaturated C=O). HR-CI^+ MS: *m/z* 385.2211 (calc. for $C_{20}H_{32}O_7$, 385.2226); CIMS MS *m/z* (rel. int.): 385 $[M]^+$ (12), 367 $[M-H_2O]^+$ (72), 349 $[M-2H_2O]^+$ (10), 322 (7), 279 (17), 251 (83), 233 (100), 215 (98) 191 (40), 149 (47). ^1H NMR (400 M Hz, $CDCl_3$): δ 7.03 (1H, *d*, *J* = 2.3 Hz, H-3), 5.10 (1H, *br t*, *J* = 2.5 Hz, H-3), 4.00 (1H, *q*, *J* = 6.5 Hz, H-3′), 2.81 (1H, *d*, *J* = 2.3 Hz, H-5), 2.42 (1H, *br d*, *J* = 14 Hz, H-9α), 2.32 (1H, *br d*, *J* = 14 Hz, H-9β), 1.49 (3H, *s*, H-13), 1.45 (3H, *s*, H-12), 1.38 (3H, *s*, H-5′), 1.26 (3H, *d*, *J* = 6.5 Hz, H-4′), 1.23 (3H, *s*, H-15), 0.99 (3H, *s*, H-14).

3α-(3′-Chloro-2′-hydroxy-2′-methylbutanoyl)cuauhtemone (**4**)

Colourless gum; IR: $\nu_{max}^{CHCl_3}$ cm^{-1}: 3400 (OH), 1735 (C=O, ester), 1670 (C=O, α,β-unsaturated C=O). HR-CI^+ MS: *m/z* 387.1916 (calc. for $C_{20}H_{32}O_5Cl$, 387.1938); CIMS MS *m/z* (rel. int.): 387 $[M]^+$ (55), 370 (100), 334 (10), 236 (90), 217 (85), 193 (44), 175 (15). ^1H NMR (400 M Hz, $CDCl_3$): δ 4.79 (1H, *br t*, *J* = 2.5 Hz, H-3), 4.28 (1H, *q*, *J* = 6 Hz, H-3′), 2.88 (1H, *dd*, *J* = 13, 5 Hz, H-5), 2.14 (1H, *br d*, *J* = 14 Hz, H-9α), 2.20 (1H, *br d*, *J* = 14 Hz, H-9β), 1.95 (3H, *br s*, H-12), 1.78

(3H, *br s*, H-13), 1.45 (3H, *d*, $J = 6$ Hz, H-4′), 1.36 (3H, *s*, H-5′), 1.19 (3H, *s*, H-15), 0.89 (3H, *s*, H-14).

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