Phytochemistry, Vol. 24, No. 12, pp. 3053–3055, 1985.
Printed in Great Britain.

0031–9422/85 $3.00 + 0.00

CUAUTHEMONE DERIVATIVES FROM *TESSARIA INTEGRIFOLIA* AND *PLUCHEA SYMPHYTIFOLIA*

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(*Received* 7 *February* 1985)

Key Word Index—*Tessaria integrifolia*; *Pluchea symphytifolia*; Compositae; sesquiterpenes; eudesmanes; cuauthemone derivatives.

Abstract—The aerial parts of *Tessaria integrifolia* afforded in addition to known compounds nine further cuauthemone derivatives and those from *Pluchea symphytifolia* also a further sesquiterpene of this type. The structures of two pairs of similar compounds are revised from 11-hydroxy to 11-peroxy derivatives.

INTRODUCTION

The generic limits of *Tessaria* and *Pluchea* have been discussed in detail from the anatomic point of view [1]. As a result *T. integrifolia* Ruiz. et Pavon remains the only species of the genus. Nothing was known on the chemistry of this species and we have therefore studied a sample collected in Costa Rica.

RESULTS AND DISCUSSION

The aerial parts of *Tessaria integrifolia* afforded the bisthienyl derivative **18**, β-selinene, squalene, the dimeric phenylpropane derivative **17**, which was prepared previously from the corresponding diisovalerate by lithium alanate reduction [2], and the cuauthemone derivatives **6** [3], **1–5** and **10–13**. The structures of **1–5** were deduced from their ^{1}H NMR spectra (Table 1) which were close to that of the known angelate **6** [3]. The nature of the ester group at C-4 followed from the characteristic ^{1}H NMR signals.

The structures of **10–13** also could be deduced from the ^{1}H NMR spectra (Table 1) which differed from those of **1–5** by the absence of olefinic methyl signals which were replaced by singlets for methyls on an oxygen bearing carbon. Furthermore new downfield narrowly split signals were present, obviously due to olefinic protons in the β-position to a carbonyl group. The spectra of **10** and **11**, which were both senecioates, differed only in the chemical shift of the olefinic proton and by a singlet at δ7.92 in the ^{1}H NMR spectrum of **10**. The latter is characteristic for hydroperoxide protons. Accordingly, compound **10** showed a very small molecular ion in its mass spectrum corresponding to $C_{20}H_{30}O_6$ which by loss of H_2O_2 led to *m/z* 332 ($C_{20}H_{28}O_4$). Addition of triphenylphosphine transformed **10** to the carbinol **11**. The absence of the peroxy group caused a clear upfield shift of the olefinic signal. Spin decoupling allowed the assignment of most signals except those of H-1 and H-2 which were obscured multiplets. Comparison of the data with those of similar eudesmane derivatives led to the proposed structures [4]. The ^{1}H NMR spectra of **12** and **13** (Table 1) indicated that these ketones only differed from **10** and **11** by the ester group at C-4, its nature followed from the typical signals.

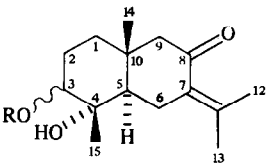
A sample of the aerial parts of *Pluchea symphytifolia* (Miller) Gills collected in Jamaica gave taraxasteryl acetate, thymohydroquinone dimethyl ether, the thiophene acetylenes **19** and **20**, 5-angeloyloxycarvotagetone [3] as well as the cuauthemone derivatives **7** [5], **8** [3], **9** [6], **12, 13, 14, 15** and **16** [4]. The structure of **15** followed from the ^{1}H NMR spectrum (Table 1) which was close to that of the corresponding angelate **13**. However, due to the presence of a 4α-acetoxy group the H-6 signal was shifted upfield. The presence of a hydroperoxide again followed from a singlet at δ7.74. This signal was overlooked in two pairs of similar cuauthemone derivatives, two 3β-angeloyloxy compounds (**14** and the corresponding 4-*O*-acetate) isolated from *Pluchea suaveolens* [5] and two 3β-2-methylbutyrates from *Epaltes brasiliensis* [7]. The structures of these compounds have to be revised from 11-hydroxy to 11-peroxy derivatives.

The chemistry of *Tessaria* and, at least of a large part, of *Pluchea* seems to be very similar. Cuauthemone derivatives are widespread in *Pluchea* but have been also reported from *Epaltes* [7] and *Blumea* [4].

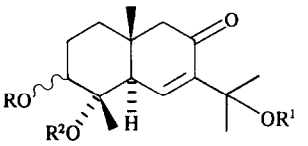
These genera, however, are also placed in the *Pluchea* group of the subtribe Inulinae [8]. The dimeric dihydroconiferyl alcohol **17** and the bisthiophene **18** have not been reported previously from any member of this group while disubstituted monothiopheneacetylenes are widespread in this group. Further investigations of representatives of the *Pluchea* group may show whether these compounds are useful chemotaxanomic markers.

EXPERIMENTAL

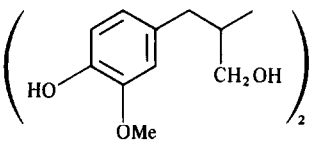
The air dried plant material was extracted with Et_2O–petrol–MeOH (1:1:1) at 20° for 12 hr. The extracts obtained were separated as described previously [9]. From the extract of the flowering aerial parts of *Tessaria integrifolia* (360 g, collected in March 1983 in Costa Rica, voucher deposited in the US National Herbarium) five CC (silica gel) fractions were taken:



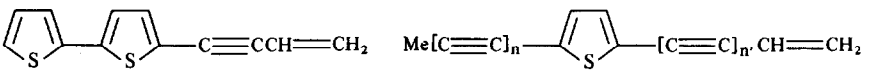
	1	2	3	4	5	6	7	8	9
R	αiBu*	αSen*	αMesen*	αMeval*	αAc	αAng*	βAng	αEpang*	αEpang (4–OAc)



	10	11	12	13	14	15	16
R	αSen	αSen	αAng	αAng	βAng	αEpang	αAng
R^1	OH	H	H	OH	OH	OH	OH
R^2	H	H	H	H	H	Ac	Ac



17



18 **19** n = 2, n′ = 1 **20** n = 1, n′ = 2

* iBu = $COCHMe_2$; Sen = $COCH{=}CMe_2$; MeSen = $COCH{=}C(Me)Et$ (*E*); Meval = $COCH_2CH(Me)Et$; Ang = $COC(Me){=}CHMe$ (*Z*); Epang = $COC(Me)—CHMe$ (O)

1 (petrol), 2 (Et_2O–petrol, 1:9), 3 (Et_2O–petrol, 1:3 and 1:1), 4 (Et_2O) and 5 (Et_2O–MeOH, 9:1). TLC (silica gel, PF 254, petrol) of fraction 1 gave 50 mg β-selinene, TLC (Et_2O–petrol, 1:9) of fraction 2 afforded 10 mg squalene and 7 mg **18**. Fraction 3 contained a mixture of triterpenes and fraction 4 was separated by TLC (Et_2O–petrol, 3:2, two developments) affording a broad band which by HPLC (RP 8, MeOH–H_2O, 7:3, always *ca* 100 bar, flow rate 3 ml/min) gave a mixture (4*a*, R_t = 3.5 min), 1 mg **1** (R_t = 4.1 min), a second mixture (4*b*, R_t = 5.3 min), 3 mg **3** (R_t = 8 min) and 1 mg **4** (R_t = 9.0 min). Repeated TLC of fraction 4*a* (CH_2Cl_2–C_6H_6–Et_2O, 2:2:1, three developments) gave 2 mg **13** (R_f 0.22), 1 mg **10** (R_f 0.20), 1.5 mg **12** (R_f 0.15) and 1 mg **11** (R_f 0.1). Repeated TLC of 4*b* (CH_2Cl_2–C_6H_6–Et_2O, 9:9:1, four developments) gave 20 mg **6** (R_f 0.65) and 7 mg **2** (R_f 0.50). TLC (Et_2O–petrol, 4:1) of fraction 5 gave a broad band (R_f 0.45) which was separated by HPLC (RP 8, MeOH–H_2O, 3:2) affording 0.5 mg **5** (R_t = 4.7 min), 20 mg **17** (R_t = 5.2 min) and 0.5 mg **11** (R_t = 8.5 min).

The extract of the aerial parts (100 g) of *Pluchea symphytifolia* (voucher Jam 2, deposited in the US National Herbarium) gave four CC (silica gel) fractions: 1 (Et_2O–petrol, 1:9), 2 (Et_2O–petrol, 1:3), 3 (Et_2O–petrol, 1:1) and 4 (Et_2O and Et_2O–MeOH, 9:1). TLC of fraction 1 (Et_2O–petrol, 1:19) gave 2 mg **19** and 2 mg **20**. TLC of fraction 2 (Et_2O–petrol, 1:3) gave 6 mg thymohydroquinone dimethyl ether, 80 mg taraxasteryl acetate and 30 mg 2-angeloyloxycarvotagetone. TLC of fraction 3 (Et_2O–petrol, 1:1, several developments) gave 30 mg **7**, 5 mg **13** and 5 mg **14**. TLC of fraction 4 (Et_2O–petrol, 3:2, several developments) gave 270 mg **7**, 200 mg **9**, 30 mg **8**, 8 mg **15**, purified by HPLC (RP 8, MeOH–H_2O, 3:2, R_t = 10.2 min), 4 mg **16** and 20 mg **12**.

Cuauthemone-3-O-*isobutyrate* (**1**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1740 (CO_2R), 1685, 1620 (C=CC=O); MS *m/z* (rel. int.): 322.214 $[M]^+$ (82) (calc. for $C_{19}H_{30}O_4$: 322.214), 234 $[M - RCO_2H]^+$ (12), 216 $[234 - H_2O]^+$ (36), 201 $[216 - Me]^+$ (16), 71 $[C_3H_7CO]^+$ (100); $[\alpha]_D^{20°} = +164$ ($CHCl_3$; *c* 0.07).

Cuauthemone-3-O-*senecioate* (**2**). Colourless oil;

Table 1. ^{1}H NMR spectral data of compounds **1–5**, **10–13** and **15** (400 MHz, $CDCl_3$, TMS as internal standard)

	1	2	3	4	5	10	11	12	13	15
H-3	4.81 *br t*	4.85 *br t*	4.86 *br t*	4.83 *br t*	4.83 *br t*	4.90 *br t*	4.90 *br t*	4.98 *br t*	4.99 *br t*	5.87 *br t*
H-5	1.98 *dd*	2.02 *dd*	2.02 *dd*	1.98 *dd*	1.99 *dd*	2.85 *d*	2.83 *d*	2.80 *d*	2.79 *d*	3.10 *d*
H-6	2.99 *dd*	3.00 *dd*	3.00 *dd*	3.00 *dd*	2.99 *dd*	7.25 *d*	2.06 *d*	7.06 *d*	7.25 *d*	6.79 *d*
H-6′	1.80 *br dd*	1.82 *m*	1.82 *br dd*	1.82 *br dd*	1.80 *br dd*					
H-9	2.23 *s*	2.24 *s*	2.27 *d*	2.24 *s*	2.24 *s*	2.31 *s*	2.33 *s*	2.33 *s*	2.30 *s*	2.37 *d*
H-9′			2.22 *d*							2.29 *d*
H-12	2.04 *d*	2.03 *d*	2.03 *d*	2.04 *d*	2.03 *d*	1.49 *s*	1.45 *s*	1.46 *s*	1.48 *s*	1.48 *s*
H-13	1.85 *d*	1.84 *d*	1.84 *d*	1.84 *d*	1.84 *d*	1.47 *s*	1.43 *s*	1.44 *s*	1.47 *s*	1.52 *s*
H-14	0.95 *s*	0.95 *s*	0.96 *s*	0.96 *s*	0.94 *s*	0.98 *s*	0.99 *s*	1.00 *s*	0.95 *s*	0.95 *s*
H-15	1.26 *s*	1.26 *s*	1.27 *s*	1.26 *s*	1.25 *s*	1.28 *s*	1.26 *s*	1.29 *s*	1.27 *s*	1.55 *s*
OCOR	2.63 *qq*	5.75 *qq*	5.72 *tq*	2.17 *dd*	—	5.75 *qq*	5.76 *qq*	6.16 *qq*	6.13 *qq*	3.05 *q*
				2.39 *dd*						
	1.22 *q*	2.19 *d*	2.20 *br q*	0.95 *d*		2.20 *d*	2.21 *d*	2.05 *dq*	2.02 *dq*	1.30 *d*
	1.21 *d*	1.92 *d*	1.09 *t*	0.90 *t*		1.92 *d*	1.94 *d*	1.96 *dq*	1.93 *dq*	1.58 *s*
			2.19 *d*							
OAc	—	—	—	—	2.13 *s*	—	—	—	—	2.03 *s*
OOH						7.92 *s*			8.03 *s*	7.74 *s*

J (Hz): Compounds **1–5**: 2, 3 = 2′, 3 = 3; 5, 6 = 4; 5, 6′ = 13; 6, 6′ = 16; 6′, 12 = 2; 6′, 13 ~ 1 (compound **3**: 9, 9′ = 15); compounds **10–13** and **15**: 2, 3 = 2′, 3 = 2.7; 5, 6 = 2.4 (compound **15**: 9, 9′ = 16); OiBu: 2, 3 = 2, 4 = 7; OSen: 2, 4 = 2, 5 = 1; OMesen: 2, 4 = 2, 6 = 1; 4, 5 = 7; OMeval: 2, 2′ = 15; 2, 3 = 3, 6 = 4, 5 = 7; OAng: 3, 4 = 7; 3, 5 = 4, 5 = 1; OEpang: 3, 4 = 5.

IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1725 (C=CCO$_2$R), 1690 (C=CCO); MS *m/z* (rel. int.): 334.214 [M]$^+$ (26) (calc. for $C_{20}H_{30}O_4$: 334.214), 234 [M − RCO$_2$H]$^+$ (8), 216 [234 − H$_2$O]$^+$ (14), 83 [C$_4$H$_7$CO]$^+$ (100), 55 [83 − CO]$^+$ (50); $[\alpha]_D^{20°}$ = +93 ($CHCl_3$; *c* 0.31).

Cuauthemone-3-O-(4-*methylsenecioate*) (**3**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1725 (C=CCO$_2$R), 1685 (C=CC=O); MS *m/z* (rel. int.): 348.230 [M]$^+$ (22) (calc. for $C_{21}H_{32}O_4$: 348.230), 234 [M − RCO$_2$H]$^+$ (6), 216 [234 − H$_2$O]$^+$ (14), 97 [C$_5$H$_9$CO]$^+$ (100), 69 [97 − CO]$^+$ (21); $[\alpha]_D^{20°}$ = +93 ($CHCl_3$; *c* 0.31).

Cuauthemone-3-O-(3-*methylvalerate*) (**4**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1740 (CO$_2$R), 1685 (C=CC=O); MS *m/z* (rel. int.): 350.246 [M]$^+$ (78) (calc. for $C_{21}H_{34}O_4$: 350.246), 234 [M − RCO$_2$H]$^+$ (14), 216 [234 − H$_2$O]$^+$ (28), 99 [C$_5$H$_{11}$CO]$^+$ (36), 71 [99 − CO]$^+$ (50), 55 (100); $[\alpha]_D^{20°}$ = +38 ($CHCl_3$; *c* 0.06).

Cuauthemone-3-O-*acetate* (**5**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1740 (OAc), 1680 (C=CC=O); MS *m/z* (rel. int.): 294.183 [M]$^+$ (100) (calc. for $C_{17}H_{26}O_4$: 294.183), 234 [M − HOAc]$^+$ (12), 216 [234 − H$_2$O]$^+$ (24), 201 [216 − Me]$^+$ (18).

3α-*Senecioyloxy*-4α-*hydroxy*-11-*peroxy*-*eudesm*-6-*èn*-8-*one* (**10**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1725 (C=CCO$_2$R), 1680 (C=CC=O); MS *m/z* (rel. int.): 366 [M]$^+$ (0.01), 332.197 [M − H$_2$O$_2$]$^+$ (0.5) (calc. for $C_{20}H_{28}O_4$: 332.198), 317 [332 − Me]$^+$ (5), 315 [332 − OH]$^+$ (3), 215 [315 − RCO$_2$H]$^+$ (4), 83 [C$_4$H$_7$CO]$^+$ (100), 55 [83 − CO]$^+$ (29). To 1 mg **10** in 0.5 ml $CDCl_3$ 5 mg triphenyl phosphine was added. After 5 min the ^{1}H NMR spectrum was identical with that of **11**.

3α-*Senecioyloxy*-4α,11-*dihydroxy*-*eudesm*-6-*en*-8-*one* (**11**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1725 (C=CCO$_2$R), 1660 (C=CC=O); MS *m/z* (rel. int.): 332.199 [M − H$_2$O]$^+$ (1) (calc. for $C_{20}H_{28}O_4$: 332.199), 317 [332 − Me]$^+$ (5), 314 [332 − H$_2$O]$^+$ (5), 215 [314 − OCOR]$^+$ (30), 214 [314 − RCO$_2$H]$^+$ (10), 83 [C$_4$H$_7$CO]$^+$ (100), 55 [83 − CO]$^+$ (42).

3α-*Angeloyloxy*-4α,11-*dihydroxy*-*eudesm*-6-*en*-8-*one* (**12**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1725 (C=CCO$_2$R), 1670 (C=CC=O); MS *m/z* (rel. int.): 332.199 [M − H$_2$O]$^+$ (1) (calc. for $C_{20}H_{28}O_4$: 332.199), 317 [332 − Me]$^+$ (21), 217 [317 − RCO$_2$H]$^+$ (7), 83 [C$_4$H$_7$CO]$^+$ (100), 55 [83 − CO]$^+$ (43); $[\alpha]_D^{22°}$ = +99 ($CHCl_3$; *c* 0.08).

3α-*Angeloyloxy*-4α-*hydroxy*-11-*peroxy*-*eudesm*-6-*en*-8-*one* (**13**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH), 1725 (C=CCO$_2$R), 1670 (C=CC=O); MS *m/z* (rel. int.): 332.199 [M − H$_2$O$_2$]$^+$ (1) (calc. for $C_{20}H_{28}O_4$: 332.199), 317 [332 − Me]$^+$ (12), 83 [C$_4$H$_7$CO]$^+$ (100), 55 [83 − CO]$^+$ (68).

3α-[2,3-*Epoxy*-2-*methylbutyryloxy*]-4α-*acetoxy*-11-*peroxy*-*eudesm*-6-*en*-8-*one* (**15**). Colourless oil; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1740 (OAc, CO$_2$R), 1680 (C=CO); MS *m/z* (rel. int.): 390.204 [M − H$_2$O$_2$]$^+$ (0.1) (calc. for $C_{22}H_{30}O_6$: 390.204), 365 [M − OAc]$^+$ (2), 231 [365 − RCO$_2$H, H$_2$O]$^+$ (22), 61 (100).

Acknowledgements—We thank Dr. R. M. King for identification of the plant material, the Deutsche Forschungsgemeinschaft and the Fonds der Chemie for financial support.

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