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HUMULENE DERIVATIVES FROM *ACRITOPAPPUS PRUNIFOLIUS**

FERDINAND BOHLMANN, CHRISTA ZDERO, ROBERT M. KING† and HAROLD ROBINSON†

Institute for Organic Chemistry, Technical University of Berlin, D-1000, Berlin 12, West Germany; †Smithsonian Institution, Washington DC 20560, U.S.A.

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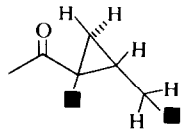
Key Word Index—*Acritopappus prunifolius*; Compositae; Eupatorieae; sesquiterpenes; humulene derivatives; cadinene derivatives; new carbon skeleton; eudesmane derivative.

Abstract—The investigation of *Acritopappus prunifolius* afforded in addition to known compounds two new derivatives of γ-humulene, a rearranged α-humulene derivative with a new carbon skeleton, a furanocadinene and a eudesmane alcohol. The structures were elucidated by spectroscopic methods. The chemotaxonomic situation is discussed briefly.

INTRODUCTION

So far, five species from the small Brazilian genus *Acritopappus* (tribe Eupatorieae) have been investigated [1, 2]. Labdane and clerodane derivatives were isolated from all species, but also some eudesmane, cadinane and dehydronerolidol derivatives were present. Furthermore, most species contained humulene and the widespread trideca pentaynene. We have now investigated a new species, *Acritopappus prunifolius* K. et R. The roots afforded traces of trideca pentaynene, stigmasterol, squalene, dammadienyl acetate, α- and γ-humulene, germacrene D, the obliquine derivative **1** [3], the angelate **2** [4] and three further sesquiterpenes, the ketone **3**, the alcohol **5** and the acetate **6**, also present in the aerial parts. The structure of **3** followed from the ^{1}H NMR data of **3** and those of the alcohol obtained by boranate reduction (Table 1). The molecular formula, $C_{15}H_{24}O$, together with the IR band at 1675 cm^{-1} and an olefinic proton signal in the ^{1}H NMR spectrum indicated the presence of a bicyclic sesquiterpene ketone whilst a high field double doublet at δ 0.12 (C_6D_6) indicated the presence of a cyclopropane ring. Spin decoupling showed that the corresponding proton was coupled with two protons, which displayed a double doublet at δ 2.14 and a four-fold doublet at 1.24. As the first two signals showed a coupling of 3.5 Hz with each other, the only explanation was a geminal coupling of two cyclopropane protons, though the chemical shift of the second signal was extremely unusual. As this signal was shifted in the spectrum of the corresponding alcohol by 0.8 ppm to higher field, the chemical shift was obviously influenced by the deshielding effect of the keto group. The four-fold doublet at δ 1.24 was further coupled with a double doublet at 0.91 and a broadened doublet at 1.33 leading to the sequence **A**. Further decouplings starting with the signal of the olefinic proton showed that the sequence **B** was present too.

The ^{1}H NMR spectrum further showed three methyl singlets and that the signals of the protons at C-2 were shifted downfield. This led to the structure **3**, as obviously C-2 had to be connected with the keto group in **A**. Inspection of a model showed that all couplings observed agreed quite nicely with this assumption, if the conformation **11** or its mirror image was assumed with both, C-14 and C-15, parallel at the same side. This conformation further explained, why only one alcohol was obtained with boranate. It also explained the strong deshielding effect of the keto group. **3** is probably formed from α-humulene (**10**) as shown in the scheme. We have named the new skeleton acriprunin. The structure of the alcohol **5** followed from the molecular formula and the ^{1}H NMR data (Table 2), though several signals were overlapping multiplets. The Eu(fod)$_3$ induced shifts showed that the 4α-position of the tertiary hydroxyl was very likely. The signals at δ 3.04 and 2.56 showed a *W*-coupling and consequently were those of H-6α and H-8α. The unusual downfield shift of the H-6α signal required a deshielding effect of the hydroxyl group, which therefore must also be α-orientated. Spin decoupling allowed the assignment of further signals. As the H-6β signal was a broadened double doublet with larger couplings, the presence of a *trans*-fused decalin was obvious. The most likely structure therefore seemed to be **5**, closely related to **8** [5], which was present in the aerial parts, which further afforded germacrene D, γ-humulene, α-bisabolol, stigmasterol, lupeol and its Δ12,13-isomer, lupeyl acetate and three new sesquiterpenes, the humulene derivatives **6** and **7** as well as the furanocadinane derivative **9**. The structures of **6** and **7** followed from the ^{1}H NMR data (Table 1), which were similar to those of γ-humulene. The position of the ester groups were deduced from the missing olefinic methyl signal, which was replaced by a broadened singlet around δ 4.5. Though some signals



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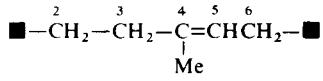


B

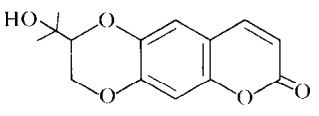
* Part 385 in the series "Naturally Occurring Terpene Derivatives". For Part 384 see Bohlmann, F. and Zdero, C. (1982) *Phytochemistry* **21**, 139.

Table 1. ^{1}H NMR spectral data of compounds **3**, **4**, **6** and **7** (400 MHz, TMS as internal standard)

	3			**4**		**6**	**7**
	(C_6D_6)	($CDCl_3$)	Δ*	($CDCl_3$)	Δ*	($CDCl_3$)	($CDCl_3$)
H-1	—	—	—	3.83 *d*	0.37	5.52 *dd(br)*	5.52 *dd(br)*
H-2α	2.84 *ddd*	3.13 *ddd*	0.13	1.92 *dddd*	0.16	2.38 *m*	
H-2β	2.11 *ddd*	2.13 *ddd*	0.20	1.53 *dddd*	0.24		
H-3α	1.96 *d(br)*	2.2 *m*	0.13	1.79 *br*	0.15	2.30 *m*	
H-3β	2.37 *ddd*		0.14	2.56 *ddd*	0.09		
H-5	5.30 *ddq*	5.20 *ddq*	0.12	5.68 *d(br)*	0.06	5.83 *d*	5.85 *d*
H-6α	1.98 *dd*	2.09 *dd*	0.06	2.16 *dd*	0.03	5.43 *d*	5.45 *d*
H-6β	1.77 d(br)	1.85 d(br)	0.03	1.83 d(br)	0.03		
H-7α	0.91 *dd*	1.08 *m*	0.04	1.3 *m*	0.10	1.44 *m*	1.43 *m*
H-7β	1.33 *d(br)*	1.46 *dd*	0.06				
H-8	1.24 *dddd*	1.08 *m*	0.24				
H-8′	—	—	—	—			
H-9α	0.12 *dd*	0.26 *dd*	0.10	−0.26 *dd*	0.25	2.04 *m*	
H-9β	2.14 *dd*	1.79 *dd*	0.22	0.99 *dd*	0.20		
H-12	0.90 *s*	1.06 *s*	0.04	0.87 *s*	0.10	0.95 *s*	0.95 *s*
H-13	0.85 *s*	0.95 *s*	0.03	0.97 *s*	0.04		
H-14	0.94 *s*	1.16 *s*	0.09	1.20 *s*	0.02	4.43 *s(br)*	4.53 *s(br)*
H-15	1.54 *dd*	1.75 *dd*	0.04	1.66 *s(br)*	0.03	4.91 *s(br)* 4.88 *s(br)*	4.92 *s(br)* 4.88 *s(br)*
OCOR	—	—	—	—	—	2.04 *s*	6.03 *qq* 1.97 *dq* 1.87 *dq*

* Δ-values after addition of $Eu(fod)_3$.

J(Hz): compound **3**: 2α,2β = 14; 2α,3α = 12; 2α,3β = 3.5; 2β,3α = 4.5; 2β,3β = 3; 3α,3β = 13; 5,6α = 10.5; 5,6β = 5,15 = 1.5; 6α,6β = 15; 6β,15 = 6β,7β = 1.5; 7α,7β = 15; 7α,8 ~ 7; 7β,8 ~ 1; 8,9α = 7; 8,9β = 10; 9α,9β = 3.5; compound **4**: 1α,2α = 1; 1α,2β = 5.3; 2α,2β = 15; 2α,3α = 2; 2α,3β = 14; 2β,3α = 2.5; 2β,3β = 5; 3α,3β = 15; 5,6α = 11.5; 5,6β = 2; 6α,6β = 14; 8,9α = 6; 8,9β = 10; 9α,9β = 3.5; compounds **6** and **7**: 1,2 = 8; 5,6 = 16; OAng: 3′,4′ = 7; 3′,5′ = 4′,5′ = 1.5.



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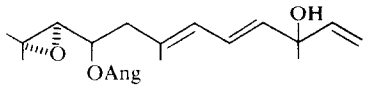

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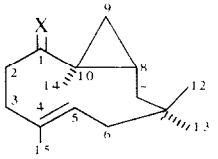
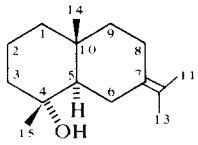


3 X = O
4 X = βOH,H



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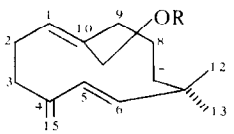

6 R = Ac
7 R = Ang

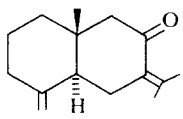

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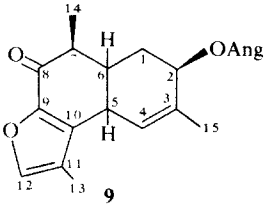
Table 2. ^{1}H NMR spectral data of compounds **5** and **9** (400 MHz, $CDCl_3$, TMS as internal standard)

	5	(C_6D_6)	Δ*	**9**			
H-6α	2.81 *ddd*	3.04 *ddd*	0.49	H-1α	2.33 *ddd*	H-13	2.08 *d*
H-6β	1.6 *m*	1.66 *dd(br)*	0.25	H-1β	1.78 *ddd*	H-14	1.32 *d*
H-8α	2.49 *dddd*	2.56 *dddd*	0.11	H-2α	5.39 *dd(br)*	H-15	1.72 *s(br)*
H-8β	2.39 *dd(br)*	1.94 *dd(br)*	0.10	H-4	5.69 *s(br)*	OCOR	6.10 *qq*
H-12	1.69 *s(br)*	1.82 *s(br)*	0.0	H-5β	3.67 *dd(br)*		2.00 *dq*
H-13	1.66 *s(br)*	1.73 *s(br)*	0.02	H-6β	2.40 *dddd*		1.91 *dq*
H-14	0.95 *s*	0.86 *s*	0.15	H-7α	2.58 *dq*		
H-15	1.13 *s*	1.04 *s*	0.40	H-12	7.38 *q*		

Δ* values after addition of $Eu(fod)_3$.

J(Hz): compound **5**: 5,6α = 2; 5,6β = 12; 6α,6β = 14; 6α,8α = 2; 8α,8β = 14; 8α,9α = 4; 8α,9β = 2; compound **9**: 1α,1β = 13; 1α,2 = 7; 1α,6 = 3; 1β,2 = 8; 1β,6 ~ 6; 4,5 ~ 3; 6β,7α = 9; 7α,14 = 7; 12,13 = 1.3; 3′,4′ = 7; 3′,5′ = 4′,5′ = 1.7.



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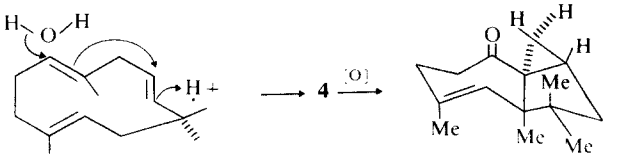

10 11

were overlapping multiplets, spin decoupling allowed their assignments. The ^{1}H NMR data of **9** were similar to those of furanocadinane and cadinane derivatives isolated previously [6, 7]. Spin decoupling allowed the assignment of all signals. The presence of a *cis*-decalin derivative followed from the small coupling $J_{5,6}$, while the couplings of H-2 indicated the β-orientation of the ester group. The absolute configuration, however, was not determined. No diterpenes were isolated from this species. The compounds isolated show relationships to those isolated before. The main constituent **8** is present in *A. confertus* [1], which also contains humulene, the precursor of **3**, **6** and **7**. α- and γ-humulene were isolated from two further species [1], while cadinanes were present in two species [1, 2]. The dehydronerolidol derivative **2** has been isolated from *A. longifolius* [2] while **1** was one of the constituents of *A. hagei* [1]. The absence of diterpenes is remarkable. They are absent too in the closely related genus *Radlkoferotoma* where compounds like **2** are characteristic.

EXPERIMENTAL

The air-dried plant material, collected in north-eastern Brazil, voucher RMK 8749 (deposited in the U.S. National Herbarium) was extracted with Et_2O–petrol (1:2) and the extracts obtained were separated by CC (Si gel) and repeated TLC (Si gel). The roots (40 g) afforded traces of tridecapentaynene, 2 mg stigmasterol, 2 mg squalene, 3 mg dammadienyl acetate, 1 mg α- and 5 mg γ-humulene, 2 mg germacrene D, 2 mg **1**, 3 mg **2**, 4 mg **3** (Et_2O–petrol, 1:10), 4 mg **5** (Et_2O–petrol, 1:3) and 2 mg **6**, while the aerial parts (200 g) gave 70 mg germacrene D, 40 mg γ-humulene, 30 mg α-bisabolol, 20 mg lupeyl acetate, 60 mg lupeol and 20 mg of its Δ12,13-isomer, 5 mg stigmasterol, 30 mg **6** (Et_2O–petrol, 1:10), 3 mg **7** (Et_2O–petrol, 1:10), 50 mg **8** and 8 mg **9** (Et_2O–petrol, 1:1).

Acriprunin-1-one (**3**). Colourless gum, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1675 (cyclopropyl ketone); MS *m/z* (rel. int.): 220.183 $[M]^+$ (7) ($C_{15}H_{24}O_3$), 205 $[M - Me]^+$ (13), 177 $[205 - CO]^+$ (9), 121 $[C_9H_{13}]^+$ (100), 107 $[C_8H_{11}]^+$ (76);

$$[\alpha]_{24}^{\lambda} = \frac{589}{-41.7} \quad \frac{578}{-42.2} \quad \frac{546}{-48.3} \quad \frac{436\,\text{nm}}{-80.6} \quad (c = 0.2,\ CHCl_3).$$

To 3 mg **3** in 1 ml MeOH were added 10 mg $NaBH_4$ followed after 5 min by dil. H_2SO_4. TLC (Et_2O petrol, 1:3) afforded 2.5 mg **4**, colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600.

4α-Hydroxyeudesm-7(11)-ene (**5**) Colourless oil, IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600 (OH); MS *m/z* (rel. int.): 222.198 $[M]^+$ (41) ($C_{15}H_{26}O$), 204 $[M - H_2O]^+$ (88), 189 $[204 - Me]^+$ (100), 161 $[204 - C_3H_7]^+$ (84).

14-Acetoxy-γ-humulene (**6**). Colourless oil, $bp_{0.1}$ 130° (bath temp.); IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3080, 1645, 895 (C=CH_2), 1740, 1240 (OAc), 1605, 980 (*trans* CH=CH); MS *m/z* (rel. int.): 262.193 $[M]^+$ (0.5) ($C_{17}H_{26}O_2$), 202 $[M - HOAc]^+$ (27), 187 $[202 - Me]^+$ (39), 159 $[202 - C_3H_7]^+$ (86), 91 $[C_7H_7]^+$ (100).

14-Angeloyloxy-γ-humulene (**7**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3080, 1645, 895 (C=CH_2), 1605, 975 (*trans* CH=CH), 1715 (C=CCO_2R); MS *m/z* (rel. int.): 302.225 $[M]^+$ (0.5) ($C_{20}H_{30}O_2$), 202 $[M - RCO_2H]^+$ (16), 187 $[202 - Me]^+$ (18), 159 $[202 - C_3H_7]^+$ (28), 83 $[C_4H_7CO]^+$ (100), 55 $[83 - CO]^+$ (88).

2β-Angeloyloxy-1,2,5,6-tetrahydrochromolaenin-8-one (**9**). Colourless gum; IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1725, 1640 (C=CCO_2R), 1683 (C=CC=O); MS *m/z* (rel. int.): 328.167 $[M]^+$ (0.5) ($C_{20}H_{24}O_4$), 228 $[M - RCO_2]^+$ (100), 213 $[228 - Me]^+$ (64), 185 $[213 - CO]^+$ (27), 83 $[C_4H_7CO]^+$ (74), 55 $[83 - CO]^+$ (95), $\alpha_D = +9.4°$ ($c = 0.77$, $CHCl_3$).

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