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FURTHER SESQUITERPENE LACTONES FROM COSTA RICAN EUPATORIEAE

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Key Word Index—*Ayapana elata*; *Critonia hebebotrya*; *C. quadrangularis*; *Koanophyllon pittieri*; Compositae; sesquiterpenes; sesquiterpene lactones; tremetone derivatives; ent-labdanes.

Abstract—The aerial parts of *Ayapana elata* afforded two new germacranolides. The configuration at C-3 in one of them was the same as that of some bejaranolides, the structures of which therefore have to be revised. *Critonia quadrangularis* gave in addition to known compounds three elemanolides, a germacranolide, an isodaucane derivative and tremetone derivative. *Critonia hebebotrya* contained large quantities of known diterpene acids. *Koanophyllon pittieri* gave two epimeric ent-labdanes. The structures were elucidated by highfield NMR spectroscopy.

INTRODUCTION

The genus *Ayapana* (tribe Eupatorieae) is placed in the subtribe Ayapaninae together with the genera *Polyanthina*, *Heterocondylius*, *Condylium* and *Isocarpha* [1]. As the latter is new to the tribe it was of interest to compare its chemistry with that of other genera. So far *Isocarpha* gave tremetone derivatives [2] and furanoheliangolides [3] which are common in the tribe while the other genera afforded mainly tremetone derivatives [4, 5] which are also reported from *Ayapana* species [6, 7]. The central American genus *Critonia* is placed in the subtribe Critoniinae [1]. From the genera which are placed in this group so far mainly different types of sesquiterpene lactones but also several diterpenes have been reported. We now have studied a further *Ayapana* species as well as two *Critonia* species and a *Koanophyllon* species from Costa Rica. The results will be discussed in this paper.

RESULTS AND DISCUSSION

The aerial parts of *Ayapana elata* (Steetz) King et Robinson afforded as main constituent the furanoheliangolide budlein A (**8**) [8], ayapin and the two germacranolides **9** and **10**. The structure of **9** clearly followed from the ^{1}H NMR spectrum (Table 1) which was close to that of other bejaranolides [9, 10]. The nature of the ester group followed from the typical signals of an isovalerate residue. The ^{1}H NMR spectrum of **10** (Table 2) indicated that this lactone was closely related to **9**. The presence of a 3-hydroxy group was deduced from the broadened double doublet at δ4.91. The observed coupling, together with inspection of a model, gave no clear answer concerning the configuration at C-3. We therefore confirmed the stereochemistry by NOE difference spectroscopy. Clear effects were observed between H-5, H-3 and H-7, between H-8, H-7 and H-13′, between H-15, H-6 and H-2β as well as between H-14 and H-2β. These results clearly established the configurations and also the preferred conformation. Comparison of the ^{1}H NMR data with those of some similar lactones with oxygen functions at C-3 showed that the proposed configurations have to be revised (**12** and **13** in [9], **19** and **20** in [10], **6** in [11] and **33–35** in [12]).

The aerial parts of *Critonia hebebotrya* DC gave cyperene, germacrene D, ent-kaurenic acid and daniellic acid [13].

The aerial parts of *C. quadrangularis* (DC) King et Robinson afforded germacrene D, squalene, stigmasterol, β-sitosterol, the sesquiterpene lactones costunolide, novanin A [14], kauniolide [15], inunolide and 4,5-epoxyinunolide [16], the isomer **1**, the elemanolides **2** [17], **3–5** [17] and **6**, euparin, the tremetone derivative **13** as well as the isodaucane aldehydes **11** [19] and **12**.

The structure of **1** followed from the ^{1}H NMR spectrum (Table 2). Though several signals were overlapping multiplets they could be assigned by spin decoupling. The couplings of H-1 and comparison of the data with those of similar lactones indicated the proposed stereochemistry. The ^{1}H NMR spectra of **3** and **4** (Table 2) were in part close to that of **2** [17]. However, the exomethylene signals (H-13) were replaced by a methyl doublet at δ1.18 and doublet quartets at 2.77 and 2.81, respectively. The stereochemistries of these isomers were elucidated by NOE difference spectroscopy. In the case of **3** clear effects were observed between H-8, H-11 and H-7, between H-7, H-11, H-8 and H-5 as well as between H-14, H-1, H-2t, H-3′, H-6β and H-9β. Furthermore a W-coupling between H-9 and H-14 was observed. This required a conformation as in isoalantolactone with a β-orientated methyl at C-11. In the ^{1}H NMR spectrum of **4** the couplings of H-8 were nearly the same as those of **2**. NOEs were observed between H-7 and H-8, between H-14 and H-15 as well as between H-5, H-2t, H-3 and H-15. As the ^{1}H NMR spectra of both 11β,13-dihydro **5** [17] and synthetic 11β,13-H **2** [18] differed from that of **4** this lactone most likely was the 11-epimer of 11β,13-dihydro **5** [17]. The couplings of H-5 indicated a boat-like confor-

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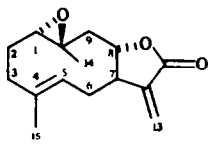

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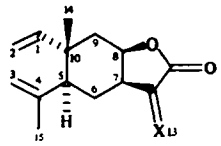
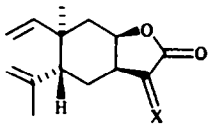


2 3
X = CH_2 β-Me,H



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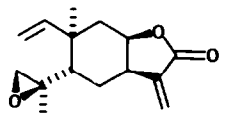
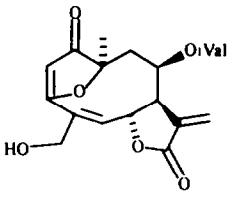
5 X = CH_2



6
7 4-epi



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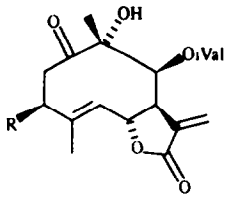
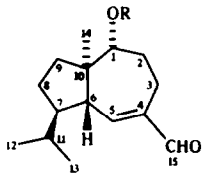
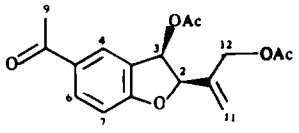


9 10
R = H OH



11 11Ac 12 12Ac
R = H Ac H Ac
6,7-epi



13

mation of the six-membered ring which would explain the different couplings of H-8.

The ^{1}H NMR spectrum of **6** (Table 2) was close to that of **5** [17]. However, the signals of the isopropenyl groups were replaced by a pair of doublets at δ2.27 and 2.24 and a singlet at δ0.95 (in C_6D_6). Accordingly, the presence of an epoxide was very likely. Epoxidation of **5** afforded a mixture of C-4 epimers where the major product was identical with the natural compound. NOE difference spectroscopy with **6** gave clear effects between H-15, H-1, H-3′, H-5, H-6 and H-14 as well as between H-3, which showed a W-coupling with H-15, and H-5 while in the case of the epimer **7**, H-15 showed effects with H-14, H-5 and H-3′ but not with H-1. An effect between H-3 which showed a W-coupling with H-15, and H-6β only was observed in the case of **7**. All data therefore agreed with the proposed configurations of **6** and **7**.

^{1}H NMR spectrum of **12** (see Experimental) was similar to that of **11** [19] but several couplings and chemical shifts were different. All signals could be assigned by spin decoupling and NOE difference spectroscopy with the acetates of both compounds showed that **12** was the 6,7-epimer of **11**. Thus in the case of **12** clear effects were observed between H-14, H-2α and H-9α, between H-6 and H-1 as well as between H-5 and H-7 while in the case of **11** NOEs between H-14, H-6 and H-2α as well as between H-7, H-6, H-5 and H-1 were observed.

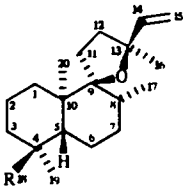
The structure of **13** also followed from the ^{1}H NMR spectrum which was close to that of the corresponding alcohol [20] (see Experimental). The coupling $J_{2,3}$ indicated a *cis*-relationship of the hydrogens at C-2 and C-3. From the aerial parts of *C. sexangularis* costunolide was isolated.

The aerial parts of *Koanophyllon pittieri* (Klatt) K. et R. gave a mixture of diterpene acids (**14** and **14a**) which could not be separated. Reduction with lithium alanate gave the corresponding alcohols (**15** and **15a**) which could be separated as their phenyl acetates **16** and **16a**. The ^{1}H NMR spectrum of **14** and **14a** (see Experimental) were close to that of a 9,13-epoxy-ent-labd-14-en-18-acid with determined absolute configuration from an *Austrobrickellia* species which, however, had a keto group at C-7 [21] and **15** and **15a** were also close to that of the corresponding alcohol [21]. The spectra of **16** and **16a** differed slightly in the signals of H-14–H-20. NOE difference spectroscopy allowed the assignment of the

Table 1. ^{1}H NMR spectral data of compounds **9** and **10** (400 MHz, $CDCl_3$, TMS as internal standard)

H	9	10
2	2.87 *m*	3.05 *dd* 2.57 *dd*
3	2.30 *m*	4.91 *dd* (*br*)
5	5.09 *dq*	5.16 *d* (*br*)
6	5.00 *dd*	5.08 *dd*
7	2.66 *m*	2.61 *m*
8	5.71 *ddd*	5.71 *ddd*
9	2.00 *m*	2.00 *m*
13	6.24 *d*	6.25 *d*
13	5.52 *d*	5.54 *d*
14	1.30 *s*	1.31 *s*
15	1.93 *d*	1.95 *d*
OR	2.12 *m*	2.12 *m*
	2.05 *m*	2.05 *m*
	0.91 *d*	0.52 *d*
0.90 *d*	0.90 *d*	0.91 *d*

J[Hz]: 5,6 = 10.5; 5,15 = 1.2; 6,7 = 9; 7,8 = 2; 7,13 = 3.5; 7,13′ = 3; 8,9 = 6.5; 8,9′ = 11; compound **10**: 2,2′ = 13; 2,3 = 11.5; 2′,3 = 4.5; OiVal: 3,4 = 3,5 = 7.



14 **15** **16**
R = CO_2H CH_2OH CH_2OCOCH_2Ph

(**14a** – **16a** are C-13-epimers)

configuration at C-13 where the esters were epimeric. Thus in the case of **16** clear effects were obtained between H-19, H-20 and H-18 as well as between H-16, H-14, H-15t and H-8. Inspection of a model showed that the latter effect required the proposed configuration at C-8. The epimer **16a** also showed NOEs between H-19, H-20 and H-18, between H-16 and H-14 but not between H-16 and H-8.

In the subtribe Critoniinae simple sesquiterpene lactones of low oxidation level are widespread [22]. However, in several cases these compounds are replaced by ent-labdane derivatives [23]. This is also the case in the genus *Critonia*. In one species dehydronerolidol derivatives and unsaturated amides are reported [24]. In *Koanophyllon* species no sesquiterpene lactones are reported. Again labdanes and some rearranged types are present [25, 26]. In the subtribe Ayapaninae tremetone derivatives are widespread but highly oxygenated germacranolides have now been isolated not only from an *Isocarpha* species but also from an *Aypana* species. This may be an indication that the former genus really belongs to the Eupatorieae.

EXPERIMENTAL

The air dried plant material was extracted with MeOH–Et_2O–petrol (1:1:1) and the extracts obtained were separated as reported previously [27]. The vouchers are deposited in the National Herbarium of Costa Rica. The aerial parts of *Ayapana elata* (390 g), voucher 86410, collected in February 1985 in San Carlos, Costa Rica, gave by CC (silica gel) and PTLC

Table 2. ^{1}H NMR spectral data of compounds **1**, **3**, **4**, **6** and **7** (400 MHz, $CDCl_3$, TMS as internal standard)

H	1	3	4	6 (C_6D_6)	7 (C_6D_6)
1	2.80 *dd*	5.74 *dd*	5.98 *dd*	5.30 *dd*	5.70 *dd*
2	2.10 *m*	4.93 *dd*	4.99 *d*	4.67 *dd*	4.77 *dd*
2′	1.50 *m*	4.96 *dd*	4.95 *d*	4.74 *dd*	4.87 *dd*
3	2.27 *m*	4.86 *dq*	4.90 *dq*	2.27 *d* (*br*)	2.18 *d* (*br*)
3′		4.60 *dq*	4.68 *s* (*br*)	2.24 *d*	2.08 *d*
5	5.36 *t* (*br*)	1.94 *dd*	2.18 *dd*	0.82 *dd*	1.21 *dd*
6	2.60 *m*	1.49 *m*	1.67 *ddd*	1.85 *ddd*	1.54 *ddd*
6′	2.10 *m*	1.43 *m*	1.59 *ddd*	1.45 *ddd*	1.40 *ddd*
7	2.97 *m*	2.38 *m*	2.72 *dddd*	2.55 *m*	2.48 *m*
8	4.47 *m*	4.47 *ddd*	4.65 *ddd*	4.13 *ddd*	4.09 *ddd* (*br*)
9	2.15 *dd*	2.04 *dd*	1.98 *dd*	1.51 *ddd*	1.43 *ddd*
9′	1.98 *dd*	1.67 *ddq*	1.86 *dd*	0.96 *dd* (*br*)	1.01 *dd* (*br*)
11	—	2.81 *dq*	2.77 *dq*	—	—
13	6.33 *d*	1.18 *d*	1.18 *d*	6.26 *dd*	6.20 *dd*
13′	5.68 *d*			5.20 *d*	4.92 *d*
14	1.34 *s*	1.03 *d*	0.98 *s*	0.59 *s*	0.61 *s*
15	1.72 *d*	1.70 *dd*	1.75 *s* (*br*)	0.95 *s*	1.04 *s*

J[Hz]: compound **1**: 1,2 = 3; 1,2′ = 11; 5,6 ≈ 7; 5,15 = 1; 7,13 = 3; 7,13′ = 2.5; 8,9 = 4; 8,9′ = 11; 9,9′ = 14; compound **3**: 1,2 = 17.5; 1,2′ = 11; 2,2′ = 1; 3,3′ = 3,15′ = 1.5; 3′,15 = 0.8; 5,6 = 4; 5,6′ = 12; 7,8 = 8,9′ = 4; 7,11 = 11,13 = 7; 8,9 = 2.5; 9,9′ = 16; 9′,14 = 0.8; compound **4**: 1,2 = 17.5; 1,2′ = 11; 3,3′ = 3,15 = 1.5; 5,6 = 7; 5,6′ = 5; 6,7 = 6; 6′,7 = 8; 7,8 = 8,9 = 5.5; 7,11 = 11,13 = 8; 8,9′ = 5; 9,9′ = 15; compounds **6** and **7**: 1,2 = 17.5; 1,2′ = 11; 2,2′ = 1; 3,3′ = 5; 5,6 = 3.5; 5,6′ = 13; 6,6′ = 14; 6,7 = 1.5; 6′,7 = 6; 7,8 = 7.5; 7,9 = 0.8; 7,13 = 3.5; 7,13′ = 3; 8,9 = 6; 8,9′ = 11; 8,13 = 0.5; 9,9′ = 13.5.

(silica gel, PF 254) 10 mg ayapin. The polar CC fraction (Et_2O) gave by PTLC (Et_2O) 30 mg **8** (R_f 0.20), 8 mg **9** (R_f 0.64) and 5 mg **10** (R_f 0.36). The aerial parts of *Critonia quadrangularis* (465 g, voucher 108498, collected in January 1985 near Santa Cruz, Costa Rica) gave by CC and PTLC 50 mg germacrene D, 500 mg squalene, 160 mg stigmasterol, 40 mg β-sitosterol and a polar fraction which was separated by medium pressure chromatography (silica gel, ϕ 30–60 μ). Further separation by PTLC finally gave 5 mg **5**, 45 mg kauniolide, 2 mg **2**, 3 mg costunolide, 2.5 mg **4** (R_f 0.67, Et_2O–petrol, 3:7), 1.6 mg inunolide, 5 mg **3** (R_f 0.60, Et_2O–petrol, 3:7), 3.6 mg novanin A and 1 mg **6** (R_f 0.33, Et_2O–petrol, 1:1). The most polar CC fraction (Et_2O) gave by PTLC (C_6H_6–CH_2Cl_2–Et_2O, 9:9:1) 4β,5α-epoxyinunolide, 2 mg **1** (R_f 0.23), 2 mg **13** (R_f 0.3) and a mixture of **11** and **12**, the acetates of which could be separated by TLC (same solvent: R_f 0.60 and 0.70, respectively).

The aerial parts of *C. hebebotrya* (voucher 82–6, 230 g) gave by CC and TLC 10 mg cyperene, 160 mg germacrene D, 4 g ent-kaurenic acid and 8 g daniellic acid.

The aerial parts of *C. sexangularis* (800 g, voucher RMK 7077, collected in Guatemala) gave 40 mg costunolide.

The aerial parts (850 g) of *Koanophyllon pittieri* (voucher 108547, collected in February 1985 near San Carlos, Costa Rica) gave a CC fraction (Et_2O–petrol, 1:1) which gave by PTLC (Et_2O–petrol, 1:1) 60 mg of a mixture of **14** and **14a** which could not be separated even by HPLC. Reduction with $LiAlH_4$ gave **15** and **15a** which also could not be separated. Esterification with phenyl acetyl chloride/C_5H_5N gave **16** and **16a** which were separated by PTLC (Et_2O–petrol, 1:25, three developments). The resultant broad band was divided in such a way that only the upper part (**16a**) and the lowest part (**16**) was eluted with Et_2O.

1α,10β-*Epoxygermacra*-4E,11(13)-*dien*-12,8α-*olide* (**1**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1780 (γ-lactone), 1275, 1145, 1130, MS *m/z* (rel. int.): 248.141 $[M]^+$ (calc. for $C_{15}H_{20}O_3$: 248.141) (10), 233 $[M-Me]^+$ (8), 230 $[M-H_2O]^+$ (8), 95 (100), 81 (74), 68 (70), 67 (70); $[\alpha]_D^{22°}$ +98 ($CHCl_3$; *c* 0.2).

11α,13-*Dihydroelemanolide* (**3**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3070, 1030, 930, 910 (C=CH_2), 1785 (γ-lactone); MS *m/z* (rel. int.): 234.162 $[M]^+$ (calc. for $C_{15}H_{22}O_2$: 234.162), (12), 219 $[M-Me]^+$ (12), 134 (48), 93 (84), 81 (72), 69 (100), 68 (92); $[\alpha]_D^{22°}$ +17 ($CHCl_3$; *c* 0.4).

11α,13-*Dihydroelemaasteiractinolide* (**4**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3070, 1030, 930, 910 (C=CH_2), 1780 (γ-lactone); MS *m/z* (rel. int.): 234.162 $[M]^+$ (calc. for $C_{15}H_{22}O_2$: 234.162) (8), 219 $[M-Me]^+$ (15), 161 (55), 119 (74), 93 (100), 81 (46), 69 (46), 68 (98), 67 (48); $[\alpha]_D^{22°}$ +27 ($CHCl_3$; *c* 0.25).

3,4β-*Epoxy elemasteiractinolide* (**6**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3090, 1640, 930 (C=CH_2), 1780 (γ-lactone); MS *m/z* (rel. int.): 248.141 $[M]^+$ (calc. for $C_{15}H_{20}O_3$: 248.141) (4), 233 $[M-Me]^+$ (29), 81 (87), 69 (66), 67 (73), 55 (100). Reaction of **5** with *m*-chloroperbenzoic acid in $CHCl_3$ afforded a mixture of **6** and **7** (*ca* 4.5:1).

8β-*Isovaleryloxy*-10α-*hydroxy*-1-*oxo*-*germacra*-4E,11(13)-*diene*-12,6α-*olide* (**9**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3460 (OH), 1780 (γ-lactone), 1740 (CO_2R), 1710 (C=O); MS *m/z* (rel int.): 262.120 $[M-RCO_2H]$, calc. for $C_{15}H_{18}O_4$: 262.120) (6), 244 $[262-H_2O]^+$ (3), 85 $[RCO]^+$ (82), 57 $[85-CO]^+$ (100); $[\alpha]_D^{22°}$ +17 ($CHCl_3$; *c* 0.64).

8β-*Isovaleryloxy*-3β,10α-*dihydroxy*-1-*oxo*-*germacra*-4E,11(13)-diene-12,6α-olide (**10**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 3600, 3460 (OH), 1780 (γ-lactone), 1740 (CO_2R), 1700 (C=O); MS *m/z* (rel. int.): 278.115 $[M-RCO_2H]^+$ (calc. for $C_{15}H_{18}O_5$: 278.115) (1.6), 260 $[278-H_2O]^+$ (2), 152 (28), 85 $[RCO]^+$ (72), 57 $[85-CO]^+$ (100); $[\alpha]_D^{22°}$ +47 ($CHCl_3$; *c* 0.17).

1α-*Acetoxy*-6β,7αH-10α-*methylisodauc*-4-*en*-14-*al* (**12** Ac). MS *m/z* (rel. int.): 278.188 $[M]^+$ (calc. for $C_{17}H_{26}O_3$: 278.188) (12), 218 $[M-HOAc]^+$ (44), 175 $[218-C_3H_7]^+$ (52), 123 $[C_9H_{15}]^+$ (100); ^{1}H NMR ($CDCl_3$): δ4.78 (*dd*, H-1), 1.31 (*dddd*, H-2) 1.78 (*m*, H-2β), 2.98 (*dd* (*br*), H-3) 1.89 (*m*, H-3β), 6.59 (*d* (*br*), H-5), 2.35 (*dd*, H-6), 2.05 (*m*, H-7), 1.88 and 1.66 (*m*, H-8), 1.48 and 1.43 (*m*, H-9), 1.63 (*dqq*, H-11), 0.90 (*d*, H-12), 0.88 (*d*, H-13), 0.80 (*s*, H-14), 9.37 (*s*, H-15) (*J* [Hz]: 1,2α = 11.5; 1,2β = 4; 2α,2β = 2α,3β = 13; 2α,3α = 2; 2β,3α = 6; 3α,3β = 15; 5,6 = 5; 6,7 = 10.5; 11,12 = 11,13 = 6.5).

3β,12-*Diacetoxytremetone* (**13**). IR $\nu_{max}^{CCl_4}$ cm^{-1}: 1750, 1740 (OAc), 1690 (PhC=O); MS *m/z* (rel. int.): 318.110 $[M]^+$ (calc. for $C_{17}H_{18}O_6$: 318.110) (10), 258 $[M-HOAc]^+$ (92), 216 $[258-ketene]^+$ (100), 201 $[216-Me]^+$ (40), 173 $[201-CO]^+$ (26), 95 (84); ^{1}H NMR ($CDCl_3$): δ5.29 (*d*, H-2), 6.36 (*d*, H-3), 8.03 (*s* (*br*) H-4), 8.00 (*dd*, H-6), 6.98 (*d*, H-7), 2.56 (*s*, H-9), 5.50 and 5.46 (*s* (*br*), H-11), 4.69 (*s* (*br*), H-12); OAc: 2.08, 2.03 *s* (*J* [Hz]: 2,3 = 6; 4,6 = 1.5; 6,7 = 8).

9β,13α- *and* 13β-*Epoxy*-8βH-*ent*-*labd*-14-*en*-18-*oic acid* (**14** *and* **14a**). Colourless oily mixture which could not be separated. ^{1}H NMR ($CDCl_3$, in parentheses epimer): 0.93 (0.93) (*s*, H-20), 1.00 (0.95) (*d*, H-17), 1.13 (1.11) (*s*, H-19), 1.27 (1.25) (*s*, H-16), 2.47 (2.40) (*dd*, H-5), 4.93 (4.86) (*dd*, H-15c), 5.18 (5.12) (*dd*, H-15t), 6.00 (5.98) (*dd*, H-14); ^{13}C NMR ($CDCl_3$, in parentheses epimer): 179.6 (179.6) *s*, 146.8 (144.9) *d*, 110.3 (110.0) *t*, 92.3 (92.1) *s*, 82.5 (82.5) *s* and 51.7, 43.0, 42.5, 40.7 *d* and 47.9, 47.7, 41.8, 41.3 *s* and 37.5, 36.6 (3 ×), 32.5, 32.1, 29.9, 29.2 (2 ×), 28.6, 20.0, 19.9, 17.6, 17.4 *t* and 28.0, 27.6, 18.6, 18.5, 17.9, 17.9, 16.7, 16.5 *q*.

Compounds **15** *and* **15a**. ^{1}H NMR ($CDCl_3$): δ0.76 (0.75) (*s*, H-19), 0.94 (0.94) (*s*, H-20), 1.02 (0.97) (*d*, H-17), 1.26 (1.24) (*s*, H-16), 3.41 (3.40) and 3.14 (3.13) (H-18), 6.01 (5.96) (*dd*, H-14), 5.14 (5.13) (*dd*, H-15t), 4.94 (4.88) (*dd*, H-15c).

Compound **16**. ^{1}H NMR ($CDCl_3$): δ6.03 (*dd*, H-14), 5.20 (*dd*, H-15t), 4.96 (*dd*, H-15c), 1.28 (*s*, H-16), 1.01 (*d*, H-17), 3.88 and 3.67 (*d*, H-18), 0.77 (*s*, H-19), = 0.93 (*s*, H-20); OCOR: 3.64 and 3.60 *d* (*J* = 14 Hz), 7.32 *m*; $[\alpha]_D^{22°}$ = +11 ($CHCl_3$; *c* 0.1); MS *m/z* (rel. int.): 424.300 $[M]^+$ (calc. for $C_{28}H_{40}O_3$: 424.300) (36), 288 $[M-RCO_2H]^+$ (4), 207 (11), 151 (100), 91 (44).

Compound **16a**. ^{1}H NMR ($CDCl_3$): 1.87 (*m*, H-8), 5.99 (*dd*, H-14). 5.14 (*dd*, H-15t), 4.90 (*dd*, H-15c), 1.27 (*s*, H-16), 0.97 (*d*, H-17), 3.88 and 3.71 (*d*, H-18), 0.78 (*s*, H-19), 0.93 (*s*, H-20); OCOR: as 16 (*J* [Hz]: 14,15t = 17; 14,15c = 11; 15c,15t = 1.5; 18,18′ = 11, 8,17 = 7.5; MS *m/z* (rel. int.): 424.300 $[M]^+$ (calc. for $C_{28}H_{40}O_3$: 424.300) (24), 288 $[M-RCO_2]^+$ (5), 207 (32), 151 (96), 91 (100); $[\alpha]_D^{22°}$ +10 ($CHCl_3$; *c* 0.1).

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