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3α-ANGELOYLOXY-2α-HYDROXYCATIVIC ACID, A NEW DITERPENE FROM *BRICKELLIA PANICULATA**

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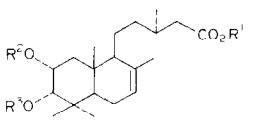
Key Word Index—*Brickellia paniculata*, Compositae, diterpene, 3α-angeloyloxy-2α-hydroxycativic acid

Abstract—The investigation of *Brickellia paniculata* resulted in the isolation of a new diterpene of the labdane type It was identified as 3α-angeloyloxy-2α-hydroxycativic acid by chemical and spectroscopic methods.

INTRODUCTION

As part of our chemical systematic study of the tribe Eupatorieae (Compositae) we have previously analysed *Brickellia secundiflora* [1] We have now undertaken the study of the herbaceous part of *Brickellia paniculata*, which resulted in the isolation of a new diterpene of the labdane type which was shown to be 3α-angeloyloxy-2α-hydroxycativic acid (**1a**). Its structure was established by physical methods and chemical modifications During the preparation of this paper the isolation of the methyl ester (**1b**) was published but the C-13 stereochemistry was not assigned [2].



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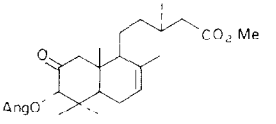
1a $R^1 = R^2 = H$, R^3 = Ang
1b R^1 = Me, R^2 = H, R^3 = Ang
1c R^1 = Me, R^2 = Ac, R^3 = Ang



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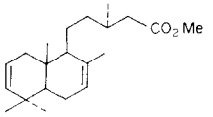

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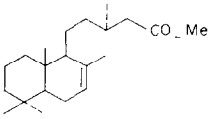

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RESULTS AND DISCUSSION

3α-Angeloyloxy-2α-hydroxycativic acid (**1a**), $C_{25}H_{40}O_5$, $[\alpha]_D + 11\,1°$, was an oily labdane type diterpene, which showed the typical IR absorption bands at 3460–2600 cm^{-1} due to a hydroxyl group(s) and at 1710 cm^{-1} due to the carbonyl of an acid group Absorption bands at 1720, 1650 and 800 cm^{-1} indicated the presence of an α,β-unsaturated ester and double bonds

The presence of a one-proton broad quartet at δ6 06 (J = 7 Hz) in the ^{1}H NMR spectrum [3], together with strong mass spectral peaks at m/z 83 (C_5H_7O, 100 0%), 55 (C_4H_7, 85 0%) and a peak at m/z 320 $[M - C_5H_8O_2]^+$ indicated the presence of an angelate moiety in **1a**. Further mass spectral peaks at m/z 182 ($C_{11}H_{18}O_2$) and 122 (C_9H_{14}), which might be formed by a retro-Diels–Alder process, suggested that **1a** should be a diterpene related to cativic acid [4]

The ^{1}H NMR spectrum of **1a** (Table 1) showed the five methyl signals of the labdane skeleton, a vinyl one at δ1 88, three tertiary ones at 0 84 (3H), 0 88 (3H), 1 02 (3H) and a secondary one at 0 98 (3H, *d*, J = 7 Hz) A doublet of a doublet of doublets at 4.18 (J = 3,4, and 12 Hz) was assigned to H-2 on a carbon bearing a hydroxyl group, since this signal was shifted downfield to 5.3 upon acetylation and the doublet at 5.02 (J = 3 Hz) to H-3 on the carbon bearing the ester function Finally a broad one-proton signal at 5 38 was assigned to the vinyl proton at C-7

Concerning the stereochemistry at C-2 and C-3, the large coupling constant (J = 12 Hz) between H-2 and one of the H-1 protons indicated that H-2 must be axial. Similarly, the small coupling constant (J = 3 Hz) of the H-3 doublet indicated that this proton must be equatorial.

Confirmation of the structure and stereochemistry of

Table 1 ^{1}H NMR spectral data of compounds **1a**, **1c**, **2** and **3***

	1a†	**1c**†	**2**†	**3**
H-2	4 18 *ddd*	5 3 *br d*	–	5 4 *m*
H-3	5 02 *br d*	5 06 *br d*	4 5 *s*	5 4 *m*
H-7	5 38 *br s*	5 38 *br s*	5 37 *br s*	5 4 *m*
H-16	0 98 *d*	0 94 *d*	0 94 *d*	0 95 *s*
H-17	1 88 *br s*	1 68 *br s*	1 66 *s*	1 67 *br s*
H-18	1 02 *s*	1 07 *s*	1 04 *s*	0 96 *s*
H-19	0 88 *s*	0 9 *s*	0 95 *s*	0 82 *s*
H-20	0 84 *s*	0 86 *s*	0 8 *s*	0 8 *s*
OMe	–	3 64 *s*	3 6 *s*	3 65 *s*
Ac	—	2 06 *s*	—	–

*Run at 100 MHz in $CDCl_3$ with TMS as internal standard, values are in ppm (δ) J (Hz) 1α 2β = 12, 1β,2β = 4, 2β,3β = 3, 13,16 = 7

†OAng 6 06 *qq*, 1 93 *dq*, 2 02 *dq*

*Contribution No. 606 of the Instituto de Química de la U N A M

1a was achieved by preparing the cativic acid methyl ester (**4**). Jones oxidation of the methyl ester (**1b**) resulted in the keto-ester (**2**) which was reduced under Wolf–Kishner conditions and the reaction product esterified with diazomethane to afford the diene (**3**) (IR ν_{max} cm^{-1}. 1740, 1650; UV λ_{max} nm 203; $[\alpha]_D$ +6 8°), which could be formed from the reduction product by a base catalysed elimination under the reaction conditions. The mass spectrum of **3** showed a molecular ion peak at *m/z* 318 and a significant peak at *m/z* 236 (22.0%), due to the loss of C_6H_{10} from the A-ring by a retro-Diels–Alder process

Catalytic hydrogenation of the diene (**3**) gave a dihydro derivative which was identical in all aspects with an authentic sample of methyl cativate (**4**) prepared from a sample of cativic acid previously isolated from *Stevia jalisciencis* [5]

EXPERIMENTAL

Brickellia paniculata was collected in Oaxaca in July 1980 A voucher specimen Quijano 51, is on deposit at the Herbarium of the Instituto de Biología (U N A M), Mexico Dried leaves and flowers (1 5 kg) were extracted with $CHCl_3$ at room temp The $CHCl_3$ extract, after removing long-chain hydrocarbons (80 g), was separated by CC over Si gel (300 g) using petrol–$CHCl_3$ and $CHCl_3$–Me_2CO mixtures as eluants

3α-Angeloyloxy-2α-hydroxycativic acid (**1a**) Chromatography fractions eluted with $CHCl_3$–Me_2CO (9 1) afforded **1a** (5 3 g) as an oil $[\alpha]_D$ +11 1° ($CHCl_3$, *c* 0 915) UV λ_{max}^{EtOH} nm (ε) 215 (7313) IR λ_{max}^{film} cm^{-1} 3450–2600, 1720, 1710, 1650, 800. MS *m/z* 420 $[M]^+$, 402 $[M-H_2O]^+$, 320 $[M-C_5H_8O_2]^+$, 83 $[C_5H_7O]^+$ (100), 55 $[C_4H_7]^+$

Acetate (**1c**) A soln of 100 mg **1b** in 1 ml Ac_2O and 0 5 ml pyridine was allowed to stand at room temp The reaction was monitored by TLC and when completed, excess Ac_2O and pyridine were removed under vacuum and the resultant residue purified by TLC yielding the acetate (**1c**) (96 mg) as an oil IR ν_{max}^{film} cm^{-1} 1735, 1730, 1715, 1640 UV λ_{max}^{MeOH} nm (ε) 209 (14167) MS *m/z* 476 $[M]^+$, 417 $[M-C_2H_3O_2]^+$, 376 $[M-C_5H_8O_2]^+$, 316 $[M-C_2H_4O_2-C_5H_8O_2]^+$, 83 $[C_5H_7O]^+$ (100).

Oxidation of **1b** Jones oxidation of **1b** (600 mg) afforded the oily keto-ester (**2**) (520 mg) $[\alpha]_D$ +12 5° ($CHCl_3$, *c* 0 47) UV λ_{max}^{EtOH} nm (ε) 213 (10472) IR ν_{max}^{film} cm^{-1} 1735, 1730, 1650, 1380, 1370 MS *m/z* 432 $[M]^+$, 332 $[M-C_5H_8O_2]^+$, 83 $[C_5H_7O]^+$, 55 $[C_4H_7]^+$

Wolf–Kishner reduction of **2** A 120 mg sample of **2** was heated for 2 hr with ethylene glycol (3 ml), KOH (50 mg) and hydrazine hydrochloride (30 mg) in a sealed tube at 180–200° After cooling, H_2O was added and the product extracted with $CHCl_3$ The mixture was methylated with CH_2N_2 to give 8 mg of the diene (**3**) $[\alpha]_D$ +6 8° ($CHCl_3$, *c* 0 27) UV λ_{max}^{film} nm (ε) 203 (4505) IR ν_{max}^{film} cm^{-1} 1740, 1665 MS *m/z* 318 $[M]^+$, 303 $[M-Me]^+$, 236 $[M-C_6H_{10}]^+$, 189 $[M-C_7H_{13}O_2]^+$, 107 $[C_8H_{11}]^+$ (100)

Hydrogenation of **3**. Catalytic hydrogenation of **3** (20 mg) in EtOAc using PtO_2 as catalyst gave, after TLC purification, a dihydro derivative which was identified as methyl cativate (**4**) (IR, ^{1}H NMR, MS), $[\alpha]_D$ −8 6° ($CHCl_3$, *c* 0 23) (lit −7 5° [6])

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