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BATUDIOIC ACID AND FLAVONOIDS FROM *BACCHARIS TUCUMANENSIS*

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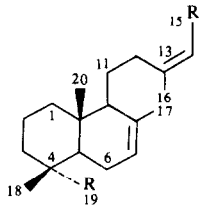
Key Word Index—*Baccharis tucumanensis*; Compositae; new labdane derivative; batudioic acid; (13*Z*)-lab-7,13-dien-15,18-dioic acid; flavonoids; xanthomicrol; scutellarein-7,4′-dimethyl ether.

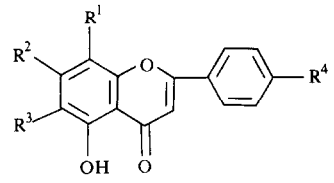
Abstract—Batudioic acid, a new labdane type diterpene, was isolated from aerial parts of *Baccharis tucumanensis*. Its structure was determined by spectral analysis and some chemical transformations. Xanthomicrol and scutellarein-7,4′-dimethyl ether were also isolated.

INTRODUCTION

In continuation of our investigation on the genus *Baccharis* (tribe Astereae) [1], we report here the isolation of batudioic acid (**1**) a new labdane type diterpene dicarboxylic acid, together with the previously known flavonoids xanthomicrol (**2**) [2] and scuttellarein-7,4′-dimethyl ether (**3**) [3] (see Experimental from *Baccharis tucumanensis* H. et A.



1 R = CO_2H
1a R = CO_2Me
1b R = CH_2OH
1c R = CH_2OAc



	R^1	R^2	R^3	R^4
2	OMe	OMe	OMe	OH
3	H	OMe	OH	OMe

RESULTS AND DISCUSSION

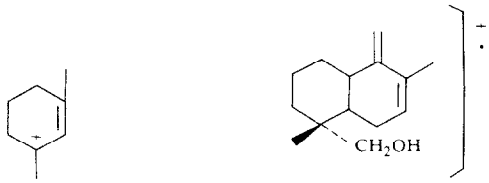
Compound **1** was purified as its dimethyl ester (diazomethane) (**1a**). Its MW (362) was deduced from the $[M-MeOH]^+$ fragment (high resolution mass spectrometry) and was consistent with a molecular formula $C_{22}H_{34}O_4$. The UV spectrum showed λ_{max}^{MeOH} nm (log ϵ) 233 (4.15) due to an α,β-unsaturated carboxyl function.

The ^1H NMR spectrum of **1** contained a broad singlet and multiplet at δ5.66 and 5.33 respectively. The signal at δ5.66 was coupled with a broad singlet at 1.91 and the multiplet at 5.33 with one at 1.73. This was verified by spin decoupling experiments which showed clearly the presence of two allylic methyl groups. Sharp singlets at δ1.20 and 0.73 were consistent with the presence of two tertiary methyl groups. The ^1H NMR spectrum of **1a** contained singlets for methoxyl groups at δ3.66 and 3.60 (–OMe). This confirms the dibasic nature of the original product. The olefinic proton signals appeared at δ5.63 and 5.30, coupled respectively with the allylic methyl groups at 1.83 and 1.73. The tertiary methyl groups showed resonance at δ1.20 and 0.76. The above data suggested the labdane structures **1** and **1a** for batudioic acid and its dimethyl ester.

Further evidence of the nature of the side chain was obtained from the mass spectrum of **1a** which contained ions at *m/z* 249 $[M-113]^+$ due to allylic cleavage of the C-11–C-12 bond and at *m/z* 114 due to a retro-Diels–Alder rearrangement on the side chain. The stereochemistry of the side chain was assigned on the basis of the chemical shift of H-16 (δ 1.83), which was as expected for the *Z* isomer [4].

The remaining allylic system had to be located in C-7–C-8 of the labdane nucleus. This was supported from the resonance pattern and by the *m/z* 109 fragment (**4**) [5].

Moreover, the chemical shift of H-18 (δ1.20) was indicative that the second carboxyl group was placed on C-19. As definitive proof of the structure, a substance (**1b**) with similar spectral properties to villenol [6] was obtained from **1a** by reducion with lithuim aluminium hydride [7]. The mass spectrum of **1b** was very similar to that villenol (see Experimental). In the



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^{1}H NMR spectrum the chemical shift of H-19 and H-19′ (AB quartet centred at δ3.23, J = 11 Hz) was shifted 0.45 ppm upfield relative to that of villenol. This difference may be rationalized if the C-19 hydroxymethylene was C-4α equatorial [8, 9].

The ^{1}H NMR spectrum of the diacetate **1c** was similar to the spectrum of the reduction product, except for the presence of a signal for two acetyl groups at δ2.03 and the corresponding paramagnetic shift shown by H-15 (δ4.56, *d*, J = 7 Hz) and H-19, H-19′ (AB quartet, δ3.73, J = 11 Hz). Except for the last signal (AB quartet) this ^{1}H NMR spectrum closely resembled that of villenol diacetate.

All these data are in good agreement with the proposed structure for batudioic acid. The stereochemistry at C-5, C-9 and C-10 in the new diterpene was not established.

EXPERIMENTAL

^{1}H NMR: 60 MHz, $CDCl_3$, TMS as int. standard; MS: 70 eV, direct inlet.

Dried aerial parts of *B. tucumanensis* H. et A. (voucher No. 19 Inst. M. Lillo), collected near El Cadillal, Tucumán, Argentina (1900 g) were extracted with $CHCl_3$ twice. The $CHCl_3$ soluble portion was partitioned with 5% Na_2CO_3. The aq. phase was adjusted to pH 3.0 with dil. HCl and the acids extracted into Et_2O. Evaporation of the Et_2O yielded 950 mg of acids.

The acid fraction was methylated with CH_2N_2 in Et_2O. The mixture was purified by repeated CC on Si gel with *n*-hexane and *n*-hexane–C_6H_6 mixtures as eluents. The fraction eluted with *n*-hexane–C_6H_6 (1:1) contained batudioic acid dimethyl ester (**1a**) (830 mg).

Batudioic acid (*lab* - 7, 13 Z - *dien* - 15, 18 - *dioic acid*) (**1**) Oil. IR ν_{max}^{KBr} cm^{-1}: 3500–2400 (CO_2H) 1680, 1650 (C=C–CO_2H); ^{1}H NMR: δ 0.73 (3H, *s*, H-20), 1.20 (3H, *s*, H-18), 1.73 (3H, *br s*, H-17), 1.91 (3H, *br s*, H-16), 2.70 (2H, *m*, H-12 and H-12′), 5.33 (1H, *m*, $W_{1/2}$ = 8.0 Hz, H-7), 5.66 (1H, *m*, $W_{1/2}$ = 5.0 Hz, H-14).

Batudioic acid dimethyl ester (**1a**). Colourless oil. IR ν_{max}^{film} cm^{-1}: 2920, 1720, 1645 (C=C–CO_2Me) 1150 (ester) 850; UV λ_{max}^{MeOH} nm (log ϵ): 233 (4.15); ^{1}H NMR: δ 0.76 (3H, *s*, H-20), 1.20 (3H, *s*, H-18), 1.73 (3H, *br s*, H-17), 1.83 (3H, *d*, J = 1.0 Hz, H-16), 2.73 (2H, *m*, H-12 and H-12′), 3.60 (3H, *s*, OMe), 3.66 (3H, *s*, OMe), 5.30 (1H, *m*, $W_{1/2}$ = 10.0 Hz, H-7), 5.63 (1H, *br s*, $W_{1/2}$ = 4.0 Hz, H-14); MS *m/z* (rel. int.): 362 [M]$^+$ (1.8), 330.2137 [M – MeOH]$^+$ (9.2) ($C_{21}H_{30}O_3$), 315 [M – MeOH – 15]$^+$ (2.0), 249 (87), 235 (7.4), 189 (83), 175 (15), 121 (19), 114 (100), 109 [(5), 21], 81 [113 – MeOH]$^+$ (77);

$[\alpha]_{23°}^{\lambda}$	589	578	546	436	365
	−12.7	−13.1	−14.4	−21.8	−28.6

($CHCl_3$; *c* 1.29).

Batudiol (**1b**). Obtained from **1a** by reduction with $LiAlH_4$ [7]. Yield 90%. IR ν_{max}^{film} cm^{-1}: 3320, 2900, 1665, 1430, 1030, 820; ^{1}H NMR: δ0.75 (3H, *s*, H-20), 0.80 (3H, *s*, H-18), 1.73 (6H, *br s*, H-16 and H-17), 3.23 (2H, AB quartet, J = 11.0 Hz, H-19 and H-19′), 4.10 (2H, *d*, J = 7.0 Hz, H-15 and H-15′), 5.38 (2H, *m*, $W_{1/2}$ = 11.0 Hz, H-7 and H-14); MS *m/z* (rel. int.): 306 [M]$^+$ (1.3), 288 [M – 18]$^+$ (1), 275 [M – 31]$^+$ (1), 220 [(5), 85], 205 (9), 202 (12), 109 [(4), 98], 81 (100);

$[\alpha]_{23°}^{\lambda}$	589	578	546	436	365
	−7.31	−8.07	−8.20	−11.26	−12.98

($CHCl_3$; *c* 0.78).

Diacetyl batudiol (**1c**). **1b** with Ac_2O–C_5H_5N at room temp. overnight followed by the usual work-up gave **1c**, colourless oil, yield 93%. IR ν_{max}^{film} cm^{-1}: 2920 1735, 1715, 1230, 1035; ^{1}H NMR: δ0.73 (3H, *s*, H-20), 0.90 (3H, *s*, H-18), 1.73 (6H, *br s*, H-16 and H-17), 2.03 (6H, *s*, two OAc), 3.73 (2H, AB quartet, J = 11.0 Hz, H-19 and H-19′), 4.56 (2H, *d*, J = 7.0 Hz, H-15 and H-15′), 5.36 (2H, *m*, H-7 and H-14).

Xanthomicrol (**2**) *and scutellarein* - 7, 4′ - *dimethyl ether* (**3**). The identity of xanthomicrol was confirmed by comparison with published physical and spectroscopic data [2]. The structure of scutellarein - 7, 4′ - dimethyl ether (**3**) was deduced from its UV (NaOMe, NaOAc, NaOAc–H_3BO_3, $AlCl_3$ and $AlCl_3$–HCl), ^{1}H NMR and mass spectral data.

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