

BISNORDITERPENES WITH A BARBACENANE SKELETON FROM *BARBACENIA FLAVA*

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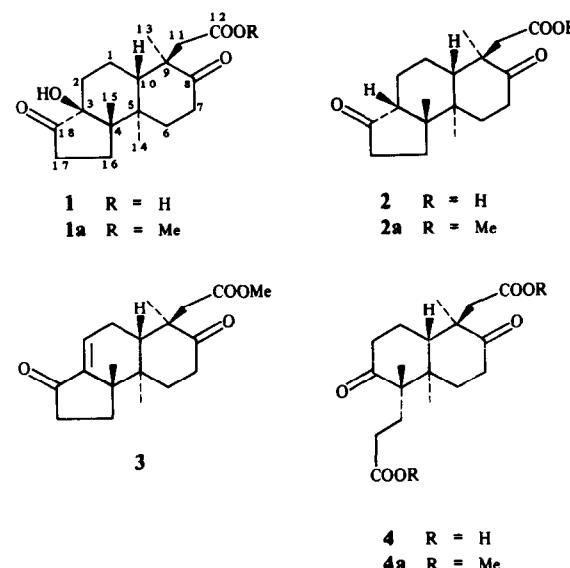
Abstract—The isolation of two new barbacenane bisnorditerpenes from *Barbacenia flava* is described. Their structures were established by spectroscopic data and chemical interconversion.

INTRODUCTION

We have previously reported the isolation and X-ray structure determination of barbacenic acid (1) [1], a bisnorditerpene with a novel skeleton from the hexane extracts of the stem, roots and leaf sheaths of *Barbacenia flava* Martius ex Schultes. The present paper describes the structural elucidation of two other diterpenes of the same plant, one with the same skeleton and the other a structurally correlated *seco* derivative.

RESULTS AND DISCUSSION

The bisnorditerpene (2), $C_{18}H_{26}O_4$, was isolated as the free acid and converted into the corresponding methyl ester (2a) ($C_{19}H_{28}O_4$) with diazomethane. The IR spectrum of 2 showed two strong carbonyl broad absorptions at 1755 and 1725 cm^{-1} and a band for an hydroxyl group at 3524 cm^{-1} , which was absent in its methyl ester (2a).



The 1H NMR spectrum of 2 in $CDCl_3$ plus C_5D_5N showed signals for three tertiary methyl groups at δ 0.80, 1.00 and 1.25, a broad signal at δ 6.48 (1H), exchangeable with D_2O , due to a proton of the carboxylic acid group, and two doublets for two geminal protons at δ 2.45 and 2.74 ($J = 18$ Hz). These two doublets and the fragmentation pattern with losses of 59 and 73 mass units in the MS of 2 and 2a, respectively, suggested the presence of a $\blacksquare-CH_2CO_2H(Me)$ residue.

These data, in combination with the comparative analysis of the proton noise decoupled and SFORD ^{13}C NMR spectrum, allowed expansion of the molecular formula to $(CO)_2\blacksquare-CH_2CO_2H(C_3(CH_2)_6(Me)_3$ and enabled us to assign structure 2 to the diterpenic acid.

Conclusive proof of this structure was provided in the following manner. Dehydration of 1a with $POCl_3$ -pyridine yielded the corresponding unsaturated carbonyl compound (3), which was catalytically hydrogenated, affording a product that was identical in all aspects to methyl ester 2a.

The *seco*-barbacenane bisnorditerpene (4), $C_{18}H_{26}O_6$, was also isolated as the free acid. Reaction of 4 with diazomethane showed the presence of two carboxylic acid functions (4a, $C_{20}H_{30}O_6$). The IR spectrum of 4a presented an intense peak at 1750 cm^{-1} and a broad band at 1703 cm^{-1} . The 1H NMR spectrum showed signals for three methyl groups at δ 1.06, 1.10 and 1.20, two carbomethoxyl groups at δ 3.70 (6H), and two doublets for two geminal protons at δ 2.48 and 3.00 ($J = 16$ Hz). The loss of 73 mass units in the MS spectrum established the presence of a $\blacksquare-CH_2CO_2Me$ residue as in 2a. The ^{13}C NMR spectrum of 4a showed characteristic chemical shifts for two methyl ester groups (two singlets at δ 174.4 and 172.3 and two quartets at δ 51.6 and 51.4), a single methyne at δ 41.4 and three sp^3 quaternary carbons at δ 54.5, 48.3 and 43.0. The intensity of the signal at δ 214.0 indicated the presence of two carbonyl groups. On the other hand, the chemical shifts for the signal of the carbonyl groups showed them to be adjacent to neopentilic carbons. These spectral data support the assigned structure 4a. Treatment of 1a with Jones reagent followed by diazomethane esterification [2] furnished 4a, identical

in all aspects to the natural bisnorditerpene isolated as a minor component.

The fact that compound **4** occurs in the same plant with **1** and **2** allows us to consider **1** as a possible biogenetic precursor for the former diterpenoid.

EXPERIMENTAL

Mps: uncorr. ^1H and ^{13}C NMR: TMS as int. stand.; TLC: Kieselgel 60PF (Merck), the analytical chromatograms were examined by spraying with a 0.2% soln of $\text{Ce}(\text{SO}_4)_2$ in 1 M H_2SO_4 followed by heating on a hot plate.

Barbacenia flava was collected in the Serra do Cipó, State of Minas Gerais, Brazil. Stem, roots and leaf sheaths (3.5 kg) were cut into small pieces and extracted with hexane followed by EtOH. The EtOH soln was concd *in vacuo*. The crude extract (224 g, 6.4%) thus obtained was redissolved in MeOH, filtered to remove waxes and evapd at red. pres. 24 g of this material was absorbed on 30 g of silica gel 60 and after evapn of the solvent, placed on top of a column of 490 g of the same adsorbent. Elution was started with hexane and the polarity of the eluent increased gradually. Compounds were eluted in the following order, although in the first chromatographic fractionation, the separations were not clear-cut, often requiring purification on smaller columns or by prep. TLC.

Barbacenic acid (**1**). Colourless crystals from hexane-EtOAc (3:1), mp 219–222°. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3532, 1732, 1140, 1050, 914 and 898; ^1H NMR (100 MHz, $\text{CDCl}_3 + \text{C}_5\text{D}_5\text{N}$ gts.): δ 0.85 (3H, s), 1.11 (3H, s), 1.18 (3H, s), 2.45 (1H, d, $J = 18$ Hz), 2.74 (1H, d, $J = 18$ Hz) and 7.63 (1H, br s, exchangeable with D_2O); MS m/z (rel. int.): 304 [M–18]⁺ (2), 294 (33), 286 (6), 263 (9), 251 (82), 191 (41), 177 (47), 123 (48), 55 (21), 43 (80) and 41 (100).

Methyl barbacenoate (**1a**). Mp 137–139°; $|\alpha|^{24}$:

+40	+45	+53	+73
589	578	546	436

(CHCl_3 ; c 0.60); IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3500, 1738, 1704 and 1050; ^1H NMR (100 MHz, CDCl_3): δ 0.88 (3H, s), 0.99 (3H, s), 1.16 (3H, s), 2.46 (1H, d, $J = 18$ Hz), 2.86 (1H, d, $J = 18$ Hz) and 3.58 (3H, s); ^{13}C NMR (25.2 MHz, CDCl_3): 16.0 (q), 16.5 (q), 20.3 (t), 23.0 (q), 27.3 (t), 27.9 (t), 29.2 (t), 34.4 (t), 34.9 (t), 38.8 (s), 41.9 (d), 44.1 (t), 48.0 (s), 49.0 (s), 51.6 (q), 75.8 (s), 172.4 (s), 215.5 (s) and 216.7 (s); MS m/z (rel. int.): 336 [M]⁺ (3), 321 (1), 318 (2), 308 (17), 277 (10), 276 (36), 265 (29), 263 (49), 191 (48), 55 (80) and 41 (100).

3-Deoxybarbacenic acid (**2**). Colourless crystals from hexane-EtOAc (6:1), mp 200–202°. IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 3524, 2925, 1755, 1725, 1415, 1230, 1193, 1059, 909, 830 and 754; ^1H NMR (100 MHz, $\text{CDCl}_3 + \text{C}_5\text{D}_5\text{N}$ gts.): δ 0.80 (3H, s), 1.00 (3H, s), 1.20 (3H, s), 2.40 (1H, d, $J = 18$ Hz), 2.76 (1H, d, $J = 18$ Hz) and 6.48 (1H, br s, exchangeable with D_2O); ^{13}C NMR (25.2 MHz, CDCl_3): δ 16.6 (q), 19.6 (t), 20.5 (t), 26.4 (q), 28.4 (t), 29.4 (t + q), 36.5 (t), 38.7 (s + s), 42.8 (d), 45.1 (t), 45.6 (t), 46.1 (s), 56.8 (d), 172.6 (s) and 218.4 (s + s); MS m/z (rel. int.): 306 [M]⁺ (1), 291 (6), 288 (12), 273 (8), 248 (10), 247 (48), 124 (34) and 97 (100).

Methyl 3-deoxybarbacenoate (**2a**). Colourless oil; IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 2929, 1722, 1700, 1427, 1332 and 1007; ^1H NMR (100 MHz, CDCl_3): δ 0.92 (3H, s), 0.99 (3H, s), 1.30 (3H, s), 2.40 (1H, d, $J = 18$ Hz), 2.90 (1H, d, $J = 18$ Hz) and 3.62 (3H, s); MS m/z (rel. int.): 320 [M]⁺ (1), 305 (9), 248 (20) and 247 (100).

3-Oxo-17-carboxy-3,18-seco-barcacenic acid (**4**). Colourless crystals from hexane-EtOAc (4:1), mp 214–216°; ^1H NMR (100 MHz, $\text{CDCl}_3 + \text{C}_5\text{D}_5\text{N}$ gts.): δ 0.96 (3H, s), 1.16 (3H, s), 1.21

(3H, s), 2.58 (1H, d, $J = 16$ Hz), 2.86 (1H, d, $J = 16$ Hz) and 9.50 (2H, br s, exchangeable with D_2O); MS m/z (rel. int.): 338 [M]⁺ (5), 320 (7), 302 (5), 55 (80) and 41 (100).

Methyl 3-oxo-17-carboxy-3,18-seco-barcacenoate (**4a**). Colourless crystals from hexane-EtOAc (6:1), mp 122–124°;

$ \alpha ^{25}$	+62	+68	+78	+155	+347
	589	578	546	436	365

(CHCl_3 ; c 60). IR $\nu_{\text{max}}^{\text{KBr}}$ cm^{-1} : 2904, 1750, 1703, 1428 and 1007; ^1H NMR (100 MHz, CDCl_3): δ 1.06 (3H, s), 1.10 (3H, s), 1.20 (3H, s), 2.48 (1H, d, $J = 16$ Hz), 3.00 (1H, d, $J = 16$ Hz) and 3.70 (6H, s); ^{13}C NMR (25.2 MHz, CDCl_3): 15.9 (q), 17.3 (q), 23.0 (q), 24.3 (t), 25.2 (t), 28.0 (t), 30.0 (t), 34.8 (t), 38.0 (t), 41.4 (d), 43.0 (s), 43.7 (t), 48.3 (t), 51.4 (q), 51.6 (q), 54.5 (s), 172.3 (s), 174.4 (s) and 214.0 (s); MS m/z (rel. int.): 366 [M]⁺ (30), 335 (23), 293 (15), 261 (70), 223 (35), 177 (100) and 55 (96).

Dehydration of methyl barbacenoate (**1a**). To a soln of **1a** (38 mg) in pyridine (1 ml) cooled to 0°, POCl_3 (0.5 ml) was added. After 2 hr, H_2O (2 ml) was added and the mixture was extracted with CHCl_3 (3×10 ml). The organic layers were washed with H_2O (2×10 ml), dried over Na_2SO_4 , filtered and the CHCl_3 was removed *in vacuo*. The crude reaction mixture (35.2 mg) was purified by prep. TLC (silica gel; hexane-EtOAc 3:1, twice developed) to give **3** (16.0 mg), mp 80–83°. UV $\lambda_{\text{max}}^{\text{EtOH}}$ nm (log ϵ): 244 (3.63); IR $\nu_{\text{max}}^{\text{CHCl}_3}$ cm^{-1} : 2963, 1717, 1702 and 1654; ^1H NMR (100 MHz, CDCl_3): δ 1.07 (3H, s), 1.15 (3H, s), 1.18 (3H, s), 2.40 (1H, d, $J = 18$ Hz), 2.90 (1H, d, $J = 18$ Hz), 3.63 (3H, s) and 6.60 (1H, t, $J = 4$ Hz); ^{13}C NMR (25.2 MHz, CDCl_3): 17.0 (q), 22.8 (q), 23.0 (q), 25.1 (t), 27.0 (t), 29.8 (t), 35.2 (t + s), 35.8 (t), 36.9 (s), 39.1 (d), 42.8 (t), 48.1 (s), 51.5 (q), 129.7 (d), 144.3 (s), 172.1 (s), 206.1 (s) and 214.0 (s); MS m/z (rel. int.): 318 [M]⁺ (21), 287 (40), 286 (100), 271 (28), 269 (10), 268 (37), 258 (10), 253 (15), 245 (42) and 123 (92).

Catalytic hydrogenation of **3**. A soln of **3** (11 mg) in EtOAc (1 ml) was hydrogenated over PtO_2 (2 mg) at 40 psi. After 40 min, the catalyst was filtered off and washed with EtOAc. Evapn of the filtrate under red. pres. yielded a crystalline compound (6 mg), identical in all respects with ester **2a**, obtained from the natural product.

Oxidation of **2a** *with Jones reagent*. To a soln of **2a** (10 mg) in Me_2CO (2 ml) was added dropwise Jones reagent under stirring and to the point of a persistent brown colour. The excess of reagent was consumed by addition of a few drops of *i*-PrOH and, after removal of the solvent *in vacuo*, the residue was extracted with CHCl_3 . The organic extract was washed with H_2O , dried (Na_2SO_4), filtered and evaporated to yield an oil, which was reacted with CH_2N_2 . Filtration through silica-gel afforded ketester **4a** as a colourless oil, identical in all respects with the natural product.

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