

Glaziovianol, a New Terpenoid Hydroquinone from *Auxemma glazioviana*

Galberto M. da Costa,[†] Telma L. G. de Lemos,^{*,†} Otilia D. L. Pessoa,[†] Francisco J. Q. Monte,[†] and Raimundo Braz-Filho[‡]

Departamento de Química Orgânica e Inorgânica, Universidade Federal do Ceará, CP 12200 60451-970 Fortaleza, Ceará, Brazil, and Setor de Química de Produtos Naturais-LCQI-CCT, Universidade Estadual do Norte Fluminense, 28015-620 Campos, Rio de Janeiro, Brazil

Received December 23, 1998

A novel terpenoid hydroquinone named glaziovianol (**1**) and three known compounds 6-formyl-2-methoxy-9-methyl-7,8-dihydro-1,4-phenanthrenedione, *ent*-19-oxo-16 β H-kauran-17-oic acid, and *rel*-8 α -hydroxy-5-hydroxymethyl-2-methoxy-8 α -methyl-7,8,8a,9-tetrahydro-1,4-anthracenedione were isolated from the EtOH extract of *Auxemma glazioviana* wood. The structures were established using spectroscopic analysis (1D and 2D NMR, MS, IR).

Previous work with *Auxemma oncocalyx* allowed the identification of several terpenoid quinones, classified as cordiachromes.^{1,2} In continuation of our phytochemical investigation of *Auxemma* species, a specimen of *A. glazioviana* Taub., popularly known as "pau branco louro", which inhabits mainly the Ceará State, of northeastern Brazil was collected. The wood of this plant, used largely in civil constructions, is resistant to fungi and termite attack. The trunk bark is used in folk medicine for the treatment of cuts and wounds.³

In this paper we describe the isolation and structure determination of three known compounds: *ent*-19-oxo-16 β H-kauran-17-oic acid,⁴ 6-formyl-2-methoxy-9-methyl-7,8-dihydroxy-1,4-phenanthrenedione, and *rel*-8 α -hydroxy-5-hydroxymethyl-2-methoxy-8 α β -methyl-7,8,8a,9-tetrahydro-1,4-anthracenedione,^{1,2} and a novel terpenoid hydroquinone, glaziovianol (**1**). Their structures were elucidated based on spectral analysis, including 2D NMR experiments and NOE difference NMR measurements of **1**. The diterpene *ent*-19-oxo-16 β H-kauran-17-oic acid is reported for the first time in the Boraginaceae family.

An ethanol extract of *A. glazioviana* trunk heartwood was chromatographed over Si gel to yield (**1**), 6-formyl-2-methoxy-9-methyl-7,8-dihydroxy-1,4-phenanthrenedione, *ent*-19-oxo-16 β H-kauran-17-oic acid, and *rel*-8 α -hydroxy-5-hydroxymethyl-2-methoxy-8 α β -methyl-7,8,8a,9-tetrahydro-1,4-anthracenedione. The HBBD-¹³C NMR spectrum of **1** revealed signals corresponding to 16 carbon atoms. Chemical shifts and comparative analysis of HBBD- and DEPT-¹³C NMR spectra were used to recognize the carbon signals as corresponding to one carbonyl, six aromatics, and nine sp³: two quaternaries, two methines, four methylenes, and one methyl. The presence of a carbonyl ketone group was also revealed by an absorption at ν_{\max} 1699 cm⁻¹ observed in the FT-IR spectrum. The ¹H NMR, HBBD-¹³C NMR and DEPT-¹³C NMR spectra of **1** are consistent with the molecular formula C₁₆H₁₈O₅, confirmed by an [M]⁺ at *m/z* 289.9822, in the HREIMS. These data suggest that **1** is a hydroquinone similar to other compounds isolated from *Auxemma oncocalyx*,^{1,2} *Cordia elaeagnoids*,⁵ and *Cordia alliodora*.⁶

The presence of two phenolic hydroxyl groups was confirmed by conversion of **1** to the diacetate **2**. Hydrogen-

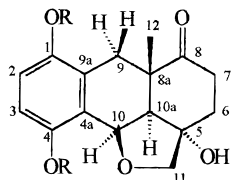
carbon direct connectivities of **1** and **2** were determined from a HMQC spectrum. The HMBC spectrum of **1** and **2** revealed coupling between hydrogen and carbon atoms via two (²J_{CH}) and three (³J_{CH}) bonds. The *p*-hydroquinone system was recognized by chemical shifts observed in the ¹³C and ¹H NMR spectra of **1**. This deduction was confirmed by the HMBC spectrum, indicating interaction of the hydroxyl hydrogen HO-1 with quaternary carbons C-1 and C-9a, and HO-4 with C-4 and C-4a. Subtraction of the *p*-hydroquinone moiety (C₆H₄O₂) from the molecular formula C₁₆H₁₈O₅ gives a partial molecular formula C₁₀H₁₄O₃ for the remaining terpenoid system, containing one carbonyl, two quaternary, two methine, four methylene, and one methyl carbon atoms, along with a tertiary hydroxyl group observed in the ¹H NMR of **1**. The presence of only three oxygen atoms in this moiety and four signals assigned to oxygenated carbons observed in the ¹³C NMR spectra of **1** indicated the existence of one ether function. The location of the tetrahydrofuran ring involving the carbon atoms CH-10, CH-10a, and C-5 was defined from the HMBC spectrum of **2**. The heteronuclear long-range interaction between the tertiary methyl carbon CH₃-12 [**1/2**: δ_C 19.53/18.80 and δ_H 0.94 (s)/1.02 (s)] and hydrogens 2H-9 [**1/2**: δ_H , 2.97 (d, *J* = 16.5 Hz) and 2.07 (d, *J* = 16.5 Hz)/2.96 (d, *J* = 16.5 Hz) and 2.27 (d, *J* = 16.5 Hz), ³J_{CH}] and H-10a [**1/2**: δ_H 2.13 (d, *J* = 3.3 Hz)/2.22 (d, *J* = 5.4 Hz), ³J_{CH}] revealed by HMBC spectra of **1** and **2** were also used to locate the methyl at carbon C-8a [**1/2** δ_C 41.62/41.68], which also showed coupling with 3H-12 (²J_{CH}, **1** and **2**), 2H-9 (²J_{CH}, **2**), H-10a (²J_{CH}, **2**), 2H-7 (³J_{CH}, **1**), and H-10 (³J_{CH}, **1** and **2**). The coupling constant values corresponding to vicinal spin-spin interaction [³J_{H,H} = 3.3 (**1**) and 5.4 Hz (**2**)] between hydrogens H-10 [δ_H 5.05 (**1**) and 5.13 (**2**)] and H-10a [δ_H 2.13 (**1**) and 2.22 (**2**)] observed in the ¹H NMR spectra of **1** and **2** are consistent with the syn relationship of these hydrogens. The trans B/C ring junction was suggested by the singlet at δ_H 0.94 corresponding to a tertiary methyl group (3H-12), whereas the *cis*-isomer signal appears at δ_H 1.05.^{7,8} Relative configurations at C-5, C-8a, C-10, and C-10a were assigned based on results obtained by NOE difference spectra: (a) irradiation at δ_H 0.94 (3H-12 β) resulted in 0.7% NOE at δ_H 3.86 (H-11 α) and 1.0% NOE at δ_H 2.97 (H-9 β); (b) irradiation at δ_H 5.05 (H-10 α) showed 4.9% NOE at δ_H 2.13 (H-10 α) and 3.5% NOE at δ_H 3.86 (H-11 α); (c) irradiation at δ_H 2.07 (H-9 α) revealed 6.6% NOE at δ_H 2.97 (H-9 β) and 2.9% NOE at δ_H 2.13 (H-10 α); (d) irradiation at δ_H 3.86 (H-11 β) resulted in 3.0%

* To whom correspondence should be addressed. Tel.: 55-85-2889954. Fax: 55-85-2889782. E-mail: tlemos@dqi.ufc.br.

[†] Universidade Federal do Ceará.

[‡] Universidade Estadual do Norte Fluminense.

NOE at δ_H 5.05 (H-10 α), 2.0% NOE at δ_H 5.21 (HO-5 α), and 1.0% NOE at 5.05 (H-10 α); (e) irradiation at δ_H 3.86 (H-11 α) showed 1.5% NOE at δ_H 0.94 (3H-12 β); (f) irradiation at δ_H 2.13 (H-10 α) yielded 1.6% NOE at δ_H 5.24 (HO-5 α) and 0.6% NOE at δ_H 5.05 (H-10 α). These deductions were confirmed by $^1H\{^1H\}$ NOE difference spectra of the diacetyl derivative **2**.



- 1 R = H
2 R = Ac

Experimental Section

General Experimental Procedures. Melting points were determined using a melting point apparatus and above 290° were uncorrected. IR spectra were obtained on a Perkin–Elmer 1000 FT-IR instrument, using KBr pellets. Optical rotations were measured on a Perkin–Elmer 341 digital polarimeter. The NMR spectra were recorded on a Bruker DRX 500 [500 MHz (1H) and 125 MHz (^{13}C)] spectrometer. Chemical shifts were recorded in δ (ppm) from the solvent absorption relative to TMS, $CDCl_3$ (δ 7.24 and 77.0 ppm), and $DMSO-d_6$ (2.49 and 39.5 ppm). TLC: Si gel 60 (Carlo Erba), hexane–EtOAc (20:80) and spots visualized by UV (254 and 366 nm) and spraying reagent with a mixture of vanillin–perchloric acid–EtOH.

Plant Material. *A. glazioviana* was collected in January 1997, in Cristais, Ceará State, Brazil, and identified by Professor Afrânio Gomes Fernandes, botanist of the Universidade Federal do Ceará, where a voucher specimen is deposited (Herbarium Prisco Bezerra, no. 18639).

Extraction and Isolation. Dried and powdered heartwood (1.0 kg) was exhaustively extracted with EtOH at room temperature. Repeated chromatography on Si gel using hexane and EtOAc yielded 6-formyl-2-methoxy-9-methyl-7,8-dihydroxy-1,4-phenanthrenedione (9.0 mg), *ent*-19-oxo-16 β H-kauran-17-oic acid (16.0 mg), *rel*-8 α -hydroxymethyl-5-hydroxymethyl-2-methoxy-8 β -methyl-7,8,8a,9-tetrahydro-1,4-anthracenedione (75.0 mg), and a new compound **1** (115.6 mg).

Glaziovianol (**1**): obtained as a colorless amorphous powder (115.6 mg), mp > 290 °C; $[\alpha]_D^{20} = 97.3^\circ$ (c 0.03, DMSO); IR (KBr) ν_{max} 3436, 3225, 1698, 1618, 1483, 1312, 1207 cm^{-1} ; HREIMS m/z 289.9822 ($[M]^+$, $C_{16}H_{18}O_5$, 75%), 258.9719 ($[M - CH_3O]^+$, $C_{15}H_{15}O_4$, 18%), 186.9621 ($[M - C_5H_{11}O_2]^+$ and/or $[M - CH_3O - C_4H_8O]^+$, $C_{11}H_7O_3$, 15%), 175.0756 ($[M - CH_3O -$

$- C_4H_8O_2]^+$, $C_{11}H_{11}O_2$, 100%); 1H (500 MHz, $DMSO-d_6$) δ 6.58 (1H, d, $J = 8.2$ Hz, H-2), 6.49 (1H, d, $J = 8.2$ Hz, H-3), 2.35 (1H, t, $J = 14.2$ Hz, H-6), 2.08 (1H, m, H-6), 2.64 (1H, m, H-7), 2.30 (1H, m, H-7), 2.97 (1H, d, $J = 16.6$ Hz, H-9), 2.07 (1H, d, $J = 16.6$ Hz, H-9), 5.05 (1H, d, $J = 3.3$ Hz, H-10), 2.13 (1H, d, $J = 3.3$ Hz, H-10a), 3.86 (2H, br s, H₂-11), 0.94 (3H, s, Me-12), 8.61 (1H, s, HO-1), 8.45 (1H, s, HO-4), 5.24 (1H, s, HO-5); ^{13}C NMR (125 MHz, $DMSO-d_6$) δ 215.1 (s, C-8), 150.0 (s, C-4), 148.1 (s, C-1), 123.3 (s, C-9a), 121.5 (s, C-4a), 115.4 (d, C-2), 113.2 (d, C-3), 82.3 (t, C-11), 78.9 (s, C-5), 73.3 (d, C-10), 53.1 (d, C-10a), 41.6 (s, C-8a), 35.8 (t, C-7), 33.1 (t, C-9), 32.7 (t, C-6), 19.5 (q, C-12).

1,4-Di-O-acetylglaziovianol (2). Glaziovianol (**1**, 30 mg) was treated with Ac_2O in the presence of pyridine (2:1) at room temperature. The reaction mixture was washed with copper sulfate solution and extracted with $CHCl_3$. The organic phase was evaporated under reduced pressure to yield diacetate **2** (26.3 mg, 84.3%): IR (KBr) ν_{max} 3422, 1764, 1716, 1474, 1191 cm^{-1} ; 1H (500 MHz, $CDCl_3$) δ 7.02 (1H, d, $J = 8.7$ Hz, H-2), 6.97 (1H, d, $J = 8.7$ Hz, H-3), 2.38 (1H, dt, $J = 4.0, 14.4$ Hz, H-6), 2.16 (1H, ddd, $J = 2.2, 5.7, 14.4$ Hz, H-6), 2.63 (1H, ddd, $J = 5.7, 14.4$ and 18.3 Hz, H-7), 2.45 (1H, ddd, $J = 2.2, 4.0, 14.4$ Hz, H-7), 2.96 (1H, d, $J = 16.5$ Hz, H-9), 2.27 (1H, d, $J = 16.5$ Hz, H-9), 5.13 (1H, d, $J = 5.4$ Hz, H-10), 2.22 (1H, d, $J = 5.4$ Hz, H-10a), 4.03 (1H, d, $J = 9.7$ Hz, H-11), 3.99 (1H, d, $J = 9.7$ Hz, H-11), 1.02 (3H, s, Me-12), 2.31 (3H, s, Me-Ac), 2.27 (3H, s, Me-Ac); ^{13}C NMR (125 MHz, $CDCl_3$) δ 213.5 (s, C-8), 169.8 (s, Ac), 169.3 (s, Ac), 148.4 (s, C-4), 147.1 (s, C-1), 129.5 (s, C-9a), 127.6 (s, C-4a), 122.9 (d, C-2), 121.7 (d, C-3), 82.9 (t, C-11), 80.0 (s, C-5), 73.3 (d, C-10), 53.6 (d, C-10a), 41.7 (s, C-8a), 35.3 (t, C-7), 32.9 (t, C-9), 32.6 (t, C-6), 20.9 (q, Ac), 20.8 (q, Ac), 18.8 (q, C-12).

Acknowledgment. The authors are grateful to CNPq, CAPES, FUNCAP, and BNB for financial support; to Prof. A. G. Fernandes for botanic identification, to CENAUREMN/UFC for the NMR spectra; to Profa. M. A. S. Lima for the MS data; and to Dr. Victor Rumjanek for reading the manuscript.

References and Notes

- (1) Pessoa, O. D. L.; Lemos, T. L. G.; Silveira, E. R.; Braz-Filho, R. *Nat. Prod. Lett.* **1993**, *2*, 145–150.
- (2) Pessoa, O. D. L.; Lemos, T. L. G.; Carvalho, M. G.; Braz-Filho, R. *Phytochemistry* **1995**, *40*, 1777–1786.
- (3) Braga, R. *Plantas do Nordeste, Especialmente do Ceará*, 2nd ed.; Imprensa Oficial: Fortaleza, Ceará, Brasil; 1960.
- (4) Buckingham, J., McDonald, F. M., Bradley, H. M., Eds. *Dictionary of Natural Products*, Chapman and Hall: London, 1994; Vol. 3, p 3484 (compound in **K-00101**).
- (5) Manners, G. D. *J. Chem. Soc., Perkin Trans. 1* **1983**, 39–43.
- (6) Manners, G. D.; Jurd, L. *J. Chem. Soc., Perkin Trans. 1* **1977**, *4*, 405–410.
- (7) Moir, M.; Thomson, R. H.; Hausen, B. M. *J. Chem. Soc., Chem. Commun.* **1972**, 363–364.
- (8) Moir, M.; Thomson, R. H.; *J. Chem. Soc., Perkin Trans. 1* **1973**, *13*, 1352–1357.

NP980575Y