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A NAPHTHOQUINONE FROM *NEWBOULDIA LAEVIS* ROOTS

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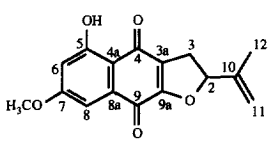
Key Word Index—*Newbouldia laevis*; Bignoniaceae; roots; naphthoquinones.

Abstract—The structure of a new naphthoquinone, isolated from the dichloromethane extract of *Newbouldia laevis* roots, has been established by means of mass and ^{1}H NMR spectroscopy as 5-hydroxy-7-methoxydehydroiso-α-lapachone. © 1998 Elsevier Science Ltd. All rights reserved

INTRODUCTION

An additional naphthoquinone has been isolated during our continuing work [1] on the roots of *Newbouldia laevis*. Its structure has been determined as 5-hydroxy-7-methoxydehydroiso-α-lapachone (**1**).



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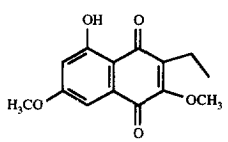

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RESULTS AND DISCUSSION

The dichloromethane extract was first fractionated by CC on silica gel. Further separations by MPLC on RP-18 and gel filtration on Sephadex LH-20 yielded the 11 naphthoquinones described before [1], as well as the minor compound **1** (0.5 mg).

The structure of **1** was determined by means of UV, mass and ^{1}H NMR spectroscopy. Unfortunately, the small quantity isolated and its instability in $CDCl_3$ solution prevented further NMR experiments. The UV spectrum of **1** (λ_{max} at 207, 263 and 320 nm) exhibited the same bands as 5,7-dihydroxydehydroiso-α-lapachone (λ_{max} at 217, 264 and 323 nm [1]). Therefore, it was suggested that **1** was a naphthoquinone with a structure similar to that of 5,7-dihydroxydehydroiso-α-lapachone.

The EI-mass spectrum ($[M]^+$ at *m/z* 286) showed a fragmentation pattern which was typical of a derivative of dehydroiso-α-lapachone without substitution in position C-3 [2]; peaks were observed at $[M-15]^+$, $[M-28]^+$, $[M-43]^+$ and $[M-71]^+$. The assignment of further fragments was based on the cleavage of the dehydroiso-α-lapachone nucleus. According to Bowie *et al.* [3], fragments at *m/z* 104, 105 and 133 indicate an unsubstituted aromatic moiety. Any substituent on this part would produce fragments of higher mass according to the mu of the substituent. The difference of 46 mu (*m/z* 150, 151 and 179 for **1**) compared with the mass of the unsubstituted quinone, suggested that the aromatic moiety was substituted with either two hydroxyl and a methyl group or a hydroxyl and a methoxyl group.

The ^{1}H NMR spectrum confirmed that **1** was a C-3 unsubstituted derivative of dehydroiso-α-lapachone: the signals of the isopropenyl group were found at δ 1.80 (*s*, 3H), δ 5.01 (*s*, H-11, *cis* to Me) and δ 5.12 (*s*, H-11, *trans* to Me), the C-2 proton was observed at δ 5.42 (*dd*, J = 10.9, 8.8 Hz) and the two protons of C-3 gave signals at δ 3.32 (*dd*, J = 17.1, 10.9 Hz, 1H) and δ 3.01 (*dd*, J = 17.1, 8.8 Hz, 1H). Further signals were attributed to two *meta*-coupled aromatic protons (δ 7.21, *d*, J = 2.4 Hz, 1H and δ 6.62, *d*, J = 2.4 Hz, 1H), a chelated hydroxyl group at δ 12.38, indicating a hydroxyl group at position C-5 or C-8, and an aromatic methoxyl group (δ 3.89, *s*, 3H). With this information, **1** was determined to be either 5-hydroxy-7-methoxydehydroiso-α-lapachone or 8-hydroxy-6-methoxydehydroiso-α-lapachone.

For juglone-type naphthoquinones (5-hydroxy-1,4-naphthoquinones), the shift of the chelated hydroxyl proton in the ^{1}H NMR gives evidence for the position of this hydroxyl group. According to Lillie and Musgrave [4], the chemical shift of the chelated hydroxyl proton in $CDCl_3$ is influenced by the substituents in the quinone ring. This value is independent of the sample concentration. Wagner *et al.* [5] proved the validity of this rule by selective-INEPT spectroscopy and formulated a general rule: hydroxyl groups of

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Table 1. ^{1}H NMR data ($CDCl_3$) of aromatic protons and substituents of the aromatic moiety of compounds **1** (500 MHz) and **2**

	1	**2**
HO-5	12.38 (*s*)	12.47 (*s*)
H-6	6.62 (*d*, J = 2.4 Hz)	6.59 (*d*, J = 2.2 Hz)
H_3CO-7	3.87 (*s*)	3.87 (*s*)
H-8	7.21 (*d*, J = 2.4 Hz)	7.10 (*d*, J = 2.2 Hz)

Values for **2** from ref. [7].

aryl-unsubstituted 8-hydroxynaphtho[2,3-*b*]furandiones appear in the ^{1}H NMR spectrum more upfield than hydroxyl protons of the corresponding 5-hydroxy isomer. In the model compounds, the signal of this proton is found at 11.64 ppm (8-hydroxydehydroiso-α-lapachone) [2] and at 12.23 ppm (5-hydroxydehydroiso-α-lapachone) [1]. As a methoxyl group in a *meta*-position has little influence (−0.09 ppm [6]) on the shift of the chelated hydroxyl proton, the shift at δ 12.38 for **1** gives evidence that this compound is 5-hydroxy-7-methoxydehydroiso-α-lapachone. It is a new natural product.

These findings were in good agreement with the literature values for demethoxylomandrone (**2**) [7], the structure of which was confirmed by synthesis. This naphthoquinone is very similarly substituted at C-3a and C-9a and has exactly the same groups attached to the aromatic moiety as **1**. A comparison between the ^{1}H NMR values of the aromatic protons and the substituents on the aromatic moieties of **1** and **2** is given in Table 1.

EXPERIMENTAL

General. TLC: silica gel 60 F_{254} Al sheets (Merck). CC: silica gel (63–200 μm; Merck). MPLC: home-packed LiChroprep RP-18 column (15–25 μm; 460 × 26 mm i.d.). Mps: uncorr. ^{1}H NMR: in $CDCl_3$ at 499.87 MHz. Signals were referenced to the solvent peak ($CDCl_3$, δ 7.26). EI-MS and D/CI-MS: triple-stage quadrupole instrument. The purity of the compound was checked by HPLC (gradient: MeCN–H_2O) (0.05% TFA) 1:4 → 9:1 in 30 min (1 ml min^{-1}) using a Nova-Pak RP-18 column (4 μm, 150 × 3.9 mm i.d.).

Plant material. Roots of *N. laevis* Seem. were collected in 1994 in Seredou, province of Macenta, Guinea. A voucher specimen (No. 94084) is deposited at the Institut de Pharmacognosie et Phytochimie, Lausanne, Switzerland.

Extraction and isolation. Powdered roots (958 g) were extracted at room temp. successively with CH_2Cl_2 and MeOH, to afford 6.8 g and 107.6 g of extract, respectively. A portion of the CH_2Cl_2 extract (6.5 g) was subjected to CC on silica gel, using mixts of petrol, EtOAc, $CHCl_3$ and MeOH of increasing polarity, giving frs 1–12. Compound **1** (0.5 mg) was isolated from fr. 3 by MPLC with MeOH–H_2O (3:2).

5-Hydroxy-7-methoxydehydroiso-α-lapachone (**1**). Red needles, mp > 300°. UV λ_{max}^{MeOH} nm (log ε): 207 (3.84), 263 (3.67), 320 (3.32). ^{1}H NMR (500 MHz, $CDCl_3$): δ 12.38 (1H, *s*, HO-5), 7.21 (1H, *d*, J = 2.4 Hz, H-8), 6.62 (1H, *d*, J = 2.4 Hz, H-6), 5.42 (1H, *dd*, J = 10.9, 8.8 Hz, H-2), 5.12 (1H, *s*, H-11, *trans* to CH_3), 5.01 (1H, *s*, H-11, *cis* to CH_3), 3.89 (3H, *s*, H_3CO-7), 3.32 (1H, *dd*, J = 17.1, 10.9 Hz, H-3), 3.01 (1H, *dd*, J = 17.1, 8.8 Hz, H-3), 1.80 (3H, *s*, H-12). EI/MS *m/z* (rel. int.): 287 (16), 286 $[M]^+$ (100), 271 (14), 258 (16), 243 (61), 215 (9), 179 (6), 151 (15), 150 (18), 122 (10).

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