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4-HYDROXYPHENYLPROPAN-7,8-DIOLS AND DERIVATIVES FROM *NARVALINA DOMINGENSIS*

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Key Word Index—*Narvalina domingensis*; Compositae; phenylpropanoids; 4-hydroxyphenylpropan-7,8-diol.

Abstract—Investigation of a Haitian medicinal plant, *Narvalina domingensis*, afforded, *erythro*- and *threo*-4-hydroxyphenylpropan-7,8-diol and their 7-*O*-methyl ether, 7-*O*-ethyl ethers and 4-*O*-isovaleric acid esters. The structures were elucidated by spectroscopic analyses.

INTRODUCTION

Narvalina domingensis (local name: evil-eye), is a small tree *ca* 2.5 m in height with upward branches, rigid leaves and several flower tubes with oily heads. This plant is used as a traditional medicine in Haiti. The repulsive odour that it gives off when it is dry is believed to neutralize the evil-eye, which is a disease symptom probably due to malnutrition in children. Phytochemical investigation of the aerial parts of the title species afforded *erythro*- and *threo*-4-hydroxyphenylpropan-7,8-diols and several derivatives thereof. This paper describes their structural elucidation.

RESULTS AND DISCUSSION

Compounds were purified by means of chromatography, as described in the Experimental section.

^{13}C NMR spectra indicated that all compounds have a symmetrical benzene ring with hydroxyl and 1,2-propanediol substituents (Table 1). This evidence was supported by ^{1}H NMR spectroscopy, showing two AB doublet signals (2H each) in the aromatic region and a doublet methyl signal (3H).

Compound **1** was obtained as colourless crystals. From the elemental composition, $C_9H_{12}O_3$, determined by HR-EI mass spectrometry, the structure of **1** was elucidated to be 4-hydroxphenylpropan-7,8-diol. Although its 4-methoxyl derivative has been known since 1939 as anetholglycol, isolated from *Ruta montana* [1] and its glucosides were isolated from *Foeniculum vulgare* [2], as far as we know this compound was first isolated from nature.

Compound **2** was isolated as crystals and its spectroscopic data were similar to those of the aforementioned compound. The most significant difference was the coupling constant of the H-7 proton [δ 4.23 (*d*, J = 7 Hz)], which indicated that these compounds were diastereomers. From the coupling constants, compound **1** was expected to be the *erythro*-form and compound **2** the *threo*-form [3]. The elution order of the two compounds on a reverse-phase column also supported this assumption [4].

Compound **3** was obtained as a colourless oil. The only difference was an additional methoxyl group at δ_C 56.5 and δ_H 3.21 (3H, *s*). Based on the ^{13}C NMR chemical shifts of the C-7 and C-8 positions, the ether linkage was tentatively placed on the hydroxyl group at C-7. However, due to the scarcity of sample, further experimentation could not be performed.

Compounds **4** and **5** were respective diastereomers like **1** and **2**. An additional functional group was an ethoxyl group. Similar to the previous compound, **3**, the position of ethyoxylation was expected to be the hydroxyl group at C-7. This was confirmed by an acetylation experiment on **5**, in which the doublet of the quartet proton at δ 3.78 showed a significant downfield shift to δ 5.09. Therefore, the structures of **4** and **5** were elucidated to be *erythro*- and *threo*-4-hydroxyphenylpropan-7,8-diol 7-*O*-ethyl ethers.

Compounds **6** and **7** were also analogous compounds with a different modification. A doublet methyl signal (6H) in the ^{1}H NMR spectrum, and methine, methylene and carbonyl carbons in the ^{13}C NMR spectrum indicated the presence of isovalerate (Table 1). Since,

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Table 1. ^{13}C NMR data for 4-hydroxyphenylpropan-7,8-diols **1**–**7** ($CDCl_3$, 100 MHz)

Carbon No	1*	2*	3	4	5	6	7
1	134.2	134.1	130.1	130.7	131.1	137.9	138.5
2,6	129.3	129.4	129.0	129.0	128.9	127.7	127.8
3,5	115.8	116.0	115.4	115.2	115.3	121.5	121.7
4	157.8	158.1	155.9	155.4	155.7	150.2	150.2
7	78.9	80.2	88.9	85.1	87.1	77.1	78.9
8	72.4	73.0	71.7	70.8	71.5	71.2	72.2
9	18.4	19.2	18.9	18.1	17.9	17.3	18.8
1′	–	–	56.5	64.1	64.1	171.6	171.5
2′	–	–	–	15.3	15.2	43.4	43.4
3′	–	–	–	–	–	25.9	25.9
4′,5′	–	–	–	–	–	22.4	22.4

*Data for CD_3OD.

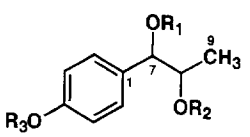
in the ^1H NMR spectrum, no acylation-induced downfield shift was observed for the H-7 and -8 protons, the structures of **6** and **7** were elucidated to be the 4-*O*-isovalerates of **1** and **2**, respectively.

EXPERIMENTAL

General. Mps: uncor. ^1H NMR and ^{13}C NMR: 400 MHz and 100 MHz, respectively, with TMS as int. standard. EI-MS: 70 eV. Prep. HPLC: ODS Inertsil (GL Science, Tokyo): 20 mm × 250 mm with H_2O–MeOH at 6 ml min^{-1} (A) or 6 mm × 250 mm with H_2O–MeOH at 1.6 ml min^{-1} (B); detection, UV at 254 nm.

Plant material. Aerial parts of *N. domingensis* Cass were collected in Haiti in 1991. The plant was identified by A. de A. and a voucher specimen is deposited in the Herbarium of the Faculty of Science, El-Minia University, Egypt.

Extraction and isolation. Air-dried aerial parts (300 g) were extracted with CH_2Cl_2–MeOH (1:1) (800 ml). The extract (13 g) was separated by silica gel (200 g) CC into four frs with solvent systems of Et_2O–*n*-hexane (3:1) (fr. 1, 143 mg), (5:1) (fr. 2, 433 mg), (8:1) (fr. 3, 69 mg) and Et_2O (fr. 4, 1.19 g). The residue of fr. 4 was separated by silica gel (50 g) CC using a gradient solvent system [Et_2O–*n*-hexane (1:4, 1 l)→(9:1, 1 l), frs of 8 g being collected] to give a mixt. of compounds **1** and **2** (405 mg) in frs 61–66. Final purification of the mixt. by prep. HPLC (A) with H_2O–MeOH (4:1) afforded **1** (150 mg) (14 min) and **2** (200 mg) (19 min) in crystalline states.



	R_1	R_2	R_3
1,2	H	H	H
3	CH_3	H	H
4,5	CH_3CH_2	H	H
5a	CH_3CH_2	CH_3CO	CH_3CO
6,7	H	H	$(CH_3)_2CHCH_2CO$

The residue of fr. 2 was separated similarly to the previous fr. by silica gel CC [Et_2O–*n*-hexane (1:4, 1 l)→(9:1, 1 l), frs of 8 g being collected]. From frs 70–78 and 84–90, **5** (10 mg) and **3** (5.5 mg) were obtained in crystalline states, respectively. The residue of frs 79–80 was further purified by prep. TLC on silica gel developed with Et_2O–*n*-hexane (4:1) to give **4** (4.0 mg) as an oil. The residue (110 mg) in frs 101–110 was a mixt. of **6** and **7**, and a small quantity of this residue was separated by prep. HPLC (B) [7 mg (6.3 min) and 4 mg (13.3 min), respectively].

erythro-4-*Hydroxyphenylpropan*-7,8-*diol* (**1**). Crystals, mp 153–154° (MeOH). $[\alpha]_D^{25}$ +23.1° (MeOH, *c* 0.56). IR ν_{max}^{KBr} cm^{-1}: 3200, 1610, 1595, 1505, 1445, 1405, 1365, 1240, 1080, 1025, 945, 880, 825. UV λ_{max}^{MeOH} nm (log ε): 225 (3.86), 277 (3.12). ^1H NMR (CD_3OD): δ 1.12 (3H, *d*, J = 6 Hz, H_3-9), 3.83 (H, *dq*, J = 5 and 6 Hz, H-8), 4.39 (H, *d*, J = 5 Hz, H-7), 6.76 (2H, *d*, J = 9 Hz, H-3 and 5), 7.18 (2H, *d*, J = 9 Hz, H-2 and 6); ^1H NMR ($CDCl_3$): δ 1.10 (3H, *d*, J = 6 Hz, H_3-9), 4.06 (H, *dq*, J = 4 and 6 Hz, H-8), 4.60 (H, *d*, J = 4 Hz, H-7), 6.83 (2H, *d*, J = 9 Hz, H_2-3 and 5), 7.24 (2H, *d*, J = 9 Hz, H-2 and 6). ^{13}C NMR (CD_3OD): Table 1. HR-EIMS *m/z*: 168.0795 $[M]^+$ ($C_9H_{12}O_3$ requires 168.0787), 151.0796 $[M-OH]^+$ ($C_9H_{11}O_2$ requires 151.0759).

threo-4-*Hydroxyphenylpropan*-7,8-*diol* (**2**). Crystals, mp 109–111° (MeOH). $[\alpha]_D^{25}$ −42.5° (MeOH, *c* 0.71). IR ν_{max}^{KBr} cm^{-1}: 3400, 1610, 1595, 1505, 1455, 1435, 1385, 1240, 1170, 1135, 1105, 1070, 1025, 885, 835, 795. UV λ_{max}^{MeOH} nm (log ε): 224 (3.91), 277 (3.21). ^1H NMR (CD_3OD): δ 0.93 (3H, *d*, J = 6 Hz, H_3-9), 3.76 (H, *qd*, J = 6 and 7 Hz, H-8), 4.23 (H, *d*, J = 7 Hz, H-7), 6.76 (2H, *d*, J = 9 Hz, H-3 and 5), 7.18 (2H, *d*, J = 9 Hz, H-2 and 6); ^1H NMR ($CDCl_3$): δ 1.05 (3H, *d*, J = 6 Hz, H_3-9), 3.84 (H, *m*, H-8), 4.32 (H, *d*, J = 8 Hz, H-7), 6.38 (2H, *d*, J = 9 Hz, H-3 and 5), 7.22 (2H, *d*, J = 9 Hz, H-2 and 6). ^{13}C NMR (CD_3OD): Table 1. HR-EIMS *m/z*: 168.0797 $[M]^+$ ($C_9H_{12}O_3$ requires 168.0787).

threo-4-*Hydroxyphenylpropan*-7,8-*diol* 7-O-*methyl ether* (**3**). Crystals, mp 118–120°. $[\alpha]_D^{28}$ −81.2°

(MeOH, *c* 0.44). UV λ_{max}^{MeOH} nm (log ε): 226 (4.04), 276 (3.27). ^{1}H NMR ($CDCl_3$): δ 0.97 (3H, *d*, $J = 6$ Hz, H_3-9), 3.21 (3H, s, H_3-1′), 3.79 (H, *d*, $J = 8$ Hz, H-7), 3.83 (H, *qd*, $J = 6$ and 8 Hz, H-8), 6.83 (2H, *d*, $J = 9$ Hz, H-3 and 5), 7.14 (2H, *d*, $J = 9$ Hz, H-2 and 6). HR-EIMS *m/z*: 182.0965 $[M]^+$ ($C_{10}H_{14}O_3$ requires 182.0943), 151.0790 $[M - CH_3O]^+$ ($C_9H_{11}O_2$ requires 151.0759).

erythro-4-*Hydroxyphenylpropan*-7,8-*diol* 7-O-*ethyl ether* (**4**). Oil. $[\alpha]_D^{28}$ +39.5° (MeOH, *c* 0.25). UV λ_{max}^{MeOH} nm (log ε): 226 (3.82), 277 (3.11). ^{1}H NMR ($CDCl_3$): δ 1.11 (3H, *d*, $J = 6$ Hz, H_3-9), 1.18 (3H, *t*, $J = 7$ Hz, H_3-2′), 3.35 (H, *qd*, $J = 7$ and 9 Hz, H-1′a), 3.45 (H, *qd*, $J = 7$ and 9 Hz, H-1′b), 3.91 (H, *dq*, $J = 5$ and 6 Hz, H-8), 4.12 (H, *d*, $J = 5$ Hz, H-7), 6.82 (2H, *d*, $J = 9$ Hz, H-3 and 5), 7.18 (2H, *d*, $J = 9$ Hz, H-2 and 6). ^{13}C NMR ($CDCl_3$): Table 1. HR-EIMS *m/z*: 196.1085 $[M]^+$ ($C_{11}H_{16}O_3$ requires 196.1099).

threo-4-*Hydroxyphenylpropan*-7,8-*diol* 7-O-*ethyl ether* (**5**). Crystals, mp 114–115° (MeOH). $[\alpha]_D^{25}$ −90.6° (MeOH, *c* 0.35). UV λ_{max}^{MeOH} nm (log ε): 226 (4.01), 277 (3.23). ^{1}H NMR ($CDCl_3$): δ 0.96 (3H, *d*, $J = 6$ Hz, H_3-9), 1.17 (3H, *t*, $J = 7$ Hz, H_3-2′), 3.31 (H, *dq*, $J = 7$ and 9 Hz, H-1′a), 3.39 (H, *dq*, $J = 7$ and 9 Hz, H-1′b), 3.78 (H, *qd*, $J = 6$ and 8 Hz, H-8), 3.88 (H, *d*, $J = 8$ Hz, H-7), 6.82 (2H, *d*, $J = 9$ Hz, H-3 and 5), 7.15 (2H, *d*, $J = 9$ Hz, H-2 and 6). ^{13}C NMR ($CDCl_3$): Table 1. HR-EIMS *m/z*: 196.1096 $[M]^+$ ($C_{11}H_{16}O_3$ requires 196.1099), 150.0699 $[M - CH_3CH_2OH]^+$ ($C_9H_{10}O_2$ requires 150.0680).

erythro-4-*Hydroxyphenylpropan*-7,8-*diol* 4-*isovalerate* (**6**). Oil. $[\alpha]_D^{28}$ +15.1° (MeOH, *c* 0.46). UV λ_{max}^{MeOH} nm (log ε): 226 (4.04), 277 (3.27). ^{1}H NMR ($CDCl_3$): δ 1.06 (6H, *d*, $J = 7$ Hz, H_3-4′ and 5′), 1.08 (3H, *d*, $J = 6$ Hz, H_3-9), 2.29 (H, *nona*, $J = 7$ Hz, H-3′), 2.43 (2, *d*, $J = 7$ Hz, H_2-2′), 3.99 (H, *dq*, $J = 4$ and 6 Hz, H-8), 4.66 (H, *d*, $J = 4$ Hz, H-7), 7.07 (2H, *d*, $J = 9$ Hz, H-3 and 5), 7.37 (2H, *d*, $J = 9$ Hz, H-2 and 6). ^{13}C NMR ($CDCl_3$): Table 1. HR-EIMS *m/z*: 252.1346 $[M]^+$ ($C_{14}H_{20}O_4$ requires 252.1361), 234.1234 $[M - H_2O]^+$ ($C_{14}H_{18}O_3$ requires 234.1256).

threo-4-*Hydroxyphenylpropan*-7,8-*diol* 4-*isovalerate* (**7**). Oil. $[\alpha]_D^{28}$ −16.9° (MeOH, *c* 0.29). UV λ_{max}^{MeOH} nm (log ε): 216 (4.07), 261 (2.94). ^{1}H NMR ($CDCl_3$): δ 1.06 (6H, *d*, $J = 7$ Hz, H_3-4′ and 5′), 1.08 (3H, *d*, $J = 6$ Hz, H_3-9), 2.27 (H, *nona*, $J = 7$ Hz, H-3′), 2.43 (2H, $J = 7$ Hz, H_2-2′), 3.84 (H, *m*, H-8), 4.39 (H, *d*, $J = 7$ Hz, H-7), 7.07 (2H, *d*, $J = 8$ Hz, H_2-3 and 5), 7.36 (2H, *d*, $J = 8$ Hz, H_2-2 and 6). HR-EIMS *m/z*: 252.1338 $[M]^+$ ($C_{14}H_{20}O_4$ requires 252. 1361), 234. 1219 $[M - H_2O]^+$ ($C_{14}H_{18}O_3$ requires 234.1256).

Acetylation. Compound **5** (5.3 mg) was acetylated with 250 μl each of Ac_2O and pyridine at 20° for 18 hr. The reagents were evapd off under a stream of N_2 and then the residue was purified by prep. TLC on silica gel 60 developed with benzene–Me_2CO (9:1) and eluted with $CHCl_3$–MeOH (9:1)] to give 6.3 mg (83%) of a diacetate (**5a**) as a colourless oil. *Diacetate.* $[\alpha]_D^{28}$ −38.1° (MeOH, *c* 0.42). UV λ_{max}^{MeOH} nm (log ε): 216 (3.82), 260 (2.38). ^{1}H NMR ($CDCl_3$): δ 1.09 (3H, *d*, $J = 6$ Hz, H_3-9), 1.16 (3H, *t*, $J = 7$ Hz, H_3-2′), 2.02 (3H, *s*, CH_3CO- on 8-OH), 2.30 (3H, *s*, CH_3CO- on 4-OH), 3.35 (H, *qd*, $J = 7$ and 9 Hz, H-1′a), 3.45 (H, *qd*, $J = 7$ and 9 Hz, H-1′b), 4.27 (H, *d*, $J = 6$ Hz, H-7), 5.09 (H, *qui*, $J = 6$ Hz, H-8), 7.07 (2H, *d*, $J = 9$ Hz, H-3 and 5), 7.31 (2H, *d*, $J = 9$ Hz, H-2 and 6). ^{13}C NMR ($CDCl_3$): δ 15.1 (C-2′), 16.1 (C-9), 21.2 and 21.3 (CH_3CO-× 2), 64.9 (C-1′), 72.6 (C-8), 82.9 (C-7), 121.3 (C-3 and 5), 128.5 (C-2 and 6), 136.4 (C-1), 150.4 (C-4), 169.3 and 170.4 ($CH_3\underline{C}O$-× 2). HR-EIMS *m/z*: 280.1312 $[M]^+$ ($C_{15}H_{20}O_5$ requires 280.1311), 238.1181 $[M - CH_2{=}C{=}O]^+$ ($C_{13}H_{18}O_4$ requires 238.1205).

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