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ARYLALKANONES FROM *HORSFIELDIA GLABRA*

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Key Word Index—*Horsfieldia glabra*; Myristicaceae; arils; arylphenyl alkanones; arylalkenone; lignans.

Abstract—Besides the new compounds 1-(2,4,6-trihydroxyphenyl)-9-phenylnonan-1-one and 1-(2,6-dihydroxyphenyl)-4-methyl-4-tridecen-1-one, the known 1-(2,6-dihydroxyphenyl)-11-phenylundecan-1-one, (+)-asarinin, (−)-dihydrocubebin and trimyristin were isolated from the methanol extract of arils of *Horsfieldia glabra*.

INTRODUCTION

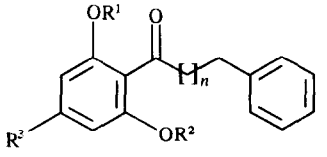
Horsfieldia glabra Warb. which is indigenous to Thailand, is a large tree. Its bark and leaves have been used as an aromatic to treat intestinal affections. The bark is also a remedy for sores and pimples [1]. Although the chemical constituents of *H. iryaghedhi* Warb. have been previously investigated [2–4], nothing has been published so far on the constituents of *H. glabra*. We report here the isolation of trimyristin [3], (+)-asarinin [3],(−)-dihydrocubebin [3] and of polyketides including the known **1a** [5] and the novel **1b** and **2a**.

RESULTS AND DISCUSSION

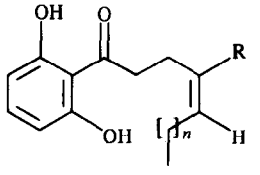
The molecular formula $C_{21}H_{26}O_4$ of compound **1b** was determined by low-resolution mass spectrometry and NMR H count. It was recognized as a diarylnonanone by the ^{1}H NMR signals for a phenyl group and a 2,4,6-trihydroxybenzoyl group, as well as for eight methylene units, two of which were vicinal to carbonyl or aryl moieties. An aluminium trichloride shift and a 1650 cm^{-1} band were both indicative of an *ortho*-hydroxycarbonyl substituted aryl. The mass spectrum was compatible with the structure showing the base peak at *m/z* 153 (trihydroxybenzoyl ion), a peak of high relative intensity at *m/z* 168 $[C_6H_3(OH)_3C(OH)=CH_2]^+$ and a peak of moderate intensity at *m/z* 91 (tropylium ion). Acetylation led to the diacetate **1c** (δ 2.36, 2.35, 2*s*, 2OAc) and the triacetate **1d** (δ 2.29, *s*, OAc and δ 2.25), *s*, 2OAc).

The structure of the diarylnonanoid **1b** belongs to the type previously detected in the fruits of *Myristica malabarica* Lam. [6]. The most significant difference between **1b** and the malabaricones is the phloroglucinol unit in the former is replaced by a resorcinol unit in the latter.

Compound **2a**, $C_{20}H_{30}O_3$, was characterized by ^{1}H NMR as a tridecenoylresorcinol comprising a 2,6-dihydroxybenzoyl group and a single olefinic proton (δ 5.34, *t*, $J=5.5$ Hz). The double bond must be separated by two CH_2 groups from the carbonyl since the ^{1}H NMR spectrum shows signals for two α-protons (δ 3.14, *t*, $J=7$ Hz) and for four allylic protons (δ 2.02, *br d* and δ 1.71, *t*, $J=7$ Hz). Double resonance at one of the allylic frequencies (δ 1.71) transforms the triplet (δ 3.14) due to both α-protons, to a singlet, but does not affect the triplet (δ 5.34) due to the olefinic proton. Double resonance at the other allylic methylene frequency (δ 2.02) transforms the triplet (δ 5.34), due to the olefinic proton, to a singlet. This evidence, together with a ^{1}H NMR multiplet (δ 1.32–1.25) for 15 protons (six methylene groups plus one methyl group) leads to the conclusion that the olefinic proton is on C-5 while a methyl group is on C-4.



1a n = 9, R^1 = R^2 = R^3 = H
1b n = 7, R^1 = R^2 = H, R^3 = OH
1c n = 7, R^1 = H, R^2 = Ac, R^3 = OAc
1d n = 7, R^1 = R^2 = Ac, R^3 = OAc



2a n = 7, R = Me
2b n = 10, R = H

The termination of the methylene chain by a methyl group is recognized by the triplet at δ0.88. The mass spectrum was in agreement with the structure, showing the parent ion peak at m/z 318 and the base peak at m/z 137 (dihydroxybenzoyl ion).

The methyl substituted double bond and the side chain with an odd number of carbons distinguishes **2a** biosynthetically from the acyl resorcinol (**2b**) previously isolated from *Virola sebifera* Aubl. and *V. elongata* (Benth.) Warb. [7].

EXPERIMENTAL

Isolation of constituents from Horsfieldia glabra. Fruits, collected in the Karnchanaburi province, Thailand, were separated into pericarp, arils and seeds. Air-dried, powdered arils (310 g) were percolated with petrol and then extracted with MeOH. The methanolic soln was evapd. The CH_2Cl_2 soluble portion of the residue (20 g) was submitted to CC (160 g silica gel, petrol–$CHCl_3$ 9:1). 28 500 ml fractions were collected. Fraction 14–28 were combined, evapd and the residue (2 g) was crystallized from MeOH–CH_2Cl_2 (4:1) to give trimyristin (300 mg). By further elution of the column with petrol–$CHCl_3$ (4:1), 20 additional 500 ml fractions were collected and evaporated. The residue (1.5 g) was crystallized from MeOH–Et_2O to give a colourless solid (400 mg), HCl purified by prep. TLC (silica gel, petrol–$CHCl_3$) to give **2a** (200 mg). The mother liquor was purified by prep TLC (silica gel, petrol–$CHCl_3$) to give (+)-asarinin (500 mg). Upon further elution of the column with petrol–$CHCl_3$ (3:2) five fractions were collected. Evapn and recrystallization from MeOH–CH_2Cl_2 gave **1a** (250 mg). Elution with petrol–$CHCl_3$ (1:1) gave 15 additional fractions. The first five of these fractions were evapd. The residue (200 mg) was recrystallized from petrol–CH_2Cl_2 to give (−)-dihydrocubebin (80 mg). The last 10 of these fractions were evapd to give an amorphous solid (500 mg). After crystallization from $CHCl_3$–MeOH, **1b** (350 mg) was obtained as a white solid.

Trimyristin. Mp 55–57° (MeOH) (lit. 56.5–57 [3]).

(+)-*Asarinin.* Mp 123–124° (petrol) (lit. 122.5–123° [2]); $[\alpha]_D^{25}$ 115° ($CHCl_3$, *c* 2.0) (lit. +122° [2]).

(−)-*Dihydrocubebin.* Mp 100–102° (lit. 101–102° [3]); $[\alpha]_D^{25}$ −30° ($CHCl_3$, *c* 2.0) (lit. −32.3° [3]).

1-(2,6-*dihydroxyphenyl*)-11-*Phenylundecan*-1-*one*(**1a**). Mp 69–71° (petrol) (lit. 69–71° [5]).

1-(2,4,6-*trihydroxyphenyl*)-9-*Phenylnonan*-1-*one* (**1b**). Mp 71–72° (MeOH), UV λ_{max}^{MeOH} nm (log ε): 224 (4.20), 286 (4.21); $\lambda_{max}^{MeOH+AlCl_3}$ nm (log ε): 220 (3.85), 307 (4.36), 355 (4.28); $\lambda_{max}^{MeOH+AlCl_3+HCl}$ nm (log ε): 220 (3.70), 307 (4.30), 355 (4.22); IR ν_{max}^{KBr} cm^{-1}: 3500 (OH), 1650 (CO), 1600, 1570 (Ar). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.24 (*br s*, C_6H_5), 5.9 (*br s*, H-3′, H-5′, OH), 3.04 (*t*, J = 7 Hz, CH_2-2), 2.60 (*t*, J = 8 Hz, CH_2-9), 1.33 (*br s*, 6 CH_2); MS m/z (rel. int.): 342 $[M]^+$ (24), 324 (12), 308 (10), 290 (10), 279 (5), 265 (2), 251 (5), 237 (5), 220 (5), 205 (5), 192 (5), 181 (70), 168 (94), 153 (100), 149 (40), 126 (18), 91 (40).

Acetylation of **1b** (30 mg, Ac_2O 3 ml, pyridine 1 ml, room temp, over-night) gave a mixture separated by prep. TLC (silica gel), into **1c** (30 mg) and **1d** (3 mg). *Diacetate* **1c** , viscous oil, IR ν_{max}^{film} cm^{-1}: 3450 (OH), 1780 (CO), 1650 (CO), 1590 (Ar); ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.29 (*s*, C_6H_5), 6.66 (*d*, J = 2 Hz, H-5′), 6.48 (*d*, J = 3 Hz, H-3′), 2.89 (*t*, J = 7 Hz, CH_2-2), 2.60 (*t*, J = 7 Hz, CH_2-9), 2.36 (*s*, OAc), 2.35 (*s*, OAc), 1.66 (*br s*, 3 CH_2), 1.33 (*s*, 3 CH_2); MS m/z (rel. int.): 426 $[M]^+$ (15), 384 (10), 342 (10), 324 (10), 308 (5), 181 (60), 168 (80), 153 (10), 149 (30), 91 (30). *Triacetate* **1d**, mp 42–43° (MeOH), IR ν_{max}^{KBr} cm^{-1}: 1780 (CO), 1700 (CO), 1615 (Ar); ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.93 (*s*, H-3′, H-5′), 2.71 (*t*, J = 7 Hz, CH_2-2), 2.60 (*t*, J = 7 Hz, CH_2-9), 2.29 (*s*, OAc), 2.25 (*s*, 2 OAc), 1.61 (*br s*, 3 CH_2) 1.31 (*br s*, 3 CH_2); MS m/z (rel. int.): 468 $[M]^+$ (10), 426 (10), 384 (10), 342 (15), 324 (10), 308 (5), 290 (5), 205 (5), 181 (20), 165 (70), 153 (100), 149 (50), 91 (40).

1-(2,6-*dihydroxyphenyl*)-4-*Methyl*-4-*tridecen*-1-*one* (**2a**), mp 42–44° (MeOH), UV λ_{max}^{MeOH} nm (log ε): 202 (3.89), 223 (3.82), 269 (3.70), 341 (3.12); $\lambda_{max}^{MeOH+NaOH}$ nm (log ε): 211 (4.45), 239 (3.81), 285 (3.61), 383 (3.28); $\lambda_{max}^{MeOH+AlCl_3}$ nm (log ε): 232 (3.78), 296 (3.74), 390 (3.30); IR ν_{max}^{KBr} cm^{-1}: 3300 (OH), 1600, 1590 (Ar); ^{1}H NMR (300 MHz, $CDCl_3$) δ: 10.03 (*br s*, 2 OH), 7.22 (*dd*, J = 7, 7 Hz, H-4′), 6.40 (*d*, J = 7 Hz, H-3′, H-5′), 5.34 (*t*, J = 5.5 Hz, H-5), 3.14 (*t*, J = 7 Hz, CH_2-2), 2.02 (*br d*, CH_2-6), 1.71 (*t*, J = 7 Hz, CH_2-3), 1.32 (*br s*, Me-4, 3 CH_2), 1.25 (*br s*, 3 CH_2), 0.88 (*t*, Me-13); MS m/z (rel. int.): 318 $[M]^+$ (10), 292 (5), 274 (5), 229 (5), 219 (5), 189 (10), 176 (10), 165 (60), 152 (67), 137 (100), 123 (15), 81 (30).

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