



2,3-Dehydro-4 α -hydroxy-longilactone, a novel quassinoid and two known phenyl propanoids from *Eurycoma longifolia* Jack

Chin-Hoe Teh^a, Hiroshi Morita^b, Osamu Shiota^c, Kit-Lam Chan^{a,*}

^a School of Pharmaceutical Sciences, Universiti Sains Malaysia, 11800 Penang, Malaysia

^b Faculty of Pharmaceutical Sciences, Hoshi University, Ebara 2-4-41, Shinagawa-ku, Tokyo 142-8501, Japan

^c Faculty of Pharmaceutical Sciences at Kagawa Campus, Tokushima Bunri University, 1314-1 Shido, Sanuki City, Kagawa 769-2193, Japan

ARTICLE INFO

Article history:

Received 24 March 2009

Received in revised form 9 September 2009

Accepted 9 November 2009

Keywords:

Simaroubaceae

Eurycoma longifolia

Novel longilactone-type quassinoid

Phenyl propanoids

ABSTRACT

A phytochemical study on the root of *Eurycoma longifolia* Jack afforded a novel 2,3-dehydro-4 α -hydroxy-longilactone (1) and two known phenyl propanoids, 2,3-dihydroxy-1-(4'-hydroxy-3'-methoxyphenyl)-propan-1-one (2) and scopolin (3), isolated from this plant for the first time. All structures were characterised by spectroscopic analysis (1D and 2D NMR experiments, HRMS, UV, IR and optical rotation) and by comparison with known data. This is the first report of a C₁₉ quassinoid from the Simaroubaceae family possessing an unsubstituted vinyl function and a C-4 methyl group of β -configuration in ring A.

© 2009 Elsevier Ltd. All rights reserved.

1. Introduction

Eurycoma longifolia Jack (Simaroubaceae), a small tree identified by various local names as 'Tongkat Ali' (Malaysia), 'Pasakbumi' (Indonesia), 'Cay ba binh' (Vietnam) and 'lan-don' (Thailand), continues to generate considerable research interest because of its diverse medicinal values. In Malaysia, the roots of *E. longifolia* are widely prepared as additives in health supplements and beverages, e.g. isotonic drink, coffee and tea, to increase virility, libido and sexual prowess (Ang, Chan, Gan, & Yuen, 1997; Ang, Lee, & Kiyoshi, 2004; Ang & Sim, 1998). Previous phytochemical investigations have shown that the plant contains mainly quassinoids (Chan, Iitaka, Noguchi, Sugiyama, Saito, & Sankawa, 1992; Chan, Lee, Sam, Tan, Noguchi, & Sankawa, 1991; Morita, Kishi, Takeya, Itokawa, & Iitaka, 1993a), tirucallene-type triterpenes (Itokawa, Kishi, Morita, & Takeya, 1992), squalene derivatives (Itokawa, Kishi, Morita, Takeya, & Iitaka, 1991; Morita, Kishi, Takeya, Itokawa, & Iitaka, 1993b), biphenyl-*neo*-lignans (Morita, Kishi, Takeya, & Itokawa, 1992), anthraquinones (Lin, Peng, Wang, Lee, & Wang, 2001), canthin-6-one alkaloids (Kardono, Angerhofer, Tsauri, Padmawinata, Pezzuto, & Kinghorn, 1991), α -carboline alkaloids (Kardono et al., 1991) and dimeric dihydrobenzofuran (Kuo, Su, Damu, & Wu, 2004a). Some of these compounds were found to possess antiulcer (Tada, Yasuda, Otani, Doteuchi, Ishihara, & Shiro, 1991), anthelmintic (Jiwajinda et al., 2002), antimalarial (Chan, Choo, Abdullah, & Is-

mail, 2004; Chan, O'Neill, Phillipson & Warhurst, 1986; Kuo, Damu, Lee, & Wu, 2004b), and cytotoxic activities (Itokawa, Takeya, Hito-tsubyanagi, & Morita, 2000; Morita et al., 1993a). In our continuing search for marker compounds to fingerprint the bioactive root extract of *E. longifolia* and analysis of the chemical content in health supplements and beverages, a new quassinoid, 2,3-dehydro-4 α -hydroxy-longilactone (1), was discovered, along with two known phenyl propanoid structures, 2,3-dihydroxy-1-(4'-hydroxy-3'-methoxyphenyl)-propan-1-one (2) and scopolin (3), being reported for the first time from this species. This paper describes the isolation and structural elucidation of these compounds.

2. Materials and methods

2.1. General

The optical rotations were determined with a Jasco DIP 370 digital polarimeter. The ultraviolet (UV) spectra were recorded on a Perkin Elmer Lambda 45 spectrophotometer (Perkin Elmer Instrument; Norwalk, CT, USA). The infrared (IR) measurements of the solid compounds (1 and 3) were performed with a Nicolet Fourier Transform Infrared Nexus (USA) spectrometer equipped with Thermo Nicolet OMNIC V6.0 software, using the potassium bromide disc method. The infrared spectrum of the liquid sample (2) was recorded on a Perkin Elmer System 2000 FT-IR spectrometer. The compound was applied on a zinc selenide (ZnSe) disc and scanned over the range 4000–650 cm⁻¹. HRFABMS and HRESIMS were measured on a Micromass LCT spectrometer (Waters; Milford, MA,

* Corresponding author.

E-mail address: klchan@usm.my (K.-L. Chan).

USA). ^1H and 2D NMR spectra of 1, 2 and 3 were recorded in Bruker AM 500, Bruker Avance 600 and Varian INOVA 500 spectrometers, respectively, using TMS as an internal standard. All the extracts, the fractions from chromatographic separations, and the isolated pure compounds were examined by TLC on Kieselgel 60-F₂₅₄ plates (Merck No. 5544; Darmstadt, Germany) and the spots were examined in an ultraviolet cabinet (Raytech, USA) at 254 and 365 nm. The developed TLC plates were sprayed with a solution of 10% H₂SO₄ in ethanol (v/v) and heated to 110 °C for 5 min. Column chromatography was performed, using resin of styrene and divinylbenzene (Diaion HP 20, Mitsubishi; Tokyo, Japan), silica gel (Merck No. 7734 or 9385; Darmstadt, Germany) or amino silica gel (Chromatorex; Fuji Silysia). Centrifugal thin-layer chromatography was carried out with silica gel 60 PF₂₅₄ containing gypsum (Merck No. 7749; Darmstadt, Germany).

2.2. Plant material

The roots of *E. longifolia* Jack were identified and purchased in Perak, Malaysia by a pharmaceutical company, Hovid Berhad, in Ipoh. A voucher specimen (No. 785-117) was deposited in Penang Botanical Garden, Penang, Malaysia.

2.3. Extraction and isolation

The air-dried powdered roots of *E. longifolia* (11.6 kg) were extracted with 6 × 4 l of 95% MeOH for 6 days at 60 °C. The combined MeOH extract was evaporated to dryness to yield 485 g of dark brown residue which was next chromatographed on a Diaion HP 20 column with a H₂O–MeOH (1:0–0:1) gradient to afford 4 fractions (Fr 1–4). Fr 2 was concentrated under vacuum to give 52.2 g of residue. The residue was resuspended in water and then partitioned successively, with ethyl acetate and saturated *n*-butanol, to yield three subfractions. The *n*-BuOH subfraction (20.4 g) was further fractionated on a silica gel column, using a CHCl₃–MeOH (1:0–1:1) gradient, to obtain 7 portions (A1–A7). A2 was further subjected to centrifugal silica gel TLC and eluted with CHCl₃–MeOH (93:7, v/v), followed by two successive column chromatographies (silica gel, CHCl₃–MeOH 1:0–1:1, then amino silica gel, CHCl₃–MeOH 1:0–0:1), to give compound 1 (1.6 mg). A3 was further purified by repeated centrifugal TLC with stepped gradients of CHCl₃–MeOH (1:0–1:1) to afford compound 2 (3.2 mg). Compound 3 (15.2 mg) was obtained by separation of A5 on five succes-

sive centrifugal TLC passages, using a mixture of CHCl₃–MeOH (15:1, v/v).

2,3-Dehydro-4 α -hydroxylongilactone (1): for ^1H and ^{13}C NMR data, see Table 1. 2,3-Dihydroxy-1-(4'-hydroxy-3'-methoxyphenyl)-propan-1-one (2): colourless liquid; $[\alpha]_D^{27} + 56^\circ$ (c 0.05, CH₃OH); HRESIMS m/z 235.0574 (calcd. for C₁₀H₁₂O₅Na⁺, [M + Na]⁺ 235.0582); UV (MeOH) λ_{max} 202, 231, 280 and 306 nm; IR (ZnSe) ν_{max} 3524, 2920, 2860, 2333, 1672, 1426, 1286, 1106, 1054 and 1030 cm⁻¹; ^1H and ^{13}C NMR data of (2) are similar to those previously published (Baderschneider & Winterhalter, 2001).

Scopolin (3): amorphous powder; $[\alpha]_D^{27} - 46^\circ$ (c 0.05, CH₃OH); HRESIMS m/z 355.1027 (calcd. for C₁₆H₁₉O₉⁺, [M + H]⁺ 355.1029); UV (MeOH) λ_{max} 203, 228, 251, 291 and 341 nm; IR (KBr) ν_{max} 3357, 2901, 1704, 1618, 1573, 1511, 1393, 1279 and 1082 cm⁻¹; ^1H NMR (CD₃OD, 500 MHz): δ 3.41 (1H, br t, $J = 9.52, 8.79$ Hz, H-4'), 3.48 (1H, m, H-3'), 3.52 (1H, m, H-5'), 3.54 (1H, m, H-2'), 3.70 (1H, dd, $J = 12.2, 2.3$ Hz, H-6a'), 3.91 (1H, dd, $J = 12.2, 5.6$ Hz, H-6b'), 3.91 (1H, s, OMe), 5.07 (1H, d, $J = 7.32$ Hz, H-1'), 6.31 (1H, d, $J = 9.52$ Hz, H-3), 7.18 (1H, s, H-8), 7.21 (1H, s, H-5), 7.90 (1H, d, $J = 9.52$ Hz, H-4); ^1H NMR (C₅D₅N, 500 MHz): δ 3.71 (1H, s, OMe), 4.16 (1H, m, H-5'), 4.33 (1H, m, H-4'), 4.35 (1H, m, H-2'), 4.37 (1H, m, H-3'), 4.37 (1H, m, H-6a'), 4.52 (1H, br d, $J = 12.0$ Hz, H-6b'), 5.77 (1H, d, $J = 7.08$ Hz, H-1'), 6.32 (1H, d, $J = 9.52$ Hz, H-3), 7.01 (1H, s, H-5), 7.49 (1H, s, H-8), 7.63 (1H, d, $J = 9.52$ Hz, H-4); ^{13}C NMR (CD₃OD, 125 MHz): δ 57.1 (CH₃, OMe), 62.4 (CH₂, C-6'), 71.2 (CH, C-4'), 74.7 (CH, C-2'), 77.8 (CH, C-3'), 78.4 (CH, C-5'), 102.0 (CH, C-1'), 105.2 (CH, C-8), 110.8 (CH, C-5), 114.5 (CH, C-3), 139.0 (C, C-10), 145.6 (CH, C-4), 148.3 (C, C-6), 150.7 (C, C-9), 151.8 (C, C-7), 163.5 (C = O, C-2); ^{13}C NMR (C₅D₅N, 125 MHz): δ 56.3 (CH₃, OMe), 62.4 (CH₂, C-6'), 71.1 (CH, C-4'), 74.6 (CH, C-2'), 78.6 (CH, C-3'), 79.2 (CH, C-5'), 101.9 (CH, C-1'), 104.3 (CH, C-8), 109.9 (CH, C-5), 113.0 (C, C-10), 114.0 (CH, C-3), 143.5 (CH, C-4), 146.9 (C, C-6), 150.0 (C, C-9), 151.2 (C, C-7), 161.1 (C = O, C-2).

3. Results and discussion

3.1. Phytochemical investigation

Compound 1 was obtained as a colourless solid of $[\alpha]_D^{20} + 16.4^\circ$ (c 0.3, CH₃OH) and showed a pseudo-molecular ion peak at m/z 367.1760 [M–H][–] (calcd. for C₁₉H₂₇O₇, 367.1757) in the HRESIMS, and the molecular formula was established as C₁₉H₂₈O₇. The molecular formula was further confirmed by HRFABMS at m/z 369.1922, [M + H]⁺ (calcd. for C₁₉H₂₉O₇, 369.1913). IR absorptions at 3410 cm⁻¹ and 1760 cm⁻¹ revealed the presence of a hydroxyl and a carbonyl lactone, respectively. The ^1H NMR spectrum of 1 (Table 1) displayed the presence of two vinyl proton signals at δ_{H} 5.84 (1H, d, $J = 10.2$ Hz) and 5.74 (1H, dd, $J = 10.2$ Hz), five oxymethine proton signals at δ_{H} 5.54 (1H, br s), 4.77 (1H, d, $J = 11.7$ Hz), 4.42 (2H, s, overlap of H-1 and H-7) and 4.09 (1H, br s), four methine signals at δ_{H} 2.40 (1H, d, $J = 5.3$ Hz), 2.49 (1H, s), 2.60 (1H, d, $J = 11.7$ Hz) and 2.77 (1H, m) and four methyl singlets at δ_{H} 1.86 (3H, s) and 1.71 (9H, s, overlap). From the ^{13}C NMR spectrum of compound 1 (Table 1), the presence of 19 carbon atoms was ascertained with the carbon signals at δ_{C} 73.6, 67.4, 76.1, 76.0 and 87.0 assigned to five oxymethines, δ_{C} 56.0, 43.2, 52.1 and 27.8 to four *sp*³ methines, δ_{C} 130.8 and 134.6 to two *sp*² methines, δ_{C} 177.4 to a lactone carbonyl, δ_{C} 71.5 to an oxygenated quaternary carbon, δ_{C} 43.9 and 44.7 to two *sp*³ quaternary carbons, and δ_{C} 24.3, 14.8, 21.2 and 15.3 to four methyls. By comparison with previously reported spectroscopic data (Itokawa, Qin, Morita, Takeya, & Iitaka, 1993; Morita, Kishi, Takeya, Itokawa, & Tanaka, 1990), 1 appeared similar in skeleton to longilactone but displayed no UV absorption band ascribable to an α , β -unsaturated ketone in ring A. Instead, the NMR of 1 showed two unusually low field

Table 1
 ^1H and ^{13}C NMR spectroscopic data of compound 1 in pyridine-*d*₅.

Position	Compound 1	
	δ_{C} (150 MHz)	δ_{H} (600 MHz)
1	76.1	4.42 (br s)
2	130.8	5.74 (d, $J = 10.2$ Hz)
3	134.6	5.84 (d, $J = 10.2$ Hz)
4	71.5	
5	52.1	2.60 (d, $J = 11.7$ Hz)
6	67.4	4.77 (d, $J = 11.7$ Hz)
7	87.0	4.42 (s)
8	43.9	
9	43.2	2.49 (s)
10	44.7	
11	73.6	5.54 (br s)
12	76.0	4.09 (br s)
13	27.8	2.77 (m)
14	56.0	2.40 (d, $J = 5.3$ Hz)
15	177.4	
18-methyl	24.3	1.71 (s)
19-methyl	14.8	1.71 (s)
20-methyl	21.2	1.86 (s)
21-methyl	15.3	1.71 (s)

Download English Version:

<https://daneshyari.com/en/article/1190669>

Download Persian Version:

<https://daneshyari.com/article/1190669>

[Daneshyari.com](https://daneshyari.com)