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Short communication

Occurrence of non-heterocyclic resveratrol tetramer in *Vatica chinensis*

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ABSTRACT

A resveratrol (Res) tetramer, vaticanol L (**1**), was isolated from the stem of *Vatica chinensis* (Dipterocarpaceae). The structure was identified on the basis of spectroscopic evidence and absolute configuration elucidated from circular dichroism data. This is the first report on oligostilbenoids that shows the occurrence of a Res tetramer without a heterocyclic ring. A biogenetic pathway to **1** is proposed.

1. Introduction

The building block Res produces various oligomers in plants upon successive phenoxy radical coupling (Riviere et al., 2012 Sotheeswaran and Pasupathy, 1993). During production of oligomers, the number of asymmetric carbons usually increases in proportion to the oligomerization degree. Oligomerization in the family Dipterocarpaceae occurs in a highly regio- and stereoselective fashion to yield oligomers as larger building blocks as well as enantiomers (Ito et al., 2014). (−)-ε-Viniferin is a representative example of these (Kurihara et al., 1990), in which two asymmetric methine carbons bear an *R* configuration that elaborates the stereochemical homogeneity of oligomers of its downstream biosynthetic products (trimers and octamers), as inferred by the same absolute configuration in the 1,2-diaryldihydrobenzofuran skeleton (Ito et al., 2014). In 1993 Sotheeswaran and Pasupathy classified oligostilbenoids from plants into two groups depending on whether they possess dihydrobenzofuran rings (group A) or not (group B) according to a biogenetical prospect (Sotheeswaran and Pasupathy, 1993). Comprehensive research into the structural diversity of oligostilbenoids from this family has been conducted in our laboratory over the last decade. This has resulted in the isolation and structural elucidation of various group A compounds as the majority (Ito et al., 2009, 2013a, b, 2015, 2014, 2012). In the minority, group B compounds, there are no examples of further oligomerization of building blocks of dimers except for a fused 2,7-dihydrooxepine-quinone methide derivative (vaticanol K) from *Vatica chinensis* (Ito and Iinuma, 2015). In the present study, we focused on the oligostilbenoids with high polarity from this plant and achieved the isolation and determination of the absolute configuration of a new Res tetramer, vaticanol L (**1**). It is a dimeric dimer that does not undergo a loss of hydroxy group during coupling. The occurrence of non-heterocyclic Res tetramer belonging to group B is reported here for the first time.

2. Materials and methods

2.1. General experimental procedure

The following instruments were used: a JASCO P-1020 polarimeter for optical rotations; a JASCO J-820 spectrometer (in MeOH solution) for UV and CD spectra; a JEOL JNM AL-400 spectrometer for ^{1}H and ^{13}C NMR spectroscopy (chemical shift values in ^{1}H NMR spectra were presented as δ values with TMS as the internal standard); and Shimadzu LCMS-IT-TOF mass spectrometer for ESIMS. Moreover, a Shimadzu HPLC system (Shimadzu Corporation, Japan) was used in this study. The system consisted of an SCL-10AVP system controller, two LC-6AD pumps, a DGU-20A3 on-line degasser, a CTO-10AVP column oven, a SIL-10AXL autosampler, and an SPD-10A UV–vis detector. The chromatographic data were collected and processed using Shimadzu CLASS-VP software (version 6.14, Shimadzu Corporation, Japan). The following adsorbents were used for purification: analytical TLC: Merck Kieselgel 60 F_{254} (0.25 mm); column chromatography: Merck Kieselgel 60, Fuji Silysia Chemica`l Chromatorex DMS

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(DM1020), Waters Sep-Pak C_{18} cartridges, Pharmacia Fine Chemicals AB Sephadex LH-20; preparative HPLC: Capcell Pak C_{18} column (UG120, 250 × 10 mm i.d., SHISEIDO, Japan). Energy-minimized stereostructures were obtained using PCMODEL 9.3 (Serena Software, USA).

2.2. Plant material

The stem bark of *V. chinensis* L. were collected in India in June 2000 and identified by Dr. Veliah Chelladurai at the Survey of Medicinal Plant Unit, Central Council for Research in Ayurveda and Siddha, India. A voucher specimen (number DP-022) has been deposited in the Gifu Pharmaceutical University.

2.3. Extraction and isolation

The dried and ground stem of *V. chinensis* (1.0 kg) were extracted with acetone (5 L, 24 h × 3) at room temperature, which produced a dry solid mass of 74 g, 46 g, and 29 g, respectively. A part of the acetone extract (70 g) was subjected to column chromatography (70 × 5 cm) on silica gel (900 g), eluted with a mixture of $CHCl_3$/MeOH with increasing polarity; nine fractions (^{A}Fr.A–I) were obtained. The sixth fraction (^{A}Fr. F, $CHCl_3$–MeOH (6:1), 17 g) was further fractionated by dimethylchlorosilane (DMS) CC (4 cm × 50 cm) eluted with a mixture of H_2O/MeOH with stepwise decrease in the H_2O ratio to produce six subfractions (^{A}Fr. F_1–^{A}Fr. F_6). Vaticanol L (25.0 mg) was obtained from ^{A}Fr. F_4 (H_2O/MeOH 3:2, 2.5 g) by further purification using column chromatography over Sephadex LH-20 (MeOH), vacuum liquid chromatography through silica gel [EtOAc–$CHCl_3$–MeOH–H_2O (80:40:11:2)], and RPCC through Sep-Pak cartridge (H_2O/MeOH) followed by HPLC [Capcell Pak C_{18}, (UG120), H_2O/CH_3CN 4:1]. (−)-ε-Viniferin (26 mg) and (−)-ampelopsin *F* (32 mg) were purified from the third fraction [^{A}Fr. C, $CHCl_3$–MeOH (8:1), 2.1 g] using Sephadex LH-20CC (MeOH) and Sep-Pak C_{18} cartridges.

Table 1
^{1}H and ^{13}C NMR spectral data of 1.

No.	δ_H	δ_C	No.	δ_H	δ_C
1a		135.5	1c		138.3
2a(6a)	6.58 (d, 8.4)	129.7	2c(6c)	7.48 (d, 8.4)	131.9
3a(5a)	6.56 (d, 8.4)	116.0	3c(5c)	6.58 (d, 8.4)	115.1
4a		155.7[a]	4c		156.0
7a	3.42 (s)	50.4	7c	4.25 (d, 12.0)	54.7
8a	3.86 (s)	52.5	8c	4.72 (d, 12.0)	58.2
9a		147.6	9c		150.5
10a		113.5	10c		122.2
11a		157.4	11c		155.0
12a	5.96 (d, 2.4)	101.5	12c	6.37 (d, 2.0)	102.3
13a		156.8	13c		159.0
14a	6.33 (d, 2.4)	105.2	14c	6.30 (d, 2.0)	106.8
1b		137.7	1d		142.0
2b(6b)	6.82 (d, 8.4)	130.0	2d(6d)	6.57 (s)	127.9
3b(5b)	6.73 (d, 8.4)	115.6[b]	3d(5d)	6.57 (s)	115.6[b]
4b		155.8[a]	4d		156.2
7b	3.94 (br s)	43.4	7d	3.58 (br s)	58.6
8b	3.57 (br s)	53.3	8d	4.27 (br s)	55.0
9b		146.8	9d		149.9
10b		127.8	10d	6.29 (d, 2.0)	107.1
11b		151.0	11d		159.2
12b	6.15 (s)	103.8	12d	6.34 (t, 2.0)	101.3
13b		156.2	13d		159.2
14b		119.8	14d	6.29 (d, 2.0)	107.1

Values are in ppm (δ_H and δ_C). Measured in acetone-d_6 at 400 MHz (^{1}H NMR) and 100 MHz (^{13}C NMR). All protons and carbons were assigned by DQF-COSY, HMQC and HMBC spectra.
[a] Interchangeable.
[b] Overlapping.

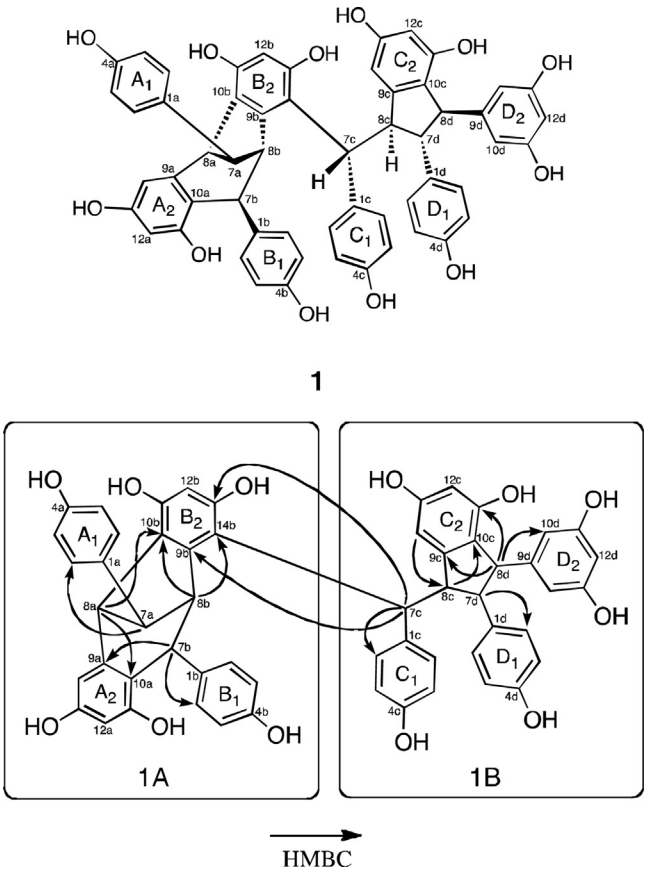

Fig. 1. CH long-range correlations in the HMBC spectrum of 1.

2.4. Vaticanol L

A pale yellow solid, $[\alpha]_D^{25}$ +27 (c 0.10, MeOH); UV λ_{max} (MeOH): 230 (4.80), 280 (4.04); CD (*c* 11.1 μM, MeOH) nm (Δε) 210 (+48.6), 231 (−37.1), 226 (−35.8), 244 (+1.2), 249 (−1.1), 257 (+4.8); IR ν (KBr disk): 3334, 1610, 1512, 1448, 1235 cm^{-1}; ^{1}H and ^{13}C NMR spectroscopic data in acetone-d_6, Table 1; ESIMS (positive), *m/z* 931.2712 $[M+Na]^+$ (calculated for $C_{56}H_{44}O_{12}$ Na, 931.2725).

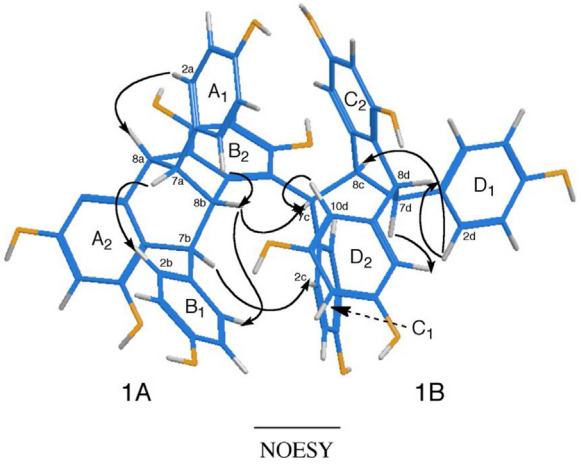

Fig. 2. Stereo structures and NOESY correlations for 1.
3D structures are generated by employing PCMODEL 9.3 (Serena Software, Box 3076, Bloomington, IN 47,402-3076) molecular-modeling program software using MMFF94 force field (MM2 type) for energy minimization.