Two Diphenylpropan-1,2-diol Syringates from the Roots of *Erythrina variegata*

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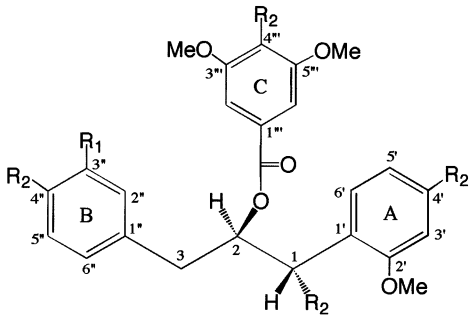
Two new diphenylpropan-1,2-diols, eryvarinols A (**1**) and B (**2**), were isolated from the roots of *Erythrina variegata*. Their structures were elucidated as 1-(4-hydroxy-2-methoxyphenyl)-2-(4-hydroxy-3,5-dimethoxybenzoyloxy)-3-(4-hydroxyphenyl)propan-1-ol (**1**) and its 3″-prenyl derivative (**2**) on the basis of spectroscopic and chemical evidence. Both these compounds are unusual diphenylpropan-1,2-diols with a syringyl group.

The genus *Erythrina* (Leguminosae) is distributed in the tropical and subtropical regions of the world and encompasses over 100 species. The antibacterial and antiinflammatory properties of *Erythrina variegata* L. are utilized in Chinese herbal medicine for the treatment of pyrexia, scabies, and septicemia.[1] Phytochemical studies of the nonalkaloidal secondary metabolites of this plant revealed the presence of some antibacterial isoflavonoids, a cinnamylphenol (eryvariestyrene),[2] three flavonoids (abyssinone V, erycristagallin, and 4′-hydroxy-6,3′,5′-triprenylflavonone) with phospholipase A_2 inhibitory (antiinflammation) activity,[3] and two isoflavones (erythrinin B and euchrenone b_{10}) that inhibit the activity of the Na^+/H^+ exchange system.[4] Previously, we reported the isolation of five new isoflavonoids (eryvarins A−E) from the roots and wood of this plant.[5,6] In this paper we describe the isolation and structural elucidation of two new diphenylpropan-1,2-diol 4-hydroxy-3,5-dimethoxybenzoates (syringates), eryvarinols A (**1**) and B (**2**), from the roots of *E. variegata* cultivated in Pakistan.



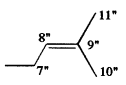
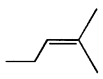
	R_1	R_2
1	H	OH
2		OH
2a		OAc

Table 1. ^{1}H NMR Data for Eryvarinols **1** and **2** in Acetone-d_6 (600 MHz)

position	**1**	**2**
1	5.19 d (4.4)	5.20 d (4.4)
2	5.53 td (5.9, 4.4)	5.52 ddd (8.1, 4.4, 3.6)
3	2.91 d (5.9)	2.88 m
3′	6.45 d (2.2)	6.46 d (2.2)
5′	6.45 dd (8.1, 2.2)	6.45 dd (8.8, 2.2)
6′	7.39 d (8.1)	7.39 d (8.8)
2″	7.03 d (8.8)	6.90 d (2.2)
3″	6.67 d (8.8)	
5″	6.67 d (8.8)	6.66 d (8.1)
6″	7.03 d (8.8)	6.85 dd (8.1, 2.2)
7″		3.18 d (7.3)
8″		5.15 t (7.3)
10″, 11″		1.60 s
2‴, 6‴	7.20 s	7.22 s
OMe-2′	3.80 s	3.81 s
OMe-3‴, 5‴	3.85 s	3.85 s

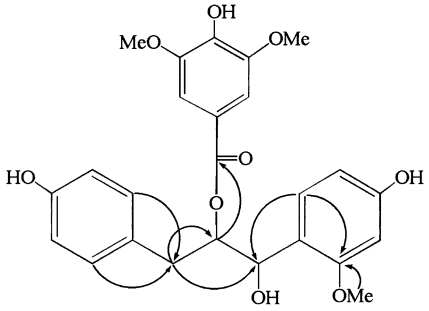


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Figure 1. Selected HMBC correlations for compound **1**.

Eryvarinol A (**1**) was isolated as an amorphous powder. Its molecular formula, $C_{25}H_{26}O_9$, was determined using negative HRFABMS at *m*/*z* 469.1491. The IR spectrum of **1** revealed the presence of an ester carbonyl (1700 cm^{-1}) and hydroxyl (3400 cm^{-1}) groups. Spin−spin networks of signals of ^{1}H (Table 1) and ^{13}C NMR spectra of **1** were elucidated using ^{1}H−^{1}H COSY, HSQC, and HMBC (Figure 1) spectra. The ^{1}H NMR spectrum of **1** exhibited signals of ABX-type aromatic protons (δ 6.45, 6.45, and 7.39) and a methoxyl group (δ 3.80) for a 4-hydroxy-2-methoxyphenyl group (A ring), A_2B_2-type aromatic protons (δ 6.67 and 7.03) for a 4-hydroxyphenyl group (B ring), and two equivalent aromatic protons (δ 7.20) and two equivalent methoxyl groups (δ 3.85) for a syringyl group (C ring). A set of aliphatic proton and carbon signals (δ_H 2.91, 5.19, and 5.53; δ_C 35.7, 69.5, and 78.6, respectively) in the ^{1}H and ^{13}C NMR

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spectra demonstrated the presence of a 1,3-disubstituted propane-1,2-diol moiety. The attachment of the 4-hydroxy-2-methoxyphenyl moiety (A ring) to the C-1 position was revealed by the identification of a cross-peak between an aromatic proton at C-6′ (δ 7.39) and an aliphatic carbon at C-1 (δ 69.5) in the HMBC spectrum. The location of the 4-hydroxyphenyl group (B ring) at the C-3 position was also established by the HMBC experiment that revealed a correlation from the aromatic protons at C-2″ (6″) (δ 7.03) to an aliphatic carbon at C-3 (δ 35.7). The attachment of the syringyl group to the C-2 position was identified from the HMBC spectrum, revealing a correlation from an aliphatic proton at C-2 (δ 5.53) to an ester carbonyl carbon (δ 165.8). These results were confirmed using the NOESY spectrum of **1**. The relative configuration of two chiral carbons, C-1 and C-2, was established as the *erythro* form using the NOESY spectrum, which revealed NOE correlations between H-1 (δ 5.19) and H-2, H-1 and H-3 (δ 2.91), H-3 and H-6′, and H-3′ (δ 6.45) and OMe-3‴ (5‴) (δ 3.85). The structure of eryvarinol A was therefore characterized as 1-(4-hydroxy-2-methoxyphenyl)-2-(4-hydroxy-3,5-dimethoxybenzoyloxy)-3-(4-hydroxyphenyl)propan-1-ol (**1**).

Eryvarinol B (**2**) was isolated as an amorphous powder. The molecular formula was determined to be $C_{30}H_{34}O_9$ using its negative HRFABMS (*m*/*z* 537.2180). The UV and IR spectra of **2** were similar to those of **1**. Acetylation of **2** gave a tetraacetate (**2a**). The ^{1}H NMR spectrum of **2a** revealed a downfield shift of the C-1 position (δ 6.51), indicating the presence of a hydroxyl group at the C-1 position of **2**. Except for the B ring moiety [a 3-methyl-2-butenyl (prenyl) group (δ_H 1.60, 3.18, and 5.15; δ_C 17.7, 25.8, 29.0, 123.8, and 132.0) and ABX type aromatic protons (δ_H 6.66, 6.85, and 6.90; δ_C 115.4, 128.1, 128.4, 130.2, 131.5, and 154.0)], the ^{1}H and ^{13}C NMR spectra (in acetone-d_6) of **2** exhibited the same structural features found in compound **1**. The location of the prenyl group at the C-3″ position was confirmed with the HMBC spectrum of **2**, which revealed correlations from methylene protons at C-7″ (δ 3.18) to a quaternary carbon at C-3″ (δ 128.1) and an oxygenated quaternary carbon at C-4″ (δ 154.0) and from an aromatic proton at C-2″ (δ 6.90) to a carbon at C-7″ (δ 29.0). The attachment of the prenylated hydroxyphenyl moiety (B ring) to the C-3 position was decided from the HMBC spectrum, revealing correlations from methylene protons at C-3 (δ 2.88) to an aromatic carbon at C-2″ (δ 131.5) and from an aromatic proton at C-6″ (δ 6.85) to an aliphatic carbon at C-3 (δ 35.8). The assignment of the *erythro* orientation of the carbons C-1 and C-2 was obtained using the NOESY spectrum that revealed NOE interactions between H-1 (δ 5.20) and H-2 (δ 5.52), H-1 and H-3, H-3 and OMe-2′ (δ 3.81), and H-6′ (δ 7.39) and H-2‴ (6‴) (δ 7.22). The structure of eryvarinol B was therefore characterized as 1-(4-hydroxy-2-methoxyphenyl)-2-(4-hydroxy-3,5-dimethoxybenzoyloxy)-3-(4-hydroxy-3-prenylphenyl)propan-1-ol (**2**). This is the first report of benzoylated diphenylpropan-1,2-diols that occur naturally.

Experimental Section

General Experimental Procedures. Optical rotations were measured on a JASCO DIP-370 digital polarimeter. UV spectra were recorded on a Beckman DU-530 spectrophotometer, and IR spectra were measured on a JASCO IR-810 spectrophotometer. ^{1}H NMR spectra were obtained on JEOL JNM-A 600 and 400 and JNM-E 500 MHz spectrometers, while ^{13}C NMR spectra were recorded at 150.8 and 100.4, and 125.7 MHz on the same instruments. Mass spectra were determined on a JEOL JMS-D 300 spectrometer and a QSTAR Pulsar quadrupole TOF mass spectrometer (AB/MDS-Sciex). Column chromatography was performed using Si gel (230−400 mesh). Thin-layer chromatography was performed using Merck precoated Si gel 60 F_{254} plates. UV light and iodine vapor were used for the detection of compounds.

Plant Material. The roots of *E. variegata* were obtained from Karachi, Pakistan, in April 2000. A voucher specimen (No. 000413) was deposited in the Department of Natural Product Chemistry in the Faculty of Pharmacy, Meijo University.

Extraction and Isolation. The finely powdered roots (0.47 kg) were extracted with acetone (12 L), and the extract was evaporated to give a dark green residue (28.8 g). The residue was divided into *n*-hexane-, $CHCl_3$-, and EtOAc-soluble fractions. The $CHCl_3$-soluble fraction (19.26 g) was applied to a Si gel column, which was eluted with solvents of varying polarity of CH_2Cl_2, CH_2Cl_2−acetone (10:1→1:1), and CH_2Cl_2−MeOH (10:1) (each fraction, 200 mL) to give 42 fractions. Fraction 22 (747 mg) was subjected to Si gel column chromatography using $CHCl_3$−acetone (3:1), followed by Si gel column chromatography using *n*-hexane−acetone (1.5:1), to give **2** (10 mg; 0.0021% yield). Fractions 23−24 (537 mg) were purified by Si gel column chromatography using $CHCl_3$−acetone (2:1), followed by Si gel column chromatography using *n*-hexane−acetone (5:1→1:1), to give **1** (7 mg; 0.0015% yield).

Eryvarinol A (1): amorphous powder; $[\alpha]^{23}_D$ −74° (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ϵ) 206 (4.66), 228 (sh, 4.36), 279 (4.05) nm; IR (KBr) ν_{max} 3400, 1700, 1620 cm^{-1}; ^{1}H NMR, see Table 1; ^{13}C NMR (150.8 MHz, acetone-d_6) δ 165.8 (COO), 158.8 (C-4′), 158.7 (C-2′), 156.6 (C-4″), 148.2 (C-3‴, 5‴), 141.3 (C-4‴), 131.3 (C-2″, 6″), 130.1 (C-1″), 129.9 (C-6′), 122.0 (C-1‴), 121.4 (C-1′), 115.8 (C-3″, 5″), 108.0 (C-2‴, 6‴), 107.7 (C-5′), 99.5 (C-3′), 78.6 (C-2), 69.5 (C-1), 56.7 (OMe-3‴, 5‴), 55.8 (OMe-2′), 35.7 (C-3); HMBC (H/C) 5′/1′ 5′/3′ 5′/4′ 6′/4′ 2″/1″ 2″/4″ 3″/1″ 3″/4″ 3″/5″ 5″/1″ 5″/4″ 6″/1″ 6″/4″ 2‴/1‴ 2‴/3‴ 2‴/4‴ 2‴/6‴ 2‴/COO 6‴/1‴ 6‴/2‴ 6‴/4‴ 6‴/5‴ 6‴/COO OMe-3‴/3‴ OMe-5‴/5‴; FABMS (negative) *m*/*z* 469 ([M − H]$^+$, 10), 367 (30), 275 (100); HRFABMS (negative) *m*/*z* 469.1491 (calcd for $C_{25}H_{25}O_9$, 469.1497).

Eryvarinol B (2): amorphous powder; $[\alpha]^{23}_D$ −62° (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ϵ) 205 (4.69), 224 (sh, 4.42), 279 (4.07) nm; IR (KBr) ν_{max} 3400, 1700, 1620 cm^{-1}; ^{1}H NMR (600 MHz, CD_3OD)[7] δ 1.55 (3H, s, H-10″), 1.58 (3H, s, H-11″), 2.79 (1H, dd, *J* = 14.7, 8.8 Hz, H-3), 2.91 (1H, dd, *J* = 14.7, 3.7 Hz, H-3), 3.11 (2H, d, *J* = 7.3 Hz, H-7″), 3.77 (3H, s, OMe-2′), 3.85 (6H, s, OMe-3‴, 5‴), 5.04 (1H, t, *J* = 7.3, H-8″), 5.16 (1H, d, *J* = 5.1 Hz, H-1), 5.46 (1H, ddd, *J* = 8.8, 5.1, 3.7 Hz, H-2), 6.38 (1H, dd, *J* = 8.8, 2.2 Hz, H-5′), 6.39 (1H, d, *J* = 2.2 Hz, H-3′), 6.57 (1H, d, *J* = 8.1 Hz, H-5″), 6.79 (1H, d, *J* = 2.2 Hz, H-2″), 6.79 (1H, dd, *J* = 8.1, 2.2 Hz, H-6″), 7.17 (2H, s, H-2‴, 6‴), 7.30 (1H, d, *J* = 8.8 Hz, H-6′); ^{13}C NMR (150.8 MHz, acetone-d_6) δ 165.7 (COO), 158.8 (C-4′), 158.7 (C-2′), 154.0 (C-4″), 148.2 (C-3‴, 5‴), 141.3 (C-4‴), 132.0 (C-9″), 131.5 (C-2″), 130.2 (C-1″), 129.9 (C-6′), 128.4 (C-6″), 128.1 (C-3″), 123.8 (C-8″), 122.0 (C-1‴), 121.4 (C-1′), 115.4 (C-5″), 108.0 (C-2‴, 6‴), 107.7 (C-5′), 99.4 (C-3′), 78.6 (C-2), 69.5 (C-1), 56.7 (OMe-3‴, 5‴), 55.7 (OMe-2′), 35.8 (C-3), 29.0 (C-7″), 25.8 (C-11″), 17.7 (C-10″); FABMS (negative) *m*/*z* 537 ([M − H]$^+$, 100), 446 (51), 444 (34), 313 (7), 297 (51), 295 (13); HRFABMS (negative) *m*/*z* 537.2180 (calcd for $C_{30}H_{33}O_9$, 537.2123).

Acetylation of Compound 2. A mixture of **2** (6 mg), acetic anhydride (0.5 mL), and pyridine (0.5 mL) was stirred at room temperature overnight. The reaction mixture was evaporated to dryness, and the resulting residue was purified by Si gel column chromatography with benzene−EtOAc (10:1) as eluting solvent to give the tetraacetate **2a** (3 mg, 38%) as a colorless oil: $[\alpha]^{23}_D$ −65° (*c* 0.1, MeOH); UV (MeOH) λ_{max} (log ϵ) 205 (4.76), 260 (4.02) nm; IR (KBr) ν_{max} 1760, 1720, 1610 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.61 (3H, s, H-10″), 1.65 (3H, s, H-11″), 2.05 (3H, s, OAc-1), 2.25 (3H, s, OAc-4″), 2.31 (3H, s, OAc-4‴), 2.35 (3H, s, OAc-4′), 2.76 (1H, dd, *J* = 14.7, 9.0 Hz, H-3), 3.01 (1H, dd, *J* = 14.7, 4.4 Hz, H-3), 3.11 (2H, d, *J* = 7.3 Hz, H-7″), 3.83 (3H, s, OMe-2′), 3.84 (6H, s, OMe-3‴, 5‴), 5.06 (1H, t, *J* = 7.3 Hz, H-8″), 5.80 (1H, ddd, *J* = 9.0, 4.4, 3.7 Hz, H-2), 6.51 (1H, d, *J* = 3.7 Hz, H-1), 6.66 (1H, d, *J* = 2.2 Hz,

H-3′), 6.71 (1H, dd, $J = 8.1$, 2.2 Hz, H-5′), 6.86 (1H, d, $J = 8.1$ Hz, H-5″), 6.99 (1H, d, $J = 2.2$ Hz, H-2″), 7.02 (1H, dd, $J = 8.1$, 2.2 Hz, H-6″), 7.20 (2H, s, H-2‴, 6‴), 7.45 (1H, d, $J = 8.1$ Hz, H-6′); FABMS (positive) *m*/*z* 647 $[M - AcOH + H]^+$; Qq-TOFMS *m*/*z* 647 $[M - AcOH + H]^+$.[8]

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(7) Although the splitting pattern of H-3 in the ^{1}H NMR spectrum of acetone-d_6 appeared as a multiplet [δ 2.88 (2H, m)], the ^{1}H NMR spectrum in CD_3OD demonstrated a different pattern for the H-3 [δ 2.79 (1H, dd, $J = 14.7$, 8.8 Hz) and 2.91 (1H, dd, $J = 14$, 7, 3.7 Hz)].
(8) The FABMS and Qq-TOFMS for **2a** gave no molecular ion peak and showed a fragment peak at *m*/*z* 647, corresponding to the removal of acetic acid.

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