# Ferreirinol, a New 3-Hydroxyisoflavanone from *Swartzia polyphylla*

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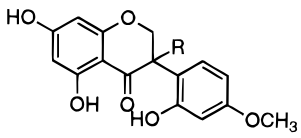
Reinvestigation of an EtOH extract of *Swartzia polyphylla* (Leguminosae) led to the isolation of a new 3-hydroxyisoflavanone, ferreirinol (**3**). The structure was elucidated from $^1$H NMR, $^{13}$C NMR, and EIMS data.

*Swartzia polyphylla* A. DC. (Leguminosae) is a tree found in the Amazon region of Peru. Its wood is used in construction, and alcohol extracts of the duramen (heartwood) are used in healing.[1] An EtOH extract of the dried, ground heartwood of *Swartzia polyphylla* showed significant inhibition ($IC_{50}$ = 31 $\mu$g/mL) of protein kinase C (PKC) activity.[2] PKC is a $Ca^{+2}$ and phospholipid-dependent protein kinase involved in signal transduction, cellular proliferation, and cellular differentiation.[3] The EtOH extract of *Swartzia polyphylla* also demonstrated antibacterial and antifungal activity. Fractionation of the methylene chloride-soluble material derived from the EtOH extract of *Swartzia polyphylla*, guided in part by an assay for inhibition of PKC, led to the isolation of the known isoflavanoids, biochanin A, dihydrobiochanin A, ferreirin (**1**), dalbergioidin, and naringenin, and a new prenylated isoflavanone, dihydrolicoisoflavone.[2] The need to isolate additional quantities of dihydrolicoisoflavone for further testing prompted the reexamination of crude fractions obtained in the previous isolation work. This reexamination resulted in the isolation of a small amount (4 mg) of a new 3-hydroxyisoflavanone, ferreirinol (**2**). This compound is the fifth example of a relatively rare class of flavonoids.[4−7]




**1**: R = H
**2**: R = OH

The structure of **2** was determined by analysis of spectroscopic data. EIMS gave a parent ion at *m/z* 318 suggesting a molecular formula of $C_{16}H_{14}O_7$. The $^1$H-NMR and COSY spectra of **2** showed an ABX aromatic system; a doublet at 7.36 ppm (8.4 Hz) was coupled to a doublet of doublets at 6.35 ppm (8.3, 2 Hz), which was further coupled to a doublet at 6.34 ppm (2 Hz). Two aromatic protons appeared as two coupled but overlapping doublets, integrating for one proton each, at 6.0 ppm (2 Hz) and 6.03 ppm (2 Hz). These resonances indicated a flavanoid structure in which the A-ring contained hydroxy or methoxy moieties at C-5 and C-7 and the B-ring contained hydroxy or methoxy moieties at C-4′ and C-2′ or C-3′. A three-proton singlet at 3.83 ppm indicated an aromatic methoxy group, and the fragment ion at *m/z* 166 in the MS indicated that the methoxy was in the B-ring, leaving two hydroxy moieties in the A-ring and one in the B-ring. The placement of the B-ring and one additional hydroxy moiety was determined from the $^{13}$C-NMR data. A methylene resonance at 74.0 ppm indicated that both substituents must be either at C-2 or C-3. If the B-ring and hydroxy moiety were at C-2, then this resonance would represent the C-3 and should appear further upfield (ca. 40−50 ppm). Consequently, the B-ring and hydroxy moiety must be located at C-3, resulting in a 3-hydroxyisoflavanone structure, and this methylene resonance must represent the 2-carbon. This assignment is in good agreement with the data for echinoisoflavanone, another 3-hydroxyisoflavanone.[4] The assignment is further supported by the two one-proton doublets at 4.3 ppm (12 Hz) and 4.8 ppm (12 Hz) due to the C-2 protons. These resonances are coupled to one another in the COSY spectrum, but are not coupled to any other protons in the spectrum. The chemical shifts are in good agreement with the analogous resonances in the spectra of the known 3-hydroxyisoflavanones, echinoisoflavanone[4] and secondifloran.[5] Comparison of the $^1$H-NMR data for the B-ring with data for with ferreirin (**1**) and the known 3-hydroxyisoflavanone, bolusanthin,[6] indicated the substitution pattern to be the same as ferreirin. Thus, ferreirinol must have structure **2**.

As noted, the isolation work on *S. polyphylla* had been guided by PKC inhibition bioassays. Unfortunately, access to this bioassay was unavailable when **2** was isolated, and it was not screened for activity. However, **2** is only the fifth representative of this unusual class of compounds, and it seems likely that additional representatives will be found in the future. A second 3-hydroxyisoflavanone was also isolated from *S. polyphylla*, but in quantities too small to characterize completely.

## Experimental Section

**General Methods.** $^1$H-NMR spectra were recorded in $Me_2CO$-$d_6$ on a General Electric QE-300 spectrometer at 300 MHz ($^1$H) or 75 MHz ($^{13}$C) using residual $Me_2CO$ as an internal standard. $^{13}$C-NMR assignments were based on literature data[5,6] and heteronuclear correlated spectra. IR spectra were measured on a Perkin-Elmer model 1600 FT-IR spectrometer. Specific rotations were measured on a Perkin-Elmer model 141 polarimeter. LREIMS were measured on a Finnigan TSQ4500 mass spectrometer. PKC inhibition assays were carried out at Sphinx Pharmaceuticals Corporation in Durham, NC.

**Plant Material.** The plant material was collected from the Amazon region of Peru in 1990, by Dr.

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Franklyn Ayala Flores, Director of the Herbarium Amazonense at the Universidad Nacional de la Amazonia Peruana, where voucher specimens are preserved.

**Extraction and Isolation.** The dried, ground heartwood of *Swartzia polyphylla* (1.135 kg) was percolated in a Soxhlet extractor with 11 L of 95% EtOH for 24 h. The resulting extract was concentrated down *in vacuo* to give a dark tar (199.0 g). This material was partitioned between $CH_2Cl_2$ (3 × 500 mL) and $H_2O$ (500 mL). The material that would not dissolve in either phase was active, and fractionation of this material by column chromatography, guided by bioassays, led to the isolation of large amounts of biochanin A and small amounts of the other flavonoids. Examination of the $CH_2Cl_2$-soluble material by TLC showed additional amounts of the minor flavonoids. Thus, 2 g of the $CH_2Cl_2$ layer were subjected to column chromatography in $CH_2Cl_2$−$CH_3CN$−$H_2O$ (90:9.7:0.3). Fractions were examined by TLC, and similar fractions were combined. Those fractions containing flavonoids were subjected to preparative TLC runs using Si gel 60 developed with MeOH−$CH_2Cl_2$ (95:5) to isolate all six flavonoids in amounts sufficient for compound identification. Known flavonoids were identified from EIMS and $^1$H-NMR data. During the effort to isolate additional quantities of dihydrolicoisoflavone, 2 g of the $CH_2Cl_2$ layer was subjected to column chromatography in $CH_2Cl$−97% $CH_3CN$ (9:1). Fractions were spotted against dihydrolicoisoflavone, sprayed with Gibb's reagent,[8] and the individual spots were isolated by preparative TLC, resulting in the isolation of 4 mg of **3**, whose structure was identified from EIMS and $^1$H-NMR and $^{13}$C-NMR data.

**Ferreirinol (2):** amorphous white solid; $[\alpha]^{20}_D$ +160° (*c* 4.0 × $10^{-3}$ g/mL, ETOH); IR (KBr) $\nu$ max 3389, 3260, 2931, 2848, 1642, 1454 $cm^{-1}$; UV (EtOH) $\lambda$ max (log $\epsilon$) 204 (4.01), 286 nm (3.76); $^1$H NMR ($Me_2CO$-$d_6$) $\delta$ 3.83 (3H, s, $OCH_3$), 4.21 (1H, d, $J$ = 12 Hz, H-2), 4.83 (1H, d, $J$ = 12 Hz, H-2), 6.0 (1H, d, $J$ = 2 Hz, H-8), 6.03 (1H, d, $J$ = 2 Hz, H-6), 6.34 (1H, d, $J$ = 2 Hz, H-3′), 6.35 (1H, dd, $J$ = 8, 2 Hz, H-5′), 7.36 (1H, d, $J$ = 8 Hz, H-6′); $^{13}$C NMR ($Me_2CO$-$d_6$) $\delta$ 55.5 ($OCH_3$), 74.0 (C-2), 93.7 (C-8), 95.0 (C-6), 103.4 (C-3′), 106.9 (C-5′), 128.4 (C-6′), 198.0 (C-4); EIMS *m*/*z* 318 $[M]^+$, 166, 152.

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