

SUPPORTING INFORMATION

Sceptrin as a Potential Biosynthetic Precursor to Complex Pyrrole-Imidazole Alkaloids: The First Total Synthesis of Ageliferin

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Experimental Data for Compounds

General Procedures. Yields refer to chromatographically and spectroscopically (^1H NMR) homogeneous materials, unless otherwise stated. Reagents were purchased at the highest commercial quality and used without further purification, unless otherwise stated. NMR spectra were recorded on either Bruker DRX-600, DRX-500, AMX-500 and AMX-400 or Varian Inova-400 instruments and calibrated using residual undeuterated solvent as an internal reference. The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, quin = quintuplet, sext = sextet, sep = septet, b = broad. Electrospray ionization (ESI) mass spectrometry (MS) experiments were performed on an API 100 Perkin Elmer SCIEX single quadrupole mass spectrometer at 4000V emitter voltage. High-resolution mass spectra (HRMS) were recorded on a VG ZAB-ZSE mass spectrometer using MALDI (matrix-assisted laser-desorption ionization). Microwave irradiation was performed using a Biotage (formerly Personal Chemistry) "Emrys Creator" apparatus.

Ageliferin 2: A solution of sceptrin (6 mg, 0.0097 mmol) in H_2O (1.4 mL) was heated to 195 °C (temperature set to 200 °C, but only reaches 195) for 1 min in a microwave (see Figure S4 for heating profile). The solvent was removed by lyophilization to give crude ageliferin (ca. 45 % conversion by NMR), which was purified by HPLC to give **2** (2.4 mg, 40%) along with recovered sceptrin (3.1 mg, 52%). HPLC was performed on an Agilent series 1100 machine using an Agilent Eclipse XDB 5 μm C8 4.6 X 150 mm column. Solvent A: 10% MeCN/ H_2O

with 0.1% TFA; Solvent B: MeCN with 0.1% TFA. 5 min., 10 % B. 40 min., 40% B.

Retention time: 29.55 minutes. ^1H NMR (600 MHz, D_2O) \square 7.12 (d, $J = 1.8$ Hz, 1 H), 7.11 (d, $J = 1.8$ Hz), 6.83 (d, $J = 1.8$ Hz), 6.79 (d, $J = 1$ Hz), 6.61 (s, 1 H), 3.93 (d, $J = 6.6$ Hz, 1 H), 3.34-3.66 (m, 4 H), 2.78-2.81 (m, 1 H), 2.45-2.48 (m, 3 H).

Sceptrin- d_2 : A solution of sceptrin (0.5 mg 0.0008 mmol) in CD_3OD (0.75 mL) was heated to 80 °C for 5 minutes in a microwave. The formation of sceptrin- d_2 was observed by the disappearance of the ^1H NMR signal at 6.57 ppm. (400 MHz, CD_3OD), see Figure S5.

Injection Date : 1/30/2004 7:05:02 PM
Sample Name : natagel
Acq. Operator : dan
Location : Vial 1
Inj Volume : 10 µl
Acq. Method : C:\HPCHEM\1\METHODS\DANO.M
Last changed : 1/30/2004 6:58:40 PM by dan
(modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\DEF_LC.M

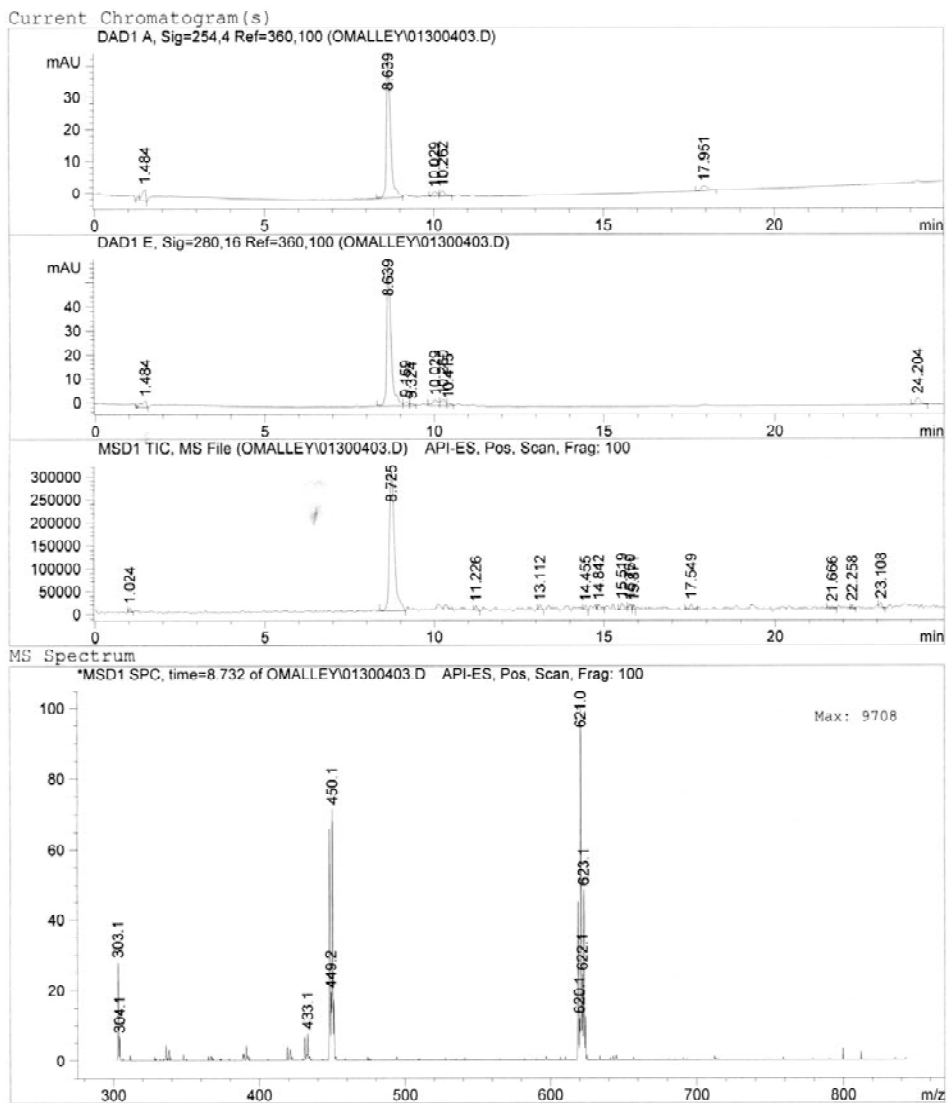


Figure S1. LC/MS of natural ageliferin (2).

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Acq. Operator : dan
Location : Vial 1
Inj Volume : 10 µl
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(modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\DEF_LC.M

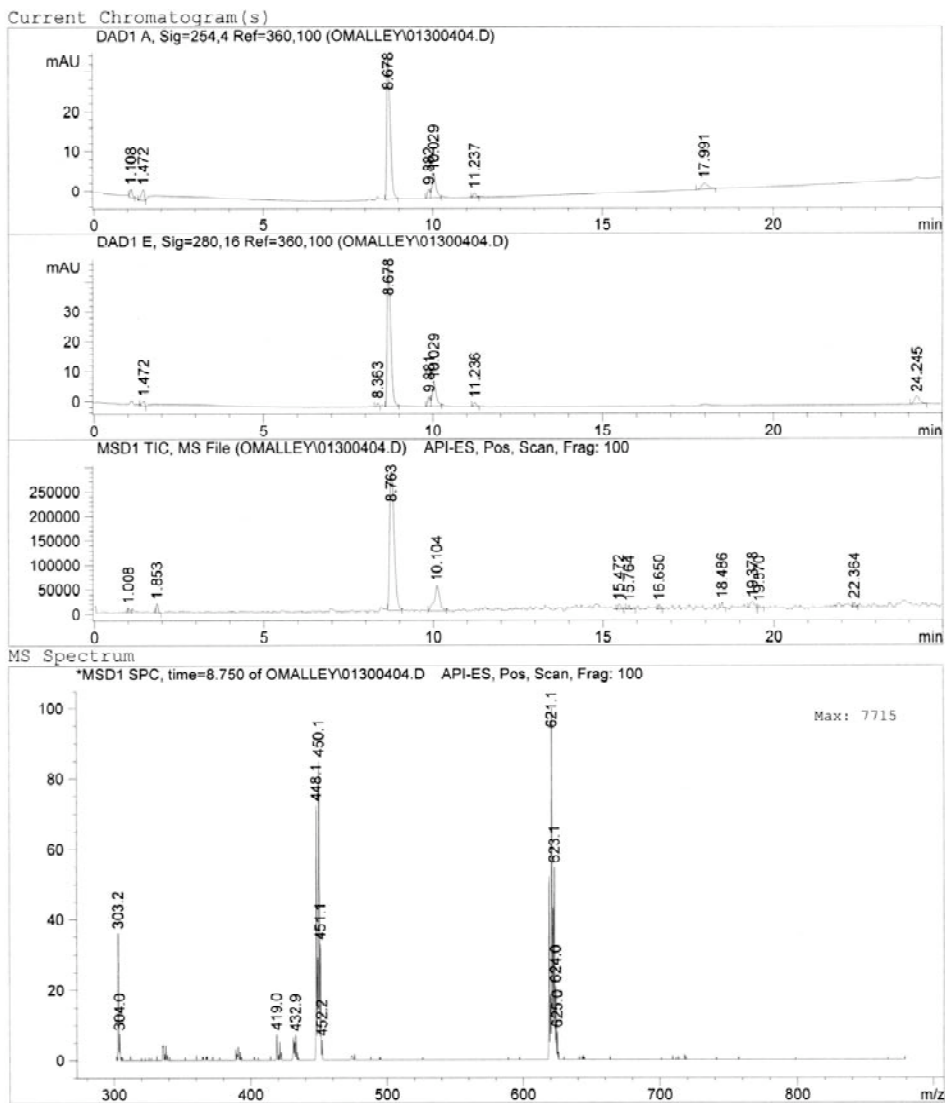


Figure S2. LC/MS of synthetic ageliferin (2).

Injection Date : 1/30/2004 8:09:44 PM
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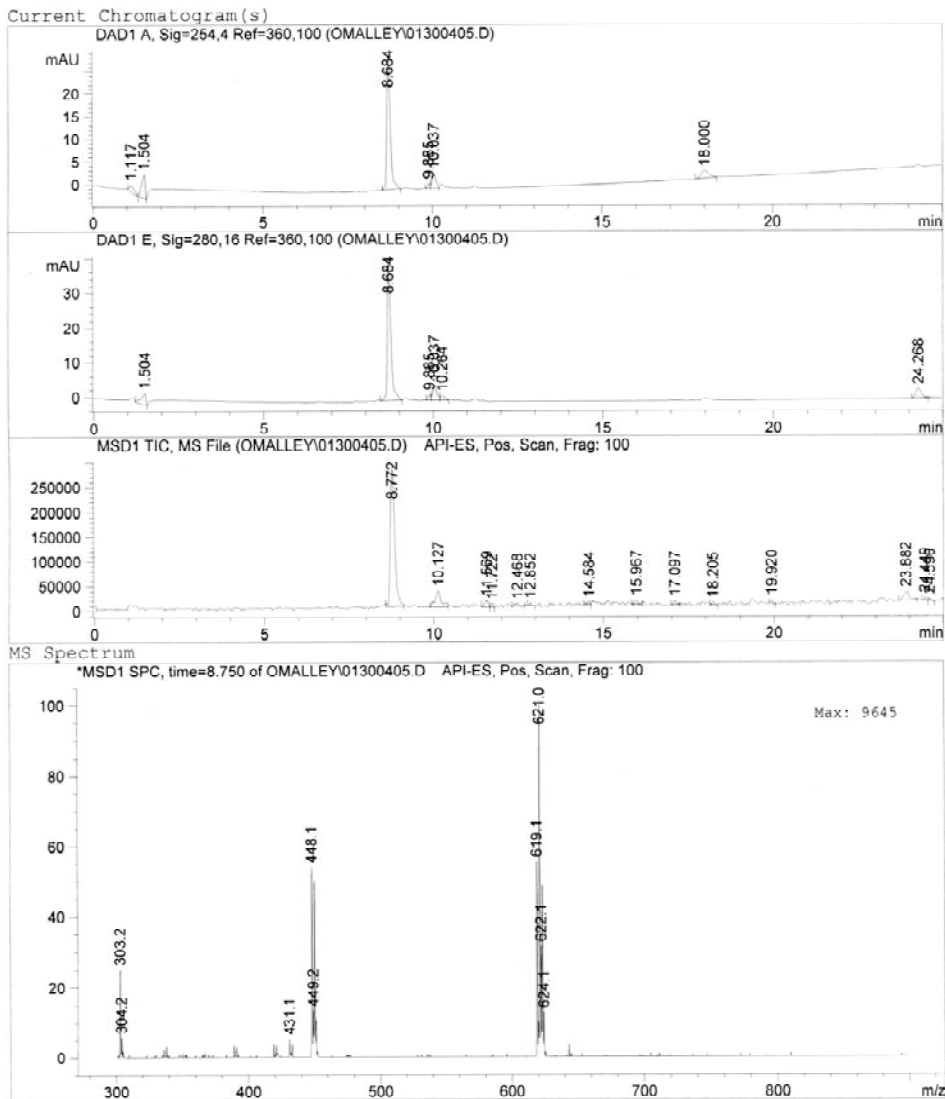


Figure S3. LC/MS of synthetic+natural ageliferin (2) co-injection.

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User: Alex
Status: OK
Date: 26-January-2004 at 11:50
Comment: Sceptrin 200 1.5min

Process parameters

Temperature: 200°C
Time: 90 s
Fixed Hold Time: Off
Absorption Level: Normal
Pre-stirring: 0 s

Graphs

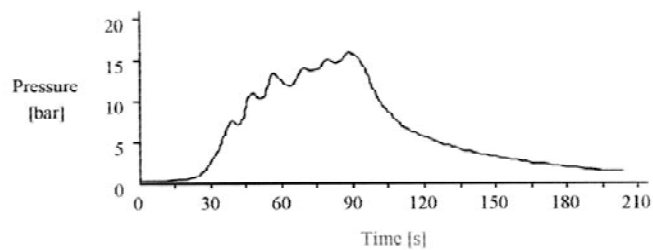
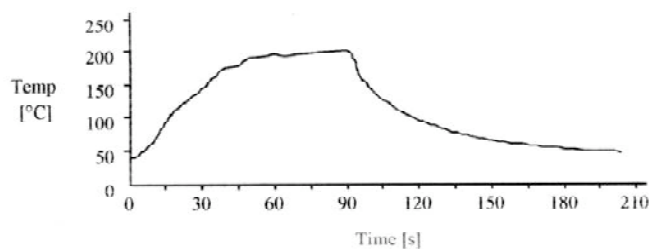


Figure S4. Reaction profile for the sceptrin to ageliferin conversion (Scheme 1).

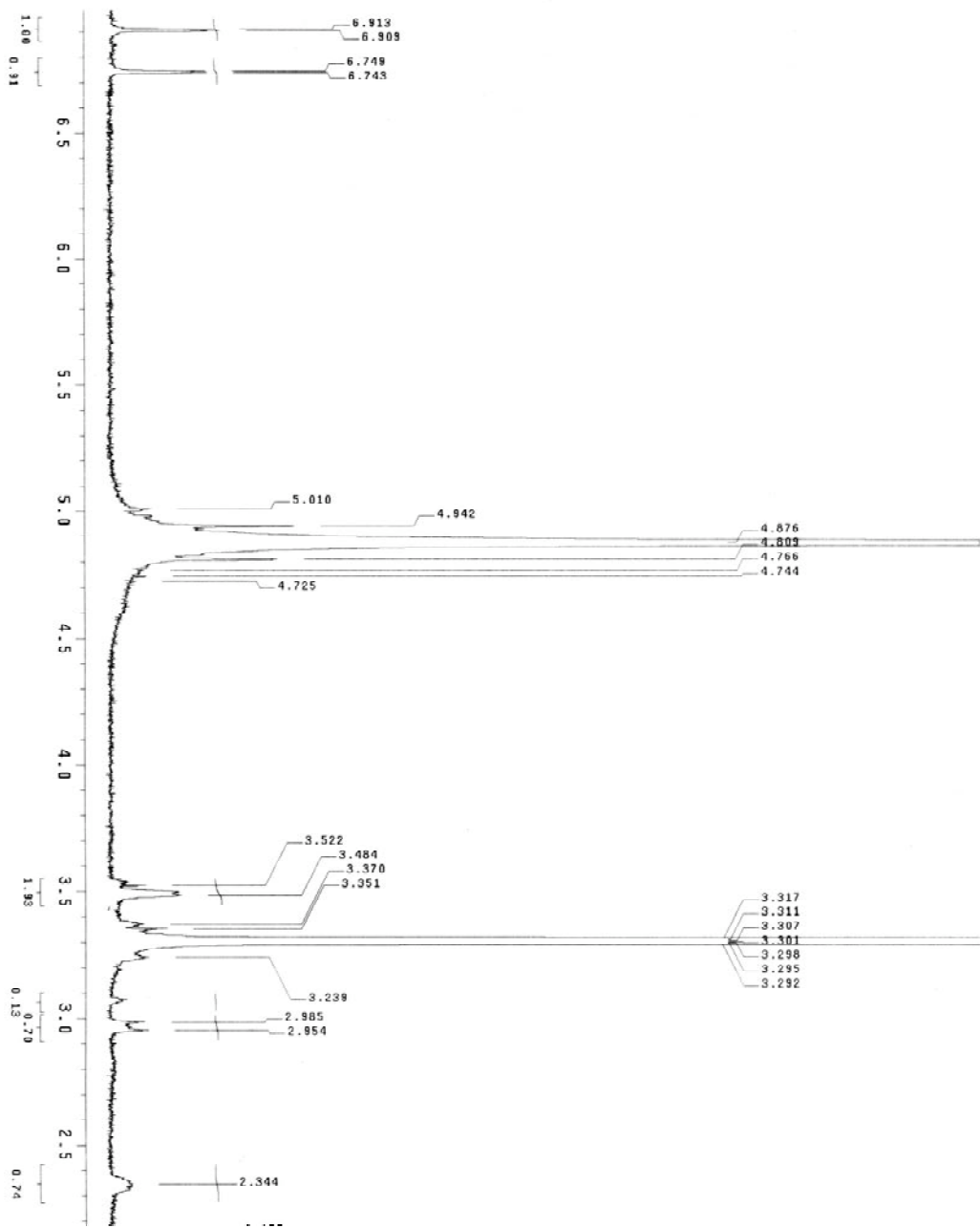


Figure S5. ¹H NMR (400 MHz, CD₃OD) of sceptrin-*d*₂.