

Two 6-Substituted 5,6-Dihydropyran-2-ones from *Piper reticulatum*

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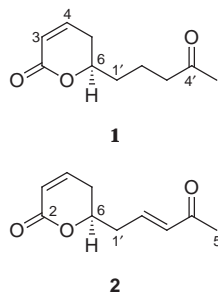
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The Me₂CO extract of the aerial parts of *Piper reticulatum* yielded two 6-substituted 5,6-dihydropyran-2-ones **1** and **2** and dihydrowisanidine. The structures of **1** and **2** were elucidated by spectroscopic methods.

The 6-substituted 5,6-dihydro-2*H*-pyran-2-ones show a wide range of biological activities. They act as plant-growth inhibitors, insect antifeedants, and antifungal and antitumor agents. This class of compounds has been isolated from 13 plant families, mainly the Annonaceae, Labiatae, Lauraceae, and Piperaceae.¹ From the Piperaceae, *Piper methysticum* is the only species to date that has yielded compounds of this class—the pharmacologically active 6-styryl-5,6-dihydro-2*H*-pyran-2-ones.^{2,3}

In our continuing studies of *Piper* species occurring in Trinidad,^{4–8} we wish to report the isolation of two new compounds, 6-(*R*)-(4'-oxopentyl)-5,6-dihydro-2*H*-pyran-2-one (**1**) and its dehydro derivative (**2**), as well as dihydrowisanidine, from *Piper reticulatum* L. (Piperaceae). The chemistry of this plant has not been studied previously, and there have been no reports of its use in folk medicine.



The crude acetone extract of the aerial parts of *P. reticulatum* was subjected to vacuum–liquid chromatography (VLC) followed by repeated column and preparative TLC. The least polar compound **1** was obtained as a colorless oil. Its IR spectrum showed absorption bands at 1720, 1695, and 1635 cm⁻¹ for α,β -unsaturated lactone and ketone moieties. The 500 MHz ¹H NMR spectrum suggested structure **1**. It showed two 1H doublets of triplets at δ 6.02 ($J = 10, 2$ Hz) and δ 6.90 ($J = 10, 4$ Hz), a 2H multiplet at δ 2.34 and a 1H multiplet at δ 4.42 suggesting a 6-substituted α,β -unsaturated lactone.¹ A methyl singlet at δ 2.16, a triplet at δ 2.52, and a broad 4H multiplet centered at δ 1.75 suggested the presence of a 4'-oxopentyl side chain. The EIMS also supported the assigned structure. It gave [M]⁺ at m/z 182.0947 (indicating a molecular

formula C₁₀H₁₄O₃) and fragment ions at m/z 97 ([C₅H₅O₂]⁺) and 85 ([C₅H₉O]⁺) resulting from cleavage of the C-6, C-1' bond. The ¹³C NMR spectrum showed the expected 10 carbons: one ester and one ketonic carbonyl, two olefinic, one oxymethine, and five sp³ carbons. Two-dimensional NMR experiments (HMQC, ¹H–¹H COSY, and HMBC) facilitated the assignment of all the ¹H NMR and ¹³C NMR signals. Assignment of C-1' and C-2', for which the signal of the attached protons overlapped, was achieved by means of the HMBC spectrum. The proton at C-5 (δ 2.34) showed cross peaks with the signal of C-3 (δ 121.35), C-4 (δ 145.08), C-6 (δ 77.42) and to the signal at δ 34.01 but not to that at δ 19.00. This enabled us to assign the signal at δ 34.01 to C-1' and that at δ 19.00 to C-2'.

The observed negative Cotton effect at 257 nm in the CD spectrum of **1** led to the assignment of the *R*-configuration at C-6.⁹ Therefore, the structure of **1** was assigned as 6-(*R*)-(4'-oxopentyl)-5,6-dihydro-2*H*-pyran-2-one.

Compound **2** was also a colorless oil, with spectral characteristics very similar to those of **1**. Its IR spectrum (1710, 1670, 1620 cm⁻¹) was consistent with the presence of an α,β -unsaturated lactone and ketone functionalities. The absence of the 4H multiplet at δ 1.75 in the ¹H NMR spectrum of **1** and the presence of two additional doublets of triplets at δ 6.82 ($J = 17, 7$ Hz) and δ 6.17 ($J = 17, 1$ Hz) suggested that **2** was a dehydro derivative of **1**. This suggestion was supported by the HREIMS of **2**, which gave a [M + H]⁺ at m/z 181.0859 for a molecular formula of C₁₀H₁₂O₃. The structure was confirmed by 2D NMR (HMQC, ¹H–¹H COSY, and HMBC) data, which allowed full assignment of all the ¹H and ¹³C NMR signals. Accordingly, compound **2** was assigned as 6-(*R*)-(4'-oxopent-2'-enyl)-5,6-dihydro-2*H*-pyran-2-one.

The HREIMS of the most polar compound **3** gave [M]⁺ at m/z 303.1482 corresponding to a molecular formula of C₁₇H₂₁NO₄. This compound was previously obtained from *Piper guineense*, and the MS, IR, and ¹H NMR data were in close agreement with those reported for dihydrowisanidine.¹⁰ The ¹³C NMR spectrum, previously unreported, fully supported the structure.

Experimental Section

General Experimental Procedures. NMR spectra were recorded on a Varian Unity-500 spectrometer in CDCl₃ solution with TMS as internal standard. HMQC

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and HMBC experiments were optimized for $^1J_{C-H}$ of 125 Hz and $^{2/3}J_{C-H}$ of 8 Hz, respectively. Mass spectra were obtained on a VG70–250S spectrometer. IR spectra were run using a Pye Unicam SP-200 spectrophotometer, and UV spectra were recorded on an HP8452 diode array instrument. Optical rotations at 589.3 nm were measured on a Schmidt–Haensch Polartronic D polarimeter, and CD spectra were recorded on a JASCO J-710 spectropolarimeter. TLC (on 0.25- and 1-mm layers) and VLC were carried out with Si gel 60 PF₂₅₄₊₃₆₆ (Merck), and for column chromatography Si gel 60 (Merck) 70–230 mesh was utilized.

Plant Material. Aerial parts of *P. reticulatum* were collected at Maracas waterfall, St. Joseph, Trinidad, in May 1993. A voucher specimen (no. 32606) is on deposit at the National Herbarium of Trinidad and Tobago on the U.W.I. Campus, St. Augustine, Trinidad.

Extraction and Isolation. The dried, ground plant material (2.4 kg) was exhaustively extracted with Me₂CO (16 L). Evaporation of the Me₂CO *in vacuo* gave a crude extract (67.23 g), a portion (39.7 g) of which was subjected to VLC eluting with petroleum ether–Me₂CO mixtures of increasing polarity. The fraction eluting with 40% Me₂CO was further purified by column chromatography and preparative TLC (CHCl₃–Me₂CO, 9:1) to yield 14.4 mg of pure **1**. The fractions eluting with 45% Me₂CO (596.6 mg) and 50% Me₂CO (504.2 mg) were subjected to repeated preparative TLC (petroleum ether–Me₂CO, 7:3, × 3) to yield 17.2 mg of **2** and 46.3 mg of **3**, respectively.

6-(R)-(4'-Oxopentyl)-5,6-dihydro-2H-pyran-2-one (1): colorless oil; $[\alpha]^{25}_D -96.3^\circ$ (*c* 0.98, CHCl₃); UV (MeOH) λ_{max} (log ϵ) 210 (2.45) nm; CD (MeOH, *c* 0.07) λ_{max} ($\Delta\epsilon$) 257 (–0.4); IR (film) ν_{max} 1720, 1695, 1635 cm^{–1}; ¹H NMR (CDCl₃, 500 MHz) δ 1.75 (4H, m, H₂-1', H₂-2'), 2.16 (3H, s, Me-5'), 2.34 (2H, m, H-5), 2.52 (2H, t, *J* = 7 Hz, H-3'), 4.42 (1H, m, H-6), 6.02 (1H, dt, *J* = 10, 2 Hz, H-3), 6.90 (1H, dt, *J* = 10, 4 Hz, H-4); ¹³C NMR (CDCl₃, 125 MHz) δ 208.47 (C-4'), 164.40 (C-2), 145.09 (C-4), 121.35 (C-3), 77.72 (C-6), 42.94 (C-3'), 34.01 (C-1'), 30.00 (C-5'), 29.24 (C-5), 19.01 (C-2'); EIMS (70 eV) *m/z* [M + H]⁺ 183 (15), 167 (6), 165 (15), 140 (47), 139 (9), 125 (12), 111 (12), 97 (100), 85 (12), 71 (29), 84 (10),

69 (39), 68 (82), 57 (11); HREIMS *m/z* [M]⁺ 182.0947 (C₁₀H₁₄O₃ requires 182.0943).

6-(R)-(4'-Oxopent-2'-enyl)-5,6-dihydro-2H-pyran-2-one (2): colorless oil; $[\alpha]^{25}_D -33.3^\circ$ (*c* 0.3, CHCl₃); UV (MeOH) λ_{max} (log ϵ) 218 (3.18) nm; IR (film) ν_{max} 1710, 1620, 1610 cm^{–1}; ¹H NMR (CDCl₃, 500 MHz) δ 2.28 (3H, s, H-5'), 2.38 (2H, m, H-5), 2.68 (2H, m, H-1'), 4.60 (1H, m, H-6), 6.06 (1H, dt, *J* = 10, 2 Hz, H-3), 6.18 (1H, dt, *J* = 17, 1 Hz, H-3'), 6.82 (1H, dt, *J* = 17, 7 Hz, H-2'), 6.90 (1H, dt, *J* = 10, 4 Hz, H-4); ¹³C NMR (CDCl₃, 125 MHz) δ 198.07 (C-4'), 163.71 (C-2), 144.63 (C-4), 140.79 (C-2'), 134.39 (C-3'), 121.49 (C-3), 76.15 (C-6), 37.55 (C-1'), 29.01 (C-5), 27.06 (C-5'); EIMS (70 eV) *m/z* [M + H]⁺ 181 (3), 165 (5), 134 (2), 111 (2), 97 (100), 84 (41), 83 (41), 69 (50), 68 (21); HREIMS *m/z* [M + H]⁺ 181.0859 (C₁₀H₁₃O₃ requires 181.0864).

Dihydrowisanidine (3): oil; ¹³C NMR (CDCl₃, 125 MHz) δ 164.87 (C-11), 152.30 (C-2), 145.02 (C-4), 146.16 (C-5), 140.62 (C-4), 121.81 (C-10), 121.67 (C-1), 109.68 (C-6), 100.9 (–OCH₂O–), 94.57 (C-3), 56.31 (OMe), 46.47 (C-4'), 45.76 (C-1'), 32.97 (C-8), 29.04 (C-7), 26.09 (C-3'), 24.32 (C-2'); HREIMS *m/z* [M]⁺ 303.1482 (C₁₇H₂₁NO₄ requires 303.1470).

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