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A New Heterocyclization Product of Adhyperforin from Hypericum perforatum (St. John's Wort)

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From the aerial parts of Hypericum perforatum L. we have isolated phloroglucinol 1 (see the formula), a homologue of 2, the latter isolated previously from the same extract and identified by 2D NMR (DQF COSY, PS NOESY, TOCSY, HSQC and HMBC) [1]. Compounds 1 and 2 are the heterocyclization products of adhyperforin and the well-known antibiotic hyperforin, respectively. The only difference between the ¹H NMR spectra of 1 and 2 was that concerning alkanoyl side chain at C-1. Instead of two methyl doublets (0.97 and 1.08) typical for an isobutyryl group observed in the ¹H NMR spectrum of 2 [1], compound 1 contained a triplet (0.78) of a methyl group (H-16) next to a methylene + a methyl doublet at 1.08 (H-17) characteristic for 2-methylbutyryl moiety. In addition, the molecular mass of 1 was higher by 14 amu.

Ethanol extraction of the air-dried ground aerial parts of H. perforatum (6.3 kg), collected at mountain Ozren (southeast Serbia) during the flowering season in July 1994, fractionation of the crude extract with supercritical CO₂ at different pressures and temperatures into five fractions (F₁-F₅), and isolation from F₂ of 2 and a degradation product 3 (with the same basic skeleton as 2, and OH instead of Me₂COH at C-6), was reported previously [1,2]. Continuing this work, 10 g (out of 17.1 g) of F₃ was subjected to silica gel chromatography column, starting elution with toluene and gradually increasing polarity by addition of EtOAc. Compound 1 (pale yellow viscous oil, 16 mg) was isolated from a fraction eluted with 2% (v/v) EtOAc in toluene by preparative TLC (n-hexane-EtOAc, 7.5:2.5). A fraction eluted with 3-4% (v/v) EtOAc in toluene yielded additional quantity (78 mg) of 2.

Spectroscopic data for compound 1:

¹H NMR (200 MHz, CDCl₃): 4.55 (dd, 5.6, 11.0, H-6); 2.66 (dd, 11.0, 13.2, H-7B); 0.78 (t, 7.3, H-16); 1.09 (d, 6.4, H-17); 3.01 (dd, 7.6, 14.5, H-18A); 3.16 (dd, 6.8, 14.5, H-18B); 5.07 (m, H-19), 1.64 (br s,
H-21); 1.70 (br s, H-22); 1.22 (s, H-24); 1.39 (s, H-25); 4.92 (br t, ca 6.5, H-27); 1.70 (br s, H-29); 1.57 (br s, H-30); 1.05 (s, H-31); 5.07 (m, H-34); 1.60 (br s, H-36); 1.64 (br s, H-37).

DCI-MS (isobutane): (M+H)$^+$ 567.

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References and Notes

2. Antibiogram tests revealed a moderate activity of 3 against G+ bacteria (Micrococcus luteus and Staphylococcus aureus) and a low activity of 2 against M. luteus and no activity against S. aureus. Neither of them exhibited activity against G- bacteria (Escherichia coli) [1]. Rapid decomposition of 1 (after few days), possibly due to traces of acidic impurities, did not allow antibiogram tests.

Sample Availability: not available.

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