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

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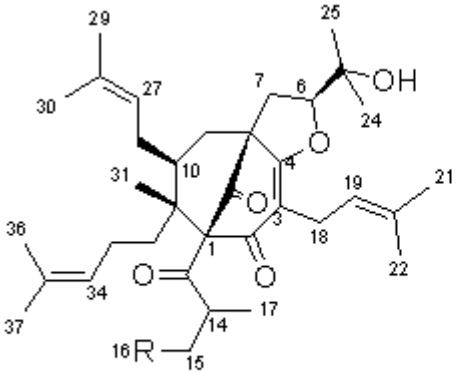
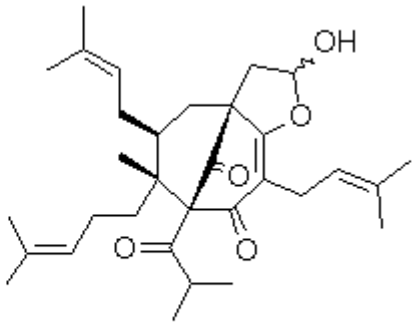


1 R=Me
2 R=H



3

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 ^{1}H 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 ^{1}H 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 CO_2 at different pressures and temperatures into five fractions (F_1-F_5), and isolation from F_2 of **2** and a degradation product **3** (with the same basic skeleton as **2**, and OH instead of Me_2COH at C-6), was reported previously [1,2]. Continuing this work, 10 g (out of 17.1 g) of F_3 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**:

^{1}H NMR (200 MHz, $CDCl_3$): 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

1. Trifunovic, S.; Vajs, V.; Macura, S.; Juranic, N.; Djarmati, Z.; Jankov, R.; Milosavljevic S. *Phytochemistry* **1998**, *49*, 1305-1310.
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.