

## Drummondins A—C: Three Novel Rottlerin-type Antibiotics from *Hypericum drummondii*

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The structures of three novel rottlerin-type antibiotics, isolated from *Hypericum drummondii*, drummondin A (**1**), B (**2**), and C (**3**), with unusual acyl side chains, have been established from spectral data.

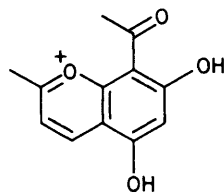
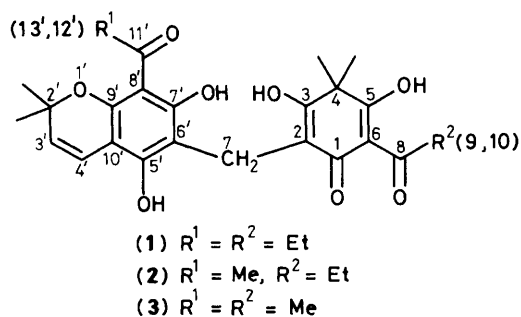
Our continued interest in discovering antibiotics from higher plants has led us to undertake a chemical and a biological investigation of the native Mississippi weed *Hypericum drummondii* (Grev. & Hook.) T. & G. Drummondins (**1**)—(**3**) were isolated from the hexane extract of the roots of *Hypericum drummondii* by a bio-assay-directed isolation procedure. In this communication we report drummondin A (**1**), B (**2**), and C (**3**), the first three rottlerin-type antibiotics from the genus *Hypericum* possessing linear side chains. The novel structures of our compounds invalidate the generalization in the literature that all rottlerin-type phloroglucinols isolated from the genus *Hypericum* possess branched side chains.<sup>1</sup>

The i.r. spectra of all three compounds showed broad absorption in the 3000 cm<sup>-1</sup> region and this, coupled with intense peaks at 1600—1650 cm<sup>-1</sup>, suggested the presence of an enolic 1,3-diketo system or a 2-hydroxyaryl ketone.<sup>2,3</sup> The very low field ( $\delta$  18, exchangeable proton) signal in the <sup>1</sup>H n.m.r. spectra of these compounds further suggests the presence of an enolizable  $\beta$ -triketone system. This correlation, together with signals for methyl groups absorbing at  $\delta$  1.49 in the <sup>1</sup>H n.m.r. spectrum, strongly indicated the presence of a 3-acyl filicinic acid moiety in the compounds.

In addition the <sup>1</sup>H n.m.r. spectra showed a singlet for geminal methyl groups (2'-Me) at  $\delta$  1.49 and also exhibited a pair of doublets (*ca.*  $\delta$  5.4 and 6.7, 3'-H, 4'-H respectively) consistent with the presence of a 2,2-dimethylpyran moiety. The 7-methylene bridge protons connecting the above two moieties appeared as a broad singlet at *ca.*  $\delta$  3.5. Both the <sup>1</sup>H and <sup>13</sup>C n.m.r. spectra of these compounds show certain anomalies which can be explained by the expected tautomerization of the acylfilicinic acid system.<sup>3</sup>

The above <sup>1</sup>H n.m.r. spectral data of these compounds suggested a close resemblance to the rottlerin-type phloroglucinol uliginosin B isolated from *Hypericum uliginosum* HBK.<sup>4</sup> The differences in the <sup>1</sup>H n.m.r. data were in the region of  $\delta$  1—4 indicating different acyl groups in our compounds. The <sup>1</sup>H n.m.r. spectra did not show any evidence for the presence of branched alkyl groups which were present in the acyl moieties of all other rottlerin-type phloroglucinols reported from the genus *Hypericum* to date.<sup>1,4—7</sup>

Drummondin A (**1**) (C<sub>26</sub>H<sub>30</sub>O<sub>8</sub>, yellow crystals from hexane, m.p. 130—132 °C) showed two <sup>1</sup>H n.m.r. quartets centred at  $\delta$  3.25 (q, *J* 7.5 Hz) and 3.12 (q, *J* 7.5 Hz). These were coupled with two almost overlapping triplets at  $\delta$  1.18 (t, *J* 7.5 Hz) and  $\delta$  1.20 (t, *J* 7.5 Hz). Taken in conjunction



(4)

these facts strongly suggested two n-propionyl substituents attached to the two carbocyclic rings of the compound. The  $^{13}\text{C}$  n.m.r. signals for the n-propionyl moiety were seen at  $\delta$  34.8 ( $\text{CH}_2$ ), 8.6 (Me) and 37.1 ( $\text{CH}_2$ ), 8.9 (Me).

Drummondin B (2) ( $\text{C}_{25}\text{H}_{28}\text{O}_8$ , yellow crystals from hexane, m.p. 136–138 °C) showed in the  $^1\text{H}$  n.m.r. only one quartet centred at  $\delta$  3.25 (q,  $J$  7.5 Hz) coupled to a triplet at  $\delta$  1.18 (t,  $J$  7.5 Hz) which suggested a propionyl moiety in one of the carbocyclic rings. There was a new singlet at  $\delta$  2.69 integrating for three protons which indicated an acetyl moiety

in the system. The  $^{13}\text{C}$  n.m.r. provided additional information since there were signals for the acetyl moiety at  $\delta$  32.6 (Me) and for the n-propionyl moiety at  $\delta$  34.8 ( $\text{CH}_2$ ) and  $\delta$  8.6 (Me). Based on the fragment ion (4) at  $m/z$  219 (100%) in the mass spectrum, the n-propionyl group was placed in the filicinic acid moiety and the acetyl group on the dimethylpyran moiety.

Drummondin C (3) ( $\text{C}_{24}\text{H}_{26}\text{O}_8$ , yellow crystals from hexane, m.p. 184–187 °C) showed two singlets in the  $^1\text{H}$  n.m.r. at  $\delta$  2.74 and 2.69 each integrating for three protons. This suggested two acetyl groups in the compound. This was confirmed by the  $^{13}\text{C}$  n.m.r. signals at  $\delta$  29.3 and 32.2 for the two methyl groups.

The complete  $^{13}\text{C}$  n.m.r. assignments and the establishment of the linear fusion of the chromene ring were established unequivocally by extensive SINEPT experiments.<sup>8</sup>

The drummondins possess antibiotic activity comparable to, or better than, that of streptomycin against the Gram positive bacteria *Staphylococcus aureus* and *Bacillus subtilis*.

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