# Drummondins A—C: Three Novel Rottlerin-type Antibiotics from *Hypericim 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.

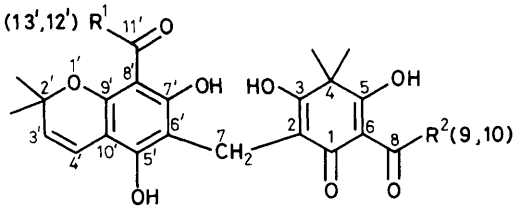
Our continued interest in discovering antibiotics from higher plants has led us to undertake a chemical and a biological investigation of the native Mississipi weed *Hypericum drummondii* (Grev. & Hook.) T. & G. Drummondins (**1**)—(**3**) were isolated from the hexane extract of the roots of *Hypericum 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.[1]

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

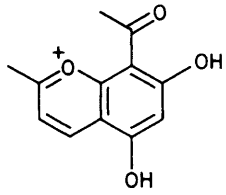
In addition the $^1H$ n.m.r. spectra showed a singlet for geminal methyl groups (2′-Me) at δ 1.49 and also exhibited a pair of doublets (*ca.* δ 5.4 and 6.7, 3′-H, 4′-H respectively) consistent with the presence of a 2,2-dimethylpyran moiety. The 7-methylene bridge protons connecting the above two moieties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

The above $^1H$ n.m.r. spectral data of these compounds suggested a close resemblance to the rottlerin-type phloroglucinol uliginosin B isolated from *Hypericum uliginosum* HBK.[4] The differences in the $^1H$ n.m.r. data were in the region of δ 1—4 indicating different acyl groups in our compounds. The $^1H$ 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.[1,4—7]

Drummondin A (**1**) ($C_{26}H_{30}O_8$, yellow crystals from hexane, m.p. 130—132 °C) showed two $^1H$ n.m.r. quartets centred at δ 3.25 (q, *J* 7.5 Hz) and 3.12 (q, *J* 7.5 Hz). These were coupled with two almost overlapping triplets at δ 1.18 (t, *J* 7.5 Hz) and δ 1.20 (t, *J* 7.5 Hz). Taken in conjunction



(1) $R^1 = R^2 = Et$
(2) $R^1 = Me$, $R^2 = Et$
(3) $R^1 = R^2 = Me$



(4)

these facts strongly suggested two n-propionyl substituents attached to the two carbocyclic rings of the compound. The $^{13}C$ n.m.r. signals for the n-propionyl moiety were seen at δ 34.8 ($CH_2$), 8.6 (Me) and 37.1 ($CH_2$), 8.9 (Me).

Drummondin B (**2**) ($C_{25}H_{28}O_8$, yellow crystals from hexane, m.p. 136—138 °C) showed in the $^1H$ n.m.r. only one quartet centred at δ 3.25 (q, *J* 7.5 Hz) coupled to a triplet at δ 1.18 (t, *J* 7.5 Hz) which suggested a propionyl moiety in one of the carbocyclic rings. There was a new singlet at δ 2.69 integrating for three protons which indicated an acetyl moiety in the system. The $^{13}C$ n.m.r. provided additional information since there were signals for the acetyl moiety at δ 32.6 (Me) and for the n-propionyl moiety at δ 34.8 ($CH_2$) and δ 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**) ($C_{24}H_{26}O_8$, yellow crystals from hexane, m.p. 184—187 °C) showed two singlets in the $^1H$ n.m.r. at δ 2.74 and 2.69 each integrating for three protons. This suggested two acetyl groups in the compound. This was confirmed by the $^{13}C$ n.m.r. signals at δ 29.3 and 32.2 for the two methyl groups.

The complete $^{13}C$ n.m.r. assignments and the establishment of the linear fusion of the chromene ring were established unequivocally by extensive SINEPT experiments.[8]

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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