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## COUMARINS FROM *ERIOSTEMON SPICATUS*

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**ABSTRACT.**—Eight coumarins have been isolated from the aerial parts of *Eriostemon spicatus* (Rutaceae). Six were characterized as the known compounds scopoletin, dracunculin, heraclenin, deoxybruceol, ramosin [1], and anisocoumarin F [2]. The other two appear to be novel and have been identified as (+)-7-(3-methylbut-2-enyloxy)-8-(2-hydroxy-3-methylbut-3-enyl) coumarin [3] and (+)-7-(3-methylbut-2-enyloxy)-8-(4-hydroxy-3-methylbut-2-enyl) coumarin [4] on the basis of spectroscopic analysis.

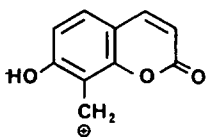
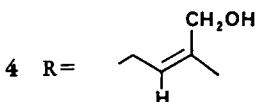
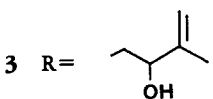
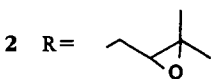
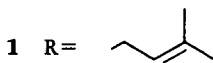
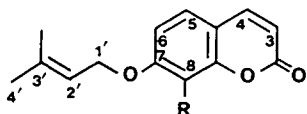
Western Australia is a rich source of plants in the Rutaceae, few of which have been examined for their secondary metabolites. As part of a survey of the chemistry of species of the genus *Eriostemon* (1,2), carried out in collaboration with the Western Australian Herbarium, we have recently examined the aerial parts of *Eriostemon spicatus* A. Rich. This slender woody perennial, which grows only to a height of 60 cm (3), has not previously been studied.

### RESULTS AND DISCUSSION

From the combined petroleum-ether- and EtOAc-soluble extractives, a total of eight coumarins have been isolated and identified. Six of these proved to be known compounds, of which scopoletin, ramosin [1], and anisocoumarin F [2] were identified by direct comparison with samples isolated previously from other Australian Rutaceae (4). Dracunculin (7,8-methylenedioxy-6-methoxycoumarin) and heraclenin [8-(2,3-epoxy-3-methylbutoxy)furocoumarin] were identified by comparison of extensive spectral data with those already reported; the location of the methoxyl group in dracunculin was confirmed by an nOe study. The unusual pentacyclic monoterpene-substituted coumarin (–)-deoxybruceol was identified by comparison with a sample recently isolated from *Eriostemon brucei* (2).

The two remaining coumarins, isolated in small amounts only, appear to be novel 7-prenyloxy-8-prenyl derivatives. The less polar of these showed no  $[M]^+$  in eims, the largest fragment being  $[M - C_5H_8]^+$ , but fabms revealed  $[M + 1]^+$  at  $m/z$  315, compatible with an empirical formula of  $C_{19}H_{22}O_4$ . The  $^1H$ -nmr spectrum showed two AB quartets indicative of H-3/H-4 and H-5/H-6. The 1'-methyleneoxy protons were observed as non-equivalent double doublets resonating at  $\delta$  4.64 and 4.68 coupling to an olefinic proton at  $\delta$  5.50. The latter showed long-range coupling to two vinylic methyls, thus completing a 3-methylbut-2-enyloxy system. For the C-8 substituent a double doublet at  $\delta$  4.57 could be assigned to an oxymethine proton and was observed to couple to two methylene protons to form an ABX system. Finally, two broad singlets (1H each) together with a vinylic methyl were indicative of an isopentenyl moiety. These observations required the presence of either a 1-hydroxy or 2-hydroxy-3-methylbut-3-enyl system. A major fragment **a** at  $m/z$  175 in the eims eliminates the possibility of the 1-hydroxy side chain. On this basis the new coumarin has been assigned structure 3.

The second new coumarin showed  $[M]^+$  in the hreims for 314 ( $C_{19}H_{22}O_4$ ), and the  $^1H$ -nmr spectrum again indicated a 7-prenyloxy-8-prenylcoumarin



a

but with changes relating to the C-8 substituent. In this compound, a benzylic methylene ( $\delta$  3.60) was observed, coupling to an olefinic proton. The remaining signals were for a single vinylic methyl and a 2H singlet at  $\delta$  4.40 attributable to an hydroxymethyl. A NOESY experiment revealed a strong interaction between this hydroxymethyl and the benzylic methylene protons, requiring them to have a *cis* relationship and therefore requiring the *Z* configuration, as in structure 4. The NOESY additionally showed an interaction between the methyleneoxy protons (C-1') and H-6, adding further proof to the assignment of this substituent to C-7.

## EXPERIMENTAL

**GENERAL EXPERIMENTAL PROCEDURES.**—All nmr experiments were run on a Bruker AMX400 instrument using standard Bruker programs and  $\text{CDCl}_3$  as solvent. Hreims were obtained using an AEI-MS-902 double focusing spectrometer with direct probe insert, operating at 70 eV and elevated temperature. Petroleum

ether refers to the bp 60–80° fraction. Fabms was obtained on a VG ZAB-E high resolution spectrometer using NOBA matrix.

**PLANT MATERIAL.**—A voucher specimen, PERTH 01195328, has been deposited at the Western Australian Herbarium, Perth.

**EXTRACTION AND ISOLATION OF COUMARINS.**—Dried, ground, aerial parts (80 g) were extracted in a Soxhlet with petroleum ether, then EtOAc, and finally MeOH. Petroleum ether and EtOAc extracts were concentrated separately and proved to be identical on tlc analysis. These were bulked and subjected to vlc over Si gel, eluting with petroleum ether containing increasing amounts of EtOAc. Elution with 10–15% EtOAc gave a mixture which was separated by preparative tlc over Si gel [solvent toluene-EtOAc (8:1), 2 developments] to give 1 (30 mg), sitosterol (7 mg), and 3 (2 mg). Similar treatment of the 20% EtOAc fraction gave deoxybruceol (2 mg). Preparative tlc of the 25% EtOAc fraction eluting with  $\text{CHCl}_3$  (Si gel plates, 3 developments) yielded 2 (5 mg). The 50% EtOAc fraction, after preparative tlc [Si gel, toluene-EtOAc (85:15)] gave dracunculin (2 mg), heraclenin (18 mg), and 4 (2 mg). The final eluate, on concentration, gave scopoletin (10 mg).

**Ramosin [1].**—Needles from petroleum ether/EtOAc: mp 68–69.5° [lit. (5) 68–69°]. Identical (uv, ir,  $^1\text{H}$  nmr, eims) with an authentic sample (4).

**Anisocoumarin F [2].**—Amorphous:  $[\alpha]_{\text{D}} +22.5^\circ$  ( $c = 0.1$ ,  $\text{CHCl}_3$ ) [lit. (6) +27.5°]. Identical (uv, ir,  $^1\text{H}$  nmr, eims) with an authentic sample (4).

**Scopoletin.**—Needles from petroleum ether/EtOAc: mp 202° [lit. (7) 202–203°]. Identical (uv, ir,  $^1\text{H}$  nmr, eims) with an authentic sample (4).

**Heraclenin.**—Needles from  $\text{CHCl}_3$ : mp 107–108° [lit. (8) 107–108°];  $[\alpha]_{\text{D}} +25^\circ$  ( $c = 0.1$ ,  $\text{CHCl}_3$ ) [lit. (8) +23°]; eims  $m/z$  286.0841 (calcd for  $\text{C}_{16}\text{H}_{14}\text{O}_5$ , 286.0642); uv, ir,  $^1\text{H}$  nmr in agreement with literature (8).

**Dracunculin.**—Gum: eims  $m/z$  220.0374 (calcd for  $\text{C}_{11}\text{H}_8\text{O}_5$ , 220.0372); uv, ir,  $^1\text{H}$  nmr in agreement with literature (9).

(–)-**Deoxybruceol.**—Gum: eims  $m/z$  312.1352 (calcd for  $\text{C}_{19}\text{H}_{20}\text{O}_4$ , 312.1362); uv, ir, optical rotation,  $^1\text{H}$  nmr in agreement with literature (2).

**7-(3-Methylbut-2-enyloxy)-8-(2-hydroxy-3-methylbut-3-enyl)coumarin [3].**—Gum:  $[\alpha]_{\text{D}} +15^\circ$  ( $c = 0.1$ ,  $\text{CHCl}_3$ ) uv max (log  $\epsilon$ ) (EtOH) 245 (3.64), 255 (3.62), 321 (4.03); ir max (KBr) 3400, 1725, 1605, 1280, 1245, 1120, 1095;  $^1\text{H}$  nmr  $\delta$  1.78 (3H, br s, 3'-Me), 1.82 (3H, br s, 3'-Me), 1.91 (br s, 3''-Me), 3.21 (1H, dd,  $J = 14.0, 5.4$

Hz, H-1''), 3.30 (1H, dd,  $J = 14.0, 8.2$  Hz, H-1''), 4.57 (1H, dd,  $J = 8.2, 5.4$  Hz, H-2''), 4.64 (1H, dd,  $J = 12.0, 7.2$  Hz, H-1'), 4.68 (1H, dd,  $J = 12.0, 7.2$  Hz, H-1'), 4.90 (1H, br s, H-4''), 4.96 (1H, br s, H-4''), 5.50 (1H, br t,  $J = 7.2$  Hz, H-2'), 6.26, 7.64 (2H, ABq,  $J = 9.5$  Hz, H-3, H-4), 6.89, 7.35 (2H, ABq,  $J = 8.6$  Hz, H-6, H-5); eims  $m/z$  (rel. int.)  $[M - C_5H_8]^+$  246 (6), 228 (6), 175 (53), 69 (100); fabms  $m/z$   $[M + H]^+$  315.

7-(3-Methylbut-2-enyloxy)-8-(4-hydroxy-3-methylbut-2-enyl)coumarin [4].—Gum: uv max (log  $\epsilon$ ) (EtOH) 248 (3.43), 254 (3.45), 323 (3.88); ir max (KBr) 3420, 1725, 1605, 1280, 1245, 1120, 1070, 830;  $^1H$  nmr  $\delta$  1.77 (3H, br s, 3'-Me), 1.80 (3H, br s, 3''-Me), 1.82 (br s, 3'-Me), 3.60 (2H, d,  $J = 7.1$  Hz, H-1''), 4.40 (2H, s, H-4''), 4.65 (2H, d,  $J = 6.7$  Hz, H-1'), 5.23 (1H, br t,  $J = 7.1$  Hz, H-2''), 5.50 (1H, br t,  $J = 6.7$  Hz, H-2'), 6.25, 7.65 (2H, ABq,  $J = 9.5$  Hz, H-3, H-4), 6.86, 7.31 (2H, ABq,  $J = 8.5$  Hz, H-6, H-5); hreims  $m/z$  (rel. int.) 314.1531 (calcd for  $C_{19}H_{22}O_4$ , 314.1518) (7), 246 (21), 215 (8), 203 (19), 187 (24), 175 (29), 69 (100).

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