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NMR ASSIGNMENTS FOR THE PENTACYCLIC COUMARINS BRUCEOL AND DEOXYBRUCEOL

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ABSTRACT.—Full and unambiguous assignments are reported for the ^1H - and ^{13}C -nmr spectra of bruceol [1] and deoxybruceol [2].

Two pentacyclic coumarins, bruceol [1] and deoxybruceol [2], known only from *Eriostemon brucei* F. Muell. (Rutaceae), were originally characterized primarily by means of X-ray studies on halogenated derivatives, and (\pm)-deoxybruceol has been synthesized (1-4). As a consequence, little use was made of nmr studies in their structure elucidation. We have recently re-isolated both compounds and have carried out an exhaustive nmr analysis leading to the unambiguous assignment of both ^1H and ^{13}C data. The results of this study are reported here.

RESULTS AND DISCUSSION

Bruceol [1], gave mp, optical rotation, and uv and ir spectra comparable with those published previously (1). The ^1H -nmr spectrum (Table 1) revealed resonances for all 20 protons, including a discrete hydroxyl proton (δ 2.38) showing coupling to an oxymethine proton (δ 3.83). The lactone ring protons showed

the typical AB pattern for H-3 and H-4, with the latter exhibiting 3J "zig-zag" coupling to H-8. By means of a ^1H - ^1H COSY-45 experiment it was possible to trace all interactions in the terpene-derived part of the molecule, starting from the oxymethine H-2' through H-1', to H-6', H-5' and finally H-4'. Important features noted were: (a) the small J -values observed for H-1', indicative of its equatorial configuration; (b) the highly shielded chemical shift for the axial H-5' (δ 0.54), which can be attributed to its lying above the aromatic coumarin nucleus and within its shielding cone; (c) the absence of any observable coupling between H-5' and H-6' equatorial protons and unusually large axial-equatorial coupling between $\text{H}_{\text{eq}}-5'$ and $\text{H}_{\text{ax}}-6'$ (5.3 Hz), which suggests that this ring must be twisted out of the normal chair conformation.

Further assignments in both the ^1H - and ^{13}C -nmr spectra were achieved by means of an HMBC (5) study in which 1J , 2J , and 3J heteronuclear interactions were observed (6) (Table 2). All nine carbons of the coumarin nucleus could be assigned on the basis of 2J and 3J ^1H - ^{13}C interactions. Assignments for the terpenoid fragment commenced from the geminal dimethyl system which could be identified by 3J coupling of the protons of one methyl to the carbon of the other methyl. This permitted identification of the quaternary C-7' and C-6' methine carbons. The remaining methyl resonance can therefore be assigned to C-3', and through its interactions C-3', C-2', and C-4' carbons can be identified.

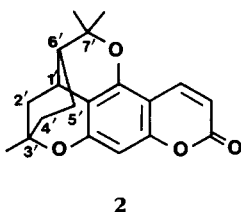
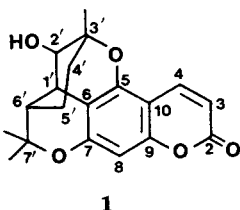


TABLE 1. ^1H -nmr (400 MHz) and ^{13}C -nmr (100 MHz) Spectral Data for **1** and **2**.

Position	^1H		^{13}C	
	1	2	1	2
2			162.0	162.1
3	6.11 d (9.6)	6.11 d (9.7)	110.4	110.9
4	7.84 dd (9.6, 0.6)	7.86 dd (9.7, 0.6)	138.2	138.4
5			154.2	153.7
6			110.2	112.5
7			158.5	160.0
8	6.48 d (0.6)	6.44 d (0.6)	97.2	97.1
9			154.7	154.7
10			105.9	105.2
1'	2.88 t (2.2)	2.86 ddd (4.6, 2.8, 1.7)	36.2	28.1
2'	3.83 dd (7.1, 2.2)	ax 1.90 dd (13.4, 1.7)	70.9	35.0
(OH)	2.38 d (7.1)	eq 2.24 ddd (13.4, 4.6, 3.2)		
3'			79.3	76.5
3'-Me	1.46 s	1.41 s	24.5	28.9
4'	ax 1.48 ddd (13.2, 11.5, 5.3)	1.48 ddd (14.9, 11.6, 5.4)	36.7	37.4
	eq 1.90 dd (13.2, 5.3)	1.81 ddd (14.9, 6.4, 2.8)		
5'	ax 0.54 (dtd (13.4, 11.5, 5.3)	0.64 dtd (14.0, 11.6, 6.4)	21.7	22.1
	eq 1.20 dt (13.4, 5.3)	1.31 dt (14.0, 5.4)		
6'	2.31 ddd (11.5, 5.3, 2.2)	2.13 ddd (11.6, 5.4, 2.8)	47.4	46.4
7'			86.5	86.6
7'-Me	1.59 s	1.60 s	29.6	24.3
7'-Me	1.04 s	1.06 s	24.3	29.7

C-1' and C-5' could now be assigned by default, but this is not necessary as H-2' shows ^1H - ^{13}C coupling to C-1' but not to C-5'. Finally H-1' revealed a total of eight 2J and 3J couplings, through which it showed the C-C connectivity from the terpene moiety through into the coumarin nucleus.

The ^1H - and ^{13}C -nmr assignments for deoxybruceol [**2**] were made in a similar

manner. The ^1H - ^1H COSY-45 spectrum revealed the presence of a 4J (W-bond) coupling between H-2' and H-4' equatorial protons. As no such coupling was observed in **1**, this would suggest that in the former the H-2' proton was axial, a fact not immediately obvious from the coupling of H-2' to H-1' in **1** (which could have been equatorial-equatorial or axial-equatorial).

TABLE 2. HMBC-Derived ^1H - ^{13}C Correlations for **1**.

^1H	^{13}C	
	2J	3J
H-3	162.0 (C-2)	105.9 (C-10)
H-4		154.2 (C-5), 154.7 (C-9)
H-8	154.7 (C-9), 158.5 (C-7)	105.9 (C-10), 110.2 (C-6)
7'-Me (δ 1.59)	86.5 (C-7')	24.3 (7'-Me), 47.4 (C-6')
7'-Me (δ 1.04)	86.5 (C-7')	29.6 (7'-Me), 47.4 (C-6')
3'-Me (δ 1.44)	79.3 (C-3')	70.9 (C-2'), 36.7 (C-4')
H-2'	36.2 (C-1'), 79.3 (C-3')	24.5 (3'-Me), 47.4 (C-6')
H-1'	47.4 (C-6'), 70.9 (C-2')	21.7 (C-5'), 79.3 (C-3')
	110.2 (C-6)	86.5 (C-7'), 154.2 (C-5), 158.5 (C-7)

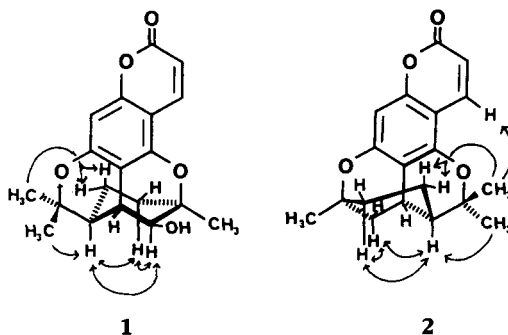


FIGURE 1. NOESY interactions between protons of the geranyl moieties of bruceol [1] and deoxybruceol [2].

Further evidence for the relative stereochemistry of the protons in the geranyl-derived system of [1] came from a NOESY experiment. This showed clearly the axial H-2', H-4', and H-6' protons (Figure 1) and also the proximity of the more shielded of the geminal dimethyl resonances to the highly shielded H_{ax}-5' proton. In 2 a weak cross peak could be seen in the NOESY due to interaction between the more shielded of the geminal dimethyl resonances and H-4, an effect that is only possible where C-7' is angular (as in 2) rather than linear (as in 1).

EXPERIMENTAL

GENERAL EXPERIMENTAL PROCEDURES.—All nmr experiments were run on a Bruker AMX400 instrument using CDCl₃ as solvent. Details of the procedures adopted have been published previously (6). For the HMBC study D₆ was set for 70 msec, optimizing for ¹H-¹³C ²J or ³J of 7 Hz. Eims 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.

PLANT MATERIAL.—Collections of *E. brucei* (PERTH 01185403; PERTH 01194356) were made in Western Australia in 1989. Voucher specimens have been deposited at the Western Australian Herbarium, Perth.

EXTRACTION AND ISOLATION OF 1 AND 2.—Preliminary tlc analysis of the two samples showed them to be identical, and they were consequently bulked (460 g) and extracted (Soxhlet) with petroleum ether. The concentrated petroleum ether extract was subjected to vlc over Si

gel, eluting with petroleum ether containing increasing amounts of EtOAc. Concentration of the 5% EtOAc fraction and subsequent preparative tlc over Si gel [solvent, toluene-EtOAc (17:3)] gave 2 (10 mg). Concentration of the 50–70% EtOAc eluent followed by preparative tlc over Si gel [solvent, CHCl₃-MeOH (90:3)] gave 1 (20 mg).

Bruceol [1].—Needles from hexane: mp 209–211° [lit. (1) 201°], [α]_D -275° (c = 0.2, CHCl₃) [lit. (1) -297°]; uv max (EtOH) 235, 256, 260, 321 nm; ir max (KBr) 3420, 1720, 1620, 1570, 1445, 1335, 1255, 1140, 1050, 1010, 925, 820, 750 cm⁻¹; ¹H and ¹³C nmr see Table 1; eims *m/z* (rel. int.) 328.1306 (calcd for C₁₉H₂₀O₅, 328.1311) (88), 313 (12), 295 (9), 257 (44), 245 (100).

Deoxybruceol [2].—Gum: [α]_D -122° (c = 0.2, CHCl₃) [lit. (2) -127°]; uv max (EtOH) 228, 250, 261, 330 nm; ir max (KBr) 1720, 1620, 1570, 1445, 1390, 1315, 1260, 1110, 1010, 920, 820, 750 cm⁻¹; ¹H and ¹³C nmr see Table 1; eims *m/z* (rel. int.) 312.1352 (calcd for C₁₉H₂₀O₄, 312.1362) (63), 297 (23), 269 (29), 229 (100), 201 (5).

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