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(−)-5-*EXO*-HYDROXYBORNEOL: ISOLATION AND NMR SPECTRAL ASSIGNMENTS

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During an investigation of the alkaloids of *Hedycarya angustifolia* A. Cunn. (Monimiaceae) (1), a plant endemic to Australia, the nonalkaloidal fraction produced a white crystalline compound that analyzed for $C_{10}H_{18}O_2$ by microanalysis. ^{1}H-nmr evidence for the presence of three methyl groups, two -CHOH-CH_2- units, and the absence of any olefinic carbon signals in the carbon spectrum suggested a trimethyl-bicyclo-[2,2,1]heptane diol structure for this compound. Because the configurations and ^{1}H-nmr assignments of compounds in this series have been debated for several years (2–4), we undertook a detailed investigation of the nmr spectroscopic properties of this compound in several solvents.

^{1}H- and ^{13}C-nmr spectra were recorded in $CDCl_3$, DMSO-d_6, and pyridine-d_5-D_2O (9:1) as summarized in Tables 1 and 2. The chemical shift values obtained in the last solvent, which afforded the best spectral resolution, were selected for discussion. A one-proton doublet at 2.01 ppm, coupled to only one other proton signal, at 2.37 ppm, provides a good entry point for the analysis of the ^{1}H spectrum. The C-4 proton in bicyclo[2,2,1] systems does not show coupling to the *endo* protons at C-3 and C-5 due to the proximity of the respective dihedral angles to 90° (4). Therefore, the doublet at 2.01 ppm can be assigned to H-4, while the two geminally coupled one-proton signals at 2.37 and 1.22 ppm can be assigned to the 3-*exo* and 3-*endo* protons, respectively. The absence of coupling between H-4 and a second *exo* proton indicates the presence of an *exo* substituent, a hydroxy group in this case, at C-5.

The 3-*exo* and 3-*endo* protons are themselves coupled, J=9.8 and 2.7 Hz, respectively, to a methine proton signal

TABLE 1. ^{1}H-Nmr Assignments of (−)-5-*exo*-Hydroxyborneol [**1**] in Different Solvents.

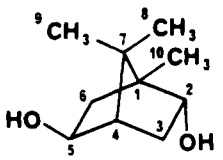
Proton	$CDCl_3$	Pyridine-d_5/D_2O	DMSO-d_6	Multiplicity	Coupling (Hz)
2-*exo*	3.89	4.21	4.44	ddd	$J_{2\text{-}exo,\,3\text{-}exo}$=9.77, $J_{2\text{-}exo,\,3\text{-}endo}$=2.7
3-*exo*	2.28	2.37	2.07	ddd	$J_{3\text{-}exo,\,3\text{-}endo}$=12.7 $J_{3\text{-}exo,\,4}$=4.9
3-*endo*	0.79	1.22	0.63	dd	
4	1.72	2.01	1.54	d	
5-*endo*	3.91	4.38	4.62	dd	$J_{5\text{-}endo,\,6\text{-}endo}$=8.0, $J_{5\text{-}endo,\,6\text{-}exo}$=2.9
6-*exo*	1.39	1.81	1.12	ddd	$J_{6\text{-}exo,\,6\text{-}endo}$=13.6, $J_{6\text{-}exo,\,2\text{-}exo}$=1.9
6-*endo*	2.36	3.01	2.22	dd	
8-H_3	0.84	0.90	0.76	s	
9-H_3	1.11	1.45	1.02	s	
10-H_3	0.89	1.10	0.76	s	
OH	1.62	5.42	3.64	br	

TABLE 2. Carbon-13 Nmr Assignments of (−)-5-*exo*-Hydroxyborneol [**1**] in Different Solvents.

Carbon	DMSO-d_6	Pyridine/D_2O	$CDCl_3$	Multiplicity
1	47.47	50.68	50.65	s
2	71.74	74.76	75.46	d
3	33.53	36.81	36.28	t
4	50.13	53.42	52.94	d
5	71.60	74.85	75.75	d
6	36.06	39.35	38.35	t
7	44.53	47.72	47.70	s
8	16.84	19.98	19.68	q
9	18.51	21.68	21.48	q
10	10.21	13.40	12.77	q

at 4.21 ppm that must be on a carbon bearing a hydroxy function. Because it is known that 2,3-*exo,exo* coupling is greater than 2,3-*exo,endo* coupling (4), the 2-hydroxy function must occupy an *endo* position. For the same reasons the two signals at 3.01 and 1.81 ppm, which showed coupling to the 5-*endo* proton signal at 4.38 ppm (J=8.0 and 2.9 Hz, respectively), can be assigned to the 6-*endo* and 6-*exo* protons. Only the 2-*exo* and 6-*exo* protons showed 1,3 coupling (J=1.9 Hz).

These data, together with the negative molecular rotation, indicated the structure (−)-5-*exo*-hydroxyborneol [**1**]



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for this compound. This compound was previously recorded as a chemical or microbial oxidation product of (−)-borneol (5), but it has not previously been isolated from a higher plant.

Assignment of the three methyl signals was achieved by nOe. Thus, irradiation of the signal at 1.45 ppm caused the enhancement of the signal due to the 6-*exo* proton, while irradiation of the signal at 0.90 ppm enhanced both the 2- and 3-*exo* protons. On the other hand, irradiation of the signal at 1.10 ppm resulted in enhancement of the 2-*exo*, 6-*exo*, and 6-*endo* protons, thereby enabling assignment of the signals at 1.45, 0.90, and 1.10 ppm to be made to C-9, C-8, and C-10, respectively.

The chemical shifts of the protonated carbons were assigned by a HETCOR (6) experiment, while the two quaternary carbon signals could be distinguished by selective INEPT (7) experiments. Thus, separate irradiation of the methyl protons at 1.45 and 0.90 ppm caused enhancement of the methine carbon signal at 53.42 ppm and the quaternary carbon signal at 50.13 ppm, thereby enabling the assignment of these two signals to C-4 and C-1, respectively.

EXPERIMENTAL

GENERAL.—Melting points were determined on a Kofler-type hot-stage apparatus and are uncorrected. Optical rotations were measured with a Perkin-Elmer Model 241 polarimeter. Ir spectra were determined with a Varian MAT 112S double focusing mass spectrometer at 80 eV. The ^{1}H-nmr spectra were obtained with either a Nicolet NMC 360 instrument operating at 360 MHz or a Varian XL-300 instrument operating at 300 MHz. TMS was used as the internal standard and chemical shifts are reported in δ ppm downfield from TMS.

The heteronuclear COSY (HETCOR) experiment was performed on a Varian XL 300 spectrometer using standard Varian pulse sequences. The acquisition time was 88.5 msec and a delay time of 1.0 sec was used. Spectral widths of 11574.1 Hz and 2730.7 Hz were employed.

Selective INEPT experiments were performed on a Nicolet NMC 360 spectrometer. Data sets of

16K covering a spectral width of 10 MHz were acquired. Proton pulse widths were calibrated using a sample of HOAc in 10% C_6D_6 ($^{1r}J=6.7$ Hz) in a 5-mm nmr tube (8). The radio frequency field strength for the soft proton pulse was on the order of 25 Hz for these experiments.

PLANT MATERIAL.—The material was collected from around Little Grassy Creek, King Island, Tasmania, in 3 batches between March 1978 and March 1982. A specimen is deposited in the herbarium at the University of Tasmania, Hobart, Australia.

ISOLATION.—Leaves and twigs of *H. angustifolia* were air dried, powdered, and exhaustively extracted with MeOH. The MeOH extract was concentrated in vacuo, dissolved in glacial HOAc, and poured into an excess of H_2O. The aqueous phase was filtered, evaporated to dryness, redissolved in 5% aqueous H_2SO_4, and extracted with Et_2O. The Et_2O-soluble, nonalkaloidal fraction after repeated recrystallization from MeOH afforded (−)-5-*exo*-hydroxyborneol [**1**] as white needles (0.25% of the dry wt) mp 256–257° [lit. (5), 258–259° in sealed tube], $[\alpha]^{27}D$ −16° (*c*=0.5, MeOH); ir ν max (KBr) 3300, 2950, 1450 cm^{-1}; ^1H nmr see Table 1; ^{13}C nmr see Table 2; ms *m/z* (%) $[M]^+$ 170 (7), $[M-1]^+$ 169 (15), 154 (98), $[M-OH]^+$ 153 (100), 146 (50), 123 (70), 112 (25), 110 (80); calcd for $C_{10}H_{18}O_2$, C 70.58, H 10.58; found: C 70.73, H 10.71.

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