Tetrahedron Letters No. 33, pp 3053 - 3056.
©Pergamon Press Ltd. 1979. Printed in Great Britain.

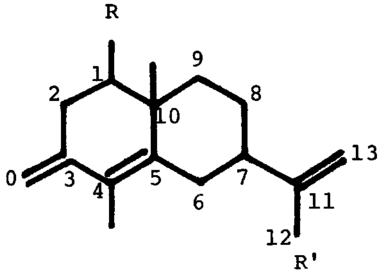
0040-4039/79/0808-3053$02.00/0

HETEROPHYLLOL, A NEW SESQUITERPENE ISOLATED FROM PARSONSIA HETEROPHYLLA A. CUNN

Nigel J. Eggers
Chemistry Division, DSIR, Private Bag, Petone, New Zealand
and
Alan J. Jones*
National NMR Centre, Australian National University, Canberra,
A.C.T., 2600, Australia

Summary: The structure of a new sesquiterpene, heterophyllol, is described. Derivatives, proton and carbon-13 nmr analyses were employed.

We wish to report evidence for the structure determination and conformation of heterophyllol 1 a new sesquiterpene isolated during a study of the alkaloids of Parsonsia heterophylla A. Cunn (Apocyanaceae).[1]

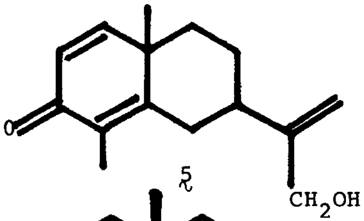


1 R=OH, R'=CH_2OH

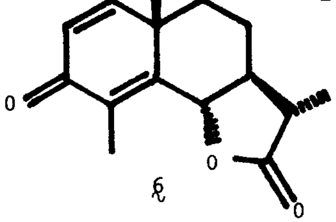
2 R=H, R'=CH_2OH

3 R=OAc, R'=CH_2OAc

4 R=OH, R'=CHO



5



6

The methanol extract was chromatographed on silica gel to give heterophyllol 1, $C_{15}H_{22}O_3$ (microanalysis and M^+ 250.1575): colourless needles, mp 132-133°; $[\alpha]_D^{20}$ + 47.9° (c, 0.37 in EtOH); IR(KBr), cm^{-1}, 3405, 3340 (OH), 1653, 1607 (α,β-unsaturated ketone)[2], 898 (vinylidene)[2]; UV(MeOH) λmax nm(logε), 249(4.18)(α,β-unsaturated ketone)[2]. The most readily characterised resonances in the proton nmr spectrum ($CDCl_3$) are at δ1.18 (3H, s, tertiary $C-CH_3$)[2], 1.76 (3H, s, olefinic $C-CH_3$)[2], 3.8(1H, dd, J 6.5, 11.4 Hz, $C\underline{H}OH$), 4.17(2H, bs, $C\underline{H}_2OH$)[2], 4.99 and 5.14 (each 1H, bm and bm, J<1Hz, vinylidene CH_2)[2]. Similarly, the ^{13}C nmr spectrum ($CDCl_3$) exhibits characteristic functionalities at δ197.17 (α,β-unsaturated ketone)[3], 161.04, 152.56 and 129.75 (quaternary olefinic C-atoms), 109.31 (vinylidene CH_2), 74.55 and 65.22 (hydroxymethine and hydroxymethylene carbons, respectively). Other ^{13}C resonances and their assignments are given in the Table. A bicyclic structure analogous to the monohydroxyl derivatives **2**[2] of α-cyperone is suggested. The ring substitution pattern and a partial stereochemistry of **1** may be deduced from reactions and nmr parameters.

Thus, acetylation of **1** yielded a diacetate **3**. Consequently, ^{13}C substituent shifts are observed throughout the molecules, though most significantly at the vinylidene carbons (upfield 5.3 and downfield 3.1 ppm for the quaternary and methylene carbons, respectively) indicating that one of the hydroxyl functions in **1** is adjacent to the vinylidene group. Oxidation of **1** with manganese dioxide gave an aldehyde **4**: MS M^+248(43)$C_{15}H_{20}O_3$, 204(100); IR($CHCl_3$) cm^{-1}, 1690 (α,β-unsaturated aldehyde); UV(MeOH) 220(3.57), 245(3.61). The proton nmr spectrum ($CDCl_3$) of **4** showed the presence of the aldehyde function δ9.57(1H, s, CHO) and substantial shifts in the vinylidene methylene proton resonances now at δ6.09 and 6.36 (2H, dd, J1.1). Similarly the carbon-13 spectrum exhibited an α,β-unsaturated aldehyde resonance at δ194.12 with concomitant shifts in the vinylidene function δ109.30 and 152.56 in **1** to 133.26 and 153.66 in **4**. Comparison of the ^{13}C shifts in **1**, **3** and **4** enables differentiation, for assignment purposes, between the carbon atoms. Note, for example, that the methyl carbon ^{13}C shifts in the series are nearly constant (∿11.0ppm) for the olefinic methyl but the other methyl group exhibits changes in the diacetate **3** (17.60ppm) compared with **1** and **4** (16.31ppm). The close proximity of the latter methyl group to one of the oxygen functions is thus indicated.

The position and configuration of the secondary alcohol substituent in **1** follows from: First, the facile dehydration of **1** using 5% KOH/MeOH yields a cross-conjugated dienone **5**: MS M^+ 232(58) $C_{15}H_{20}O_2$, 214(31), 199(100); UV(MeOH) 238(3.93), 264(3.77). The proton nmr spectrum of **5**($CDCl_3$) showed additional olefinic resonances at δ6.73 and 6.19 (2H, dd, J10.0, CH=CH). The ^{13}C spectrum ($CDCl_3$) also showed the additional olefinic group δ156.62 and 125.77 with loss of the hydroxymethine and methylene resonances at δ74.55 and 42.49 in **1**. Further, the ^{13}C shifts of the carbonyl carbon δ186.32 in **5** is typical of a cross-conjugated dienone.[4] The ^{13}C shifts given in the Table for the A-ring in **5** correspond closely to those in α-santonin **6**[4]. Secondly, base catalysed deuterium exchange of **1** (0.1M methoxide, ^2H_2O) produced a product the proton spectrum of which lacked a signal at δ2.62, while the dd pattern at δ3.8 in **1** was reduced to a singlet. The ^{13}C spectrum showed "washing out" of the signal at δ42.49 with reduction in intensity of the signal at δ41.33, the consequence of ^2H exchange at C-2 and reduction of the nuclear Overhauser enhancement at C-10 now coupled $^3J_{C^2H}$ to C-2. It is noteworthy that no deuterium exchange

Table

^{13}C Chemical Shifts of Heterophyllol (1) and Related Compounds

	δ ^{13}C ppm. (TMS)				
C-position	1	3	4	5	6[3]
1	74.55	75.34	74.48	156.62	155.1
2	42.49	41.11	42.47	125.77	125.9
3	197.17	195.55	197.01	186.32	186.0
4	129.75	130.27	130.11	129.02	128.4
5	161.04	159.56	160.01	159.64	151.5
6	(27.18)	(26.67)	(26.34)	(26.52)	81.5
7	40.95	39.23	37.58	42.07	54.0
8	(33.25)	(32.83)	(32.51)	(32.88)	23.3
9	37.88	37.51	36.2_2	37.70	39.3
10	41.33	40.10	41.23	40.06	41.7
11	152.56	147.34	153.66	151.92	41.2
12	65.22	66.02	194.12	64.64	-
13	109.31	112.35	133.26	108.88	-
4'	11.03	11.07	11.0_3	10.25	10.9
10'	16.31	17.60	16.27	23.33	25.3
C=O(OAc)	-	170.61, 170.12	-	-	-
CH_3(OAc)	-	21.00, 20.94	-	-	-

Parentheses indicate reverse assignment possible.

ccurred at C-6, presumably the consequence of steric-hindrance by the olefinic methyl group at C-4. The configuration of the C-1 function in **1**, **3** and **4** follows from the *vicinal* couplings between H-1 and H-2e,2a (*av*. 6.0 and 12.0Hz), the larger being an axial-axial value, making the oxygen functional group equatorial. The *geminal* coupling $^2J_{2e,2a}$ (16.4Hz) was only distinguishable in **3**.

With the exception of the features already discussed the proton nmr spectra of heterophyllol **1** and its derivatives **3**-**5** are quite complex (due to overlap) even at high field (270MHz)[5]. The protons H-6 through H-9 form a complex coupled 7-spin system, with overlap occurring at ∿δ2.6 with the ABX system associated with H-2e,2a and H-1. However, homonuclear decoupling experiments[6] on the more resolved spectrum of the aldehyde **4** enable determination of the regions associated with the geminal protons and the methine attributable to H-7. Thus, in **4** the assignments are δ2.85 (1H, dq, J13.5, 3.0, 2.0Hz, H-6e), 2.61 (4H, m, H-2a,2e, H-7a, H-8e), 2.19 (1H, dt, J13.0, 3.3, 3.3Hz, H-9e), 2.10 (1H, overlapping pair of dd, J13, 13, 2Hz, H-6a), 1.66 (1H, qd, J13.0, 12.4, 12.0, 3.0Hz, H-8a), and 1.43 (1H, td, J13.0, 13.0, 4.5Hz, H-9a). In **1** there is more overlap in the region attributed to H-6a, H-9e, while H-6e appears to be a simpler dd pattern. Analysis of the larger coupling magnitudes listed requires a number of *geminal* and axial-axial interactions only met with if the conformation of the B-ring is a chair with the C-7 substituent in the *equatorial* configuration. In particular, the three large couplings (1 geminal, 2 axial-axial) at H-8a and two large couplings (1 geminal, 1 axial-axial) at H-6a demand this stereochemistry. At this juncture an analysis of the long range couplings would add little to the conclusions.

References and Notes

1. Herbarium accession number CHR 354426 (Parsonsia heterophylla), Botany Division, DSIR, Private Bag, Christchurch, New Zealand.
2. H. Hikino, C. Konno, Y. Ikeda, N. Izumi, T. Takemoto, *Chem. Pharm. Bull.*, *23*, 1231 (1975)
3. D. H. Marr and J. B. Stothers, *Can. J. Chem.*, *43*, 596 (1965)
4. P. S. Pregosin, E. W. Randall, T.B.H. McMurry, *J.C.S. Perkin I*, 299 (1972)
5. All ^{1}H and ^{13}C spectra were determined at 270MHz and 67.89MHz, respectively, using a Bruker HFX-270 spectrometer in the Fourier mode.
6. As an example of the homonuclear decoupling experiments irradiation at the overlapped region at δ2.6(H-2a,2e, H-7a, H-8e) produced the following changes: δ3.8(s, H-1a), 2.85(dd, J∿13, 2Hz, H-6e), 2.10 (bdd, J∿13, 2Hz, H-6a), 1.66 (btd, J∿13, 12, 3Hz, H-8a).

Acknowledgements: We thank Dr. R. Hodges for the high resolution mass spectrum and Mr. A. P. Druce for identification of the plant specimen.

(Received in USA 16 May 1979)