Two-dimensional nuclear magnetic resonance of sesquiterpenes. 4— Application to complete assignment of 1H and 13C NMR spectra of some aromadendrane derivatives

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The total assignment of the 1H and 13C NMR spectra of five aromadendrane derivatives, (+)-aromadendrene (1), (−)-alloaromadendrene (2), (+)-ledene (3),

(−)-dehydroaromadendrane (4), (−)-globulol (5) and (+)-viridiflorol (6) has been performed. The 13C spectral assignment of globulol was achieved from DEPT and double quantum coherence measurements. The concerted application of 1H–1H homonuclear and 1H–13C heteronuclear two-dimensional chemical shift correlations provided other 13C and all 1H chemical shifts. Moreover, the 1H assignment for compounds 1–3 was reexamined from the high-field analysis of proton–proton coupling constants.

INTRODUCTION

During the course of our investigations on the chemical composition of niaouli (*Melaleuca viridiflora*) essential oil, we have isolated a sesquiterpene alcohol identified as (+)-viridiflorol (6) (Fig. 1).[1] Within the context of our NMR studies on sesquiterpene compounds,[2-5] the complete 1H and 13C NMR chemical shift assignments, using two-dimensional techniques, are presented for 6 and five related aromadendrane derivatives, (+)-aromadendrene (1), (−)-alloaromadendrene (2), (+)-ledene (3), (−)-dehydroaromadendrane (4) and (−)-globulol (5). The

knowledge of the 1H and 13C NMR chemical shifts of such tricyclo[6.3.0.0^{2,4}]undecane skeletons, commonly found in the hydrocarbon fraction of essential oils, should be useful in the determination of new sesquiterpenic structures.

EXPERIMENTAL

Compounds 1–5 were purchased from Fluka. (+)-Viridiflorol (6) was obtained from niaouli (*Melaleuca viridiflora*) leaves. The isolation and purification of 6 from the niaouli essential oil (obtained from the leaves by steam distillation) was achieved according to a reported process.[1]

Carbon-13 and two-dimensional spectra were recorded on a Bruker AM-200 spectrometer and 1H conventional NMR spectra were obtained on a Bruker AM-400 apparatus. The NMR spectra were measured as solutions in chloroform-*d* in 10- and 5-mm o.d. tubes for 13C and 1H, respectively. Tetramethylsilane (TMS) was used as internal standard in both measurements. Proton–proton coupling constants were extracted from high-field resolution-enhanced 1H spectra using the Gaussian multiplication technique.[6] Resonance multiplicities for 13C were established via the acquisition of DEPT spectra obtained for proton pulses $P = 90°$ (CH only) and $P = 135°$ (CH and CH_3 differentiated from CH_2). For the DEPT sequence,[7] the width of a 13C 90° pulse was 13 µs, the width of a 1H 90° pulse was 29 µs and the $(2J)^{-1}$ delay was set equal to 3.7 ms.
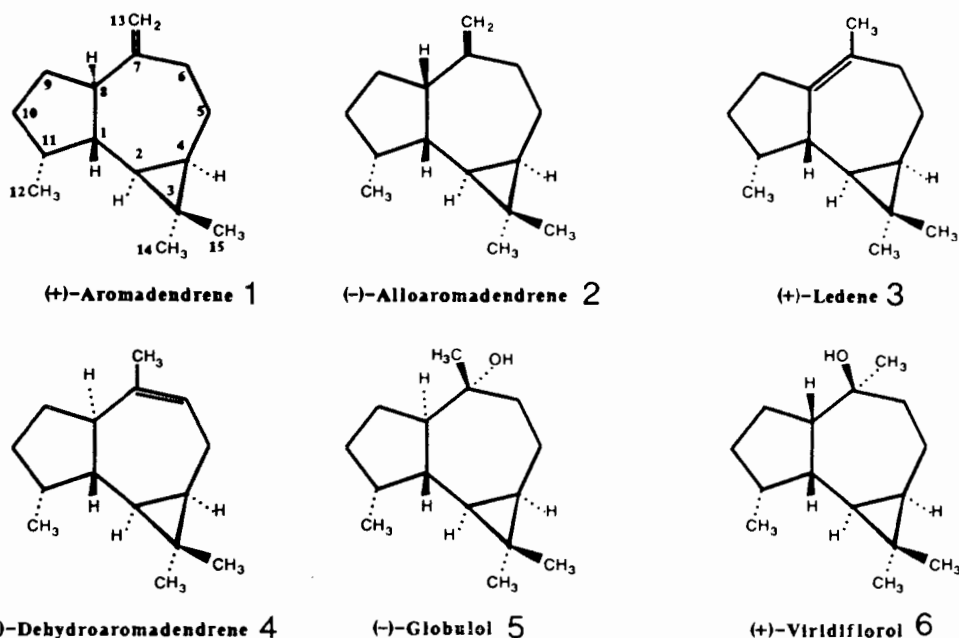

Figure 1. Structures of aromadendrane derivatives 1–6: (+)-aromadendrene (1), (−)-alloaromadendrene (2), (+)-ledene (3), (−)-dehydroaromadendrane (4), (−)-globulol (5) and (+)-viridiflorol (6).

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The homonuclear ^1H–^1H shift correlated two-dimensional diagrams were obtained using the COSY-45 pulse sequence.[8–10] The spectral widths were $F_2 = 1500$ and $F_1 = \pm750$ Hz, allowing a digital resolution of 1.47 Hz. The spectra were collected as 2048×1024 blocks of data and were processed by sinusoidal multiplication in each dimension, followed by symmetrization of the final data matrix. Other parameters were as follows: number of increments in t_1, 512; scans, 32; phase cycling, 16; and relaxation delay, 1 s.

The heteronuclear two-dimensional ^1H–^{13}C chemical shift correlation experiments were obtained with proton decoupling in the F_1 dimension[11,12] (XHCORRD in the operating Bruker software). The spectra were acquired with $4K \times 256$ data points and a

data acquisition of 512×128 increments in t_1 and a zero filling in the F_1 dimension. Spectral widths of 8600 and ±750 Hz were employed in the F_2 (^{13}C) and F_1 (^1H) domains, respectively. Data were processed using unshifted sine-bell functions for weighting in both dimensions. The refocusing delay was 1.85 ms, the mixing delay 3.7 ms, the relaxation delay 1 s and sixteen phase cycling steps were employed.

The two-dimensional ^{13}C–^{13}C double quantum coherence spectrum[13,14] was acquired using spectral widths of 4400 Hz, a 32-step phase cycling and data acqustion of 704×128 increments in t_1 to provide, after zero filling in the F_1 dimension, a matrix of 8192×256. Data files were processed using exponential broadening in both dimensions. The delay for the creation of the double

quantum coherence was 7.1 ms, corresponding to a coupling of 35 Hz, and the relaxation delay was 2 s.

RESULTS AND DISCUSSION

The carbon and proton chemical shifts for aromadendrane derivatives 1–6 are given in Tables 1 and 2, respectively.

The complete assignment of the carbons in the ^{13}C NMR spectrum of globulol (5) follows from the 2D-INADEQUATE pulse sequence which establishes the carbon bonding pattern in the molecule. In the carbon–carbon connectivity plot, the C-2—C-4 bond is missing because on the one hand it forms a strongly coupled AB system,[15] and on the other our experiment

Table 1. ^{13}C NMR chemical shifts of aromadendrane derivatives 1–6[a]

Carbon	1[b]	2	3	4	5	6
C-1	44.01	42.24	40.25	42.74	39.68	39.85
C-2	29.32	23.59	30.68	26.72	28.55	22.52
C-3	19.94	17.23	18.64	18.86	19.33	18.43
C-4	27.71	24.87	25.83	26.53	26.93	28.71
C-5	24.92	22.20	22.41	23.28	20.24	18.90
C-6	39.17	35.76	36.82	121.93	44.73	37.91
C-7	154.00	152.32	124.60	139.31	75.06	74.48
C-8	53.80	50.84	139.80	49.99	57.16	58.36
C-9	29.53	28.27	31.79	32.45	26.29	25.85
C-10	35.23	31.26	32.88	31.33	34.69	29.26
C-11	35.44	37.86	37.48	34.26	36.42	38.53
C-12	17.15	16.44	15.77	18.18	16.09	16.33
C-13	105.66	109.78	21.82	24.88	20.24	32.14
C-14	28.74	28.65	28.53	28.72	28.71	28.71
C-15	15.75	15.89	15.68	15.31	15.80	16.12

[a] In ppm from TMS.
[b] Values from Ref. 4.

Table 2. ^1H NMR chemical shifts of aromadendrane derivatives 1–6[a]

Proton	1	2	3	4	5	6
H-1	1.39	1.86	2.56	1.76	1.23	1.84
H-2	0.62	0.24	0.66	0.57	0.51	0.11
H-4	0.70	0.55	0.55	0.83	0.59	0.61
H-5	1.98 (α), 1.02 (β)	1.84 (α), 1.24 (β)	1.72, 1.64	2.08	1.79 (α), 0.91 (β)	1.60 (β), 1.45 (α)
H-6	2.43 (β), 2.08 (α)	2.34 (α), 2.28 (β)	2.25 (β), 2.19 (α)	5.35	1.73, 1.53	1.66, 1.57
H-8	2.24	2.65	—	2.32	1.91	1.80
H-9	1.70 (α), 1.59 (β)	1.88, 1.73	2.40 (α), 2.06 (β)	1.96, 1.18	1.78, 1.43	1.63, 1.57
H-10	1.88 (β), 1.21 (α)	1.73 (β), 1.32 (α)	1.66 (β), 1.23 (α)	1.99, 1.13	1.67 (β), 1.24 (α)	1.78 (β), 1.27 (α)
H-11	2.12	2.07	2.03	2.10	2.02	1.98
H-12	0.94	0.94	0.95	0.90	0.92	0.93
H-13	4.64	4.74, 4.71	1.57	1.67	1.09	1.14
H-14	1.06	1.01	0.99	1.05	1.01	1.03
H-15	1.00	0.96	1.06	1.02	0.98	1.00

[a] In ppm from TMS.

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was optimized for the detection of sp^3–sp^3 carbon connections [$^1J(CC) = 35$ Hz]. One bond carbon–carbon coupling constants for 5 are presented in Table 3.

A heteronuclear shift correlated experiment with proton decoupling in the F_1 dimension was then performed on 5. This two-dimensional diagram gives the correspondence between peaks in the ^{13}C spectrum and the signals for the directly bonded proton in the ^1H spectrum. Therefore, from the slices of the chemical shift correlation diagram, it is possible to assign easily the entire proton spectrum. A similar scheme was applied in the determination of the proton network of aromadendrene (1) using our previously reported ^{13}C assignment[4] for this compound.

The ^1H and ^{13}C spectral parameters for sesquiterpenes 2–5 were deduced from the concerted application of homonuclear and heteronuclear chemical shift correlations, which establishes proton assignments from the evidence of proton–proton couplings and then correlates these assignments with the ^{13}C spectrum. In this respect, information similar to that available from the concerted use of carbon–carbon and carbon–proton connectivity experiments can be obtained.

Stereochemical assignments of the proton resonances for 1–3 had been carried out from the ^1H NMR spectra obtained at 400 MHz and analysed as first order; the resulting proton–proton coupling constants are presented in Table 4. Finally, for all these derivatives, examination of Dreiding models suggested that only the C-15 methyl experiences shielding γ-gauche steric interaction,[16]

Table 3. Natural abundance one-bond ^{13}C—^{13}C coupling constants in globulol (5) determined from double quantum coherence

Pairs of carbons	^1J (Hz)
1–2	45.3
1–8	32.3
1–11	33.3
2–3	14.6
3–4	14.6
3–14	43.3
3–15	44.9
4–5	43.3
5–6	33.3
6–7	37.8
7–8	38.3
7–13	40.6
8–9	33.4
9–10	32.7
10–11	32.8
11–12	36.1

Table 4. ^1H–^1H coupling constants for aromadendrane derivatives 1–6

Pairs of protons	1	2	3	4	5	6
			^2J (Hz)			
5α–5β	−14.3	−14.4				
6α–6β	−13.3	−13.7	−18.0			
9α–9β	−11.6		−16.5			
10α–10β	−11.9		−11.8			
			^3J (Hz)			
1–2	11.0	10.9	10.9	11.4	10.8	9.5
1–8	10.6	6.6				
1–11	10.5	9.9	8.6			
2–4	9.4	9.3	9.5	9.4	9.5	9.5
4–5α	5.9	5.9	5.3	7.0	6.0	6.1
4–5β	10.9	10.9	11.1	10.3	11.2	11.1
5α–6α	1.8	6.6				
5α–6β	6.1	4.3				
5β–6α	13.3	9.5	10.0			
5β–6β	1.4	7.0				
8–9α	5.8	8.2				
8–9β	10.6	9.8				
9α–10α	5.9		7.1			
9α–10β	2.2		5.8			
9β–10α	11.5		10.1			
9β–10β	6.0		5.0			
10α–11	10.0	9.9	10.1			
10α–12	6.2	8.0	5.9			
11–12	7.4	6.7	7.0	6.8	6.7	6.6

allowing the ^{13}C assignment of both gem-methyl groups from chemical shift considerations.

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