Pergamon

PII: S0031-9422(96)00863-1

Phytochemistry, Vol. 45, No. 3, pp. 537–544, 1997

0031-9422/97 $17.00+0.00

OXYGENATED BISABOLANES FROM *ALPINIA DENSIBRACTEATA*

LAI-KING SY and GEOFFREY D. BROWN*

Department of Chemistry, The University of Hong Kong, Pokfulam Rd, Hong Kong

(*Received in revised form* 11 *November* 1996)

Key Word Index—*Alpinia densibracteata*; Zingiberaceae; bisabolane sesquiterpenes; menthane monoterpenes.

Abstract—Seven novel oxygenated bisabolane sesquiterpenes and four oxygenated menthane monoterpenes have been isolated from the dichloromethane extract of *Alpinia densibracteata* in addition to known bisabolanes and menthanes. The structures of these compounds were established by NMR spectroscopy and by some chemical transformations.

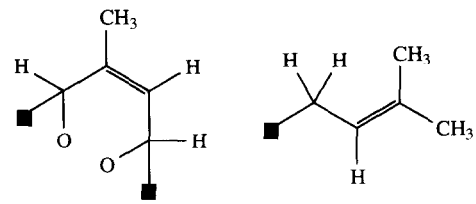
INTRODUCTION

Alpinia densibracteata T.L. Wu and Senjen is a perennial herb found growing in shady woodland in Hong Kong. No previous chemical studies have been undertaken with *A. densibracteata*, although chemical investigation of other members of the genus *Alpinia* have indicated the presence of diarylheptanes, labdane diterpenes, various classes of sesquiterpenes and menthane monoterpenes [1].

RESULTS AND DISCUSSION

Extraction of the aerial parts of *A. densibracteata* with CH_2Cl_2 afforded two stereoisomeric endoperoxides **1** and **2**. Mass spectroscopic analysis of these compounds proved difficult. Thus, HREIMS of **1** showed only weak ions at m/z 220 $[M-16]^+$ and 204 $[M-32]^+$ (molecular formula $C_{15}H_{24}O$ and $C_{15}H_{24}$, respectively), whilst CIMS gave a relatively low intensity molecular ion at m/z 237 $[M+1]^+$. The diagnostic region of the IR spectrum of **1** showed only peaks due to sp^2 and sp^3 carbon–hydrogen bonds and carbon–carbon double bonds (1684; 1663 cm^{-1}). ^{13}C NMR and DEPT confirmed the presence of 15 carbons with 24 directly attached protons; whilst a more detailed analysis of chemical shifts indicated the presence of four alkene ($\delta^{13}C$ 141.3 C, 131.3 C, 126.0 CH and 124.6 CH) and only two oxygenated methine carbons ($\delta^{13}C$ 76.1 CH and 73.0 CH). In consequence, compound **1** must contain two double bonds, in addition to the two oxygen atoms of an endoperoxide linkage and an additional carbocyclic ring to satisfy the fourth double bond equivalent required by the molecular formula $C_{15}H_{24}O_2$.

Analysis of the chemical shifts and coupling constants for those signals which were clearly resolved in the ^1H spectrum such as the alkene protons (δ^1H 6.31 and 5.10), oxygenated methines (δ^1H 4.58 and 4.38) and methyl singlets (δ^1H 1.93, 1.68 and 1.60), in collaboration with the results of ^1H–^1H COSY, established the following sub-structures:



These two sub-structures and the remaining methyl, two methylene and two methine groups were unambiguously assembled into structure **1** by means of single bond and long range ^{13}C–^1H correlations and ^1H–^1H COSY experiments (^{13}C and ^1H data reported in Table 1).

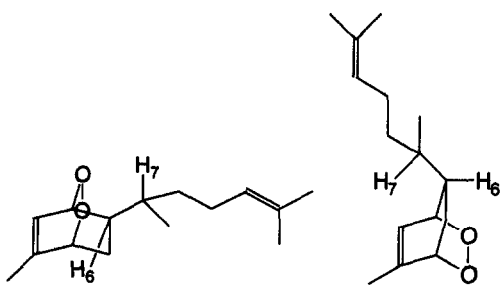
As was the case for compound **1**, compound **2** showed only $[M-16]^+$ and $[M-32]^+$ peaks under HREIMS, and gave a surprisingly low intensity $[M+1]^+$ signal in CIMS. Compound **2** was of very similar polarity to **1** and showed an identical pattern of connectivities in ^1H–^1H and ^{13}C–^1H correlation experiments. The most significant differences between the two compounds were noted in the ^1H chemical shifts at positions 6 and 7 (Table 1). H-6 in compound **1** was shifted strongly upfield as compared with **2**, consistent with its location in the shielding region of the endocyclic double bond in **1**. Conversely, H-7 was strongly shielded in **2** as compared with **1**, indicating

* Author to whom correspondence should be addressed.

Table 1. NMR data for compounds **1–4** ($CDCl_3$)

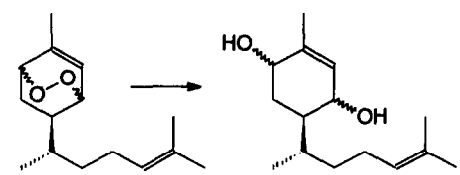
	δ_C*				δ_H†			
Assignment	**1**	**2**	**3**	**4**	**1**	**2**	**3**	**4**
1	73.0	73.9	73.1	73.6	4.58	4.60	4.56	4.59
2	126.0	122.9	126.0	122.8	6.31	6.18	6.32	6.20
3	141.3	142.0	141.3	142.2				
4	76.1	75.7	76.1	75.6	4.38	4.43	4.38	4.43
5	27.4	28.4	27.8	28.5	1.82	2.30	1.82	2.35
					1.70	1.10	1.70	1.10
6	40.0	40.1	41.6	41.7	1.25	2.10	1.10	1.91
7	34.8	36.7	30.5	32.6	1.81	1.05	1.90	1.05
8	34.3	34.5	21.3‡	20.4‡	1.57	1.40	0.99‡	0.89‡
					1.12	1.15		
9	25.0	24.8	20.8‡	19.8‡	2.05	2.05	0.97‡	0.84‡
					1.90	1.90		
10	124.6	124.4	18.6	18.5	5.10	5.05	1.93	1.94
11	131.3	131.6						
12	17.7	17.7			1.60	1.60		
13	25.7	25.7			1.68	1.68		
14	17.4	16.1			0.99	0.81		
15	18.6	18.6			1.93	1.94		

* 125 MHz.
† 500 MHz.
‡ Assignments interchangeable within column.



1 **2**

Fig. 1. Relative stereochemistry of **1** and **2**.



1 *cis* **5**

2 *trans* **6**

Fig. 2. Reduction of the endoperoxide linkage in **1** and **2**.

that H-7 was located in the shielding region of the endocyclic double bond in **2**. These differences are consistent with **2** being diastereoisomeric with **1**: in particular the chemical shifts of H-6 and H-7 suggested that **1** was the *cis*-endoperoxide and **2** was the *trans*-form (Fig. 1).

The presence of an endoperoxide linkage in **1** and **2** was confirmed by $LiAlH_4$ reduction which yielded the 1,4-dihydroxybisaboladienes **5** and **6** (Fig. 2) as identified by 2D-NMR spectroscopy (Table 2). The NMR data for compound **6** were in fair agreement with a dihydroxybisaboladiene of incompletely defined stereochemistry [2] reported previously as a natural product (allowing for some obvious misprints in Table 2 of ref. 2). Compound **5** was also isolated from the extract of *A. densibracteata* as a natural product.

The menthane monoterpene endoperoxides **3** and **4**, which can be considered as the C_{10} analogues of bisabolane sesquiterpene endoperoxides **1** and **2**, were also isolated from the extract and their structures established by 2D-NMR. The data in Table 1 show strong similarities between the NMR spectra for **1** and **3** and also between those of **2** and **4**, suggesting that **3** is the menthane *cis*-endoperoxide and **4** the *trans*-form. These *cis* and *trans* endoperoxides have been obtained previously both by synthesis and as natural products [3–6] and comparison with literature spectra confirmed the identities of **3** and **4** (this is the first report of full NMR data and assignments for these compounds, however).

The absolute stereochemistry of **3** and **4** was established in two ways. Optical rotation values were of opposite sign to those given for the *cis* (1*R*, 4*S*, 6*S*) and *trans* (1*S*, 4*R*, 6*S*) endoperoxides previously isolated as natural products [4]. Thus, **3** and **4** were assigned as mirror image forms 1*S*,4*R*,6*R* and 1*R*,4*S*,6*R*, respectively (they are consequently new as natural products). $LiAlH_4$ reduction of **3** and **4** (cf. Fig. 2) resulted in 1,4-dihydroxymenthenes **7** and **8** as

Table 2. NMR data for compounds **5–8** ($CDCl_3$

	δ_C*				δ_H†			
Assignment	**5**	**6**	**7**	**8**	**5**	**6**	**7**	**8**
1	65.4	69.2	65.0	69.4	4.14	3.96	4.14	3.95
2	125.9	130.0	125.8	129.7	5.69	5.54	5.69	5.54
3	141.9	136.7	142.0	137.0				
4	71.3	68.0	71.2	68.0	4.03	3.97	4.03	3.99
5	30.7	29.8	30.9	30.0	2.06	1.73	2.12	1.75
					1.80	1.45	1.41	1.45
6	43.1	40.6	45.1	42.4	1.27	1.65	1.12	1.57
7	32.9	30.5	28.4	26.5	1.65	1.98	1.69	2.10
8	33.9	35.2	20.9‡	17.2‡	1.72	1.32	0.97‡	0.99‡
					1.60	1.32		
9	25.2	26.1	20.4‡	20.9‡	2.10	2.02	0.99‡	0.86‡
					2.10	2.02		
10	124.8	124.6	18.8	20.4	5.12	5.12	1.81	1.81
11	133.6	131.4						
12	17.7	17.7			1.61	1.61		
13	25.7	25.7			1.69	1.68		
14	17.1	14.4			0.97	0.82		
15	18.8	20.5			1.81	1.81		

*125 MHz.
† 500 MHz.
‡ Assignments interchangeable within column.

expected (fully characterized for the first time by 2D-NMR, Table 2). Comparison of the spectra and optical rotations for **7** (1*S*,4*R*,6*R*) and **8** (1*R*,4*S*,6*R*) agreed with those of *p*-menthenediols reported in the literature from natural and synthetic sources [3, 4, 7–10], thereby confirming the absolute stereochemistry for **3** and **4**. Further analysis of the extract revealed that both **7** and **8** were also present as natural products in *A. densibracteata*.

The absolute stereochemistry at the 6-position for bisabolanes **1** and **2** is assumed to be *R* by analogy with the menthane endoperoxides on biogenetic grounds. The extract also contained the aromatic compound **9**, identified from its NMR spectra and optical rotation ($[\alpha]_D = +23°$) as the known compound (*S*)-α-curcumene [11]. We have assumed that bisabolanes **1** and **2** from *A. densibracteata* have 7*S* stereochemistry since **9** is likely to share a common biosynthetic precursor with **1** and **2**. This stereochemistry for the 6 and 7 positions is also that commonly encountered for bisabolanes from the Zingiberaceae.

In addition to the bisabolane endoperoxides **1** and **2**, the CH_2Cl_2 extract of *A. densibracteata* also afforded three bisabolane hydroperoxides **10–12**. As was the case for the endoperoxides, obtaining good mass spectra for these hydroperoxides was problematic. Compound **10** showed a weak cluster of ions between *m/z* 252 and 254 and clusters of fragment ions between *m/z* 232 and 238, and 217 and 221, which could be ascribed to a molecular formula $C_{15}H_{26}O_3$ incorporating both hydroperoxide and alcohol functional groups. The IR spectrum showed the presence of an OH group, while a full NMR analysis (obtained as previously) established the bisabolane skeleton incorporating double bonds at positions 1 and 9 with oxygenation at 3 and 11 (Table 3). A survey of the literature showed the ^{13}C chemical shift for C-11 (δ 82.1) was consistent with a hydroperoxide (typical values δ_C 81.8–81.9 ppm) [12, 13] rather than an alcohol function (typical values δ 70.6–70.8 ppm) [13–16].

Compound **11** was of comparable polarity to **10** and gave a similar mass spectrum. 2D-NMR analysis established a bisabolane skeleton with unsaturation at positions 1 and 11 and oxygenation at 3 and 10. ^1H and ^{13}C chemical shifts at the 10 position (and also for neighbouring positions) were consistent with substitution of a hydroperoxide group (typical values δ^1H 4.2–4.5; $\delta^{13}C$ 89.8–90.3) [13, 17–19] rather than a hydroxyl group (typical values δ^1H 3.9–4.1; $\delta^{13}C$ 75.1) [13, 19].

Compound **12** was identified as a bisabolatriene incorporating an 11-hydroperoxide group (as for **10**), with an additional exocyclic double bond as compared with **10** and hydroxylation at the 4-position rather than the 3-position. Analysis of the ^1H NMR coupling constants showed that the Δ^9-double bond was *trans* and the absence of large couplings for H-4 demonstrated that this proton was *pseudo*-equatorial (consequently 4-OH was axial).

Compound **13** gave a molecular ion corresponding to molecular formula $C_{15}H_{26}O_2$ and its structure was established as a 3,4-dihydroxybisaboladiene by 2D-NMR as previously (Table 4). Partial NMR data

Table 3. NMR data for compounds **10–12**($CDCl_3$)

	δ_C*			δ_H†		
Assignment	**10**	**11**	**12**	**10**	**11**	**12**
1	133.5	133.9	136.1	5.65	5.59	5.71
2	133.7	133.7	126.4	5.59	5.67	6.11
3	67.5	67.4	145.0			
4	37.1	37.2	70.0	1.85	1.85	4.46
				1.55	1.52	
5	20.7	20.4	28.4	1.56	1.52	1.90
				1.52	1.48	1.40
6	40.3	40.4	32.9	2.02	2.02	2.65
7	36.8	36.8	35.5	1.65	1.55	1.85
8	37.2	30.0	37.7	2.14	1.40	2.12
				1.97	1.40	2.02
9	130.7	28.9	130.4	5.68	1.65	5.64
					1.45	
10	134.6	89.8	135.4	5.54	4.30	5.58
11	82.1	143.8	81.5			
12	24.4‡	17.2	25.3‡	1.32‡	1.73	1.28‡
13	24.2‡	114.3	22.5‡	1.34‡	5.03	1.38‡
					5.02	
14	16.3	15.8	15.6	0.87	0.83	0.84
15	29.7	29.7	113.8	1.29	1.28	5.02; 4.95

* 125 MHz.
† 500 MHz.
‡Assignments interchangeable within column.

Table 4. NMR data for compounds **13–15** ($CDCl_3$)

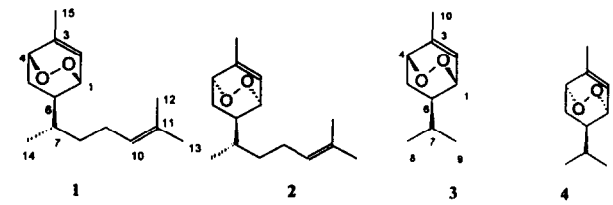
	δ_C*			δ_H†		
Assignment	**13**	**14**	**15**	**13**	**14**	**15**
1	133.1	132.1	69.2	5.66	5.71	4.03
2	131.8	132.0	125.7	5.61	5.61	5.39
3	70.7	71.2	137.4			
4	73.6	73.5	30.5	3.79	3.81	2.00
						1.92
5	27.4	28.8	20.9	1.83	1.83	1.62
				1.70	1.73	1.30
6	36.5	38.6	46.5	2.30	2.15	1.32
7	36.3	32.0	31.0	1.61	1.72	1.92
8	34.2	20.0‡	35.5	1.40	0.92‡	1.32
				1.24		1.32
9	25.9	19.9‡	26.2	2.05	0.93‡	2.00
				1.88		2.00
10	124.5	23.5	124.8	5.09	1.30	5.12
11	131.6		131.2			
12	17.7		17.7	1.61		1.61
13	25.7		25.7	1.69		1.68
14	16.2		14.4	0.87		0.82
15	23.8		23.1	1.31		1.67

* 125 MHz.
† 500 MHz.
‡ Assignments interchangeable within column.

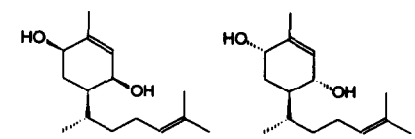
reported for both 6*R* and 6*S* *trans*-3,4-dihydroxybisaboladienes [2, 20] were almost identical with **13**, and gave good agreement with our full assignments (**13** is assumed to be 6*R* by analogy with other bisabolanes isolated from *A. densibracteata*). Compound **14** was identified as the menthane dihydroxy analogue of **13**, since it gave almost identical ^{13}C and ^{1}H resonances to **13** (assigned by 2D-NMR techniques) for

positions on and around the cyclohexane ring (Table 4). Several diastereoisomeric 3,4-dihydroxymenthenes have been reported previously as natural products [21], although there is limited NMR data available for comparison. Compound **15** was isolated as an inseparable mixture with nerolidol. In spite of this, it was still possible to assign all ^{13}C and ^{1}H resonances in **15** by application of high-resolution 2D-NMR spectroscopy. H-1 in **15** presented a broad peak containing unresolved couplings with an appearance comparable to that of H-1 in **5**. The stereochemistry for the 1-OH group in **15** has been tentatively assigned on this basis.

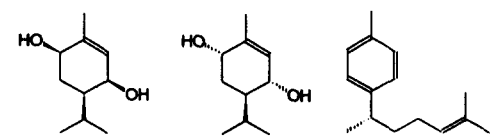
Compounds **16** and **17** were identified as cinnamate esters of 2-hydroxycineole. Both compounds showed strong molecular ions in HREIMS corresponding to the molecular formula $C_{19}H_{24}O_3$. Chemical shift for NMR resonances associated with the cinnamate moiety were nearly identical between **16** and **17**, whilst the most significant differences in the chemical shifts for the cineole portion (assigned from 2D-NMR spectra)



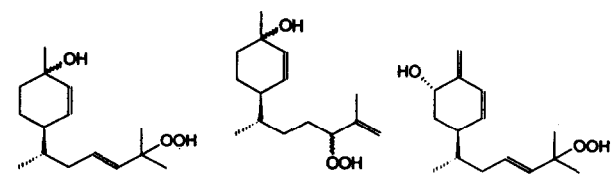
1 **2** **3** **4**



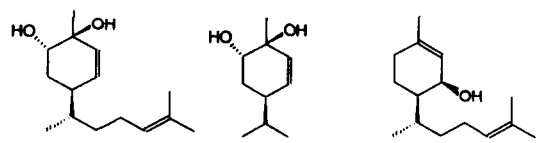
5 **6**



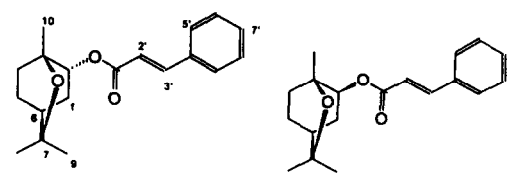
7 **8** **9**



10 **11** **12**



13 **14** **15**



16 **17**

Table 5. NMR data for compounds **16** and **17** ($CDCl_3$)

	δ_C*		δ_H†	
Assignment	**16**	**17**	**16**	**17**
1	32.8	32.4	2.70; 1.40	2.15; 1.98
2	72.9	73.0	4.83	4.81
3	71.0	71.1		
4	26.1	29.8	1.95; 1.65	1.82; 1.55
5	22.0	21.9	2.05; 1.55	2.05; 1.45
6	33.9	33.4	1.60	1.55
7	73.8	73.8		
8	28.6	28.9	1.31	1.30
9	28.9	28.1	1.26	1.34
10	24.3	23.1	1.10	1.11
1′	166.5	166.9		
2′	118.4	118.5	6.43	6.52
3′	144.8	144.8	7.67	7.72
4′	134.3	134.5		
5′/9′	128.1	128.1	7.54	7.53
6′/8′	128.9	128.9	7.39	7.38
7′	130.3	130.3	7.39	7.38

* 125 MHz.
† 500 MHz.

occurred for protons at H-1 (Table 5). This suggested that **16** and **17** were diastereoisomeric with respect to the orientation of the 2-cinnamate substituent. A small coupling (J = 1.9 Hz) was observed for H-2 in **16**, in addition to the two larger couplings expected with H-1, but no such coupling was noted for **17**. This coupling must be due to a four-bond interaction with a proton in the 4-methylene group. Such long-range coupling is only favoured if the coupling protons can adopt a 'W'-conformation, i.e. if H-2 is equatorial in **16**, requiring a *trans* stereochemistry for the epoxide linkage and the cinnamate substituent. The proposed stereochemistry was confirmed by NOESY experiments which demonstrated an enhancement between H-2 and the 9-methyl for compound **16** but not for **17**.

EXPERIMENTAL

General. ^{1}H(500 MHz) and ^{13}C(125 MHz) NMR; $CDCl_3$ with TMS as int. standard single-bond and long-range ^{13}C-^{1}H correlation experiments (HETCOR) were normally recorded with 1024 data points in F_2 and 256 points in F_1, whilst high resolution experiments had 4096 data points in F_2 and 1024 data points in F_1. PFG-HSQC and PFG-HMBC spectra were normally recorded with 2048 data points in F_2 and 128 data points in F_1, whilst high resolution experiments had 8192 data points in F_2 and 1024 data points in F_1. EI-MS: 70 eV; FTIR: CCl_4; TLC: plates were visualized using *p*-anisaldehyde; HPLC: PREP-SIL 20 mm × 25 cm column, flow rate 8 ml min^{-1}.

Isolation of compounds **1–5**, **7–18**. Extraction of the aerial parts of *A. densibracteata* (1 kg) collected whilst fruiting in October from Pokfulam Country Park on Hong Kong Island with CH_2Cl_2, followed by drying and rot. evap. yielded a green gum (14.71 g w/w, 1.47%). The various components of the extracts were isolated by CC followed by HPLC: **1** (48.4 mg; 3% EtOAc–97% hexane), **2** (18.7 mg; 3% EtOAc–97% hexane), **3** (22.7 mg; 3% EtOAc–97% hexane), **4** (22.9 mg; 3% EtOAc–97% hexane), **5** (4.5 mg; 50% EtOAc–50% hexane–1% AcOH), **7** (4.1 mg; 50% EtOAc–50% hexane–1% AcOH), **8** (6.1 mg; 50% EtOAc–50% hexane–1% AcOH) **9** (31.6 mg; hexane), **10** (8.3 mg; 25% EtOAc–75% hexane), **11** (2.5 mg; 25% EtOAc–75% hexane), **12** (2.6 mg; 25% EtOAc–75% hexane), **13** (10.5 mg; 50% EtOAc–50% hexane), **14** (10.3 mg; 50% EtOAc–50% hexane), **15** (13.1 mg; 15% EtOAc–85% hexane), **16** (6.6 mg; 15% EtOAc–85% hexane), **17** (7.8 mg; 25% EtOAc–75% hexane).

A voucher specimen of the plant is deposited in the University of Hong Kong Herbarium (GDBROWN 95/2).

1,4-*Epidioxy-bisabola*-2,10-*diene* (1S,4R,6R) (**1**). Colourless oil, $[\alpha]_D$ −3.5° ($CHCl_3$; *c*4.4). IR ν_{max} cm^{-1}: 2968, 2931, 2914, 2856, 1684, 1663, 1445, 1381, 1263; HREIMS *m/z* (rel. int.): 220.1825 [M − 16, Δ = 0.2 mmu for $C_{15}H_{24}O$] (0.3); 204.1871 [M − 32, Δ = 0.7 mmu for $C_{15}H_{24}$] (8), 161 (30), 132 (40), 120 (80), 109 (100), 105 (50); CIMS *m/z*: 237 [M + 1]$^+$ (26), 220 (54), 177 (40), 147 (28), 135 (62), 119 (100), 109 (100); ^{1}H NMR δ ($CDCl_3$): 6.31 (1H, *d*, *J* = 6.5 Hz), 5.10 (1H, *t*, *J* = 7.1 Hz), 4.58 (1H, *d*, *J* = 6.5 Hz), 4.38 (1H, *d*, *J* = 1.5 Hz), 2.05 (1H, *m*), 1.93 (3H, *d*, *J* = 1.4 Hz), 1.68 (3H, *s*), 1.60 (3H, *s*), 1.25 (1H, *td*, *J* = 10.5, 4.8 Hz), 0.99 (3H, *d*, *J* = 6.7 Hz).

1,4-*Epidioxy-bisabola*-2,10-*diene* (1R,4S,6R) (**2**). Colourless oil, $[\alpha]_D$ = +0.6°C ($CHCl_3$; *c* 1.8). IR ν_{max} cm^{-1}: 2968, 2914, 2855, 1446, 1379; HREIMS *m/z*

(rel. int.): 220.1826 [M−16, Δ = 0.3 mmu for $C_{15}H_{24}O$] (0.3), 204.1882 [M−32, Δ = −0.4 mmu for $C_{15}H_{24}$] (12), 161 (6), 119 (100); 109 (6); CIMS *m/z* 237 $[M+1]^+$ (42), 219 (49), 203 (100), 161 (16), 147 (10), 135 (28), 119 (40), 109 (35), ^{1}H NMR δ ($CDCl_3$): 6.18 (1H, *td*, *J* = 2.6, 1.8 Hz), 5.05 (1H, *m*), 4.60 (1H, *m*), 4.43 (1H, *dd*, *J* = 4.3, 1.8 Hz), 2.30 (1H, *m*), 1.94 (3H, *d*, *J* = 1.6 Hz), 1.68 (3H, *s*), 1.60 (3H, *s*), 0.81 (3H, *d*, *J* = 6.6 Hz).

1,4-*Epidioxy*-p-*menth*-2-*ene* (1S,4R,6R) (**3**). Colourless oil, $[\alpha]_D = +18.8°$ ($CHCl_3$; *c* 1.5). IR ν_{max} (cm^{-1}): 2963, 2939, 2914, 1447, 1271; EIMS *m/z* (rel. int.): 136 $[M-32]^+$ (50), 119 (30), 93 (100); CIMS 169 $[M+1]^+$ (30), 151 (35), 136 (100), 123 (30); ^{1}H NMR δ ($CDCl_3$) 6.32 (1H, *dt*, *J* = 6.4, 1.6 Hz), 4.56 (1H, *d*, *J* = 6.4 Hz), 4.38 (1H, *dd*, *J* = 3.5.1.7 Hz), 1.93 (3H, *d*, *J* = 1.6 Hz), 1.82 (1H, *dt*, *J* = 13.4, 4.2 Hz), 1.70 (1H, *ddd*, *J* = 13.2, 10.7, 2.3 Hz), 1.10 (1H, *ddd*, *J* = 20.7, 4.8, 1.1 Hz), 0.99 (3H, *d*, *J* = 7.2 Hz), 0.97 (3H, *d*, *J* = 7.0 Hz).

1,4-*Epidioxy*-p-*menth*-2-*ene* (1R,4S,6R) (**4**). Colourless oil, $[\alpha]_D = +22.2°$ ($CHCl_3$; *c* 1.7). IR ν_{max} (cm^{-1}): 2963, 2937, 2912, 2874, 1470, 1445, 1286; CIMS *m/z* (rel. int.): 151 (20), 136 (100), 123 (20); ^{1}H NMR δ ($CDCl_3$): 6.20 (1H, *m*), 4.59 (1H, *m*), 4.43 (1H, *m*), 1.94 (3H, *s*), 1.91 (1H, *m*), 0.89 (3H, *d*, *J* = 6.5 Hz), 0.84 (3H, *d*, *J* = 6.6 Hz).

3-*Hydroxy*,11-*hydroperoxy*-*bisabola*-1,9-*diene* (**10**). Gum. IR ν_{max} cm^{-1}: 3360, 2964, 2922, 2871, 1459, 1377; EIMS *m/z*: 252–254 (1), 232–238 (5), 217–221 (10), 203 (27), 161 (17), 147 (27), 138 (63), 109 (100); ^{1}H NMR δ ($CDCl_3$: 5.60 (4H, *m*), 2.14 (1H, *dt*, *J* = 13.9, 6.9 Hz), 1.97 (1H, *dt*, *J* = 13.9, 7.0 Hz), 1.34 (3H, *s*), 1.32 (3H, *s*), 1.29 (3H, *s*), 0.87 (3H, *d*, *J* = 6.9 Hz).

3-*Hydroxy*-10-*hydroperoxy*-*bisabola*-1,10-*diene* (**11**). Gum. IR ν_{max} cm^{-1}: 3350 *br*, 2964, 2932, 2872, 1450, 1375, 1263; EIMS *m/z* (rel. int.): 252–254 (1), 232–238 (5), 218–222 (8), 153 (42), 132 (100), 109 (54); ^{1}H NMR δ ($CDCl_3$: 5.67 (1H, *d*, *J* = 10.0 Hz), 5.59 (1H, *d*, *J* = 10.0 Hz), 5.03 (1H, *s*), 5.02 (1H, *s*), 4.30 (1H, *t*, *J* = 6.6 Hz); 1.73 (3H, *s*), 1.28 (3H, *s*), 0.83 (3H, *d*, *J* = 6.9 Hz).

4-*Hydroxy*-11-*hydroperoxy*-*bisabola*-1,3(15),9-*triene* (**12**). Gum IR ν_{max} (cm^{-1}): 3411, 2959, 2922, 2878, 1458, 1263; EIMS *m/z* (rel. int.): 250 (15); 235 (20), 217 (15), 161 (40), 151 (40), 135 (80), 109 (100); ^{1}H NMR δ ($CDCl_3$) 6.11 (1H, *d*, *J* = 9.5 Hz), 5.71 (1H, *d*, *J* = 9.5 Hz), 5.64 (1H, *ddd*, *J* = 15.7, 9.0, 4.7 Hz), 5.58 (1H, *d*, *J* = 15.7 Hz), 5.02 (1H, *s*), 4.95 (1H, *s*), 4.46 (1H, *br s*), 1.38 (3H, *s*), 1.28 (3H, *s*), 0.84 (3H, *d*, *J* = 6.9 Hz).

3,4-*Dihydroxy*-*bisabola*-1,10-*diene* (**13**). Gum, $[\alpha]_D = -10.1$ ($CHCl_3$; *c* 1.35). IR ν_{max} cm^{-1}: 3411, 2959, 2930, 2862, 1458, 1367, 1259; EIMS *m/z* (rel. int.) 238.1936 [M^+, Δ = −0.3 mmu for $C_{15}H_{26}O_2$] (10), 220 (25), 193 (30), 177 (100), 151 (40), 136 (65), 111 (70), 109 (75); ^{1}H NMR δ ($CDCl_3$): 5.66 (1H, *dd*, *J* = 10.2, 1.8 Hz), 5.61 (1H, *d*, *J* = 10.2 Hz), 5.09 (1H, *m*), 3.79 (1H, *dd*, *J* = 7.1, 3.2 Hz), 2.30 (1H, *m*); 1.69 (3H, *s*), 1.61 (3H, *s*); 1.31 (3H, *s*), 0.87 (3H, *d*, *J* = 6.8 Hz).

3,4-*Dihydroxy*-p-*menth*-1-*ene* (**14**). Gum, $[\alpha]_D = -23.7$ ($CHCl_3$; *c* 10.92). IR ν_{max} cm^{-1}: 3450, 2961, 2932, 2874, 1460, 1369, 1261; CIMS *m/z* 170 (1), 169 (3), 153 (16), 135 (84), 126 (100), 111 (74), 93 (23), 71 (29); EIMS *m/z* (rel. int.); 126 (100), 111 (44); ^{1}H NMR δ ($CDCl_3$): 5.71 (1H, *dd*, *J* = 10.1, 2.6 Hz), 5.61 (1H, *d*, *J* = 10.2 Hz), 3.81 (1H, *dd*, *J* = 7.6, 3.4 Hz), 1.30 (3H, *s*); 0.93 (3H, *d*, *J* = 6.8 Hz), 0.92 (3H, *d*, *J* = 6.8 Hz).

2α-*Cinnamoyl cineole* (**16**). Gum, $[\alpha]_D = -8.6°$ ($CHCl_3$; *c* 1.21). IR ν_{max} cm^{-1}: 1715, 1643, 1450, 1371, 1315, 1171; EIMS *m/z* (rel. int.): 300.1719 [M^+, Δ = 0.6 mmu for $C_{19}H_{24}O_3$] (60), 152 (30), 131 (70), 126 (100), 108 (65); ^{1}H NMR δ ($CDCl_3$): 7.67 (1H, *d*, *J* = 16.0 Hz), 7.54 (2H, *m*), 7.39 (3H, *m*), 6.43 (1H, *d*, *J* = 16.0 Hz), 4.83 (1H, *ddd*, *J* = 9.7, 3.3, 1.9 Hz); 2.70 (1H, *ddd*, *J* = 13.6 9.7, 3.3 Hz), 1.40 (1H, *ddd*, *J* = 13.6, 3.8, 3.3 Hz); 1.31 (3H, *s*), 1.26 (3H, *s*), 1.10 (3H, *s*). NOESY correlations were observed from δ 4.83 to 1.10, 1.26 and 2.70; 2.70 to 1.26; 2.05 to 1.31.

2β-*Cinnamoyl cineole* (**17**). Gum, $[\alpha]_D = +10.2°$ ($CHCl_3$; *c* 0.84). IR ν_{max} cm^{-1}: 2959, 2930, 1715; EIMS *m/z* (rel. int.): 300.1718 [M^+, Δ = 0.7 mmu for $C_{19}H_{24}O_3$] (55), 169 (10), 152 (27), 131 (81), 126 (100), 108 (68); ^{1}H NMR δ ($CDCl_3$): 7.72 (1H, *d*, *J* = 16.0 Hz), 7.53 (2H, *m*), 7.38 (3H, *m*), 6.52 (1H, *d*, *J* = 16.0 Hz), 4.81 (1H, *dd*, *J* = 10.0, 3.0 Hz); 1.34 (3H, *s*), 1.30 (3H, *s*), 1.11 (3H, *s*). NOESY correlations were observed from δ 4.81 to 1.11, 1.55 and 2.15; 1.98 to 1.34; 2.05 to 1.30

Reduction of **1**–**4** *to* **5**–**8**. **1** (22.1 mg) was reduced by $LiAlH_4$ (1:1 mol equiv) in dry Et_2O under a dry N_2 atmosphere, according to a standard procedure [8]. The progress of the reduction was monitored by TLC. After normal work-up, the reaction yielded **5** (15.3 mg; 69%). Reduction of **2** (12.0 mg) yielded **6** (8.5 mg; 71%); reduction of **3** (11.4 mg) gave **7** (6.0 mg; 53%); reduction of **4** (10.2 mg) yielded **8** (4.0 mg; 39%).

Acknowledgements—We would like to thank the CRCG for funding this research and Drs Richard Cortlett and Richard Saunders of the Department of Ecology and Biodiversity for help in identification of *Alpinia densibracteata*.

REFERENCES

1. Tang, W. and Eisenbrand, G.,*Chinese Drugs of Plant Origin*. Springer, Berlin, 1992, p. 87.
2. Ohshiro, M., Kuroyanagi, M. and Ueno, A., *Phytochemistry*, 1990, **29**, 2201.
3. Del R. Cuenca, M., Catalan, C. A. N., Diaz, J. G. and Herz, W., *Journal of Natural Products*, 1991, **54**, 1162.
4. De Pascual Teresa, J., Bellido, I. S., Torres, C., Sastre, B. A. and Grande, M., *Phytochemistry*, 1981, **20** 163.

5. Turner, J. A. and Herz, W., *Journal of Organic Chemistry*, 1977, **42**, 1895.
6. Bohlmann, F. and Zdero, C., *Phytochemistry*, 1982, **21**, 139.
7. Gonzalez, A. G., Bermejo Barrera, J., Bermejo Barrera, J. L. and Massanet, G. M., *Anales de Quimica*, 1972, **68**, 319.
8. Stolow, R. D. and Sachdev, K., *Tetrahedron*, 1965, **21**, 1889.
9. D'Agostino, M., De Simone, F., Zollo, F. and Pizza, C., *Phytochemistry*, 1990, **29**, 3656.
10. Delford, J. J. *et al.*, *Acta Crystallographica C*,1988, **44**, 765.
11. Honwad, V. K. and Rao, A. S., *Tetrahedron*, 1965, **21**, 2593.
12. Rucker, G., Schenkel, E., Manns, D., Falkenberg, M. and Marek, A., *Phytochemistry* 1996, **41**, 297.
13. Appendino, G., Gariboldi, P. and Menichini, F., *Phytochemistry*, 1985, **24**, 1729.
14. Stoessl, A., Stothers, J. B. and Ward, E. W. B., *Canadian Journal of Chemistry*, 1975, **53**, 3351.
15. Miyazawa, M. and Kameoka, H., *Phytochemistry*, 1983, **22**, 1040.
16. Kitagawa, I., Yoshioka, N., Kamba, C., Yoshikawa, M. and Hamamoto, Y., *Chemistry and Pharmaceutical Bulletin*, 1987, **35**, 928.
17. Luo, S., Ning, B., Hu, W. and Xie, J., *Journal of Natural Products*, 1991, **54**, 573.
18. Bohlmann, F., Castro, V. and Ziesche, J., *Revista Latinoamericana de Quimica*, 1991, **14**, 103.
19. Bohlmann, F., Jakupovic, J., Ahmed, M. and Schuster, A., *Phytochemistry*, 1983, **22**, 1623.
20. Zdero, C., Bohlman, F. and Scott, R., *Phytochemistry*, 1987, **26**, 1999.
21. De Pascual Teresa, J., Torrese, C., Gonzalez, M. S., Grande, M. and Bellido, I. S., *Phytochemistry*, 1983, **22**, 2749.