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Terpenoids from the liverwort *Chandonanthus hirtellus*

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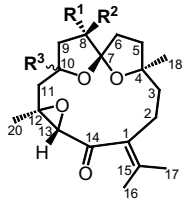
ABSTRACT

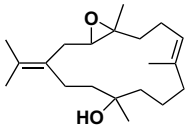
A new bicyclogermacrane sesquiterpenoid, two new cembrane diterpenoids and five new dolabellane diterpenoids, along with known terpenoids, have been isolated from the Malaysian liverwort *Chandonanthus hirtellus*. The structures of the new compounds were established by spectroscopic and chemical methods in addition to X-ray crystallographic studies.

1. Introduction

Liverworts are well known to produce a wide variety of compounds, such as terpenoids and aromatic compounds as their major constituents.[1,2] Many of these compounds possess bioactivities and/or exhibit intense bitterness.[1,2] The leafy liverwort *Chandonanthus hirtellus* (Web.) Mitt., produces sesquiterpenes and cem diterpenoids chandonanthone (**1**), isochandonanthone (**2**) (8-*epi*-chandonanthone) and setiformenol (**3**).[3–6] Cembranes are rare in liverworts and have been reported only from this genus. A recent study of West Malaysian *C. hirtellus* led to the isolation of eight new compounds, i.e., (+)-3β-acetoxybicyclogermacra-1(10)(*E*),4(*E*)-diene (**4**), two cembranes 8,10-di*epi*-chandonanthone (**5**) and β-1,15-dihydro-8,10-di*epi*-chandonanthone (**6**), five dolabellanes 2,10-diacetoxy-7,8,18,19-diepoxydolabell-3(*E*)-en-14-one (**7**), 2,10,14-triacetoxy-7,8,18,19-diepoxydolabell-3(*E*)-ene (**8**), 10,14-diacetoxy-7,8-epoxydolabella-3(*E*),18-dien-2α-ol (**9**), 2,10-diacetoxy-7,8-epoxydolabella-3(*E*),18-diene (**10**) and dolabella-3(*E*),7(*E*),18-trien-2α-ol (**11**), as well as the known terpenoids (−)-(6*S*,7*S*)-sesquiphellandrene (**12**)[7–9] and friedelin (**13**). Friedelin was identified by comparing with an authentic sample (TLC and ^{1}H NMR spectroscopy).



1 R^1=H; R^2=CH_3; R^3=α-H
2 R^1=CH_3; R^2=H; R^3=α-H
5 R^1=CH_3; R^2=H; R^3=β-H



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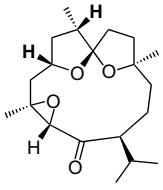

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Table 1
^{1}H (500 MHz), HMBC and ^{13}C (125 MHz) NMR spectroscopic data for **4** in $CDCl_3$ (*J* in Hz in parentheses)

Position	δ_H	HMBC		δ_C
		^2J	^3J	
1	5.01 (ddt, 10.6, 5.8, 1.4)	C-2	C-3, 9	119.8 d
2	2.25 (m)	C-1, 3	C-4, 10	30.6 t
3	5.22 (t, 3.0)	C-2, 4	C-1, 5, 15, C=O(OAc-3)	79.1 d
4	—	—	—	126.1 s
5	4.68 (dd, 11.6, 1.4)	C-4	C-3, 7, 11, 15	126.3 d
6	1.33 (dd, 12.0, 8.4)	C-5, 7, 11	C-4, 8, 12, 13	26.8 d
7	0.70 (ddd, 12.0, 8.8, 2.8)	C-6, 8, 11	C-5, 12	30.3 d
8	1.94 (ddd, 14.3, 6.9, 3.2), 1.26 (dd, 13.9, 4.6)	C-7, 9	C-6, 10	27.0 t
9	2.46 (dt, 13.0, 3.2), 1.76 (dt, 4.2, 12.0)	C-8, 10	C-1, 7	37.1 t
10	—	—	—	143.5 s
11	—	—	—	20.3 s
12	1.09 (s)	C-11	C-6, 7, 13	29.1 q
13	1.03 (s)	C-11	C-6, 7, 12	15.4 q
14	1.69 (s)	C-10	C-1, 9	21.1 q
15	1.48 (s)	C-4	C-3, 5	15.7 q
Me(OAc-3)	2.02 (s)	C=O(OAc-3)	—	21.3 q,
C=O(OAc-3)				170.2 s

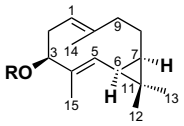
2. Results and discussion

2.1. (+)-3β-Acetoxybicyclogermacra-1(10)(*E*),4(*E*)-diene (4)

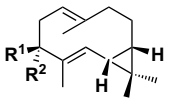
The sesquiterpenoid, $C_{17}H_{26}O_2$ (*m*/*z* 262.1931), was obtained as a colourless oil. The ^{1}H and ^{13}C NMR spectra (Table 1) showed the presence of two vinyl methyl groups [δ_H 1.69 (s, H_3-14) and 1.48 (s, H_3-15); δ_C 21.1 (C-14) and 15.7 (C-15)], two tertiary methyl groups [δ_H 1.09 (s, H_3-12) and 1.03 (s, H_3-13); δ_C 29.1 (C-12) and 15.4 (C-13)], two trisubstituted alkenes [δ_H 5.01 (1H, ddt, *J*=10.6, 5.8 and 1.4 Hz, H-1) and 4.68 (1H, dd, *J*=11.6 and 1.4 Hz, H-5); δ_C 143.5 (C-10), 126.3 (C-5), 126.1 (C-4) and 119.9 (C-1)], one oxygenated methine [δ_H 5.22 (1H, t, *J*=3.0 Hz); δ_C 79.1 (C-3)] and one acetate group [δ_H 2.02 (3H, s); δ_C 170.2 (C) and 21.3 (CH_3)]. Three methylenes, two methines and one shielded quaternary carbon [δ_C 20.3 (C)] were also present. Based on the calculation of the degree of unsaturation, compound **4** was bicarbocyclic. HMBC correlations (Table 1) were used to elucidate the structure. H_3-12 and H_3-13 correlated to C-6, C-7, C-11 and to each other, which indicated the presence of a cyclopropane ring. H_3-15 correlated to the oxygenated carbon (C-3), two olefinic carbons (C-4 and C-5) suggested that the OAc group was allylic to an alkene. The correlations between H-5 and C-3, C-15, C-7 and C-11 linked the structures discussed above. Complete analysis of the HMBC correlations led to the identification of a unique structure 3-acetoxybicyclogermacra-1(10),4-diene.

The geometry of the double bonds deduced from the relative shielded chemical shifts of the vinyl methyls (δ_C 21.1 and 15.7) was consistent with the *E* germacrene.[10] The relative stereochemistry between H-6 and H-7 was deduced from the coupling constant, which is typical of a cyclopropane ring, the large *J*=8.6 Hz implies a cis position. In addition, the clear NOESY correlations between H-6 and H-7 also suggested that they were cis. The stereochemistry of the acetoxy group was confirmed as follows. By comparison of the NMR spectroscopic data of **4** with those of **14** and **15**, it was found that both of the ^{1}H and ^{13}C NMR spectra of **4** were exactly same as those of **14**[11,12] while differed from those of **15** [δ_H 4.85 (H-3 and H-1/5), 0.59 (H-7); δ_C 80.7 (C-3), 125.4 (C-5)],[10] which indicated that the relative stereochemistry of the acetoxy group was same to that of **14**, as cis to the cyclopropane ring. However, the specific optical rotation {$[\alpha]_D$ +28 (*c* 1.0, $CHCl_3$)} of **4** is of opposite sign to that of **14** {lit.[11] $[\alpha]_D$ −13.7}. Therefore, the compound was determined to be (+)-3β-acetoxygermacra-1(10)(*E*),4(*E*)-diene. The two geminal methyl groups were differentiated by the NOESY correlations between H-12 to H-6 and H-7.

Methanolysis of **4** gave the corresponding alcohol, (−)-bicyclogermacra-1(10)(*E*),4(*E*)-dien-3β-ol (**16**) (colourless oil, $C_{15}H_{24}O$, *m*/*z* 220.1818). Further comparison of the NMR spectroscopic data of **16** (see Experimental section) with those of the hydrolysis product of **15**, (3*S*)-*trans*-3-hydroxybicyclogermacrene (**17**) [δ_H 4.06 (H-3), 0.63 (H-7); δ_C 79.7 (C-3)] revealed that their NMR spectra were not exactly same. This indicated that their relative stereochemistry was different,[11,12] which provided further evidence that the absolute stereochemistry of **4** was different from that of **15**.



4 R=Ac
16 R=H



14 R^1=H, R^2=OAc
15 R^1=OAc, R^2=H
17 R^1=OH, R^2=H

2.2. 8,10-Di*epi*-chandonanthone (5)

The major metabolite, 8,10-di*epi*-chandonanthone (**5**), $C_{20}H_{30}O_4$ (*m*/*z* 334.2148), was obtained as colourless cubes from hexane/EtOAc (3:1). Its ^{1}H and ^{13}C NMR spectroscopic data (see Experimental section) were very close to those of chandonanthone (**1**) and isochandonanthone (**2**).[3] Small chemical shift differences in the ^{13}C NMR spectra suggested that **5** only differed from **1** and **2** in the stereochemistry. As suitable crystals were available, the crystal structure of **5** was determined (Fig. 1) and this established that **5** was 8,10-di*epi*-chandonanthone.

2.3. β-1,15-Dihydro-8,10-di*epi*-chandonanthone (6)

A minor compound, β-1,15-dihydro-8,10-di*epi*-chandonanthone (**6**), $C_{20}H_{32}O_4$ (*m*/*z* 336.2304), was also obtained as colourless cubes. Its ^{1}H and ^{13}C NMR spectra (see Table 2) were rather similar to those of **5**, the major differences were that the carbonyl group was more deshielded [δ_C 209.4] and that the conjugated double bond and two vinyl methyls signals were replaced by those of an isopropyl group and a methine. Compound **6** was obviously a 1,15-dihydro derivative of **5** and this was confirmed using HMBC spectroscopy (Table 2). X-ray crystallography (see Fig. 2) was used to determine the relative stereochemistry of **6**, which was shown to be β-1,15-dihydro-8,10-di*epi*-chandonanthone.

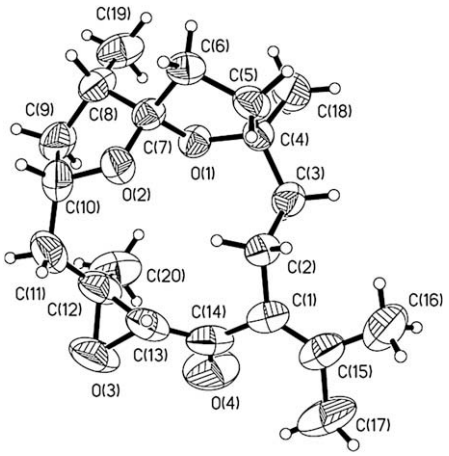


Figure 1. ORTEP drawing of **5**, showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii at calculated positions.

Table 2
^{1}H (500 MHz), HMBC and ^{13}C (125 MHz) NMR spectroscopic data for **6** in $CDCl_3$ (*J* in Hz in parentheses)

Position	δ_H	HMBC		δ_C
		^2J	^3J	
1	2.05 (m)	—	C-3	61.0 d
2	2.17 (m), 1.98 (m)	C-3	C-4	34.4 t
3	1.62 (m), 1.25 (m)	C-4, 5	C-1, 18	39.1 t
4	—	—	—	85.3 s
5	2.19 (m), 1.53 (m)	C-4	C-3, 7, 18	32.0 t
6	2.38 (m), 1.76 (m)	—	C-4	23.0 t
7	—	—	—	115.7 s
8	2.08 (m),	C-7, 9, 19	C-6	40.6 d
9	1.89 (m)	C-8, 10	C-7, 11, 19	36.6 t
10	4.20 (dddd, 12.5, 10.2, 6.5, 3.7)	C-9	C-7	75.2 d
11	2.21 (dd, 14.8, 1.0), 1.76 (m)	C-10, 12	C-9, 13, 20	42.8 t
12	—	—	—	62.6 s
13	3.97 (s)	C-12, 14	C-11	64.0 d
14	—	—	—	209.4 s
15	1.95 (m)	C-1, 16, 17	—	31.0 d
16	1.03 (d, 6.5)[a]	C-15	C-1, 17	22.3[a] q
17	0.92 (d, 6.9)[a]	C-15	C-1, 16	22.1[a] q
18	1.11 (s)	C-4	C-3, 5	29.0 q
19	0.99 (d, 6.5)	C-8	C-7, 9	12.7 q
20	1.48 (s)	C-12	C-11, 13	18.1 q

[a] Signals within a column are interchangeable.

2.4. 2α,10α-Diacetoxy-7,8,18,19-diepoxydolabell-3(*E*)-en-14-one (7)

The diterpenoids was obtained as colourless cubes, $C_{24}H_{34}O_7$ (*m*/*z* 434.2321). The ^{1}H and ^{13}C NMR spectra (see Table 3) showed the presence of a ketone [δ_C 216.6], a trisubstituted alkene, two oxygenated methines, a trisubstituted oxirane [δ_H 3.10 (d, *J*=9.7 Hz, H-7); δ_C 62.5 (CH) and 59.6 (C)], a 1,1-disubstituted oxirane [δ_H 2.72 (d, *J*=5.1 Hz) and 2.68 (d, *J*=5.1 Hz); δ_C 56.4 (C) and 53.7 (CH_2)], two acetates, four tertiary methyl groups, two saturated quaternary carbons, four methylenes and two methines. These NMR spectroscopic data accounted for six double bonds equivalents, the molecule was therefore bicarbocyclic. The HMBC correlations of the methyl groups were used as the starting points to deduce the structure (Fig. 3). H_3-15 correlated to an oxygenated methine (C-2), the ketone (C-14), one methine (C-11) and C-1 indicated that the methyl group was attached to the quaternary carbon (C-1), which most likely is a ring junction. H_3-20 correlated to the disubstituted oxirane carbons and C-12 suggested that the oxirane connected to C-12 with Me-20 as another substituent. Similarly, H_3-17 showed correlations with the other oxirane carbons and one methylene. The gross structure was determined by further HMBC spectroscopy as 2,10-diacetoxy-7,8,18,19-diepoxydolabell-3(*E*)-en-14-one. This was confirmed by X-ray crystallographic analysis (Fig. 4), which also allowed a determination of the relative configuration. The asymmetric unit contained two independent molecules, which differed only in their conformation. Although several attempts at methanolysis and hydrolysis of the acetate groups of **7** were made, only decomposition of the starting material was observed.

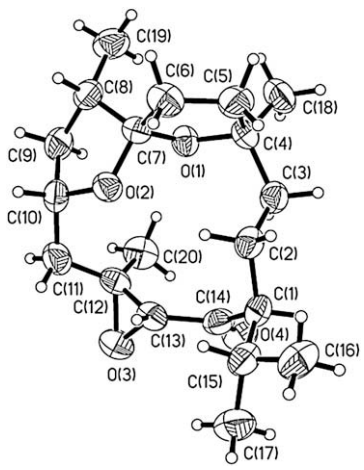


Figure 2. ORTEP drawing of **6**, showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii at calculated positions.

Table 3
^{1}H (500 MHz), HMBC and ^{13}C (125 MHz) NMR spectroscopic data for **7** in $CDCl_3$ (*J* in Hz in parentheses)

Position	δ_H	HMBC		δ_C
		^2J	^3J	
1	—	—	—	56.3[a] s
2	5.49 (d, 8.8)	C-1, 3	C-4, 11, 15, C=O(OAc-2)	75.5 d
3	4.85 (dd, 8.8, 1.4)			117.9 d
4	—			140.2 s
5	2.33 (m)		C-16	35.8 t
6	1.98 (dt, 17.5, 6.1), 1.68 (m)	C-5, 7	C-8	22.8 t
7	3.10 (d, 9.7)	C-6, 8	C-5, 9	62.5 d
8	—	—	—	59.6 s
9	2.71 (dd, 14.1, 11.4), 1.53 (br d, 9.9)	C-8, 10	C-7, 11	42.2 t
10	5.08 (dd, 11.6, 1.9)	C-9, 11	C-1, 8, 12, C=O(OAc-10)	71.7 d
11	2.82 (d, 10.2)	C-1, 12	C-2, 9, 15	43.4 d
12	2.38 (m)	C-11, 13	C-1, 10, 19, 20	39.2 d
13	2.49 (dd, 17.6, 8.3), 2.15 (dd, 17.6, 12.0)	C-12, 14	C-1, 11, 18	41.6 t
14	—	—	—	216.6 s
15	0.85 (s)	C-1	C-2, 11, 14	15.6 q
16	1.78 (s)	C-4	C-3, 5	18.4 q
17	1.56 (s)	C-8	C-7, 9	21.1 q
18	—	—	—	56.4[a] s
19	2.72 (d, 5.1), 2.68 (d, 5.1)	C-18	C-12, 20	53.7 t
20	1.49 (s)	C-18	C-12, 19	17.4 q
Me(OAc-2)	1.98 (s)	C=O(OAc-2)	—	21.3 q,
C=O(OAc-2)				169.7 s
Me(OAc-10)	1.95 (s)	C=O(OAc-10)	—	20.9 q,
C=O(OAc-10)				168.7 s

[a] Note: the signals are interchangeable.

2.5. 2α,10α,14α-Triacetoxy-7,8,18,19-diepoxydolabell-3(*E*)-ene (8)

The triacetate was obtained as a colourless oil, $C_{26}H_{38}O_8$ (*m*/*z* 479.2667). When the ^{1}H and ^{13}C NMR spectra of **8** (see Table 4) were compared to those of **7**, it was observed that **8** and **7** differed only in that the ketone group of the latter had been replaced by a secondary acetoxy group in **8**. This was confirmed using HMBC correlations (Table 4). The close similarity in the chemical shifts and coupling constants indicated that the relative stereochemistry of **8** was the same as that of **7**. The relative stereochemistry of the new chiral centre (C-14) was deduced from the clear NOESY correlation between H-14 and H_3-15 (Fig. 5), which showed that H-14 and Me-15 were cis to each other.

2.6. 10α,14α-Diacetoxy-7,8-epoxydolabella-3(*E*),18-dien-2α-ol (9)

The metabolite **9** was obtained as a colourless oil, $C_{24}H_{36}O_6$ ($[M-AcOH]^+$ *m*/*z* 360.2294). The ^{1}H and ^{13}C NMR spectra of **9** (see

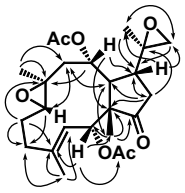


Figure 3. Selected HMBC correlations of **7**.

Table 5) were very similar to those of **8**. However, the signals for the 1,1-disubstituted epoxy group had been replaced by those of a 1,1-disubstituted alkene [δ_H 5.02 (br s) and 4.92 (br s); δ_C 145.2 (C) and 113.9 (CH_2)]. One set signals of an acetoxy group was also absent while a shielding of H-2 [δ_H 4.33 (d, J=7.9 Hz)] was observed. Therefore, it was deduced that one of the acetoxy groups was hydrolyzed to a secondary alcohol, which was confirmed by the chemical shift of C-2 [δ_C 73.8 (CH)]. The compound was identified as 10α,14α-diacetoxy-7,8-epoxydolabell-3(*E*),18-dien-2-ol by HMBC correlations (Table 5). The relative stereochemistry of the compound was assumed to be the same as that of **7** due to the similarity of the NMR spectroscopic data, which was confirmed by analysis of the NOESY correlations (Fig. 6).

2.7. 2α,10α-Diacetoxy-7,8-epoxydolabella-3(*E*),18-diene (10)

The diterpenoid was obtained as a colourless oil, $C_{24}H_{36}O_5$ (m/z 404.2574). The ^{1}H and ^{13}C NMR spectra of **10** (see Table 6) showed the presence of two alkenes, one of which was trisubstituted whilst the other was 1,1-disubstituted. Two oxygenated methines, a trisubstituted epoxide, two vinyl methyls, two tertiary methyl groups and two acetoxy groups were also present along with five methylenes and two methines. Comparison of NMR spectra indicated that **10** only differed from **8** in the absence of one acetoxy group and the replacement of the 1,1-disubstituted epoxy group with a 1,1-disubsituted alkene. Therefore the compound was deduced to be 2α,10α-diacetoxy-7,8-epoxydolabella-3,18-diene, which was confirmed by HMBC correlations. Likewise, the relative stereochemistry of the compound was assumed to be the same as that of **8** due to the similarity of the NMR spectroscopic data.

Table 4
^{1}H (500 MHz), HMBC and ^{13}C (125 MHz) NMR spectroscopic data for **8** in $CDCl_3$ (J in Hz in parentheses)

Position	δ_H	HMBC		δ_C
		^2J	^3J	
1	—	—	—	50.2 s
2	5.42 (d, 9.3)	C-1, 3	C-4, 11, 14, 15, C=O(OAc-2)	74.9 d
3	5.04 (d, 9.3)			119.8 d
4	—	—	—	139.9 s
5	2.34 (m)			35.7 t
6	2.03 (m & o), 1.67 (m & o)	C-5	C-8	23.4 t
7	3.06 (d, 7.9)	C-6	C-5	61.5 d
8	—	—	—	59.2 s
9	2.66 (m), 1.55 (m & o)	C-8, 10	C-7, 11	41.9 t
10	4.92 (dd, 11.6, 2.3)	C-9, 11	C-1, 8, 12, C=O(OAc-10)	71.4 d
11	2.65 (m)	C-1, 10, 12	C-2, 9, 18	44.3 d
12	2.63 (m)	C-11, 18	C-1, 9, 20	41.3 d
13	2.14 (m), 1.65 (m)	C-12, 14; C-12, 14	C-1, 11; C-2, 18, OAc-14	34.4 t
14	4.85 (dd, 9.3, 6.5)	—	C-2, 15, OAc-14	80.7 d
15	0.87 (s)	C-1	C-2, 11, 14	20.8 q
16	1.80 (s)	C-4	C-3, 5	18.1 q
17	1.56 (s)	C-8	C-7, 9	21.6 q
18	—	—	—	56.5 s
19	2.66 (m, 2H)	C-18	C-12, 20	53.9 t
20	1.47 (s)	C-18	C-12, 19	17.8 q
Me(OAc-2)	2.04 (s)	C=O(OAc-2)	—	21.4 q,
C=O(OAc-2)				169.4 s
Me(OAc-10)	1.97 (s)	C=O(OAc-10)	—	21.4 q,
C=O(OAc-10)				169.9 s
Me(OAc-14)	2.04 (s)	C=O(OAc-14)	—	21.0 q,
C=O(OAc-14)				170.7 s

Note: 'o' means the signals are overlapped with other signals.

Methanolysis of **10** resulted in a selectively cleaved product, 10α-acetoxy-7,8-epoxydolabella-3(*E*)18-dien-2α-ol (**18**). In the ^{1}H and ^{13}C NMR spectra of **18** (see Experimental section), the secondary alcohol signals are readily identified [δ_H 3.02 (d, J=9.7 Hz, H-2); δ_C 76.0 (CH, C-2)]. Oxidation of **18** afforded 10α-acetoxy-7,8-epoxydolabella-3(*E*),18-dien-2-one (**19**), as a colourless oil. Its NMR spectra showed that the allylic secondary alcohol had been converted to an α,β-unsaturated ketone [δ_C 203.3 (C)].

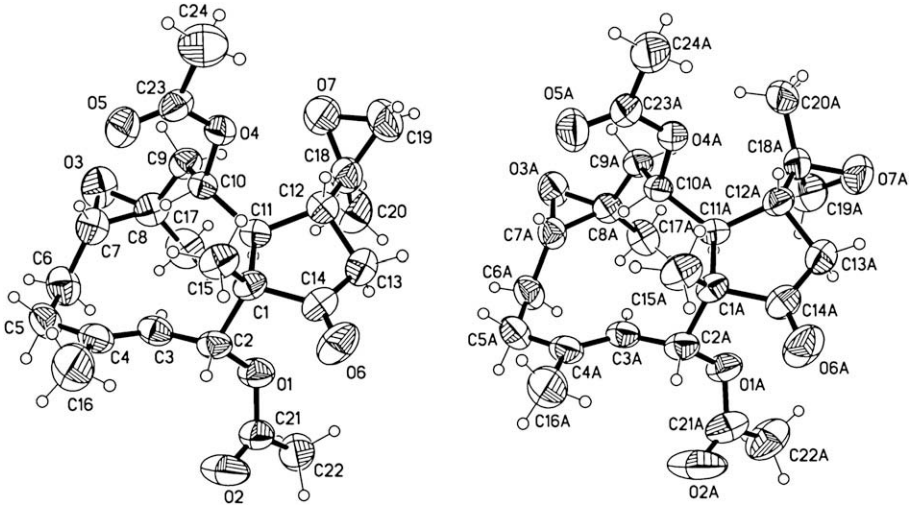
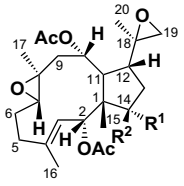
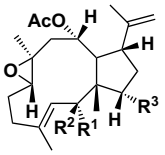


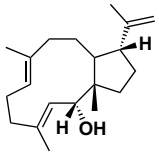
Figure 4. ORTEP drawing of **7**, showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level and H atoms are shown as small spheres of arbitrary radii at calculated positions.



7 R^1,R^2=O
8 R^1=OAc; R^2=H



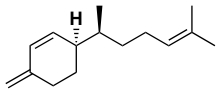
9 R^1=OH; R^2=H; R^3=OAc
10 R^1=OAc; R^2=R^3=H
18 R^1=OH; R^2=R^3=H
19 R^1,R^2=O; R^3=H



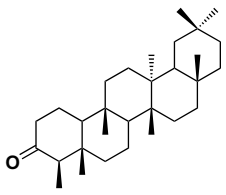
11

2.8. Dolabella-3(*E*),7(*E*),18-trien-2α-ol (11)

The triene was obtained as a colourless oil, $C_{20}H_{32}O$ (*m*/*z* 288.2463). Its ^1H and ^{13}C NMR spectra (see Table 7) indicated the presence of three vinyl methyl groups and one tertiary methyl. A 1,1-disubstituted alkene, two trisubstituted double bonds and a secondary alcohol were also present. Comparison of the NMR spectroscopic data with those of **18** showed that **11** retained the 1,1-disubstituted alkene and allylic alcohol moieties of **18** but that the trisubstituted epoxy group had been replaced by a trisubstituted alkene and the absence of the acetoxy group. This suggested that the compound was dolabella-3(*E*),7(*E*),18-trien-2α-ol. This was confirmed by analysis of the HMBC correlations. Similarly, the relative stereochemistry of **11** was assumed to be the same as that of **8** due to the similarity of the NMR spectroscopic data.



12



13

Although dolabellanes are commonly found in marine organisms,[13,14] they are considered to be important chemical markers of *Barbilophozia* species of the Lophozioideae.[15] They were also found in *Odontoschisma denudatum*[16,17] and *Pleurozia gigantea*.[18] This study has shown that dolabellanes are indeed an important marker for the Lophozioideae, as *C. hirtellus* is also a member of this subfamily. Comparison of the structures reveals some characteristic features of dolabellanes from different sources (Table 8). The Lophozioideae generally produces compounds (**7**–**11** and **20**–**23**), which are oxidized at C-2, C-10 and C-18 with a double bond and an epoxide in the macrocycle.[6,15,19] The *Odontoschisma* dolabellanes (**24**–**29**), on the other hand, usually lack epoxide groups and are oxidized at C-6 and C-12,[16,17] whereas the dolabellane (**30**) from *Pleurozia* lacks epoxides and is oxidized at C-18.[18] In addition, the reported stereochemistry of **30** has the C-1 methyl and C-12 substituent cis, whilst in all the other dolabellanes these groups are trans. A closer examination of the details of the *Pleurozia* work revealed that the structure is based on rather tenuous evidence.[18] However, the fusicoccanes **31**–**33**, which were isolated from the same species, also have a cis relationship between the two substituents.[18] The liverwort dolabellanes (especially those from the Lophozioideae) have similar features to those (**34**–**36**) from marine organisms, such as sea hares and brown algae, which are in accord with the proposal that brown algae and liverworts share a common evolutionary ancestor.[20–22] The sea hares presumably do not synthesize dolabellanes themselves but obtain them from a dietary source.[14]

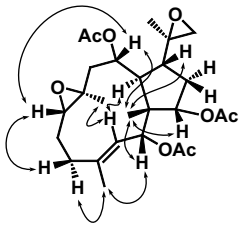
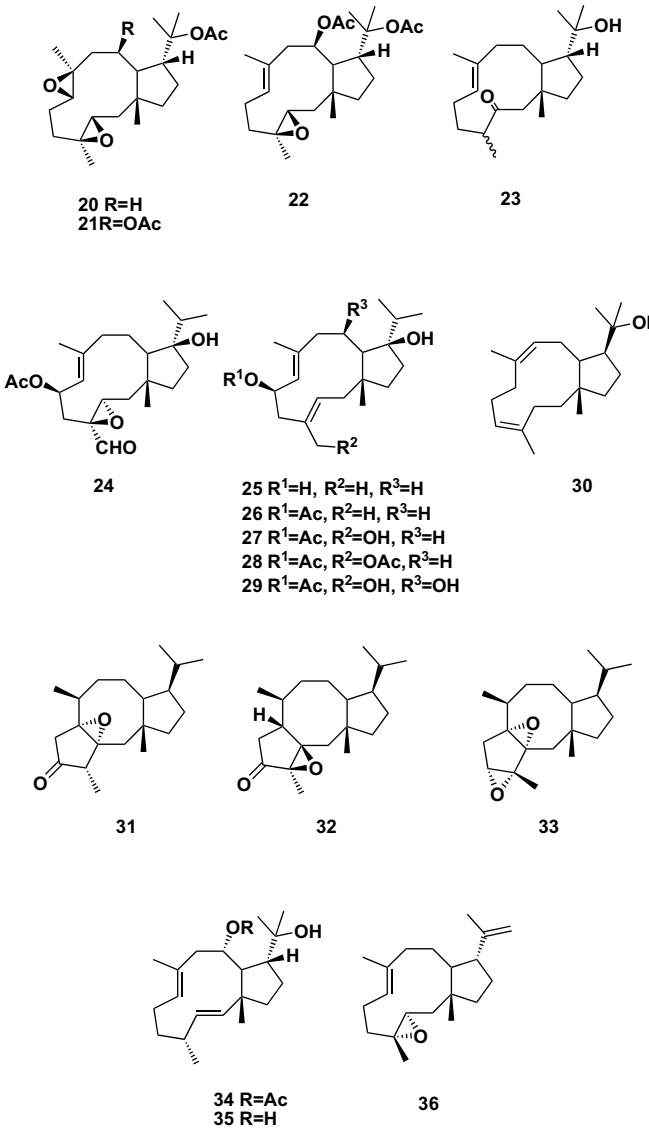


Figure 5. Important NOESY correlations of **8**.

Table 5
^1H (500 MHz), HMBC and ^{13}C (125 MHz) NMR spectroscopic data for **9** in $CDCl_3$ (*J* in Hz in parentheses)

Position	δ_H	HMBC		δ_C
		^2J	^3J	
1	—	—	—	49.8 s
2	4.33 (d, 7.9)	C-1, 3	C-4, 11, 14	73.8 d
3	4.96 (d, 6.9)			121.9 d
4	—			137.0 s
5	2.31 (m, 2H)			36.1 t
6	1.98 (dt, 7.5, 5.0), 1.70 (m)	C-7	C-8, C-8	23.2 t
7	2.99 (d, 9.3)	C-6, 8	C-5, 9	62.3 d
8	—	—	—	59.5 s
9	2.31 (m), 1.38 (dd, 13.4, 2.5)	C-8, 10; C-8, 10	C-7, 11, 17; C-11, 17	42.3 t
10	4.90 (dd, 11.6, 2.8)	C-9, 11	C-1, 8, 12, C=O(OAc-10)	72.6 d
11	2.64 (d, 11.6)	C-1, 12	C-2, 9, 18	44.0 d
12	2.85 (dt, 5.4, 12.5)	C-11, 13, 18	C-10, 19, 20	41.9 d
13	2.04 (dd, 11.6, 6.0), 1.76 (dd, 11.1, 2.1)	C-12, 14; C-12, 14	C-1, 11; C-1, 18	37.2 t
14	4.97 (dd, 10.6, 6.5)	C-1, 13	C-2, 15, C=O(OAc-14)	83.0 d
15	0.84 (s)	C-1	C-2, 11, 14	20.6 q
16	1.73 (s)	C-4	C-3, 5	18.8 q
17	1.52 (s)	C-8	C-7, 9	21.2 q
18	—	—	—	145.2 s
19	5.02 (br s), 4.92 (br s)		C-12	113.9 t
20	1.85 (s)	C-18	C-12, 19	19.2 q
Me(OAc-10)	2.00 (s)	C=O(OAc-10)	—	21.3 q,
C=O(OAc-10)				169.6 s
Me(OAc-14)	2.15 (s)	C=O(OAc-14)	—	21.3 q,
C=O(OAc-14)				170.0 s



3. Experimental

3.1. General experimental details

^{1}H NMR and ^{13}C NMR: Bruker DPX300, Bruker AMX500 or Bruker DRX500 in $CDCl_3$; MS: Finnigan TSQ-7000 LC/triple quadrupole MS; IR: BIO-RAD Excalibur series FTS 3000; Optical rotation: Perkin–Elmer 241 polarimeter; X-ray diffraction: Bruker AXS SMART APEX CCD diffractometer; CC was carried out on normal phase silica gel 60 (Merck, 40–63 μm); Sephadex LH-20 (MeOH/CH_2Cl_2=1:1 as eluent) was used for gel permeation chromatography (GPC); HPLC were on Lichrosorb 10 DIOL, 250×4.60 mm, Luna 5 μ C_{18}, 250×4.60 mm and Partisil 10 silica, 250×4.60 mm.

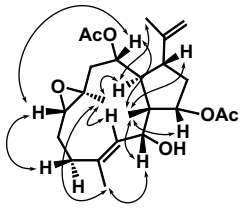


Figure 6. Selected NOESY correlations of **9**.

Table 6
^{1}H (500 MHz), HMBC and ^{13}C (125 MHz) NMR spectroscopic data for **10** in $CDCl_3$ (*J* in Hz in parentheses)

Position	δ_H	HMBC		δ_C
		^2J	^3J	
1	—	—	—	47.8 s
2	5.30 (d, 8.5)	C-1, 3	C-4, 11, 14, 15, C=O(OAc-2)	78.4 d
3	4.89 (br d, 8.7)			119.9 d
4	—			138.1 s
5	2.28 (m), 1.74 (m)		C-3, 7	35.7 t
6	1.94 (dt, 14.9, 3.9), 1.63 (m)	C-5, 7	C-4, 8	22.9 t
7	3.01 (d, 9.9)	C-6, 8	C-5, 9	62.4 d
8	—	—	—	59.6 s
9	2.29 (m), 1.38 (dd, 13.5, 2.3)		C-7, 11, 17	42.2 t
10	4.97 (dd, 10.0, 2.5)	C-9, 11	C-1, 8, 12, C=O(OAc-10)	72.7 d
11	2.30 (m)	—	C-2, 9, 13, 18	46.3 d
12	2.82 (dt, 6.0, 11.2)	C-11	C-10, 13, 19, 20	47.4 d
13	1.56 (m)	C-12, 14	C-1, 11, 18	31.3 t
14	1.70 (m), 1.32 (m)	C-1, 13	C-2, 12	37.4 t
15	0.82 (s)	C-1	C-2, 11, 14	22.2 q
16	1.73 (s)	C-4	C-3, 5	18.4 q
17	1.46 (s)	C-8	C-7, 9	21.0 q
18	—	—	—	146.8 s
19	4.96 (br s), 4.87 (br s)	C-18	C-20	112.5 t
20	1.83 (s)	C-18	C-12, 19	19.4 q
Me(OAc-2)	2.06 (s)	C=O(OAc-2)	—	21.2[a] q,
C=O(OAc-2)				170.2 s
Me(OAc-10)	1.99 (s)	C=O(OAc-10)	—	21.3[a] q,
C=O(OAc-10)				169.9 s

[a] Interchangeable within the same column.

3.2. Plant material

C. hirtellus (Web.) Mitt. was collected on Gunung Brinchang in the Cameron Highlands, Malaysia in April, 2004. A voucher specimen (WYM 04-1, SINU) was deposited at SINU Herbarium at Raffles Museum of Biodiversity Research, National University of Singapore.

Table 7
^{1}H (500 MHz), HMBC and ^{13}C (125 MHz) NMR spectroscopic data for **11** in $CDCl_3$ (*J* in Hz in parentheses)

Position	δ_H	HMBC		δ_C
		^2J	^3J	
1	—	—	—	49.6 s
2	3.99 (d, 9.3)	C-1, 3	C-4, 14, 15	73.7 d
3	5.15 (d, 8.7)	C-2	C-1, 5, 16	126.2 d
4	—	—	—	140.3 s
5	2.27 (m), 2.06 (br d, 18.0)	C-4, 6	C-3, 16	39.4 t
6	2.36 (ddd, 23.6, 12.5, 4.6), 2.02 (m)	C-5, 7	C-4, 8	25.5 t
7	4.79 (dd, 11.1, 4.2)	—	C-9	124.2 d
8	—	—	—	136.7 s
9	1.81 (m), 1.64 (m)	C-8	C-7, 11, 17	37.8 t
10	1.22 (m), 1.13 (m)	C-9, 11	C-1, 8, 12	27.3 t
11	1.72 (m)	C-1, 10, 12	C-2, 9, 13	45.4 d
12	2.47 (ddd, 9.7, 7.4, 2.8)	C-11, 18	C-20	55.1 d
13	1.78 (m), 1.52 (m)	C-14	C-1, 11	26.8 t
14	1.43 (ddd, 12.0, 8.8, 2.8), 1.12 (br d, 13.9)	C-1, 13	C-11, 12, 15	31.8 t
15	0.99 (s)	C-1	C-2, 11, 14	19.1 q
16	1.65 (d, 1.4)	C-4	C-3, 5	16.4 q
17	1.49 (s)	C-8	C-7, 9	16.9 q
18	—	—	—	147.7 s
19	4.80 (d, 2.3), 4.66 (dd, 2.3, 1.4)	—	C-12	111.4 t
20	1.77 (s)	C-18	C-12, 19	18.5 q

Table 8
Comparison of the features of dolabellanes from different sources

	Sources	Oxidized positions	Other features within the large ring	Orientations of the side chain on C-12
20–23	*Barbilophozia*[15–17] (Lophozioideae, Jungermanniaceae)	C-10 and C-18	Alkenes and epoxides	trans to the C-1 methyl
7–11	*C. hirtellus* (Lophozioideae, Jungermanniaceae)	Typically C-2, C-10 and C-18	Alkenes and epoxides	trans to the C-1 methyl
24–29	*O. denudatum*[18,19] (Adelanthaceae)	C-6 and C-12	Typically alkenes	trans to the C-1 methyl
30	*P. gigantea* [20] (originally Pleuroziaceae) (recently close to *Metzgeria* and *Aneura*)	C-18	Alkenes	cis to the C-1 methyl
34	*Dolabella californica*[21] (sea hare)	C-10 and C-18	Alkenes	trans to the C-1 methyl
35	*Dictyota dichtoma*[22] (brown alga)	C-10 and C-18	alkenes	trans to the C-1 methyl
36	*Glossophora galapagensis*[23] (brown alga)	NA	Alkenes and epoxides	trans to the C-1 methyl

3.3. Extraction and isolation

The powdered plant material (27 g) was extracted with diethyl ether (ca. 300 ml×2) at room temperature. The combined crude extracts (1.9 g) were chromatographed on a column of silica gel eluted with an EtOAc/hexane gradient followed by methanol to give seven fractions. One third of the first fraction (209 mg) was separated by reversed phase HPLC (C_{18}, 94% MeOH/H_2O) to afford the sesquiterpene **12** (14.3 mg). The second fraction (193 mg) was purified with Sephadex LH-20 to remove the triglycerides and gave a mixture (84 mg), which was then purified by a silica gel column (3% EtOAc/hexane) to afford **12** (21 mg) and **4** (11.4 mg). The third fraction (125 mg) was separated on Sephadex LH-20 followed by purification on HPLC (silica gel, 5% acetone/hexane) to afford friedelin (1.0 mg). The fourth fraction (106 mg) was purified on Sephadex LH-20, and then by CC (10% EtOAc/hexane) and reversed phase columns (C_{18}, 75% MeCN/H_2O) to afford **11** (1.2 mg). The fifth fraction (140 mg) was purified on Sephadex LH-20 and followed with purification on HPLC (DIOL, 15% acetone/hexane) to afford the major compound **10** (32 mg). The sixth fraction (500 mg) was purified on Sephadex LH-20 and DIOL CC (9% acetone/hexane) to give a mixture (150 mg); one third of which was separated by HPLC (silica gel, 22% EtOAc/hexane) to give the major compound **5** (30 mg) and the minor compound **6** (2.2 mg). The seventh fraction (300 mg) was subjected to Sephadex LH-20 and CC (43% EtOAc/hexane) to afford three fractions fr.71, fr.72 and fr.73. Fr.71 (12 mg) was purified by HPLC (silica gel, 45% EtOAc/hexane) to afford **9** (4.5 mg). Fr.72 (14 mg) was separated by HPLC (DIOL, 36% EtOAc/hexane) to afford **8** (4.9 mg). Fr.73 (19 mg) was purified by HPLC (silica gel, 47% EtOAc/hexane) to afford **7** (18 mg).

3.3.1. (+)-cis-3β-Acetoxybicyclogermacra-1(10)(E),4(E)-diene (**4**)

Colourless oil; $[\alpha]_D$ +28 (*c* 1.0, $CHCl_3$); FTIR ν_{max} (liquid film, cm^{-1}) 2921, 2859, 1738, 1452, 1371, 1240, 1178, 1151, 1042, 1021, 865, 849; ^1H NMR and ^{13}C NMR spectra—see Table 1; HREI-MS 262.1931 ($C_{17}H_{26}O_2$ requires 262.1926), 220.1827 ($C_{15}H_{24}O$ calcd as 220.1821), 202.1719 ($C_{15}H_{22}$ requires 202.1716); EIMS *m*/*z* (rel int.) 262 (M^+, 8), 220 (9), 202 (45), 191 (81), 159 (91), 133 (86), 109 (100), 95 (78), 81 (67), 43 (81).

3.3.2. 8,10-Diepi-chandonanthone (**5**)

Colourless cubes (from EtOAc/hexane, 3:1); mp 127.1–130.3 °C; $[\alpha]_D$ +86 (*c* 2.0, EtOH); UV λ_{max} (EtOH, nm): 256.6 (3.89); FTIR ν_{max} (KBr, cm^{-1}) 2963, 2934, 2877, 1686, 1621, 1462, 1453, 1376, 1246, 1218, 1171, 1138, 1055, 1007, 977, 899, 868; ^1H NMR 4.20 (1H, dddd, *J*=12.5, 10.2, 6.5 and 3.7 Hz), 3.97 (1H, s), 2.92 (1H, dt, *J*=13.4 and 2.8 Hz), 2.40 (1H, dt, *J*=12.5 and 6.5 Hz), 2.28 (1H, dd, *J*=14.8 and 3.7 Hz), 2.08 (2H, m), 2.04 (2H, m), 2.02 (1H, m), 1.97 (3H, s), 1.85 (1H, ddd, *J*=14.3, 12.5 and 6.5 Hz), 1.81 (3H, s), 1.76 (2H, m), 1.52 (1H, m), 1.36 (1H, dt, *J*=13.2 and 3.2 Hz), 1.35 (3H, s), 1.12 (3H, s), 0.98 (3H, d, *J*=6.5 Hz); ^{13}C NMR 198.9 (C, C-14), 145.4 (C, C-1), 134.1 (C, C-15), 115.5 (C, C-7), 84.8 (C, C-4), 74.9 (CH, C-10), 66.3 (CH, C-13), 62.2 (C, C-12), 42.7 (CH_2, C-11), 40.6 (CH, C-8), 38.6 (CH_2, C-3), 37.1 (CH_2, C-5), 34.8 (CH_2, C-9), 33.1 (CH_2, C-6), 27.5 (CH_3, C-18), 22.8 (CH_2, C-2), 22.4 (CH_3, C-16), 22.1 (CH_3, C-17), 18.3 (CH_3, C-20), 13.0 (CH_3, C-19); HREI-MS 334.2148 ($C_{20}H_{30}O_4$ calcd as 334.2136); EIMS *m*/*z* (rel int.) 334 (M^+, 11), 301 (19), 238 (15), 209 (39), 191 (21), 163 (40), 151 (56), 137 (52), 121 (48), 109 (39), 95 (100), 69 (38), 43 (54).

3.3.3. β-1,15-Dihydro-8,10-diepi-chandonanthone (**6**)

Colourless needles (from EtOAc/hexane, 3:1); mp 132.3–135.9 °C; $[\alpha]_D$ −29 (*c* 0.2, $CHCl_3$); FTIR ν_{max} (KBr, cm^{-1}) 2964, 2928, 2871, 1710, 1647, 1458, 1379, 1004, 889; ^1H NMR and ^{13}C NMR spectra—see Table 2; HREI-MS 336.2304 ($C_{20}H_{32}O_4$ calcd as 336.2292); EIMS *m*/*z* (rel int.) 336 (M^+, 59), 318 (17), 308 (37), 293 (22), 275 (23), 209 (59), 185 (92), 123 (89), 109 (100), 97 (95), 69 (86).

3.3.4. 2α,10α-Diacetoxy-7,8,18,19-diepoxydolabell-3(E)-en-14-one (**7**)

Colourless cubes (from MeOH); mp 163.1–164.7 °C; $[\alpha]_D$ +55 (*c* 1.7, $CHCl_3$); FTIR ν_{max} (liquid film, cm^{-1}) 2968, 2938, 1742, 1452, 1374, 1233, 1072, 1036, 1023, 817, 755; ^1H NMR and ^{13}C NMR spectra—see Table 3; HREIMS 434.2321 ($C_{24}H_{34}O_7$ calcd as 434.2295); EIMS *m*/*z* (rel int.) 434 (M^+, 2), 391 (2), 374 (4), 332 (7), 314 (10), 299 (6), 271 (6), 221 (12), 201 (18), 179 (36), 153 (42), 135 (56), 95 (58), 43 (100).

3.3.5. 2α,10α,14α-Triacetoxy-7,8,18,19-diepoxydolabell-3(E)-ene (**8**)

Colourless oil; $[\alpha]_D$ +1 (*c* 0.5, $CHCl_3$); FTIR ν_{max} (liquid film, cm^{-1}): 2988, 2884, 1734, 1455, 1373, 1241, 1046, 755; ^1H NMR and ^{13}C NMR spectra—see Table 4; HRFABMS 479.2667 ($C_{26}H_{39}O_8$ calcd as 479.2634); FABMS *m*/*z* (rel int.) 479.3 {$[M+H]^+$, 13}, 419.3 (100), 149.0 (43).

3.3.6. 10α,14α-Diacetoxy-7,8-epoxydolabella-3(E),18-dien-2α-ol (**9**)

Colourless oil; $[\alpha]_D$ +17 (*c* 0.6, $CHCl_3$); FTIR ν_{max} (liquid film, cm^{-1}) 3497, 3073, 2936, 1734, 1644, 1452, 1376, 1242, 1117, 1047, 1023, 892, 736; ^1H NMR and ^{13}C NMR spectra—see Table 5; HREIMS $[M-AcOH]^+$ 360.2294 ($C_{22}H_{32}O_4$ calcd as 360.2292); EIMS *m*/*z* (rel int.) 420 (M^+, 1), 360 (3), 300 (25), 203 (90), 150 (100), 95 (53).

3.3.7. 2α,10α-Diacetoxy-7,8-epoxydolabella-3(E),18-diene (**10**)

Colourless oil; $[\alpha]_D$ +25 (*c* 3.6, $CHCl_3$); FTIR ν_{max} (liquid film, cm^{-1}) 3073, 2955, 2873, 1734, 1451, 1372, 1238, 1020, 756; ^1H NMR and ^{13}C NMR spectra—see Table 6; HREIMS 404.2574 ($C_{24}H_{36}O_5$ calcd as 404.2553); EIMS *m*/*z* (rel int.) 404 (M^+, 2), 344 (6), 302 (6), 284 (18), 269 (15), 241 (15), 175 (81), 151 (68), 133 (69), 119 (64), 107 (71), 95 (54), 43 (100).

3.3.8. Dolabella-3(E),7(E),18-trien-2α-ol (**11**)

Colourless oil; $[\alpha]_D$ −3 (*c* 0.1, $CHCl_3$); FTIR ν_{max} (liquid film, cm^{-1}) 3441, 3071, 2953, 2920, 1641, 1451, 1376, 992, 886; ^1H NMR and ^{13}C NMR spectra—see Table 7; HREI-MS 288.2463 ($C_{20}H_{32}O$ calcd as 288.2445); EIMS *m*/*z* (rel int.) 288 (M^+, 8), 270 (20), 255 (13), 247 (15), 227 (19), 189 (19), 175 (22), 161 (35), 149 (44), 134 (100), 123 (89), 107 (76), 94 (66), 81 (65).

*3.3.9. (−)-(6R,7S)-Sesquiphellandrene (**12**)*

Colourless oil; $[\alpha]_D$ −2.8 (*c* 1.2, $CHCl_3$), {lit.[9] −7.8 (*c* 0.8, $CHCl_3$)}; ^{1}H NMR 6.14 (1H, dd, *J*=10.2 and 2.3 Hz, H-2), 5.68 (1H, d, *J*=10.2 Hz, H-1), 5.11 (1H, tt, *J*=6.9 and 1.4 Hz, H-10), 4.75 (1H, s, H-15), 4.73 (1H, s, H-15), 2.45 (1H, dt, *J*=15.3 and 3.9 Hz, H-4), 2.28 (1H, ddt, *J*=13.4, 3.7 and 1.4 Hz, H-4), 2.21 (1H, br s, H-6), 2.03 (1H, m, H-9), 1.93 (1H, m, H-9), 1.71 (1H, m, H-5), 1.61 (3H, s, H-13), 1.55 (3H, s, H-12), 1.53 (1H, m, H-7), 1.39 (2H, m, H-5 and H-8), 1.21 (1H, m, H-8), 0.84 (3H, d, *J*=6.9 Hz, H-14); ^{13}C NMR 143.8 (C, C-3), 135.2 (CH, C-1), 131.3 (C, C-11), 129.5 (CH, C-2), 124.8 (CH, C-10), 109.8 (CH_2, C-15), 40.6 (CH, C-6), 36.6 (CH, C-7), 34.3 (CH_2, C-8), 30.4 (CH_2, C-4), 26.0 (CH_2, C-9), 25.7 (CH_3, C-13), 24.5 (CH_2, C-5), 17.6 (CH_3, C-12), 15.9 (CH_3, C-14).

*3.3.10. Methanolysis of (+)-cis-3β-acetoxybicyclogermacra-1(10)(E),4(E)-diene (**4**)*

Compound **4** (9.0 mg) and K_2CO_3 (200 mg) were dissolved in 5 ml methanol and stirred until TLC showed that the reaction was complete. The product (7.6 mg) was obtained as a colourless oil, (−)-bicyclogermacra-1(10)(*E*),4(*E*)-dien-3β-ol (**16**). Colourless oil; $[\alpha]_D$ −31 (*c* 0.6, $CHCl_3$); FTIR ν_{max} (liquid film, cm^{-1}) 3413, 2921, 2861, 1711, 1660, 1455, 1379, 1217, 1196, 1053, 1013, 849, 758, 666; ^{1}H NMR 5.01 (1H, ddt, *J*=11.1, 5.1 and 1.4 Hz), 4.88 (1H, dd, *J*=11.6 and 1.4 Hz), 4.44 (1H, t, *J*=2.8 Hz), 2.46 (1H, dt, *J*=12.9 and 3.2 Hz), 2.28 (1H, dt, *J*=13.4 and 4.0 Hz), 2.18 (1H, ddd, *J*=13.9, 11.1 and 2.8 Hz), 1.92 (1H, ddd, *J*=14.3, 6.9 and 2.8 Hz), 1.73 (1H, dt, *J*=4.1 and 13.0 Hz), 1.64 (3H, d, *J*=0.9 Hz), 1.47 (3H, d, *J*=0.9 Hz), 1.36 (1H, dd, *J*=11.6 and 8.3 Hz), 1.31 (1H, dd, *J*=12.5 and 4.6 Hz), 1.11 (3H, s), 1.06 (3H, s), 0.70 (1H, ddd, *J*=12.1, 8.8 and 2.8 Hz); ^{13}C NMR 142.8 (C), 130.3 (C), 125.1 (CH), 120.0 (CH), 77.5 (CH), 37.2 (CH_2), 32.5 (CH_2), 30.5 (CH), 29.2 (CH_3), 27.0 (CH_2), 26.7 (CH), 21.0 (CH_3), 20.4 (C), 16.0 (CH_3), 15.5 (CH_3); HREIMS 220.1818 ($C_{15}H_{24}O$ calcd as 220.1821), 202.1719 ($C_{15}H_{22}$ calcd as 202.1716); EIMS *m*/*z* (rel int.) 220 (M^+, 13), 202 (10), 191 (30), 159 (36), 137 (43), 121 (70), 109 (100), 95 (65), 81 (40), 43 (36).

*3.3.11. Methanolysis of 2α,10α-diacetoxy-7,8-epoxydolabella-3(E),18-diene (**10**)*

Compound **10** (10 mg) was methanolyzed as described above; the product (9.3 mg), 10-acetoxy-7,8-epoxydolabella-3(*E*)18-dien-2α-ol (**18**), was obtained as a colourless oil; $[\alpha]_D$ +39 (*c* 0.4, $CHCl_3$); FTIR ν_{max} (liquid film, cm^{-1}) 3449, 3073, 2951, 2874, 1730, 1641, 1451, 1376, 1244, 1044, 1020, 886; ^{1}H NMR 4.96 (2H, m), 4.85 (1H, q, *J*=1.4 Hz), 4.18 (1H, br d, *J*=8.7 Hz), 3.02 (1H, d, *J*=9.7 Hz), 2.79 (1H, m), 2.26 (3H, m), 1.83–2.06 (2H, m), 1.99 (3H, s), 1.83 (3H, s), 1.70 (3H, s), 1.61 (1H, m), 1.51 (3H, s), 0.77 (3H, s); ^{13}C NMR 170.0 (C), 147.2 (C), 136.5 (C), 123.8 (CH), 112.5 (CH_2), 76.0 (CH), 73.1 (CH), 62.6 (CH), 59.8 (C), 48.6 (C), 47.8 (CH), 44.9 (CH), 42.4 (CH_2), 37.3 (CH_2), 35.8 (CH_2), 31.6 (CH_2), 23.0(CH_2), 22.6 (CH_3), 21.4 (CH_3), 21.1 (CH_3), 19.5 (CH_3), 18.7 (CH_3); HREIMS 362.2458 ($C_{22}H_{34}O_4$ calcd as 362.2448); EIMS *m*/*z* (rel int.) 362 (M^+, 2), 302 (12), 284 (19), 269 (14), 245 (21), 175 (58), 161 (44), 151 (75), 133 (81), 121 (81), 107 (87), 95 (83), 81 (80), 43 (100).

*3.3.12. Oxidation of 10α-acetoxy-7,8-epoxydolabella-3(E)18-dien-2α-ol (**18**)*

Alcohol **18** (9.0 mg) was oxidized with Collins' reagent to give 10α-acetoxy-7,8-epoxydolabella-3(*E*),18-dien-2-one (**19**) (8.7 mg). Colourless oil; $[\alpha]_D$ −58 (*c* 0.8, $CHCl_3$); FTIR ν_{max} (liquid film, cm^{-1}) 3075, 2961, 2936, 2874, 1733, 1682, 1623, 1456, 1376, 1241, 1049, 1024, 939, 890.4, 734; ^{1}H NMR 6.41 (1H, s), 5.48 (1H, dd, *J*=11.5 and 3.1 Hz), 4.85 (1H, br s), 4.81 (1H, t, *J*=1.6 Hz), 3.12 (1H, dd, *J*=10.8 and 2.2 Hz), 3.01 (1H, dd, *J*=11.7 and 8.0 Hz), 2.62 (1H, ddd, *J*=13.2, 8.0 and 1.4 Hz), 2.38 (2H, m), 2.29 (1H, dd, *J*=13.5 and 11.6 Hz), 2.17 (1H, m), 2.05 (3H, s), 1.93 (3H, s), 1.76 (1H, m), 1.74 (3H, s), 1.47 (2H, m), 1.40 (1H, dd, *J*=13.5 and 2.8 Hz), 1.25 (2H, m), 1.15 (3H, s), 1.13 (3H, s); ^{13}C NMR 203.3 (C), 170.1 (C), 152.5 (C), 147.1 (C), 123.1 (CH), 112.6 (CH_2), 75.5 (CH), 71.6 (CH), 61.3 (CH), 58.8 (C), 56.8 (CH), 50.1 (CH), 46.5 (CH), 43.2 (CH_2), 37.4 (CH_2), 32.9 (CH_2), 30.0 (CH), 25.0 (CH_2), 21.4 (CH_3), 20.5 (CH_3), 19.9 (2×CH_3), 18.5 (CH_3); HREI-MS 360.2300 ($C_{22}H_{32}O_4$ calcd as 360.2292); EIMS *m*/*z* (rel int.) 360.2 (M^+, 4), 300 (10), 285 (10), 257 (9), 201 (31), 175 (48), 151 (81), 133 (83), 121 (73), 107 (88), 95 (92), 82 (81), 43 (100).

3.4. Crystallographic analysis

All of the data were collected on Bruker AXS SMART APEX CCD diffractometer. Sadabs[23] was used for absorption corrections, λ=0.71073 Å. Tables of atomic co-ordinates, bonds lengths and angles, anisotropic displacement parameters and hydrogen atom co-ordinates are deposited with the Cambridge Crystallographic Data Center.[†]

*3.4.1. Crystallographic analysis of 8,10-diepi-chandonanthone (**5**)*

$C_{20}H_{30}O_4$, Mr 334.44, orthorhombic, space group $P2_12_12_1$, *a*=8.6420(11) Å, *b*=12.0138(16) Å, *c*=18.429(2) Å, α=β=γ=90°, *V*=1913.4(4) Å^3, *Z*=4, density (calculated)=1.161 Mg/m^3, *F*(000)=728, μ=0.079 mm^{-1}. Data were collected using a crystal size ca. 0.60×0.56×0.40 mm^3 (CCDC 256149).

*3.4.2. Crystallographic analysis of β-1,15-dihydro-8,10-diepi-chandonanthone (**6**)*

$C_{20}H_{32}O_4$, Mr 336.46, hexagonal, space group $P6_2$, *a*=18.6172(9) Å, *b*=18.6172(9) Å, *c*=9.2951(9) Å, α=β=90°, γ=120°, *V*=2790.1(3) Å^3, *Z*=6, density (calculated)=1.201 Mg/m^3, *F*(000)=1104, μ=0.082 mm^{-1}. Data were collected using a crystal size ca. 0.30×0.20×0.18 mm^3 (CCDC 256148).

*3.4.3. Crystallographic analysis of 2α,10α-diacetoxy-7,8,18,19-diepoxydolabell-3(E)-en-14-one (**7**)*

$C_{24}H_{34}O_7$, Mr 434.51, triclinic, space group *P*1, *a*=8.9853(4) Å, *b*=9.5870(4) Å, *c*=14.4060(6) Å, α=76.7830(10)°, β=82.8560(10)°, γ=86.1660(10)°, *V*=1197.76(9) Å^3, *Z*=2, density (calculated)=1.205 Mg/m^3, *F*(000)=468, μ=0.088 mm^{-1}. Data were collected using a crystal size ca. 0.40×0.28×0.20 mm^3 (CCDC 256150).

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[†] CCDC contains the supplementary crystallographic data for this paper (please refer to sections 3.4.1–3.4.3 for the reference numbers). These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html, or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033; e-mail: deposit@ccdc.cam.ac.uk.

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