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FURTHER BRIAREOLATE ESTERS AND BRIAREOLIDES FROM THE CARIBBEAN GORGONIAN OCTOCORAL *BRIAREUM ASBESTINUM*[1,2]

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Abstract: Eight new diterpenes were isolated from *Briareum asbestinum* collected off south-west Tobago. Six metabolites (**4**) - (**9**) are briareolate esters while (**10**) and (**11**) are related to the briareolides. The structures of all compounds were determined by 2D NMR spectroscopy and correlation with known compounds. The structure of compound **4** was confirmed by X-ray analysis. Compounds **4**, **7**, **9** and **11** showed weak activity in the brine shrimp bioassay.

Our previous investigations of the Caribbean gorgonian octocoral *Briareum asbestinum* (Pallas) yielded six diterpenes including methyl briareolate (**1**) the first briarein diterpene containing a C-19 methyl ester and the derivatives (**2**) and (**3**), which we now designate briareolate esters A, B and C, respectively.[1,2] We have made further collections of *B. asbestinum* at Milford Bay and Buccoo Reef in south-west Tobago and now report the isolation and structure determination of briareolate esters D-I **4** - **9** and briareolides J **10** and K **11** from this organism. Compounds **5**, **6**, **8**, and **10** were isolated from the specimen collected at Milford Bay while compounds **4**, **7**, **9**, and **11** were isolated from the Buccoo Reef specimen.

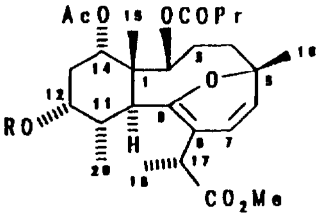
Briareolate ester D **4** was isolated as a crystalline solid, mp 160-163°, and had the molecular formula $C_{27}H_{40}O_9$ as determined by HREIMS data. The IR spectrum had absorptions due to hydroxy (3500 cm^{-1}) and carbonyl (1735 and 1690 cm^{-1}) functionalities. In addition to a secondary hydroxy group, the ^{1}H and ^{13}C NMR spectra revealed the presence of one butyroxy, an acetoxy, a carbomethoxy, a ketone, a trisubstituted olefinic bond and a trisubstituted epoxide.

The COSY, HMQC and HMBC experiments readily located the butyrate at C-2 and the acetate at C-14. The connectivities from C-1 through to C-8 and to C-17 and the relationship of the latter to C-18 and C-19 were easily traced. The environment of the C-7/C-8 epoxide, with C-17 directly attached to one side and C-6 on the other, was established by HMBC correlations of C-8 to H-7 and H-17 and vicinal coupling between H-6 and H-7. In addition, the C-9 carbonyl showed HMBC correlations with H-7, H-10 and H-17. Complete ^{1}H assignments for compounds **4** - **9** are given in Table 1 with ^{13}C assignments in Table 2.

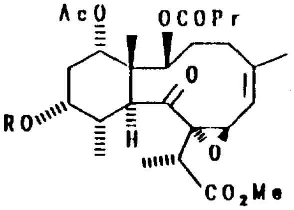
Table 1. ^{1}H NMR Assignments of Compounds (4) - (9).[a]

Position	**4**	**5**	**6**	**7**	**8**	**9**
2	5.45 (8.3)	5.50 (8.1)	5.50 (8.0)	4.98 (6.6; 2.0)	4.95 (10.5; 1.5)	5.21 (8.0)
3	2.27 (m) 1.53 (m)	2.24 (m) 1.54 (m)	2.25 (m) 1.52 (m)	1.87 (m) 1.87 (m)	2.09 (m) 1.38 (m)	2.47 (m) 1.72 (m)
4	2.58 (18.0; 8.0) 2.22 (m)	2.59 (18.0; 7.0) 2.22 (m)	2.59 (18.0; 9.0) 2.20 (m)	2.37 (m) 2.10 (m)	2.33 (m) 1.35 (m)	2.47 (m) 2.47 (m)
6	5.37 (7.0)	5.38 (6.3)	5.38 (7.0)	6.07 (4.0)	5.59 (9.0)	5.34 (bd, 7.0)
7	4.42 (7.0)	4.46 (6.3)	4.46 (7.0)	6.63 (4.0;2.0)	5.93 (9.0)	4.35 (7.0)
10	2.93 (11.0)	3.07 (11.5)	3.07 (11.0)	3.54 (11.0)	3.64 (10.5)	3.05 (12.0)
11	2.11 (m)	2.22 (m)	2.21 (m)	2.01 (m)	2.22 (m)	2.75 (m)
12	3.70 (dq,10.0; 3.3)	4.99 (q, 3.3)	5.01 (q, 3.1)	3.65 (m)	5.08 (q, 3.3)	- -
13	2.08 (m) 1.87 (dt, 12.0; 3.3)	2.13 (dt, 16.0; 3.3) 1.84 (dt, 16.0; 3.3)	2.11 (dt, 16.0; 3.3) 1.85 (dt,16.0; 3.3)	2.03 (m) 1.93 (m)	2.09 (m) 2.09 (m)	5.91 (10.0)
14	4.92 (t, 3.3)	4.72 (t, 3.3)	4.71 (t, 3, 3)	4.95 (t, 3.0)	4.89 (t, 3.0)	6.41 (10.0)
15	0.97 (s)	0.96 (s)	0.96 (s)	1.21 (s)	1.39 (s)	1.07 (s)
16	1.75 (bs)	1.74 (bs)	1.74 (bs)	2.17 (t, 1.5)	1.35 (s)	1.77 (bs)
17	2.31 (q, 7.0)	2.33 (q, 7.0)	2.33 (q, 7.0)	3.47 (q, 7.0)	3.71 (q, 7.0)	2.31 (q, 7.0)
18	1.37 (7.0)	1.34 (7.0)	1.35 (7.0)	1.37 (7.0)	1.34 (7.0)	1.40 (7.0)
20	0.90 (7.0)	0.76 (7.0)	0.76 (7.0)	0.92 (7.0)	0.85 (7.0)	0.98 (7.0)
OCH_3	3.65 (s)	3.66 (s)	3.65 (s)	3.65 (s)	3.84 (s)	3.68 (s)
C-2 Ester	2.23 (t, 7.1) 1.61 (m) 0.94 (t, 7.5)	2.22 (t, 7.1) 1.58 (m) 0.94 (t, 7.2)	2.23 (m) 1.60 (m) 0.93 (t, 8.0)	2.21 (t, 7.5) 1.61 (m, 7.5) 0.93 (t, 7.5)	2.18 (m) 1.58 (m) 0.92 (t, 8.0)	2.40 (t, 7.5) 1.72 (m, 7.5) 1.00 (t, 7.5)
C-12 Ester	- - - - - -	2.03 (s) - - - -	2.23 (m) 1.65 (m) 0.95 (t, 8.0)	- - - - - -	2.05 (s) - - - -	- - - - - -
C-14 Ester	2.07 (s)	2.01 (s)	2.01 (s)	2.05 (s)	1.95 (s)	- -

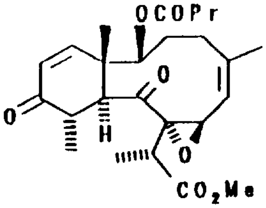
[a] Spectra were recorded at 500.0 MHz in $CDCl_3$ with TMS as internal standard. Assignments are based on COSY, HMQC and HMBC experiments with coupling constants (Hz) in parenthesis. When multiplicity is not noted, a doublet is implied.



(1) R = PrCO
(2) R = H; (8) R = Ac



(4) R = H
(5) R = Ac; (6) R = PrCO



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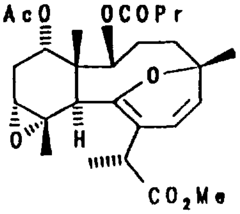

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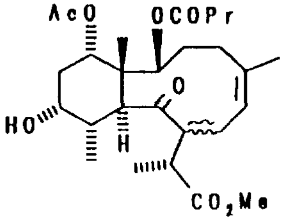

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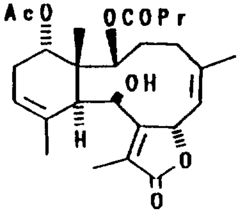
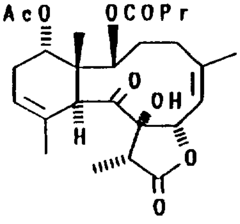


(10)



(11)

Initial stereochemical assignments for 4 were carried out with the aid of vicinal coupling constants and selective n.O.e. measurements. Initially H-12 was misassigned as α-axial (i.e. different from 1 and 2) due to the observation of a 10 Hz coupling to this proton. However, an axial orientation for H-12 should give rise to two large couplings to the β-axial H-11 and H-13. Closer inspection of the COSY and HMQC spectra indicated that H-12 was coupled strongly to a doublet at δ 1.97 which showed no correlation with a carbon in the HMQC spectrum and thus must be the OH proton. Selective irradiation of the δ 1.97 doublet gave a 6.7% enhancement of H-10 , confirming the α-axial orientation of the OH group and consequently the β-equatorial orientation of H-12. Consistent with this was the absence of large splittings of H-12 other than to the OH proton.

A further series of selective n.O.e. measurements were carried out to deduce other stereochemical features. Irradiation of the C-16 methyl singlet caused a 10% enhancement of H-6, consistent with a Z-orientation of the C-5/C-6 double bond, while irradiation of H-7 caused enhancements of 14.8% for H-2 and 10.9% for H-10. On the other hand irradiation of H-2 caused only a 1.5% enhancement of H-10. At the same time, irradiation of H-17 caused a significant (2.5%) enhancement of H-6 but a negligible (<0.5%)

Table 2. ^{13}C NMR Assignments of Compounds (4) - (9).[a]

Position	4	5	6	7	8	9
1	47.0	46.6	47.0	44.8	45.6	45.8
2	78.6	79.2	78.6	73.6	78.0	81.8
3	29.6	29.5	29.5	30.8	28.6	29.6
4	32.6	32.3	32.7	28.7	34.8	32.6
5	145.3	145.5	145.4	144.8	75.2	146.2
6	114.5	114.6	114.6	123.5	130.1	114.9
7	62.7	62.9	62.6	138.1	120.4	63.5
8	69.7	69.7	69.8	144.3	117.6	68.9
9	209.4	209.9	209.9	205.7	151.1	206.9
10	42.1	43.3	43.1	45.8	37.3	49.8
11	36.6	34.7	34.6	38.9	31.8	40.5
12	69.7	70.6	70.0	71.0	72.5	198.8
13	31.2	28.6	28.8	31.5	30.9	126.7
14	74.3	72.6	72.4	75.6	74.0	150.9
15	12.3	12.3	12.1	14.4	14.9	14.2
16	26.2	26.6	26.2	27.2	23.6	26.1
17	39.3	39.6	39.3	44.2	37.7	39.3
18	12.6	12.7	12.7	18.9	14.4	12.5
19	172.1	172.2	172.3	174.6	174.7	172.0
20	16.2	16.0	15.7	16.9	15.1	12.5
OCH_3	51.5	51.9	51.6	51.8	52.0	51.6
C-2 Ester	173.5	173.6	173.5	173.3	172.6	173.0
	36.3	36.4	36.3	36.3	36.4	36.4
	18.1	18.4	18.2	18.1	18.2	18.5
	13.6	14.0	13.6	13.7	13.7	13.7
C-12 Ester	- -	170.0	173.0	- -	170.2	- -
	- -	21.1	36.5	- -	21.1	- -
	- -	- -	18.5	- -	- -	- -
	- -	- -	13.7	- -	- -	- -
C-14 Ester	169.9	170.5	170.5	169.1	170.1	- -
	21.6	21.3	21.5	21.3	21.0	- -

[a] Spectra were recorded in $CDCl_3$ at 125 MHz with TMS as the internal standard. All assignments are based on HMQC and HMBC experiments.

enhancement of H-7. Examination of molecular models showed that this set of observations could only be explained if the epoxide had a *trans* stereochemistry.

To confirm this, an X-ray crystal structure determination of **4** was carried out. The results, illustrated in Figure 1, confirmed the *trans* stereochemistry of the epoxide, the α-orientation of the OH group and the Z-geometry of the C-5/C-6 double bond. The solution conformation must be relatively similar to the crystal structure conformation, since the latter gives an H-2/H-7 distance of 1.91Å, H-2/H-10 of 2.42Å and H-7/H-10 of 2.19Å, generally consistent with the solution n.O.e. measurements.

Briareolate ester E **5**, $C_{29}H_{42}O_{10}$, was isolated as an amorphous powder and had IR absorptions due to ester (1735 cm^{-1}) and ketone (1710 cm^{-1}) carbonyls. The ^1H NMR spectrum was similar to that of **4** except that the oxymethine proton at δ 3.70 had shifted downfield to δ 4.99 in **5** in addition to the appearance of a new acetate methyl at δ 2.03. Compound **5** is therefore the 12-acetoxy analogue of **4**.

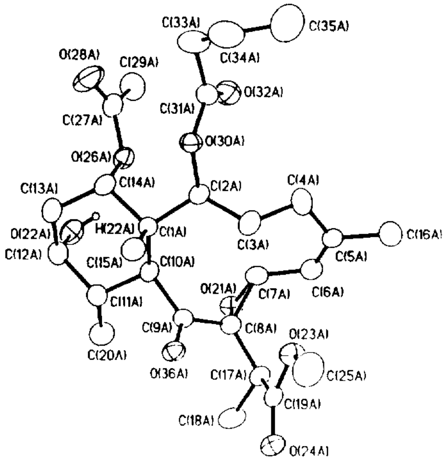


Figure 1. ORTEP Drawing of Compound 4.

Briareolate ester F **6**, the least polar of the compounds isolated, had the molecular formula $C_{31}H_{46}O_{10}$, indicated by ^{13}C and ^1H NMR spectra and confirmed by high resolution mass spectrometry. The IR spectrum showed ester (1735 cm^{-1}) and ketone (1710 cm^{-1}) absorbances. The ^1H and ^{13}C NMR spectra also confirmed the functional groups as two butyroxy, one acetoxy, a carbomethoxy, a ketone, a trisubstituted olefinic bond and a trisubstituted epoxide. The HMBC experiment showed that the acetate was at C-14 while the butyrates were at C-2 and C-12. The shape of the proton signals in **4**, **5**, and **6** indicate that they all have the same stereochemistry.

Briareolate ester G **7** was a crystalline compound, mp 99.5-101. The UV absorptions at λ_{max} 232 nm (log ε 3.74) and 288 nm (log ε 3.67) suggested that an extended conjugated system was present. Four olefinic

Table 3. ^{13}C and ^{1}H NMR Assignments of Compounds (**10**) and (**11**).[a]

Position	**10**[b]		**11**	
	δ_C	δ_H	δ_C	δ_H
1	42.6	- -	46.6	- -
2	74.0	5.30 (bs)	72.8	4.95 (5.9; 2.2)
3	26.2	2.89 (bd, 12.0) 2.07 (m)	34.6	1.72 (m) 1.72 (m)
4	29.9	1.49 (bs) 1.46 (bs)	29.7	2.53 (15.0; 3.1) 2.17 (m)
5	145.3	- -	147.7	- -
6	121.9	5.10 (bs)	120.3	5.48 (m)
7	79.5	6.08 (bd, 9.0)	84.2	5.13 (9.8)
8	161.1	- -	87.4	- -
9	68.6	5.02 (bs)	209.7	- -
10	45.8	3.29 (bs)	50.7	3.96 (bs)
11	132.0	- -	130.0	- -
12	122.8	5.47 (bs)	121.9	5.48 (m)
13	28.0	2.53 (bd, 18.0) 2.12 (m)	26.4	2.35 (14.6; 3.1) 2.13 (m)
14	75.5	5.12 (bs)	71.8	4.77 (t, 3.0)
15	17.7	1.40 (s)	15.2	0.89 (s)
16	24.1	1.83 (bs)	26.7	2.18 (bs)
17	127.3	- -	42.4	2.96 (q, 7.0)
18	10.2	2.00 (s)	7.6	1.13 (7.0)
19	174.2	- -	174.8	- -
20	22.1	1.59 (bs)	23.6	1.56 (bs)
C-2 Ester	172.2 36.6 18.3 13.7	- - 2.30 (m, 7.0) 1.68 (sext, 7.0) 0.98 (t, 7.0)	173.3 36.1 18.2 13.7	- - 2.27 (t, 8.0) 1.63 (sext, 8.0) 0.95 (t, 8.0)
C-14 Ester	170.6 21.1	- - 1.95 (s)	170.4 21.2	- - 1.98 (s)

[a] Spectra were recorded at 500 MHz for protons and 125 MHz for carbon in $CDCl_3$ with TMS as the internal standard. Values in parenthesis are coupling constants in Hz. When multiplicity is not noted, a doublet is implied. [b] Spectra recorded at 50°C.

carbons, C-5 to C-8, had signals at δ_C 144.8, 123.5, 138.1 and 144.3, respectively. In addition, the COSY correlation between H-6 (δ 6.07, bd, 4.0 Hz) and H-7 (δ 6.63, dd, 4.0, 2.0 Hz) was evident. The highest peak in the HREIMS for $C_{23}H_{32}O_6$ suggested an M^+-C_3H_7COOH fragment. The molecular formula, $C_{27}H_{40}O_8$, was corroborated by ^1H and ^{13}C NMR data, which indicated the presence of a hydroxy in the molecule (ν_{max} 3500 cm^{-1}) in addition to one acetate, a butyrate and a carbomethoxy group. The location of the hydroxy was determined by HMBC correlations to be at C-12, with the butyrate at C-2 and the acetate at C-14. The stereochemistry in ring A at the relevant carbons and at C-2 was assumed to be as for **4** - **6** since the position and shape of the proton resonances were similar. By analogy with other briareins in this series, the $\Delta^{5,6}$ bond will be expected to be Z and the δ_C for C-16 (δ 27.2) is consistent with this assignment.[3] The flexibility of the ten-membered ring and small coupling constant for H-6/H-7 (4 Hz) made it difficult to define the conformation across the C-6/C-7 bond. The geometry across the $\Delta^{7,8}$ bond was not determined. The compound was fairly unstable and decomposition precluded any further experimentation.

Briareolate ester H **8**, $C_{29}H_{42}O_9$, had ^1H and ^{13}C NMR data virtually identical with briareolate ester A **1** except for the replacement of a butyrate group in **1** by an acetate in compound **8**.[1] It is therefore the 12-OAc analogue of **1**. The butyrate at C-2 was readily identified by HMBC correlations between position 2 and C-1, C-10, C-14 and C-15 on the one hand and of the carbonyl of the butyrate moiety on the other. The stereochemistry was determined by comparison of the NMR data with those of briareolate esters A and B[1,2] and confirmed by a NOESY experiment.

Briareolate ester I **9** was the most polar compound isolated. The spectral data indicated a molecular formula of $C_{25}H_{34}O_7$, with butyroxy, carbomethoxy, ketone, α,β-unsaturated ketone, trisubstituted epoxide and trisubstituted olefinic moieties. High resolution NMR experiments established all the connectivities from C-1 to C-8; it was further extended through to C-17 and to C-19 via $^{2,3}J_{CH}$ connectivities involving C-17 (δ 39.33) and its proton (δ 2.31, q, 7.0 Hz). While the C-8/C-9 connectivity was not established directly, the $^3J_{CH}$ correlation between C-9 (δ 206.9) and both H-17 (δ 2.31) and H-7 (δ 4.35) could be clearly seen as well as the $^2J_{CH}$ coupling between C-9 and H-10 (δ 3.05 d, 12.0 Hz). The structure of ring A including the α,β-unsaturated ketone was established by $^{2,3}J_{CH}$ connectivities involving all positions in the ring and the COSY correlation between H-13 (δ 5.91, d, 10.0 Hz) and H-14 (δ 6.41, d, 10.0 Hz). The relative stereochemistry suggested by analogy with compounds **1**, **2** and **3** was further supported by NOESY experiments.

Briareolide J **10** was obtained as an amorphous powder and HREIMS denoted a molecular formula, $C_{26}H_{36}O_7$. The functional groups were ascertained to be acetate, butyrate, hydroxy (ν_{max} 3450 cm^{-1}), two trisubstituted double bonds and an α,β-unsaturated γ-lactone (uv λ_{max} 235 nm, log ϵ 3.75). The HMBC correlations for this compound were done at 50° in order to sharpen the peaks. The vicinal methylene carbons at C-3 and C-4 were identified from the 2D COSY spectrum. The relationships involving C-4, C-5, C-6 and C-16 were made via $^3J_{CH}$ connectivities between H-4 and C-16 and H-16 and C-6 as well as $^2J_{CH}$ correlation between H-16 and C-5. Further direct connectivities from C-6 to C-9 and to C-17, C-18 and C-19 on the one hand and from C-10 to C-14 and C-1 on the other, as well as the relative positions of C-15 and C-20 to the rest of the structure as shown were all discernible from the HMBC data. In order to locate the acyl groups, the HMBC experiment was repeated this time at 70° in C_6D_6. Compound **10** is closely related to briareolides A to I which were reported from *B. asbestinum* collected off Puerto Rico.[4] The relative stereochemistry is suggested as shown by analogy with these compounds.

Briareolide K **11** was isolated as a colourless gum, $C_{26}H_{36}O_8$, and had acetate and butyrate groups, in addition to ketone, hydroxy (ν_{max} 3425 cm^{-1}) and γ-lactone (ν_{max} 1785 cm^{-1}) functionalities. Also, two trisubstituted double bonds were present. The complete structure was determined by comparison of the NMR data (Table 3) with that of **10** and confirmed by HMBC experiments. The stereochemistry was based on analogy with briareolides A - I since the coupling constants for H-2, H-7, H-10 and H-14 were all similar.[4] Compounds **4**, **7**, **9** and **11** showed weak activity (LD_{50} 400-500 μg/ml) in the brine shrimp bioassay.[5] Caribbean collections of *B. asbestinum* continue to yield briarane and asbestinane diterpenes,[1,2,4,6-8] and there has been a recent report of eunicellane-based diterpenes from this organism.[9] However, the unusual methyl briareolate esters A - J have thus far been reported only from specimens collected off Tobago.

EXPERIMENTAL

The general experimental, instrumentation used and extraction procedures were as described previously.[1] Two samples of *Briareum asbestinum* were collected off south-west Tobago and voucher specimens, are housed at the Institute of Marine Affairs, Trinidad and Tobago.

General Experimental Procedures:

The first sample (1.7 kg dried weight after extraction) was collected from Milford Bay (- 15 meters) in March 1994 and gave 18.8 g of a crude EtOAc residue. Vacuum liquid chromatography (VLC) of this extract (9.3 g) on silica gel using $CHCl_3$ with increasing quantities of EtOAc, followed by column chromatography of the resulting fractions using hexane/EtOAc mixtures, and subsequent TLC gave briareolate ester F (**6**), (10 mg, 0.001%), briareolate ester H (**8**), (5 mg, 0.0005%), briareolate ester E (**5**), (9 mg, 0.0009%), and briareolide J (**10**), (30 mg, 0.003%).

The second sample of *B. asbestinum*, collected at Buccoo Reef (- 8 m), gave an EtOAc soluble gum (8.1 g, 1.3%) which was separated by VLC as before, followed by column chomatography and preparative TLC to give briareolide K (**11**) (6 mg, 0.001%), briareolate ester D (**4**) (46 mg 0.008%), briareolate ester G (**7**), (22 mg, 0.004%), and briareolate ester I (**9**) (6 mg, 0.001%).

Briareolate ester D (4) - Crystalline solid: mp 160-163° (Pet. ether/EtOAc); $[\alpha]_D$ -120.0° (*c* 0.20, $CHCl_3$); IR (nujol) 3500, 1735, 1690 cm^{-1}; EIMS 508 (M^+, 89%), 407 (5), 361 (8), 245 (34), 227 (67), 197 (46), 181 (56), 109 (66), 71 (100); *Exact mass*: 508.2689 calcd. for $C_{27}H_{40}O_9$ 508.2672.

Briareolate ester E (5) - Amorphous powder: $[\alpha]_D$ -74.7° (c 0.28, $CHCl_3$); IR (nujol) 1735, 1710 cm^{-1}; EIMS 550 (M^+, 46%), 448 (10), 360 (6), 343 (10), 283 (11), 255 (26), 227 (71), 199 (38), 181 (35), 135 (37), 71 (100); *Exact mass*: 550.2796 calcd. for $C_{29}H_{42}O_{10}$ 550.2778.

Briareolate ester F (6) - Amorphous powder: $[\alpha]_D$ -62.1° (c 0.29, $CHCl_3$); IR (nujol) 1735, 1710 cm^{-1}; EIMS 578 (M^+, 54%), 550 (1), 508 (2), 474 (14), 311 (9), 283 (10), 255 (26), 227 (64), 199 (36), 181 (32), 71 (100); *Exact mass*: 578.3089 calcd. for $C_{31}H_{46}O_{10}$ 578.3091.

Briareolate ester G (7) - Crystalline solid: mp 99.5-101° (Pet. ether/Me_2CO); $[\alpha]_D$ -121.7° (c 0.23, $CHCl_3$); UV (MeOH) 232 nm (log ϵ 3.74) and 288 nm (log ϵ 3.67); IR ($CHCl_3$) 3500, 1730, 1640 cm^{-1}; EIMS 404 (M^+ - C_3H_7COOH, 100%), 361 (14), 287 (45), 239 (45), 207 (74), 181 (27), 71 (61); *Exact mass*: 404.2208 (M^+ - C_3H_7COOH) calcd. for $C_{23}H_{32}O_6$ 404.2199).

Briareolate ester H (8) - Colourless gum: $[\alpha]_D$ +127.3° (c 0.27, $CHCl_3$); UV (MeOH) 220 nm (log ϵ 3.50), 285 nm (log ϵ 3.58); IR ($CHCl_3$) 1730, 1640 cm^{-1}; EIMS 534 (M^+ , 3%), 474 (15), 446 (100), 403 (30), 387 (17), 287 (44), 239 (14), 207 (70), 181 (14); *Exact mass*: 534.2834 calcd. for $C_{29}H_{42}O_9$ 534.2829.

Briareolate ester I (9) - Colourless gum: $[\alpha]_D$ -113.2° (c 0.22, $CHCl_3$); UV (MeOH) 228 nm (log ϵ 3.70); IR ($CHCl_3$) 1735, 1685 cm^{-1}; EIMS 446 (M^+, 36%), 376 (12), 343 (13), 271 (15), 243 (21), 197 (38), 173 (22), 123 (59), 93 (39), 71 (100); *Exact mass*: 446.2284 calcd. for $C_{25}H_{34}O_7$ 446.2305.

Briareolide J (10) - Amorphous powder: $[\alpha]_D$ +57.8° (c 0.28, $CHCl_3$); UV (MeOH) 235 nm (log ϵ 3.75); IR (nujol) 3450, 1740, 1630 cm^{-1}; EIMS 460 (M^+, 6%), 372 (6), 312 (18), 279 (7), 224 (100), 206 (51), 188 (31), 160 (24), 132 (34), 119 (48), 71 (55); *Exact mass*: 460.2469 calcd. for $C_{26}H_{36}O_7$ requires 460.2461.

Briareolide K (11) - Amorphous solid: $[\alpha]_D$ +116.1° (c 0.16, $CHCl_3$); IR (nujol) 3425, 1785, 1730, 1620 cm^{-1}; EIMS 476 (M^+, 1%), 416 (9), 388 (22), 332 (36), 295 (21), 212 (27), 133 (69), 119 (79), 71 (100); *Exact mass*: 476.2414 calcd. for $C_{26}H_{36}O_8$ 476.2410.

X-ray Analysis - Crystals of (4), $C_{27}H_{40}O_9$, are orthorhombic, with space group $P2_12_12_1$, a=8.831(3), b=16.1966(13), c=37.728(4) Å, V=5397(2) $Å^3$ and D_c=1.249 $Mg.m^{-3}$ for Z=8. A total of 6567 unique reflections (2.5>2θ>27.0) were collected using graphite monochromated Mo-Kα radiation, λ=0.71073 Å, μ(Mo-Kα)=0.093 mm^{-1}, T=173(2)K on a Siemens P4 diffractometer. The structure was solved by direct methods and refined by full-matrix least-squares[10] based on F^2 (only very large negative intensities were suppressed). No absorption correction was applied. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were included in calculated positions and are treated as riding atoms. The hydroxyl hydrogen atoms were refined with isotropic thermal parameters, R_1=0.0470, wR_2=0.1161 for 4833 reflections with $F>4\sigma(F)$ and R_1=0.0703, wR_2=0.1312 (all data). Minimum and maximum peaks in the final ΔF map were -0.269 and 0.496 e.Å^{-3}. The structure contains two crystallographically independent molecules which have different conformations of the *-OCOPr* group. Details of molecular dimensions, atomic coordinates, thermal parameters and listings of observed and calculated structure factors have been deposited with the Cambridge Crystallographic Data Centre.

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