Structural and Stereochemical Reassessment of Sclerophytin-Type Diterpenes

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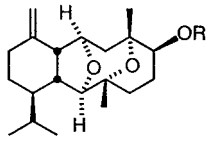
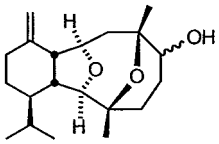
Received July 27, 2001

A complete reassessment of the structural assignments of the sclerophytin diterpenes is provided.

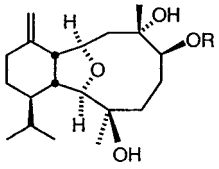
Marine invertebrates are a rich source of oxygenated diterpenoids.[1−4] Among those isolated from the soft coral *Sclerophytum capitalis* are sclerophytins A and B, originally formulated by their discoverers as **1** and **2**.[5] The novel structural features of these oxygen-bridged heterocycles and the significant cytotoxic properties of **1** have attracted some defining synthetic work.[6−9] In consideration of the fact that synthetic **3** and **4** both proved to differ significantly from the originally isolated marine metabolites, an extensive NMR analysis of **2** was undertaken, the results of which identified sclerophytin B to be **6**.[10] This thorough investigation also implicated sclerophytin A to be **5** since its simple acetylation leads to **6**.[5,7,8]



1, R=H
2, R=Ac



3, α-OH
4, β-OH

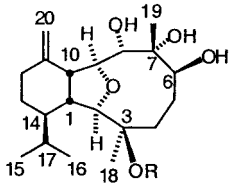


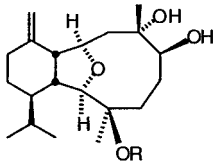
5, R=H
6, R=Ac

Other members of the sclerophytin family, many of which are thought to play an important biological role in the survival of the coral population, have previously been identified. In light of the recently confirmed structural features of **5** and **6**, the time is considered to be appropriate for a critical reevaluation of the prior assignments accorded to these congeners. This comprehensive analysis forms the subject of this paper.

Results and Discussion

The structural assignment accorded to sclerophytin C, initially elucidated mainly by various NMR experiments, was ultimately confirmed by means of an X-ray crystallographic analysis.[11] On this basis, the definition of its absolute configuration as represented by **7** is considered secure.





7, R=Ac (sclerophytin C)[11,12]
8, R=H (sclerophytin D)[11]
9, R=$COCH_2CH_2CH_3$ (litophynol B)[13]

10, R=Ac (sclerophytin E)[11]
11, R=H (sclerophytin F)[11]

The structural features reported for sclerophytin D[11] are based on the close correspondence of the ^{1}H and ^{13}C NMR data exhibited by **7** and **8** and the added fact that sclerophytins C and D afford identical acetylation products. More specifically, the ^{1}H NMR shifts exhibited by **7** and **8** coincide within 0.02 ppm except for H-1 (−0.03 ppm), H-6 (+0.04 ppm), and H-17 (−0.03 ppm), while the ^{13}C chemical shifts coincide within 0.2 ppm except for C-4 (+0.7 ppm), C-10 (+0.5 ppm), C-11 (+0.4 ppm), C-1 (+0.3 ppm), and C-8 (+0.3 ppm). Particularly striking is the similarity of the carbon shifts in the vicinity of C-3: for **7**, 91.4 (d, C-2), 86.2 (s, C-3), 34.5 (t, C-4), and 23.0 (q, C-18); for **8**, 91.4 (d, C-2), 86.2 (s, C-3), 35.2 (t, C-4), and 23.0 (q, C-18). The ^{13}C chemical shifts reported for sclerophytins E and F show a similarly close correspondence[11] (Table 1). This degree of similarity is considered unusual in light of the fact that acetylation of a tertiary alcohol will typically result in a noticeable downfield shift of the oxygen-bearing carbon (on the order of several ppm) and a slight upfield shift (on the order of 0−3 ppm) of the immediately adjacent carbons.

The finding that the acetylation of **7** and **8** affords identical 3,6,8-triacetate derivatives also holds interest. For **8**, the implication is that, beyond esterification of the two secondary hydroxyls, acetylation occurs regioselectively at the tertiary C-3−OH site, but not at the tertiary C-7−OH position. This may conceivably reflect a kinetic preference caused by greater steric hindrance surrounding the 7-OH substituent.

The implicit assumption has been made that **7** and **8** (both isolated from *Sclerophytum capitalis*) possess the same absolute stereochemistry.[11] Significant optical rotations of the same sign are indeed reported for both **7** [mp 87 °C; $[\alpha]_D$ −104.8 (*c* 0.124, $CHCl_3$)] and **8** [gummy solid; $[\alpha]_D$ −138 (*c* 0.150, $CHCl_3$)], which may be construed to support this assumption. However, a much lower optical rotation has been reported in a subsequent paper[12] that describes the isolation of sclerophytin C [mp 94−95 °C; $[\alpha]_D$ −16.1 (*c* 0.32, $CHCl_3$)] and several other diterpenoids from *Cladiella australis*. A similarly small optical rotation has been reported for litophynol B (**9**) [colorless oil; $[\alpha]^{28}_D$ −17.6 (*c* 3.1, $CHCl_3$)], which is the 3-butanoyl analogue of sclerophytin C isolated from *Litophyton* sp.[13]

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10.1021/np0103822 CCC: $22.00
Published on Web 01/15/2002

Table 1. Comparison of Reported ^{13}C Chemical Shifts for Sclerophytin B and Related Compounds[a]

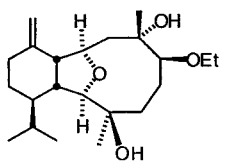
position	sclerophytin A[b] δC ($CDCl_3$)	sclerophytin B[c,d] δC ($CDCl_3$)	sclerophytin B (ref 10) δC ($CDCl_3$)	patagonicol[c,e] δC (C_6D_6, 55 °C)	"sclerophytin F methyl ether"[c,f] δC ($CDCl_3$)	sclerophytin F[c,g] δC ($CDCl_3$)	sclerophytin E[h,i] δC ($CDCl_3$)
1	45.2d	45.5 (+0.3)	45.5d	45.3d (+0.1)	44.6d (−0.6)	45.4d (+0.2)	45.2d (−0.2)
2	90.5d	90.5d (0.0)	90.5d	91.1d (+0.6)	90.5d (0.0)	91.9d (+1.4)	92.0d (+0.1)
3	74.8s	74.8s (0.0)	74.9s	74.4s (−0.4)	76.1s (+1.3)	86.6s (+11.8)	86.3s (−0.3)
4	39.9t	39.8t (−0.1)	39.8t	40.9t (+1.0)	41.0t (+1.1)	35.9t (−4.0)	36.1t (+0.2)
5	29.4t	28.1t (−1.3)	28.1t	27.2t (−2.2)	30.0t (0.6)	30.5t (+1.1)	30.4t (−0.1)
6	79.9d	85.0s (+5.1)	85.1d	88.4d (+8.5)	90.5d (+10.6)	80.1d (+0.2)	80.1d (0.0)
7	77.0s	75.9s (−1.1)	75.9s	76.1s (−0.9)	74.9s (−2.1)	77.0s (0.0)	77.0s (0.0)
8	45.4t	45.5t (+0.1)	45.4t	45.1t (−0.3)	45.1t (−0.3)	45.8t (+0.4)	45.7t (−0.1)
9	78.2d	78.0d (−0.2)	78.0d	78.6d (+0.4)	78.1d (−0.1)	78.2d (0.0)	78.2d (0.0)
10	52.6d	53.2d (+0.6)	53.2d	53.8d (+1.2)	53.0d (+0.4)	52.9d (+0.3)	52.9d (0.0)
11	147.9s	147.9s (0.0)	147.9s	148.4s (+0.5)	147.9s (0.0)	147.6s (−0.3)	147.6s (0.0)
12	31.6t	31.9t (+0.3)	31.6t	31.9t (+0.3)	31.6t (0.0)	31.4t (−0.2)	31.4t (0.0)
13	24.9t	24.8t (−0.1)	24.8t	25.2t (+0.3)	24.9t (0.0)	24.7t (−0.2)	24.8t (+0.1)
14	43.7d	43.6d (−0.1)	43.6d	44.0d (+0.3)	43.7d (0.0)	43.9d (+0.2)	43.9d (0.0)
15	16.0q	16.1q (+0.1)	15.6q	15.7q (−0.3)	15.9q (−0.1)	15.7q (−0.3)	16.1q (+0.4)
16	22.0q	21.9q (−0.1)	21.9q	22.1q (+0.1)	22.0q (0.0)	21.9q (−0.1)	21.9q (0.0)
17	29.1d	29.0d (−0.1)	29.0d	29.3q (+0.2)	29.0d (−0.1)	29.1d (0.0)	29.0d (−0.1)
18	30.3q	30.2q (−0.1)	30.3q	29.9q (−0.4)	23.9q (−6.4)	23.2q (−7.1)	23.2q (0.0)
19	23.1q	23.7q (+0.6)	23.7q	24.8q (+1.7)	25.9q (+2.8)	22.3q (−0.8)	22.6q (+0.3)
20	109.1t	109.2t (+0.1)	109.3t	109.2t (+0.1)	109.1t (0.0)	109.3t (+0.2)	109.3t (0.0)
other		171.8s	171.9s	64.8t	57.0q		170.1s
		21.5q (OAc)	21.5q (OAc)	15.3q (OEt)	(OMe)		22.7q (OAc)

[a] The numbering scheme of refs 5 and 11 has been applied uniformly. [b] Sclerophytin A from *Sclerophytum capitalis* (compound **5** in ref 5): colorless needles, mp 187 °C (no optical rotation data given); the chemical shifts taken from ref 5 have been rounded to one significant digit; the entries for C-5 and C-13 are marked "can be interchanged" in ref 5; the original entry for C-7 in ref 5 reads "77.01 (d)", presumably due to a typographical error. [c] Numbers in parentheses are chemical shift differences from sclerophytin A. [d] Sclerophytin B from *Sclerophytum capitalis* (compound **6** in ref 5): colorless needles, mp 190−192 °C (no optical rotation data given); the chemical shifts taken from ref 5 have been rounded to one significant digit; the original entry for C-7 in ref 5 reads "75.87 (d)", presumably due to a typographical error; the chemical shifts given for C-5 and C-17 in ref 5 have to be exchanged; the original entry for C-17 in ref 5 reads "28.07 (m)", presumably due to a typographical error. [e] Patagonicol from *Alcyonium patagonicum* (compound **1** in ref 14): mp 172.5−174 °C, $[\alpha]_D$ +7.5 (*c* 0.0042, CH_3OH); the entries for C-3 and C-7 are marked "can be interchanged" in ref 14. [f] Sclerophytin F methyl ether from *Cladiella krempfi* (compound **2** in ref 15): colorless prisms, mp 202−203 °C (no optical rotation data given); the original entry for C-2 and C-6 in ref 15 reads "90.5 (d, C-2, C-6)". [g] Sclerophytin F from *Sclerophytum capitalis* (compound **VII** in ref 11): gummy solid, $[\alpha]_D$ +55 (*c* 0.20, $CHCl_3$). [h] Numbers in parentheses are chemical shift differences from sclerophytin F. [i] Sclerophytin E from *Sclerophytum capitalis* (compound **VI** in ref 11): gummy solid, $[\alpha]_D$ +88 (*c* 0.42, $CHCl_3$); the original entry for C-19 in ref 11 reads "24.6", presumably due to a typographical error.

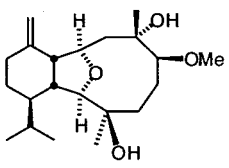
We conclude that although the similarity of the ^{13}C chemical shifts reported for the vicinity of C-3 in sclerophytins C and D is rather unusual, the evidence appears sufficiently conclusive that **8** does indeed possess the structure reported for it.[11]

The structural definition and absolute stereochemistry of sclerophytins E and F were previously reported to be **10** and **11** for two reasons:[11] (a) analogy to sclerophytins C and D (**7**and **8**); (b) ^{13}C spectral comparisons with sclerophytins A and B *under the assumption that the structures assigned to this pair of diterpenoids are those originally proposed by Alam*.[5] However, these assignments are necessarily incompatible with the revised structural assignments[10] to sclerophytins A and B, which have been confirmed by total synthesis.[7−9]

In this context, two additional congeners, both of which are closely related in structure to sclerophytins A, B and E, F and which have been subjected to X-ray crystallographic analysis, serve as important reference points.[14,15] The ^{13}C NMR data reported for patagonicol (**12**)[14] correspond poorly with those reported for sclerophytin F,[11] but show reasonable correlation with those of sclerophytins A and B when proper allowance is made for the different substitution at C-6 and the different solvent and temperature employed (Table 1). Similarly, the crystallographic analysis of sclerophytin F methyl ether (**13**)[15] reveals the stereochemistry of this compound to be analogous to that originally assigned to sclerophytin F.[11] Once again, the ^{13}C chemical shifts reported for **13**[15] correspond poorly with those cited for sclerophytin F,[11] but correspond reasonably well with those of patagonicol and sclerophytin A (once again taking into account their different substitution at C-6), although a single large discrepancy in the ^{13}C chemical shift reported for C-18 of **13**[15] is puzzling (see Table 1). These observations are consistent with the revised structural assignments for sclerophytins A and B and with the assumption that the structures reported for sclerophytins E and F[11] are incorrect.



12 (patagonicol)[14]



13 (sclerophytin F methyl ether)[15]

Comparison of the ^{13}C NMR data for sclerophytins A and F (see Table 1) shows close correspondence except for C-3 ($\Delta\delta$ +11.8) and the immediately adjacent C-2 ($\Delta\delta$ +1.4), C-4 ($\Delta\delta$ −4.0), and C-18 ($\Delta\delta$ −7.1). Differences in chemical shifts for the remaining carbons do not exceed ±0.4 ppm except for C-5 ($\Delta\delta$ +1.1) and C-19 ($\Delta\delta$ −0.8). These observations suggest to us a difference in relative stereochemistry at C-3 between sclerophytins A and F. This proposition is also consistent with the fact that the ^{13}C NMR data reported for sclerophytin F do not correspond with those of any of the three diastereomers of sclerophytin A with respect to stereochemistry at C-6 and C-7, which have also been made available by total synthesis.[8] However, the close correspondence of the ^{13}C NMR data reported for sclerophytins E/F and analogues with those reported for sclerophytins C/D[11] (except for the immediate vicinity of C-8) remains an unresolved puzzle, as it appears to preclude differences in relative configuration at C-3.

It is conceivable that some of the unexplained inconsistencies and discrepancies so far pointed out are due to incorrect assignments of selected ^{13}C chemical shifts or

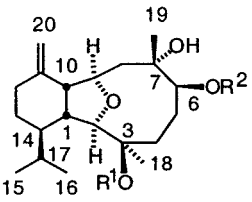
Table 2. Comparison of Reported ^{13}C Chemical Shifts for Sclerophytin B and Related Compounds[a]

	sclerophytin A[b]	sclerophytin B[c]	sclerophytin B (ref 10)	compound **2** in ref 19[d]	litophynin E[e]	litophynin E acetate[f]	sclerophytin E[g]
position	δC ($CDCl_3$)	δC ($CDCl_3$)	δC ($CDCl_3$)	δC	δC ($CDCl_3$)	δC ($CDCl_3$)	δC ($CDCl_3$)
1	45.2d	45.5 (+0.3)	45.5d		45.5d (+0.3)	45.9 (+0.7)	45.2d
2	90.5d	90.5d (0.0)	90.5d	90.5d (0.0)	92.1d (+0.1)	92.3 (+0.3)	92.0d
3	74.8s	74.8s (0.0)	74.9s	74.6s (−0.3)	86.5s (+0.2)	86.6 (+0.3)	86.3s
4	39.9t	39.8t (−0.1)	39.8t		36.2t (+0.1)	36.0 (−0.1)	36.1t
5	29.4t	28.1t (−1.3)	28.1t		30.5t (+0.1)	29.3 (−1.1)	30.4t
6	79.9d	85.0d (+5.1)	85.1d	85.0d (−0.1)	80.2d (+0.1)	84.9 (+4.8)	80.1d
7	77.0s	75.9s (−1.1)	75.9s	75.8s (−0.1)	76.9s (−0.1)	75.7 (−1.3)	77.0s
8	45.4t	45.5t (+0.1)	45.4t		45.9t (+0.2)	46.1 (+0.4)	45.7t
9	78.2d	78.0d (−0.2)	78.0d	77.9d (−0.1)	78.3d (+0.1)	78.2 (0.0)	78.2d
10	52.6d	53.2d (+0.6)	53.2d		53.7d (+0.8)	53.9 (+1.0)	52.9d
11	147.9s	147.9s (0.0)	147.9s	147.8s (−0.1)	147.6s (0.0)	147.7 (+0.1)	147.6s
12	31.6t	31.9t (+0.3)	31.6t		31.5t (+0.1)	31.6 (+0.2)	31.4t
13	24.9t	24.8t (−0.1)	24.8t		24.6t (−0.2)	24.8 (0.0)	24.8t
14	43.7d	43.6d (−0.1)	43.6d		44.0d (+0.1)	44.0 (+0.1)	43.9d
15	16.0q	16.1q (+0.1)	15.6q	15.5q (−0.1)	15.7q (−0.4)	15.5 (−0.6)	16.1q
16	22.0q	21.9q (−0.1)	21.9q	21.8q (−0.1)	22.0q (+0.1)	21.9q (0.0)	21.9q
17	29.1d	29.0d (−0.1)	29.0d	27.5d (−1.5)	29.1d (+0.1)	29.1d (+0.1)	29.0d
18	30.3q	30.2q (−0.1)	30.3q	30.0q (−0.3)	23.2q (0.0)	23.1 (−0.1)	23.2q
19	23.1q	23.7q (+0.6)	23.7q	23.6q (−0.1)	22.7q (+0.1)	23.8 (+1.2)	22.6q
20	109.1t	109.2t (+0.1)	109.3t	109.1t (−0.2)	109.4t (+0.1)	109.4 (+0.1)	109.3t
other		171.8s	171.9s	171.7s (−0.2)	172.3s, 37.4t,	171.8, 21.4	170.1s
		21.5q	21.5q	21.3q (−0.2)	18.4t, 13.7q	(OAc)	22.7q
		(OAc)	(OAc)	(OAc)	(OCO*n*C_{3H7})	172.3, 37.5,	(OAc)
						18.5, 13.7	
						(OCO*n*C_{3H7})	

[a] The numbering scheme of refs 5 and 11 has been applied uniformly. [b] Sclerophytin A from *Sclerophytum capitalis* (compound **5** in ref 5): colorless needles, mp 187 °C (no optical rotation data given); the chemical shifts taken from ref 5 have been rounded to one significant digit; the entries for C-5 and C-13 of compound **5** are marked "can be interchanged" in ref 5; the original entry for C-7 of compound **5** in ref 5 reads "77.01 (d)", presumably due to a typographical error. [c] Sclerophytin B from *Sclerophytum capitalis* (compound **6** in ref 5): colorless needles, mp 190−192 °C (no optical rotation data given); the chemical shifts taken from ref 5 have been rounded to one significant digit; the original entry for C-7 in ref 5 reads "75.87 (d)", presumably due to a typographical error; the chemical shifts given for C-5 and C-17 in ref 5 have to be exchanged; the original entry for C-17 in ref 5 reads "28.07 (m)", presumably due to a typographical error; numbers in parentheses are chemical shift differences from sclerophytin A. [d] 6-Acetoxycladiell-11(17)ene-3,7-diol from *Cladiella australis* (compound **2** in ref 19): colorless crystals, mp 68 °C, $[\alpha]^{26}_D$ +38 (*c* 0.5, $CHCl_3$); only partial NMR data are given in ref 19; the NMR solvent, presumably $CDCl_3$, is not specified in ref 19; the partial 1H chemical shifts listed for compound **2** in ref 11 match very closely those for sclerophytin B (refs 5,7,10): 3.69s (H-2), 5.63d (*J* = 6 Hz, H-6), 4.12m (H-9), 0.98d (3H, *J* = 8, H-15), 0.70d (3H, *J* = 8, H-16), 1.78m (H-17), 1.13s (3H, H-18), 1.25s (3H, H-19), 4.65br s (H-20), 4.62br s (H-20′), 2.08s (Ac); numbers in parentheses are chemical shift differences from authentic sclerophytin B. [e] Litophynin E from *Litophyton* sp. was first described as compound **5** in ref 16, colorless viscous oil, $[\alpha]^{20}_D$ −13.1 (*c* 0.21, $CHCl_3$), but NMR data were provided only for the derived monoacetate (compound **9** in ref 16). Curiously, ref 13 describes litophynin E from *Litophyton* sp. as a colorless oil, $[\alpha]^{27}_D$ +12.6 (*c* 3.1, $CHCl_3$); numbers in parentheses are chemical shift differences from sclerophytin E. [f] Litophynin E monoacetate (compound **9** in ref 16): colorless oil (no optical rotation data given); the chemical shifts taken from ref 16 have been rounded to one significant digit; numbers in parentheses are chemical shift differences from sclerophytin E. [g] Sclerophytin E from *Sclerophytum capitalis* (compound **VI** in ref 11): gummy solid, $[\alpha]_D$ +88 (*c* 0.42, $CHCl_3$); the original entry for C-19 in ref 11 reads "24.6", presumably due to a typographical error.

even to typographical errors. A clear resolution of these issues would require a close reexamination of the originally described compounds by NMR, or at least detailed scrutiny of authentic NMR spectra. Another available alternative would be the total synthesis of additional specific members of this series. However, since the originally proposed structures of sclerophytins E and F are clearly incorrect, the stereochemical assignments for several other compounds described elsewhere,[12,13,16] which are based on analogy with sclerophytin E, will require revision to parallel the true structure of this marine metabolite.

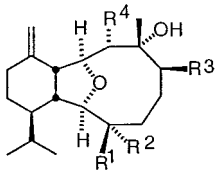
Faulkner et al. have described the isolation of sclerophytins C and E and four closely related analogues (see Supporting Information). The latter carry alternative substituents at C-6 (isovaleroyloxy or ethoxy instead of hydroxy) or C-3 (butanoyloxy instead of acetoxy).[12] The structure and stereochemistry proposed for these six compounds, including the sclerophytin E analogues **14**−**16**, parallels Alam's assignments for **7** and **10**[11] on the basis of the close correspondence of their ^{13}C NMR data.



10 (sclerophytin E (R^1 = Ac, R^2 = H))[12]
14 (3-butanoyl analog of sclerophytin E (R^1 = butyryl, R^2 = H))[12]
15 (6-ethoxy analog of sclerophytin E (R^1 = Ac, R^2 = Et))[12]
16 (6-isovaleroyl analog of sclerophytin E (R^1 = Ac, R^2 = isovaleroyl))[12]

Litophynol B (**9**) and litophynin E (**17**) have also been identified and come under scrutiny.[13] Both **17** and its 6-acetoxy derivative **18** had been previously described by Ochi and co-workers.[16] Interestingly, while the stereochemical assignment offered for litophynol B parallels that for sclerophytin C,[11] the structure proposed for litophynin E involves opposite stereochemistry at C-7. This latter assignment originates from a comparison of ^1H and ^{13}C NMR shifts of the 6-acetoxy derivative **18** with a related $\Delta^{6,7}$ compound (litophynin A[17]) and from NOESY spectra of

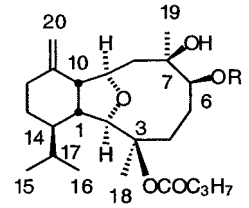
Table 3. Proposed Structural Assignments of Sclerophytin Diterpenes



compound	R1	R2	R3	R4	refs	notes	revision
sclerophytin A	OH	Me	OH	H	5	*a, c*	yes
sclerophytin B	OH	Me	OAc	H	5	*a, d*	yes
patagonicol	OH	Me	OEt	H	14	*e*	no
"sclerophytin F methyl ether"	OH	Me	OMe	H	15	*f*	no
6-acetoxycladiellenediol	OH	Me	OAc	H	19	*b, g*	yes
sclerophytin C	OAc	Me	OH	OH	11, 12	*h*	no
sclerophytin D	OH	Me	OH	OH	11	*i, j*	no
6-ethoxy sclerophytin C	OAc	Me	OEt	OH	12	*i*	no
litophynol B	OBu	Me	OH	OH	13	*i, o*	no
sclerophytin E	Me	OAc	OH	H	11, 12	*b, k, n*	yes
sclerophytin F	Me	OH	OH	H	11	*a, l, n*	yes
3-butanoyloxy sclerophytin E	Me	OBu	OH	H	12	*b, m, n, o*	yes
6-isovaleroyl sclerophytin E	Me	OAc	OiVal	H	12	*b, m, n, o*	yes
6-ethoxy sclerophytin E	Me	OAc	OEt	H	12	*b, m, n*	yes
litophynin E	Me	OBu	OH	H	13, 16	*b, m, n, o*	yes
6-acetoxy litophynin E	Me	OBu	OAc	H	16	*b, m, n, o*	yes

[a] Originally proposed structure proven incorrect. [b] Strong circumstancial evidence that originally proposed structure is incorrect. [c] Inferred from NMR analysis of sclerophytin B (ref 10) and subsequently confirmed by total synthesis (refs 7−9). [d] Extensive NMR analysis (ref 10); acetylation of sclerophytin A yields sclerophytin B (refs 5, 7, 8). [e] X-ray crystallography; reported NMR data correspond reasonably well with those of sclerophytin A (see Table 1). [f] X-ray crystallography (see note in ref 15); reported NMR data correspond reasonably well with those of sclerophytin A (see Table 1). [g] Correspondence of reported partial NMR data suggests identity to sclerophytin B (see Table 2). [h] X-ray crystallography. [i] Close correspondence of reported ^{13}C NMR data with those of sclerophytin C. [j] Acetylation of sclerophytins C and D yields identical triacetate (ref 11). [k] Close correspondence of reported ^{13}C NMR data with those of sclerophytin F (see Table 1). [l] Close correspondence of reported ^{13}C NMR data with those of sclerophytin A except for the immediate vicinity of C-3 suggests the true structure of sclerophytin F may be the C-3 epimer of sclerophytin A (see Table 1). [m] Close correspondence of reported ^{13}C NMR data with those of sclerophytin E (see Table 2). [n] Stereochemical assignment in the sclerophytin E/F series remains tentative: the close correspondence of the ^{13}C NMR data reported for sclerophytins E/F and analogues with those reported for sclerophytins C/D (except for the immediate vicinity of C-8) remains an unresolved puzzle, as it appears to preclude a difference in relative configuration at C-3 (see ref 11). [o] Bu = $COCH_2CH_2CH_3$, iVal = $COCH_2CHMe_2$

18.[16] However, the rationale provided for the C-6/C-7 stereochemical assignment to **18** is unconvincing.[18] In actuality, litophynol B (**9**) appears to be the 3-butanoyl analogue of sclerophytin C, and litophynin E (**17**) gives evidence of being the corresponding acylated derivative of sclerophytin E. In both instances, close correspondence of the ^{13}C NMR data with those reported for the parent systems is seen (Table 2).



17, litophynin E (R = H)[13,16]
18, 6-acetoxy analog of litophynin E (R = Ac)[16]

Equally questionable is the structure reported for a 6-acetoxycladiell-11(17)-ene-3,7-diol.[19] The authors claim incorrectly that the ^1H and ^{13}C NMR data for this compound compare well with those of sclerophytin F. They also report that lithium aluminum hydride reduction of this compound afforded sclerophytin F, but no data are reported to support this claim. Furthermore, the C-7 stereochemical assignment according to the abstract and discussion differs from the structural formula depicted in the text. In actuality, the partial ^1H and ^{13}C NMR data reported for this substance correspond very well to those of sclerophytin B (Table 2), which suggests that the authors may actually have isolated sclerophytin B and converted it to sclerophytin A upon hydride reduction.[20]

In conclusion, a reassessment of prior structural assignments of sclerophytin-type diterpenes was undertaken, and structural revisions are proposed in several cases as summarized in Table 3. The revised structural assignments proposed for the sclerophytin E/F subset remain tentative.

Supporting Information Available: A tabular summary of the reported properties of sclerophytin-type compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

References and Notes

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(5) Sharma, P.; Alam, M. *J. Chem. Soc., Perkin Trans. 1* **1988**, 2537. Note that the structural formulas **5** (sclerophytin A) and **6** (sclerophytin B) in ref 5 represent relative stereochemistry at C-2, C-3, C-7, and C-8 rather mysteriously, disagree with the pertinent discussion in ref 5 with respect to relative stereochemistry at C-1 and C-10, and leave the relative stereochemistry at C-14 unspecified. Partial clarification is gained from the summarizing passage: "These data support the assigned relative stereochemistry for the quaternary methyls, 2-H, 9-H, and 10-H. The proton 6-H has an -configuration..." near the bottom of page 2538 of ref 5. Note further that all remaining structural formulas in ref 5, as well as the structural formulas **I** (sclerophytin A), **II** (sclerophytin B), and **III** (cladiellin) in ref 11, leave the relative stereochemistry at C-1, C-10, and C-14 unspecified, while the remaining structural formulas **IV**−**VII** (sclerophytins C−F) in ref 11 represent relative stereochemistry at C-1, C-10, and C-14 explicitely. Our depiction of the "originally formulated" structures for sclerophytins A and B as **1** and **2** takes into account the analogy with sclerophytins C−F with respect to relative stereochemistry at C-14 which is implicitly assumed in refs 5 and 11.

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(15) Sarma, N. S.; Chavakula, R.; Nageswara Rao, I.; Kadirvelraj, R.; Guru Row, T. N.; Saito, I. *J. Nat. Prod*. **1993**, *56*, 1977. Note that the structural formulas and discussion presented in ref 15 are incorrect with respect to the relative configuration at C-3 of sclerophytin F methyl ether. Structure **13** correctly represents the relative stereochemistry of sclerophytin F methyl ether as implicated by the crystallographic data, deposited by the authors with the Cambridge Crystallographic Data Centre. We thank Professor Larry Overman and co-workers for bringing this fact to our attention.
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(18) Note also that the pertinent structure **9a** on page 2185 of ref 16 contains two errors: the structure should show OH instead of H as the 7β-substituent, and the legend should read R = COC_3H_7 instead of R = $COCH_3$.
(19) Sreenivasa Rao, D.; Shreedara, C.; Venkata Rao, D.; Bheemasankara Rao, C. *Ind. J. Chem., Sect. B* **1994**, *33B*, 198.
(20) Note, however, the completely different melting points reported for sclerophytin B[5] and the 6-acetoxycladiell-11(17)ene-3,7-diol[19] (consult Supporting Information).

NP0103822