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Sesterterpene Lactones from a Sponge Species of the Genus *Dactylospongia*

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Abstract: A new species of sponge in the genus *Dactylospongia* has yielded two new isomeric sesterterpene lactones [1] and [2]. The structures and relative stereochemistry were determined from 1-D and 2-D nmr studies and an X-ray structure of [2]. These hexacyclic compounds are probably identical with cyclisation products [4] and [5] of luffolide [3] which has been isolated from a *Luffariella* sponge.

Sponges from the family Thorectidae (Order, Dictyoceratida) have yielded a diverse range of bio-active terpenoid compounds. The three species of the genus *Dactylospongia* which have been examined[1-3] have all yielded sesquiterpene quinones. In a continuing search for biologically active compounds from South Pacific sponges, we have examined extracts from a new species of the genus *Dactylospongia* collected in New Caledonia. We report here the structures of two new cheilanthane sesterterpenes isolated by flash chromatography of a dichloromethane extract.

Compound **1**, mp 248-251°, $[\alpha]_D^{25}$ -15° (*c* 0.02, $CHCl_3$), $C_{27}H_{40}O_6$ (HREIMS: *m/z* 460.2829, required 460.2825), showed i.r. absorptions for a saturated γ-lactone (1798 cm^{-1}) and an acetate carbonyl (1738 cm^{-1}). The nmr spectra (Table 1) confirmed the presence of the lactone and acetate functions, and as all protons were carbon-bound, the remaining two oxygen atoms were present as ethers. Compound **1** was thus deduced to be hexacyclic. Accurate mass measurement of a peak at *m/z* 191 ($C_{14}H_{23}$) in the mass spectrum indicated that all six oxygen atoms were present in one region of the molecule. The ^{13}C nmr spectrum (100 MHz) showed the presence of three high field quaternary carbons (δ33.3, 37.2, 37.5) and four tertiary methyl groups (δ15.1, 16.1, 21.4, 33.3). These shifts were compatible with a *trans-A/B-trans-B/C* tricyclic skeleton with a *gem*-dimethyl group at C-4 and axial methyl groups at the ring junctions C-8 and C-10. Also, high field carbon signals (δ18.5, 18.6 and 20.5) could be attributed to C-2, C-6 and C-11 lying γ to the axial methyl groups, while low field carbon signals (δ39.9 and 40.0) together with their associated high field axial proton signals (δ0.74, 0.75) in the ^1H nmr (400 MHz) spectrum could be attributed to carbons β to the axial methyl groups, i.e., C-1 and C-7. Methine proton signals at δ0.76 and 0.81 could be attributed to axial H-5 and H-9 confirming that rings A/B and B/C were *trans*-fused. Examination of the phase-sensitive double quantum filtered COSY (COSYPHDQ) spectrum revealed the presence of a six-spin system ($CH_2CH_2CH_2$) corresponding to C-1--C-3 protons, and a five-spin system (CH-CH_2-CH_2) corresponding to C-5--C-7 protons. A ten-spin system (CH-CH_2-CH_2-CH-CH-CH_2-CH{OAc}) was also observed, in which the initial seven-spin system could be assigned to C-9--C-11--C-14 protons, and the latter three-spin system was a side-chain extension consistent with the connectivity at C-14 found in luffolide [3].[4]

The remaining signals in the ^1H and ^{13}C nmr spectrum were due to an acetate-bearing methine group (δ5.18;71.8) which was assigned to C-16 at the terminus of the ten-spin system, a methylene group (δ1.38, 2.05; 20.5) assigned to C-15, two acetal methine groups (δ5.48, 5.72; 114.1, 102.8), an acetoxy group (δ2.17; 21.1, 170.2), a lactone group (δ171.1), an isolated methylene group (δ2.70, 2.92; 38.9) which was deduced to be adjacent to the lactone carbonyl group, and an oxygenated quaternary carbon (δ90.1). Long range heteronuclear correlation experiments optimised for J = 7 Hz and 14 Hz showed that the signals at δ171.1 and δ(38.9; 2.70, 2.92) were associated with those at δ90.1 and δ(102.8; 5.72) indicating that these nuclei constituted the lactone ring. The signal at δ 90.1 was the key in the structure elucidation, as not only did it

Table 1. ^{13}C and ^{1}H Nmr Data for Compound 1

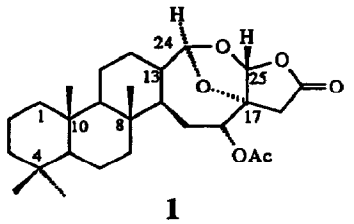
Carbon	δ(^{13}C)	δ(^{1}H),*mult.*(*J*(Hz))[A], Assign.	COSYPHDQ	XHCORR[C]	NOESYPH
C1	40.0	0.74, *m*[B], α	H1β,2α,2β		
		1.74, *m*[B], β	H1α,2α,2β		
C2	18.6	1.32, *m*[B], β	H1α,1β,2α,3α,3β	H1β,3β	
		1.54, *m*[B], α	H1α,1β,2β,3α,3β		
C3	41.9	1.10, *dt*, (13.4, 13.4, 4.0), α	H2α,2β,3α	H20,21	
		1.35, *m*[B], β	H2α,2β,3β		
C4	33.3	-		H20,21,3α	
C5	56.4	0.76, *m*[B], α	H6α,6β	H20,21,3β	
C6	18.6	1.40, *m*[B], β	H5,6α,7α,7β	H7β	
		1.54, *m*[B], α	H5,6β,7α,7β		
C7	40.0	0.75, *m*[B], α	H6α,6β,7β		H14
		1.64, *m*[B], β	H6α,6β,7α		
C8	37.2	-		H23,11α,13,15α	
C9	59.1	0.81, *m*[B], α	H11α,11β	H12β,11β	H12α
C10	37.5	-		H22,2α,2β	
C11	20.5	1.28, *m*[B], β	H9,11α,12α,12β	H9,12α,13	H12α
		1.68, *m*[B], α	H9,11β,12α,12β		
C12	31.6	1.18, *dt*, (12.6, 12.6, 4.0), α	H11α,11β,12β,13	H24,13,9	H11α,12β,24
		1.81, *m*[B], β	H11α,11β,12α,13		H12α,13,24
C13	44.9	1.70, *dd* br, (10.5, *ca.* 13)[D], β	H12α,12β,14	H24,15α,11β	H24,12β,15β,11β
C14	45.2	1.48, *t*, (10.5), α	H13,15β	H23,24,16,12β	H7α,15α,12α
C15	26.9	1.38, *ddd*, (15.2, 10.5, 2.0)[B], β	H14,15α,16	H14	H25,15α,13,16,14
		2.05, *dd*, (15.2, 4.5), α	H15β,16		H15β,14,16
C16	71.8	5.18, *dd*, (4.5, 2.0), β	H15α,15β		H25,18β,15β,15α
C17	90.1	-		H25,24,18β,15α	
C18	38.9	2.70, *d*, (17.9), β	H18α		H16,25
		2.92, *d*, (17.9), α	H18β		
C19	171.1	-		H18α,18β,25	
C20	33.3	0.85, *s*, 4α-CH_3			
C21	21.4	0.80, *s*, 4β-CH_3			
C22	16.1	0.80, *s*, 10β-CH_3			
C23	15.1	0.76, *s*, 8β-CH_3		H7α,9,14	
C24	114.1	5.48, *s*, α		H25,13	H12β,12α,13
C25	102.8	5.72, *s*, β		H18α	H16,15β,18β
C26	170.2	- CH_3COO-		H27	
C27	21.1	2.17, *s*, CH_3COO-			

[A] The coupling constant(s) were determined from analysis of the one-dimensional spectrum. [B] Resonance in the one-dimensional spectra obscured by overlapping signals, in these cases δH was found from the carbon/proton correlation and/or the COSYPHDQ spectrum. [C] Long range experiment. [D] Determined from analysis of crosspeak in COSYPHDQ spectrum.

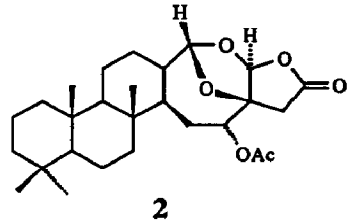
correlate with the acetate-bearing methine proton, but it also showed strong correlation to the acetal proton at δ5.48, which in turn was back-correlated to the other acetal carbon at δ102.8. A complementary C-H correlation between δ5.72 and δ114.1 was also observed. The final connectivity was determined to be between the 13-CH group at δ(44.9; 1.70) and 24-CH group at δ(114.1; 5.48) on the basis of a heteronuclear correlation. No proton-proton coupling was observed between H-13 and H-24 in either the ^{1}H or the COSYPHDQ spectra.

Examination of the Dreiding model indicated that the dihedral angle between the respective protons approximates to 90°. Similarly, no coupling was observed between H-14 and the H-15α due to a similar dihedral angle.

The relative stereochemistry was determined from two phase sensitive NOESY (NOESYPH) experiments acquired for mixing times of 0.3 s and 0.8 s, respectively. The axial H-7α proton showed strong *nOe* to H-14 which in turn showed a strong *nOe* to H-15 (δ2.05), therefore suggesting an α-orientation for the respective protons. H-15 (δ1.38) exhibited strong *nOe* to H-16, H-25 and H-13, indicating a β-orientation for these protons. In turn, H-25β showed moderate *nOe* to H-18β. The acetal proton at δ5.48 (H-24) did not show any *nOe* to H-25β, but showed strong *nOe* to H-12β, moderate *nOe* to H-12α, and weak *nOe* to H-13β . Therefore, H-24 was assigned an α-orientation. The multiplicity of H-12α in the COSYPHDQ spectrum indicated that it had an axial orientation. Examination of the Dreiding model indicated that the torsion angles between H-24 and H-12α and H-12β approximate to 80° and 30° respectively. From this, and the fact that the crosspeak for H-13 and the signal for H-14 which each exhibited two large coupling constants indicative of their axial orientation, rings C/D were assigned a *trans*-fused junction.



1



2

Compound 2, mp 238-240°, $[\alpha]_D^{25}$ -71° (*c* 0.03, $CHCl_3$), $C_{27}H_{40}O_6$ (HREIMS: *m/z* 460.2828, required 460.2825), also showed absorptions for a saturated γ-lactone ring (1801 cm^{-1}) and an acetate carbonyl (1745 cm^{-1}). The ^1H and ^{13}C nmr spectra[5] each showed close similarity with those of **1**; analysis of its COSYPHDQ, XHCORRD and long range XHCORR spectra indicated that **2** had the same skeleton as **1** but that the chirality of certain centres in the ring D/E moiety differed. The H-14 signal (δ1.05) which appeared as a triplet (*J* = 10.5 Hz) indicated that ring C/D had a *trans* ring junction as in **1**. The multiplicity of H-16 (δ5.40, *t*, J = 3.3 Hz) was also consistent with the same stereochemistry at C-17. H-25 (δ6.21) was deshielded by *ca.* 0.5 ppm, while H-24 (δ5.60, *d*, J = 1.7 Hz) was now coupled to H-13.

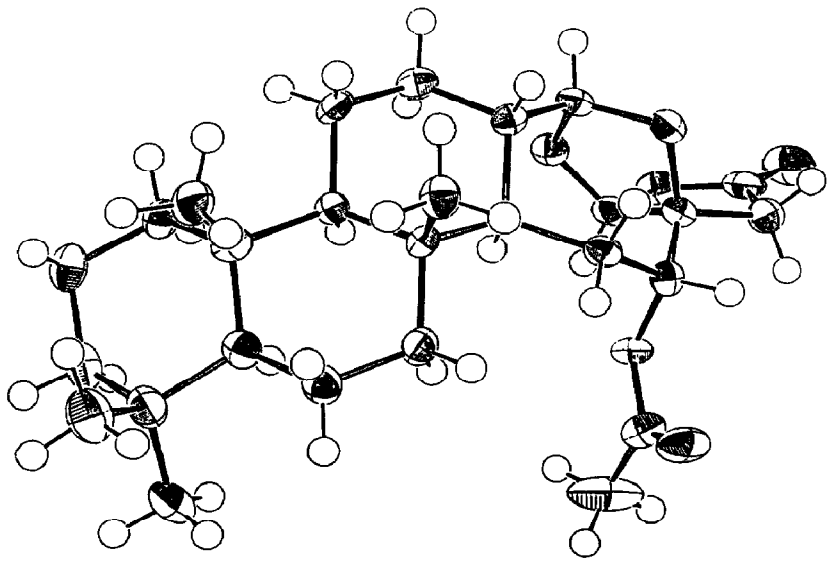
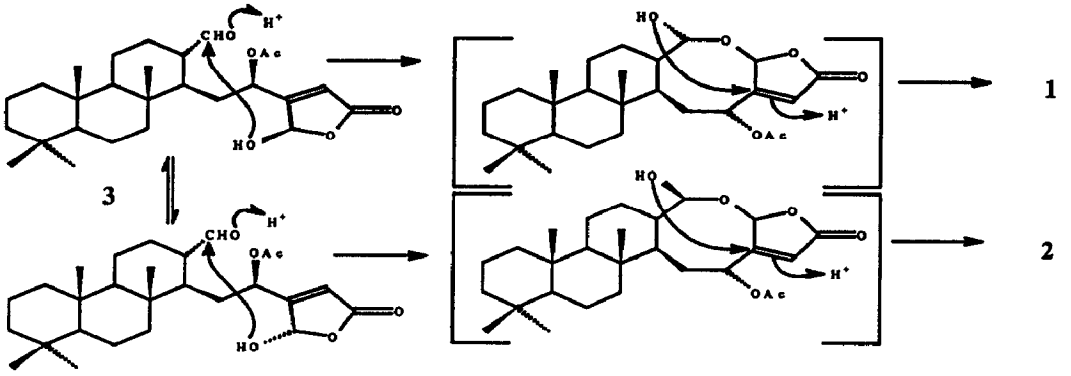


Figure 1. ORTEP Projection of Compound **2**

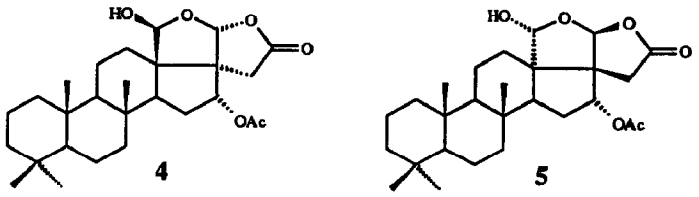
The stereochemistry of the D/E ring moiety was determined from NOESYPH experiments as before. H-7α (δ0.77) showed a strong *nOe* to H-14α (δ1.05), which in turn showed a strong *nOe* to H-25 (δ6.21), thereby confirming the α orientation of the respective protons. Similarly, the *nOe*'s between H-24 (δ5.60) and H-13β (δ1.58), and H-12β (δ1.66) were consistent with a β orientation for H-24.

The relative stereochemistry of **2** was confirmed by a single crystal X-ray analysis (**Fig. 1**). The chirality of the centres C-17, C-24 and C-25 in **2** is opposite to that of the respective centres in **1**. Biosynthetically, **1** could be derived from **3** as shown (**Scheme 1**), and epimerisation of the hemiacetal carbon C-25 of **3** would lead to the formation of **2**



Scheme 1. Possible biosynthesis of **1** and **2** from **3**

The nmr spectra of **1** and **2** are almost identical with those recorded[4] for **4** and **5** which are cyclisation products of luffolide (**3**), and thus it is probable that the structures of **4** and **5** should be revised to **1** and **2** respectively.



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5. δ(^{13}C;^{1}H) of **2** are (C1--C27) **40.3**, t; 0.81, *m*, α; 1.79, *td* (13.4, 13.4, 4.0), β; **18.5**, t; 1.31, *m*, β; 1.54, *m*, α; **42.0**, t; 1.10, *dt* (13.4, 13.4, 4.0), α; 1.36, *m*, β; **33.3**, s; **56.2**, d; 0.80, *m*, α; **18.6**, t; 1.40, *m*, β; 1.58, *m*, α; **39.9**, t; 0.77, *m*, α; 1.68, *m*, β; **37.1**, s; **58.9**, d; 0.75, *m*, α; **37.5**, s; **19.5**, t; 1.25, *m*, β; 1.64, *m*, α; **27.7**, t; 1.22, *m*, α; 1.66, *m*, β; **44.9**, d; 1.58, *m*, β; **43.7**, d; 1.05, *t* (10.5), α; **30.1**, t; 1.59, *ddd* (15.4, 10.5, 3.3), β; 1.88, *dd* (15.4, 3.3), α; **72.9**, d; 5.40, *t* (3.3), β; **86.9**, s; **40.3**, t; 2.78, *d* (18.1), α; 2.93, *d* (18.1), β; **171.1**, s; **33.3**, q; 0.85, *s*, 4α-Me; **21.4**, q; 0.79, *s*, 4β-Me; **16.4**, q; 0.80, *s*, 10β-Me; **14.4**, q; 0.77, *s*, 8β-Me; **113.0**, d; 5.60, *d* (1.7), β; **103.2**, d; 6.21, *s*, α; **169.8**, s, CH_3COO; **21.2**, q; 2.14, *s*, CH_3COO.

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