Cyclic Peroxides and Related Norterpenes from a Southern Australian Marine Sponge, *Mycale* sp.

Robert J. Capon,* Simone J. Rochfort, and Simon P. B. Ovenden

Department of Chemistry, University of Melbourne, Parkville, Victoria 3052, Australia

Received July 2, 1997[⊗]

Investigation of a southern Australian marine sponge, *Mycale* sp., resulted in isolation of the known norsesterterpenes **1**−**3** as well as two new isomeric norsesterterpenes, mycaperoxide C methyl ester (**4**) and mycaperoxide D methyl ester (**5**), and six new norterpenes (**6**−**11**).

Following the 1979 report[1] of muqubilin from a Red Sea *Prianos* sp., marine sponges have become a recognized source of novel norterpene cyclic peroxides. Norterpene cyclic peroxides are remarkably stable, usually occur as carboxylic acids, and have been reported to possess antibiotic, anticancer, and/or antiviral activity. Typically converted to the methyl esters to facilitate isolation, known norterpene cyclic peroxides feature familiar acyclic, monocyclic, and bicyclic carbon skeletons, as well as the rare trunculin carbon skeleton. Biosynthetically related metabolites include norterpene dienes from an Australian *Mycale* sp.[2] and a norterpene ketone from a specimen of *Sigmosceptrella laevis* collected off Papua, New Guinea.[3] In pursuing new examples of this structure class we secured geographically distinct collections of three Australian sponge genera, *Mycale*, *Latrunculia*, and *Sigmosceptrella*, known to yield norterpene cyclic peroxides. This report describes the results of our investigations into the chemistry of a *Mycale* sp. collected by hand (scuba) near Durras on the mid-south coast of New South Wales, Australia.

Results and Discussion

The crude ethanol extract of the *Mycale* specimen was concentrated under reduced pressure and methylated with CH_2N_2 prior to chromatographic purification which subsequently yielded three known cyclic peroxides (**1**−**3**)[3−6] as well as two previously undescribed cyclic peroxides (**4** and **5**) (Chart 1). The same sponge also yielded six new norterpenes (**6**−**11**) as well as the unprecedented steroidal lactone mycalone, the structure of which has already been reported.[7] The reisolates of **1**−**3** possessed spectroscopic characteristics identical with those of authentic samples. The characterization and structure elucidation of the new compounds **4**−**11** are described below.

Mycaperoxide C methyl ester (**4**) possessed a molecular formula ($C_{25}H_{44}O_5$, Δ mmu −1.6) requiring four double bond equivalents. A comparison of selected signals in the NMR spectra of **4** with that of **3** (Tables 1 and 2) confirmed a common cyclic peroxide moiety. The bicyclic moiety in **4** lacked the $\Delta^{10,11}$ double bond common to **3**, featuring instead an oxygenated quaternary carbon (^{13}C: 73.2 ppm) and tertiary methyl (^{1}H: δ 1.16, ^{13}C: 30.4 ppm) indicative of an axial C-10 tertiary alcohol. This assignment was confirmed by spectroscopic comparison with the known compounds **12** and **13**.[8] Literature reports document that the ^{13}C NMR chemical shift for the C-8 CH_3 in **12** and **13** is diagnostic of the C-8 relative stereochemistry, with an equatorial methyl carbon (31.7 ppm) resonating downfield of that for the corresponding axial methyl carbon (24.3 ppm).[8]

It has been shown for a large number of labdane diterpenes in which the asymmetric ring system is separated by two methylene groups from an asymmetric center in the side chain that the molar rotation contributions for the two chiral subunits are additive.[9] We have successfully used this technique to assign absolute stereochemistry to a number of marine natural products.[5,10−15] On the basis of the optical properties of **14** and **15**, the $[\phi]_D$ attributed to the cyclic peroxide moiety C-1 to C-7 must be either −244° (2*S*,3*S*,6*S*) or +244° (2*R*,3*R*,6*R*).[5] Likewise, three examples exist in the literature of compounds in which the sole chiral unit is the C-9 to C-18 bicyclic moiety of **4**, such that the $[\phi]_D$ for this chiral unit can be determined to be between +29° and +107° (9*R*,10*S*,13*S*,18*R*) or −29° and −107° (9*S*,10*R*,13*R*,18*S*).[16] The experimentally measured $[\phi]_D$ for **4** (−304°) is therefore indicative of a 2*S*,3*S*,6*S*,9*S*,-10*R*,13*R*,18*S* absolute stereochemistry. This stereochemistry is consistent with a common biosynthetic sequence with **1**−**3**, the absolute stereochemistries of which have already been unambiguously determined.

Mycaperoxide D methyl ester (**5**) possessed a molecular formula ($C_{25}H_{44}O_5$, Δ mmu −0.3) isomeric with **4**. Comparison of the NMR data between **4** and **5** (Tables 1 and 2) confirmed a common cyclic peroxide moiety, with the only significant spectroscopic difference between the two metabolites occurring in the bicyclic portion of the molecule. The chemical shift of the C-10 CH_3 resonance in **5** was upfield (24.4 ppm) of that in **4** (30.4 ppm), indicative of an equatorial rather than axial C-10 tertiary alcohol. Attempts to assign an absolute stereochemistry to **5** via the same $[\phi]_D$ approach as described above required knowledge of the $[\phi]_D$ contribution for the C-10 to C-18 bicyclic unit. Unfortunately, the chemical literature does not provide adequate $[\phi]_D$ measurements for suitable model compounds of known absolute stereochemistry. The co-occurrence of **5** with **4** would, however, imply a common biosynthetic origin, allowing *tentative* assignment of the absolute stereochemistry for **5** as shown.

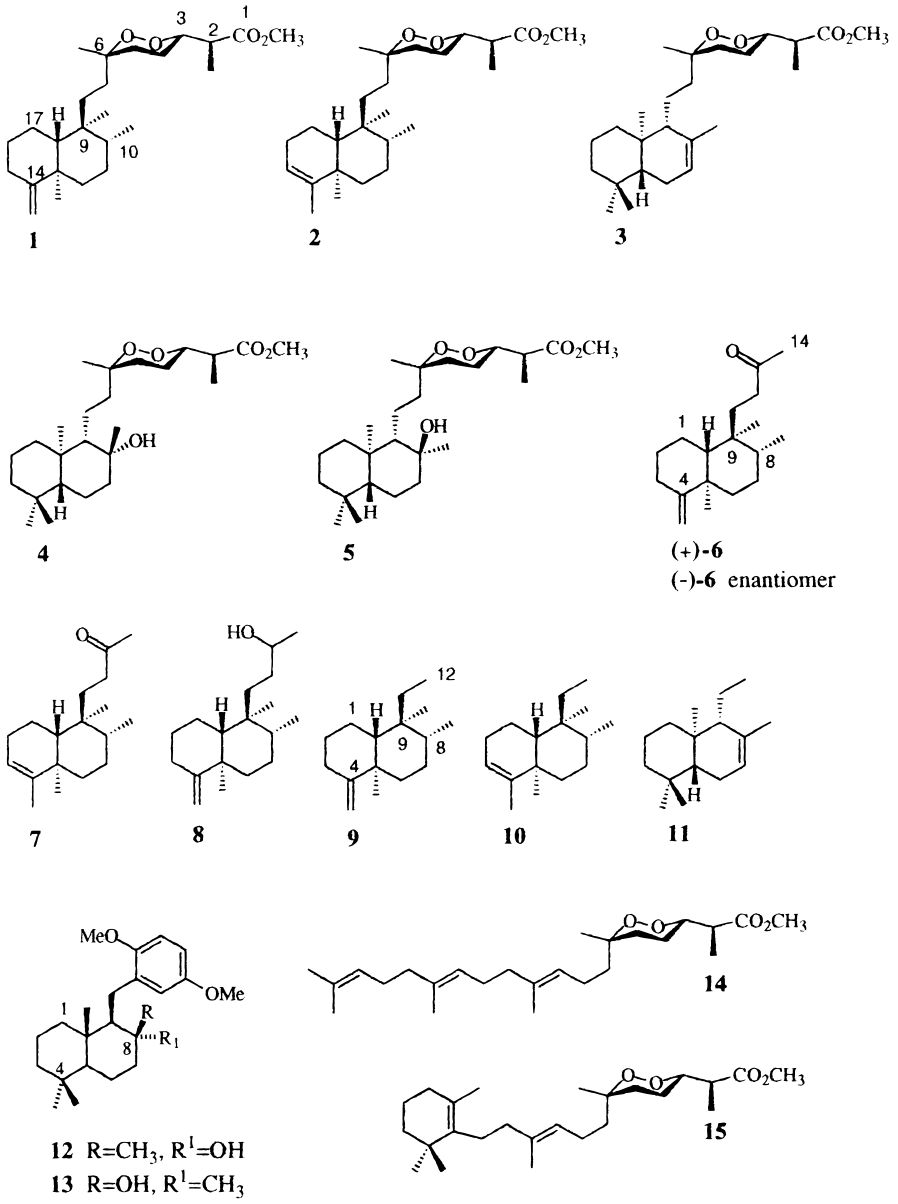
Ketone (+)-**6** ($C_{18}H_{30}O$, Δ mmu −0.9) was spectroscopically identical with but possessed a specific rotation (+43°) opposite to that (−41°) of the known marine natural product (−)-**6**.[3] The absolute stereochemistry

* To whom correspondence should be addressed: Tel.: +61 3 9344 6468. Fax: +61 9347 5180. E-mail: r.capon@chemistry.unimelb.edu.au.

[⊗] Abstract published in *Advance ACS Abstracts,* November 15, 1997.

S0163-3864(97)00313-3 CCC: $14.00

Chart 1



of (−)-**6** was originally assigned on biosynthetic grounds to be common with that of its cometabolite sigmosceptrellin A, which is itself the enantiomer of the free acid of **1**. The absolute stereochemistry of sigmosceptrellin A had been first established by CD analysis in 1982[3] but was later revised by Horeau analysis in 1985[4] and by degradation and asymmetric synthesis in 1988.[6] Consequently, the absolute stereochemistry of (+)-**6** can be assigned as shown, fully consistent with that attributed to the coisolates **1**−**5**.

The ketone **7** possessed a molecular formula ($M^+ - H$, Δ mmu −1.9) isomeric with that of **6**. Comparison of the NMR data between **6** and **7** revealed the only significant spectroscopic difference to be the absence of the olefinic methylene resonance (^{1}H: δ 4.50; ^{13}C: 102.6 (t) and 160.5 (s) ppm) and the appearance of an olefinic methine and methyl resonance (^{1}H: δ 5.19 and 1.60; ^{13}C: 18.0 (q), 120.4 (d) and 144.4 (s) ppm). These observations suggested that **7** was an endocyclic double bond isomer of **6**. This conclusion was confirmed by comparison of the NMR data for the bicyclic portion of **7** with that for the known marine natural product **2**.[5] The $[\phi]_D$ for **7** (−109°) was in good agreement with that ascribed to the chiral bicyclic unit in **2** (−147°), thereby defining a common absolute stereochemistry.

The alcohol **8** possessed a molecular formula ($C_{18}H_{32}O$, Δ mmu −0.6) requiring three double bond equivalents. Examination of the NMR data confirmed that **8** possessed the same bicyclic unit as **6**. Further comparison of the NMR data for **6** and **8** revealed that the latter lacked the characteristic ketone carbon (^{13}C: 209.5 ppm) in favor of an oxygenated methine (^{1}H: δ 3.68; ^{13}C: 69.1 ppm) and a secondary methyl (δ 1.18;^{13}C: 23.6 ppm), indicative of a C-13 secondary alcohol functionality. Although lack of material precluded an independent determination of stereochemistry about C-13, co-occurrence of **8** with **1**−**7** permits the *tentative* partial assignment of absolute stereochemistry as shown.

Metabolites **9**−**11** were isolated as a mixture inseparable by HPLC. Analytical resolution by GC and subsequent analysis by GC/MS revealed the three compounds to be isomeric (M^+ 220u) ($C_{16}H_{28}$) in a ratio of approximately 4:2:1. Inspection of the ^{1}H NMR data suggested an exocyclic $=CH_2$ group at C-4 (δ 4.50) for **9**, together with olefinic protons at C-3 (δ 5.08) for **10** and C-7 (δ 5.38) for **11**. The ^{13}C NMR data (Table 3) of

Table 1. ^{13}C NMR ($CDCl_3$) Data for **4**, **5**, **(+)-6**, **7**, **8**, and **3**

	compounds					
carbon no.	**3**	**4**	**5**	**(+)-6**	**7**	**8**
1	174.4 (s)	174.3 (s)	174.4 (s)			
2	42.7 (d)	42.6 (d)	42.6 (d)			
3	81.2 (d)	81.2 (d)	81.4 (d)			
4	22.7 (t)	22.6 (t)	22.7 (t)			
5	32.2 (t)	32.1 (t)	33.0 (t)			
6	80.3 (s)	80.2 (s)	80.1 (s)	209.5 (s)	209.7 (s)	69.1 (d)
7	37.5 (t)	38.4 (t)	37.7 (t)	37.6 (t)[a]	37.6 (t)[a]	34.2 (t)[a]
8	20.9 (t)	18.2 (t)	18.1 (t)	37.3 (t)[a]	36.7 (t)[a]	37.3 (t)[a]
9	55.3 (d)	59.0 (d)	61.8 (d)	38.8 (s)[b]	38.2 (s)[b]	40.0 (s)[b]
10	135.5 (s)	73.2 (s)	74.2 (s)	36.8 (d)	36.4 (d)	36.6 (d)
11	122.0 (d)	42.1 (t)	43.1 (t)	33.0 (t)[a]	31.5 (t)[a]	33.1 (t)[a]
12	23.8 (t)	19.0 (t)	20.3 (t)	31.4 (t)[a]	27.4 (t)[d]	32.4 (t)[a]
13	50.2 (d)	56.0 (d)	56.1 (d)	40.0 (s)[b]	38.1 (s)[b]	39.0 (s)[b]
14	33.0 (s)	33.2 (s)	33.2 (s)	160.5 (s)	144.4 (s)	160.7 (s)
15	42.3 (t)	42.0 (t)	42.0 (t)	28.7 (t)[d]	120.4 (d)	28.7 (t)[d]
16	18.8 (t)	18.3 (t)	18.5 (t)	27.4 (t)[d]	26.8 (t)[d]	27.5 (t)[d]
17	39.2 (t)	39.2 (t)	39.6 (t)	21.6 (t)	18.2 (t)	21.6 (t)
18	37.0 (s)	39.0 (s)	38.9 (s)	48.9 (d)	46.6 (d)	48.6 (d)
1-CO_2CH_3	51.9 (q)	51.9 (q)	51.9 (q)			
2-CH_3	12.7 (q)	12.6 (q)	12.7 (q)			
6-CH_3	23.9 (q)	23.9 (q)	23.6 (q)	30.0 (q)	30.0 (q)	23.6 (q)
14-CH_2				102.6 (t)		102.4 (t)
9-CH_3				20.7 (q)[c]	19.8 (q)[c]	20.8 (q)[c]
10-CH_3	21.8 (q)	30.4 (q)	24.4 (q)	18.0 (q)[c]	18.1 (q)[c]	18.2 (q)[c]
13-CH_3				16.0 (q)[c]	16.0 (q)[c]	16.0 (q)[c]
14-CH_3	33.2 (q)	33.4 (q)	33.4 (q)		18.0 (q)[c]	
	22.0 (q)	21.6 (q)	21.4 (q)			
18-CH_3	13.6 (q)	15.2 (q)	15.5 (q)			

[a–d] Shifts indicated with similar letters may be exchanged within a column. For purposes of comparison, the NMR data for **6**–**8** are presented with the numbering scheme common to the norterpene cyclic peroxides **3**–**5**.

Table 2. Selected ^1H (400 MHz, $CDCl_3$) Data for **3**–**5**

proton no.	compound		
	3	**4**	**5**
2-H	2.57	2.56	2.54
3-H	4.24	4.23	4.24
CO_2CH_3	3.69	3.68	3.69
2-CH_3	1.13	1.12	1.12
6-CH_3	1.12	1.13	1.10

Table 3. ^{13}C NMR (100 MHz, $CDCl_3$) Data for **9**–**11**

carbon no.	compound		
	9	**10**	**11**
1	21.6 (t)	18.1 (t)	31.1 (t)[a]
2	27.5 (t)[a]	26.9 (t)	18.8 (t)
3	28.7 (t)[a]	120.5 (d)	42.3 (t)
4	161.0 (s)	144.6 (s)	33.0 (s)
5	38.1 (s)[b]	42.2 (s)[b]	50.8 (d)
6	33.2 (t)[a]	27.5 (t)	23.8 (t)
7	37.4 (t)	30.4 (t)	121.9 (d)
8	35.8 (d)	35.4 (d)	*
9	38.2 (s)[b]	38.4 (s)[b]	57.1 (d)
10	47.9 (d)	45.6 (d)	*
11	30.3 (t)[a]	36.8 (t)	33.6 (t)[a]
12	7.2 (t)	7.2 (t)	*
9-CH_3	20.8 (q)	19.9 (q)	*
8-CH_3	18.2 (q)	18.0 (q)	21.9 (q)[c]
4-CH_2	102.3 (t)		
4-CH_3		18.4 (q)	33.3 (q)
			22.1 (q)[c]
10-CH_3			13.5 (q)

[a–c] Shifts indicated with similar letters may be exchanged within a column. *These carbons could not be assigned due to the low intensity and signal overlap.

9 and **10** could be fully assigned by comparison to the related cyclic peroxides **1** and **2**. Similar comparisons between **3** and **11** allowed most of the carbon skeleton to be assigned; however, due to the small amount of **11** present not all the carbons were observed. Although the absolute stereochemistry of **9**–**11** could not be determined independently, on biosynthetic grounds they were nominally assigned the same stereochemistry as the co-occurring cyclic peroxides **1**–**3**. Given that **9**–**11** could not be separated and independently characterized, the structure assignments as shown must be deemed only *tentative*.

The natural free acids of **4** and **5** are isomeric with norsesterterpene cyclic peroxides mycaperoxide A and B isolated from a Thai sponge, *Mycale* sp.,[17] and for this reason are allocated the trivial names mycaperoxide C and D, respectively. The norsesterterpene cyclic peroxides **1**–**5** are very likely derived from a common cyclization event on a acyclic biosynthetic precursor such as **14**, varying only in the manner in which the intermediate C-10 carbocation is quenched. Loss of H^+ from C-11 would lead to **3**, direct quenching with H_2O to **4** and **5**, and Wagner–Meerwin rearrangement followed by subsequent loss of H^+ from either the C-14 CH_3 or C-15 to **1** and **2**, respectively. Similarly, the norterpenes **6**–**8** can be viewed as oxidative degradation products of **1** and **2**. The biosynthetic origins of the hydrocarbons **9**–**11** is less obvious, although very likely involving a cyclization event common to **1**–**5**.

Experimental Section

General Experimental Procedures. The general experimental procedures are as previously described.[18]

Collection, Extraction, and Isolation. A fresh specimen of a *Mycale* sp. (277.9 g dry weight, Museum of Victoria registry no. F77035) collected by scuba (−20m) off Durras on the mid south coast of NSW, Australia, was immersed in EtOH and stored at −20 °C. [This specimen of *Mycale* was a massive-lobate growth form, 10–30 mm thick; color in ethanol gray-beige; texture highly compressible and easily torn; oscules conspicuous with raised membranous lip; the

surface transparent and microscopically hispid; spicules include subtylostyles (fusiform, straight or slightly curved, length 190−210 μm); anisochelae (length 20−25 μm); sigmas (c-shaped, fusiform length 50−80 μm); the ectosome is a tangential layer of single spicules over an almost continuous palisade of pulmose spicule bundles formed by the protruding choanosomal primary fibers, the whole being ~500 μm thick and detachable; the choanosome consists of a wide-spaced almost rectangular reticulation of fibers (50−100 μm thick) cored by multispicular tracts of 5−10 subtylostyles in the subectosomal region, becoming less organized deeper in the sponge; detritus occasionally coring primary ascending fibers; interstitial collagen light and filled with scattered megascleres and microscleres.] The decanted EtOH extract was concentrated under reduced pressure, methylated with ethereal diazomethane, and fractionated by normal phase (2.0 mL/min 5%, 10%, 15%, or 20% EtOAc/petroleum spirits) and C_{18} reversed-phase (2 mL/min MeOH or 5% H_2O/MeOH) HPLC to yield the five cyclic peroxide methyl esters **1** (201 mg, 0.072%), **2** (101 mg, 0.036%), **3** (13 mg, 0.005%), **4** (14 mg, 0.005%), and **5** (4 mg, 0.001%) as well as the six norterpenes **6** (18 mg, 0.006%), **7** (5 mg, 0.002%), **8** (8 mg, 0.003%), and **9**−**11** (8 mg, 0.003%).

Mycaperoxide C methyl ester (4): colorless oil; IR ν_{max} ($CHCl_3$) 3680, 1736 cm^{-1}; $[\alpha]_D$ −71° (*c* 1.1, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.82, 0.87, and 0.96 (3s, 14_a-CH_3, 14_b-CH_3, and 18-CH_3), 1.12 (d, *J* 6.2 Hz, 2-CH_3), 1.13 (s, 6-CH_3), 1.16 (s, 10-CH_3), 1.85 (ddd, *J* = 4.4, 13.5, 13.5 Hz), 2.56 (m, 2-H), 3.68 (s, CO_2CH_3), 4.23 (m, 3-H); ^{13}C NMR Table 1; EIMS (15 eV) *m/z* 424 (M^+, 3), 406 (3), 374 (6), 203 (6), 191 (28), 171 (42), 123 (42), 109 (63), 95 (79), 81 (71), 69 (100), 53 (58); HREIMS *m/z* 424.3173 (calcd for $C_{25}H_{44}O_5$, 424.3189).

Mycaperoxide D methyl ester (5): colorless oil; IR ν_{max} ($CHCl_3$) 3680, 1732 cm^{-1}; $[\alpha]_D$ −52° (*c* 0.3, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.78, 0.78, and 0.87 (3s, 14_a-CH_3, 14_b-CH_3, and 18-CH_3), 1.10 (s, 6-CH_3), 1.12 (d, *J* = 7.2 Hz, 2-CH_3), 1.18 (s, 10-CH_3), 1.83 (ddd, *J* = 3.1, 3.1, 12.4 Hz), 2.10 (brt, *J* = 11.2 Hz), 2.54 (m, 2-H), 3.69 (s, CO_2CH_3), 4.24 (m, 3-H); ^{13}C NMR Table 1; EIMS (15 eV) *m/z* 424 (M^+, 5), 374 (4), 320 (3), 271 (8), 221 (27), 191 (44), 171 (32), 123 (45), 109 (64), 95 (91), 81 (75), 69 (91), 53 (100); HREIMS *m/z* 424.3186 (calcd for $C_{25}H_{44}O_5$, 424.3189).

Ketone (+)-6: colorless oil; IR ν_{max} ($CHCl_3$) 1718 cm^{-1}; $[\alpha]_D$ +43° (*c* 1.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.76 (s, 9-CH_3), 0.79 (d, *J* = 6.8 Hz, 8-CH_3), 0.96 (dd, *J* = 3.6, 11.6 Hz), 1.03 (s, 5-CH_3), 2.13 (s, 14-H_3), 4.50 (s, C4−CH_2); ^{13}C NMR Table 1; EIMS (70 eV) *m/z* 262 (M^+, 3), 229 (3), 191 (95), 175 (8), 163 (11), 135 (40), 121 (36), 109 (41), 95 (100), 81 (34), 67 (23), 53 (44); HREIMS *m/z* 262.2287 (calcd for $C_{18}H_{30}O$, 262.2297).

Ketone 7: colorless oil; $[\alpha]_D$ −41.6° (*c* 0.4, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.75 (s, 9-CH_3), 0.79 (d, *J* = 7.2 Hz, 8-CH_3), 0.99 (s, 5-CH_3), 1.60 (bs, 4-CH_3), 2.14 (s, 14-H_3), 5.19 (s, 3-H); ^{13}C NMR Table 1; EIMS (15 eV) *m/z* 262 (M^+, 5), 261 (M^+ − H, 11), 243 (29), 205 (19), 187 (25), 173 (12), 159 (15), 149 (18), 135 (48), 121 (100), 109 (54), 95 (70), 81 (47), 69 (43), 53 (74); HREIMS *m/z* 261.2437 (calcd for $C_{18}H_{29}O$, 261.2456). The sample decomposed before an IR spectrum could be acquired.

Alcohol 8: colorless oil; $[\alpha]_D$ −27° (*c* 0.2, $CHCl_3$); ^1H NMR ($CDCl_3$, 400 MHz) δ 0.73 (s, 9-CH_3), 0.78 (d, *J* = 6.4 Hz, 8-CH_3), 1.03 (s, 5-CH_3), 1.18 (d, *J* = 6.1 Hz, 14-H_3), 1.87 (m, 1H), 2.11 (very brd, *J* = 15.6 Hz, 1H), 2.28 (ddd, *J* = 5.1, 13.6, 13.6 Hz, 1H), 3.68 (brm, 13-H), 4.49 (s, C4−CH_2); ^{13}C NMR Table 1; EIMS (70 eV) *m/z* 264 (M^+, 3), 246 (1), 191 (57), 175 (5), 163 (7), 135 (12), 121 (27), 109 (37), 95 (100), 81 (38), 69 (28), 53 (47); HREIMS *m/z* 264.2447 (calcd for $C_{18}H_{32}O$, 264.2453). The sample decomposed before an IR spectrum could be acquired.

Hydrocarbons 9−11. Compounds **9**−**11** were a table mixture of colorless oils resolved by capillary GC and GC/MS (Hewlett-Packard 5890 gas chromatograph fitted with BP-1 column (15m by 0.2 mm by 0.25μm film thickness). Program: injection temperature = 40 °C, ramp = 5 °C min^{-1}, final temperature = 200 °C, retention times: **9**, 29 min 27 s, **10**, 29 min 56 s, and **11**, 30 min 15 s in an approximate ratio of 4:1:2. Selected ^1H NMR data on the individual compounds is presented below.

Hydrocarbon 9: ^1H NMR ($CDCl_3$, 400 MHz) δ 0.65 (t, *J* = 7.5 Hz, 12-H_3), 0.70 (s, 9-CH_3), 0.77 (d, *J* = 6.2 Hz, 8-CH_3), 1.04 (s, 5-CH_3), 1.86 (m, 1H), 2.09 (very brd, *J* = 13.4 Hz, 1H), 2.28 (ddd, *J* = 5.1, 13.5, 13.5 Hz, 1H), 4.50 (s, C4−CH_2); ^{13}C NMR Table 3; EIMS (15 eV) *m/z* 220 (M^+, 10), 205 (8), 191 (57), 163 (12), 149 (8), 135 (43), 121 (35), 109 (42), 95 (100), 81 (37), 69 (31), 53 (14).

Hydrocarbon 10: ^1H NMR ($CDCl_3$, 400 MHz) δ 0.69 (t, *J* = 7.4 Hz, 12-H_3), 0.70 (s, 9-CH_3), 0.99 (s, 5-CH_3), 5.08 (s, 3-H),^{13}C NMR Table 3; EIMS (15 eV) *m/z* 220 (M^+, 23), 205 (16), 191 (37), 177 (25), 163 (7), 136 (59), 123 (37), 107 (34), 95 (100), 81 (40), 69 (37), 55 (54).

Hydrocarbon 11: ^1H NMR ($CDCl_3$, 400 MHz) δ 5.38 (s, 7-H).[1] ^{13}C NMR Table 3; EIMS (15 eV) *m/z* 220 (M^+, 10), 205 (8), 191 (59), 164 (16), 149 (8), 135 (43), 121 (35), 109 (42), 95 (100), 81 (37), 69 (31), 55 (48).

Acknowledgment. We thank C. Lawler and J. Lawler for assistance in specimen collection, L. Hobbs for taxonomic analysis, and the Australian Research Council for financial support.

References and Notes

(1) Kashman, Y.; Rotem, M. *Tetrahedron Lett.* **1979**, 1707−1708.
(2) Butler, M. S.; Capon, R. J. *Aust. J. Chem.* **1991**, *44*, 77−85.
(3) Albericci, M.; Braekman, J. C.; Daloze, D.; Tursch, B. *Tetrahedron* **1982**, *38*, 1881−1890.
(4) Capon, R. J.; MacLeod, J. K. *Tetradedron* **1985**, *41*, 3391−3404.
(5) Capon, R. J.; MacLeod, J. K. *J. Nat. Prod.* **1987**, *50*, 225−229.
(6) Capon, R. J.; MacLeod, J. K.; Coote, S. J.; Davies, S. G.; Gravatt, L.; Dordor-Hedgecock, I. M.; Whittaker, M. *Tetrahedron* **1988**, *44*, 1637−1650.
(7) Rochfort, S. J.; Gable, R. W.; Capon, R. J. *Aust. J. Chem.* **1996**, *49*, 715−718.
(8) Djura, P.; Stierle, D. B.; Sullivan, B.; Faulkner, D. J. *J. Org. Chem.* **1980**, *45*, 1435.
(9) Carmen, R. M. *Aust. J. Chem.* **1966**, *19*, 629−642.
(10) Capon, R. J.; Ghisalberti, E. L.; Jefferies, P. R. *Aust. J. Chem.* **1981**, *34*, 1775−1778.
(11) Capon, R. J.; Ghisalberti, E. L.; Jefferies, P. R. *Phytochemistry.* **1983**, *22*, 1465−1467.
(12) Capon, R. J.; Faulkner, D. J. *J. Org. Chem.* **1984**, *106*, 1819−1822.
(13) Butler, M. S.; Capon, R. J. *Aust. J. Chem.* **1991**, *44*, 77−85.
(14) Butler, M. S.; Capon, R. J. *Aust. J. Chem.* **1992**, *45*, 1705−1743.
(15) Capon, R. J.; Dargaville, T. R.; Davis, R. *Nat. Prod. Lett.* **1994**, *4(1)*, 51−56.
(16) Hinder, M.; Stoll, M. *Helv. Chim. Acta* **1953**, *36*, 1995−2008.
(17) Tanaka, J.; Higa, T.; Suwanborirux, K.; Kokpol, U.; Bernardinelli, G.; Jefford, C. W. *J. Org. Chem.* **1993**, *58*, 2999−3002.
(18) Rochfort, S. J.; Capon, R. J. *Aust. J. Chem.* **1996**, *49*, 19−26.

NP970313G