350 (M^+·, 100), 135 (82), 122 (28), 107 (36); ^1H NMR ($CDCl_3$) δ 1.83 (3 H, s, 16-CH_3), 3.86 (3 H, s, OCH_3, 5.53 (1 H, dd, J = 10, 2 Hz, H-15), 5.74 (1 H, ddd, J = 10, 5, 2 Hz, H-14), 7.20 (1 H, t, J = 8 Hz, H-11), 7.27 (1 H, t, J = 8 Hz, H-10), 7.30 (1 H, d, J = 8 Hz, H-12), 7.56 (1 H, d, J = 8 Hz, H-9); ^{13}C NMR ($CDCl_3$) 188.2 (C-2), 52.4 (C-3), 54.1 (C-5), 44.5 (C-6), 61.0 (C-7), 147.5 (C-8), 121.1 (C-9), 124.3 (C-10), 127.4 (C-11), 120.4 (C-12), 152.3 (C-13), 125.8 (C-14), 134.4 (C-15), 49.2 (C-16), 27.5(C-17), 8.3 (C-18), 26.5 (C-19), 40.4 (C-20), 72.9 (C-21).

***N*-Methyltabersonine 23**: amorphous; UV (EtOH) λ_{max} 310, 338 nm; IR ($CHCl_3$) 1680, 1630 cm^{-1}; mass spectrum (70 eV, 180 °C), m/e (M^+·, 88), 122 (100); ^1H NMR ($CDCl_3$) δ 0.56 (3 H, t, J = 7 Hz, CH_3), 3.25 (3 H, s, NCH_3), 3.86 (3 H, s, CO_2CH_3), 5.48 (1 H, dd, J = 10, 2 Hz, H-15), 5.63 (1 H, ddd, J = 10, 5, 2 Hz, H-14), 6.9-7.4 (4 H, m, aromatic).

Methylation of Indolenine 18 → 21. To a stirred solution of 200 mg (0.72 mmol) of indolenine **18** in 12 mL of anhydrous THF under nitrogen was added 18 mg (0.75 mmol) of NaH. After 15 min 0.1 mL (1.6 mmol) of CH_3I was added and the mixture was stirred for 17 h at room temperature. The mixture was poured in water and extracted with CH_2Cl_2. After the normal workup the crude product was purified by PLC ($CHCl_3$/MeOH, 95/5, silica gel), yielding 39 mg (19%) of enamine **21**.

Enamine 21: amorphous; UV (EtOH) λ_{max} 225, 258, 279 nm; mass spectrum (70 eV, 200 °C), m/e 292 (M^+·, 48), 135 (100); ^1H NMR ($CDCl_3$) δ 0.55 (3 H, t, J = 8 Hz, CH_3), 2.88 (3 H, s, NCH_3), 5.43 (1 H, m, H-16), 5.60 (1 H, dd, J = 10, 2 Hz, H-15), 5.58 (1 H, m, H-14), 7.0-7.5 (4 H, m, aromatic).

Coupling of Enamine 21 with 21-Cyanoepipandoline 29. To a solution of 60 mg (0.15 mmol) of 21-cyanoepipandoline **29** in anhydrous THF under nitrogen were added 30 mg (0.15 mmol) of $AgBF_4$ in anhydrous THF and then 45 mg (0.15 mmol) of enamine **21** equally in anhydrous THF. The mixture was kept in darkness at room temperature for 3 h. The mixture was filtered on Celite and washed with 10% NH_4OH solution and then with CH_2Cl_2. This was repeated 3 times. The organic phase, after normal workup, afforded the crude product, which was purified on PLC (EtOAc/hexane, 2/35, alumina), yielding 21 mg (20%) of the dimer **30**.

Dimer 30: amorphous; UV (EtOH) λ_{max} 324 (log ϵ 4.18), 298 (4.14), 252 (4.00), 236 nm (sh); IR ($CHCl_3$) 1680, 1610 cm^{-1}; mass spectrum (70 eV, 250 °C), m/e 644 (M^+·, 75), 379 (100), 291 (50), 278 (40), 135 (40), 122 (35), 121 (20), 107 (24); ^1H NMR ($CDCl_3$) 0.57 (3 H, t, J = 7 Hz, CH_3 (C-18')), 1.00 (3 H, t, J = 7 Hz, CH_3 (C-18)), 2.86 (3 H, s, NCH_3), 3.79 (3 H, s, CO_2CH_3), 5.46 (1 H, dd, J = 10, 2 Hz, H-15'), 5.72 (1 H, m, H-14'), 6.30 (1 H, d, J = 8 Hz, H-12), 6.65 (1 H, t, J = 8 Hz, H-10), 6.84 (1 H, d, J = 8 Hz, H-12'), 6.95 (1 H, t, J = 8 Hz, H-10'), 7.05 (1 H, t, J = 8 Hz, H-11), 7.07 (1 H, d, J = 8 Hz, H-9), 7.19 (1 H, t, J = 8 Hz, H-11'), 7.23 (1 H, d, J = 8 Hz, H-9'); ^{13}C NMR ($CDCl_3$) 164.9 (C-2), 72.5 (C-3), 49.0[a] (C-5), 43.1 (C-6), 54.1 (C-7), 136.4 (C-8), 120.2[c] (C-9), 119.3 (C-10), 126.6 (C-11), 108.0 (C-12), 142.4 (C-13), 31.9 (C-14), 35.6[b] (C-15), 95.2 (C-16), 23.0 (C-17), 7.2 (C-18), 32.7 (C-19), 75.6 (C-20), 56.8 (C-21), 167.3 (C=O), 49.5 (OCH_3), 104.1 (C-2'), 50.7[a] (C-3'), 52.7 (C-5'), 35.3[b] (C-6'), 55.0 (C-7'), 136.2 (C-8'), 121.0[c] (C-9'), 116.2 (C-10'), 126.0 (C-11'), 103.5 (C-12'), 150.0 (C-13'), 122.6 (C-14'), 135.0 (C-15'), 33.8 (C-16'), 29.1 (C-17'), 7.2 (C-18'), 32.7 (C-19'), 38.0 (C-20'), 72.5 (C-21'), 26.7 (N'CH_3) (a, b, c indicates assignments may be interchanged.

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Registry No. **1**, 70545-44-7; **2**, 77784-40-8; **3**, 77784-39-5; **4**, 77794-87-7; **5**, 80293-76-1; **6**, 80338-95-0; **7**, 80293-77-2; **8**, 80293-78-3; **9**, 56698-80-7; **9** *N*-oxide, 80263-44-1; **10**, 4429-63-4; **10** *N*-oxide, 67249-34-7; **18**, 32975-46-5; **20**, 78346-69-7; **21**, 78346-70-0; **22**, 80263-45-2; **23**, 80263-46-3; **26**, 3247-10-7; **26** *N*-oxide, 38199-35-8; **27**, 66148-07-0; **28**, 66148-10-5; **29**, 78346-71-1; **30**, 78355-82-5.

Supplementary Material Available: Tables containing ^1H NMR data for **5**-**8**; ^{13}C NMR data for **1**, **2**, **4**, **5**, and **8**; mass spectral data for **1**-**8**; comparative lists of bond lengths, bond angles, and torsion angles and final atomic coordinates and thermal parameters for **1**, **6** and **7** (19 pages). Ordering information is given on any current masthead page.

Tricyclic Diterpenes from the Brown Marine Algae *Dictyota divaricata* and *Dictyota linearis*

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Received September 1, 1981

Mixed collections of two toxic brown seaweeds, *Dictyota linearis* and *D. divaricata*, were studied from five collection sites in the Honduras Bay Islands. The two known dolastane diterpenes **3** and **4** were isolated. Five new dolastanes, **5**-**9**, were also characterized. Compounds **5**-**8** were each converted to **4**. A combination of ^{13}C and ^1H NMR experiments or chemical correlations supported structural and stereochemical assignments. Several of these compounds showed interesting pharmacological properties.

Dense mats of two brown seaweeds attracted our attention while we were collecting specimens from the coral reefs of the Honduras Bay Islands in Apr 1978. A chemical study of these intertwined algae, mixture of *Dictyota linearis* (C. Ag.) and *Dictyota divaricata* (lamour), was initiated because their crude extracts showed toxicity to goldfish at 400 μg/mL (death in 90 min).[1] Seaweed extracts of the Dictyotaceae family often contain fascinating diterpeniods.[2] Not surprisingly, one of the simplest components of our toxic crude extracts seemed to be a diterpene because 20 carbons, and five methyl equivalents were evident from its NMR properties. While our work was proceeding we learned that two other laboratories had

(1) Based upon as assay procedure used by: Bakus, G. J. *Science* **1981**, *211*, 498 and references within.

(2) Gerwick, W. H.; Fenical, W.; Sultanbawa, M. U. S. *J. Org. Chem.* **1981**, *46*, 2233 and references within.

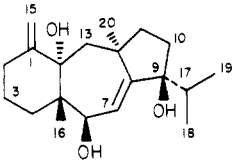
0022-3263/82/1947-0811$01.25/0

Table I. ^{1}H NMR Data (Benzene-d_6, 360 MHz)

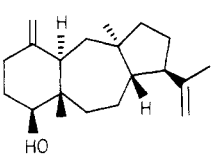
	chemical shift, δ (pattern; J, Hz)						
H[d]	3	4	5	6	7	8	9
2a	2.85 (dt, 14, 14, 6.3)	2.74 (dt, 13, 13, 6.3)	2.72 (dt, 13.5, 13.5, 6.8)	2.60 (dt, 13, 13, 6)	2.83 (dt, 14, 14, 7)	2.84 (dt, 14, 14, 6)	2.55 (dt, 13.5, 13.5, 2.7)
2e	1.65 (m)	1.64 (dd, 13, 3.8, 3.4)					1.79 (dt, 13.5, 3.6, 3.6)
3	1.65 (m)						1.50 (m)
4e	3.25 (dt, 8.1, 3.6, 3.6)	4.88 (t, 3, 3)	4.85 (t, 3.6, 3.6)		3.24 (m)	3.25 (dt, 7, 4, 4)	4.78 (t, 3.6, 3.6)
6	2.99[b] (ddd, 16.2, 14.4, 5.4) 1.70[c] (ddd, 14.7, 4.5, 3.2)	3.34[b] (dd, 15.3, 4.2)	3.14[b] (dd, 15.1, 4.2)	3.25[b] (dd, 15.3, 4.8)	3.40[b] (dd, 15, 4)	3.06[b] (dd, 14.4, 10.8)	4.43[b] (dd, 10.8, 7.2)
7	2.39[b] (ddd, 16, 14, 5) 1.84[c] (ddd, 14.2, 5.4, 3.2)	5.34 (dd, 9.2, 4.2)	5.28 (dd, 9.5, 4.3)	5.47 (dd, 7.7, 4.8)	5.37 (dd, 10, 4)	4.53[b] (dd, 10.8, 7.4)	2.85[b] (dd, 14.0, 10.8) 1.50[c] (dd)
10	2.20 (t, J_{AX} + J_{BX} = 13.5)	5.55 (br t, 4, 4)		5.55 (br t, 3.6, 3.6)		2.19 (m)	2.21 (m)
11	1.65 (m)	2.24 (br d, 16.7)		2.22 (br d, 16.8)			
11′	1.25 (ddd, 14.4, 9, 2)	2.16 (br d, 16.7)		2.09 (br d, 16.8)			
13	1.95 (d, 15.3)	2.04 (d, 14.4)	2.04 (d, 14.4)	2.06 (d, 14)	1.79 (d, 14)	1.90 (d, 14.4)	1.93 (d, 14.4)
13′	1.40 (d, 15.3)	1.84 (d, 14.4)	1.80 (d, 14.4)	1.99 (d, 14)	1.57 (d, 14)	1.41 (d, 14.4)	1.50 (d)
15	4.77 (br s)	4.80 (br s)	4.80 (br s)	4.78 (br s)	4.76 (br s)	4.76 (br s)	4.69 (br s)
15′	4.72 (br s)	4.74 (br s)	4.75 (br s)	4.61 (br s)	4.60 (br s)	4.68 (br s)	4.50 (br s)
17	2.60 (sp, 7.2)	2.41 (sp, 7.2)	1.82 (sp, 7.2)	2.42 (sp, 7.2)	1.56 (sp, 7)	2.78 (sp, 7)	2.72 (sp, 7.2)
Me_{16}	0.66 (s)	0.78 (s)	0.70 (s)	0.92 (s)	0.65 (s)	0.59 (s)	0.44 (s)
Me_{18}[a]	0.98 (d, 7.2)	1.14 (d, 7.2)	1.11 (d, 7.2)	1.14 (d, 7.2)	1.13 (d, 7)	1.02 (d, 7)	1.39 (d, 7.2)
Me_{19}[a]	0.925 (d, 7.2)	1.12 (d, 7.2)	0.84 (d, 7.2)	1.11 (d, 7.2)	0.83 (d, 7)	0.86 (d, 7)	1.30 (d, 7.2)
Me_{20}	1.425 (s)	1.51 (s)	1.47 (s)	1.39 (s)	1.18 (s)	1.58 (s)	1.48 (s)
C_4 OH	3.15 (d, 8.1)				3.11 (d, 8)	3.17 (d, 7)	3.45 (s)
C_{14} OH	2.235 (s)	3.70 (s)	3.60 (s, C_9 OH)		2.25 (s)	2.69 (s, C_7 OH)	
OAc		1.66 (s)	1.53 (s)				1.60 (s), 1.55 (s)

[a] Assignments that can be switched. [b] Axial. [c] Equatorial. [d] See the numbering scheme in structure 1.

isolated tricyclic diterpenes from *D. divaricata* (Caribbean, Virgin Islands)[3-5] and *D. linearis* (Pacific, Japan).[6] These tricyclic diterpenes were members of the dolastane class which was first observed from a gastropod mollusc, *Dolabella auricularia*[7] (e.g., dolatriol, 1), and subsequently observed from an alcyonarian, *Clavularia inflata* (e.g., hydroxyclavularadiene, 2).[8] We have isolated five new dolastane alcohols, **5–9**, and report now their chemical, spectroscopic, and bioactive properties.

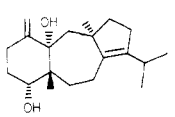


1



2

(3) Fenical et al. secured the structure of 4 by its conversion to the corresponding diol i whose structure was solved by X-ray crystallography;[4] however, only relative stereochemistry could be established as 4S*,14S*[5]. Consequently, only relative stereochemistry is implied for all new natural products reported here.



i

(4) Sun, H. H.; McConnell, O. J.; Fenical, W.; Hirotsu, K.; Clardy, J. *Tetrahedron* **1981**, *37*, 1237.

(5) This follows IUPAC 1968 Tentative Rules, Section E, Fundamental Stereochemistry, for designating chiral centers were the relative but not absolute configuration is known (section E-5.10): *J. Org. Chem.* **1970**, *35*, 2849.

(6) (a) Ochi, M.; Watanabe, M.; Miura, I.; Taniguchi, M.; Tokoroyama, T. *Chem. Lett.* **1980**, 1229. (b) Ochi, M.; Watanabe, M.; Kido, M.; Ichikawa, Y.; Miura, I.; Tokoroyama, T. *Ibid* **1980**, 1233.

Results and Discussion

Five different mixed *Dictyota* collections were examined, representing two from Roatan Island and one each from

(7) Pettit, G. R.; Ode, R. H.; Herald, C. L.; Von Dreele, R. B.; Michel, C. *J. Am. Chem. Soc.* **1976**, *98*, 4677.

(8) (a) Braekman, J. C.; Daloze, D.; Schubert, R.; Albericci, M.; Tursch, B.; Karlsson, R. *Tetrahedron* **1978**, *34*, 1551. (b) Bowden, B. F.; Braekman, J. C.; Coll, J. C.; Mitchell, S. J. *Aust. J. Chem.* **1980**, *33*, 927.

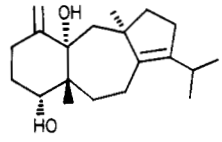
Table II. ^{13}C NMR Data ($CDCl_3$, 25 MHz)[a]

	chemical shift, δ				
C[b]	3	4	5	6	9
1	152.3	155.0	150.9	149.8	149.6
2	30.6	30.8	30.1	37.2[e]	36.4[c]
3	26.7	26.9	26.5	23.2	26.8[c]
4	80.5	82.3	81.6	32.1[e]	81.7
5	44.1[c]	43.9[c]	42.4[c]	41.4[c]	44.0
6	28.3	28.4	28.0	35.1[e]	65.5
7	22.1	112.5	117.7	114.5	26.3[c]
8	139.2[d]	151.6[d]	156.9	154.1[d]	149.6[d]
9	138.4[d]	149.6[d]	79.4	153.9[d]	146.4[d]
10	27.3	125.6	28.9	124.7	27.1[c]
11	42.9	41.9	41.2	43.4	42.4
12	50.8[c]	45.8[c]	45.9[c]	45.4[c]	
13	47.6	50.1	43.0	50.9	47.7
14	81.1	80.1	86.2	79.5	78.3
15	109.2	109.4	109.5	108.6	110.2
17	26.7	25.7	34.4	25.6	25.4
Me_{16}	17.5	20.0	17.1	19.9	18.3
Me_{18}	20.3[e]	21.3[e]	18.9[e]	22.3	20.2[e]
Me_{19}	21.2[e]	22.1[e]	19.7[e]	22.3	21.4[e]
Me_{20}	26.7	27.6	24.2	27.6	27.1
		169.4	169.3		174.7, 169.1
OAc		22.1	21.1		20.2, 20.2

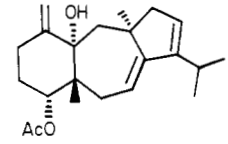
[a] Assignments based upon off resonance multiplets and comparison to standard shifts. [b] See the numbering scheme in structure 1. [c-e] Assignments may be switched.

the other major islands (Hog Island, Utila, and Guanaja). The diterpene composition in each collection varied as might be expected on the basis of our past experience with red seaweed terpenes.[9]

Alcohols 3[6] and 4[3] of known structure (see Tables I and II) were encountered. Fine crystalline threads of diol 3



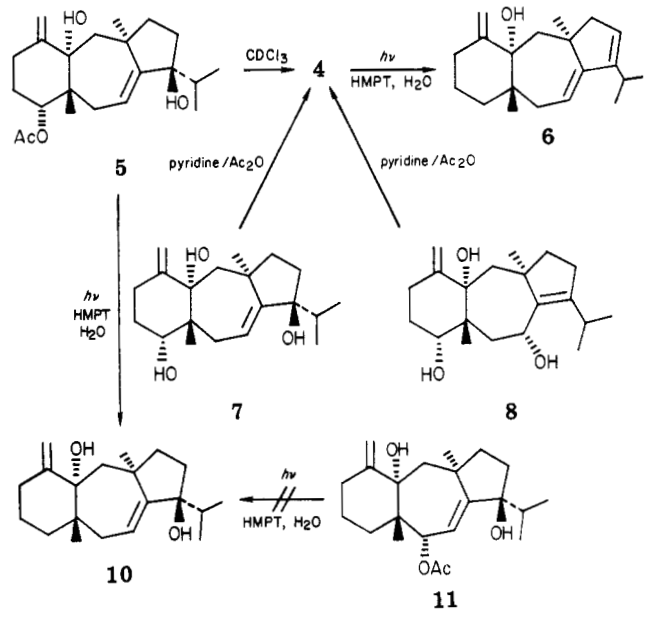
3



4

($C_{20}H_{32}O_2$) were deposited from the crude hexane extracts of the Utila Island collection. The ol acetate 4 ($C_{22}H_{32}O_3$) was a minor component from a Roatan Island ("Lost Paradise") collection. The major component of the "Lost Paradise" oil, diol acetate 5 ($C_{22}H_{34}O_4$), was closely related to 4. Several complimentary NMR observations showed that 5 was a hydrated product of 4. These included the position of the ^{13}C NMR C_9–C_{10} signals in 4 at δ 149.6 (s) and 125.6 (d) compared to δ 79.4 (s) and δ 28.9 (d) in 5, the four olefin ^1H signals in 4 vs. three in 5 (Table I), a significant upfield shift of the H_{17} septet in 5 (δ 1.82) vs. that in 4 (δ 2.4), and finally the larger Δδ between Me_{18} and Me_{19} in 5 (Δδ = 0.27 ppm) vs. that in 4 (Δδ = 0.02 ppm). Identical ^1H and/or ^{13}C shifts between 4 and 5 at C_4, C_5, Me_{16}, and Me_{20} and J's to H_{4e} showed that the stereochemistry at each chiral center, *except* C_9, was identical. Dehydration of 5 to 4 occurred when it was stored in $CDCl_3$ for long periods[3] (Scheme I). This facile dehydration raised suspicions that 4 might be an artifact. But this was not true because ^1H NMR (360 MHz) of a crude extract of a frozen sample (from "Lost Paradise") exhibited characteristic signals for 4.

Scheme I



A photochemically induced deacetylation[10] converted 5 to 10 and 4 to 6 in good yield, and this provided further support for an acetate at C_4 in both 5 and 4. The synthetic alcohol 6 ($C_{20}H_{30}O$) was identical with a natural product isolated as a minor component from a Roatan Island collection. Remaining unresolved was the C_9 stereochemistry in 5, and two strategies were considered. The first, which was unsuccessful, involved an attempt to relate 5 via synthetic product 10 to 6-*O*-acetyldolatriol (11) whose structure is known from X-ray analysis.[7] Subjecting 11 to the photochemical deacetylation gave a complex mixture which did not contain 10. A correlation of OH–Me ^1H NMR shift effects provided more positive results. It is well-known that an H or Me group is deshielded when coplanar to a nearby OH group.[11] The usual shift magnitude for an H or Me 1,3 to an OH ranges from 0.4 to 0.6 ppm. Consistent with this is the relatively low-field position ($CDCl_3$) of Me_{20} (δ 1.36) vs. Me_{16} (δ 0.74) in 3 due to a syn 1,3 Me–OH orientation.[6] By contrast, the slightly upfield shift of the 1 Me_{20} (δ 1.19)[7] is diagnostic of its trans relationship to the C_9OH. Consequently, the shift ($CDCl_3$) of the 5 Me_{20} (δ 1.19) indicates that it and C_9OH are trans as shown.

Concentration of the Guanaja crude extract yielded a triol 7 ($C_{20}H_{32}O_3$) as a pure crystalline substance (cubes, mp 179–180 °C). Its limited solubility precluded ^{13}C NMR study, yet its ^1H NMR properties clearly showed that 7 was the parent triol of 5. The characteristic NMR shift ($CDCl_3$) of Me_{20} (δ 1.21) established its trans relationship to C_9OH. The remaining structure and stereochemical features were pinned down by conversion of 7 to 4 during acetylation.

A second triol isomer, 8 ($C_{20}H_{32}O_3$, mp 163–166 °C) cocrystallized with diol 3 from the Utila crude extract. The C_7 OH(H) substituent and the stereochemistry were confirmed on the basis of comparison of the 8 H_7 NMR properties ($CDCl_3$; δ 4.65, J = 11, 7 Hz) to those of the related diol acetate 12 reported by Fenical[4] [C_7 OAc(H),

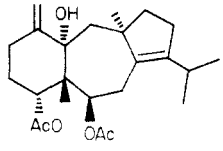
(9) (a) Crews, P.; Kho-Wiseman, E.; Montana, P. *J. Org. Chem.* **1978**, *43*, 116. (b) Crews, P.; Kho-Wiseman, E. *Ibid* **1977**, *42*, 2812, (c) Crews, P.; Campbell, L.; Heron, E. *J. Phycol.* **1977**, *13*, 297.

(10) (a) Still, W. C.; Tsai, M.-Y. *J. Am. Chem. Soc.* **1980**, *102*, 3654. (b) Murry, R. K.; Ford T. M. *J. Org. Chem.*. **1979**, *44*, 3504. (c) Deshayes, H.; Pete, J.-P.; Portella, C. *Tetrahedron Lett.* **1976**, 2019.

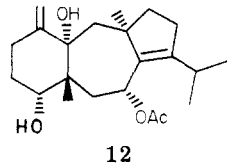
(11) Diagnostic examples include: (a) Carr, J. B.; Huitric, A. C. *J. Org. Chem.* **1964**, *29*, 2508. (b) Lemieux, R. V.; Stevens, J. D. *Can. J. Chem.* **1966**, *44*, 249. (c) Zücher, R. F. *Helv. Chim. Acta* **1963**, *46*, 2054.

δ 5.92, J = 11, 7 Hz). As above, the remaining structural and stereochemical features were established by conversion of 8 to 4 during acetylation.

A diacetate alcohol (9, $C_{24}H_{36}O_5$) was isolated from the Roatan Island collections, and it was completely characterized on the basis of spectroscopic arguments. Diagnostic ^{13}C NMR signals were evident for two OAc's [δ 174.7 (s), 169.1 (s), 20.2 (q), 20.2 (q)], a >C=C< [δ 149.6 (s), 146.4 (s)], a >C=CH_2 [δ 149.6 (s), 110.2 (t)], and three oxygen-bearing sp^3 C's [δ 81.7 (d), 78.3 (s), 65.5 (d)]. A magnificent spin-decoupling result (benzene-d_6, 360 MHz) revealed several other subfeatures. Irradiation of a featureless multiplet at δ 1.47 simultaneously removed the coupling from four separate protons (H_{3a}, H_{3e}, H_{7e}, and H_{13}) which simplified multiplets for six other protons (H_{2a}, H_{2e}, H_{4a}, H_{6a}, H_{7a}, and $H_{13'}$). Assignments based upon this included an isolated CH_2 [δ 1.93 (d), 1.47 (d), J = 13 Hz], a $CCH_2CH_2CH(OAc)C$ as part of a six-membered ring [H_{4e}, δ 4.78 (bt), J = 4, 4 Hz; H_{3a} and H_{3e}, δ 1.47 (m); H_{2a}, δ 2.55 (dt), J = 14, 14, 3 Hz; H_{2e}, δ 1.79 (dt), J = 14, 4, 4 Hz], and an isolated $CH_2CH(OAc)$ as part of a seven-membered ring [H_{6a}, δ 4.43 (dd), J = 10.8, 7.2 Hz; H_{7a}, δ 2.85 (dd), J = 10.8, 14.0 Hz; H_{7e}, δ 1.47]. Attachment of acetates at both CH–O sites was required by the relatively deshielded ^1H shifts of both methine multiplets (δ 4.78 and 4.43). Assignment of a pseudoequatorial OAc at C_6 vs. C_7 was possible by comparison to the much more deshielded allylic H_7 in 12[4] at δ 5.9 and consideration of the H_7 J's = 10.9 and 7.2 Hz. The remaining stereochemial features at C_5, C_{12}, and C_{14} could be assigned on the basis of the near-identity of ^{13}C and ^1H shifts at C_4, Me_{16}, and Me_{20} between 9 and 3.



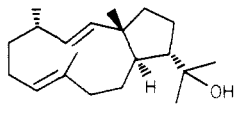
9



12

Several of the above metabolites showed pharmacological activity.[12] Diol 4 at 16 μg/mL exhibited a 71% reversible histamine antagonism on guinea pig ileum preparations. Compound 5 showed a 27% increase of the twitch height at 16 μg/mL in a rat hemidiaphragm preparation while 8 showed a 48% decrease at the same concentration. This latter compound also exhibited a 17% inhibition of cell division in an urchin egg assay.

The close similarity between natural products such as 7 from seaweeds and herbivorous mollusc metabolites such as 1[7] is not surprising.[13] Alternatively, the similarity in biosynthetic capability between soft corals as illustrated by natural products such as 2[8] and similar seaweed metabolites such as 3–9 is less common. There seems to be only one other parallel diterpenoid-type example. Bicyclic diterpenes including 13 from the brown algae *Glossophora*



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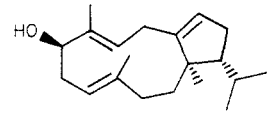

14

galapagensis[13] and *Dictyota dichotoma*[14] and from the herbivorous mollusc *Dolabella californica*[15] are biogenetically related to a methyl-rearranged bicyclic diterpene, 14, recently reported from an unidentified soft coral.[16]

Experimental Section

Our general analytical, chemical, and chromatographic methods have been described previously.[17] Collections of *Dictyota divaricata* and *Dictyota linearis* were made from each of the major Bay islands of Honduras, Central America, during Mar 1978, July 1979, or July 1980. Collections were from a depth of −10 to −30 ft, and locations were on Roatan Island ("Lost Paradise" and Dixon's Cove), Hog Islands (northeast inner coves of Cachino Grande), Utila (Jack O'Neil's cay), and Guanaja (Michael Rock). All collections were mixtures of the two *Dictyota* species that were difficult to separate. Each collection was immediately frozen and stored until extracted with hexanes in a Soxhlet apparatus. Concentration of the hexanes extract sometimes yielded a crystalline deposit within a few days at room temperature. Flash chromatography of the concentrated extract with petroleum ether, petroleum ether/benzene (1:1), and finally benzene gave fractions which were further purified by HPLC. Prior to chromatography each crude oil was examined by ^1H NMR (benzene-d^6, 360 MHz) to estimate the composition of the major diterpenes. A sample of *Dictyota* from "Lost Paradise" (Roatan Island) was carefully separated into *D. linearis* and *D. divaricata*, and diterpenes 4 and 5 could be identified in the ^1H NMR of the crude extract of the former while 4 could be seen in the latter.

Amijiol or (4*S,14*S*)-4,14-Dihydroxydolasta-1(15),9-diene (3).** The Utila Island crude hexanes concentrate deposited impure 3 which after recrystallization gave two types of crystals (50 mg) which after hand separation both showed a melting point of 141–143 °C. The separate ^1H NMR (360 MHz) of these crystals were identical. Alternatively, HPLC fraction 16 (12 mg) from the "Lost Paradise" (Roatan Island) collection gave fine crystalline threads of 3 whose ^1H and ^{13}C NMR (Tables I and II) were similar to those reported in the literature[6]: $[\alpha]_D$ −98° ($CHCl_3$) vs. $[\alpha]^{20}_D$ −126° ($CHCl_3$); mass spectrum, *m/e* 286 ($M^+ - H_2O$), 268 ($M^+ - 2H_2O$), 253, 55 (base peak).

(4*S,14*S**)-4-Acetoxy-14-hydroxydolasta-1(15),7,9-triene (4).** High-performance LC fraction 12 (6 mg) of one of the semipure oils from the "Lost Paradise" extract gave 4 as a yellow oil: $[\alpha]_D$ −133.8° (*c* 1.0, CH_3OH) vs. −128.5°;[3] ^1H and ^{13}C NMR spectra (Tables I and II) and the mass spectrum [*m/e* 344 (M^+), 326 ($M^+ - H_2O$), 91 (base peak)] were similar to those reported in the literature[4]; UV (EtOH) λ_{max} 243 nm (ε 3600).

(4*S,9*R**,14*S**)-4-Acetoxy-9,14-dihydroxydolasta-1(15),7-diene (5).** High-performance LC fraction 12 (16 mg) of one of the semipure oils from the "Lost Paradise" extract gave 5 as a crystalline material: mp 151 °C; $[\alpha]_D$ −40° (*c* 1.0, CH_3OH); ^1H and ^{13}C NMR data in Tables I and II; ^1H NMR ($CDCl_3$ 360 MHz) δ 5.49 (dd, J = 10, 4 Hz, H_7), 4.88 (br s, H_{15}), 4.80 (br t, J = 4 Hz, H_{4e}), 4.77 (br s, H_{15}), 3.02 (dd, J = 15 Hz, 4, H_{6a}), 2.66 (m, H_{2a}), 2.10 (s, OAc), 1.19 (s, Me_{20}), 0.99 (d, J = 7 Hz, Me_{18} or Me_{19}), 0.85 (s, Me_{16}), 0.78 (d, J = 7 Hz, Me_{19} or Me_{18}).

(14*S)-14-Hydroxydolasta-1(15),7,9-triene (6).** High-performance LC fraction 6 (2 mg) of the semipure oil from Dixon's Cove gave 6 as a clear oil: ^1H and ^{13}C NMR data in Tables I and II; mass spectrum, *m/e* 286 (M^+), 271 ($M^+ - CH_3$), 55 (base peak).

(4*S,9*R**,14*S**)-4,9,14-Trihydroxydolasta-1(15),7-diene (7).** Concentration of the crude hexanes extract from the Guanaja oil yielded 7 as a crystalline material: mp 179–180 °C; 150 mg (0.04%); $[\alpha]_D$ −161° ($CHCl_3$); ^1H NMR [360 MHz (Table I in benzene-d_6) $CDCl_3$] δ 5.61 (dd, J = 10, 4 Hz, H_7), 4.92 (s, H_{15}), 4.79 (s, H_{15}), 3.74 (d, J = 8 Hz, C_4OH), 3.45 (br t, H_{4a}), 3.35 (dd, J = 15, 4 Hz, H_{6a}), 2.65 (s, OH), 2.87 (ddd, J = 7, 4, 4 Hz, H_{2a}), 1.93 (d, J = 15 Hz, H_{13}), 1.74 (d, J = 15 Hz, H_{13}), 1.48 (sp, J = 7 Hz, H_{17}), 1.21 (s, Me_{20}), 1.02 (d, J = 6.8 Hz, Me_{18}), 0.82 (d, J

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= 6.8 Hz, Me_{19}), 0.77 (s, Me_{16}); mass spectrum, m/e 302 ($M^+ - H_2O$).

(4S*,7S*,14S*)-4,7,14-Trihydroxydolasta-1(15),8-diene (8). Reconcentration of the crude hexanes extract from Utila yielded impure crystalline **8**. Fractional recrystallization from benzene/hexanes gave fine needles: mp 163-166 °C; 371 mg (0.03%); $[\alpha]_D$ -112° ($CHCl_3$); ^1H NMR [(benzene-d_6 in Table I) $CDCl_3$] δ 0.72 (s, Me_{16}), 0.89 (d, J = 7 Hz, Me_{18}), 0.93 (d, J = 7 Hz, Me_{19}), 1.49 (s, Me_{20}); Mass spectrum, m/e 320 (M^+), 302 ($M^+ - H_2O$); exact mass m/e 302.211, calcd for $C_{20}H_{30}O_2$ 302.2244.

(4S*,6R*,14S*)-4,6-Diacetoxy-14-hydroxydolasta-1(15),8-diene (9). High-performance LC fraction 14 (6 mg) of the semipure oil from Dixon's Cove gave **9** as a yellow oil: $[\alpha]^{25}_D$ -144.6° (c 1.0, CH_3OH), ^1H and ^{13}C NMR data in Tables I and II; mass spectrum, m/e 404 (M^+), 338, 80 (base peak).

Dehydration of 5 to 4. Compound **5** stored in $CDCl_3$ at room temperature for several days quantitatively dehydrated to **4** as determined both by ^1H and ^{13}C NMR. The progress of this dehydration could easily be followed by monitoring the shift of (^1H NMR, benzene-d_6) multiplets of H_{17} (δ 1.82), H_6 (δ 3.14), and H_7 (δ 5.28) to H_{17} (δ 2.41), H_6 (δ 3.34), and H_7 (δ 5.34), respectively, and the appearance of H_{10} (δ 5.55).

Deacetylation of 4 to 6. A nitrogen-purged solution of compound **4** (1 mg) in 9.5 mL hexamethylphosphoric triamide (HMPT) and 0.5 mL distilled H_2O in a quartz tube was irridated with a low-pressure mercury lamp (λ = 2537 Å) for 5 h. Diethyl ether (20 mL) was added to the product mixture followed by washing with portions of H_2O (4 × 20 mL). Flash chromatography on silica gel (hexanes/diethyl ether), 95:5) gave **6** (<1 mg) whose ^1H NMR (360 MHz, benzene-d_6) was the same as that of the natural product isolated above (Table I).

Deacetylation of 5 to 10. Using the same procedure as described above, compound **5** (13 mg) in HMPT (1.9 mL) and water (0.1 mL) yielded, after silica gel flash chromatography (hexanes/diethyl ether, 1:1), pure **10** (3.4 mg) which showed the following: ^1H NMR (100 MHz, benzene-d_6) δ 5.36 (dd, J = 10, 4 Hz, H_7), 4.76 (s) and 4.58 (s), H_{15} and $H_{15'}$), 3.02 (dd, J = 14, 4 Hz, H_{6a}), 2.54 (dt, J = 10, 10, 4 Hz, H_{2a}), 1.16 (s, Me_{20}), 1.14 (d, J = 7 Hz, Me_{18}), 0.84 (s, Me_{16}), 0.82 (d, J = 7 Hz, Me_{19}).

Acetylation of 7 to 4. To compound **7** (13 mg) in 2 mL of dry pyridine was added 2 mL of freshly distilled acetic anhydride. This was stirred for 48 h at room temperature and diluted with 80 mL of benzene. It was washed with several portions of 1% HCl followed by $NaHCO_3$ solution (saturated). The organic layer was dried with $MgSO_4$, and the solvent was removed under vacuum. The residue was chromatographed by high-performance LC to give **4** whose ^1H NMR (360 MHz, benzene-d_6) matched that of an authentic sample.

Acetylation of 8 to 4. By employment of the above procedure, **8** (50 mg) yielded **4** whose ^1H NMR (360 MHz, benzene-d_6) matched that of an authentic sample.

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Registry No. **3**, 75744-70-6; **4**, 79203-55-7; **5**, 80243-66-9; **6**, 80243-67-0; **7**, 80243-68-1; **8**, 80243-69-2; **9**, 80243-70-5; **10**, 80243-71-6; **11**, 80299-50-9.

Synthesis of (*E*)-1-Aryl-2-methyl-3-alkyl-2-propen-1-ones via Allylic Sulfoxide–Sulfenate Ester Rearrangements

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A synthon for vinyl anion **2** has been designed as the cornerstone for a versatile synthesis of (*E*)-1-aryl-2-methyl-3-alkyl-2-propen-1-ones (**1**). The choice of the allylic sulfoxide–sulfenate ester rearrangement as a synthesis conduit leads to formation of the desired *E* isomers stereoselectively. Attempted tetrahydropyran ring opening of enone **7c** was not successful.

As a prelude to a convergent organochemical preparation of members of the maytansine[1] family of antileukemic[2] ansa macrolides,[3] a general synthesis of (*E*)-1-aryl-2-methyl-3-alkyl-2-propen-1-ones (**1**) has been designed. The constraints of the synthesis plan mandated the intermediacy of an (*E*)-1-aryl-2-methyl-2-propen-1-one d_3 reagent,[4] i.e., the operational equivalent of the vinyl anion **2**.

Table I. Overall Yields of Purified Ketones 7 from Allylic Sulfides 3

compd	% yield	compd	% yield
7a	41	7c	39
7b	50	7d	49

Results and Discussion

Appropriation of synthetic methodology pioneered by Evans and his co-workers[5] resulted in a suitable synthon

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