1.6, 14.0, 22.5, 25.0, 29.4, 31.6, 37.5, 65.5, 122.1. Anal. Calcd for $C_{14}H_{31}NOSi_2$: C, 58.88; H, 10.94; N, 4.90. Found: C, 59.03; H, 10.99; N, 4.97.

1-[Bis(1-methylethyl)amino]-1-[bis(trimethylsilyl)-amino]-2-[(trimethylsilyl)oxy]-1-octene (7e). A solution of **1e** (0.21 g, 1.0 mmol) in THF (5 mL) was added to LDA (2.2 mmol), TMEDA (2.2 mmol), and TMSCl (2.2 mmol) in THF (5 mL). After 2 h at −78 °C and overnight at 25 °C, an anhydrous workup afforded a 60:40 mixture of **3e:7e**, as deduced from spectral data. IR: 1255 (s), 1265 (s) cm^{-1}. ^1H NMR: δ 0.14 (s, 18 H), 0.18 (s, 9 H), 0.87 (m, 3 H), 1.19 (d, J = 7 Hz, 6 H), 1.2–1.55 (m, 8 H), 2.12 (m, 2 H), 3.47 (septet, J = 7 Hz, 2 H). ^{13}C NMR: δ 2.2, 3.1, 14.1, 22.7, 24.6, 27.3, 29.8, 31.8, 33.9, 49.4, 133.4, 133.9.

2-Phenyl-2-(trimethylsilyl)-2-[(trimethylsilyl)oxy]-ethanenitrile (3f). A solution of LDA (0.16 mol) in THF (250 mL) at −78 °C was treated with **1f** (30.0 g, 0.146 mol) followed by TMSCl (35.0 g, 0.32 mol). **1f** and TMSCl were added neat and not precooled. After overnight at 25 °C, an anhydrous workup followed by short-path distillation gave 37.4 g of **3f**, bp 71–84 °C (0.2 mm), which VPC (120 °C) showed to be over 95% pure (88% yield). IR: 2220 (w), 1600 (w), 1250 (s) cm^{-1}. ^1H NMR: δ 0.08 (s, 9 H), 0.15 (s, 9 H), 7.32 (m, 5 H). ^{13}C NMR: δ −4.9, 1.0, 69.2, 121.4, 124.4, 127.0, 128.2, 138.7. Anal. Calcd for $C_{14}H_{23}NOSi_2$: C, 60.59; H, 8.35; N, 5.05. Found: C, 60.60; H, 8.25; N, 4.92.

In another experiment, a solution of LDA (2.4 mmol) in THF (10 mL) was treated at −78 °C with **1f** (0.44 g, 2.1 mmol) and then with TMSCl (0.26 g, 2.4 mmol). Two hours after the mixture was allowed to warm to 25 °C, the solution was concentrated under vacuum to ca. 2 mL. A sample was then withdrawn by syringe under argon and its IR spectrum obtained (vs THF) in matched cells (0.1 mm). The spectrum showed a band at 2095 (2070 sh) cm^{-1} with A = 1.1.

1-[Bis(1-methylethyl)amino]-1-[bis(trimethylsilyl)-amino]-2-phenyl-2-[(trimethylsilyl)oxy]ethene (7f). To a mixture of LDA (8.8 mmol) and TMEDA (1.33 mL, 8.8 mmol) in THF (20 mL) at −78 °C were added **1f** (0.88 g, 4.0 mmol) and TMSCl (1.22 mL, 9.6 mmol) sequentially. After overnight at 25 °C, TMSCl (0.8 mL, 6.4 mmol) was added, and the mixture was worked up (anhydrous) after 2 h to give 1.68 g of crude material which NMR analysis indicated contained **7f** together with a small amount of **1f** and other $SiMe_3$-containing impurities. Kugelrohr distillation (middle cut, 90–110 °C, 0.2 mm) afforded a sample for spectral data. ^1H NMR: δ −0.17 (s, 9 H), 0.22 (s, 18 H), 0.85 (d, J = 7.0 Hz, 12 H), 3.54 (septet, J = 7.0 Hz, 2 H), 7.0–7.5 (m, 5 H). ^{13}C NMR: δ 2.1, 2.9, 24.3, 51.1, 127.4, 127.9, 132.4, 132.8, 137.1, 139.3. Due to air-sensitivity and high molecular weight, further purification of **7f** proved difficult. Preparative VPC (2 ft × 0.25 in. 3% SE-30, 180 °C, 1 h retention time) afforded an analytical sample which NMR analysis indicated had undergone partial isomerization to a 2:1 mixture of **7f** and its geometrical isomer [^1H NMR: −0.14 (s, 9 H), −0.06 (s, 18 H), 1.30 (d, J = 7.0 Hz, 12 H), 3.58 (septet, J = 7.0 Hz, 2 H), 7.0–7.35 (m, 5 H)]. Anal. Calcd for $C_{23}H_{46}N_2OSi_3$: C, 61.27; H, 10.28; N, 6.21. Found: C, 62.03; H, 9.78; N, 6.24.

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Diterpenoids from the Gorgonian *Solenopodium stechei*

Stephen J. Bloor,[1] Francis J. Schmitz,* M. Bilayet Hossain, and Dick van der Helm*

Department of Chemistry and Biochemistry, University of Oklahoma, Norman, Oklahoma 73019-0370

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Twenty-five new diterpenoids with representatives from three skeletal classes, briareins, eunicellins, and cembranes, have been isolated from a Pacific gorgonian, *Solenopodium stechei*. The structural diversity of the diterpenoids isolated indicates significant biosynthetic versatility for this gorgonian. Stecholides **1–20** are diterpene lactones of the briarein family distinguished by the presence of an α,β-epoxide group in the lactone ring. These structures were deduced by spectroscopic analyses. The structure of solenopodin D, **24**, a eunicellin-type diterpenoid, was established by X-ray analysis while the structures of three other solenopodins, **20–23**, were confirmed by spectral analyses and comparison to data for **24**. Solenopodins A–D are the only eunicellin-type diterpenoids isolated to date which do not have an ether bridge across the 10-membered carbocyclic ring. Only one cembranoid, **25**, was isolated. Diterpenoids **1**, **3**, and **20** show cytotoxicity to murine leukemia cells (P388).

Gorgonians (order Gorgonacea, phylum Cnidaria) and soft corals (Alcyonacea, phylum Cnidaria), have proven to be rich sources of terpenoids.[2] As part of our continuing search for bioactive compounds we have studied the encrusting Indopacific gorgonian *Solenopodium stechei* which was collected at Dalton Reef on the Great Barrier Reef off Australia. Taxonomically, the genus *Solenopodium* is very difficult to distinguish from the Caribbean *Briareum* genus[3] which has yielded a variety of diterpenoids, the majority of which belong to the diterpene skeletal class first observed in briarein-A obtained from *Briareum asbestinum*.[4] In addition to species of the genus *Briareum*, briareins have also been isolated from one species of soft coral (*Minabea* sp.),[5] several sea pens (Pennatulaceae),[6-12] and the sea pansy *Renilla*.[13]

An earlier report on another *Solenopodium* sp. collected in the vicinity of Palau described a group of six briarein-type diterpenes.[14] The present study resulted in the

(1) Taken in part from the Ph.D. Dissertation of S. J. Bloor, University of Oklahoma, 1986.
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Table I. Proton NMR Data for 1–6

H	1	2	3	4	5	6
2	4.82	4.85	4.82	4.85	4.79	4.82
	d 6.6	d 6.7	d 6.6	d 6.4	d 6.6	d 6.6
3	3.10	2.85	3.10	2.85	3.09	2.85
	dd 16; 12.8	dd 13; 12.9	dd 16; 13	dd 15.3; 13.1	dd 15.8; 12.9	dd 15.8; 12.8
3′	1.93	2.00	1.92	2.00	1.93	2.00
	ddd 16; 6.6; 5.3	ddd 13; 5.5; 6.7	ddd 16; 6.6; 5.7	m	ddd 16; 6.6; 5.8	m
4	5.02	5.05	5.02	5.05	5.04	5.07
	dd 12.8; 5.3	dd 12.9; 5.5	dd 13; 12.7	dd 13.1; 5.4	dd 12.9; 5.4	dd 12.8; 5.4
6	5.48	5.50	5.48	5.49	5.48	5.49
	bd 10	bd 10	bd 10	bd 10	bd 10	bd 10
7	5.95	5.80	5.95	5.79	5.95	5.79
	d 10	d 10	d 10	d 10	d 10	d 10
9	4.47	5.75	4.46	5.76	4.47	5.76
	dd 6.5; 3.7	d 3.7	dd 6.5; 3.7	d 3.6	dd 6.7; 3.8	d 3.5
10	2.30	2.41	2.30	2.42	2.30	2.40
	d 3.7	d 3.7	d 3.7	d 3.6	d 3.8	d 3.5
12	3.07	3.03	3.07	3.02	3.08	3.03
	bd 5.4	bd 5.5	bd 5.2	d 5.3	bd 6	d 5
13	2.17	2.11	2.17	2.12		2.07
	ddd 15.8; 5.4; 3	ddd 17; 5.5; 3.6	ddd 15.8; 5.2; 3	ddd 16; 5.3; 3	2.12 (2 H) m	(2 H) m
13′	2.08	2.06	2.08	2.04		
	dd 15.8; 1	dd 17; 2	dd 15.8; 1	dd 16; 2		
14	4.68	4.67	4.69	4.69	4.73	4.72
	bs (dd) (3; 1)	bs	bs	bs	bs	bs
15	1.19 s	1.03 s	1.19 s	1.03 s	1.20 s	1.03 s
16	2.20 bs	2.21 s	2.20 bs	2.22 d 1.4	2.19 d 1.4	2.21 bs
18	1.68 s	1.68 s	1.68 s	1.69 s	1.68 s	1.69 s
20	1.35 s	1.41 s	1.35 s	1.41 s	1.35 s	1.41 s
OH at C-9	2.88 d 6.5		2.86 d 6.5		2.70 d 6.7	
acetate methyls	2.05 s	2.21 s	2.05 s	2.21 s	2.05 s	2.21 s
		2.06 s		2.06 s		2.06 s
		1.99 s		2.00 s		2.03 s
	1.99 s		1.99 s		2.03 s	
					1.99 s	
other esters	2.26 t	2.26 t	2.31 q	2.31 q		2.00 s
	1.64 m	1.13 m	1.11 t	1.11 t		
	0.95 t	0.96 t				

isolation of 25 new diterpenoids, of which 20 have the briarein skeleton, four have the eunicellin skeleton,[15] and one has a regular cembranoid skeleton. The presence of all three of these classes of compounds provides circumstantial support for a biosynthetic pathway in which a cembrene skeleton is the precursor to both the briarein skeleton (via C-3/C-8 cyclization) and the eunicellin skeleton (via C-2/C-11 cyclization).

The briarein-type compounds have been designated stecholides[16] and the eunicellin-type metabolites, solenopodins. The stecholides are distinguished by an α,β-epoxy lactone ring found thus far in only a few other briareins.[17] The eunicellin-type compounds reported here, **21–24** (see Chart I), lack the ether bridge found in the 10-membered ring in nearly all the other metabolites of this class of marine metabolites.[17,18]

Specimens were frozen immediately after collection and subsequently freeze-dried. Conventional extraction procedures were used, and the extracts were fractionated extensively using normal- and reversed-phase adsorbents to give the 25 new diterpenoids, see the Experimental Section. Compounds **2** and **13** were distinctively major diterpene metabolites (~60 mg each) while all others were minor components (1–7 mg each).

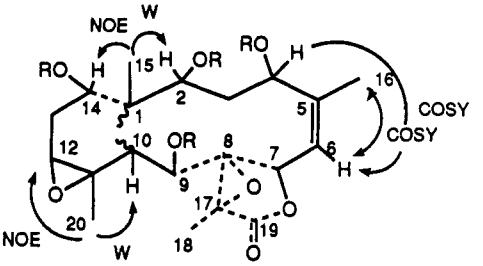

Figure 1. Partial structures confirmed for **2** from ^{1}H NMR decoupling experiments, NOE, and *W* couplings.

A molecular formula of $C_{30}H_{40}O_{12}$ was established for stecholide A acetate, **2**, from HRMS (592.252, calcd 595.256), plus ^{1}H NMR and ^{13}C NMR data (see Tables I and II). The ^{1}H NMR spectrum contained signals for three acetates at 2.21, 2.06, and 1.99 ppm, and three separate signals comprising the two methylenes and the methyl group of a butyrate ester. Subtraction of the 10 carbons associated with the ester groups left 20 carbons, suggestive of a diterpene skeleton (7 unsaturations). The IR spectrum indicated the absence of hydroxyl groups. From extensive ^{1}H decoupling experiments and a ^{1}H–^{1}H COSY experiment it was possible to determine three separate spin systems which map out the proton sequences H-1 to H-7, H-9 to H-10, and H-12 to H-14, see Figure 1 and coupling assignments in Table I. Allylic couplings were detected in the COSY spectrum between H-6 and H-4/H-16, thus confirming the C-4 to C-6 with branching C-16 array. *W* coupling between H-2 and H-15 indicated

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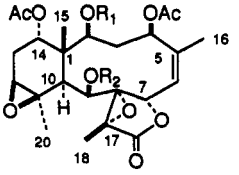
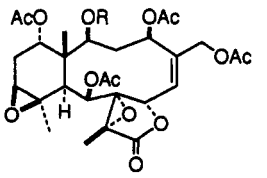
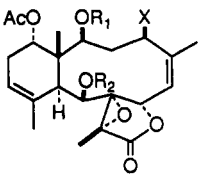
Chart I



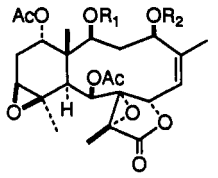
	R_1	R_2	
1	$C(O)C_3H_7$	H	Stecholide A
2	$C(O)C_3H_7$	Ac	Stecholide A Acetate
3	$C(O)C_2H_5$	H	Stecholide B
4	$C(O)C_2H_5$	Ac	Stecholide B Acetate
5	Ac	H	Stecholide C
6	Ac	Ac	Stecholide C Acetate



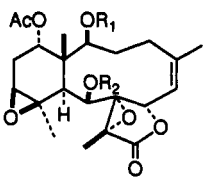
7 R = $C(O)C_3H_7$ 16-Acetoxystecholide A Acetate
8 R = $C(O)C_2H_5$ 16-Acetoxystecholide B Acetate
9 R = Ac 16-Acetoxystecholide C Acetate



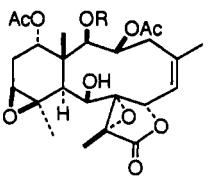
	R_1	R_2	X	
10	$C(O)C_3H_7$	OAc	OAc	(11,12-Deoxystecholide A Acetate)
16	$C(O)C_3H_7$	H	H	(11,12-Deoxystecholide E)



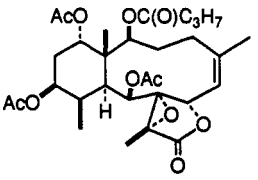
	R_1	R_2	
11	$C(O)C_3H_7$	H	Stecholide D
12	$C(O)C_3H_7$	$C(O)C_3H_7$	



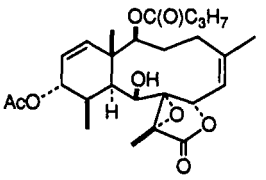
	R_1	R_2	
13	$C(O)C_3H_7$	H	Stecholide E
14	$C(O)C_3H_7$	Ac	Stecholide E Acetate
15	$C(O)C_2H_5$	H	Stecholide F



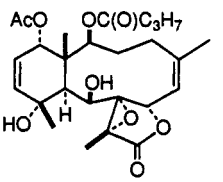
17 R = $C(O)C_3H_7$ 3-Acetoxystecholide E



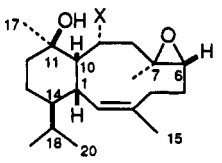
18 11,12-Deoxy-11-H,12-acetoxy-stecholide E Acetate



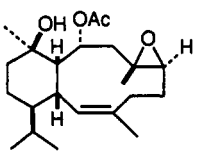
19 Stecholide G



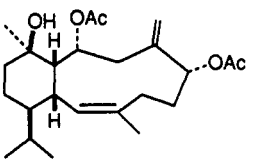
20 Stecholide H



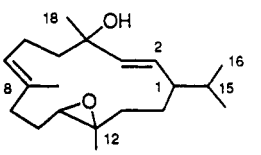
21 X = OAc Solenopodin A
23 X = H Solenopodin C



22 Solenopodin B



24 Solenopodin D



25 (tentative)

the C-15/C-1/C-2 connection.

Although further couplings to link these partial structures were not evident, NOE's observed between Me-20, H-12, and H-9 provided evidence for the spatial proximity of these groups. An NOE observed between H-15 and H-14 supported the connection from C-14 to C-1 to C-15. The proton chemical shifts of Me-15 and Me-20 suggested attachment to a ring junction carbon and an epoxide-bearing carbon, respectively. These combined data were compared with known compounds, especially those previously isolated from gorgonians of the *Briareum* genus. The most favorable comparisons could be made with those having the briarein skeleton, which commonly possesses an α-methyl γ-lactone. A fifth carbonyl signal in the ^{13}C NMR spectrum of **2** suggested the presence of this feature. The remaining methyl absorption in the ^{1}H NMR spectrum is a singlet at 1.68 ppm consistent with a methyl group attached to a quaternary carbon bearing oxygen. Since all of the protons of **2** were accounted for by the above and only one oxygen atom remained, it could be concluded that the lactone ring must contain an α,β-epoxide. This was supported by the ^{13}C NMR spectrum which had nine signals in the 60–80 ppm range, only seven of which were accounted for by the partial structures in Figure 1. The α,β-epoxy lactone feature is relatively rare among the briarein compounds, having been reported previously in only two recent investigations.[17,19] Placement of this lactone so as to link C-7 and C-9 of the structures in Figure 1 and then linking of C-10 to C-14 yielded the structure shown in Figure 1 which possesses the well-known briarein skeleton.

The locus of the butyrate vs the acetate groups was deduced from ^{13}C NMR data. The ^{13}C NMR signal assignments of C-2, -4, and -14 were made from single frequency on-resonance decoupling experiments by irradiating the H-2, -4, and -14 signals individually. Comparison of the ^{13}C NMR data of **2** with that of **4** and **6** which have propionate and acetate esters, respectively, replacing the butyrate moiety established that only C-2 is affected by

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Table II. ^{13}C NMR Data for 1–6

C	1	2[a]	3	4	5	6
1	45.8	45.5 s	45.9	45.6	45.8	45.5
2	72.3	71.9 d[b]	72.3	72.0	72.7	72.3
3	38.3	38.3 t	38.2	38.5	38.2	38.4
4	72.4	72.4 d[b]	72.4	72.4	72.4	72.3
5	145.1	145.3 s	145.2	145.4	143.2	145.3
6	122.4	122.3 d	122.5	122.3	122.5	122.4
7	73.8	73.5 d	73.7	73.5	73.7	73.5
8	70.9	70.3 s	71.0	70.3	70.9	70.3
9	72.6	69.8 d	72.6	69.9	72.6	69.8
10	42.6	42.2 d	42.6	42.2	42.6	42.2
11	62.4	63.5 s	63.6	63.5	63.6	63.5
12	61.4	60.9 d	61.4	60.9	61.4	60.8
13	25.1	24.9 t	25.2	25.0	25.2	25.0
14	73.4	73.6 d[b]	73.5	73.6	73.4	73.5
15	16.1	15.5 q	16.0	15.5	16.1	15.5
16	25.4	25.4 q	25.4	25.4	25.3	25.4
17	62.4	62.4 s	c	62.6	c	62.6
18	9.4	10.0 q	9.4	10.0	9.0	10.0
19	171.6	170.7 s	c	171.0	c	171.0
20	24.5	24.5 q	24.5	24.5	24.5	24.4
acetate methyls	21.1	21.1	21.1	21.1	21.0	21.5
	21.1	21.1	21.1	21.1	21.0	21.1
		21.5		21.5	21.0	21.1; 21.1
other esters	36.1		27.6			
	18.2; 13.7		8.8			
ester carbonyls	173.0	167.4	173.8	167.4	b	170.5
	170.4	170.3	170.1	170.3	b	170.4
	170.2	170.1; 167.4	170.1	170.1; 167.4	b	170.1; 167.4
butyrate		13.7; 18.1; 36.1				
propionate				8.8; 27.6		

[a] Multiplicities by DEPT exp. [b] Assignment confirmed by SFORD. [c] Signal not observed.

these replacements. The observed chemical shift difference (0.4 ppm) is consistent with that observed (0.32 ppm) for the C-2 carbon signal in briantheins Y (butyrate at C-2) versus Z (acetate at C-2),[20] and hence the butyrate moiety in **2** is at C-2.

The relative stereochemistries for most of the substituents on the 10-membered ring were determined by analysis of proton–proton coupling constants and NOE experiments. A *W* coupling between H-15 and H-2 places the H-2 proton on the α-face (relative to an arbitrary assignment of Me-15 as β). An NOE between H-2 and H-10 placed both of these protons on the α-face and established the ring junction as trans. NOE's between H-16 and H-6 confirmed the *Z* nature of the double bond and another NOE between H-16 and H-2 demonstrated that the vinyl moiety is folded downward to place the H-16 and H-2 protons close to each other. Given this constraint it follows that the NOE noted between H-16 and H-4 means that the latter is α-oriented. The large coupling between H-6 and H-7 suggests an antiparallel orientation of these two protons, placing H-7 on the β-face. H-7 in turn exhibits an NOE with the more downfield of the H-3 protons, assigned as H-3β. Consistent with this assignment is the large coupling observed between H-3β and H-4α. The small coupling between H-9 and H-10 suggests these protons are almost orthogonal. The previously mentioned NOE between Me-15 and H-14 places the acetate group at C-14 on the α-side.

The β-configuration is assigned to the epoxide on the six-membered ring since the C-11/C-12 carbon chemical shifts, 61–63 ppm, are virtually identical to those of related 11,12β-epoxybriareins[17] and distinctly different from 11,12α-epoxybriareins such as stylatudide,[7] minabein-10,[5] and briareolide C,[19] i.e., 58–60 ppm. The 8,17-epoxide is assigned the α-configuration because the ^{13}C NMR shifts of these carbons are virtually identical to those of the briareins reported by Bowden et al.[17] and briareolide C,[19] for which the 8,17α-epoxy configuration has been confirmed. Thus the complete structure of stecholide A acetate with all relative stereochemistry is described by formula **2**.

Two minor metabolites exhibiting spectral data very similar to that of **2** were readily identified as **4** and **6**, C-2 propionate and acetate analogues of **2**, since the only differences in their proton NMR spectra were signals associated with the relevant CH_2 groups. The only noticeable ^{13}C NMR chemical shift difference between **2**, **4**, and **6** was at C-2 as mentioned above.

A further series of three compounds, **1**, **3**, and **5**, were determined to be the C-9 alcohol analogues of compounds **2**, **4**, and **6**. The hydroxyl proton in each of the latter compounds appeared in the ^1H NMR spectrum as a sharp doublet, was exchangeable with CD_3OD, and was coupled to H-9 (dd). A fourth alcohol, **11**, was determined to be the C-4 alcohol analogue of compound **2** by virtue of the upfield shift of H-4 relative to that in **2** and the removal of a small coupling to H-4 upon addition of CD_3OD to the sample.

Compounds **7**, **8**, and **9** possessed mass spectral molecular ions which were 58 amu's larger than those of **2**, **4**, and **6**, respectively. This difference is consistent with replacement of a hydrogen in **2**, **4**, or **6** with an acetoxy group. The ^1H NMR spectra of **7**, **8**, and **9** each showed two new signals which corresponded to a pair of methylene protons deshielded by oxygen. These protons were coupled to the vinyl proton, H-6. The absence of the vinyl methyl signal, coupled with the appearance of an extra acetate signal, established that these compounds were 16-acetoxy versions of **2**, **4**, and **6** since the remainder of the spectra of all these metabolites were nearly identical.

A second trisubstituted double bond was apparent in the ^{13}C NMR spectrum of **10**, and no absorptions were

(20) van der Helm, D.; Loghry, R. A.; Matson, J. A.; Weinheimer, A. J. *J. Crystallograph. Spectrosc. Res.* **1986**, *16*, 713; Grode, S. H.; James, T. R.; Cardellina, J. H. III; Onan, K. D. *J. Org. Chem.* **1983**, *48*, 5203.

Table III. Proton NMR Data for 7–12

H	7	8	9	10	11	12
2	4.90 d 6.4	4.91 d 6.4	4.87 d 6.3	4.95 d 6.5	4.78 d 6.4	4.85 d 6.5
3	2.88	2.88	2.88	2.94	2.79	2.85
	dd 15; 13	dd 15; 13	dd 15; 12.6	dd 15; 12.5	dd 15; 12	dd 14; 13
	2.0 m	2.0 m	2.0 m	2.0 m	2.00 m	2.00 m
4	5.01	5.00	5.02	5.08	4.25	5.06
	dd 13; 5.1	dd 13; 5.2	dd 12.6; 5.1	dd 12.5; 5.1	dd 12; 5.3	dd 12.3; 5
6	5.47 bd 10	5.45 bd 10	5.46 bd 10	5.49 bd 9.8	5.51 bd 9.6	5.49 bd 9.6
7	5.81 d 10	5.81 d 10	5.81 d 10	5.80 d 9.8	6.10 d 9.6	5.79 d 9.6
9	5.75 d 3.8	5.74 d 3.7	5.75 d 3.7	5.72 d 3.3	5.74 d 3.6	5.76 d 3.6
10	2.43 d 3.8	2.43 d 3.7	2.23 d 3.7	2.79 bs	2.42 d 3.6	2.42 d 3.6
12	3.03 d 5.8	3.04 d 5.8	3.04 d 5.8	5.42 bd 6.6	3.02 d 5.4	3.02 d 6
13	2.21	2.10	2.0	2.05	2.0	2.12
	m	ddd 15.6; 5.3; 3	(2 H) m	(2 H) m	m	ddd 16; 5.3; 3
	2.0	2.03				2.04
	m	dd 15.6; 2				dd 16; 2
14	4.75 bs	4.75 bdd 3; 2	4.80 bs	4.71 bs	4.69 bs	4.68 bs [dd] [4; 2][a]
15	1.03 s	1.03 s	1.04 s	1.01 s	1.04 s	1.06 s
16	5.35	5.35	5.34	2.21 bs	2.14 bs	2.22 d 2
	dd 16.3; 2.1	dd 16.4; 2	dd 16.4; 2			
	4.77	4.78	4.76			
	dd 16.3; 2.1	dd 16.4; 2	dd 16.4; 2			
18	1.69 s	1.69 s	1.69 s	1.62 s	1.68 s	1.69 s
20	1.40 s	1.39 s	1.40 s	1.85 bs	1.41 s	1.41 s
acetate methyls	2.21 s	2.21 s	2.22 s	2.21 s	2.19 s	2.20 s
	2.13 s	2.13 s	2.13 s	2.06 s	1.99 s	2.00 s
	2.06 s	2.05 s	2.06 s	1.85 s		
	2.02 s		2.03 s			
			2.02 s			
other esters	2.27 t	2.32 q				
	1.60 m	1.10 t				
	0.95 t					
butyrate				2.28 t	2.26 t	2.28, 2.27 t
				1.64 m	1.63 m	1.64, 1.62 m
				0.96 t	0.95 t	0.92, 0.91 t

[a] Bracketed data obtained from decoupling experiments.

evident for an 11,12-epoxide as in **2**. In the ^1H NMR spectrum of **10**, the H-12 proton signal was shifted from 3.03 ppm to 5.42 ppm (relative to **2**) and was coupled to the methyl signal at 1.7 ppm; the latter is thus assigned to Me-20. The H-10 resonance was broadened due to allylic coupling with H-12 (confirmed by decoupling). Since the remainder of the NMR spectra of **10** could be matched with that of **2**, **10** was deduced to be 11,12-deoxystecholide A acetate.

Compound **12** was identified as a bis-butyrate based on mass and NMR data. The second butyrate was assigned to the C-4 position since butyrylation of **11** yielded a product identical by TLC and ^1H NMR with **12**.

Analysis of the spectral data for **13** established a molecular formula of $C_{26}H_{36}O_9$. The ^1H NMR spectrum indicated the presence of a butyrate ester, an acetate ester, and one proton exchangeable with CD_3OD. Although a molecular ion was not observed in the LRMS, ions corresponding to sequential losses of butyric acid and acetic acid from the molecular ion were evident. The characteristic signals of the α,β-epoxy γ-lactone found in the other stecholides were present in the ^{13}C NMR spectrum. The ^1H NMR spectrum of **13** was quite similar to that of **1**. The signals due to H-13, -13′, and -14 were almost identical to those of **1**, suggesting that these two compounds possess the same type of substituted six-membered ring. The similarity extended to the H-9 and H-10 signals, although the H-9 resonance was somewhat broader, as was that of the hydroxyl proton to which it was coupled. However, decoupling established that **13** has a methylene group at C-4 rather than an oxygenated methine as in **1**. A small allylic coupling was observed between H-6 and one of the protons at C-4. Thus stecholide E, **13**, is 4-deacetoxystecholide A. NOE experiments confirmed the stereochemical similarity of **13** to stecholide A acetate (**2**). Several minor metabolites closely related to **13** were readily determined by spectral comparisons to be **14** (the C-9 acetate of **13**), **15** (the C-2 propionate version of **13**), and **16** (the 11, 12-deoxy analogue of **13**).

Another minor component, **17**, was determined to have the same molecular formula as stecholide A (**1**). The ^1H NMR spectrum of **17** differed considerably from that of **1**, but these differences were limited to the signals from protons at C-2, -3, and -4. Both methylene protons at C-4 (identified by the coupling of one of these to the vinyl proton at C-6) were coupled to a proton at 5.72 ppm, which must be H-3. Another signal, a singlet at 4.93 ppm, was assigned to the remaining C-2 position. An orthogonal arrangement of the H-2 and H-3 protons would account for the absence of coupling. An NOE between H-10 and H-2 indicates the configuration at the ring junction is identical to that of **2**. Therefore the ester group at C-3 must be trans to the C-2 ester in order that H-2 and H-3 be orthogonal. The butyrate is assigned to the C-2 position by analogy with all the related metabolites. Thus structure **17** is proposed for 3-acetoxystecholide E.

The remaining briarein metabolites, **18**, **19**, and **20**, have different substitution patterns in the six-membered ring than do **1**–**17**. The ^1H NMR spectrum of the first of these, **18** ($C_{30}H_{42}O_{11}$), contained signals for three acetates and one butyrate. No hydroxyl absorption was observed in the IR spectrum. A series of ^1H NMR decoupling experiments established that the C-2 to C-7 section of **18** was identical to the same section in **14**. However, decoupling showed that there is a hydrogen at C-11 and that C-12 is still oxygenated (ascribed to OAc). The coupling constants between H-10, -11, and -12 are typical of axial/equatorial coupling constants for six-membered rings. Assuming H-10 is axial, then H-11 must be equatorial. The large coupling (10.5 Hz) between H-12 and one of the H-13 protons must

Table IV. ^{13}C NMR Data for 7–12

C	7	8	9	10	11	12
1	45.4	45.5	45.4	45.2	45.5	45.5
2	71.9	72.0	72.3	71.8	71.1	71.9
3	38.7	38.6	38.6	38.4	41.1	38.7
4	70.0	70.1	70.0	72.6	73.8	72.2
5	142.5	142.6	142.6	145.2	147.8	145.4
6	120.9	120.8	120.9	122.3	122.0	122.3
7	73.1	73.0	73.0	73.4	72.9	73.5
8	70.4	70.4	70.4	70.3	70.4	70.3
9	68.9	68.9	68.9	68.3	69.9	69.9
10	42.0	42.0	42.1	43.5	42.2	42.2
11	63.3	63.3	63.3	133.4	63.5	63.5
12	61.2	61.2	61.2	120.8	60.8	60.9
13	24.3	24.3	24.2	26.0[a]	25.5	25.0
14	73.4	73.4	73.3	73.8	73.3	73.6
15	15.7	15.7	15.7	15.1	15.0	15.5
16	65.5	65.5	65.5	25.4[a]	25.0	25.0
17	62.6	62.6	62.6	63.3	62.6	62.6
18	10.1	10.0	10.0	9.6	10.0	10.0
19	170.8	170.8	170.8	170.8	171.1	*b*
20	25.1	25.1	25.2	24.7[a]	24.5	24.5
ester carbonyls	169.9	169.8	169.8	172.9	173.0	173.9
	167.3	167.3	167.3	169.9	170.3	170.6
	170.0	170.0	169.9	168.7	167.5	*b*
	173.2	174.0; 170.9	171.0; 170.7			*b*
acetate methyls	20.9	20.9	20.9	21.6	21.5	21.5
	20.9; 21.6	21.0; 21.5	20.9; 21.5	21.3		21.1
		20.7	20.7; 20.9	21.1		
butyrates	13.7			36.1	36.2	36.1, 36.1
	18.0			18.1	18.1	18.4, 18.1
	36.1			13.7	13.7	13.7, 13.4
propionate		8.7; 27.5				

[a] Interchangeable assignments. [b] Signals not observed.

Table V. Proton NMR Data for 13–18

H	13	14	15	16	17	18
2	4.88 d 6.5	4.91 d 6.3	4.89 d 6.2	5.00 d 5.6	4.93 s	5.11 d 7.8
3	2.74 ddd	2.53 m (ddd)[a]	2.74	2.84 m (bdd)	5.72	2.60
	15.5; 14.5; 5.3	(15.8, 16.5, 5.3)[a]	ddd 18; 12; 6.2	(18; 13; 5)[a]	dd 12.6; 5.5	ddd 16.5; 15.3; 5
	1.7 m (dddd)	1.70 m	1.6 m	1.60 m (bdd)		1.68 m
	(15.5, 6.5, 4.3, 2)[a]			(18; 5.6; 4.5)[a]		
4	2.51 bddd 15.0	2.54	2.53	2.47	2.88 ddd	2.47 bd 15 (5)[a]
	(5.3, 2)[a]	m (bd)[a] (16)[a]	vbd 13.5	bdd 15; 5	13.4; 5.5; 0.5	1.94 m (ddd)
				2.0 m (ddd)	2.01 dd	(15.3; 15; 4.5)[a]
	1.95 ddd	2.0 m	1.98 ddd	(15; 13; 5)[a]	12.6; 13.4	
	15; 14.5; 4.3		13.5; 12; 4.5			
6	5.37 bd 9.8		5.38 bd 10	5.38 bd 9.8	5.48 bd 10	5.25 bd 8.8
7	5.52 d 9.8	5.38 s (2 H)	5.51 d 10	5.55 d 9.8	5.87 d 10	5.17 d 8.8
9	4.42 bd 3.5	5.7 d 3.4	4.44 dd 6.2; 3.5	4.32 bs (4.4)	4.45 dd 6.1; 4	4.97 bs
10	2.33 d 3.5	2.45 d 3.4	2.34 d 3.5	2.77 bs (4.4)	2.39 d 4	2.52 dd 5; 1.9
11						2.19 m
12	3.06 d 5.4	3.01 d 5.9	3.06 d 5.4	5.38 bs	3.06 t 3	5.09 m (dt)
						(10.5; 5.5)[a]
13	2.16	2.12	2.07	2.32 bd (ddd)	2.12 (2 H) t 3	1.88 (2 H) dd
	ddd 15.5; 5.4; 3	m	(2 H) m	18 (3; 2)[a]		10.5; 3.1
	2.06	2.04		2.0 m		
	dd 15.5; 2.1	m				
14	4.65	4.65	4.68	4.74	4.76 bt 3	4.78 t 3.1
	bs (dd) (3.2, 1)[a]	bs	bs	bs (dd) (3; 2)[a]		
15	1.15 s	1.00 s	1.16 s	1.23 s	1.14 s	1.20 s
16	2.04 bs	2.06 bs	2.05 bs	2.03 s	2.07 bs	2.02 bs
18	1.66 s	1.68 s	1.68 s	1.62 s	1.67 s	1.63 s
20	1.36 s	1.42 s	1.37 s	1.72 s	1.36 s	1.03 d 7
C-9 OH	3.00 bd		2.64 d 6.2		2.53 d 6.1	
acetate methyls	1.99 s	2.17 s	2.00 s	1.95 s	2.05 s	2.21 s
					1.99 s	2.04 s; 2.01 s
butyrate	0.94 t; 0.58 m	0.95 t; 1.62 m		2.28 t; 1.64 m	2.36 t; 1.68 m	2.21 t; 1.63 m
	2.25 t	2.26 t		0.92 t	0.99 t	0.96 t
propionate			2.28 t; 1.11 q			

[a] Data in parentheses obtained from decoupling experiments.

be an axial–axial coupling; therefore, H-12 must be axial. The chemical shifts and coupling constants for the remainder of the molecule were very similar to those of **13–15**, indicating that the relative stereochemistry of **18** is the same as in those compounds. The butyrate group in **18** has been assigned to C-2 by analogy with **1** and other stecholides.

Compound **19** ($C_{26}H_{36}O_8$) had an IR spectrum with ab-

Table VI. ^{13}C NMR Data for 13–18

C	13[a]	14	15	16	17	18
1	45.5 s	45.2	45.5	45.1	45.7	45.8
2	75.0 d	74.5	75.0	74.9[b]	72.8[b]	74.6[b]
3	32.7 t	32.8	32.6	29.4	71.0[b]	28.6
4	29.0 t	28.8	28.9	26.4	35.0	27.3
5	146.3 s	146.4	146.3	146.1	140.6	145.0
6	118.2 d	118.1	118.2	118.4	120.9	118.3
7	74.4 d	74.4	74.3	74.6[b]	74.2[b]	74.7[b]
8	71.2 s	70.6	71.1	71.5	71.1	69.0
9	72.5 d	70.5	72.7	70.8[b]	72.5[b]	70.8
10	42.4 d	42.1	42.4	44.2	42.5	41.2
11	63.3 s	63.5	63.8	134.0	64.0	29.7
12	62.5 d	60.8	61.4	120.3	61.3	75.5
13	27.4 t	27.4	27.4	26.9	25.0	31.8
14	73.4 d	73.8	73.9	71.5[b]	73.7[b]	73.7
15	15.9 q	15.4	15.9	16.6	16.3	15.5
16	25.2 q	25.0	25.2	24.6	26.6	25.2
17	62.5 s	62.6	62.5	62.3	63.3	56.7
18	9.5 q	9.5	9.4	9.4	9.4	9.0
19	170.6 s	170.5	170.6	171.1	170.4	170.6
20	24.5 q	24.4	24.4	26.9	24.5	11.1
ester carbonyls	171.8 s	171.0		172.1	173.2	177.5
	173.1 s	173.1	173.9	173.1	170.3	170.4
		167.5			163.2	
acetate methyls	21.2 q	21.2	21.1	21.3	21.1	21.3
		21.5			21.1	
butyrate	13.6 q	13.7		36.4	36.1	36.2
	18.2 t	18.2		18.3	18.3	18.4
	36.3 t	36.3		13.7	13.7	13.6
propionate			8.9; 27.4			

[a] Multiplicities determined by DEPT. [b] Signals with the same letter in a column are interchangeable.

sorptions consistent with the presence of OH, ester and lactone groups (3500, 1785, and 1730 cm^{-1}, respectively). Structural segments corresponding to C-1 (C-15) to C-4, C-6 (C-16) to C-7, and C-9 to C-14 of the briarein skeleton were traced out by interpretation of decoupling, H–H COSY, and NOE data. COSY cross-peaks between the signal ascribed to H-6 and a vinyl methyl group signal (Me-16) were also consistent with this skeleton. COSY cross-peaks between H-10 and H-15 confirmed the usual ring junction. It is interesting that H-10/H-15 coupling was not observed for the other stecholides, although it is not uncommon to observe this coupling in such a trans-fused ring array. An NOE was detected between H-15 and H-14, thus providing support for the C-14 to C-1 connection. The general structure of **19** could be completed by joining C-4 to C-5 and adding C-8 along with the remainder of the α,β-epoxy lactone moiety. By analogy with the other stecholides, the butyrate moiety was assigned to the C-2 position.

W couplings were observed between Me-15 and the H-10 and H-2 signals, confirming that the latter methine protons must be trans and antiparallel to Me-15. Unlike many of the other stecholides, an NOE between H-2 and H-10 was not observed for **19**. An NOE between Me-15, Me-20, and H-12 places these three groups on the β-face. Therefore, the ester substituent at C-12 is α-oriented. In the other stecholides the coupling constant between H-9 and H-10 is small, indicating these two protons are almost orthogonal. The large 13.5-Hz coupling observed between H-9 and H-10 in the spectrum of **19** indicates a significant change in the dihedral angle between these two protons relative to the other stecholides. NOE enhancement of both Me-20 and Me-18 is observed when H-9 is irradiated. This, combined with the magnitude of the coupling between H-9 and H-10, suggests that the hydroxyl group lies inside the 10-membered ring and is also in the plane of the ring, forcing the H-9 proton above the ring and thus increasing the dihedral angle between H-9 and H-10 to approximately 180°. The NOE observed between H-9 and Me-18 is not observed for the other stecholides. An examination of Dreiding molecular models suggests that Me-18 needs to be β in order to observe this effect and still retain a configuration which is consistent with the observed NMR data for the rest of the molecule.

A molecular formula of $C_{26}H_{36}O_9$ was determined for the final briarein compound, **20**, based upon the ^{13}C and ^{1}H NMR data. The presence of two hydroxyl groups was deduced from the IR spectrum and the number of oxygenated carbons. The largest ion observed in the mass spectrum was m/z 362, consistent with loss of butyric acid plus ketene from the proposed molecular formula. As for **19** the substitution pattern for the 10-membered ring was determined to be the same as that of **13**. The ^{13}C NMR spectrum of **19** indicated the presence of two double bonds, one of which could be accounted for as the C-5 double bond. The second double bond was disubstituted and had chemical shifts similar to the first one. This second double bond must then be part of the six-membered ring. The ^{1}H NMR spectrum had signals consistent with a cis double bond flanked at one end by the proton (4.91 ppm) of a CH-O-acyl group and at the other end by a blocked position. The proton at 4.91 ppm showed no further coupling, but an NOE was observed between this proton and the ring junction methyl (Me-15). Hence the CH-OAc group was assigned to the C-14 position. Also, the ^{13}C NMR chemical shift of C-1 is the same as for other compounds of this series which have similar substitution patterns on the adjacent carbons. A small upfield shift would be expected if the double bond were adjacent to C-1 (cf. **19**). The blocked position at C-11 is accounted for by a methylcarbinol group. The butyrate moiety is assigned to the C-2 position by analogy with all the other compounds in this series.

NOE's were detected between H-14, Me-20, and Me-15 of **20** which indicated that these protons are all on the same (β) face of the molecule. Also an NOE was observed betweeen H-9 and Me-20 just as was noted for many of the other stecholides. No NOE was observed between

Table VII. Proton NMR Data for 19–24

H	19	20	21	22	23	24
1			2.81	3.16	2.73	2.78
			ddd 6.6; 5.9; 5.1	ddd 10.3; 5; 3.4	ddd 7.5; 6; 6	ddd 6.5; 5; 5
2	4.85 d (8.9)[a]	4.82 d 9.7	5.30 bd 6.6	5.74 d 10.3	5.34 bd 7.5	5.15 bd 6.5
3	2.32 m	2.33 m				
	1.60	1.66				
	dd 15.3; 6.7; 3	dd 15.8; 9				
4	1.91	2.44	2.52	2.67	2.47	2.57
	dd 15.6; 3	dd 14.6; 9	dt 13; 13.2; 1	ddd 13; 13; 6	ddd 13.4; 13; 2.2	t 13.5
	2.55	4.6; 11	2.05	1.86	1.9	1.9
	ddd 15.6; 6.7; 2.2		m	dd (13; 5)[a]	m	m
5			2.23	2.29 dddd	2.1	2.15
			m	13; 13; 5; 4.8	m	m
			1.5 m	1.33 m	1.3 m	1.5 m
6	5.31	5.41	3.23	3.47	3.10	5.33
	bd 8.2	(2 H) s	dd 11; 4	dd 10.2; 4.8	dd 11.2; 3.5	dd 11; 4
7	5.64 d 8.2	5.41 (2 H) s				
8			2.38	2.12	2.3	2.67
			dd 14.3; 4	dd 16.1; 4.3	m	dd 15; 4
			1.15	1.96		2.46
			dd 14.3; 2.8	dd 16.1; 3.3		dd 15; 4
9	3.72	4.13	5.20	5.59	1.2–1.7	5.11
	dd 13.5; 3.7	dd 10.7; 6.4	ddd 5; 4; 2.8	bt (4.3; 3.3)[a]	m	q 4
10	3.20	2.96	2.65	2.01	1.95	2.35
	dd 13.5; 3.7	d 6.4	dd 5; 5.1	d 5	(ddd 6; 6; 6)[a]	dd (5; 4)[a]
11	2.31 m					
12	4.91 dd 5.9; 1.7	5.49 d 10.1				
13	5.85	5.81				
	dd 10; 5.9	dd 10.1; 5.5				
14	5.52 d 10	4.90 d 5.5	1.2 m	1.03 m	1.0 m	1.05 m
15	1.22 s	1.24 s	1.71 s	1.81 s	1.71 s	1.64 bs
16	1.82 s	1.85 bs	1.20 s	1.27 s[b]	1.22 s[b]	5.32 s; 4.89 s
17			1.24 s	1.49 s[b]	1.18 s[b]	1.34 s
18	1.59 s	1.67 s	2.0 m	1.82 m	1.90 m	1.9 m
19			0.70 d 6.9	0.88 d 7.5	0.78 d 7	0.89 d 7
20	0.97 d 7.3	1.46 s	0.90 d 6.9	1.06 d 7.5	0.98 d 7	0.72 d 7
acetate methyls	2.07 s	2.07 s				
			2.08 s	1.97 s		2.01 s; 2.05 s
butyrate	2.44 t; 1.74 m	2.52 t; 1.76 m				
	1.00 t	1.03 t				

[a] Data in parentheses obtained from decoupling experiments. [b] Interchangeable within column.

H-10 and H-2. However, the similarities in coupling constants between these protons and their vicinal neighbors indicated that H-10 and H-2 have the same stereochemistry in **20** as observed in **19** and the other stecholides.

In addition to the above briareins, another group of five diterpenoids with distinctively different spectral features were isolated. Four of these, solenopodins A–D, exhibited spectral data indicating they had identical carbon skeletons, see Tables VII and VIII. The overall structure of all of these were deduced by NMR analyses, but all of the relative stereochemistries could not be resolved unambiguously. Fortunately, solenopodin D crystallized and an X-ray analysis provided the structure **24** with relative stereochemistry. Confirmation of this structure provided additional support for the remaining structures deduced from spectral analyses. Solenopodins A–D, **21–24**, thus belong to the eunicellin class of diterpenes.[15,18]

Solenopodin A, **21**, $C_{22}H_{36}O_4$ based on LRMS, NMR, and IR data, showed NMR signals for one acetate group, one double bond (132.3, 131.4 ppm), an epoxide (65.5 d, 59.1 s), and two other carbons attached to oxygen (71.4 d, 72.4 s). This data accounted for three of the five degrees of unsaturation inherent in the molecular formula and hence a bicyclic skeleton was inferred for **21**. Partial structures shown in Figure 2 were deduced from decoupling and H–H COSY data combined with chemical-shift information. The 10-membered ring could be closed as shown because a small coupling was detected in the H–H COSY spectrum between H-2 and one of the H-4 protons, between the C-3 vinyl methyl protons and the other H-4

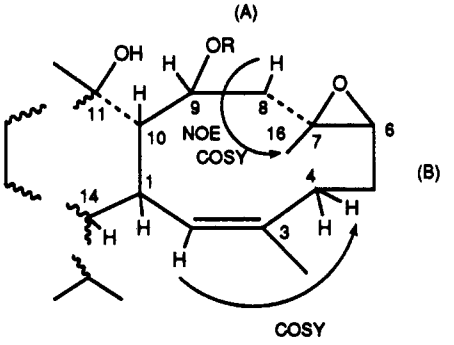

Figure 2. Partial structures confirmed for **21** from ^1H NMR decoupling experiments and NOE results.

proton, and between the epoxide methyl group (H-16) and one of the H-8 protons. Also, irradiation of the epoxide methyl signal (1.24 ppm) caused an 8% NOE on H-8.

H-10 was coupled only to H-9 and H-1, and hence the fourth bond to C-10 must be to the remaining quaternary carbon whose chemical shift, 72.4 s, requires that it bears an oxygen. This quaternary carbon must also bear the second quaternary methyl group, which has a rather low field proton shift, 1.20 ppm.

The ring junction proton, H-1, shows coupling to only one proton at position 14; hence this position must be branched, i.e. bears the isopropyl group. The remaining two methylene groups whose proton signals overlap in the 1.2–1.6 ppm region can only be added to complete a six-membered ring to give the overall structure **21**, which has

Table VIII. ^{13}C NMR Data for 19–24

C	19	20[b]	21[a]	22[a]	23[b]	24
1	43.2	45.8 s	42.3 d	48.1 d	44.8 d	42.8
2	82.0	72.9 d	132.3 d	130.9 d	130.4 d	130.9
3	23.1	24.1 t	131.4 s	128.9 s	134.3 s	130.8
4	24.4	24.9 t	33.4 t	38.6 t	35.2 t	35.4
5	142.1	144.0 s	25.4 t	24.5 t	25.3 t	30.1
6	121.0	121.0 d	65.5 d	59.3 d	65.9 d	73.2
7	73.7	73.4 d	59.1 s	58.1 s	61.1 s	118.0
8	70.7	71.5 s	44.3 t	43.1 t	38.6 t	40.6
9	68.3	68.4 d	71.4 d	70.4 d	22.2 t	72.5
10	36.3	40.9 d	50.1 d	49.0 d	47.3 d	50.6
11	32.6	72.6 s	72.4 s	72.4 s	73.2 s	73.2
12	70.3	141.3 d	28.0 t	26.4 t	28.1 t	28.6
13	123.4	120.4 s	18.5 t	20.9 t	20.0 t	19.1
14	140.4	81.8 d	35.1 d	37.2 d	36.6 d	35.4
15	19.1	22.4 q	24.7 d or q	23.1 d or q	24.9 q	22.8
16	23.9	25.1 q	21.8 q[c]	23.4 d or q[c]	18.2 q	143.5
17	58.7	61.5 s	27.3 d or q	27.0 d or q	26.8 q	27.4
18	9.4	9.7 q	28.9 d or q	26.7 d or q	26.6 d	28.7
19	170.8	170.9 s	21.7 q	21.5 d or q	22.0 q	21.3
20	13.6	27.0 q	14.8 q[c]	19.5 q[c]	17.7 q	19.1
acetate carbonyls			169.8	169.6		170.0
						170.3
acetate methyls	22.3	21.3	21.0	21.7		21.6
						21.7
butyrate	36.1	36.4				
	18.3	18.3				
	13.5	13.7				
ester carbonyls	172.7	173.1				
	169.0	172.1				

[a] Multiplicities by APT. [b] Multiplicities by DEPT. [c] Interchangeable within a column with entry having same superscript.

the same skeleton as does **24**.

An NOE was observed between the vinyl methyl group and the vinylic proton, confirming that this double bond has the *Z* configuration. A large NOE was also observed between the epoxy methine proton, H-6, and H-10; hence these protons are both shown as being β-oriented. However, no NOE was noted between the epoxide proton and the epoxide methyl, H-16, thus indicating that these groups are trans oriented as shown in **21**. A cis ring juncture is proposed for **21** since the coupling constant between the ring juncture protons (H-1, H-10) is the same as in compounds **22–24** and the cis configuration is confirmed by X-ray in **24** and by NOE effects in **22**. The configurations at C-9, C-11, and C-14 are also assigned by analogy to those found for **24**. All these assignments are in accordance with those in eunicellin and related diterpenes.[18]

A molecular formula of $C_{22}H_{36}O_4$ was also deduced for diterpene **22**, solenopodin B, on the basis of its LRMS (M^+ 364) and ^{13}C and ^1H NMR spectral data, see Tables VII and VIII and the IR spectrum (OH absorption at 3450 cm^{-1}). The ^1H NMR spectrum of **22** had many features in common with that of **21**, and indeed decoupling experiments confirmed the same partial structures as determined for **21**, see Figure 2, although the chemical shifts of the respective protons differed somewhat. The linkages between C-3 and C-4, and C-7 and C-8, were assumed by analogy to **21** and **24**, but no allylic coupling was detected between H-2 and H-4, and no NOE was observed between the epoxide methyl (H-16) and either of the H-8 protons. The H-10 signal was coupled only to H-1 (4.9 Hz) and H-9 (<1 Hz), and hence C-11 must be a quaternary center and is assigned the methylcarbinol structure as in **21** and **24**. Connecting the remainder of the 6-membered ring and the isopropyl branch by analogy with **24** yields structure **22**, but without stereochemical specification. Hence **21** and **22** appear to be stereoisomers. A small NOE was observed between the ring junction protons which argues for a cis ring junction in **22**. The *Z* configuration for the double bond was also confirmed by an NOE between H-2 and the vinyl methyl signal. However, no NOE was observed between H-6 and H-10 in contrast to the case for **21**. Nor was any NOE detected between H-6 and the epoxide methyl group, suggesting that these groups are trans oriented. Hence it seems most likely that **22** differs from **21** by having the inverted stereochemistry at the epoxide centers and the same stereochemistry elsewhere.

Low-resolution mass spectral data (M^+ 306) plus ^{13}C NMR and IR data [3600 (sharp), 3450 (br d) for OH] confirmed the formula $C_{20}H_{34}O_2$ for solenopodin C, **23**. The ^1H NMR spectrum of **23** was similar to those of **21** and **22**, the most obvious difference between **23** and **21** being the loss (in **23**) of the acetate methyl signal and the downfield multiplet corresponding to H-9 in **21**. The structure **23** is predicated on (a) decoupling experiments which confirmed the connectivity from H-1 through H-6, H-1 to H-10, H-1 to H-14 and (b) analogy with **21**, **22**, and **24**. The cis ring junction is predicted since the H-1/H-10 coupling is the same as for **21**, **22**, and **24**. An NOE was observed between the epoxide proton, H-6, and the ring junction proton, H-10, just as was observed for **21**, and hence these compounds appear to have the same epoxide stereochemistry as shown. This is also suggested by the similar upfield shift of the carbon resonance of the epoxide methyl group in these two compounds.

A small amount (1.6 mg) of diterpene **25** of molecular formula $C_{20}H_{34}O_2$ (M^+, ^{13}C and ^1H NMR, and IR data) was isolated. The compound contained a hydroxyl group but no carbonyl functionality (IR), and ^{13}C NMR data revealed the presence of two double bonds and one epoxide moiety. The double bonds are not conjugated since the UV showed only end absorption. These groups accounted for three of the four degrees of unsaturation implied by the molecular formula, and hence **25** must be monocarbocyclic. Proton NMR data revealed the presence of an isopropyl group (two doublet methyl signals coupled to the same proton signal at 1.5 ppm) and the four partial structures shown in Figure 3. Combination of this data suggested the substituted cembrane structure **25** or an alternative

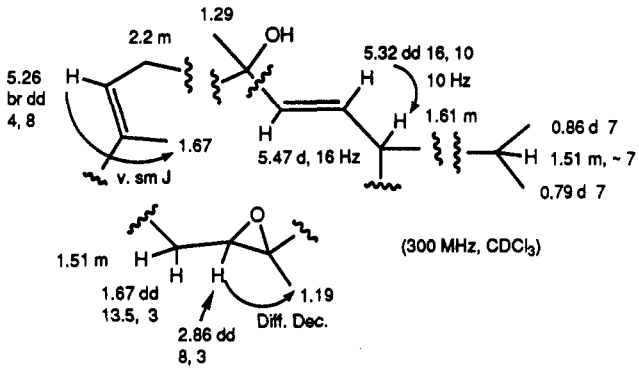

Figure 3. Partial structures deduced for **25** from ^{1}H NMR data.

cembrane with the epoxide in the 7,8-position. Structure **25**, without stereochemical specification, is the same as that of trocheliopherol which was isolated from a soft coral.[21] While the ^{13}C NMR data for **25** and trocheliopherol are very similar, there are some small, but distinct, differences in the ^{1}H NMR spectra measured in C_6D_6, confirming that the two compounds are similar, but not identical. Furthermore, their optical rotations are quite different: +55° for trocheliopherol and −28° for **25**. Unfortunately, inadequate sample was available to establish all details of the structure of this epoxy alcohol, but the evidence for a cembranoid structure such as **25** is quite strong. Since it has been noted that cembranoids isolated from a number of soft corals have opposite absolute configurations at C-1 from those obtained from gorgonians, the difference between **25** and trocheliopherol may be due to such a difference. The important finding for purposes of this study is that a cembranoid metabolite co-occurs with many briarein and eunicellin-type diterpenes. This is consistent with a biosynthetic path wherein a cembrene intermediate serves as a precursor to the briarein and eunicellin skeletons.

The absolute configuration of several briarein-type diterpenes, briarein A,[4] brianthein X,[21] and briareolide B,[20] have been determined and all are the same. Hence we speculate that the absolute configuration of all the stecholides described here have the same absolute configuration as the above three compounds which is that denoted by the stereoformulas **1–20**.

Compounds **1**, **3**, and **20** showed modest levels of cytotoxicity to murine leukemia cells (P388), ED_{50}'s of 4.5, 5.4 and 10 μg/mL.

X-ray Analysis of Solenopodin D (24). Crystal data: Solenopodin D, $C_{24}H_{38}O_5$, M_r = 406.6, orthorhombic, $P2_12_12$, a = 17.613 (4) Å, b = 28.435 (9) Å, c = 9.436 (3) Å, V = 4725.8 Å^3, Z = 8, D_x = 1.443 mg m^{-1}, $F(000)$ = 1776, μ(Cu Kα) = 5.5 cm^{-1}. The refinement converged to a final R = 0.044, R_ω = 0.044 for 4169 observed reflections ($I \geq 2\sigma(I)$), S = 1.3, D/σ = 0.08, electron density in the final difference map ±0.3 e/Å^3.

There are two independent molecules (molecules A and B) in the asymmetric unit which form a dimeric pair in the crystal. A stereoview of the dimer is shown in Figure 4. The dimeric pair is held together by two O–H···O hydrogen bonds which have the following geometries: (i) O(5)B–H···O(2)A = 2.958 (3) Å, H···O(2)A = 2.10 (4) Å and angle O–H···O of 170 (4)° and (ii) O(5)A–H···O(5)B = 2.791 (3) Å, H···O(5)B = 1.92(4)Å and angle O–H···O of 174(3)°.

The absolute configuration of solenopodin was not determined but was assigned on the basis of the configuration of sclerophytin C whose absolute configuration was determined by X-ray diffraction.[18d] The two independent molecules have the same structure but they have different hydrogen bonding patterns. Their geometrical features are almost identical; the mean difference in the endocyclic torsion angle between the two molecules is 2.2° with a maximum of 5.9° for C(2)–C(1)–C(10)–C(9). Generally, the bond distances and angles are comparable to those observed in other related structures, except for the bond angles, C(2)–C(1)–C(10) [117.0°] and C(1)–C(10)–C(9) [112.3°] which are much larger (104.5° and 101.9°, respectively, in sclerophytin C). The six-membered ring is in a chair conformation with mean |τ| of 54.4°. The absence of transannular bridging and the presence of a cis double bond [C(2)–C(3)] led to a more folded conformation for the 10-membered ring compared to those observed in eunicellin dibromide,[22] acetoxycladiellin,[23] and sclerophytin C.[18d] The root-mean-square deviation of the individual atoms from the least-squares plane through the 14 ring atoms is 0.70 Å (0.68 Å for molecule B). The corresponding deviation in slcerophytin C is 0.50 Å. The folded geometry of the 10-membered ring resulted in a very short H(C6)···H(C10) contact, 1.97 Å in molecule A and 2.10 Å in molecule B.

Experimental Section

^{1}H and ^{13}C NMR spectral data, obtained in $CDCl_3$ at 300 MHz for ^{1}H and 75 MHz for ^{13}C, for compounds **1–24** are presented in Tables I–VIII. J values are reported in hertz and chemical shifts in δ units. Assignments were aided by spin-decoupling and 2D COSY experiments. IR spectra were obtained on thin films prepared by evaporation of $CHCl_3$ solutions on NaCl plates. Mass spectra are reported as m/z (relative intensity); all low-resolution spectra were obtained at 12 eV. All optical rotations were obtained at ambient temperature, ~23 °C in $CHCl_3$.

Extraction and Partition Procedure. A detailed outline of the extraction and fractionation process is given in Schemes I–III, supplementary material. The gorgonian *S. stechei* was collected from the Dalton Reef area of the Australian Great Barrier Reef in July 1983, frozen immediately, and freeze-dried within 2 months to give 345 g of dry animal tissue. A portion of the material (150 g) was soaked in $CHCl_3$–MeOH (2:1) at rt three times: 6, 12, and 30 h. The latter two extracts were combined and partitioned following the Kupchan procedure:[24] (a) 10% aqueous MeOH (400 mL) vs hexane (2 × 400 mL), yield 240 mg; (b) 20% aqueous MeOH vs CCl_4 (2 × 300 mL), yield 225 mg; (c) 30% aqueous MeOH vs $CHCl_3$ (2 × 300 mL), yield 164 mg. The CCl_4 solubles were chromatographed over silica gel [open column, acetone–hexane (1:10)], and a selected fraction was purified further by HPLC [SiO_2 using acetone–hexane (15:85) and then C_{18} using MeOH–H_2O (7:3)] to give **2** (5 mg) and **13** (3 mg).

The remainder of the dried specimen (~190 g) was extracted with pentane at rt (2 h; 24 h; combined yield 2.16 g), CCl_4 (8 and 24 h, combined yield 750 mg), and $CHCl_3$ (24 h, 500 mg). The pentane and CCl_4 solubles plus the $CHCl_3$ solubles from the Kupchan partition above were chromatographed extensively using open silica gel columns and HPLC [silica gel and reversed-phase (C_{18})] to give compounds **1–25** as detailed in Scheme III (supplementary material). The principle solvent combinations used with normal phase adsorbents were hexane-acetone (~9:1 → 2:1 for vacuum flash chromatography; various mixtures in the range of 92:8 to ~4:1 for isocratic HPLC); MeOH–H_2O combinations for C_{18} reversed-phase HPLC (85:15 to 65:35). Percent yields are not calculated since not all of the extracts were exhaustively processed.

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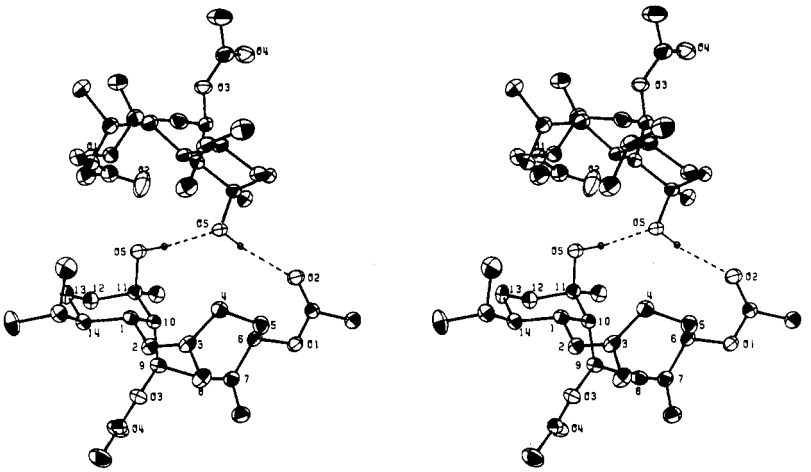

Figure 4. A stereo view of the dimeric pair (molecule A, lower, and molecule B, upper) of solenopodin D. Hydrogen atoms (except hydroxyl hydrogens) are omitted for clarity. Hydrogen bonds are indicated by dashed lines. Ring atom designation is indicated by a numeral.

Stecholide A (1): 2.3 mg, mp 113–115 °C; white solid from evaporation of acetone/hexane solution; $[\alpha]_D$ = +54.8° (*c* 0.23); IR 3450, 1780, 1740 cm^{-1}; MS 550 (M^+, 7), 490 (3), 464 (11), 463 (47), 420 (57), 124 (100); HR FAB MS *m/z* 573.2331 [calcd for $C_{28}H_{38}O_{11}Na$ (M + Na^+), 573.2312, 491.2331 [calcd for $C_{26}H_{35}O_9$ (M – OAc)$^+$, 491.2281].

Stecholide A acetate (2): 68 mg; mp 179–182 °C (from Et_2O); $[\alpha]_D$ = +45.1° (*c* 0.63); IR 1770, 1730, 1220 cm^{-1}; MS 592 (M^+, 27), 533 (16), 505 (53), 504 (20), 462 (60); HRMS (70 eV) *m/z* 592.2561 (calcd for $C_{30}H_{40}O_{12}$, 592.2520), 504.2030 (calcd for $C_{24}H_{32}O_{10}$, 504.1996).

Stecholide C (3): 1 mg; mp 123–127 °C (from C_6H_6 with hexane diffusion); $[\alpha]_D$ = +89.0° (*c* 0.09); IR 3420 (br), 1780, 1740 cm^{-1}; MS 536 (M^+, 6), 463 (20), 420 (21), 360 (15), 342 (16), 124 (100).

Stecholide B acetate (4): 2.8 mg; mp 247–249 °C (white powder from evaporation of acetone/hexane solution); $[\alpha]_D$ = +43.6° (*c* 0.28); IR 1785, 1740 cm^{-1}; MS 578 (M^+, 2), 519 (2), 462 (6), 384 (10), 320 (18), 149 (100); HRMS 578.2382 (calcd for $C_{29}H_{38}O_{12}$ 578.2363).

Stecholide C (5): 0.9 mg; mp 90–95 °C (powder from acetone/hexane); IR 3450, 1790, 1740 cm^{-1}; MS 463 (M^+ – CH_3COO, 24), 420 (29), 419 (27), 342 (18), 106 (100).

Stecholide C acetate (6): 4.8 mg; mp 251–253 °C (white solid from evaporation of acetone/hexane solution); $[\alpha]_D$ = +43.5° (*c* 0.48); IR 1780, 1740 cm^{-1}; MS 564 (M^+, 13), 505 (29), 504 (12), 462 (31), 461 (41), 110 (100).

16-Acetoxystecholide A acetate (7): 1.6 mg; mp 90–95 °C (from Et_2O); $[\alpha]_D$ = +50.6 (*c* 0.16); IR 1790, 1740 cm^{-1}; MS 650 (M^+, 3), 607 (2), 591 (4), 530 (24), 519 (24), 460 (49), 400 (100).

16-Acetoxystecholide B acetate (8): 7.0 mg, mp 229–231 °C (white powder from evaporation of acetone/hexane solution); $[\alpha]_D$ = +52.7° (*c* 0.70); IR 1780, 1740 cm^{-1}; MS 636 (M^+, 5), 593 (2), 577 (2), 519 (25), 516 (27), 460 (36), 400 (72), 82 (100).

16-Acetoxystecholide C acetate (9): 1.0 mg; mp 277–279 °C (from Et_2O); $[\alpha]_D$ = +36.0° (*c* 0.18); IR 1790, 1740 cm^{-1}; MS 622 (M^+, 4), 563 (6), 520 (11), 519 (12), 460 (33), 400 (53), 82 (100).

11,12-Deoxystecholide A acetate (10): 1.0 mg; IR 1790, 1730 cm^{-1}; MS (special tune for *m/z* 400–600) 576 (2), 517 (2), 488 (2), 429 (9), 428 (32).

Stecholide D (11): 3.6 mg; mp 85–88 °C (white solid from evaporation of acetone/hexane solution); $[\alpha]_D$ = +11.7° (*c* 0.36); IR 3450 (br), 1790, 1740 cm^{-1}; MS 462 (M^+ – $C_4H_8O_2$, 13), 444 (9), 419 (37), 402 (28), 360 (35), 106 (100).

Butyrylation of Stecholide D (11). Approximately 1 mg of stecholide D (11) was dissolved in Et_2O containing a trace of pyridine. A small amount of butyryl chloride was added, and the mixture was stirred rapidly at rt for 3 h. The product was separated from the reaction mixture by preparative TLC (eluted with 20:80 acetone–hexane). This product was shown to be identical with stecholide D butyrate (12) by TLC and ^{1}H NMR spectroscopy.

Stecholide D butyrate (12): 0.7 mg; IR 1780, 1750, 1730 cm^{-1}; MS 620 (M^+, 24), 561 (14), 533 (97), 461 (100), 384 (42).

Stecholide E (13): 60 mg; mp 96–100 °C (white powder from evaporation of acetone/hexane solution); $[\alpha]_D$ = +10.0° (*c* 0.36); IR 3420 (br), 1780 cm^{-1}; MS 404 (M^+ – C_3H_7COOH, 6), 362 (22), 344 (13), 329 (6), 273 (17), 255 (21), 124 (100).

Stecholide E acetate (14): 3.5 mg; mp 123–125 °C (from Et_2O); $[\alpha]_D$ = –2.8° (*c* 0.35); IR 1790, 1735 cm^{-1}; MS 446 (M^+ – C_3H_7COOH, 6), 403 (9), 386 (7), 344 (10), 256 (63), 82 (100).

Stecholide F (15): 2.7 mg; mp 100–103 °C (white powder from evaporation of acetone/hexane solution); $[\alpha]_D$ = +7.8° (*c* 0.27); IR 3450 (br), 1790, 1740 cm^{-1}; MS (special tune for *m/z* 350–500) 478 (M^+, 1), 463 (1), 435 (1), 418 (5), 404 (16), 376 (10).

11,12-Deoxystecholide E (16): 1.8 mg; mp 71–74 °C (from C_6H_6 with hexane diffusion); $[\alpha]_D$ = +8.3° (*c* 0.18); IR 3410 (br), 1780 cm^{-1}; MS 388 (M^+ – $C_4H_8O_2$, 3), 328 (7), 313 (4), 295 (3), 195 (21), 119 (100).

3-Acetoxystecholide E (17): 3 mg; mp 110–112 °C (from C_6H_6 with hexane diffusion); IR 1780, 1730 cm^{-1}; MS 490 (M^+ – HOAc, 4), 420 (100), 360 (9), 342 (7), 183 (13).

11,12-Deoxy-11*H*-12-acetoxystecholide E acetate (18): 2.1 mg; $[\alpha]_D$ = +14.3° (*c* 0.21); IR 1785, 1740 cm^{-1}; MS 518 (M^+ – HOAc, 6), 490 (M^+ – $C_3H_7CO_2H$, 35), 430 (20), 388 (25), 370 (65), 240 (100).

Stecholide G (19): 2.7 mg; mp 58–60 °C (powder from acetone/hexane); $[\alpha]_D$ = –16.7° (*c* 0.27); IR 3500 (br), 1786, 1730 cm^{-1}; MS 416 (M^+ – HOAc, 4), 346 (14), 328 (42), 301 (27), 221 (60), 108 (100); FD MS (15 mA) *m/z* 476 [M^+], 416, 405, 389.

Stecholide H (20): 3.2 mg; mp 84–88 °C (white powder); $[\alpha]_D$ = –57.2° (*c* 0.32); IR 3500 (br), 1780, 1740 cm^{-1}; MS 362 [M^+ – ($C_4H_8O_2$ + C_2H_2O), 1], 344 (2), 329 (1), 301 (1).

Solenopodin A (21): 1.9 mg; oil; $[\alpha]_D$ = –75.3° (*c* 0.19); IR 3480, 1740 cm^{-1}; MS 364 (M^+, 2), 346 (60), 331 (22), 303 (61), 271 (21), 243 (100); HREIMS *m/z* 364.2664 (calcd for $C_{22}H_{36}O_4$ 364.2614).

Solenopodin B (22): 1.3 mg; oil; IR 3450 (br), 1745 cm^{-1}; MS 364 (M^+, 1), 346 (70), 331 (13), 303 (32), 271 (44), 243 (100); HREIMS *m/z* 346.2457 [calcd for $C_{20}H_{34}O_3$ (M – H_2O)$^+$, 346.2508].

Solenopodin C (23): 3.6 mg; oil; $[\alpha]_D$ = +105.6° (*c* 0.36); IR 3600 (sharp), 3450 (br) cm^{-1}; MS 306 (M^+, 2), 291 (1), 288 (16), 260 (13), 245 (100).

Solenopodin D (24): 1.5 mg (from C_6H_6 with hexane diffusion); $[\alpha]_D$ = +29.3° (*c* 0.15); IR 3500 (br), 1735, 1720 cm^{-1}; MS 406 (M^+, 2), 346 (5), 328 (6), 304 (12), 286 (51), 159 (100).

Compound 25: 1.6 mg; oil; $[\alpha]_D$ = –28° (*c* 0.16); IR 3450, 985 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$), see Figure 3; ^{13}C NMR ($CDCl_3$) 15.8 (C-19), 16.1 (C-20), 19.4 (C-17), 20.7 (C-16), 23.7 (C-6), 25.1 (C-10), 28.7 (C-14), 29.6 (C-18), 32.7 (C-15), 35.3 (C-13), 36.3 (C-9), 43.7 (C-5), 47.1 (C-1), 59.8 (C-12), 61.6 (C-11), 73.9 (C-4), 127.5 (C-7), 129.6 (C-2), 131.9 (C-8), 138.9 (C-3); MS 306 (M^+, 1), 291 (1), 288 (12), 273 (10), 263 (13), 245 (39).

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Supplementary Material Available: ^1H NMR and ^{13}C NMR spectra of 1-25; X-ray experimental description, non-hydrogen atomic parameters, anisotropic thermal parameters, hydrogen atom parameters, bond distances, bond angles, and endocyclic torsion angles; and Schemes I-III describing details of fractionation of compounds 1-25 (61 pages). Ordering information is given on any current masthead page.

A Short Synthesis of (±)-β-Isocomene

Nikolaos D. Willmore,[1] Richard Goodman,[2] Hyun-Ho Lee, and Robert M. Kennedy*

Department of Chemistry, Columbia University, New York, New York 10027

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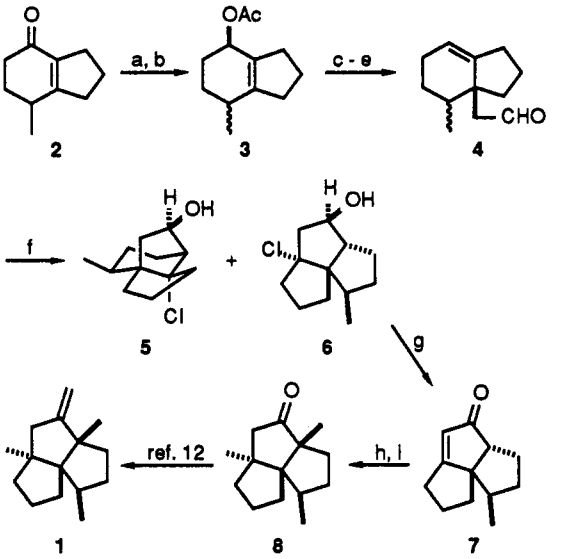
A strategy in which a Prins reaction is followed by a ring contraction has been used to synthesize (±)-β-isocomene efficiently.

Large numbers of triquinane natural products have been isolated, and efforts directed toward their synthesis have greatly expanded methodology for the construction and manipulation of cyclopentanes.[3] We report here a contribution to this field in which an intramolecular Prins reaction[4] followed by a ring contraction is applied to the synthesis of (±)-β-isocomene (1).[5]

The known[6] enone **2**, prepared[7] from cyclopentanone was reduced to give an inseparable 1:1.9 mixture of cis and trans alcohols in 95% yield.[8] Acetylation, Ireland ester enolate Claisen rearrangement,[9] and reduction afforded a 1:2 mixture of primary alcohols in 85% yield. Swern oxidation[10] gave an 84% yield of aldehydes **4** as an inseparable 1:2 mixture of diastereomers.

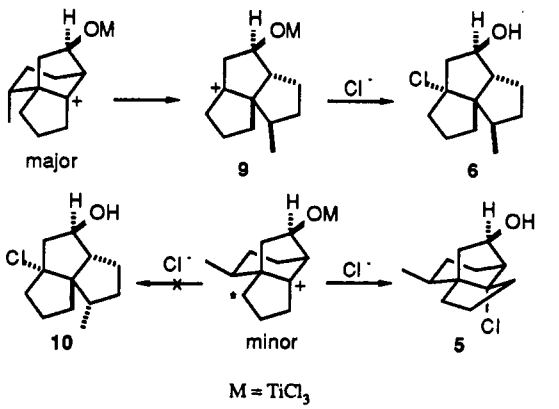
In the key step,[11] 1 equiv of a 1 M solution of $TiCl_4$ in CH_2Cl_2 was added to a 0.1 M solution of aldehydes **4** in

Scheme I[a]



[a] Key: (a) LAH, Et_2O, -78 °C; (b) Ac_2O, py; (c) LDA, TBDMSCl, THF, HMPA, -78 °C → reflux; (d) LAH, Et_2O, 0 °C; (e) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -41 °C; (f) $TiCl_4$, CH_2Cl_2, -78 °C; (g) PCC, CH_2Cl_2; DBU, THF; (h) LDA, MeI, -78 °C → RT; (i) Me_2CuLi, Et_2O, 0 °C.

Scheme II



CH_2Cl_2 at -78 °C. Reaction was immediate and complete, giving a clear, slightly yellow solution, which after being warmed to 0 °C and quenched with water afforded a 1:2.3

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(2) NSF Research Experiences for Undergraduates in Chemistry Program participant, Summer 1990.
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(8) Other reducing agents (i.e., sodium borohydride and L-Selectride (Aldrich)) were employed with similarly disappointing results.
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