Acknowledgment. We thank C. Arneson and K. Jordan for assistance in collecting sponges and nudibranchs, Dr. Klaus Rützler for identifying the sponges, Mary Kay Harper for performing antimicrobial assays, and Virginia Scott and Dr. Thomas Matthews, Syntex Corporation, for antifungal and toxicity data. This research was supported by grants from the National Science Foundation (Grants CHE86-03091 and CHE84-14054) and the National Institutes of Health (Grant AI-11969).

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Cacospongionolide: A New Antitumoral Sesterterpene, from the Marine Sponge *Cacospongia mollior*

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A sesterterpene with a new carbon skeleton, cacospongionolide (**4a**), has been isolated from the marine sponge *Cacospongia mollior*. The structure of cacospongionolide was elucidated by spectral data, using 2D-NMR spectroscopy, and by chemical transformations. Cacospongionolide is a potent antitumor agent.

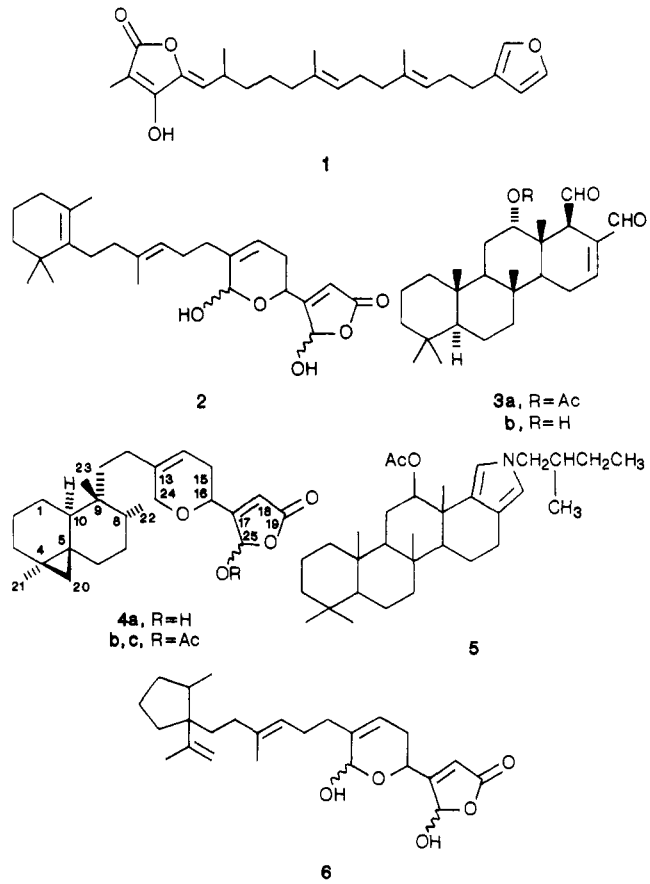
Marine organisms and in particular sponges have provided a large number of sesterterpenoids, several of which have shown a wide variety of biological activities. Some containing a tetronic acid moiety showed strong antibiotic activity against *Staphylococcus aureus*, e.g., variabilin[1] (**1**); others which were γ-hydroxybutenolides such as manoalide[2] (**2**) had analgesic and antiinflammatory properties[3]; still others were dialdehydes such as scalaradial[4] (**3a**), and its desacetyl derivative[5] **3b** had cytotoxic and/or antifeedant activity.[5]

In the course of our search for marine natural compounds that have biological activities, we have studied the marine sponge *Cacospongia mollior* (Schmidt), collected in the northern Adriatic, whose extract showed high cytotoxic activity (LD_{50} = 10 μg/mL) in the brine shrimp assay.[6] By fractionating the extract, we isolated a new sesterterpene (**4a**), named cacospongionolide, which is responsible for the biological activity.

The structure determination and some biological activities of this substance are reported in this paper.

From the same sponge, collected in the Tyrrhenian Sea, other authors have reported the isolation of sesterterpenoids with the scalarane skeleton, such as scalaradial[4] (**3a**) and the molliorins,[7] e.g., molliorin A (**5**).

Cacospongionolide, which did not give crystals suitable for X-ray analysis, had $[\alpha]_D$ 27° ($CHCl_3$, *c* 1.4) and the molecular formula $C_{25}H_{36}O_4$ from high-resolution mass measurement of the parent ion. The ultraviolet absorption at 222 nm (ε 4000) and infrared bands at 3330, 1780, and 1760 cm^{-1} were characteristic of a γ-hydroxybutenolide moiety. Its 500-MHz ^1H NMR spectrum was highly solvent dependent, and interpretation of the signals emanating from the polar moiety was difficult. In C_6D_6 solution, due to the presence of the lactol function, two sets of signals for H-16, H-18, and H-25 signals were observed, while in $CDCl_3$, a single set of broad signals was obtained. The same was true for the ^{13}C NMR spectrum. The NMR



(1) Faulkner, D. J. *Tetrahedron Lett.* **1985**, *26*, 3821.
(2) De Silva, E. D.; Scheuer, P. J. *Tetrahedron Lett.* **1980**, *21*, 1611.
(3) Jacobs, R. S.; Culver, P.; Langdon, R.; O'Brien, T.; White, S. *Tetrahedron* **1985**, *41*, 981.
(4) Cimino, G.; De Stefano, S.; Minale, L. *Experientia* **1974**, *30*, 846.
(5) Yasuda, F.; Tada, H. *Experientia* **1981**, *37*, 110.
(6) Meyer, B. N.; Ferrigni, N. R.; Putnam, J. E.; Jacobsen, L. B.; Nichols, D. E.; McLaughlin, J. L. *Planta Med.* **1982**, *45*, 31.
(7) Cafieri, F.; De Napoli, L.; Iengo, A.; Santacroce, C. *Experientia* **1979**, *35*, 157.

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Table I. NMR Spectral Data of 4a in $CDCl_3$ Solution[a]

C	^{13}C	^1H	^1H–^{13}C long-range correlation	
			J = 14 Hz	J = 8 Hz[b]
1	19.84 (t)[c]	1.38 (m), 0.68 (ddd) (15.5, 12.5, 2.8)		
2	23.2 (t)	1.45 (m), 1.12 (m)	1.54 (H-10)	
3	32.12 (t)	1.52 (m)	1.45 (H-2), 0.99 (H-21), 0.47 (H-20)	
4	17.29 (s)	–	1.45 (H-2), 1.12 (H-2), 0.99 (H-21), 0.47 (H-20), 0.08 (H-20)	
5	26.34 (s)	–	1.54 (H-10), 1.28 (H-6), 0.95 (H-7), 0.47 (H-20), 0.08 (H-20)	1.75 (H-7), 0.99 (H-21)
6	27.92 (t)	1.85 (m), 1.28 (m)	0.08 (H-20)	
7	27.68 (t)	1.75 (m), 0.95 (m)		
8	35.51 (d)	1.57 (m)	0.91 (H-22)	
9	39.04 (s)	–	1.54 (H-10), 0.92 (H-23)	1.38 (H-1), 1.17 (H-11), 0.95 (H-7)
10	41.01 (d)	1.54 (m)	0.92 (H-23), 0.47 (H-20), 0.08 (H-20)	0.68 (H-1)
11	36.82 (t)	1.37 (m), 1.17 (m)	0.92 (H-23)	1.80 (H-12)
12	26.06 (t)	1.80 (m)	5.51 (H-14)	
13	138.28 (s)	–		
14	115.8 (d)	5.51 (br s)	4.14 (H-24)	
15	29.1 (br t)	2.20 (br m)		
16	69.5 (br d)	4.40 (br)		
17	168.1 (br s)	–		
18	117.8 (br d)	6.15 (br)		
19	171.21 (s)	–		6.15 (H-18)
20	24.53 (t)	0.47 (d) (4.4), 0.08 (d) (4.4)	1.54 (H-10), 0.99 (H-21)	
21	22.37 (q)	0.99 (s)	0.08 (H-20)	1.52 (H-3), 0.47 (H-20)
22	14.18 (q)	0.91 (d) (7.1)		
23	19.84 (q)	0.92 (s)		
24	68.37 (t)	4.14 (br s)		5.51 (H-14), 1.80 (H-12)
25	98.0 (br d)	6.22 (br)		

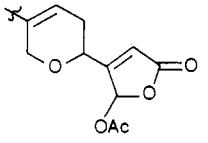
[a] Chemical shifts are referred to tetramethylsilane. Multiplicities are indicated by usual symbols. Coupling constants (hertz) are in parentheses. [b] Only correlations not observed in the experiment with J = 14 Hz are reported. [c] By DEPT sequence.

spectra of manoalide (**2**) and luffariellin A (**6**), which contain a similar polar moiety, exhibited the same phenomena.[8]

Treatment of cacospongionolide with acetic anhydride in pyridine, at room temperature, gave a mixture of two diastereoisomeric acetates (**4b**,**4c**), which were separated by silica gel chromatography.

The ^1H NMR spectrum of both acetates showed a single set of sharp signals disclosing the structure of the polar moiety of cacospongionolide, the relative stereochemistry at C-25 remaining undetermined.

The ^1H NMR spectrum of the major acetate (**4b**) shows (COSY) long-range-coupled broad singlets at δ 6.94 and 6.16, assigned to H-25 and H-18 respectively, confirming the γ-acetoxybutenolide, β-substituted moiety. Signals at δ 166.3 (s), 159.5 (s), 118.1 (d), and 92.4 (d) in the ^{13}C NMR spectrum afforded an additional proof for the proposed moiety. Moreover, the ^1H NMR spectrum shows a two-proton broad singlet at δ 4.18 (H-24), long-range coupled with an olefinic proton at δ 5.53 (H-14), which, in turn, is coupled with a nonequivalent methylene at δ 2.24 (m) and 2.12 (m) (H-15). These latter are coupled with a proton at δ 4.33 (H-16), long-range coupled with the two broad singlets of the γ-acetoxybutenolide moiety (H-18 and H-25). The two signals at δ 4.33 and 4.18 show correlations (HETCOR) with carbons at δ 69.6 (d) and 68.4 (t) leading us to propose the presence in the molecule of partial structure A.



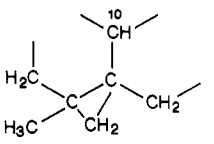
A

Similar results were obtained from the spectral investigation of the minor acetyl derivative **4c**, which exhibited small differences in the chemical shift values of some signals (see Experimental Section), due to the difference in stereochemistry at C-25.

Since the remaining signals in the ^1H NMR and ^{13}C NMR spectra of **4b**,**c** were identical with those of cacospongionolide itself, we used the NMR data of this latter to determine the structure of the remainder of the molecule.

The ^1H NMR spectrum of cacospongionolide, apart from the signals due to the partial structure A, shows three methyl signals at δ 0.91 (d, J = 7.1 Hz), 0.92 (s), and 0.99 (s) and two doublets at δ 0.08 and 0.47 which were assigned to the nonequivalent protons of the cyclopropyl methylene.

The fact that the COSY-45 spectrum shows that these latter signals do not show further coupling suggested that the cyclopropyl ring was tetrasubstituted. The ^1H–^{13}C correlation shows that the two protons at high field are part of a methylene group (δ 24.53). The long-range heteronuclear correlation, showing correlations among the protons on the cyclopropyl ring and carbon atoms at δ 41.01 (d), 32.12 (t), 27.92 (t), 26.34 (s), 22.37 (q), and 17.29 (s), allowed the identification of the quaternary carbon atoms of the cyclopropyl ring and of four carbon atoms around the cyclopropyl ring; furthermore, by observing the correlation among methyl's proton at δ 0.99 and the surrounding carbon atoms (Table I), it is possible to infer partial structure B.



B

Since it was not possible to establish by long-range HETCOR and by COSY the groups linked to the partial

(8) Kernan, M. R.; Faulkner, D. J.; Jacobs, R. S. *J. Org. Chem.* **1987**, *52*, 3081.

Table II. Magnetization Exchange by Cross Relaxation (NOE) for 4a in $CDCl_3$, as Obtained from NOESY[a]

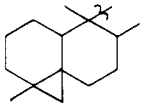
cross-peak coordinates below the diagonal δ_x–δ_x	protons correlated
0.08–0.99	H_α-20, Me-4
0.47–0.68	H_β-20, H_β-1
0.47–0.92	H_β-20, Me-9
0.68–0.92	H_β-1, Me-9
0.91–1.85	Me-8, H_α-6

[a] ^1H NOESY spectrum is recorded at 500 MHz, with the mixing time τ_m = 1 s ± 180 ms (randomly modulated). Only the cross peaks not sensitive to strong filtering were reported.

structure B, we used RELAY experiments, which showed that the methine carbon at δ 41.01 (C-10) was correlated with its proton (δ 1.54) and with the nonequivalent methylene protons on C-1 (δ 1.38 and 0.68). Moreover, the methylene carbon at δ 32.12 (C-3) had correlations with its protons (δ 1.52) and with one proton (δ 1.12) of a nonequivalent methylene (C-2, 23.2 ppm). This latter carbon was correlated with both its protons (δ 1.12 and 1.45) and with protons (δ 1.52) of the adjacent methylene (C-3).

Continuing the analysis of COSY-45, it was possible to establish that the methylene protons at δ 1.85 and 1.28 (C-6) were coupled with another nonequivalent methylene at δ 1.75 and 0.95 (C-7), which in turn was coupled with a proton at δ 1.57 (H-8).

The long-range heteronuclear correlations suggested that attached to the C-10 methine in the partial structure B is a quaternary carbon atom that is also bonded to a methyl at δ 0.92 and to the methine at δ 1.57 (H-8). These data taken altogether are in accordance with partial structure C.



C

Taking into account the molecular formula and the two partial structures A and C, two methylenes remain to be assigned. That the two methylenes connnect partial structures A and C was inferred from the following evidence. The vinyl methylene at δ 1.80 (C-12) was allylically coupled with the C-14 proton and with the nonequivalent (C-11) methylene protons at δ 1.37 and 1.17. In the long-range HETCOR spectrum, the C-11 carbon (δ 36.82) was formed coupled with the C-23 methyl protons, while the C-12 carbon (δ 26.06) was coupled to the H-14 at δ 5.51. These considerations lead to structure **4a**, without stereochemical implications.

The relative stereochemistry of the rigid part of the molecule was deduced by a NOESY spectrum and by NOEDS measurements. The NOESY spectrum exhibited the presence of NOEs (Table II) indicating that the methyl at C-9, the methylene of the cyclopropyl ring, and the proton at δ 0.68 (H-1) are oriented on the same side (β), while the Me-8 and one of the C-6 protons (δ 1.85) are oriented on the opposite side. The presence of NOE between Me-8 and the H-10 proton, observed by NOEDS, establishes that also H-10 has an α orientation. The stereochemistry at C-16 was deduced from the magnitude of the coupling constants of the H-16 in the ^1H NMR spectrum of **4b**. Since it exhibits coupling constants of 10.3, 4.3, and 1.5 Hz (the last attributable to the long-range coupling with H-18 and/or H-25), only an axial position of H-16 is in accordance with the Karplus dihedral angles relationship.

The proposed structure is unique among sesterterpenes and fits very well with the biogenetic rule, the C-10 methyl having migrated to C-9.

Cacospongionolide shows high cytotoxicity (LD_{50} = 0.1 μg/mL) in the brine shrimp assay and very high inhibition (75%) in the crown-gall potato disc assay.[9-11] Further, cacospongionolide when subjected to the fish toxicity bioassay[12] proved to be very toxic at 10 ppm and toxic at 1 ppm, using the toxicity ranking reported by Coll et al.[12]

Experimental Section

General Procedures. ^1H and ^{13}C NMR spectra were recorded at 500 and 125 MHz respectively, with TMS as internal standard on a Bruker WM 500 instrument, under Aspect 2000 control. 2D-NMR spectra were obtained by using Bruker's microprograms. COSY-45 spectra were obtained by coaddition of 16 scans at each of 256 t_1 values. A 512 × 1024 data matrix had been Fourier transformed with sine-bell filters in both domains, using DISN86 software. The digital resolution was 6.5 Hz/point in both domains. The 2D heteronuclear correlations were obtained by coaddition of 128 or 256 scans at each of 256 t_1 values, with J_{CH} = 140 Hz for polarization transfer to obtain direct C–H correlation and J_{CH} = 14 or 8 Hz for polarization transfer to obtain long-range C–H correlations. A 512 × 1024 data matrix had been Fourier transformed with Lorenz–Gauss (LB1 = −2.5, GB1 = 0.15; LB2 = −5.0, GB2 = 0.25) filters in both domains. The digital resolution was 7.4 Hz/point and 40.2 Hz/point in F1 and F2 domain, respectively. RELAY spectra were obtained by coaddition of 416 scans at each of 128 t_1 values; J_{HH} = 9 and 4 Hz were chosen for magnetization transfer. A 512 × 1024 data matrix had been Fourier transformed as for the 2D heteronuclear correlations. IR spectra were recorded on a Perkin-Elmer Model 257 Infracord. UV spectra were obtained on a Varian DMS 90 spectrophotometer. Optical rotations were measured on a Perkin-Elmer Model 141 polarimeter, using a 10-cm microcell. Low-resolution and high-resolution mass spectra were recorded on an AEI MS-50 spectrometer. Melting points were measured on a Kofler apparatus and are uncorrected. Bioassay techniques were performed as in ref 6, 11, and 12.

Extraction and Isolation of Compound. The songe *C. mollior* (Schmidt), collected by dredging (−25 m) at Rovinj (Yugoslavia), was frozen at −20 °C until extracted and was identified by Dr. G. Bavestrello, Istituto di Zoologia dell'Università di Genova. The frozen sponge (50 g, dry weight after extraction) was extracted with acetone, and after elimination of the solvent in vacuo, the aqueous residue was extracted with diethyl ether and then with 1-butanol. The extracts were submitted to the brine shrimp assay.[6] The active ethereal extract was evaporated in vacuo to obtain a brown oil (1.73 g), which was applied on a column (5 × 100 cm) of silica gel. The column was eluted with a solvent gradient system from petroleum ether, 40–70 °C, to diethyl ether. Fractions of 40 mL were collected. Fractions with the same TLC profile were combined. From fractions 90 to 105, after crystallization from MeOH, was recovered **4a** (350 mg, 0.7% dry wt).

Casospongionolide (4a): mp 163–165 °C; $[\alpha]_D$ +27° ($CHCl_3$, *c* 1.4); UV λ_{max} (MeOH) 222 nm (ε 4000); IR ($CHCl_3$) 3330 (br), 1780, 1760 cm^{-1}; NMR data, Table I; MS, *m/z* (relative intensity) 400.2637 [M^+; $C_{25}H_{36}O_4$ requires 400.2635] (12), 382 [$M - H_2O]^+$ (6), 208 (19), 205 (11), 195 (19), 192 (72), 191 (96), 190 (30), 189 (100), 177 (15).

Acetylation of Cacospongionolide (4a). A solution of cacospongionolide (**4a**, 50 mg) in pyridine (3 mL) and acetic anhydride (0.3 mL) was kept at room temperature over night. The excess reagents were removed in vacuo, and the residue was partitioned between water and diethyl ether. The ether extracts

(9) Galsky, A. G.; Kozimor, R.; Piotrowski, D.; Powell, R. G. *JNCI, J. Natl. Cancer Inst.* **1981**, *67*, 689.
(10) Ferrigni, N. R.; Putnam, J. E.; Anderson, B.; Jacobsen, L. B.; Nichols, D. E.; Moore, D. S.; McLaughlin, J. L.; Powell, R. G.; Smith C. R., Jr. *J. Nat. Prod.* **1982**, *45*, 679.
(11) Ferrigni, N. R.; McLaughlin, J. L.; Powell, R. G.; Smith, C. R., Jr. *J. Nat. Prod.* **1984**, *47*, 347.
(12) Coll, J. C.; La Barre, S.; Sammarco, P. W.; Williams, W. T.; Bakers, G. J. *Mar. Ecol.: Prog. Ser.* **1982**, *8*, 271.

were dried over anhydrous sodium sulfate, and the solvent was evaporated to obtain a mixture of acetates **4b** and **4c** (48 mg), which was separated by silica gel column, petroleum ether/diethyl ether (4:1) as eluent, to obtain acetate **4b** (29 mg, 60% yield) and acetate **4c** (18 mg, 37% yield).

Acetate 4b: mp 141–144 °C (from MeOH); $[\alpha]_D \pm 0°$ ($CHCl_3$, *c* 0.35); UV λ_{max} (MeOH) 204 (ϵ 7300); IR ($CHCl_3$) 1780, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.11 (d, 1 H, *J* = 4.4 Hz), 0.5 (d, 1 H, *J* = 4.4 Hz), 0.71 (ddd, 1 H, *J* = 15.5, 12.5, and 2.8 Hz), 0.94 (d, 3 H, *J* = 7.0 Hz), 0.95 (s, 3 H), 1.03 (s, 3 H) 2.16 (s, 3 H), 4.18 (br s, 2 H), 4.33 (ddd, 1 H, *J* = 10.3, 4.3, and 1.5 Hz), 5.53 (br d, 1 H, *J* = 3.7 Hz), 6.16 (br s, 1 H), 6.94 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 169.25 (s, $COCH_3$), 166.3 (s, C-19), 159.6 (s, C-17), 138.81 (s, C-13), 118.08 (d, C-18), 115.6 (d, C-14), 92.37 (d, C-25), 69.59 (d, C-16), 68.42 (t, C-24), 41.12 (d, C-10), 39.21 (s, C-9), 36.95 (t, C-11), 35.69 (d, C-8), 32.21 (t, C-3), 29.66 (t, C-15), 28.01 (t, C-6), 27.8 (t, C-7), 26.45 (s, C-5), 26.18 (t, C-12), 24.6 (t, C-20), 23.23 (t, C-2), 22.36 (q, C-21), 20.6 (q, $COCH_3$), 20.0 (q, C-23), 19.97 (t, C-1), 17.43 (s, C-4), and 14.22 (q, C-22); MS, *m/z* (relative intensity) 442 $[M]^+$ (5), 440 (2), 382 $[M - HAc]^+$ (10), 205 (20), 192 (100), 191 (83), 189 (83), 177 (44).

Acetate 4c: oil; $[\alpha]_D$ +17° ($CHCl_3$, *c* 0.3); UV λ_{max} (MeOH) 204 (ϵ 7100); IR ($CHCl_3$) 1780, 1750 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.11 (d, 1 H, *J* = 4.4 Hz), 0.5 (d, 1 H, *J* = 4.4 Hz), 0.71 (ddd, 1 H, *J* = 15.5, 12.5, and 2.8 Hz), 0.92 (d, 3 H, *J* = 7.0 Hz), 0.96 (s, 3 H), 1.04 (s, 3 H), 2.18 (s, 3 H), 4.13 (br s, 2 H), 4.31 (m, 1 H), 5.55 (br d, 1 H, *J* = 3.7 Hz), 6.09 (br s, 1 H), 7.04 (br s, 1 H); ^{13}C NMR ($CDCl_3$) δ 169.5 (s), 166.1 (s), 159.3 (s), 138.5 (s), 118.9 (d), 115.5 (d), 92.9 (d), 68.6 (d), 68.5 (t), 41.1 (d), 39.1 (s), 36.9 (t), 35.6 (d), 32.2 (t), 30.4 (t), 28.0 (t), 27.7 (t), 26.4 (s), 26.2 (t), 24.6 (t), 23.3 (t), 22.4 (q), 20.7 (q), 19.9 (q), 19.9 (t), 17.4 (s), and 14.1 (q); MS, *m/z* (relative intensity), 442 $[M]^+$ (5), 382 $([M - HAc]^+$ (14), 205 (21), 192 (100), 191 (86), 189 (86), and 177 (43).

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Registry No. **4a**, 116079-49-3; **4a** (acetate 1), 116079-50-6; **4a** (acetate 2), 116179-72-7.

Application of Allylboronates to the Synthesis of Carbomycin B

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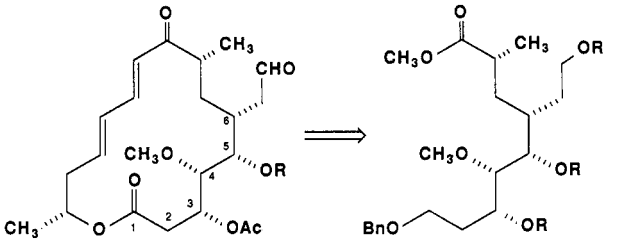
A formal synthesis of carbomycin B, a representative of the macrolide antibiotics, was achieved. The key steps of the sequence utilized allylboronates to secure the four contiguous stereogenic centers from C3 to C6. Condensation of a (*Z*)-(3-methoxyallyl)boronate with 3-(benzyloxy)propanal secures the centers at C3 and C6. Protection of the hydroxyl and oxidative cleavage of the olefin affords an aldehyde, which is coupled with (2′*E*)-[5′-(*tert*-butyldimethylsiloxy)pent-2′-enyl]-4,4,5,5-tetramethyl-2-bora-1,3-dioxolane to afford the C1–C8 portion of carbomycin B with the correct stereochemistry at the four contiguous stereogenic centers. A hydroformylation introduces C9. A series of straightforward functional group manipulations affords an intermediate identical with that prepared previously by K. C. Nicolaou. This synthesis demonstrates that the factors controlling α-asymmetric induction in simple allylboronates do not necessarily hold true with more complex highly functionalized boronates and aldehydes.

Carbomycin B (**1**) is a representative of the 16-membered ring macrolide antibiotics.[2] The groups of Nicolaou,[3] Tatsuta,[4] and Ziegler[5] have successfully accomplished total or partial syntheses of carbomycin B. All three approaches are based on modifications of the glucose framework as a means to securing chirality as well as the relative stereochemistry at positions 3–5 of the macrolide.

As an alternative to the carbohydrate approach to macrolide synthesis, we have explored the application of allylboronate methodology for securing each of the four contiguous chiral centers of carbomycin B. With the right half of the molecule **2** as an initial target structure, our design was to employ two successive allylboronate condensations to secure relative stereochemistry. On the basis of our work[6] and that of Hoffmann,[7] the relationship at

Scheme I



1a R=(Isovaleryl- α -L-mycarosyl)-D-mycaminose

1b R=H

2

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(2) (a) Hochstein, F. A.; Muri, K. *J. Am. Chem. Soc.* **1954**, *76*, 5080. (b) Freiberg, L. A.; Egan, R. S.; Washburn, W. H. *J. Org. Chem.* **1974**, *39*, 2474. (c) Woodward, R. B. *Angew. Chem.* **1957**, *69*, 50. (d) Woodward, R. B.; Weiler, L. S.; Dutta, P. C. *J. Am. Chem. Soc.* **1965**, *87*, 4662. (e) Kuehne, M.; Benson, B. W. *J. Am. Chem. Soc.* **1965**, *87*, 4660.

(3) Nicolaou, K. C.; Pavia, M. R.; Seitz, S. P. *Tetrahedron Lett.* **1979**, 2327. Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R.; Petasis, N. A. *J. Org. Chem.* **1979**, *44*, 4011. Nicolaou, K. C.; Seitz, S. P.; Pavia, M. R. *J. Am. Chem. Soc.* **1981**, *103*, 1222, 1224.

(4) Tatsuta, K.; Tanaka, A.; Fjujimoto, K.; Kinoshita, M.; Umezawa, S. *J. Am. Chem. Soc.* **1977**, *99*, 5827. Tatsuta, K.; Yamauchi, T.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 3035. Tatsuta, K.; Ameniya, Y.; Maniwa, S.; Kinoshita, M. *Tetrahedron Lett.* **1980**, *21*, 2837.

(5) Ziegler, F. E.; Gilligan, P. J. *J. Org. Chem.* **1981**, *46*, 3874. Ziegler, F. E.; Gilligan, P. J. *Tetrahedron Lett.* **1979**, 3371. Ziegler, F. E.; Chakraborty, U. R.; Weisenfeld, R. B. *Tetrahedron* **1981**, *37*, 4035.

(6) Wuts, P. G. M.; Bigelow, S. S. *J. Org. Chem.* **1982**, *47*, 2498.

(7) Hoffmann, R. W.; Kemper, B.; Metternich, R.; Lehmeier, T. *Justus Liebigs Ann. Chem.* **1985**, 2246 and references cited therein.

0022-3263/88/1953-5023$01.50/0