1.48 (s, 6 H), 3.32 (s, 3 H), 4.58 (s, 2 H), 7.02-7.55 (m, 5 H); IR (film) 1789, 1663 cm^{-1}; MS exact mass, *m/e* 335.0812 (calcd for $C_{14}H_{16}F_3NO_3S$ 335.0803).

General Procedure for the Conversion of Sulfoxides to β-Lactams. As an example, preparation of 4-(phenylthio)-2-azetidinone (**11c**) is cited. To a solution of **9c** (99 mg, 0.5 mmol) in 20 mL of CH_2Cl_2 were added at -20 °C triethylamine (251 μL, 1.8 mmol) and TMSOTf (348 μL, 1.8 mmol). The solution was stirred at -20 °C for 15 min and then quenched by addition of 5% $NaHCO_3$ solution. The organic layer was washed with 0.5% HCl solution and brine. Drying over Na_2SO_4 and removal of the solvent gave a colorless oil. A preparative silica gel TLC (5% CH_3OH-CH_2Cl_2) of this material yielded, besides the starting material (18%) and *trans*-3-(phenylthio)acrylamide (8%), 37 mg (41%) of **11c** which was recrystallized from diethyl ether: mp 72-73 °C (lit.[23] mp 72 °C); NMR ($CDCl_3$) δ 2.90 (ddd, 1 H, *J* = 15.0, 2.26, 1.3 Hz), 3.33 (ddd, 1 H, *J* = 15.0, 5.0, 2.1 Hz), 5.06 (dd, 1 H, *J* = 5.0, 2.6 Hz), 6.49 (br s, 1 H), 7.47 (m, 5 H); IR (film) 1740 cm^{-1}; MS exact mass, *m/e* 179.0411 (calcd for C_9H_9NOS 179.0405).

***N*-(Phenylmethoxy)-3,3-dimethyl-4-(phenylthio)-2-azetidinone (11a)**: yield 51%; a colorless oil; NMR ($CDCl_3$) δ 1.28 (s, 3 H), 1.32 (s, 3 H), 4.73 (s, 1 H), 5.00 (d, 1 H, *J* = 10 Hz), 5.14 (d, 1 H, *J* = 10 Hz), 7.39 (m, 5 H); IR (film) 1780 cm^{-1}; MS exact mass, *m/e* 313.1133 (calcd for $C_{18}H_{19}NO_2S$ 313.1137).

***N*-(Phenylmethoxy)-4-(phenylthio)-2-azetidinone (11b)**: yield 14%; mp 50.5-51 °C; NMR ($CDCl_3$) δ 2.51 (dd, H, *J* = 2.6 Hz), 3.01 (dd, 1 H, *J* = 14, 5 Hz), 4.81 (dd, 1 H, *J* = 5, 2.6 Hz), 5.05 (s, 2 H), 7.41 (m, 5 H); IR (film) 1780 cm^{-1}; MS exact mass, *m/e* 285.0815 (calcd for $C_{16}H_{15}NO_2S$ 285.0824).

3-Methyl-4-(phenylthio)-2-azetidinone (15 and 16). This was obtained in 41% yield as a 2.7:1 mixture of cis (**15**) and trans (**16**) isomers. The NMR spectra was assignable to each isomer, but IR and MS were taken as a mixture.[24] **15**: NMR ($CDCl_3$) δ 1.36 (d, 3 H, *J* = 7.6 Hz), 3.59 (qdd, 1 H, *J* = 7.6, 4.9, 1.5 Hz), 7.31 (m, 5 H). **16**: NMR ($CDCl_3$) δ 1.32 (d, 3 H, *J* = 7.5 Hz), 3.06 (qdd, 1 H, *J* = 7.5, 2.5, 1.0 Hz), 4.59 (d, 1 H, *J* = 2.5 Hz), 7.31 (m, 5 H); IR (film) 1762 cm^{-1}; MS exact mass, *m/e* 193.0566 (calcd for $C_{10}H_{11}NOS$ 193.0562).

Acknowledgment. I thank Drs. C. U. Kim, D. N. McGregor, and Y. Ueda for helpful discussions and the Analytical Department for recording spectra.

(23) Claus, K.; Grimm, D.; Prossel, G. *Liebigs Ann. Chem.* **1974**, 539.

(24) For the trans isomer see ref 23.

Metabolites of the Marine Prosobranch Mollusc *Lamellaria* sp.

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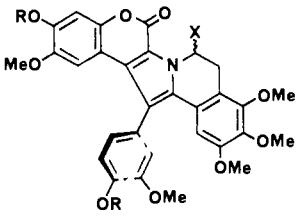
Abstract: The marine prosobranch mollusc, *Lamellaria* sp. contains four aromatic metabolites, lamellarins A-D (**1-4**). The structure of lamellarin A (**1**) was determined by an X-ray crystallographic study and the structures of lamellarins B-D (**2-4**) were assigned by interpretation of spectral data. Lamellarian A (**1**) exists in solution as a 1:1 mixture of two geometrical isomers due to restricted rotation about the C1-C11 bond. Molecular mechanics calculations revealed that the barrier to rotation was large (>600 kcal/mol).

Chemical studies of prosobranch molluscs are rare,[1] particularly when compared with the frequent investigations of opisthobranch molluscs.[2] Six specimens of a species of *Lamellaria*[3] were collected by hand during a night dive (-5 m) near Koror, Palau. Although they are prosobranchs, the *Lamellaria* sp. resembles an opisthobranch since the shell is completely concealed by dark brown, almost black, fleshy tissue. In this paper we report the structural elucidation of four aromatic metabolites, lamellarins A-D (**1-4**) (Chart I).

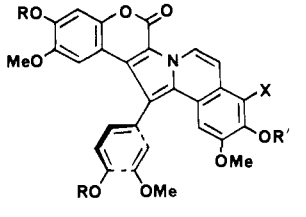
The specimens of *Lamellaria* were stored in methanol (1 L) at 4 °C for 3 years. Dichloromethane and ethyl acetate soluble materials from the methanol extract were combined and subjected to preparative thick-layer chromatography to obtain four UV-active bands. Each band was further purified by reverse-phase LC to obtain lamellarin A (**1**, 13 mg/animal), lamellarin B (**2**, 4 mg/animal), lamellarin C (**3**, 3 mg/animal), and lamellarin D (**4**, 6 mg/animal).

Lamellarin A (**1**) was obtained as pale yellow prisms, mp 168-172 °C dec, from methanol. A parent ion at *m/z* 561.1669 in the mass spectrum was appropriate for a molecular formula of $C_{30}H_{27}NO_{10}$. The highly aromatic character of lamellarin A (**1**) was apparent from the UV spectrum [326 (ε 25 000), 309 (ε 28 000), 275 (ε 33 000), 215 nm (ε 41 000)] and from the number

Chart I



1 R = H X = OH
3 R = H X = H
5 R = Ac X = OAc
7 R = Ac X = H



2 R = H R' = Me X = OMe
4 R = H R' = H X = H
6 R = Ac R' = Me X = OMe
8 R = Ac R' = Ac X = H

of signals in the aromatic region of the ^1H NMR spectrum. A simple analysis of the ^1H NMR specrum (360 MHz, acetone-d_6)

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[⊥] Visiting scholar from the Biophysics Institute, Chinese Academy of Medical Sciences, Beijing, PRC.

(1) Recent examples include: Tymiak, A. A.; Rinehart, K. L., Jr. *J. Am. Chem. Soc.* **1983**, *105*, 7396. Kosuge, T.; Tsuji, K.; Hirai, K.; Yamaguchi, K.; Okamoto, T.; Iitaka, Y. *Tetrahedron Lett.* **1981**, *22*, 3417. Coll, J. C.; Tapiolas, D. M.; Bowden, B. F.; Webb, L.; Marsh, H. *Mar. Biol. (Berlin)* **1983**, *74*, 35.

0002-7863/85/1507-5492$01.50/0

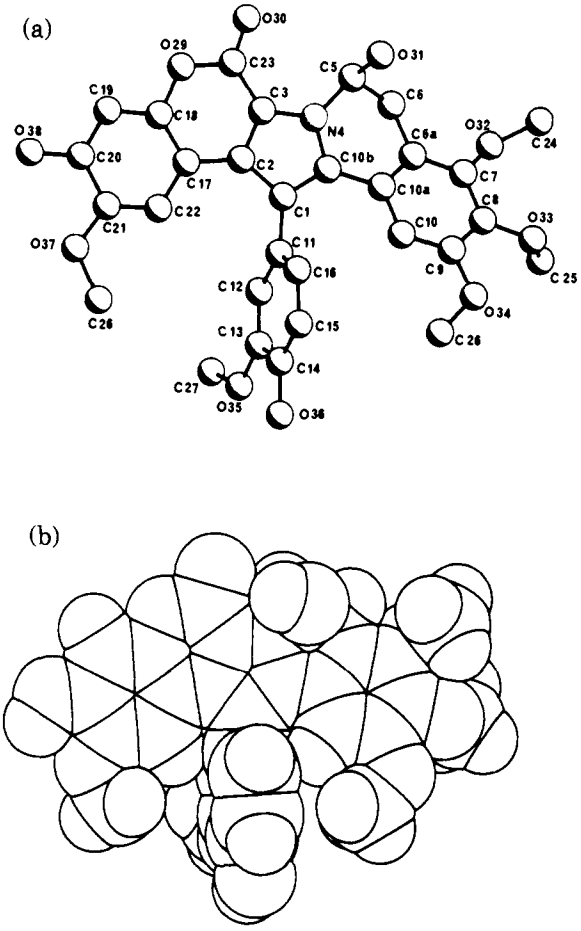

Figure 1. Two computer-generated perspective drawings of the final X-ray model of lamellarin A. In the top drawing (a) hydrogen atoms are omitted for clarity, and the remaining atoms are shown with arbitrary radii so the connectivity is clear. The bottom drawing (b) is from the same perspective, and all atoms are drawn with appropriate van der Waals radii.

required the presence of at least 48 protons and suggested that the molecule might exist in solution as a 1:1 mixture of two geometrical forms that did not interconvert on the ^{1}H NMR time scale. Acetylation of lamellarin A (**1**) with acetic anhydride in pyridine gave a mixture of triacetates **5** that could not easily be separated.

The structure of lamellarin A (**1**) was determined by a single-crystal X-ray diffraction analysis. A computer-generated perspective drawing of the final X-ray model of lamellarin A (**1**) is given in Figure 1a. Hydrogens are omitted for clarity, and the material is a naturally occurring racemate. The main pentacyclic array is essentially planar with the hydroxyl substituent at C5, $OC24H_3$ and $OC25H_3$ oriented out of this plane. The aromatic ring attached to C1 is rotated 90° to this plane and in the crystalline phase the hydroxyl at C5 is anti to the C13 methoxyl group. The observed doubling of signals in the ^{1}N NMR spectrum indicates that both syn and anti configurations exist in solution. Slow interconversion of the syn and anti forms can be accomplished, in principle, either by rotation about the C1–C11 bond or by equilibration of the carbinolamine.

Molecular mechanics calculations (MM2[4]) were used to estimate the barrier to rotation about the C1–C11 bond. The initial geometry was obtained from the X-ray positional coordinates, and this was arbitrarily given a rotational angle of 0°. Another initial geometry was generated by optimizing the X-ray geometry with MM2. The methyl group (C27) of the aromatic methoxyl was removed because its conformation during rotation was not known. The energy increased rapidly for rotations beyond about 40° in either direction. The position of the maximum energy was sensitive to the exact placement of the aromatic hydrogens, but the height of the maximum was not. The height of a typical maximum was in excess of 600 kcal/mol. The calculations also suggested that this barrier was almost completely in the van der Waals term. In order to appreciate this, a drawing of lamellarin A (**1**) with van der Waals atomic radii is shown in Figure 1b. The calculations and drawing argue strongly that ring rotation is severely hindered in these compounds and that the interconversion of the syn and anti atropisomers involving opening of the carbinolamine to a pyrrole aldehyde. Once this opening has occurred, models suggest that rotation about the C1–C11 bond is relatively unencumbered. Thus a mechanism exists for both the syn and anti forms to racemize. Interestingly, none of the lamellarins exhibited an optical rotation and all are therefore racemic.

Table I. 360-MHz ^{1}H NMR Spectral Assignments for Lamellarin A (1) in Acetone-d_6[a]

H at C no.	^{1}H NMR, δ	
5	6.97 (m, 1 H)	
6	3.11 (dd, 1/2 H, J = 16.7, 4.2 Hz)	3.12 (dd, 1/2 H, J = 16.7, 4.2 Hz)
6	3.52 (dd, 1/2 H, J = 16.7, 2.2 Hz)	3.53 (dd, 1/2 H, J = 16.7, 4.2 Hz)
10[b]	6.70 (s, 1/2 H)	6.76 (s, 1/2 H)
12	6.99 (d, 1/2 H, J = 1.8 Hz)	7.27 (d, 1/2 H, J = 1.8 Hz)
15	7.18 (d, 1/2 H, J = 8 Hz)	7.07 (d, 1/2 H, J = 8 Hz)
16	7.15 (dd, 1/2 H, J = 8, 1.8 Hz)	6.85 (dd, 1/2 H, J = 8, 1.8 Hz)
19	6.84 (s, 1 H)	
22[b]	6.66 (s, 1/2 H)	6.67 (s, 1/2 H)
24[c]	3.87 (s, 3 H)	
25[c]	3.80 (s, 3 H)	
26[d]	3.37 (s, 3 H)	
27	3.83 (s, 1 1/2 H)	3.97 (s, 1 1/2 H)
28[d]	3.44 (s, 3 H)	

[a] The signals are arbitrarily assigned to two isomers except that signals for C12, C15, and C16 are coupled as shown. [b-d] Assignments may be interchanged.

The ^{1}H NMR spectrum was assigned as indicated in Table I. In making these assignments, we have assumed that the ring current of the phenyl ring attached at C1 causes shielding of the protons at C10, C22, C26, and C28. The signals at δ 3.12 and 3.53 for the geminal protons at C6 both appear to be doublets of triplets but are actually two sets of doublets of doublets, resulting from the syn and anti configurations.

Lamellarin B (**2**) was obtained as pale yellow needles, mp 258–259 °C, from methanol. The molecular formula, $C_{30}H_{25}NO_9$, suggested that lamellarin B might result from dehydration of lamellarin A. This proposal was supported by both the UV spectrum (λ_{max} 388, 368, 284, and 206 nm), which indicated a more extensively conjugated chromophore than that of **1**, and the ^{1}H NMR spectrum, which contained five methoxyl signals at δ 3.46, 3.47, 3.89, 3.92, and 4.03 (all s, 3 H), three isolated aromatic proton signals at δ 6.79, 6.90, and 7.11 (all s, 1 H), signals at δ 7.12 (dd, 1 H, J = 8, 1,8 Hz), 7.19 (d, 1 H, J = 8 Hz), and 7.25 (d, 1 H, J = 1.8 Hz) assigned to protons at C16, C15, and C12, respectively, and two mutually coupled signals at δ 7.46 (d, 1 H, J = 7.4 Hz) and 9.16 (d, 1 Hz, J = 7.4 Hz) assigned to protons at C6 and C5, respectively. The proposed structure was confirmed by dehydration of lamellarin A (**1**) using *p*-toluenesulfonyl chloride in pyridine to obtain lamellarin B (**2**) in high yield. Acetylation of lamellarin B (**2**) gave a diacetate **6**, as expected.

Lamellarin C (**3**) crystallized from methanol as white needles, mp 225–230 °C dec. The molecular formula, $C_{30}H_{27}NO_9$, suggested that **3** was a dihydro derivative of lamellarin B (**2**). The UV spectrum (λ_{max} 312, 276, and 210 nm) indicated the same chromophore that is present in lamellarin A (**1**). The ^{1}H NMR

(2) For recent reviews, see: Faulkner, D. J. *Nat. Prod. Rep.* **1984**, *1*, 251, 551.
(3) It has been determined that the animal is a new species of *Lamellaria*. (J. R. Lance, personal communication.)
(4) Alinger, N. L. *Adv. Phys. Org. Chem.* **1976**, *13*, 1 and references therein.

spectrum (Table I) contained five methoxy signals, six aromatic proton signals, and signals at δ 3.05–3.22 (m, 2 H) (protons at C6) and 4.62 (m, 1 H) and 4.90 (m, 1 H) (protons at C5). Irradiation at δ 3.1 caused the multiplets at δ 4.62 and 4.90 to appear as mutually coupled doublets (J = 14 Hz). Acetylation of lamellarin C (**3**) produced the expected diacetate **7**.

Lamellarin D (**4**) was obtained as a pale yellow powder from methylene chloride trituration. The molecular formula, $C_{28}H_{21}NO_8$, was derived from mass spectral analysis. The UV spectrum (λ_{max} 387, 368, 280, and 212 nm) required the same chromophore as that of lamellarin B (**2**). The ^{1}H NMR spectrum contained characteristic signals at δ 9.12 (d, 1 H, J = 7.4 Hz) and 7.19 (d, 1 H, J = 7.4 Hz) for the protons at C5 and C6, three methoxyl signals, and seven additional aromatic proton signals that included four singlets. We therefore concluded that in lamellarin D (**4**), one of the methoxyl groups of lamellarin B (**2**) had been replaced by hydrogen and a second had been replaced by a phenolic hydroxyl. The new aromatic hydrogen must be at C7 since the new aromatic proton signal in the ^{1}H NMR spectrum is a singlet. The phenolic hydroxyl must be at C8 since both shielded methoxyl groups are present and the ^{1}H NMR signals associated with the aromatic ring at C1 are identical. Acetylation of lamellarin D (**4**) gave a triacetate **8**, confirming the presence of the additional phenolic group.

The majority of metabolites from molluscs can be traced to dietary sources.[2,5] While we know nothing of the diet of this *Lamellaria* sp., other species are known to feed on compound colonial tunicates.[6] However, the lamellarins do not resemble reported tunicate metabolites or any other group of marine natural products. At concentrations of 19 μg/mL, lamellarin D (**4**) caused a 78% inhibition of cell division in the fertilized sea urchin egg assay while lamellarin C (**3**) caused 15% inhibition and lamellarins A and B (**1** and **2**) were inactive.

Experimental Section

Collection, Extraction, and Isolation Procedures. Six specimens of *Lamellaria* sp. were collected at night using scuba (−5 m) at Peduliaes headland on Ngarol Island at the entrance to Malakal Harbor, Palau. The animals were stored in methanol (1 L) for 3 years at 0–5 °C. The methanol was decanted and concentrated in vacuo to obtain an aqueous suspension that was extracted sequentially with dichloromethane and ethyl acetate. Since both extracts contained the same UV-absorbing materials, the combined crude extracts were separated by preparative TLC on silica gel using 3:1 ethyl acetate–hexane as eluant to obtain four UV-active bands. The material from each band was further purified by preparative reverse-phase HPLC on silica-ODS using 32% water–68% methanol as eluant to obtain lamellarin A (**1**, 13 mg/animal), lamellarin B (**2**, 4 mg/animal), lamellarin C (**3**, 3 mg/animal), and lamellarin D (**4**, 6 mg/animal).

Lamellarin A (1): pale yellow prisms (MeOH); mp 168–172 °C dec; UV (MeOH) 326 (ε 25 000), 309 (ε 28 000), 275 (ε 33 000), 215 nm (ε 41 000); UV (MeOH + NaOH) 378 (ε 9000), 319 (ε 36 000), 287 (ε 33 000), 218 (ε 46 000); IR (KBr) 3430, 3005, 2940, 2830, 1705, 1510, 1415, 1270, 1205, 1145, 1030 cm^{-1}; ^{1}H NMR (acetone-d_6), see Table I; mass spectrum, m/z (relative intensity) 561 (38), 543 (100), 529 (10), 271 (12); HRMS, obsd m/z 561.1669, $C_{30}H_{27}NO_{10}$ requires m/z 561.1635.

Lamellarin B (2): yellow needles (MeOH); mp 258–259 °C; UV (MeOH) 388, 368, 340 (sh), 325 (sh), 304 (sh, 284, 206 nm; UV (MeOH + NaOH) 399, 318, 297, 216 nm; IR ($CDCl_3$) 3690, 3605, 3530, 3105, 2980, 2930, 1695, 1600, 1480, 1430 cm^{-1}; ^{1}H NMR (acetone-d_6) δ 3.46 (s, 3 H), 3.47 (s, 3 H), 3.89 (s, 3 H), 3.92 (s, 3 H), 4.03 (s, 3 H), 6.79 (s, 1 H), 6.90 (s, 1 H), 7.11 (s, 1 H), 7.12 (dd, 1 H, J = 8, 1.8 Hz), 7.19 (d, 1 H, J = 8 Hz), 7.25 (d, J = 1.8 Hz), 7.46 (d, 1 H, J = 7.4 Hz), 9.16 (d, 1 H, J = 7.4 Hz); mass spectrum, m/z (relative intensity) 543 (67), 393 (55), 269 (100); HRMS, obsd m/z 543.1532, $C_{30}H_{25}NO_9$ requires m/z 543.1529.

Lamellarin C (3): needles (MeOH); mp 225–230 °C dec; UV (MeOH) 332 (sh), 321, 276, 210 nm; UV (MeOH + NaOH) 382, 312, 287, 214 nm; ^{1}H NMR (acetone-d_6) δ 3.05–3.22 (m, 2 H), 3.36 (s, 3 H), 3.50 (s, 3 H), 3.87 (s, 3 H), 3.88 (s, 3 H), 3.90 (s, 3 H), 4.62 (m, 1 H), 4.90 (m, 1 H), 6.57 (s, 1 H), 6.60 (s, 1 H), 6.96 (s, 1 H), 6.97 (d, 1 H, J = 1.7 Hz), 7.07 (dd, 1 H, J = 8, 1.7 Hz), 7.13 (d, 1 H, J = 8 Hz); mass spectrum, m/z (relative intensity) 545 (100), 530 (30); HRMS, obsd m/z 545.1703, $C_{30}H_{27}NO_9$ requires m/z 545.1686.

Lamellarin D (4): powder; UV (MeOH) 387, 368, 339 (sh), 324 (sh), 302 (sh), 280, 212 nm; UV (MeOH + NaOH) 406, 316 (sh), 296, 244 (sh), 218 nm; ^{1}H NMR (acetone-d_6) δ 3.48 (s, 3 H), 3.49 (s, 3 H), 3.92 (s, 3 H), 6.87 (s, 1 H), 6.89 (s, 1 H), 7.12 (dd, 1 H, J = 8, 1.8 Hz), 7.19 (d, 1 H, J = 8 Hz), 7.19 (d, 1 H, J = 7.4 Hz), 7.24 (s, 2 H), 7.24 (d, 1 H, J = 1.8 Hz), 9.12 (d, 1 H, J = 7.4 Hz); mass spectrum, m/z (relative intensity) 499 (100), 466 (31), 438 (32); HRMS, obsd m/z 499.1261, $C_{28}H_{21}NO_8$ requires m/z 499.1267.

Single-Crystal X-ray Diffraction Analysis of Lamellarin A (1). Large clear crystals could be obtained by slow evaporation of an aqueous methanol solution. Preliminary X-ray photographs displayed only triclinic symmetry. Accurate lattice constants of a = 10.992 (1) Å, b = 11.587 (1) Å, c = 12.059 (1) Å, α = 94.60 (1)°, β = 81.97 (1)°, and γ = 67.74 (1)° were obtained from a least-squares fitting of 15 2θ values. The crystal density indicated that two fragments of composition $C_{30}H_{27}NO_{10}\cdot 2H_2O$ formed the unit cell. All unique diffraction maxima with $2\theta \leq 114°$ were collected on a fully automated four-circle diffractometer using variable-speed, 1° ω scans and graphite-monochromated Cu Kα radiation (1.54178 Å). Of the 3726 reflections surveyed in this fashion, 2521 (68%) were judged observed after correction for Lorentz, polarization, and background effects ($|F_o| \geq 3\sigma(F_o)$).[7] Since intensity statistics indicated that the most likely space group was $P\bar{1}$, a phasing attempt was initiated in this space group. This proceeded uneventfully, and a plausible 20-atom fragment was found on the initial E synthesis. Extension of this fragment with tangent formula recycling eventually led to a model consisting of all of the non-hydrogen atoms of lamellarin A and two peaks which were tentatively identified as solvent but not included at this stage. Block-diagonal least-squares refinements converged nicely, and hydrogen atoms were located on a ΔF synthesis. The two suspect peaks were included as waters of crystallization. Further refinement with anisotropic non-hydrogen atoms and isotropic hydrogens converged to a conventional crystallographic residual of 0.058 for the observed reflections. Additional crystallographic details are available as supplementary material.

Dehydration of Lamellarin A (1). p-Toluenesulfonyl chloride (5 mg) was added to a solution of lamellarin A (**1**, 3 mg) in pyridine (0.5 mL) and the reaction mixture was allowed to stand at 25 °C for 20 h. The reaction mixture was added to 2 N hydrochloric acid (10 mL) and extracted with methylene chloride (3 × 25 mL). The dichloromethane-soluble material was purified by preparative TLC on silica gel to obtain lamellarin B (**2**, 1.5 mg) identical in all respects with an authentic sample.

Preparation of Acetates 5–8. In a typical procedure, acetic anhydride (0.25 mL) was added to a solution of lamellarin A (**1**, 2 mg) in pyridine (0.5 mL), and the resulting solution was allowed to stand overnight at 25 °C. Evaporation of the reagents under high vacuum gave a residue that was purified by LC on Partisil with 1:1 hexane–ethyl acetate as eluant to obtain the triacetate **5** (1.5 mg) as a white solid.

Triacetate 5: UV (MeOH) 340 (sh), 324 (sh), 308, 277, 268 (sh), 230 nm; IR ($CHCl_3$) 3015, 2940, 1760, 1745, 1710, 1600, 1470, 1415, 1200 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.99 (s, 3 H), 2.32 (s, 3 H), 2.36 (s, 3 H), 3.18 (dd, 1 H, J = 17.4, 4.2 Hz), 3.39 (s, 3 H), 3.42 (s, 3 H), 3.78 (dd, 1 H, J = 17.4, 1 Hz), 3.78 (s, 1.5 H), 3.86 (s, 3 H), 3.87 (s, 1.5 H), 3.88 (s, 3 H), 6.59 (s, 0.5 H), 6.62 (s, 0.5 H), 7.02 (d, 1 H, J = 1.8 Hz), 7.04 (dd, 1 H, J = 8, 1.8 Hz), 7.11 (s, 0.5 H), 7.12 (s, 0.5 H), 7.22 (d, 1 H, J = 8 Hz), 7.94 (m, 1 H); mass spectrum, m/z (relative intensity) 627 (7), 584 (18), 543 (26), 42 (100); HRMS, obsd m/z 627.1734, $C_{34}H_{29}NO_{11}$ (M − AcOH) requires m/z 627.1739.

Diacetate 6: oil; UV (MeOH) 382, 363, 274, 218 nm; ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3 H), 2.37 (s, 3 H), 3.45 (s, 3 H), 3.48 (s, 3 H), 3.83 (s, 3 H), 3.95 (s, 3 H), 4.03 (s, 3 H), 6.81 (s, 1 H), 6.94 (s, 1 H), 7.17 (s, 1 H), 7.19 (d, 1 H, J = 1.8 Hz), 7.22 (d, 1 H, J = 8, 1.8 Hz), 7.29 (d, 1 H, J = Hz), 7.45 (d, 1 H, J = 7.4 Hz), 9.24 (d, 1 H, J = 7.4 Hz);

(5) Stallard, M. O.; Faulkner, D. J. *Comp. Biochem. Physiol., B: Comp. Biochem.* **1974**, *49B*, 25.

(6) Behrens, D. W. *Veliger* **1980**, *22*, 323. Lambert, G. *Veliger* **1980**, *22*, 340.

(7) All crystallographic calculations were done on a PRIME 850 computer operated by the Cornell Chemistry Computing Facility. Principal programs employed were as follows: REDUCE and UNIQUE, data reduction programs by M. E. Leonowicz, Cornell University, 1978; MULTAN 78, MULTAN 80, and RANTAN 80, systems of computer programs for the automatic solution of crystal structures from X-ray diffraction data (locally modified to perform all Fourier calculations, including Patterson syntheses), written by P. Main, S. E. Hull, L. Lessinger, G. Germain, J. P. Declercq, and M. M. Woolfson, University of York, England, 1978 and 1980; DIRDIF, written by P. T. Buerskens et al., University of Nijmegen, The Netherlands, 1981; BLS78A, an anisotropic block-diagonal least-squares refinement, written by K. Hirotsu and E. Arnold, Cornell University, 1980; PLUTO78, a crystallographic illustration program by W. D. S. Motherwell, Cambridge Crystallographic Data Centre, 1978; BOND, a program to calculate molecular parameters and prepare tables, written by K. Hirotsu, Cornell University, 1978.

mass spectrum, m/z (relative intensity) 627 (8), 585 (26), 543 (22), 42 (100); HRMS, obsd m/z 627.1711, $C_{34}H_{29}NO_{11}$ requires m/z 627.1739.

Diacetate 7: UV (MeOH) 337 (sh), 312, 278, 268 (sh), 229 nm; ^{1}H NMR ($CDCl_3$) δ 2.31 (s, 3 H), 2.35 (s, 3 H), 3.16 (m, 2 H), 3.37 (s, 3 H), 3.43 (s, 3 H), 3.81 (s, 3 H), 3.87 (s, 3 H), 3.90 (s, 3 H), 4.76 (m, 1 H), 4.82 (m, 1 H), 6.54 (s, 1 H), 6.69 (s, 1 H), 7.10 (s, 1 H), 7.10 (d, 1 H, J = 1.7 Hz), 7.13 (dd, 1 H, J = 8, 1.7 Hz), 7.22 (d, 1 H, J = 8 Hz); mass spectrum, m/z (relative intensity) 629 (28), 587 (100), 545 (76), 530 (36); HRMS, obsd m/z 629.1932, $C_{34}H_{31}NO_{11}$ requires m/z 629.1896.

Triacetate 8: UV (MeOH) 384, 364, 345, 335 (sh), 320 (sh), 308 (sh), 300 (sh), 282, 232 nm; ^{1}H NMR ($CDCl_3$) δ 2.33 (s, 3 H), 2.35 (s, 3 H), 2.37 (s, 3 H), 3.45 (s, 6 H), 3.84 (s, 3 H), 6.81 (s, 1 H), 7.08 (d, 1 H, J = 7.4 Hz), 7.17 (s, 1 H), 7.20 (d, 1 H, J = 1.8 Hz), 7.22 (s, 1 H), 7.23 (dd, 1 H, J = 8, 1.8 Hz), 7.30 (d, 1 H, J = 8 Hz), 7.41 (s, 1 H), 9.25 (d, 1 H, J = 7.4 Hz); mass spectrum, m/z (relative intensity) 625 (29), 583 (40), 541 (100), 499 (91); HRMS, obsd m/z 625.1638, $C_{34}H_{27}NO_{11}$ requires m/z 625.1584.

Acknowledgment. We thank James R. Lance for identification of the molluscs and Prof. Robert S. Jacobs for supplying the biological screening data. This research was supported by grants from the National Science Foundation (CHE 81-21471 and INT14133), the National Institutes of Health (CA 24487), and the Sea Grant Programs of California and New York.

Registry No. *anti*-**1**, 97614-62-5; *syn*-**1**, 97672-36-1; **2**, 97614-63-6; **3**, 97614-64-7; **4**, 97614-65-8; *anti*-**5**, 97614-66-9; *syn*-**5**, 97672-37-2; **6**, 97614-67-0; **7**, 97614-68-1; **8**, 97633-82-4.

Supplementary Material Available: Tables of fractional coordinates, thermal parameters, bond distances, and bond angles for lamellarin A (5 pages). Ordering information is given on any current masthead page.

General Method for Generation of 3-Siloxyallylmetallic Species and Their Synthetic Application

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Abstract: On treatment with vinylmagnesium bromide, most of the α-branched acyltrimethylsilanes initially form the corresponding 1-(trimethylsilyl)allylic alkoxides, which undergo a facile rearrangement of the silyl group from carbon to oxygen to generate 3-(trimethylsiloxy)allylmagnesium bromides, namely, homoenolate equivalents, almost quantitatively. On the other hand, use of alcohols prepared from acyl(*tert*-butyl)dimethylsilanes has made it feasible to generate lithium homoenolate equivalents bearing straight side chains. Thus, treatment of 1-(*tert*-butyldimethylsilyl)allylic alcohols with an equimolar amount of butyllithium in THF has allowed generation of the corresponding lithium homoenolates in over 80% yield irrespective of difference of electronegativities between carbon and oxygen. Under the influence of copper(I) trimethylsilylacetylide, these reagents add to enones to give the corresponding 1,6-diketone derivatives bearing enol ether moieties, which can further serve for introduction of other electrophiles or unsaturation. Oxiranes also react with these copper homoenolates to yield the corresponding 5-hydroxy ketone derivatives.

Although enolate anions have been extensively studied in synthetic organic chemistry, the characteristics and behavior of their homologous nucleophiles, namely, homoenolate anions,[1] have not been so fully elucidated up to now. Recently, their synthetic utility has been well recognized, and several studies on this subject have been described by us[2] and others.[3,4] These nucleophiles reported hitherto can be classified into two types: metal homoenolates themselves and their synthetic equivalents. A few reports have appeared on the former and several synthetic reactions using such species as nucleophiles have been described, but some limitations exist from a synthetic viewpoint on such aspects as structural limitations as well as rather poor nucleophilicities attributable to the nature of counter metal cations.[2,3]

Recent progress achieved by using organosilicon compounds has offered several new aspects to synthetic organic chemistry.[5] One of them is an introduction of enol silyl ethers[6] as enolate equivalents, which has brought about a great contribution to regiocontrol of enolate chemistry. Another interesting feature on synthetic background is expected from a possibility of generating several types of carbanionic species from the metal alkoxides through the so-called Brook–West rearrangement.[7] Based on these features we studied the generation of metal homoenolate equivalents[8] bearing enol silyl ether moieties as the masked carbonyl functionality from 1-(trimethylsilyl)allylic alcohols which can easily be prepared from acyltrimethylsilanes[9,10] with vinylmagnesium halide. In the previous paper, we reported alkylation

(1) Review: Werstiuk, N. H. *Tetrahedron* **1983**, *39*, 205.
(2) Titanium homoenolates of esters: Nakamura, E.; Kuwajima, I. *J. Am. Chem. Soc.* **1977**, *99*, 7360. Zinc homoenolates of esters: Nakamura, E.; Kuwajima, I. *Ibid.* **1984**, *106*, 3368. Homoenolates of main metal group: Nakamura, E.; Shimada, J.; Kuwajima, I. *Organometallics* **1985**, *4*, 641.
(3) (a) Caine, D.; Frobest, A. S. *Tetrahedron Lett.* **1978**, 883. (b) Goswami, R.; Corcoran, D. E. *Ibid.* **1982**, *23*, 1463. (c) Goswami, R.; Corcoran, D. E. *J. Am. Chem. Soc.* **1983**, *103*, 7182. (d) Ryu, I.; Ando, M.; Ogawa, A.; Murai, S.; Sonoda, A. *Ibid.* **1983**, *105*, 7192.
(4) Homoenolate equivalents: (a) Evans, D. A.; Andrews, G. C.; Buckwalter, B. *J. Am. Chem. Soc.* **1974**, *96*, 5560. (b) Still, W. C.; Macdonald, T. L. *Ibid.* **1974**, *96*, 5561. (c) Lesur, B.; Toye, J.; Chantrenne, M.; Ghosez, L. *Tetrahedron Lett.* **1979**, 2835. (d) De Lombaert, S.; Lesur, B.; Ghosez, L. *Ibid.* **1982**, *23*, 4251.
(5) (a) Colvin, E. W. "Silicon in Organic Synthesis"; Butterworths: London, 1981. (b) Weber, W. P. "Silicon Reagents for Organic Synthesis"; Springer-Verlag: Berlin, 1983.
(6) Brownbridge, P. *Synthesis* **1983**, 1, 85. Reference 5a, pp 198–287. Reference 5b, pp 206–272.
(7) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77.
(8) Kuwajima, I.; Kato, M. *J. Chem. Soc., Chem. Commun.* **1979**, 708. Kato, M.; Mori, A.; Oshino, H.; Enda, J.; Kobayashi, K.; Kuwajima, I. *J. Am. Chem. Soc.* **1984**, *106*, 1773.
(9) Kuwajima, I.; Abe, T.; Minami, N. *Chem. Lett.* **1976**, 993. Kuwajima, I.; Arai, M.; Sato, T. *J. Am. Chem. Soc.* **1977**, *99*, 4181. Kuwajima, I.; Kato, M.; Sato, T. *J. Chem. Soc., Chem. Commun.* **1978**, 478. Kuwajima, I.; Mori, A.; Kato, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 2368.
(10) Cohen, T.; Matz, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 6900.

0002-7863/85/1507-5495$01.50/0