Stereoselective Total Synthesis of Bengamide E from Glyceraldehyde Acetonide and a Nonracemic γ-Alkoxy Allylic Stannane

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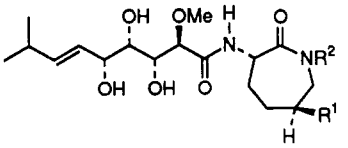
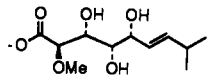
Received July 7, 1993®

The synthesis of bengamide E (**30**) was achieved starting from the furan adduct **1** of (*R*)-glyceraldehyde acetonide. The key step entailed $MgBr_2$-promoted addition of the (*S*)-γ-alkoxy allylic stannane (*S*)-**25** to the aldehyde **8** obtained from the oxidation product of furan **1** after protection as the methyl ether. The adduct of stannane (*S*)-**25** and aldehyde **8**, a 1:1 mixture of hydroxy ester **27** and lactone **28** was converted to bengamide E by aminolysis with (*S*)-2-aminocaprolactam and subsequent debenzylation with Li in NH_3.

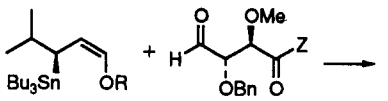
In a recent series of papers, Crews and co-workers described the isolation and structure elucidation of the bengamides, a novel family of amino acid derivatives from a choristid sponge common to coral reef communities throughout the Fiji Islands.[1] They speculate that these



Bengamide	R^1	R^2
A	$-O_2C(CH_2)_{12}CH_3$	H
B		CH_3
C		H
D		CH_3
E	H	H
F		CH_3

unusual compounds are symbiotic products derived from bacterial fatty acids, cyclized L-lysine, and a 4-carbon diketide. Bengamide A and B show potent antiparasitic and antimicrobial activity.

To date, total syntheses have been reported for bengamide E,[2-4] B,[3] and A[5] and the C_{10} side chain.[6] All employ carbohydrates[2,3,6] or natural cyclitols[4,5] as the source of the four contiguous stereocenters in the side chain. Our recent studies on carbohydrate homologation through use of chiral γ-alkoxy allylic stannanes suggested a particularly straightforward approach to assemblage of this side chain (eq 1).[7] The plan is especially appealing because it allows for the direct introduction of the (*E*)-double bond, a



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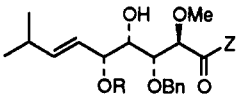
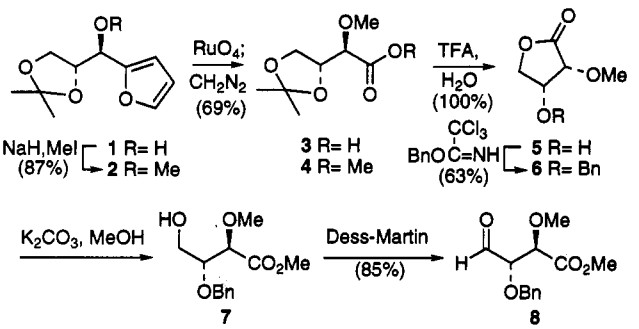


III (1)

problem that has plagued previous syntheses. It also efficiently utilizes the stereocenters of the two reactants **I** and **II** to control the introduction of new stereocenters without loss of carbon atoms.[8]

The aldehyde fragment **8**, a *meso*-tartaric acid derivative, was prepared from the furan adduct **1** of (*R*)-glyceraldehyde acetonide.[9] Methyl ether formation then oxidative



furan cleavage[10] and esterification afforded the ester **4**. Hydrolysis of the acetonide led to hydroxy lactone **5** which was benzylated[11] and then subjected to methanolysis and oxidation.[12] Attempted benzylation under basic conditions (BnBr, NaH) led to considerable dehydration of **5**.

The allylstannane component **12** was prepared from enal **9**[13] through addition of Bu_3SnLi[7,14] and protection of the hydroxystannane adduct **10** as the MOM derivative **11**.

• Abstract published in *Advance ACS Abstracts,* October 1, 1993.

(1) Adamczeski, M.; Quinoa, E.; Crews, P. *J. Org. Chem.* **1990**, *55*, 240; *J. Am. Chem. Soc.* **1989**, 111, 647. Quinoa, E.; Adamczeski, M.; Crews, P.; Bakus, G. J. *J. Org. Chem.* **1986**, 51, 4494.

(2) Kishimoto, H.; Ohrui, H.; Meguro, H. *J. Org. Chem.* **1992**, *57*, 5042 (D-glucose as starting material).

(3) Broka, C. A.; Ehrler, J. *Tetrahedron Lett.* **1991**, *32*, 5907 (L-glucose as starting material).

(4) Chida, N.; Tobe, T.; Ogawa, S. *Tetrahedron Lett.* **1991**, *32*, 1063 (L-quebrachitol as starting material).

(5) Chida, N.; Tobe, T.; Okada, S.; Ogawa, S. *J. Chem. Soc., Chem. Commun.* **1992**, 1064 (L-quebrachitol as starting material).

(6) Gurjur, M. K.; Srinvas, N. R. *Tetrahedron Lett.* **1991**, *32*, 3409 (α-D-glucoheptonic γ-lactone as starting material).

(7) Marshall, J. A.; Luke, G. P. *J. Org. Chem.* **1991**, *56*, 483.

(8) For a preliminary account of a portion of this investigation, see: Marshall, J. A.; Luke, G. P. *Synlett* **1992**, 1007.

(9) Suzuki K.; Yuki, Y.; Mukaiyama, T. *Chem. Lett.* **1981**, 1529.

(10) Danishefsky, S. J.; DeNinno, M. P.; Chen, S.-h. *J. Am. Chem. Soc.* **1988**, *110*, 3929.

(11) Iversen, T.; Bundle, D. R. *J. Chem. Soc., Chem. Commun.* **1981**, 1240.

(12) Dess, D. B.; Martin, J. C. *J. Org. Chem.* **1983**, *48*, 4155.

(13) Piers, E.; Jung, G. L.; Ruediger, E. H. *Can. J. Chem.* **1987**, *65*, 670.

(14) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481.

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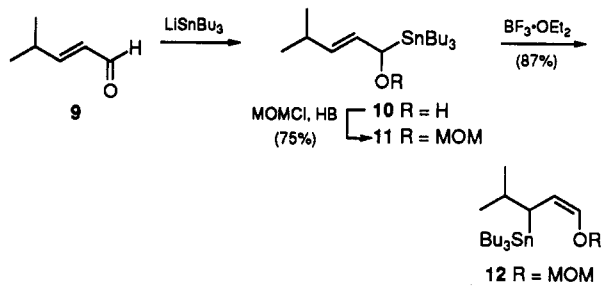
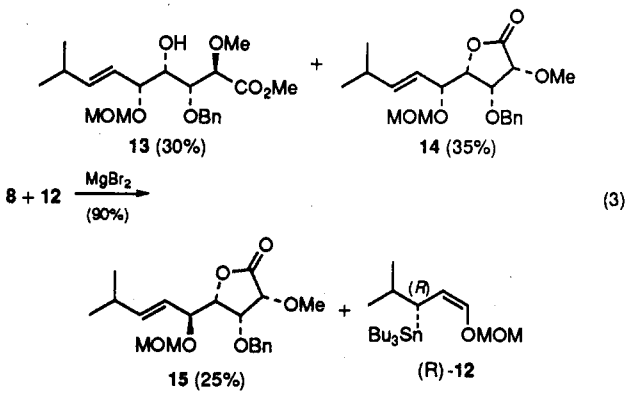
Isomerization to the γ-alkoxy allylic stannane **12** was achieved through treatment with $BF_3{\cdot}OEt_2$.[7,15]

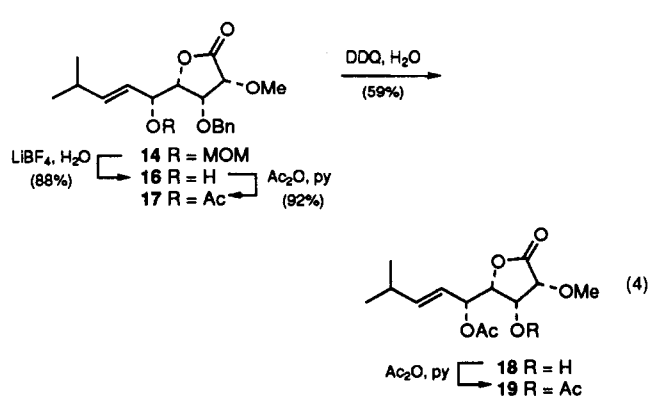


On the basis of our earlier studies with α-alkoxy aldehydes, we expected aldehyde **8** to preferentially react with the (*S*)-enantiomer of stannane **12** in the presence of $MgBr_2$ (chelation-controlled addition).[7] We hoped that the enantiodifferentiation of this reaction would be large enough to allow use of the racemic stannane thus circumventing the need to prepare the (*S*)-enantiomer. Accordingly, aldehyde **8** was treated with 3 equiv of racemic **12** under the aforementioned conditions. Three products



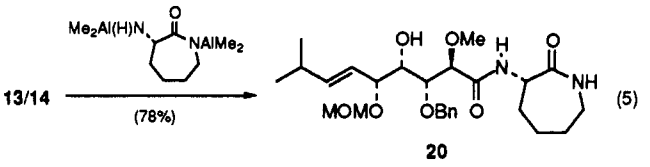
were isolated from this reaction, hydroxy ester **13** and the related lactone **14** (65% yield), the matched products, and lactone **15** (25% yield), the mismatched product derived from the (*R*)-enantiomer of stannane **12**. The recovered stannane **12** was enriched in the (*R*)-enantiomer ($[\alpha]_D$ −18°), as expected. Confirmation of this stereochemistry comes from comparison with (*S*)-**25** ($[\alpha]_D$ +72°), prepared as described below.[16]

The stereochemistry of the major matched adducts **13** and **14** was ascertained by conversion of the latter to the diacetate **19**, a compound previously prepared by Crews from a bengamide degradation product.[1] Comparison of

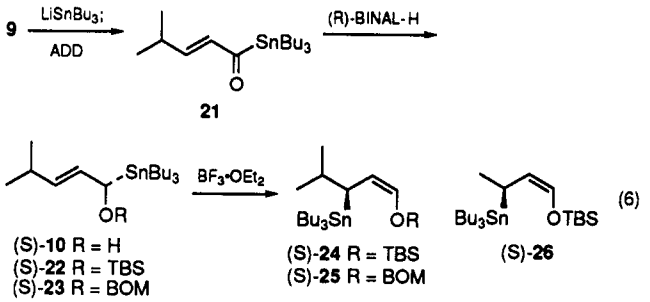


the ^1H NMR spectra confirmed their identity. Diacetate **19** has also been synthesized by Ogawa and co-workers.[4] Our rotation and mp are in good agreement with the reported values. The stereochemistry of the mismatched adduct **15** is assigned by analogy.[7]

Both ester **13** and lactone **14**, or a mixture of the two, readily underwent aminolysis with (*S*)-**2**-aminocaprolactam by Weinreb's procedure[17] to afford the protected bengamide E derivative **20** (eq 5).



At this point we decided to examine several modifications of the foregoing synthetic sequence to improve its efficiency. In view of the relatively low enantioselection of the racemic stannane **12**, we directed our attention to nonracemic (*S*) stannanes. To that end, we prepared the acylstannane **21** through *in situ* oxidation of the adduct of enal **9** and Bu_3SnLi.[15] Reduction with Noyori's (*R*)-BINAL-H reagent[18] and protection as the TBS ether afforded the (*S*)-α-silyloxy compound (*S*)-**22** which yielded the γ-isomer (*S*)-**24** after isomerization with $BF_3{\cdot}OEt_2$ (eq 6). The ee of (*S*)-**24** was estimated to be >90% based on



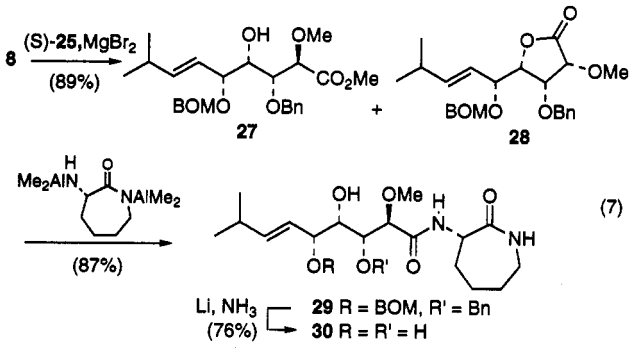
^1H NMR analysis of the *O*-methylmandelate derivatives of alcohol (*S*)-**10**.[15] The TBS ether was selected over MOM in consideration of the greater ease of cleavage in the final product.

We have previously shown that γ-(silyloxy) allylic stannanes undergo efficient $BF_3{\cdot}OEt_2$-promoted S_E' addition to aldehydes.[19] However, stannane (*S*)-**24** failed to react with aldehyde **9** in the presence of $MgBr_2{\cdot}OEt_2$. Attempts to force the issue by prolonging reaction times or raising the temperature caused decomposition of the stannane. Aldehyde **8** also failed to react with the [(silyloxy)butenyl] stannane (*S*)-**26**[19] under comparable conditions. Thus, the silyloxy substituent is the most likely source of the diminished reactivity of stannane (*S*)-**24** compared to the MOM analogue **12**.

Still hoping to simplify the eventual deprotection protocol, we chose the BOM protected γ-alkoxy allylic stannane (*S*)-**25**. This was readily prepared through

(15) Marshall, J. A.; Welmaker, G. S.; Gung, B. W. *J. Am. Chem. Soc.* **1991**, *113*, 647.
(16) (*R*)-γ-OMOM and OBOM allylic stannanes show negative rotations of similar magnitude.[15]
(17) Basha, A; Lipton, M.; Weinreb, S. M. *Tetrahedron Lett.* **1977**, 4171.
(18) Noyori, R.; Tomino, I.; Tanimoto, Y.; Nishigawa, M. *J. Am. Chem. Soc.* **1984**, *106*, 6709.
(19) Marshall, J. A.; Welmaker, G. S. *Synlett* **1992**, 537. Marshall, J. A.; Welmaker, G. S. *Tetrahedron Lett.* **1991**, *32*, 2101. Marshall, J. A.; Welmaker, G. S. *J. Org. Chem.* **1992**, *57*, 7158.

treatment of the (*S*)-α-hydroxy allylic stannane (*S*)-**10** with BOMCl and Hunig's base followed by $BF_3{\cdot}OEt_2$-promoted 1,3-isomerization (eq 6). Addition of stannane (*S*)-**25** to aldehyde **8**, as before, afforded a nearly 1:1 mixture of hydroxy ester **27** and lactone **28** in 89% yield. Subsequent



aminolysis with (*S*)-2-aminocaprolactam followed by debenzylation with Li in NH_3 afforded bengamide E (**30**) in high overall yield. The optical rotation of our synthetic sample (+27°) in methanol was comparable to that reported by Ogawa (+25°)[4] and somewhat lower than that recorded by Crews (+37°)[1] and Ohrui (+34°).[2] However, the ^1H and ^{13}C NMR spectra were in excellent agreement with those of the natural product.

The synthesis of bengamide E in 12 steps from (*R*)-glyceraldehyde acetonide illustrates the potential of nonracemic γ-alkoxy allylic stannanes for elaboration of acyclic polyols. The failure of silyloxy stannanes (*S*)-**24** and (*S*)-**26** to undergo $MgBr_2$-promoted addition to aldehyde **8** is noteworthy.[20] Additional studies to establish relative reactivities of such stannanes are in progress.[21]

Experimental Section[21]

(+)-(2*R*,3*R*)-3-(2-Furyl)-1,2-*O*-isopropylidene-3-methoxypropane (2). To a solution of 1.17 g (5.92 mmol) of alcohol **1**[9] in 12 mL of dry THF at 0 °C under N_2 was added 194 mg (7.69 mmol) of NaH (95%) in one portion. The ice bath was removed, and the reaction was allowed to warm to rt. After 25 min, 0.74 mL (11.8 mmol) of MeI was added to the orange solution. After 25 min, the reaction was quenched by the addition of H_2O and extracted with Et_2O, and the combined extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Elution with 5:1 hexanes–Et_2O afforded 1.09 g (87%) of methyl ether **2**: $[\alpha]_D^{23}$ +48.0° (*c* 2.18, $CHCl_3$); IR (thin film) ν 1092 cm^{-1}; ^1H-NMR (500 MHz, $CDCl_3$) δ 7.41 (dd (apparent t), *J* = 1.3, 1.4 Hz), 6.35 (d, *J* = 1.4 Hz), 4.37 (ddd, *J* = 6.9, 6.2, 5.3 Hz), 4.15 (d, *J* = 6.9 Hz), 4.09, 4.04 (ABX, J_{AB} = 8.6, J_{AX} = 6.2, J_{BX} = 5.3 Hz), 3.25 (s), 1.38 (s), 1.32 (d, *J* = 0.4 Hz) ppm; HRMS (EI) *m/z* 212.1046 (M^+ calcd for $C_{11}H_{16}O_4$ 212.1049). Anal. Calcd for $C_{11}H_{16}O_4$: C, 62.25; H, 7.60. Found: C, 62.13; H, 7.69.

(+)-(2*R*,3*R*) Methyl 3,4-*O*-Isopropylidene-2-methoxybutanoate (4). To a mixture of 67 mL of 3:2:3 CH_3CN–CCl_4–H_2O was added 3.12 g (14.58 mmol) of $NaIO_4$ followed by 65 mg (0.49 mmol) of $RuO_2{\cdot}H_2O$. The resulting mixture was stirred vigorously for 15 min whereupon 10.21 g (121.5 mmol) of $NaHCO_3$ was added in one portion to the light green-yellow mixture. After 10 min, a solution of 516.6 mg (2.43 mmol) of furan **2** in 2 mL of CH_3CN was added. The mixture immediately became black, and small amounts of $NaIO_4$ were added until the mixture turned light green. Once the green color persisted, the mixture was poured into H_2O and extracted with EtOAc. The aqueous layer was acidified with 10% HCl (aq) and reextracted twice with EtOAc. The extracts were washed with saturated $NaHSO_3$ until colorless. The combined extracts were dried over Na_2SO_4 and concentrated to afford 422 mg (91%) of crude acid **3**. The acid was dissolved in ~5 mL of Et_2O and cooled to 0 °C. The solution was treated with an ethereal solution of CH_2N_2 until a slight yellow color persisted. The excess CH_2N_2 was quenched by the addition of a small amount of AcOH. The resulting solution was concentrated, and the crude material was purified by flash chromatography on silica gel. Elution with 1:1 Et_2O–hexanes afforded 342 mg (69%) of ester **4**: $[\alpha]^{21}_D$+14.0° (*c* 2.34, $CHCl_3$); IR (thin film) ν 1749, 1200 cm^{-1}; ^1H-NMR (500 MHz, $CDCl_3$) δ 4.26 (ddd (apparent q), *J* = 6.3, 6.0, 5.0 Hz), 4.02, 3.99 (ABX, J_{AB} = 8.7, J_{AX} = 6.0, J_{BX} = 5.0 Hz), 3.77 (s), 3.76 (d, *J* = 6.3 Hz), 3.40 (s), 1.41 (s), 1.32 (d, *J* = 0.4 Hz) ppm; HRMS (EI) *m/z* 189.0770 [$(M - CH_3)^+$ calcd for $C_8H_{13}O_5$ 189.0763]. Anal. Calcd for $C_9H_{16}O_5$: C, 52.93; H, 7.90. Found: C, 53.07; H, 7.98.

(2*R*,3*R*)-3,4-Dihydroxy-2-methoxybutanoic Acid 1,4-Lactone (5). To a solution of 304 mg (1.49 mmol) of acetonide **4** in 5 mL of 4:1 THF–H_2O at 0 °C was added 1 mL of trifluoroacetic acid (TFA). After being stirred overnight with warming, the reaction mixture was diluted with brine and extracted with EtOAc. The combined extracts were dried over $MgSO_4$ and concentrated. Remaining TFA was removed azeotropically with benzene to afford 210 mg (quantitative) of crude lactone **5**. The material could be further purified by flash chromatography on silica gel. Elution with 1:1 EtOAc–Et_2O followed by 2:1 EtOAc–Et_2O afforded pure lactone **5**. This material was not subjected to high vacuum because of its volatility. ^1H-NMR (500 MHz, $CDCl_3$) δ 4.52 (ddd, *J* = 4.8, 3.3, 1.0 Hz), 4.32, 4.27 (ABX, J_{AB} = 10.5, J_{AX} = 1.0, J_{BX} = 3.3 Hz), 4.02 (d, *J* = 4.8 Hz), 3.67 (s), 2.72 (br) ppm. IR (film) ν 3456, 1790 cm^{-1}.

(−)-(2*R*,3*R*)-3-Benzyloxy-4-hydroxy-2-methoxybutanoic Acid 1,4-Lactone (6). To a solution of 51 mg (0.39 mmol) of β hydroxy lactone **5** in 2.2 mL of 1:1 CH_2Cl_2–cyclohexane at rt under N_2 was added 93 μL of benzyl 2,2,2-trichloroacetimidate followed by 3.4 μL of triflic acid. After 1 h, an additional 45 μL of the acetimidate was added. After another 2 h, the reaction mixture was diluted with ether and washed with water and brine. The aqueous washes were extracted with ether, and the combined extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel . Elution with 4:1 ether–hexanes followed by ether afforded 54 mg (63%) of benzyl ether **6** as a white solid: mp 90–91 °C, $[\alpha]^{24}_D$ −16.7° (*c* 1.44, $CHCl_3$); ^1H-NMR (300 MHz, $CDCl_3$) δ 7.33 (m), 4.72, 4.65 (ABq, *J* = 12.1 Hz), 4.34, 4.20 (ABX, J_{AB} = 10.2, J_{AX} = 1.4, J_{BX} = 3.4 Hz), 4.30 (ddd, *J* = 4.7, 3.4, 1.4 Hz), 4.00 (d, *J* = 4.7 Hz), 3.61 (s) ppm. IR ν 1785 cm^{-1}.

(+)-Methyl (2*R*,3*R*)-3-(Benzyloxy)-4-hydroxy-2-methoxybutanoate (7). To a solution of lactone **6** in MeOH at 0 °C was added a catalytic amount of K_2CO_3. After 25 min, the reaction mixture was poured into water and extracted with CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Elution with 3:1 Et_2O–hexanes afforded hydroxy ester **7**: $[\alpha]^{22}_D$ +28.6° (*c* 1.46, $CHCl_3$); IR (thin film) ν 3477, 1741,1104 cm^{-1}; ^1H-NMR ($CDCl_3$, 500 MHz) δ 7.35–7.26 (m), 4.64, 4.59 (ABq, *J* = 11.6 Hz), 3.98 (d, *J* = 5.1 Hz), 3.79- 3.72 (m), 3.74 (s), 3.41 (s), 1.95 (t, *J* = 6.3 Hz) ppm; HRMS (EI) *m/z* 222.0894 [$(M - CH_3OH)^+$ calcd for $C_{12}H_{14}O_4$ 222.0892]. Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.41; H, 7.13. Found: C, 61.28; H, 7.15.

Methyl (2*R*,3*S*)-3-(Benzyloxy)-4-formyl-2-methoxybutanoate (8). To a solution of 0.418 g (1.64 mmol) of alcohol **7** in 14 mL of dry CH_2Cl_2 at rt under N_2 was added 0.836 g (1.97 mmol) of the Dess–Martin periodinane reagent[12] in one portion. After 10 min, another small amount (~0.1 g) of the periodinane was added. After 25 min, the reaction mixture was diluted with Et_2O and poured into a vigorously stirring mixture of 1.8 g of $Na_2S_2O_3$ in saturated aqueous $NaHCO_3$. After two clear layers had formed (5 min), the layers were separated. The Et_2O extract was washed with saturated aqueous $NaHCO_3$ and water. The

(20) (*Z*)-Bu_3SnCH_2CH=CHOTBS undergoes $MgBr_2$-promoted addition to 2-(benzyloxy)butanal. Keck, G. E.; Abbott, D. E.; Wiley, M. R. *Tetrahedron Lett.* **1987**, *28*, 139.

(21) For typical experimental protocols see ref 15.

aqueous washes were reextracted once with Et_2O and the combined extracts were dried over $MgSO_4$ and concentrated. The crude oil was purified by flash chromatography on silica gel. Elution with 2:1 Et_2O–hexanes afforded 0.353 g (85%) of aldehyde **8**: IR (thin film) ν 1736, 1115 cm^{-1}; ^1H-NMR ($CDCl_3$, 500 MHz) δ 9.59 (d, J = 0.8 Hz), 7.35–7.26 (m), 4.79, 4.70 (ABq, J = 11.9 Hz), 4.19 (d, J = 2.9Hz), 4.12 (dd, J = 2.9, 0.8 Hz), 3.75 (s), 3.45 (s) ppm; HRMS (EI) m/z 223.0970 [(M – CHO)$^+$ calcd for $C_{12}H_{15}O_4$: 223.0970].

(±)-(*E*)-1-(Methoxymethoxy)-4-methyl-1-(tri-*n*-butylstannyl)-2-pentene (11). To a solution of 1.54 mL (11.0 mmol) of *i*-Pr_2NH in 30 mL of dry THF at 0 °C under N_2 was added 4.23 mL of 2.6 M *n*-BuLi in hexanes. After 10 min, 3.05 mL (11.0 mmol) of *n*-Bu_3SnH was slowly added. After another 15 min, the light green-yellow solution was cooled to –78 °C, and a solution of 0.981 g (10.0 mmol) of enal **9**[13] in 1 mL of THF was added dropwise. After 15 min, the reaction was quenched at –78 °C by the addition of dilute aqueous NH_4Cl. The mixture was allowed to warm and was then extracted with Et_2O. The combined extracts were dried over $MgSO_4$ and concentrated to afford hydroxy stannane **10** which was used without further purification. This material was dissolved in 20 mL of CH_2Cl_2 and cooled to 0 °C under N_2. To the solution was added 5.2 mL (30.0 mmol) of *i*-Pr_2NEt followed by 1.14 mL (15.0 mmol) of MOMCl. The reaction was allowed to slowly warm to rt. After 6 h, the reaction mixture was recooled to 0 °C and quenched by the addition of ice cold 5% aqueous HCl. The mixture was extracted with Et_2O, and the extract was washed with additional 5% HCl, water, and saturated aqueous $NaHCO_3$. The aqueous washes were reextracted once with Et_2O, and the combined extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Elution with hexanes, 2.5% ethyl acetate–hexanes, and 5% ethyl acetate–hexanes afforded 3.235 g (75%) of α-alkoxy stannane **11**: IR (thin film) ν 2954, 1017 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 5.49 (ddd, J = 15.4, 7.2, 1.0 Hz), 5.35 (ddd, J = 15.4, 6.3, 1.2 Hz), 4.66, 4.47 (ABq, J = 6.4 Hz), 4.55 (d, J = 7.2 Hz), 3.32 (s), 2.26 (oct, J = 6.7 Hz), 1.57–1.41, 1.35–1.22, 0.92–0.78 (m), 0.95 (d, J = 6.7 Hz) ppm; HRMS (EI) m/z 385.1850 [(M – CH_3OCH_2)$^+$ calcd for $C_{18}H_{37}O^{116}Sn$ 385.1862].

(±)-(*Z*)-1-(Methoxymethoxy)-4-methyl-3-(tri-*n*-butylstannyl)-1-pentene (12). To a solution of 7.745 g (17.88 mmol) of α-alkoxy stannane **11** in 72 mL of dry CH_2Cl_2 at –78 °C under N_2 was added 0.22 mL (1.79 mmol) of BF_3·OEt_2. After 10 min, the –78 °C bath was removed and the reaction mixture was allowed to warm. After being warmed for 25 min, the reaction was judged complete by TLC and was quenched by the addition of saturated aqueous $NaHCO_3$. The resulting mixture was extracted with Et_2O, and the combined extracts were dried over $MgSO_4$ and concentrated. The crude oil was purified by flash chromatography on a short column of silica gel. Elution with hexanes afforded 6.77 g (87%) of γ-alkoxy stannane **12**: IR (thin film) ν 2921, 1649, 1044 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 5.97 (dd, J = 6.2, 0.8 Hz), 4.76, 4.73 (ABq, J = 6.3 Hz), 4.52 (dd, J = 11.8, 6.2 Hz), 3.37 (s), 2.41 (ddd, J = 11.8, 7.6, 0.8 Hz), 1.87 (dsept, J = 7.6, 6.6 Hz), 1.54–1.41, 1.34–1.22, 0.89–0.71 (m), 0.92 (dd, J = 6.6, 3.0 Hz) ppm; HRMS (EI) m/z 385.1854 [(M – CH_3OCH_2)$^+$ calcd for $C_{18}H_{37}O^{116}Sn$ 385.1862]. Anal. Calcd for $C_{20}H_{42}O_2Sn$: C, 55.45; H, 9.77. Found: C, 55.64; H, 9.78.

(2*R*,3*R*,4*S*,5*R*,*E*) Methyl 3-(Benzyloxy)-4-hydroxy-2-methoxy-8-methyl-5-(methoxymethoxy)-6-nonenoate (13), (–)-(2*R*,3*R*,4*S*,5*R*,*E*)-3-(Benzyloxy)-4-hydroxy-2-methoxy-8-methyl-5-(methoxymethoxy)-6-nonenoic Acid 1,4-Lactone (14), and (2*R*,3*R*,4*S*,5*S*,*E*)-3-(Benzyloxy)-4-hydroxy-2-methoxy-8-methyl-5-(methoxymethoxy)-6-nonenoic Acid 1,4-Lactone (15). To a solution of 51 mg (0.20 mmol) of aldehyde **8** in 2.0 mL of dry CH_2Cl_2 under N_2 at –20 °C was added 115 mg (0.446 mmol) of $MgBr_2$·OEt_2 in one portion. After 45 min, a solution of 263 mg (0.608 mmol) of stannane **12** in 0.5 mL of CH_2Cl_2 was added via cannula. The reaction was allowed to warm to rt, and after 48 h, it was quenched by the addition of 4 mL of saturated aqueous $NaHCO_3$. After the mixture had stirred for 2 min, it was diluted with water and extracted with ether, the combined extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Elution from 25 to 35% ethyl acetate–hexanes afforded 68 mg (90%) of a mixture of the following: **13** (30%), **14** (35%), **15** (25%). The mixture was subjected to a second chromatography. "Clean" fractions were collected for ^1H-NMR analysis. ^1H-NMR for **13** ($CDCl_3$, 300 MHz)SPCLN δ 7.33–7.24 (m), 5.65 (dd, J = 15.6, 6.6 Hz), 5.27 (ddd, J = 15.6, 8.7, 1.3 Hz), 4.72, 4.55 (ABq, J = 6.7 Hz), 4.58, 4.52 (ABq, J = 11.2 Hz), 4.13–4.10 (m), 3.80–3.78 (m), 3.70 (s), 3.40 (s), 3.37 (s), 2.77 (d, J = 5.2 Hz), 2.29 (oct d, J = 6.7, 1.3 Hz), 0.97 (d, J = 6.8 Hz), 0.97 (d, J = 6.7 Hz) ppm. Data for **14**: $[\alpha]^{23}_D$–3.9° (*c* 1.82, $CHCl_3$); IR (thin film) ν 1790 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 7.30 (m), 5.80 (dd, J = 15.6, 6.6 Hz), 5.15 (ddd, J = 15.6, 7.6, 1.3 Hz), 4.90, 4.38 (ABq, J = 10.8 Hz), 4.68, 4.58 (ABq, J = 6.7 Hz), 4.44 (dd (apparent t), J = 8.9, 8.2 Hz), 4.20–4.17 (m), 4.12 (d, J = 3.7 Hz), 3.67 (s), 3.36 (s), 2.26 (oct, J = 6.7 Hz), 0.94 (d, J = 6.8 Hz), 0.93 (d, J = 6.8 Hz) ppm; HRMS (EI) m/z 332.1620 [(M – CH_3OH)$^+$ calcd for $C_{19}H_{24}O_5$ 332.1624]. Anal. Calcd for $C_{20}H_{28}O_6$: C, 65.92; H, 7.74. Found: C, 65.82; H, 7.80. ^1H-NMR for **15** ($CDCl_3$, 500 MHz)SPCLN δ 7.36–7.28 (m), 5.72 (dd, J = 15.6, 6.4 Hz), 5.29 (ddd, J = 15.6, 8.8, 1.4 Hz), 4.69, 4.62 (ABq, J = 11.8 Hz), 4.63, 4.43 (ABq, J = 6.8 Hz), 4.45 (m), 4.16 (dd, J = 5.8, 1.9 Hz), 4.13 (d, J = 5.9 Hz), 4.05 (dd, J = 8.8, 3.3 Hz), 3.59 (s), 3.28 (s), 2.30 (oct d, J = 6.7, 1.3 Hz), 0.97 (d, J = 6.8 Hz), 0.96 (d, J = 6.7 Hz) ppm.

(+)-(2*R*,3*R*,4*S*,5*R*,*E*)-3-(Benzyloxy)-4,5-dihydroxy-2-methoxy-8-methyl-6-nonenoic Acid 1,4-Lactone (16). To a solution of 87 mg (0.24 mmol) of MOM ether **14** in 5 mL of 5% H_2O–CH_3CN at rt under N_2 was added 1.2 mL of 1.0 M $LiBF_4$ in CH_3CN. The reaction mixture was then heated to 75 °C for 8 h. After cooling, the reaction mixture was diluted with water and extracted with ethyl acetate. The combined organic extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Elution with 1:1 ethyl acetate–hexanes afforded 67 mg (88%) of **16** as a white solid: mp 107–108 °C; $[\alpha]^{23}_D$+64.3° (*c* 1.60, $CHCl_3$); IR (thin film) ν 3455, 3324, 1790 cm^{-1}; ^1H-NMR ($CDCl_3$, 300 MHz) δ 7.31 (m), 5.80 (ddd, J = 15.6, 6.6, 1.0 Hz), 5.31 (ddd, J = 15.6, 6.8, 1.4 Hz), 4.92, 4.46 (ABq, J = 11.1 Hz), 4.53 (dd (apparent t), J = 7.0, 6.9 Hz), 4.26 (dd, J = 4.4, 3.5 Hz), 4.13 (dd, J = 7.2, 3.4 Hz), 4.10 (d, J = 4.5 Hz), 3.69 (s), 2.57 (brs), 2.25 (oct, J = 6.7 Hz), 0.95 (d, J = 6.8 Hz), 0.94 (d, J = 6.8 Hz) ppm; HRMS (EI) m/z 302.1515 [(M – H_2O)$^+$ calcd for $C_{18}H_{22}O_4$ 302.1518]. Anal. Calcd for $C_{18}H_{24}O_5$: C, 67.48; H, 7.55. Found: C, 67.23; H, 7.64.

(+)-(2*R*,3*R*,4*S*,5*R*,*E*)-5-Acetoxy-3-(benzyloxy)-4-hydroxy-2-methoxy-8-methyl-6-nonenoic Acid 1,4-Lactone (17). To a solution of 25 mg (0.079 mmol) of alcohol **16** in 1 mL of CH_2Cl_2 at rt was added 10 drops of pyridine followed by 5 drops of acetic anhydride. After being stirred overnight at rt, the reaction mixture was concentrated under reduced pressure. The crude material was purified by flash chromatography on silica gel. Elution with 35% ethyl acetate–hexanes afforded 27 mg (94%) of acetate **17** as an oil: $[\alpha]^{25}_D$+17.4° (*c* 1.06, $CHCl_3$); IR (thin film) ν 1790, 1741, 1142 cm^{-1}; ^1H-NMR ($CDCl_3$, 500 MHz) δ 7.31 (m), 5.80 (ddd, J = 15.6, 6.5, 0.8 Hz), 5.61 (dd, J = 8.3, 8.0 Hz), 5.21 (ddd, J = 15.6, 7.1, 1.4 Hz), 4.91, 4.43 (ABq, J = 11.0 Hz), 4.27 (dd, J = 9.1, 3.1 Hz), 4.21 (dd, J = 4.1, 3.1 Hz), 4.11 (d, J = 4.2 Hz), 3.68 (s), 2.21 (oct, J = 6.7 Hz), 2.03 (s), 0.91 (d, J = 6.8 Hz), 0.90 (d, J = 6.8 Hz) ppm; HRMS (EI) m/z 362.1736 (M$^+$, calcd for $C_{20}H_{26}O_6$: 362.1729); Anal. Calcd for $C_{20}H_{26}O_6$: C, 66.28; H, 7.23. Found: C, 66.35; H, 7.25.

(2*R*,3*R*,4*S*,5*R*,*E*)-5-Acetoxy-3,4-dihydroxy-2-methoxy-8-methyl-6-nonenoic Acid 1,4-Lactone (18). To a mixture of 31 mg (0.086 mmol) of benzyl ether **17** in 1.1 mL of 10:1 CH_2Cl_2–H_2O at rt was added 98 mg (0.43 mmol) of DDQ. After 20 h, the reaction mixture was diluted with CH_2Cl_2 and saturated aqueous $NaHCO_3$. The layers were separated and the CH_2Cl_2 extract was washed with saturated aqueous $Na_2S_2O_3$. The aqueous washes were reextracted once with CH_2Cl_2, and the combined extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Elution with 35 to 50% ethyl acetate-hexanes afforded 5.5 mg (24%; 63%, based on recovered **17**) of alcohol **18**. The isolated yield improved with longer reaction time (72 h) (46% yield, 59% based on recovered **17**). Some acetyl transfer (17%) was observed with this longer reaction time. ^1H-NMR (300 MHz, $CDCl_3$)of **18**: δ 5.94 (ddd, J = 15.7, 6.5, 1.0 Hz), 5.67 (dd, J = 9.0, 6.7 Hz), 5.41 (ddd, J = 15.7, 6.7, 1.4 Hz), 4.39 (m), 4.22 (dd, J = 9.0, 2.8 Hz),

4.06 (d, J = 4.5 Hz), 3.67 (s), 2.50 (bs), 2.31 (oct, J = 6.8 Hz), 2.07 (s), 0.98 (d, J = 6.8 Hz) ppm.

(−)-(2*R*,3*R*,4*S*,5*R*,*E*)-3,5-Diacetoxy-4-hydroxy-2-methoxy-8-methyl-6-nonenoic Acid 1,4 Lactone (19). To a solution of 3.5 mg (0.013 mmol) of alcohol 18 in 1.0 mL of dry CH_2Cl_2 at rt was added 10 drops of pyridine followed by 5 drops of Ac_2O. The resulting light yellow solution was allowed to stir overnight whereupon it was concentrated *in vacuo*. The crude material was purified by flash chromatography on silica gel. Elution with 25 to 35% ethyl acetate–hexanes afforded 4.1 mg (quant.) of diacetate 19: $[\alpha]_D$ −40.6°, lit[1] $[\alpha]_D$ −40°; m.p. 171 °C, lit[1] m.p. 178–179 °C; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 5.85 (ddd, J = 15.5, 6.6, 0.7 Hz), 5.63 (dd, J = 4.7, 3.2 Hz), 5.52 (dd(apparent t), J = 8.9, 8.4 Hz), 5.18 (ddd, J = 15.5, 8.3, 1.4 Hz), 4.46 (dd, J = 9.0, 3.2 Hz), 4.08 (d, J = 4.7 Hz), 3.53 (s), 2.26 (oct, J = 6.7 Hz), 2.11 (s), 2.06 (s), 0.94 (d, J = 6.8 Hz), 0.94 (d, J = 6.7 Hz) ppm.

3-(Benzyloxy)-5-(methoxymethoxy)bengamide E (20). To a solution of 73 mg (0.569 mmol) of L-(−)-α-amino-ε-caprolactam in 1.0 mL of dry CH_2Cl_2 at 0 °C under N_2 was added, dropwise, 0.57 mL of 2.0 M Me_3Al in hexane. The ice bath was removed, and the light yellow solution was allowed to stir at rt for 15 min whereupon it was recooled to 0 °C. A solution of 66 mg (0.18 mmol) of a 47:53 mixture of hydroxy ester 13 and lactone 14 in 0.5 mL of CH_2Cl_2 was then added via cannula with the aid of two 0.5 mL rinses. The reaction mixture was allowed to warm to rt and then heated to 45 °C. After heating overnight, all the solvent had evaporated. The residue was redissolved in 2 mL of CH_2Cl_2. The mixture was cooled to 0 °C and carefully diluted with 2–3 mL of saturated aqueous Rochelle's salt solution. The resulting mixture was stirred vigorously for 1 h. The two resulting layers were separated, and the aqueous layer was rextracted twice with CH_2Cl_2. The combined extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Elution with ethyl acetate to 20:1 ethyl acetate–methanol afforded 68 mg (78%) of amide 20: IR (thin film) ν 3379, 1654, 1098 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 500 MHz) δ 7.91 (d, J = 6.1Hz), 7.31–7.21 (m), 6.15 (bt, J = 6.3 Hz), 5.62 (dd, J = 15.6, 6.6 Hz), 5.26 (ddd, J = 15.6, 8.6, 1.2 Hz), 4.73, 4.49 (ABq, J = 11.3 Hz), 4.69, 4.56 (ABq, J = 6.6 Hz), 4.50 (m), 4.16 (dd, J = 8.4, 6.6 Hz), 4.00 (d, J = 3.4 Hz), 3.89 (t, J = 3.5 Hz), 3.79 (m), 3.52 (d, J = 3.4 Hz), 3.45 (s), 3.36 (s), 3.21–3.19 (m), 2.26 (oct, J = 6.7 Hz), 1.97–1.94, 1.83–1.80, 1.50–1.35 (m), 0.94 (d, J = 6.7 Hz), 0.94 (d, J = 6.7 Hz) ppm.

(−)-(1*S*,2*E*)-1-[(Benzyloxy)methoxy]-4-methyl-1-(tri-*n*-butylstannyl)-2-pentene (23). To a solution of 3.9 mL (27.5 mmol) of i-Pr_2NH in 125 mL of dry THF at 0 °C under N_2 was slowly added 11.0 mL of 2.5 M n-BuLi in hexanes. After 10 min, 7.4 mL (27.5 mmol) of Bu_3SnH was slowly added to the LDA solution. After 15 min, the green-yellow Bu_3SnLi solution was cooled to −78 °C and a solution of 2.45 g (25.0 mmol) of enal 9 in 5 mL of THF was slowly added with the aid of two 1.5-mL rinses. After 15 min, 8.20 g (32.5 mmol) of azodicarbonyldipiperidine (ADD) was added in one portion, and the −78 °C bath was replaced by an ice bath. The reaction mixture became dark red-brown in color. After 40 min, the reaction was quenched by the addition of dilute NH_4Cl (aq), and the resulting mixture was extracted with Et_2O. The extract was washed with saturated $NaHCO_3$, and the aqueous washes were rextracted once with ether. The combined extracts were dried over $MgSO_4$ and concentrated at reduced pressure under Ar. The resulting slurry was diluted with hexanes and filtered through a pad of silica gel. The filtrate was concentrated as before to afford the air-sensitive acylstannane 21 as a deep yellow oil which was used immediately without further purification.

Preparation of (*R*)-BINAL-H Reagent. To a solution of 75 mL of 1.0 M LAH in THF in 185 mL of dry THF was slowly added a solution of 3.63 g of dry EtOH in 15 mL of THF over a 30-min period, with the aid of two 2-mL rinses. Next, a solution of 22.56 g of (*R*)-binaphthol in 80 mL of THF was slowly added over 60 min. The resulting milky mixture was heated to reflux for 75 min. The mixture was allowed to cool to rt and was then cooled to −78 °C.

Reduction of Acylstannane 21. A solution of the above acylstannane 21 in 35 mL of dry THF was slowly added to the (*R*)-BINAL-H reagent over 60 min. The resulting yellow reaction mixture was kept at −78 °C overnight. The yellow color slowly faded to a faint greenish-yellow (almost white) color. After a total of 20 h, the reaction mixture was quenched at −78 °C by the addition of 4–5 mL of MeOH. After 15 min, the mixture was diluted with saturated NH_4Cl (aq) and ether and then allowed to warm to rt. The mixture was extracted with ether, and the extract was washed with additional saturated NH_4Cl (aq), H_2O, and brine. The combined aqueous washes were treated with 10% HCl to dissolve the aluminum salts, and the clear aqueous phase was extracted with ether to recover the remaining binaphthol. The combined extracts were dried over $MgSO_4$ and concentrated to a syrup that was triturated twice with hexanes to precipitate the binaphthol (recovery: 22.20 g, 98.4%)). At this point, small samples (~100 mg) of crude hydroxy stannane 10 were removed and converted to the (*R*)- and (*S*)-*O*-methylmandelates to ascertain the ee. The remaining hydroxy stannane 10 was dissolved in 30 mL of dry CH_2Cl_2 and cooled to 0 °C under N_2. To this solution was added 13.1 mL of i-Pr_2NEt followed by 4.2 mL of BOMCl. The mixture was allowed to warm to rt overnight, recooled to 0 °C, and quenched with ice-cold 5% HCl. The mixture was extracted with ether and washed with 5% HCl, H_2O, and saturated $NaHCO_3$. The extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Elution with hexanes followed by 2.5% EtOAc–hexanes afforded 3.92 g (31%) of stannane 23: $[\alpha]^{24}_D$ −62.0° (c 1.24, $CHCl_3$); IR (thin film) ν 1015 cm^{-1}; ^{1}H-NMR (500MHz, $CDCl_3$) δ 7.32, 7.27 (m), 5.51 (ddd, J = 15.4, 7.5, 1.1 Hz), 5.37 (ddd, J = 15.4, 6.6, 1.3 Hz), 4.77, 4.64 (ABq, J = 6.5 Hz), 4.66 (d, J = 7.6 Hz), 4.63, 4.50 (ABq, J = 11.7 Hz), 2.26 (oct, J = 6.7 Hz), 1.53–1.47 (m), 1.32–1.25 (m), 0.95 (d, J = 6.7 Hz), 0.95 (d, J = 6.7 Hz), 0.92–0.89 (m), 0.87 (t, J = 7.3 Hz) ppm; HRMS (EI) m/z 449.1811 [$(M-C_4H_9)^+$ calcd for $C_{22}H_{37}O_2{}^{116}Sn$ 449.1812]. Anal. Calcd for $C_{26}H_{46}O_2Sn$: C, 61.31; H, 9.10. Found: C, 61.33; H, 9.14.

(+)-(*Z*,*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-4-methyl-3-(tri-*n*-butylstannyl)-1-pentene (24). To a solution of crude hydroxy stannane (*S*)-10 (prepared as described above, from 2.45 g (25.0 mmol) of enal 9) in 50 mL of dry CH_2Cl_2 at 0 °C under N_2 was added 13.1 mL of i-Pr_2NEt followed by 6.3 mL of TBSOTf. The mixture was allowed to warm to rt overnight, recooled to 0 °C, and quenched by the addition of ice cold 5% aqueous HCl. The resulting mixture was extracted with ether, and the extract was washed with additional 5% HCl, water, and saturated aqueous $NaHCO_3$. The extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Elution with hexanes followed by 2.5% ethyl acetate–hexanes afforded stannane 24: $[\alpha]^{23}_D$+149.9° (c 1.06, $CHCl_3$); IR (thin film) ν 1093 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 6.02 (dd, J = 5.8, 0.9 Hz), 4.45 (dd, J = 11.6, 5.8 Hz), 2.46 (dd, J = 11.6, 7.6 Hz), 1.84 (oct, J = 7.4 Hz), 1.50–1.40 (m), 1.34–1.22 (m), 0.90 (s), 0.91–0.81 (m), 0.084 (s), 0.077 (s) ppm; HRMS (EI) m/z 500.2816 (M^+ calcd for $C_{24}H_{52}OSi^{116}Sn$ 500.2805). Anal. Calcd for $C_{24}H_{52}OSiSn$: C, 57.26; H, 10.41. Found: C, 57.33; H, 10.46.

(+)-(*Z*,*S*)-1-[(Benzyloxy)methoxy]-4-methyl-3-(tri-*n*-butylstannyl)-1-pentene (25). The isomerization was carried out as described for 12 on 3.91 g (7.68 g) of α-alkoxy stannane 23 affording 3.56 g (91%) of γ-alkoxy stannane 25: $[\alpha]^{24}_D$ +133.7° (c 1.63, $CHCl_3$); IR (thin film) ν 1046 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.33 (m), 6.07 (d, J = 6.2 Hz), 4.88, 4.86 (ABq, J = 6.9 Hz), 4.63, 4.57 (ABq, J = 11.6 Hz), 4.57 (dd, J = 11.8, 6.2 Hz), 2.45 (dd, J = 11.8, 7.5 Hz), 1.89 (dsept, J = 7.5, 6.6 Hz), 1.53–1.42 (m), 1.35–1.23 (m), 0.94 (d, J = 6.6 Hz), 0.94 (d, J = 6.6 Hz), 0.87 (t, J = 7.3 Hz), 0.86–0.81 (m) ppm; HRMS (EI) m/z 449.1806 [$(M - C_4H_9)^+$ calcd for $C_{22}H_{37}O_2{}^{116}Sn$ 449.1811]. Anal. Calcd for $C_{26}H_{46}O_2Sn$: C, 61.31; H, 9.10. Found: C, 61.20; H, 9.05.

(+)-(*Z*,*S*)-1-[(*tert*-Butyldimethylsilyl)oxy]-3-(tri-*n*-butylstannyl)-1-butene (26). Starting from 0.701 g (10 mmol) of crotonaldehyde (*S*)-α-hydroxy stannane of ~87% ee was prepared analogously to (*S*)-10. To a solution of 3.502 g of this crude hydroxy stannane in 20 mL of dry CH_2Cl_2 at 0 °C under N_2 was added 5.23 mL (30.0 mmol) of i-Pr_2NEt followed by 2.53 mL (11.0 mmol) of TBSCl. The reaction mixture was allowed to slowly warm to rt overnight whereupon it was recooled to 0 °C and quenched with ice-cold 5% aqeous HCl. The mixture was extracted with ether, and the extract was washed with additional 5% HCl, water, and saturated aqueous $NaHCO_3$. The

extracts were dried over $MgSO_4$ and concentrated. The crude material was purified by flash chromatography on silica gel. Elution with hexanes followed by 2.5% ethyl acetate–hexanes afforded 1.90 g (40%) of stannane **26**: $[\alpha]^{23}_D$+130.6° (*c* 2.24, $CHCl_3$); IR (thin film) 1077 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 5.95 (dd, J = 5.7, 1.1 Hz), 4.45 (dd, J = 10.9, 5.7 Hz), 2.51 (dd, 10.9, 7.5 Hz), 1.52–1.41 (m), 1.36–1.22 (m), 1.24 (d, J = 7.5 Hz), 0.90 (s), 0.91–0.78 (m), 0.092 (s), 0.083 (s) ppm; HRMS (EI) *m/z* 472.2498 (M^+ calcd for $C_{22}H_{48}OSi^{116}Sn$ 472.2492). Anal. Calcd for $C_{22}H_{48}OSiSn$: C, 55.58; H, 10.18. Found: C, 55.83; H, 10.44.

(−)-(2*R*,3*R*,4*S*,5*R*,*E*) Methyl 3-(Benzyloxy)-5-[(benzyloxy)-methoxy]-4-hydroxy-2-methoxy-8-methyl-6-nonenoate (27) and (−)-(2*R*,3*R*,4*S*,5*R*,*E*)-3-(Benzyloxy)-5-[(benzyloxy)-methoxy]-4-hydroxy-2-methoxy-8-methyl-6-nonenecarboxylic Acid 1,4-Lactone (28). To a solution of 190 mg (0.753 mmol) of aldehyde **8** in 7.5 mL of dry CH_2Cl_2 at −20 °C under N_2 was added 428 mg (1.66 mmol) of $MgBr_2{\cdot}OEt_2$ in one portion. After 45 min, a solution of 457 mg (0.897 mmol) of stannane (*S*)-**25** in 0.5 mL of CH_2Cl_2 was added via cannula with the aid of two 0.5-mL rinses. Cooling was maintained for 2 h, and then the reaction mixture was allowed to slowly warm to rt. After a total of 6 h, 1 mL of MeOH was added, and then 30 min later water was added, and the resulting mixture was stirred vigorously for 1 h. The mixture was processed as described for **13–15** to yield 645 mg of crude material. This material was partially purified by flash chromatography on silica gel. After elution with 1:1 ether-hexanes followed by 2:1 ether–hexanes, all fractions containing **27** and **28** were combined and concentrated to 356 mg (96%) of semipure material. This material was rechromatographed in a similar manner affording 308 mg (89%) of a 1.2:1 mixture of hydroxy ester **27** and lactone **28**. "Clean" fractions of pure **27** and pure **28** were collected for analysis.

27: $[\alpha]^{24}_D$ −42° (*c* 2.5, $CHCl_3$); IR (thin film) ν 3539, 1744, 1113, 1026 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.32–7.26 (m), 5.66 (dd, J = 15.6, 6.6 Hz), 5.28 (ddd, J = 15.6, 8.8, 1.2 Hz), 4.81, 4.73 (ABq, J = 6.8 Hz), 4.73, 4.51 (ABq, J = 11.7 Hz), 4.58, 4.53 (ABq, J = 11.2 Hz), 4.23 (dd, J = 8.5, 7.5 Hz), 4.13 (d, J = 6.8 Hz), 3.81 (m), 3.71 (s), 3.39 (s), 2.73 (br), 2.29 (oct, J = 6.7 Hz), 0.96 (d, J = 6.8 Hz) ppm; HRMS (positive ion FAB) *m/z* 495.2345 [(M + Na)$^+$ calcd for $C_{27}H_{36}O_7Na$ 495.2359].

28: $[\alpha]^{24}_D$−24.8° (*c* 1.20, $CHCl_3$); IR (thin film) ν 1790, 1144, 1026 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.33, 7.30 (m), 5.80 (ddd, J = 15.6, 6.6, 0.7 Hz), 5.17 (ddd, J = 15.6, 7.6, 1.4 Hz), 4.92, 4.39 (ABq, J = 10.9 Hz), 4.77, 4.73 (ABq, J = 7.4 Hz), 4.74, 4.52 (ABq, J = 11.5 Hz), 4.58 (t, J = 8.2 Hz), 4.21 (m), 4.13 (d, J = 3.9 Hz), 3.69 (s), 2.24 (oct, J = 6.8 Hz), 0.93 (d, J = 6.8 Hz), 0.92 (d, J = 6.8 Hz) ppm; HRMS (EI) *m/z* 440.2182 (M^+ calcd for $C_{26}H_{32}O_6$ 440.2199).

(−)-7-(Benzyloxy)-5-[(benzyloxy)methoxy]bengamide E (29). The procedure described for **20** was followed with 161 mg (1.26 mmol) of L-(−)-α-amino-ε-caprolactam, 1.26 mL of 2.0 M Me_3Al in hexanes, and 154 mg of a 1.2:1 mixture of **27** and **28**. The crude product was purified by flash chromatography on silica gel. Elution with ethyl acetate followed by 1:20 MeOH–ethyl acetate afforded 23 mg of recovered **27** + **28** and 142 mg (73%) of amide **29** (87%, based on recovered material): $[\alpha]^{23}_D$−8.9° (*c* 1.40, $CHCl_3$); IR (thin film) ν 3374, 3313, 1651, 1102, 1030 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.91 (d, J = 6.1 Hz), 7.32–7.25 (m), 6.12 (brt), 5.62 (dd, J = 15.6, 6.6 Hz), 5.27 (ddd, J = 15.6, 8.6, 1.2 Hz), 4.79, 4.74 (ABq, J = 6.7 Hz), 4.73, 4.50 (ABq, J = 11.3 Hz), 4.73, 4.51 (ABq, J = 11.8 Hz), 4.51 (m), 4.26 (dd, J = 8.4, 6.8 Hz), 4.01 (d, J = 3.5 Hz), 3.91 (t, J = 3.3 Hz), 3.82 (dd, J = 6.7, 3.2 Hz), 3.42 (s), 3.20 (m), 2.26 (oct, J = 6.8 Hz), 2.03–1.93 (m), 1.81 (m), 1.47–1.30 (m), 0.93 (d, J = 6.8 Hz) ppm; HRMS (positive ion FAB) *m/z* 591.3035 [(M + Na)$^+$ calcd for $C_{32}H_{44}O_7N_2$Na 591.3046].

Bengamide E (30). A solution of 136 mg (0.239 mmol) of amide **29** in 3 mL of dry THF was cooled to −78 °C under Ar. Next, ~10 mL of NH_3 was condensed in the reaction flask. To the resulting colorless mixture was added a small piece (~5 mg) of Li metal (rinsed with hexanes, cleaned with MeOH, and rinsed again with hexanes). The Li slowly dissolved, but no blue color persisted. Another small piece of Li metal was added, and almost immediately a blue color appeared and persisted. After 30 min, the reaction was quenched at −78 °C by the addition of small amounts of solid NH_4Cl until the mixture became colorless. The mixture was then allowed to warm while the solvents were removed under a stream of Ar. To the residue was added a few drops of water and 3 mL of saturated aqueous NH_4Cl. This mixture was then extracted with CH_2Cl_2 followed by ethyl acetate. The combined extracts were dried over $MgSO_4$ and concentrated affording 78 mg of crude material that was purified by flash chromatography on silica gel. Elution with 1:10 MeOH–$CHCl_3$ afforded 65.1 mg (76%) of bengamide E as a colorless, viscous oil: $[\alpha]^{21}_D$+75.6° (*c* 1.14, $CHCl_3$), $[\alpha]^{22}_D$+27.1° (*c* 1.55, MeOH) [lit.[1] $[\alpha]^{20}_D$+36.9° (*c* 4.3 × 10^{-2}, MeOH)]; IR (thin film) ν 3600–3200, 1668, 1639, 1109 cm^{-1}; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.96 (d, J = 6.4 Hz), 6.37 (brt), 5.76 (ddd, J = 15.5, 6.4, 0.6 Hz), 5.42 (ddd, J = 15.5, 7.2, 1.3 Hz), 4.52 (dd, J = 9.9, 6.4 Hz), 4.20 (dd, J = 6.5, 6.0 Hz), 3.79 (m), 3.78 (m), 3.57 (dd, J = 5.4, 1.1 Hz), 3.51 (s), 3.26 (m), 2.29 (oct d, J = 6.6, 1.0 Hz), 2.05, 2.01 (m), 1.88, 1.82, 1.77 (m), 1.61–1.38 (m), 0.97 (d, J = 6.8 Hz), 0.97 (d, J = 6.8 Hz) ppm; ^{13}C-NMR (500 MHz, $CDCl_3$) δ 175.5, 172.3, 142.1, 125.8, 81.7, 74.6, 73.0, 72.9, 60.1, 52.4, 42.4, 31.4, 31.2, 29.2, 28.4, 22.6, 22.5 ppm; HRMS (FAB) *m/z* 359.2172 [(M + H)$^+$ calcd for $C_{17}H_{31}O_6N_2$ 359.2182].

Acknowledgment. This research was supported by research grant R01-AI 31422 from the National Institute of Allergy and Infectious Diseases. We thank Professor Phillip Crews for providing spectral data and other useful information.

Supplementary Material Available: ^{1}H NMR spectra of new compounds (28 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.