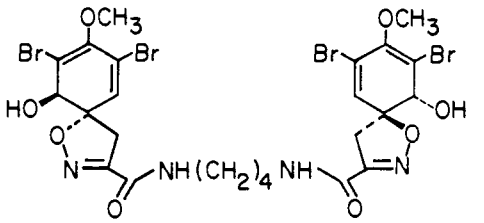
dried and triturated sequentially to provide hexane- and methanol-soluble portions. The hexane extract was more heavily labeled than the methanol extract by sodium acetate and methionine (presumably in sterols), but the reverse was true for Tyr and Phe which gave the brominated metabolites (Table I). Approximately 0.5% of the sponges' wet weight was recovered in the methanolic extract and, of this, one-third[15] corresponded to the antimicrobial[16] metabolite **3**. The dienone **3** was easily isolated as the solid, recrystallized from methanol and characterized.[17] The structures of other brominated metabolites (**1**, **2**, **4**–**6**) found in the methanol extract were assigned by comparison of TLC, HPLC, MS, and GC/MS parameters of the mixture relative to those of synthetically prepared compounds.[3b,18] The methanol extract was fractionated chromatographically (silica TLC followed by reversed-phase $C_{18}$ HPLC) to afford small amounts of radiochemically pure **4**.

Both Phe and Tyr were shown to be biosynthetic precursors of **3** (Table I), implying the ready conversion of Phe to Tyr[19] by the sponge. Improved incorporation of Tyr in the liposome feeding experiment (relative to that without liposomes) argues that this technique should prove valuable in future marine biosynthetic studies, particularly for the introduction of less polar precursors. The presence of comparable radioactivity in **3** and **4** agrees with our previous hypothesis[20] that **4** is formed from **3** via a skeletal rearrangement parallel to that observed in the mammalian biosynthesis of homogentisic acid. Although the enzymatic mechanism of the side-chain migration to form homogentisic acid is still unclear,[21] the conversion of 4-hydroxy-2,5-cyclohexadienone-4-acetic acid to homogentisic acid in aqueous alkali has been demonstrated.[22]

Crystalline **3**, isolated from sponges incubated with a mixture of [$^{15}$N]Phe and [U-$^{14}$C]Phe, was digested by the Kjeldahl procedure, and the resulting ammonium chloride was oxidized to nitrogen gas for $^{15}$N quantitation by isotope ratio mass spectrometry.[23] Table I summarizes the incorporation results. Although partial transamination of the amino acid (ca. $^2/_3$) is apparent, the observed retention of $^{15}$N relative to $^{14}$C indicates that the sponge can convert the alanine to the acetamide side chain without deamination. The biosynthetic pathway in Scheme I is consistent with our labeling studies as well as the known occurrence of bromophenol nitriles and oximes in *Verongia* species.[24] The isolation of (*p*-hydroxyphenyl)pyruvic acid oxime[25] from *Hymeniacidon sanguinea* and aerothionin (**7**)[26] from *Aplysina fistularis* supports the proposed mechanism. The intermediacy of compound **3** is currently being investigated with purified material from the $^{15}$N/$^{14}$C labeling experiment.[27,28]




7

**Acknowledgment.** Field work carried out at the Santa Catalina Marine Science Center was supported in part by the Institute of Marine and Coastal Studies and the Marine and Freshwater Biomedical Center, both at the University of Southern California. Chemical studies at the University of Illinois were supported in part by grants from the National Institute of Allergy and Infectious Diseases (AI 04769, AI 01278) and the National Institute of General Medical Sciences (GM 27029). We thank Dr. W. O. McClure, University of Southern California, and Dr. C. J. Pearce, University of Illinois, for liquid scintillation counting and gas chromatography of sponge extracts, J. C. Cook, Jr., University of Illinois, and Dr. L. Dunkerton, University of Southern California, for mass spectra, Dr. T. Kurtz, University of Illinois, for isotope ratio measurements, and Dr. R. Given, Catalina Marine Science Center, for assistance with sponge collection and identification.

(15) The amount of **3** in each methanolic extract was determined by TLC purification (silica, 4:1 $CHCl_3$–MeOH) to give a mixture of **3** and **4**, followed by UV quantitation of both compounds in methanol [**3**: $\lambda_{max}$ 255 nm (6500). **4**: $\lambda_{max}$ 222 nm (5400)].

(16) The crude extract (1:3 toluene/methanol) of the sponge was tested for antimicrobial activity by the disk method (100 μL/disk): *Bacillus subtilis* (18 mm); *Escherichia coli* (13 mm). Purified **3** was tested at 100 μg/disk: *B. subtilis* (35 mm); *E. coli* (33 mm).

(17) Physical data obtained for **3** [mp 190–191 °C; IR (Nujol) 3420, 3125, 2700, 2660, 1650 cm$^{-1}$; MS (EI), *m/z* 323, 306, 278, 264, 244, 227, 199, 185; $^1$H NMR ($CD_3COCD_3$) 7.59 (2 H), 2.97 (3 H), 2.75 (2 H) ppm; $^{13}$C NMR ($CD_3OD$) 174.5, 173, 153.2 (2 C), 121.5 (2 C), 72.8, 46.0 ppm] and its acetate [mp 168–171 °C; $^1$H NMR ($CD_3COCD_3$) 7.75 (2 H), 2.9 (4 H), 2.08 (3 H) ppm] were in agreement with values published for a synthetic sample (Sharma, G. M.; Burkholder, P. R. *Tetrahedron Lett.* **1967**, 4147–4150).

(18) Goo, Y. M. Ph.D. Thesis, University of Illinois, Urbana, IL, 1980.

(19) Weiss, U.; Edwards, J. M. "The Biosynthesis of Aromatic Compounds"; Wiley: New York, 1980; p 144.

(20) Krejcarek, G. E.; White, R. H.; Hager, L. P.; McClure, W. O.; Johnson, R. D.; Rinehart, K. L., Jr.; McMillan, J. A.; Paul, I. C.; Shaw, P. D.; Brusca, R. C. *Tetrahedron Lett.* **1975**, 507–510.

(21) Nozaki, M. *Top. Curr. Chem.* **1979**, *78*, 145–186.

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(24) Minale, L. *Pure Appl. Chem.* **1976**, *48*, 7–23.

(25) Cimino, G.; DeStefano, S.; Minale, L. *Experientia* **1975**, *31*, 756–757.

(26) McMillan, J. A.; Paul, I. C.; Goo, Y. M.; Rinehart, K. L., Jr.; Krueger, W. C.; Pschigoda, L. M. *Tetrahedron Lett.* **1981**, 39–42.

(27) We presume **3** (or the related acid or nitrile) is also the precursor for the brominated quinones and hydroquinones **5** and **6**, as shown in Scheme I, though that has not yet been demonstrated.

(28) The enzymes involved may be rather nonspecific and complementary pathways may also exist, involving, e.g., bromination of (*p*-hydroxyphenyl)-acetonitrile, oxidation of Tyr to its oxime, or oxidation of the nitrile analogue of **2** to the corresponding dienone.

## Stereospecific Conversion of Penicillin to Thienamycin

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The control of absolute stereochemistry is a critical problem in the synthesis of chiral molecules. A convenient access to chirality is the stereocontrolled modification of suitable natural products. In this paper, we wish to report a stereospecific synthesis of the potent antibiotic thienamycin[1] (**9**) from readily available 6-aminopenicillanic acid (**1**).

The strategy employed to transform the stereochemistry of penicillin, 5*R*, 6*R*, to that of thienamycin, 5*R*, 6*S*, 8*R*, takes advantage of the strong preference of β-lactam systems for trans substitution. Thus, replacement of the penicillin 6-nitrogen with acetyl (**1** → **2**) and reduction of the chelated *trans*-ketone from the β side (**2** → **3**) set the stereochemistry at C-8 and C-6 as *R* and *S*. Degradation of the thiazolidine ring to **5d** followed by trans substitution of the corresponding immonium intermediate established the remaining center C-5 as *R*. Noteworthy features of this synthesis are the stereospecific amine–borane reduction of ketone **2** and use of a novel β-carbene-anion equivalent for annelation.

(1) For previous synthesis, see: (a) Melillo, D. G.; Shinkai, I.; Liu, T.; Ryan, K.; Sletzinger, M. *Tetrahedron Lett.* **1980**, 2783. (b) Saltzman, T. N.; Ratcliffe, R.; Christensen, B. G.; Bouffard, F. A. *J. Am. Chem. Soc.* **1980**, *102*, 6161. (c) Johnston, D. B. R.; Schmitt, S. M.; Bouffard, F. A.; Christensen, B. G. *Ibid.* **1978**, *100*, 313. Kametami, T.; Huang, S.-P.; Suzuki, J.; Yokohama, S.; Shara, M. *Heterocycles* **1979**, *12*, 1301.

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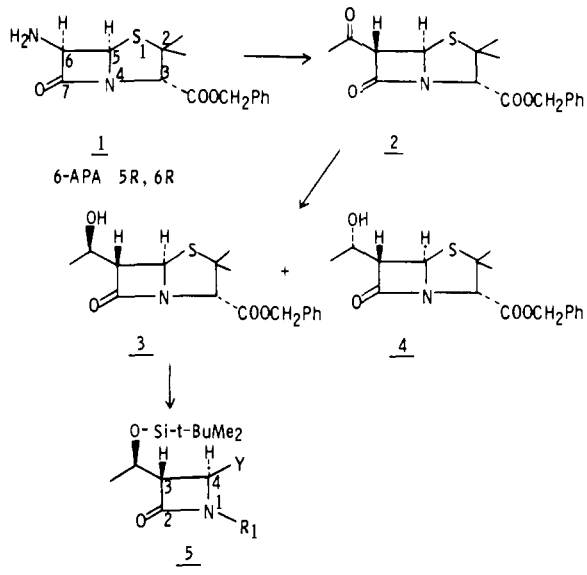


a) Y = S-CH$_2$COOMe, R$_1$ = C(CH$_3$)(CH$_3$)COOCH$_2$Ph

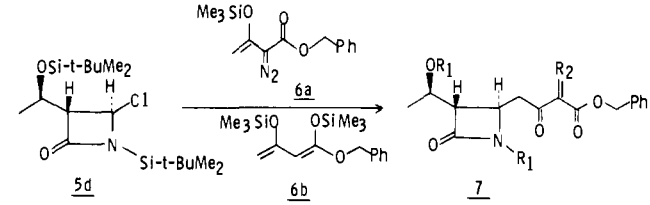
b) Y = SCH$_2$COOMe, R$_1$ = H

c) Y = SCH$_2$COOMe, R$_1$ = Si-t-BuMe$_2$

d) Y = Cl, R$_1$ = Si-t-BuMe$_2$

The reaction of benzyl 6-diazopenicillanate[2] in $CH_2Cl_2$ with excess acetaldehyde and a catalytic amount of $ZnCl_2$ at 10 °C followed by extraction with aqueous $H_3PO_4$ afforded benzyl 6-acetylpenicillanate[3,4] (**2**) in 70% yield. This ketone is of limited stability at room temperature (half-life at room temperature ca. 5 h) but could be stored at −78 °C in dry methylene chloride solution overnight without decomposition. Reduction of the magnesium chelate of **2**, formed with fivefold excess of magnesium trifluoroacetate in ether, with 2 equiv of diisopropylamine–borane[5] at 0 °C for 75 min yielded the *RSR* and *SSR* alcohols[6] **3** and **4** in a ratio of 96:4 in 55% yield, overall from 6-APA (**1**). Following protection of the hydroxy group of **3** by silylation, the thiazolidine ring was opened by treatment with methyl bromoacetate and *t*-BuOK in THF at room temperature for 4 h[7] to afford **5a** in 50% yield. Permanganate oxidation in pyridine and water[8] (25 °C, 4 h) gave β-lactam **5b** which was converted to **5d** with *t*-BuMe$_2$SiCl and TEA in DMF (25 °C, 4 h) followed by chlorinolysis with $Cl_2$ in $CCl_4$[9] (**5a** → **5d**, 57% yield).

Diazo synthon **6a** was prepared from benzyl 2-diazoacetoacetate[10] by silylation with lithium hexamethyldisilazide, $Me_3SiCl$, and tetramethylethylenediamine in THF at −78 °C, followed by warming to 0 °C, precipitating with hexane, and concentrating the filtrate in vacuo. The diazo group is a carbene precursor and, in addition, directs enolization of the carbonyl to form a terminal enol silane, which is a C-4 carbanion equivalent. Annelation of the β-lactam (**5d**) with this reagent was performed in three steps (**5d** → **7b** → **8**). The crucial silver-mediated coupling reaction

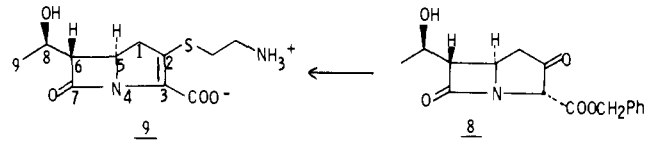


a) R$_1$ = Si-t-BuMe$_2$; R$_2$ = N$_2$

b) R$_1$ = H; R$_2$ = N$_2$

c) R$_1$ = Si-t-BuMe$_2$; R$_2$ = H$_2$

d) R$_1$ = H; R$_2$ = H$_2$



Thienamycin, 5R, 6S, 8R

of **5d** and **6a** to afford **7a** was carried out in the following manner: an ice cold solution of **5d** and **6a** (50% excess) was treated with a solution of 1 equiv of $AgBF_4$ in acetonitrile. After 2 h of reaction time at room temperature, filtration and partitioning of the filtrate with ethyl acetate and saturated NaCl solution, **7a** was obtained as a single product in 70% yield. Desilylation of this material with MeOH, $H_2O$, and concentrated HCl (90:10:2) at room temperature for 24 h afforded **7b**. An alternative route to **7b** utilized an acetoacetate dianion equivalent **6b**, analogous to the reagents of Chan[11] and Danishefsky.[12] Coupling of **5d** and **6b**, using reaction conditions described above, afforded **7c** as a single isomer in 65% yield. The trans substitution of the β-lactam was apparent from the $H_3$–$H_4$ vicinal coupling constant of 2.8 Hz. After desilylation (**7c** → **7d**), the diazo group was introduced by an ex-

(2) Sheehan, J. C.; Lo, Y. S.; *J. Org. Chem.* **1973**, *38*, 3227.

(3) Sheehan, J. C.; Chacko, E.; Lo, Y. S.; Ponzi, D. R.; Sato, E. *J. Org. Chem.* **1978**, *43*, 4856.

(4) None of the intermediates in this synthesis were crystalline. Consequently purification was affected by rapid chromatography. NMR spectra were recorded on the following spectrometers: $^1H$, 60 MHz, Perkin Elmer R-24A; $^1H$, 100 MHz, Varian XL-100; $^{13}C$, Varian CFT-20. Satisfactory spectral data (NMR, IR, and mass) were obtained on the intermediates. Diagnostic data are summarized as follows. **3**: $^1H$ NMR (acetone-$d_6$, 100 MHz) δ 1.28 (d, 3 H, $J$ = 6 Hz, CHC$H_3$), 1.41 and 1.61 (2 s, 3 H, $CH_3$), 3.26 (dd, 1 H, $J$ = 7 and 1.8 Hz, $C_6H$), 4.20 (m, 1 H, $C_8H$), 4.49 (s, 1 H, $C_3H$), 5.24 (s, 2 H, $OCH_2$), 5.33 (d, 1 H, $J$ = 1.8 Hz, $C_5$–H), 7.45 (m, 5 H, Ph). **5a**: $^1H$ NMR ($CDCl_3$, 60 MHz) δ 1.35 (d, 3 H, $J$ = 6 Hz, $CH_3$CHO), 2.05 and 2.35 (2s, 3 H, $CH_3$), 3.15 (m, 1 H, $C_3H$), 3.25 (s, 2 H, $SCH_2$), 3.75 (s, 3 H, $OCH_3$), 4.2 (m, 1 H, CHO), 5.2 (m, 3 H, O$CH_2$, $C_4H$). **5d**: $^1H$ NMR ($CDCl_3$, 60 MHz) δ 1.2 (d, 3 H, $J$ = 6 Hz, C$H_3$CHO), 3.3 (m, 1 H, $C_3H$), 4.1 (m, 1 H, $CH_3$CHO), 5.5 (d, 1 H, $J$ = 2 Hz, $C_4H$). **6a**: $^1H$ NMR ($CDCl_3$, 60 MHz) δ 0.3 (s, 9 H, SiMe), 4.2 and 5.0 (2 d, 1 H, $J$ = 2 Hz, =$CH_2$), 5.2 (s, 2 H, C$H_2$Ph), 7.3 (s, 5 H, Ph). **6b**: $^1H$ NMR ($CDCl_3$, 60 MHz) δ 0.125 (2 s, 9 H, $SiCH_3$), 4.05 and 4.18 (2 d, 1 H, $J$ = 1.5 Hz, $CH_2$=), 4.5 (s, 1 H). **7c**: $^1H$ NMR ($CDCl_3$, 100 MHz) δ 1.15 (d, 3 H, $J$ = 6.3 Hz, $CH_3$), 2.8 (dd, 1 H, $J$ = 4.5 and 2.5 Hz, $C_3H$), centered at 2.9 (*ABX*, 2 H, $J$ = 16.9, 8.2, and 4.7 Hz, $C_4CH_2$), 3.49 (s, 2 H, $CH_2CO$), 4.00 (m, 1 H, $C_4H$), 4.15 (qd, 1 H, $J$ = 6.3 and 4.4 Hz, CHOH); $^{13}C$ NMR ($CDCl_3$, internal $Me_4Si$ $\delta_c$ 22.2 ($CH_3CO$), 47.3 ($C_4$), 48.7 and 49.7 ($CH_2CO$ and $C_4CH_2$), 65.5 ($C_3$ and $CH_3CHO$), 67.1 ($OCH_2$-Ph), 172.6 ($C_2$), 199.3 ($CH_2CO$). **7b**: mp 152–153 °C dec; $^1H$ NMR ($CDCl_3$, 60 MHz) δ 1.33 (d, 3 H, $J$ = 6.3 Hz, $CH_3$), 2.04 (br, 1 H, OH), 2.88 (dd, 1 H, $J$ = 1.8 and 7.3 Hz, $C_3H$), centered at 3.31 (*ABX*, 2 H, $J$ = 7.2, 6.1, and 18.3 Hz, $C_4CH_2$), 3.97 (AB*X*, $J$ = 1.9 and 6.3, $C_4H$), 4.17 (dq, 1 H, $J$ = 6.3, CHO), 5.28 (s, 2 H, COOC$H_2$Ph), 5.95 (br, 1 H, NH) and 7.38 (s, 5 H, Ph). **8**: mp 177–179 °C; $^1H$ NMR ($CDCl_3$, 60 MHz) δ 1.39 (d, 3 H, $J$ = 6.2 Hz, $CH_3$), 1.80 (br s, 1 H, OH), centered at 2.68 (*ABX*, 2 H, $J$ = 6.8, 7.6, and 18.9 Hz, $C_1H_2$), 3.17 (dd, 1 H, $J$ = 1.9 and 7.2 Hz, $C_6H$), 4.14 (AB*X*, 1 H, $J$ = 1.9 and 7.3 Hz, $C_5H$), 4.31 (dq, $J$ = 6.2 and 7.2 Hz, –CHO–), 4.72 (s, 1 H, $C_3H$), 5.21 (s, 2 H, COOC$H_2$Ph), and 7.36 (s, 5 H, Ph).

(5) Purchased from the Callery Chem. Co., Callery, PA. For reduction of ketones by amine–boranes, see: Jones, W. M. *J. Am. Chem. Soc.* **1960**, *82*, 2528. The anhydrous $Hg(CF_3COO)_2$·$CF_3COOH$ was prepared by dissolving powdered magnesium in anhydrous TFA (an exothermic reaction!) followed by removal of excess TFA in vacuo.

(6) These compounds were first produced by a nonstereospecific method. Chromatographic separation of the diastereomers by the method of: DiNinno, F.; Beattie, T. R.; Christensen, B. G. *J. Org. Chem.* **1977**, *42*, 2960. We thank Dr. DiNinno for a sample of **3**.

(7) Brain, E. G.; McMillan, I.; Nayler, J. H. C.; Southgate, R.; Tolliday, P. *J. Chem. Soc., Perkin Trans. 1* **1975**, 562.

(8) Brain, E. G.; Elington, A. J.; Nayler, J. H. C.; Pearson, M. J.; Southgate, R. *J. Chem. Soc., Perkin Trans. 1* **1976**, 447.

(9) Kukolja, S. *J. Am. Chem. Soc.* **1971**, *93*, 6267.

(10) Prepared with 2-naphthylsulfonyl azide by the procedure of ref 13. Benzyl 2-diazoacetoacetate exhibits a strongly exothermic reaction at 90–100 °C on thermal analysis, but it is not overly sensitive to impact. This material should be handled carefully.

(11) Chan, T.; Brownbridg, P. *J. Am. Chem. Soc.* **1980**, *102*, 3534. We thank Professor Chan for a detailed procedure for the preparation of the analogous methyl ester. In our case, LiHMDS and $Me_3SiCl$ were used and the procedure had to be repeated twice to complete the formation of **6b**. On attempted distillation, O to C silyl rearrangement took place.

(12) Danishefsky, S.; Singh, R.; Gammill, R. B.; *J. Org. Chem.* **1978**, *43*, 380.

change reaction with 2-naphthylsulfonyl azide[13] to afford **7b**, identical in all respects with the sample obtained by the direct route described above. Ring closure via carbenoid insertion of **7b**, according to the published procedure,[14] in the presence of $Rh_2(OAc)_4$ afforded the bicyclic keto ester (**8**) in good yield. This was found to be identical with a sample prepared by Shinkai et al.[15] which they had previously converted to thienamycin (**9**).[16]

The key features of this synthesis are brevity, inexpensive starting material, and virtually complete stereospecificity. In addition, this transformation formally interrelates the stereochemistry of these two important antibiotics. Thus, more than half a century after its discovery penicillin proves to be a practical source of another new highly potent antibiotic.

**Acknowledgment.** We thank Drs. F. P. DiNinno, I. Shinkai, M. Sletzinger, S. H. Pines, and Professors S. Danishefsky and J. Schwartz for stimulating discussions.

(13) Hazen, G. G.; Weinstock, L. M.; Connell, R.; Bollinger, F. W. *Synth. Commun.*, submitted for publication.
(14) Ratcliffe, R. W.; Saltzmann, T. N.; Christensen, G. B. *Tetrahedron Lett.* **1980**, 31.
(15) We thank Dr. Shinkai for the comparison sample of **8** and for the procedures of the last two steps. He informed us that this sample was prepared and converted to thienamycin by an identical procedure which they have reported for the corresponding *p*-nitrobenzyl esters.[16]
(16) Sletzinger, M.; Liu, T.; Reamer, R. A.; Shinkai, I. *Tetrahedron Lett.* **1980**, *21*, 4221.

## Internal Reactions of Tetraalkylstannanes with Carbon-Centered Electrophiles

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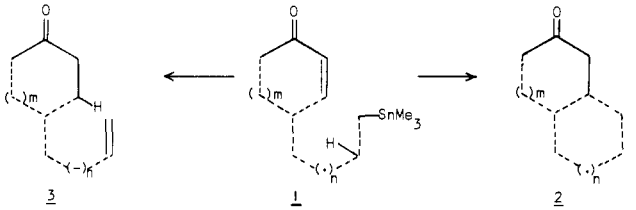
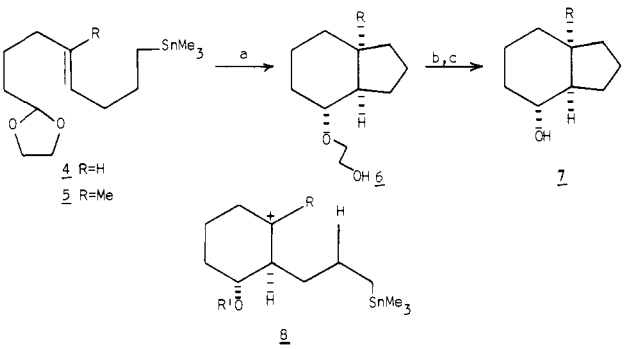
We recently uncovered a method for effecting intramolecular conjugate addition to $\alpha$-enones of unactivated carbon nucleophiles which proceeds through the mediation of novel alkyltin(IV) chemistry (e.g., **1** → **2**).[1] This approach to carbocyclization represents the first general method for internal conjugate addition to $\alpha$-enones of unactivated carbon nucleophiles,[2] a central reaction type in intermolecular carbon-carbon bond formation, and illustrates the use of the carbon-tin $\sigma$ bond as a latent carbanionic nucleophile.[3] The method employs activation of the $\alpha$-enone moiety with Lewis acids to engender a $\beta$-electrophilic site (e.g., an oxy-substituted allyl carbocation) which is sufficiently potent to react with a stereoproximate carbon-tin $\sigma$ bond.




†Research Fellow of the Alfred P. Sloan Foundation (1981-1983).
(1) Macdonald, T. L.; Mahalingam, S. *J. Am. Chem. Soc.* **1980**, *102*, 2113.
(2) For an alternate approach to internal conjugate enone addition, see: Scheffold, R.; Dike, M.; Dike, S.; Herold, T.; Walder, L. *J. Am. Chem. Soc.* **1980**, *102*, 3642.
(3) For recent examples of the use of the carbon-tin bond to promote carbon-carbon bond formation, see: (a) Yamamoto, Y.; Yatagai, H.; Naruta, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1980**, *102*, 7108. (b) Naruta, Y. *Ibid.* **1980**, *102*, 3774. (c) Trost, B. M.; Keinan, E. *Tetrahedron Lett.* **1980**, *21*, 2591. (d) Godschaly, J.; Stille, J. K. *Ibid.* **1980**, *21*, 2599. (e) Nicolau, K. C.; Claremon, D. A.; Barnette, W. E.; Seitz, S. P. *J. Am. Chem. Soc.* **1979**, *101*, 3704. (f) Luijten, J. G. A.; van der Kerk "The Bond to Carbon"; MacDiarmid, A. G., Ed.; Marcel Dekker: New York, 1968; Part II, pp 91-191.

Scheme I[a]



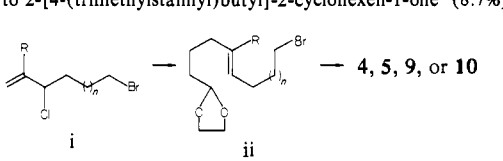

[a] Conditions: (a) $SnCl_4$ (5%), $CH_2Cl_2$, 0 °C (**4**, 83%; **5**, 58%), (b) $SOCl_2$ (1.5 equiv), LiBr (3.0 equiv), $CH_3CN$ (R = H, 95%; R = Me, 98%); (c) Li (4.0 equiv), $NH_3$, THF (R = H, 72%; R = Me, 84%).

We have extended the basic strategy illustrated by this process to other carbon-centered electrophiles by establishing that carbocations engendered from a variety of precursors including allylic and tertiary alcohols, acetals, epoxides, olefinic cyclization, and iminium ions can be employed in the initiation of internal alkyltin(IV)-mediated reaction processes. The carbon-tin $\sigma$ bond can react with these electrophiles via two distinct modes resulting either in the formation of a carbon-carbon bond via electrophilic cleavage of the carbon-tin bond (e.g., **1** → **2**) or in the transfer of a hydride $\beta$ to the trimethylstannyl moiety via an internal redox process (e.g., **1** → **3**). We report here on the substrate and reaction condition parameters which direct the mode of tin(IV)-mediated reaction to either reaction type.

The balance between these two reaction processes is sensitive to the size of the ring being formed, the substitution pattern of the electrophilic site, and the catalyst employed to initiate the reaction. Carbon-carbon bond formation is the only reaction process that we have observed in the formation of five-membered rings via this tetraalkyltin-mediated cyclization strategy. Both di- and trisubstituted carbocations undergo cyclization reactions, and $\beta$-hydride transfer does not appear to be a competitive reaction mode. For example, olefinic acetals **4** and **5**[4] undergo smooth carbocyclization (Scheme I). In the pentannulation of substrates with identical stereoelectronic, enthalpic, and entropic requirements,[6] alkyl substitution at the electrophilic site for carbon-tin bond attack appears to retard carbon-carbon bond formation but not to alter the course of reaction (e.g., to $\beta$-hydride transfer).

The ring junction stereochemistry generated during the cyclization of olefinic acetals **4** and **5** is independent both of the olefin substituent (hydrogen, methyl) and of the olefin geometry (*E* or *Z*). Cyclization of (*E*)-acetals **4** and **5** produces exclusively the *cis*-hydrindane skeleton **6** (R = H, Me)[7] implying that tri-

(4) All new compounds were characterized by infrared, mass, $^1H$ NMR, and $^{13}C$ NMR spectroscopy and by combustion analysis. Spectral and analytical data appear as supplementary material. Acetals **4** (or **5**) and **9** (or **10**) were synthesized according to the scheme outlined below. Thus, a requisite bromochloroolefin *i* (R = H, Me; *n* = 1, 2) prepared by the method of Macdonald et al.[5] was treated with the heterocuprate derived from 3-(ethylenedioxy)-1-propylmagnesium bromide[5] to afford olefinic acetals ii (R = H, Me; *n* = 1, 2) after low pressure chromotographic isolation of the predominant *E* isomer (46-63%). Subsequent stannylation ($LiSnMe_3$, $NH_3$, THF, -33 °C) of acetal bromides ii gave the desired stannyl acetals **4** (or **5**) and **9** (or **10**) (85-95%). Allylic alcohol **14** was synthesized by methyllithium addition to 2-[4-(trimethylstannyl)butyl]-2-cyclohexen-1-one[1] (8.7%).




(5) Macdonald, T. L.; Narayanan, B. A.; O'Dell, D. E. *J. Org. Chem.* **1981**, *46*, 1504.
(6) Baldwin, J. E. *J. Chem. Soc., Chem. Commun.* **1976**, 734.

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