phase, both of which contained flat aromatic cores stacked on top of each other to form columns. The columns were arranged in compact layers separated by the alkyl chains in a disordered conformation. Obviously, these special structures are a result of stereochemical demands of the cation, the stacking ability of the ancillary *ortho*-palladated ligand, and the insertion of the counteranion among the alkyl chains. The packing mode of the aromatic cores may be optimized depending on the position of the alkyl chains on the bipy residues. The lamellar morphology of the columnar phase indicates that macroscopically oriented samples could be easily produced and could be profitably exploited for their physical properties. Because columns of closely stacked aromatic units are accessible at modest temperatures, we anticipate that these materials could be used as medium-length molecular wires or chemical sensors.

Experimental Section

L: Dodecanol (ca. 2 g) was heated with Na (0.08 g) for 2 h at 80°C to yield a white precipitate of $C_{12}H_{25}ONa$. After cooling to 20°C, a suspension of 5,5′-dibromomethyl-2,2′-bipyridine (0.30 g, 0.94 mmol) in anhydrous THF (5 mL) was added dropwise. The mixture was heated under reflux for 24 h. After distillation of the solvent, the residue was purified over a chromatography column (flash silica, *n*-hexane/CH_2Cl_2, gradient of 1/1 to 0/1). The analytically pure ligand L was then obtained (0.36 g, 70%). R_f = 0.65, SiO_2, CH_2Cl_2/MeOH: 98/2; m.p. 60–62°C; UV/Vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$: 290 nm (28500); ^{1}H NMR (200.1 MHz, $CDCl_3$, 25°C): δ = 8.6 (s, 1H; H^6), 8.4 (d, ^3J = 8 Hz, 1H; H^3), 7.8 (dd, ^3J = 8 Hz, ^4J = 2 Hz, 1H; H^4), 4.6 (s, 2H; bipy-CH_2), 3.5 (t, ^3J = 6 Hz, 2H; OCH_2), 1.6 (m, 2H; OCH_2CH_2), 1.3 (broad s, 18H; $(CH_2)_9$), 0.9 (t, ^3J = 6 Hz, 3H; CH_3); ^{13}C{^{1}H} NMR (50.1 MHz, $CDCl_3$, 25°C): δ = 154.7–120.1 (aromatic C), 70.2 (bipyCH_2), 69.6 (OCH_2), 31.3 (OCH_2CH_2), 29.1 ($(CH_2)_3$), 28.9 (CH_2), 28.8 (CH_2), 28.7 (CH_2), 25.5 ($CH_3CH_2CH_2$), 22.1 (CH_3CH_2), 13.5 (CH_3); IR (KBr): $\tilde{\nu}$ = 2925 (s), 2853 (s), 1598 (w), 1553 (w), 1467 (m), 1384 (w), 1350 (w), 1109 cm^{-1} (s). FAB$^+$-MS: *m*/*z* (%): 553.4 (100) [M^+], 383.2 (32) [$M^+ - C_{12}H_{25}$]; elemental analysis calcd for $C_{36}H_{60}N_2O_2$ (552.465): C 78.21, H 10.94, N 5.07; found: C 78.09, H 10.79, N 5.02.

1a: A solution of $AgO_3SOC_{12}H_{25}$ (0.034 g, 0.090 mmol) in anhydrous CH_3CN (5 mL) was added at 20°C under argon, to a stirred suspension of $[Pd(8\text{-mq})Cl]_2$ (0.026 g, 0.045 mmol). A white precipitate of AgCl appeared instantaneously. After 2 h, the solution was filtered over celite under argon. The filtrate was evaporated to dryness, and a solution of 5,5′-di(dodecyloxymethyl)-2,2′-bipyridine (0.05 g, 0.09 mmol) in anhydrous CH_2Cl_2 (5 mL) was added. The yellow solution was stirred for 2 h, and the product was precipitated by addition of pentane (10 mL). **1a** was recovered by centrifugation as a yellow powder (0.08 g, 84%). UV/Vis (CH_2Cl_2): $\lambda_{max}(\varepsilon)$: 229 nm (45500), 243 (43800), 315 (25900); ^{1}H NMR (200.1 MHz, $CDCl_3$, 25°C): δ = 9.1 (d, 1H; aromatic H), 8.8 (s, 1H; aromatic H), 8.6 (dd, 2H; aromatic H), 8.4 (s, 1H; aromatic H), 8.2 (d, 1H; aromatic H), 8.1 (pseudo t, 2H; aromatic H), 7.9 (dd, 1H; aromatic H), 7.5 (m, 3H; aromatic H), 4.8 (s, 2H; bipy-CH_2), 4.5 (s, 2H; bipy-CH_2), 4.2 (t, ^3J = 7 Hz, 2H; O_3SOCH_2), 3.75 (s, 2H; CH_2Pd), 3.6 (m, 4H; OCH_2), 1.7 (m, 6H; OCH_2CH_2), 1.3 (broad s, 54H; $(CH_2)_{27}$), 0.9 (t, ^3J = 6 Hz, 9H; CH_3); ^{13}C{^{1}H} NMR (50.1 MHz, $CDCl_3$, 25°C): δ = 155.2–123.5 (aromatic C), 71.6 (bipyCH_2), 69.0 (OCH_2), 67.6 (O_3SOCH_2), 34.4 (CH_2Pd), 32 (CH_2), 29.8 [$(CH_2)_n$], 29.6 (CH_2), 29.4 (CH_2), 26.4 (CH_2), 26.2 (CH_2), 22.7 (CH_2), 14.2 (CH_3); IR (KBr): $\tilde{\nu}$ = 3055 (w), 2923 (s), 2854 (s), 1604 (w), 1509 (w), 1468 (m), 1386 (w), 1251 (s), 1223 (s), 1117 cm^{-1} (s). FAB$^+$-MS: *m*/*z* (%): 800.4 (100) [$M - O_3SOC_{12}H_{25}$]$^+$, expected isotopic profile, 658.3 (8) [$M - O_3SOC_{12}H_{25}$ – mq], 630.2 (30) [$M - O_3SOC_{12}H_{25} - C_{12}H_{25}$], 247.9 (45) [$M - O_3SOC_{12}H_{25}$ – L]; elemental analysis calcd for $C_{58}H_{93}N_3O_6SPd$ (1065.58): C 65.32, H 8.80, N 3.94; found: C 65.17, H 8.61, N 3.69.

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Anion Control in the Self-Assembly of a Cage Coordination Complex**

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Anion binding and recognition has attracted increasing interest because of its importance in biological and chemical processes.[1, 2] Many enzyme reactions involve the selective transformation of anions.[1] The selective extraction of anionic pollutants also requires the development of specific coordination sites.[2a] Classically, cations have been used to promote the assembly of ligands,[3] but recently interest has been shown in using anions as templates for the formation of supramolecular entities.[4]

The supramolecular interactions required for anion-assisted self-assembly involve either Lewis acid–base interactions between a metal cation and an anion[5, 6] or hydrogen-bonding

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interactions between an organic host and an anionic guest. Examples of the first type of supramolecular interaction are the 12-membered ring mercuracarborands reported by Hawthorne et al.[5a] and the isopolyoxovanadates of Müller et al.[6] In these rings and cages the metal ions interact due to their Lewis acidity with encapsulated anions. The second type of interaction has been illustrated recently by Stoddart, Williams, and co-workers,[7] who reported the formation of a supermolecule based on hydrogen-bonding interactions to a PF_6^- anion. Here we report the novel anion-assisted self-assembly of a supermolecule in which both types of supramolecular interaction (Lewis acidity from a metal and hydrogen-bonding interactions from an organic moiety) are essential for its formation.

The coordination properties of biguanide have been known for a long time, and several of its complexes have been prepared and structurally characterized.[8] Surprisingly, very few reports have appeared on the coordination chemistry of the analogous amidinothiourea ligand (Hatu; Figure 1), and indeed we are aware of only one such complex that has been structurally characterized.[9]

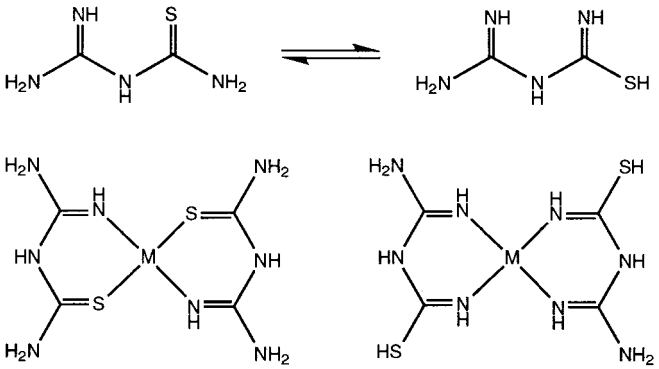

Figure 1. Two tautomeric forms of amidinothiourea and possible geometries of square-planar metal complexes with this ligand.

As part of a more general study of coordination compounds that display complementary hydrogen bonds,[10] we have investigated the coordination chemistry of the amidinothiourea ligand with Group 10 transition metals. $NiCl_2$ in methanol readily reacts with amidinothiourea to give, initially, an orange intermediate that reacts further to yield a dark green compound, which was isolated and shown by single crystal X-ray analysis to be $[Ni_6(atu)_8Cl]Cl_3$ (**1**).[11] The atu ligands coordinate to the nickel(II) centers by both guanidino nitrogen atoms to form square-planar units (Figure 2). This complexation resembles that observed in metal–biguanide complexes[8] but is in contrast to the *N*,*S* coordination mode observed in the Pd complex formed with atu.[9] The sulfur atoms of four $\{Ni(ATU)_2\}$ units act as secondary donating sites to a further two nickel(II) ions to form the cage structure.

The Ni–N and Ni–S coordination distances in **1** are unexceptional, and comparable with those observed in related biguanide[8] and thiourea[12] species respectively. The most fascinating feature of this cage structure is the encapsulation of a chloride anion (Figure 3). Primary binding of the chloride

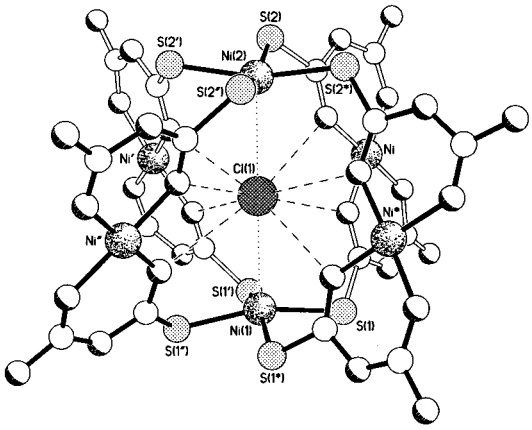

Figure 2. Structure of **1** in the crystal, showing the total encapsulation of a chloride anion through N–H···Cl hydrogen bonds. Hydrogen bonding geometries (N···Cl, H···Cl distances [Å], N–H···Cl angles [°]): 3.34, 2.45, 168; 3.29, 2.43, 149; 3.34, 2.45, 171; 3.28, 2.40, 166; 3.28, 2.39, 172; 3.30, 2.44, 161; 3.30, 2.43, 165; 3.29, 2.42, 165.

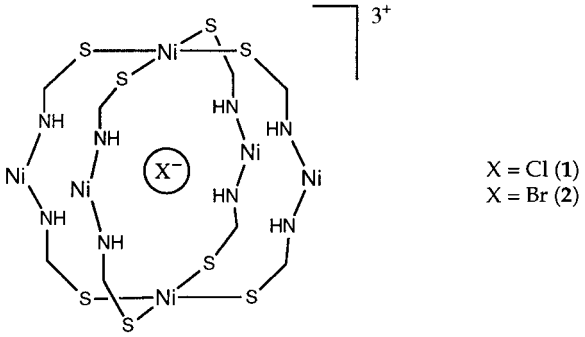

Figure 3. Schematic representation of the cage structure of **1** and the corresponding bromide species **2**.

anion is through eight N–H···Cl hydrogen bonds with N···Cl distances ranging between 3.28 and 3.34 Å. Accompanying these interactions is a marked out-of-plane distortion of each NiS_4 unit (ca. 0.33 Å) with the metal atoms approaching to 3.140(1) and 3.123(1) Å (for Ni(1) and Ni(2)) to the encapsulated chloride anion (Figure 4). This distortion suggests that there is a significant Lewis acid/base interaction between the two nickel ions and the central chloride ion. This type of interaction is similar to that previously observed in other host–guest structures such as the mercuracarborands reported by Hawthorne et al.[5a]

The remaining three charge-compensating chloride anions in **1** are also involved in N–H···Cl hydrogen bonding interactions, but to the noncoordinated acidic N–H groups (these N···Cl distances range between 3.15 and 3.23 Å). The formation of a regular extended hydrogen-bonded network is prevented by the inclusion of ten disordered methanol molecules distributed over seventeen full and partial occupancy sites throughout the asymmetric unit.

The generality of the above anion-controlled self-assembly is supported by the ability to synthesize the analogous bromine species $[Ni_6(atu)_8Br]Br_3$ (**2**). This has been structurally characterized by single crystal X-ray analysis and has been shown to have a structure that is essentially isomorphous to **1**. The encapsulated bromide is bound by eight N–H···Br

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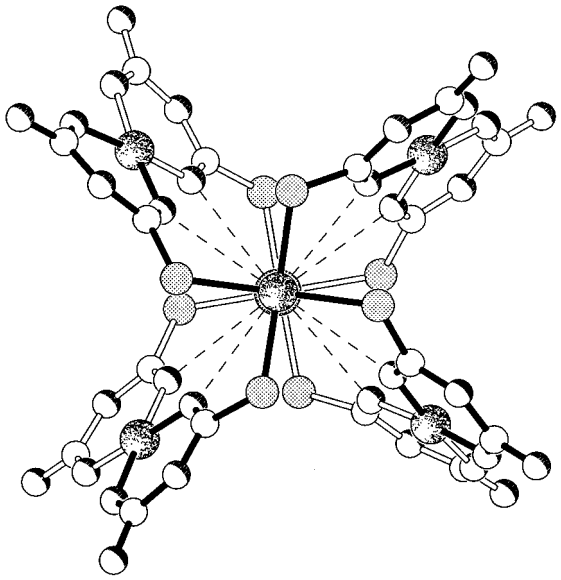

Figure 4. View, in parallel projection, down the Ni(1)···Cl(1)···Ni(2) direction of **1** showing the twisted, four-bladed propellerlike conformation of the five component complex: the two NiS_4 units have a slightly skewed (ca. 18°) square-prismatic orientation, an arrangement that is also adopted by the eight hydrogen-bonded ligand nitrogen atoms with respect to the entrapped chloride anion [twist angle ca. 15°].

hydrogen bonds with N···Br distances between 3.33 and 3.40 Å and axial Ni···Br distances of 3.128(4) and 3.134(4) Å for Ni(1) and Ni(2) respectively (the nickel atoms are again "bowed" inwards towards the encapsulated anion, here by about 0.35 Å).

The formation of the above complexes can be rationalized on the basis of the sequence of reactions shown in Equation (1). The first step may be the formation of the square-

$$4\ NiCl_2 + 8\ Hatu \rightarrow 4\ [Ni(Hatu)_2]Cl_2 \xrightarrow{2\,NiCl_2} \mathbf{1} + 8\ HCl \qquad (1)$$

planar complex $[Ni(Hatu)_2]Cl_2$. Deprotonation of the coordinated amidinothiourea ligands enables four of the molecules to act as ligands towards two additional Ni^{2+} ions to form a cage containing six nickel ions. The second step takes place in the presence of a templating anion (chloride or bromide) to form the final cage compound **1**.

Confirmation of the role of the chloride or bromide in the self-assembly process is demonstrated by the inability to form analogous cage structures with either nitrate, acetate, or perchlorate. In these cases, orange compounds characterized as salts of the simple monomer $[Ni(Hatu)_2]^{2+}$ were obtained. When, however, these salts are treated with stoichiometric amounts of either nickel or potassium chloride, the cage compound **1** is formed immediately. The ability of chloride and bromide anions to template the formation of the novel cage complexes **1** and **2** provides another elegant demonstration of the little appreciated potential role of anions in self-assembly processes. We are currently exploring how this concept can be utilized in the anion-assisted self-assembly synthesis of mixed-metal species as potential precursors for new materials with controllable physical properties.

Experimental Section

A solution of $NiCl_2 \cdot 6H_2O$ (1.03 mmol, 243 mg) in methanol (10 mL) was added to a solution of amidinothiourea (2.00 mmol, 236 mg) in methanol (30 mL) and stirred. Initially the reaction mixture had a dark orange color, which disappeared after 10 min to give a dark green solution. The reaction mixture was stirred for a further 2 h and left to stand for 12 h. After this time dark green crystals of **1** had formed, and were separated by filtration. Some of the crystals were suitable for X-ray structural analysis. An analogous procedure was followed to prepare **2** from $NiBr_2 \cdot 3H_2O$ and amidinothiourea. Crystals of **2** were obtained by slow diffusion of diethyl ether into a methanol/acetone mixture.

1: Yield: 52%; ^{1}H NMR ([D_6]methanol): $\delta = 6.2-6.4$ (br; NH); IR (KBr): $\tilde{\nu} = 3434$ (m), 3330 (m) (N–H), 1660 (vs) (C–N), 1590 (s) (C–S), 1176cm^{-1} (s). UV/Vis: $\lambda_{max} = 642$ nm; FAB-MS: *m*/*z* (%): 1395 (**1** – Cl^-; 20), 645 (**1** – 4 Cl – 3 Ni – 4 L, 90); elemental analysis calcd for $C_{16}H_{40}Cl_4N_{32}Ni_6S_8$: C 13.4, H 2.8, N 31.3; obtained: C 13.0, H 2.8, N 28.2.

2: Yield: 56%; IR (KBr): $\tilde{\nu} = 3436$ (m), 3330 (m) (N–H), 1660 (vs) (C–N), 1585 (s) (C–S), 1176cm^{-1} (s); UV/Vis: $\lambda_{max} = 645$ nm; FAB-MS: *m*/*z* (%): 645 (**2** – 4 Br – 3 Ni – 4 L, 50); elemental analysis calcd for $C_{16}H_{40}Br_4N_{32}Ni_6S_8 \cdot 3\,MeOH \cdot 3H_2O$: C 12.9, H 3.3, N 25.4; obtained: C 12.6, H 3.1, N 25.0.

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[11] Crystal data for **1**: $[C_{16}H_{40}N_{32}Ni_6S_8][Cl]_4 \cdot 10\,MeOH$, $M = 1751.8$, monoclinic, space group $P2_1/c$ (no. 14), $a = 18.971(4)$, $b = 15.523(2)$, $c = 25.555(3)$ Å, $\beta = 104.03(2)^\circ$, $V = 7301(2)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.59$ g cm^{-3}, $\mu Mo_{K\alpha} = 19.6$ cm^{-1}, $F(000) = 3616$. A dark green rhomb of dimensions $0.83 \times 0.60 \times 0.47$ mm was used. **2**: $[C_{16}H_{40}N_{32}Ni_6S_8][Br]_4 \cdot 5\,MeOH \cdot Me_2CO$, $M = 1827.5$, monoclinic, space group $P2_1/c$ (no. 14), $a = 19.045(5)$, $b = 15.862(6)$, $c = 25.771(7)$ Å, $\beta = 103.88(2)^\circ$, $V = 7558(5)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.61$ g cm^{-3}, $\mu Mo_{K\alpha} = 38.5$ cm^{-1}, $F(000) = 3672$. A green platelike rhomb of dimensions $0.30 \times 0.13 \times 0.04$ mm was used. For **1**(**2**) 12 800 (6955) independent reflections were measured at 203 K on a Siemens P4/PC diffractometer with graphite monochromated $Mo_{K\alpha}$ radiation and ω scans. The structures were solved by direct methods and were refined with full-matrix least squares based on F^2. In **1** all the major occupancy non-hydrogen atoms were refined anisotropically, but in **2**, due to a shortage of observed data, only the nickel, bromine, and sulfur atoms were refined anisotropically. In the case of **1**, a semiempirical absorption correction (based on ψ scans) was performed. The residuals in the final ΔF map were $R_1 = 0.047$ (0.093), $wR_2 = 0.097$ (0.193) for 9103 (3153) independent observed reflections [$|F_o| > 4\sigma(|F_o|)$, $2\theta \le 50^\circ$ (40°)] and 971 (444) parameters for **1** and **2** respectively. Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication no. CCDC-101 043. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

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Total Synthesis of Macrolactin A with Versatile Catalytic, Enantioselective Dienolate Aldol Addition Reactions**

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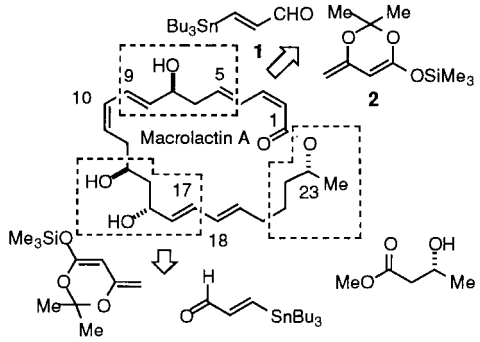
Polyene macrolide antibiotics form a diverse group of natural products that display a wide range of biological activities.[1] Impressive and elegant synthetic strategies have been used in their syntheses.[2–6] Recently, macrolactin A was isolated from a bacterium of unclassifed taxonomy, and in preliminary studies it was shown to inhibit HIV replication in T-lymphoblast cells (Scheme 1).[7] As the organism was isolated from deep-sea coring and is no longer readily available, further biological research must rely on de novo synthesis of macrolactin A. We report herein a total synthesis of macrolactin A that utilizes modern asymmetric catalytic

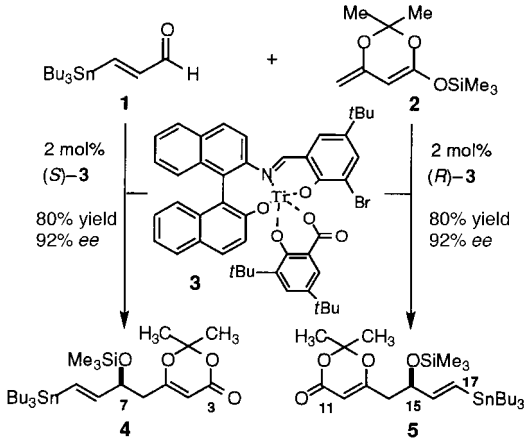


Scheme 1. Retrosynthetic analysis of macrolactin A.

C–C coupling methods in a highly convergent fashion.[8] A common enantioselective, catalytic dienolate addition reaction was used to synthesize two key fragments that contain most of the molecule's stereochemical complexity, and Pd^0 Stille coupling chemistry was used to assemble the principal fragments.

Central to our retrosynthesis (Scheme 1) was the recognition of structural homology between the three different regions that contain the stereogenic centers found in macrolactin A. In this analysis the latent 1,3-oxygenation pattern of the acetogenic macrocycle guides the disconnection of the macrocycle into three key subunits of approximately equal complexity: C(2)–C(9), C(11)–C(17), and C(18)–C(24). We speculated that the first two of these could be constructed with their attendant hydroxy-substituted stereocenters by an acetoacetate aldol addition reaction; each subunit could then be joined pairwise by Pd^0-catalyzed sp^2–sp^2 coupling reactions. Importantly, implementation of this strategy was facilitated by our recently developed catalytic, enantioselective dienolate aldol addition.[9]

Fragments **4** and **5** were synthesized by a known strategy that started with aldehyde **1**, dienolate **2**, and the enantiomeric Ti^{IV} catalysts (*S*)- and (*R*)-**3** (Scheme 2). Treatment of



Scheme 2.

propynal diethyl acetal with Bu_3SnH/BuLi/CuCN followed by mildly acidic workup conveniently provided 3-tributylstannyl-2-propenal.[10] In separate experiments with 2 mol% of (*S*)- and (*R*)- **3**, protected acetoacetate aldol adducts **4** and

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