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The Development of a New Catalytic Process: Bu_3SnH-Catalyzed Reductive Cyclization of Enals and Enones

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Abstract: By sequencing two known reactions, a new catalytic carbon-carbon bond-forming process, the Bu_3SnH-catalyzed, $PhSiH_3$-mediated reductive cyclization of enals and enones, has been developed. The addition of EtOH to the reactions leads to reproducibly good yields of the cyclized products; a rationale for including this additive is provided.

Keywords: catalysis; cyclisation; silicon and compounds; tin and compounds

Over the past several decades, a tremendous amount of effort has been directed toward the development of organotin reagents for organic synthesis.[1] Much of this work has centered on radical-based chemistry of Bu_3SnH.[2] It is a testimony to the power of these methods that these efforts have proceeded in spite of the toxicity[3] and the purification[4] issues that surround triorganotin compounds.

Recently, a variety of strategies have been pursued to address these toxicity and purification issues, one of which involves the development of alternative reagents to Bu_3SnH, such as $(Me_3Si)_3SiH$ (TTMS).[5,6] A drawback of this approach is that it forsakes the sometimes unique reactivity of Bu_3SnH.[7] We have chosen to pursue a different approach, one that focuses on the development of Bu_3SnH-*catalyzed* variants of reactions for which Bu_3SnH has been reported to serve as a useful stoichiometric reductant.[8] Such a strategy capitalizes on the quite sizable base of knowledge regarding the chemistry of Bu_3SnH and simultaneously greatly reduces the amount of Bu_3SnH that is required to effect the desired transformation.

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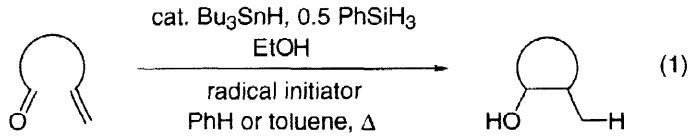
During the last few years, we have described Bu_3SnH-catalyzed variants of a number of processes, including the Barton-McCombie deoxygenation of alcohols,[9] the reduction of nitroalkanes to alkanes,[10] the conversion of azides to amines,[11] and the conjugate reduction of α,β-unsaturated carbonyl compounds.[12] In these processes, the Bu_3SnH catalyst effects the reduction of the substrate, and a silicon hydride regenerates the Bu_3SnH from the initial reduction adduct, thereby completing the catalytic cycle. In this Article, we describe the application of this general approach to the development of a Bu_3SnH-catalyzed variant of the Beckwith-Enholm cyclization of enals and enones (eq 1). Part of this study has been the subject of a preliminary report.[13]



Results and Discussion

In 1986 Beckwith reported that Bu_3SnH can effect the reductive cyclization of a δ,ε-unsaturated enal via a radical chain process (Figure 1);[14,15] others, most notably Enholm, subsequently explored the scope of this reaction.[16,17] The reductive cyclization proceeds by initial addition of a Bu_3Sn radical to a carbonyl group to produce a tin ketyl (Figure 1). Intramolecular addition of the ketyl to the olefin affords a new radical, which then abstracts a hydrogen atom from Bu_3SnH to generate the reductive cyclization product (**1**) and the chain-carrying Bu_3Sn radical.

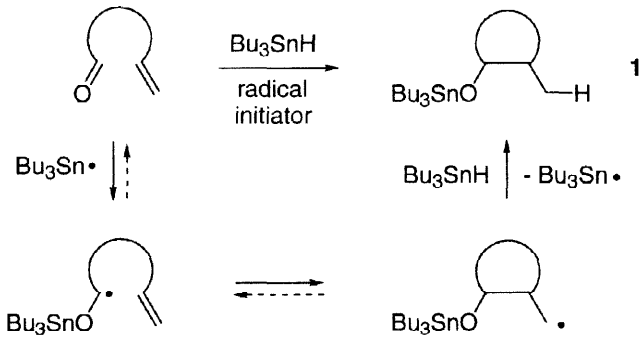


Figure 1. Beckwith-Enholm reductive cyclization of enals and enones with stoichiometric Bu_3SnH

Given that the product of the Beckwith-Enholm reaction is a tin alkoxide (Bu_3SnOR, **1**), it appeared reasonable to postulate that cyclization could be achieved with only a *catalytic* amount of Bu_3SnH, if a stoichiometric quantity of a metal hydride (M-H) capable of reducing Bu_3SnOR to Bu_3SnH were added (Figure 2, "turnover step").[18] In addition to being chemically competent for achieving the turnover step, M-H must not react with a carbonyl group or an olefin and should be non-toxic.

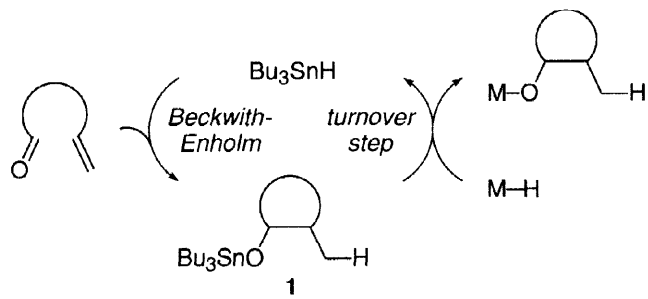
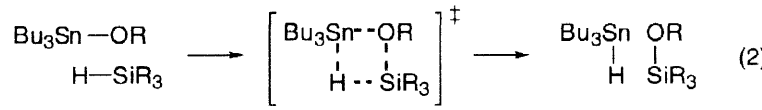


Figure 2. Proposed pathway for a Bu_3SnH-catalyzed Beckwith-Enholm reductive cyclization

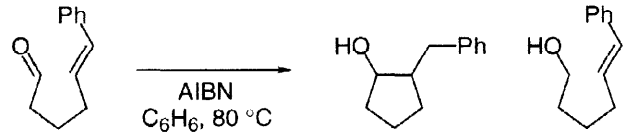
Silicon hydrides appeared to be excellent candidates for the role of stoichiometric reducing agent (M-H), since silicon hydrides can reduce Bu_3SnOR to Bu_3SnH (eq 2).[19] Furthermore, silicon hydrides are relatively innocuous[20] and do not typically react with carbonyl groups or olefins in the absence of a catalyst.[21]



(2)

Thus, two known reactions, run in sequence, seemed to provide the basis for a new catalytic process (Figure 2). When this proposal was put to the test, however, we obtained an unanticipated result. In accord with the report of Enholm,[17] reaction of enal **2** with stoichiometric Bu_3SnH resulted in very clean conversion to the cyclized product (eq 3; >185:1 cyclic:acyclic). However, when we subjected **2** to the catalytic conditions (0.10 equiv Bu_3SnH, 0.6-1.2 equiv $PhSiH_3$), we observed a significant quantity of the acyclic reduction product (eq 3; 1-13:1 cyclic:acyclic). This result is opposite from what we had anticipated--we had expected that the lower

concentration of Bu_3SnH under the catalytic conditions would lead to a cyclic:acyclic product ratio at least as large as that observed in the presence of stoichiometric Bu_3SnH.[22] Even more surprisingly, when we investigated the Bu_3SnH-catalyzed reductive cyclization of **2** with polymethylhydrosiloxane (PMHS), a less reactive silicon hydride, as the stoichiometric reducing agent, the acyclic alcohol was the *predominant* product (eq 3; 0.1:1 cyclic:acyclic).



(3)

2

Bu_3SnH (1.5 equiv)	>185 : 1
Bu_3SnH (0.10 equiv) $PhSiH_3$ (0.6-1.2 equiv)	1-13 : 1
Bu_3SnH (0.10 equiv) PMHS (5.0 equiv)	0.1 : 1

In our efforts to improve the efficiency of the Bu_3SnH-catalyzed reductive cyclization process, we decided to focus on facilitating the turnover step (see Figure 2). Because $PhSiH_3$ is, to the best of our knowledge, the most effective silicon hydride for reducing Sn-O bonds to Sn-H bonds, screening commercially available silicon hydrides seemed unlikely to be productive.

Two observations described in the literature suggested an alternative means by which we might be able to accelerate the turnover step: (1) exchange of alcohols with tin alkoxides proceeds rapidly at room temperature,[23] and (2) primary tin alkoxides are more readily reduced by silicon hydrides than are secondary or tertiary tin alkoxides.[19] Based on these observations, we postulated that the addition of a primary alcohol (e.g., EtOH) to the reaction mixture might accelerate the turnover step (Figure 3) to the point that the 1,2-reduction pathway might become insignificant.

We were pleased to discover that the addition of EtOH does indeed lead to elimination of the acyclic alcohol as a side product in the Bu_3SnH-catalyzed reductive cyclization of enal **2** (Table 1, entry 1). We have applied these reaction conditions (0.1-0.3 equiv Bu_3SnH,[24,25] 0.5 equiv $PhSiH_3$, 2.0 equiv EtOH, radical initiator, refluxing benzene or toluene) to the cyclization of a range of enals and enones (Table 1).[26] Both five- (entries 1-4) and six-membered rings (entries 5-6) are

formed efficiently in this new catalytic carbon-carbon bond-forming process. The cyclization proceeds more smoothly when the olefin bears a radical-stabilizing substituent (e.g., phenyl or ester, entries 1 and 2); otherwise, a significant amount of uncyclized alcohol is produced (29%; entry 3).[27] We observe essentially the same diastereoselection for reactions run under the catalyzed conditions as for reactions run with stoichiometric Bu_3SnH, a result consistent with the catalytic reaction proceeding via the pathway depicted in Figure 2.

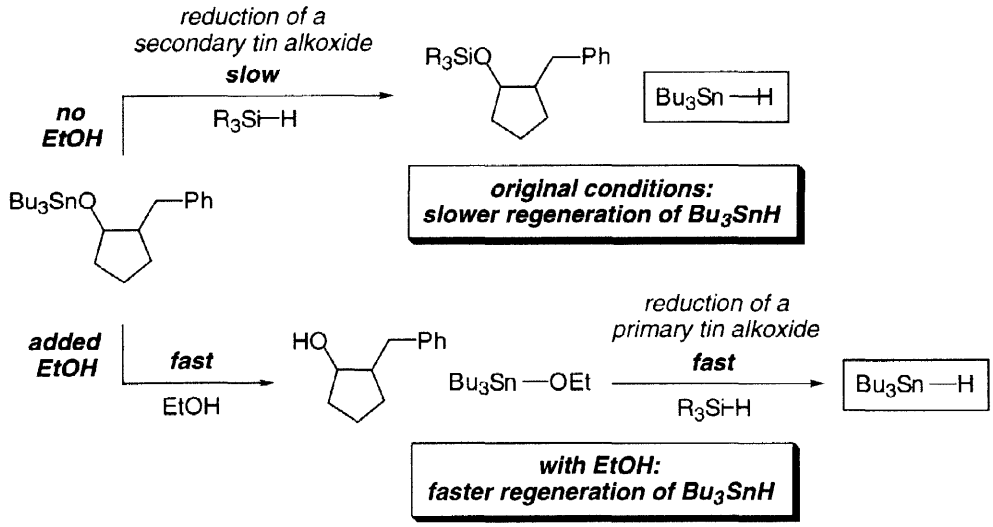
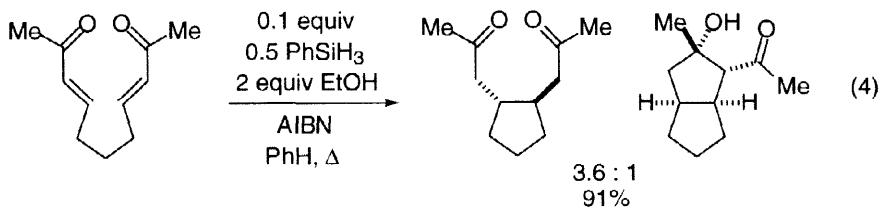


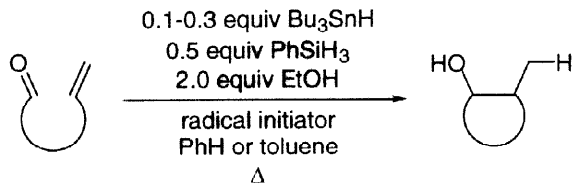
Figure 3. Proposed strategy to facilitate the turnover step (regeneration of Bu_3SnH): addition of a primary alcohol (EtOH)

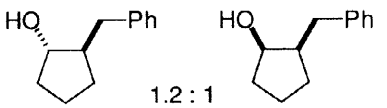
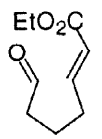
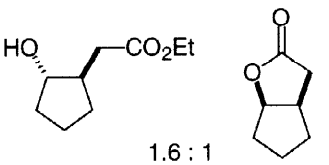
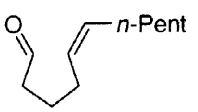
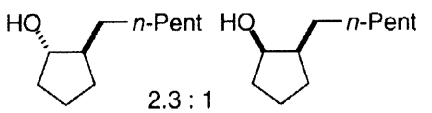
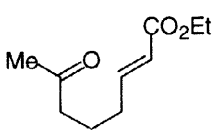
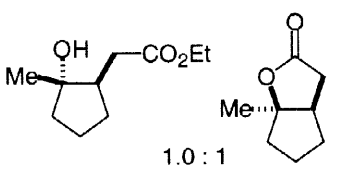
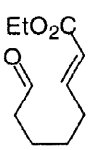
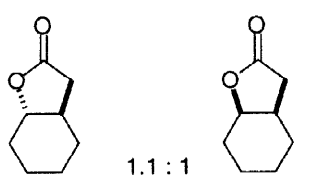
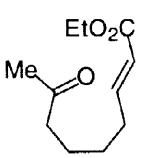
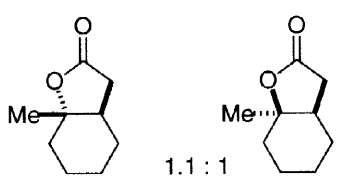
We have also demonstrated that a related reductive cyclization is susceptible to Bu_3SnH catalysis. Enholm reported in 1991 that certain activated dienes undergo intramolecular coupling upon treatment with three equivalents of Bu_3SnH.[28] We have established that this reaction can be effected in comparable yield and stereoselection using Bu_3SnH as a catalyst (0.10 equiv) and $PhSiH_3$ as the stoichiometric reductant (eq 4).



(4)

Table 1. Bu_3SnH-catalyzed reductive cyclization of enals and enones



Entry	Substrate	Products[a]	Yield[b]
1		 1.2 : 1	85
2		 1.6 : 1	71
3		 2.3 : 1	67[c]
4		 1.0 : 1	75
5		 1.1 : 1	76
6		 1.1 : 1	66

[a]Product ratios are based on analysis by capillary gas chromatography or by ^1H NMR. [b]Yields refer to isolated mixtures of the cis and trans products and are the average of two runs. [c]The acyclic 1,2-reduction product is produced in 29% yield.

The origin of 1,2-reduction in the absence of EtOH. As noted above, in the original, EtOH-free Bu_3SnH-catalyzed reductive cyclizations, we had observed simple 1,2-reduction of enal **2** to a surprising extent (eq 3). Our visual observation that metallic tin is formed in these catalyzed reactions (but not in the reactions that employ stoichiometric Bu_3SnH) led us to a possible explanation for these results: Bu_2SnH_2 is being generated under the catalytic conditions. This postulate was based on the knowledge that dialkyltin dihydrides are active catalysts for the polar reduction of aldehydes by silicon hydrides[8a] and that dialkyltin dihydrides decompose readily to tin metal.[29]

We hypothesized that Bu_2SnH_2 is being produced via an intermolecular Bu_3SnH-mediated pinacol coupling of the substrate (Figure 4).[30] Thus, a Bu_3Sn radical adds to the aldehyde to form a tin ketyl, which then adds in an intermolecular fashion to a second aldehyde. The resulting oxygen-centered radical ejects a butyl radical through a facile intramolecular S_H2 reaction at tin, thereby producing a dioxastannolane.[30] Reaction of the dioxastannolane with $PhSiH_3$ then affords Bu_2SnH_2.

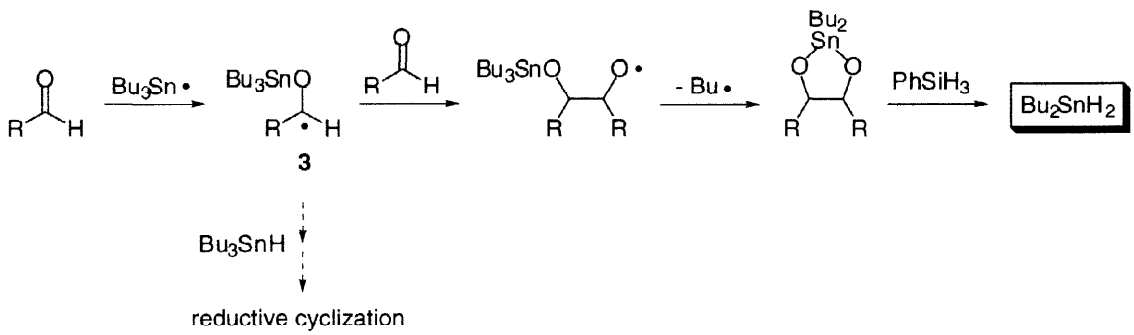
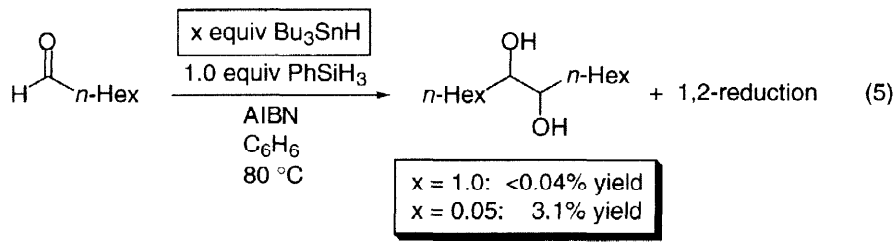


Figure 4. A possible mechanism for the formation of Bu_2SnH_2

This pathway appears to be consistent with our observation of increased 1,2-reduction under the Bu_3SnH-catalyzed reductive cyclization conditions (eq 3): when the concentration of Bu_3SnH decreases (Bu_3SnH catalysis), the partitioning of tin ketyl **3** (Figure 4) between formation of Bu_2SnH_2 and reductive cyclization shifts more toward formation of Bu_2SnH_2, since this process does not require Bu_3SnH; in contrast, the rate of reductive cyclization *is* Bu_3SnH dependent, since hydrogen atom abstraction from Bu_3SnH seems to be rate-determining.[31] The more Bu_2SnH_2 that is generated, the more 1,2-reduction occurs.

To determine the feasibility of our hypotheses, we examined the reduction of *n*-heptanal with $Bu_3SnH/PhSiH_3$. Two side-by-side reactions, which differed only in the quantity of Bu_3SnH (1.0 vs. 0.05 equiv), were carried out (eq 5). In the reaction with the higher concentration of Bu_3SnH, we were unable to detect any of the pinacol coupling product. In the low-concentration reaction, on the other hand, we found that the pinacol adduct had formed in 3% yield. Furthermore, our kinetic data for the two reactions suggest that a new, highly active catalyst for carbonyl reduction is produced in the reaction with 0.05 equivalents of Bu_3SnH (Figure 5). Collectively, these observations are consistent with the hypotheses outlined above for explaining the increased 1,2-reduction at low Bu_3SnH concentrations (eq 3).



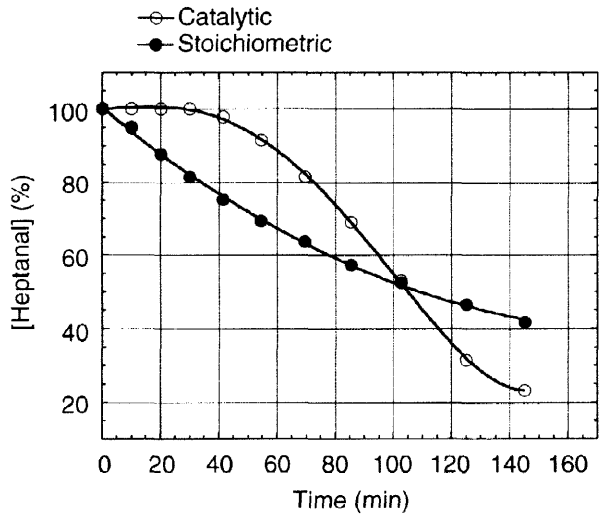


Figure 5. Evidence for the formation of a new catalytic species in the Bu_3SnH-catalyzed reduction of *n*-heptanal (eq 5)

Conclusions

We have developed a new catalytic carbon-carbon bond-forming process, the Bu_3SnH-catalyzed, $PhSiH_3$-mediated reductive cyclization of enals and enones.[32] The development of this process into a general and reliable method required that regeneration of the Bu_3SnH catalyst be efficient, and this was accomplished by adding EtOH to the reaction mixture. Otherwise, if the steady-state concentration of Bu_3SnH is very low, an undesired pinacol coupling of the substrate occurs, leading to the production of Bu_2SnH_2, which serves as a catalyst for simple 1,2-reduction of the substrate.

Experimental

General. $(Bu_3Sn)_2O$ (Gelest) and $PhSiH_3$ (Aldrich) were distilled prior to use. Absolute EtOH was obtained from Pharmco and distilled from magnesium turnings prior to use. AIBN (Eastman), 1,1′-azobis(cyclohexanecarbonitrile) (Aldrich), and tetrabutylammonium fluoride (TBAF; 1.0 M in THF) (Aldrich) were used without purification.

Solvents were distilled from the indicated drying agents: benzene (sodium/benzophenone); toluene (molten sodium).

Analytical thin layer chromatography was performed using EM Reagents 0.25 mm silica gel 60 plates, and visualization was accomplished with anisaldehyde/H_2SO_4/EtOH/HOAc or with ethanolic phosphomolybdic acid. Flash chromatography was performed on EM Reagents silica gel 60 (230-400 mesh).

^1H, and ^{13}C nuclear magnetic resonance spectra were recorded on Varian XL-300 or Unity-300 NMR spectrometers at ambient temperature. ^1H data are reported as follows: chemical shift in parts per million downfield from tetramethylsilane (δ scale), multiplicity (br = broad, s = singlet, d = doublet, t = triplet, q = quartet, and m = multiplet), integration, and coupling constant (Hz). ^{13}C chemical shifts are reported in ppm downfield from tetramethylsilane (δ scale). All ^{13}C spectra were determined with complete proton decoupling.

Gas chromatography was performed on a Hewlett Packard 5890 Series II instrument utilizing a DB-1 capillary column (J & W Scientific).

Infrared spectra were obtained on a Perkin-Elmer Series 1600 FT-IR spectrophotometer. Microanalyses were performed by E + R Microanalytical

Laboratory, Inc. High resolution mass spectra were recorded on a Finnegan MAT System 8200 spectrometer.

All reactions were carried out under an atmosphere of nitrogen or argon. Reductive cyclization reactions were carried out in sealed 10 mL Schlenk tubes under an atmosphere of nitrogen, and reaction temperatures refer to those of the oil bath.

The yields reported below may differ slightly from those reported in Table 1, since the yield data in Table 1 are the average of two runs.

Table 1, entry 1. $(Bu_3Sn)_2O$ (25 μL, 0.050 mmol), $PhSiH_3$ (62 μL, 0.50 mmol), EtOH (117 μL, 2.00 mmol), and AIBN (16 mg, 0.10 mmol in 200 μL of benzene) were added to a solution of the enal (174 mg, 1.00 mmol) in benzene (2.0 mL) in a 10 mL sealable Schlenk tube. The vessel was sealed, shaken, and placed in an oil bath at 80 °C. After 5 hours, more AIBN was added (16 mg, 0.10 mmol in 200 μL of benzene). After 7 more hours, TLC indicated that all of the starting material had been consumed. The reaction mixture was treated with TBAF (3.0 mL, 3.0 mmol), stirred for 1 h, and then subjected to an aqueous workup (15 mL of 2 N HCl). The reaction mixture was extracted with Et_2O, and the combined organic layers were dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography, which provided 149 mg (85%) of a mixture of cis and trans cyclopentanols as an analytically pure, colorless oil.

GC analysis of an aliquot taken from the unpurified reaction mixture, as well as ^1H NMR integration of the purified material, indicated that a 1.3 : 1 (trans : cis) mixture of cyclopentanols was present.

***cis*- and *trans*-2-(Phenylmethyl)cyclopentanol.** The ^1H and ^{13}C NMR spectra of the mixture were identical to those reported in the literature.[33] IR (neat) 3374, 3061, 3026, 2956, 2872, 1494, 1453, 1071, 1030, 747, 700. Anal. calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.55; H, 9.21.

Table 1, entry 2. $(Bu_3Sn)_2O$ (25 μL, 0.050 mmol), $PhSiH_3$ (62 μL, 0.50 mmol), EtOH (117 μL, 2.00 mmol), and AIBN (16 mg, 0.10 mmol in 200 μL of benzene) were added to a solution of the enal (170 mg, 1.00 mmol) in benzene (2.0 mL) in a 10 mL sealable Schlenk tube. The vessel was sealed, shaken, and placed in an oil bath at 80 °C. After 6 h, TLC and GC analyses indicated that all of the starting material had been consumed. The reaction mixture was treated with TBAF (3.0 mL, 3.0 mmol), stirred for 2 h, and then subjected to an aqueous workup (15 mL of 2 N HCl). The

reaction mixture was extracted with Et_2O, and the combined organic layers were dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography, which provided 108 mg (70%; colorless oil) of a mixture of trans hydroxyester and cis lactone.

GC analysis of an aliquot taken from the unpurified reaction mixture, as well as ^1H NMR integration of the purified material, indicated that a 1.5 : 1 (trans : cis) mixture of compounds was present.

The purified mixture was silylated, and the two components were then separated by flash chromatography. The silyl ether was then desilylated.

***(trans*-2-Hydroxycyclopentane)acetic acid ethyl ester.** Colorless oil. The ^1H NMR spectrum was identical to the partial data reported in the literature.[34] ^1H NMR (300 MHz, $CDCl_3$) δ 4.12 (q, 2H, J = 7.2), 3.83 (q, 1H, J = 6.4), 2.86 (br s, 1H), 2.43 (dd, 1H, J_1 = 16.2, J_2 = 6.6), 2.35 (dd, 1H, J_1 = 16.2, J_2 = 8.1), 2.13-2.00 (m, 1H), 1.99-1.86 (m, 2H), 1.79-1.51 (m, 3H), 1.24 (t, 3H, J = 7.2), 1.26-1.13 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.1, 78.8, 60.6, 44.4, 38.5, 34.2, 30.6, 21.8, 14.1.

***cis*-Hexahydro-2*H*-cyclopenta[b]furan-2-one.** Colorless oil. The ^1H NMR spectrum was identical to that reported in the literature.[35] ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.7, 86.3, 37.8, 35.9, 33.5, 33.4, 23.3.

Table 1, entry 3. $(Bu_3Sn)_2O$ (76 μL, 0.15 mmol), $PhSiH_3$ (62 μL, 0.50 mmol), EtOH (117 μL, 2.00 mmol), and AIBN (16 mg, 0.10 mmol in 200 μL of benzene) were added to a solution of the enal (168 mg, 1.00 mmol) in benzene (2.0 mL) in a 10 mL sealable Schlenk tube. The vessel was sealed, shaken, and placed in an oil bath at 80 °C. After 12.5 h, TLC analysis indicated that all of the starting material had been consumed. The reaction mixture was treated with TBAF (3.0 mL, 3.0 mmol), stirred for 1 h, and then subjected to an aqueous workup (15 mL of 2 N HCl). The reaction mixture was extracted with Et_2O, and the combined organic layers were dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography, which provided 167 mg (98%) of a mixture of cis and trans cyclopentanols and the simple reduction product as an analytically pure, colorless oil. Anal. calcd. for $C_{11}H_{22}O$: C, 77.58; H, 13.02. Found: C, 77.95; H, 12.86. The mixture was separated by flash chromatography to afford the three isomers as colorless oils.

^1H NMR integration of the purified material indicated that a 2.3 : 1 (trans : cis) mixture of cyclopentanols was present. The stereochemistry was determined by oxidation of the cyclopentanol to the cyclopentanone according to a literature procedure,[36] followed by reduction with Li(*sec*-Bu_3BH). The latter reaction is

known to yield the cis isomer in the reduction of 2-alkylcyclopentanones.[37] ^{1}H NMR integration indicated that 30% of the purified material was 5-undecen-1-ol (3.6 : 1 E : Z, as estimated by the relative intensities of the vinyl signals in the ^{13}C NMR).

***trans*-2-Hexylcyclopentanol.** ^{1}H NMR (300 MHz, $CDCl_3$) δ 3.80 (q, 1H, J = 5.7), 1.96-0.99 (m, 18H), 0.88 (t, 3H, J = 6.8). ^{13}C NMR (75 MHz, $CDCl_3$) δ 79.4, 48.4, 34.6, 33.9, 31.8, 30.0, 29.6, 28.2, 22.6, 21.8, 14.1. IR (neat) 3333, 2922, 2854, 1464, 1456, 1378, 1344, 1078, 1022, 972, 724. HRMS: Calcd. for $C_{11}H_{22}O$: 170.1671. Found: 170.1669.

***cis*-2-Hexylcyclopentanol.** ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.14 (td, 1H, J_1 = 4.0, J_2 = 1.2), 1.87-1.25 (m, 18H), 0.88 (t, 3H, J = 6.8). ^{13}C NMR (75 MHz, $CDCl_3$) δ 74.9, 45.8, 34.8, 31.9, 29.7, 29.2, 28.8, 28.6, 22.7, 21.8, 14.1. IR (neat) 3374, 2956, 2925, 2856, 1466, 1378, 1302, 1136, 1028, 988, 891, 724. HRMS: Calcd. for $C_{11}H_{22}O$: 170.1671. Found: 170.1669.

***E*- and *Z*-5-Undecen-1-ol.** ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.46-5.29 (m, 2H), 3.66-3.61 (m, 2H), 2.09-1.93 (m, 4H), 1.63-1.20 (m, 11H), 0.90-0.85 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 130.9, 130.4, 129.7, 129.3, 62.9, 32.5, 32.4, 32.3, 32.2, 31.5, 31.4, 29.4, 29.3, 27.2, 26.9, 25.8, 25.7, 22.5, 22.5, 14.0. IR (neat) 3331, 3004, 2926, 2856, 1458, 1378, 1061, 968, 726. HRMS: Calcd. for $C_{11}H_{22}O$: 170.1671. Found: 170.1669.

Table 1, entry 4. $(Bu_3Sn)_2O$ (25 μL, 0.050 mmol), $PhSiH_3$ (62 μL, 0.50 mmol), EtOH (117 μL, 2.00 mmol), and 1,1′-azobis(cyclohexanecarbonitrile) (24 mg, 0.10 mmol in 200 μL of toluene) were added to a solution of the enone (184 mg, 1.00 mmol) in toluene (1.0 mL) in a 10 mL sealable Schlenk tube. The vessel was sealed, shaken, and placed in an oil bath at 110 °C. After 3.5 hours, more initiator was added (24 mg, 0.10 mmol in 200 μL of toluene). After 3.5 more hours, GC analysis indicated that only a small amount of starting material remained. The reaction mixture was treated with TBAF (3.0 mL, 3.0 mmol), stirred for 1 h, and then subjected to an aqueous workup (15 mL of 2 N HCl). The reaction mixture was extracted with Et_2O, and the combined organic layers were dried ($MgSO_4$), filtered, concentrated, and purified by flash chromatography, which provided 130 mg (80%) of a mixture of trans hydroxyester and cis lactone as a colorless oil. The mixture was separated by flash chromatography to afford the two compounds as colorless oils.

A GC analysis of an aliquot taken from the unpurified reaction mixture (corrected for the relative response factors), as well as ^{1}H NMR integration of the purified material, indicated that a 1.0 : 1 (trans : cis) mixture of compounds was present.

***(trans*-2-Hydroxy-2-methylcyclopentane)acetic acid ethyl ester.** ^{1}H NMR (300

MHz, $CDCl_3$) δ 4.12 (q, 2H, J = 7.1), 2.54 (br s, 1H), 2.47-2.15 (m, 3H), 2.00-1.89 (m, 1H), 1.81-1.47 (m, 4H), 1.29-1.15 (m, 1H), 1.24 (t, 3H, J = 7.1), 1.13 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.2, 79.3, 60.6, 46.4, 41.1, 35.3, 30.3, 23.1, 20.5, 14.1. IR (neat) 3433, 2965, 2874, 1735, 1374, 1329, 1306, 1201, 1153, 1097, 1033. HRMS: Calcd. for $C_{10}H_{18}O_3$: 186.1256. Found: 186.1258.

***cis*-Hexahydro-6a-methyl-2*H*-cyclopenta[b]furan-2-one.** The ^1H and ^{13}C NMR spectra were identical to those reported in the literature.[38]

Table 1, entry 5. $(Bu_3Sn)_2O$ (76 μL, 0.15 mmol), $PhSiH_3$ (62 μL, 0.50 mmol), EtOH (117 μL, 2.00 mmol), and AIBN (16 mg, 0.10 mmol in 200 μL of benzene) were added to a solution of the enal (184 mg, 1.00 mmol) in benzene (2.0 mL) in a 10 mL sealable Schlenk tube. The vessel was sealed, shaken, and placed in an oil bath at 80 °C. After 6.5 h, TLC analysis indicated that all of the starting material had been consumed. The reaction mixture was treated with TBAF (3.0 mL, 3.0 mmol), stirred for 1 h, and then subjected to an aqueous workup (15 mL of 2 N HCl). The reaction mixture was extracted with Et_2O, and the combined organic layers were dried ($MgSO_4$), filtered, concentrated, and dissolved in CH_2Cl_2 (10 mL). A catalytic quantity of *p*-toluenesulfonic acid monohydrate was added, and the solution was stirred for 20 h, at which time GC analysis indicated that all of the initially formed trans hydroxyester had been converted to the corresponding lactone. The solution was concentrated and purified by flash chromatography, which afforded 103 mg (74%) of an analytically pure mixture of cis and trans lactones.

^1H NMR integration of the purified material indicated that a 1.1 : 1 (trans : cis) mixture of lactones was present. The stereochemistry was assigned by noting which carbinol signal grew in over the course of the acid-catalyzed lactonization. This resonance was assigned to the trans isomer.

***cis*- and *trans*-Hexahydro-2(3*H*)-benzofuranone.** Colorless oil. ^1H NMR (300 MHz, $CDCl_3$) δ 4.48 (q, cis carbinol resonance, J = 4.2), 3.75 (td, trans carbinol resonance, J_1 = 10.9, J_2 = 3.7), 2.62-1.16 (m, 11H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 177.3, 176.4, 85.0, 79.0, 44.6, 37.3, 35.7, 34.7, 30.0, 28.1, 27.6, 27.0, 25.2, 23.9, 22.6, 19.7. IR (neat) 2936, 2861, 1770, 1448, 1225, 1212, 1173, 1142, 1076, 1029, 989, 942, 931. Anal. calcd. for $C_8H_{12}O_2$: C, 68.55, H; 8.63. Found: C, 68.65; H, 8.62.

Table 1, entry 6. $(Bu_3Sn)_2O$ (51 μL, 0.10 mmol), $PhSiH_3$ (62 μL, 0.50 mmol), EtOH (117 μL, 2.00 mmol), and 1,1′-azobis(cyclohexanecarbonitrile) (24 mg, 0.10 mmol in 200 μL of toluene) were added to a solution of the enone (198 mg, 1.00 mmol) in

toluene (1.0 mL) in a 10 mL sealable Schlenk tube. The vessel was sealed, shaken, and placed in an oil bath at 110 °C. More initiator was added after 5.5 h (24 mg, 0.10 mmol in 200 μL of toluene) and after 9.5 h (12 mg, 0.050 mmol in 200 μL of toluene). After a total reaction time of 12 hours, TLC analysis indicated that very little starting material remained. The reaction mixture was treated with TBAF (3.0 mL, 3.0 mmol), stirred for 1 h, and then subjected to an aqueous workup (15 mL of 2 N HCl). The reaction mixture was extracted with Et_2O, and the combined organic layers were dried ($MgSO_4$), filtered, concentrated, and dissolved in CH_2Cl_2 (10 mL). A catalytic quantity of *p*-toluenesulfonic acid monohydrate was added, and the reaction was stirred until equilibrium was reached. The solution was concentrated and redissolved in CH_2Cl_2 in order to drive the lactonization to completion (two times). The reaction mixture was then purified by flash chromatography to afford 102 mg (66%) of an analytically pure mixture of cis and trans lactones as a colorless oil. Anal. calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.13; H, 9.46.

GC analysis of an aliquot taken from the unpurified reaction mixture indicated that a 1.1 : 1 (trans : cis) mixture of lactones was present.

***trans*-Hexahydro-7a-methyl-2(3*H*)-benzofuranone.** ^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 85.9, 46.7, 36.8, 33.2, 25.4, 24.7, 22.9, 17.4.

***cis*-Hexahydro-7a-methyl-2(3*H*)-benzofuranone.** The signals assigned to the cis isomer in the ^1H and ^{13}C NMR spectra of the mixture were identical to those reported in the literature.[38]

Eq 4. $(Bu_3Sn)_2O$ (25 μL, 0.050 mmol), $PhSiH_3$ (62 μL, 0.50 mmol), EtOH (117 μL, 2.00 mmol), and AIBN (16 mg, 0.10 mmol in 200 μL of benzene) were added to a solution of the enone (180 mg, 1.00 mmol) in benzene (2.0 mL) in a 10 mL sealable Schlenk tube. The vessel was sealed, shaken, and placed in an oil bath at 80 °C. After 7.5 h, TLC analysis indicated that all of the starting material had been consumed. The solution was concentrated and purified by flash chromatography to afford 164 mg (90%) of a mixture of the two products as an analytically pure, colorless oil. The ^1H and ^{13}C NMR spectra were identical to those reported in the literature.[39] Anal. calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.18; H, 9.99.

GC analysis of an aliquot taken from the unpurified reaction mixture, and then passed through a plug of silica gel, indicated that a 3.6 : 1 (trans : cis) mixture of isomers was present.

Control reactions. Each of the seven substrates was submitted to the conditions described in the corresponding cyclization procedure, but in the absence of $(Bu_3Sn)_2O$. In every case, little or no cyclized product (<3%) was observed by GC analysis.

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