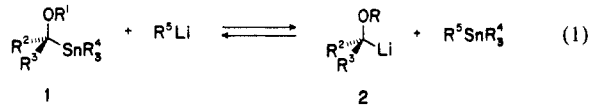
Physical Properties and Synthetic Utility of α-Alkoxyorganolithium Species As Studied through Ligand Selectivity in Tin–Lithium Exchange

J. Scott Sawyer, Andrew Kucerovy, Timothy L. Macdonald,* and Glenn J. McGarvey*

Contribution from the Department of Chemistry, University of Virginia, Charlottesville, Virginia 22901. *Received August 6, 1985*

Abstract: The effects of alkoxy substitution on tetrahedral carbanions were studied by examining ligand selectivity in the tin–lithium exchange reaction in the corresponding stannanes. The thermodynamic stability of the derived organolithium species was studied by competitive exchange experiments and low-temperature NMR to reveal an order of decreasing stability as follows: $R^1OCH_2Li > R^1OCH(R^2)Li > MeLi > R^1OCR^2R^3Li > n$-BuLi > c-HxLi ($R^1$ = methoxymethyl). The results of this study allow a conservative estimate of the destabilizing effect of alkyl substitution on tetrahedral organolithium species to be 3–4 kcal/mol, while alkoxy substitution stabilizes the alkyllithium species by about 5–6 kcal/mol relative to hydrogen. Although the origin of this heteroatom stabilization may be attributable to several factors, the facility with which a wide variety of α-alkoxyorganolithium species were found to undergo exchange to the corresponding α-alkoxyorganolithium species is indicative of the prominence of σ-induction as a major contributor. In stereochemical studies carried out on conformationally biased ketone **31**, it was unambiguously demonstrated that tin–lithium exchange takes place with retention of configuration at the carbon center and that R_3SnLi addition to ketones is a reversible process. This latter feature has allowed the stereoselective preparation of axial stannane **32M**, which serves as a useful precursor to numerous axially substituted cyclohexyl species by virtue of stereospecific replacement of the tin center by electrophiles. A number of examples have been carried out to illustrate the utility of tertiary α-alkoxyorganolithium reagents as a means of forming highly substituted, functionalized carbon–carbon bonds.

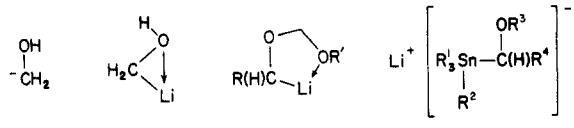
We recently communicated a study that provided experimental support for the stabilizing influence of α-alkoxy groups upon organolithium species generated via tin–lithium exchange (**1** ⇄ **2**; eq 1) and illustrated the synthetic potential of tertiary α-alkoxyorganolithium reagents (**2**: R^2, R^3 = carbon substituents) generated in this manner.[1] In this paper, we describe in detail the synthetic and mechanistic features of our prior study, expand our investigations into the underlying electronic and bonding processes responsible for the stabilization of organolithium species by α-alkoxy groups, and further illustrate the synthetic utility and reaction mechanisms of such reagents.



(1)

1 **2**

The enhancement of the thermodynamic and kinetic acidities of carbon acids by many second-, third-, and fourth-row elements is well established. However, only limited experimental data are available to document such stabilization for oxygen substitution.[2a,3] Theoretical calculations have suggested that for the hydroxide-substituted carbanion **3** in the gas phase significant stabilization (ΔG = 15.8 kcal/mol) would result from the difference between the stabilization due to a σ-inductive effect and a less significant destabilization due to a π-conjugative effect.[4,5] Moreover, the corresponding lithiohydrocarbon **4** has been calculated (in the gas phase) to possess significant nonelectronically derived stabilization due to three-membered ring lithium–oxygen bridging.[6] In the lowest energy bridged syn conformation of **4**, a stabilization energy of 9 kcal/mol was calculated relative to methane. It is anticipated that in the solution phase such bridging would be highly dependent upon the solvent, temperature, species concentration, and possibly the nature of other groups attached to the heteroatom, which in the instance of acetal-substituted organolithium species **5** could intervene via five-membered chelation.[7] In addition, kinetically dictated preferential transfer of the α-alkoxyalkyl ligand from an intermediate lithium stannylate complex **6** has been proposed to rationalize the selective reactivity of this ligand in tetraalkyltin–alkyllithium exchange processes[8] as an alternative mechanism to the formation of a thermodynamically preferred α-alkoxy lithium species.[9,10] We have endeavored to differentiate between these potential contributing effects and provide experimental data that support a primary contribution from electronic factors in α-alkoxy stabilization of organolithium species.



3 **4** **5** **6**

The synthetic potential of the tertiary α-alkoxy lithiohydrocarbons generated with facility via this tin–lithium exchange process in tetrahydrofuran (THF) or dimethoxyethane (DME) is considerable. We have demonstrated that these species can be generated stereospecifically with retention of configuration from the precursor stannane and undergo reactions stereospecifically with retention in their protonation reactions, additions to carbonyl substrates, and displacements of many alkylating agents. However,

(1) Sawyer, J. S.; Macdonald, T. L.; McGarvey, G. J. *J. Am. Chem. Soc.* **1984**, *106*, 3376.

(2) For reviews of heteroatom-substituted carbanions, see: (a) Krief, A. *Tetrahedron* **1980**, *36*, 2531. (b) Beak, P.; Reitz, D. B. *Chem. Rev.* **1978**, *78*, 275. (c) Ahlbrecht, H. *Chimia* **1977**, *31*, 391. (d) Seebach, D.; Geiss, K.-H. In *New Applications of Organometallic Reagents in Organic Synthesis*; Seyferth, D., Ed.; Elsevier: Amsterdam, 1976; p 1.

(3) (a) Cohen, T.; Matx, J. R. *J. Am. Chem. Soc.* **1980**, *102*, 6900 and references therein. (b) Bordwell, F. G.; Van der Puy, M.; Vanier, N. R. *J. Org. Chem.* **1976**, *41*, 1885. (c) Hunter, D. H.; Lin, Y.-t.; McIntyre, A. L.; Shearing, D. J.; Zvagulis, M. *J. Am. Chem. Soc.* **1973**, *95*, 8327. (d) Shatenshtein, A. I.; Gvozdeva, H. A. *Tetrahedron* **1969**, *25*, 2749. (e) Slaugh, L. H.; Bergman, E. *J. Org. Chem.* **1961**, *26*, 3158. (f) Dessy, R. E.; Kitching, W.; Psarras, T.; Salinger, R.; Chen, A.; Chivers, T. *J. Am. Chem. Soc.* **1966**, *88*, 460.

(4) Clark, T.; Korner, H.; Schleyer, P. v. R. *Tetrahedron Lett.* **1980**, 743.

(5) (a) Dill, J. D.; Schleyer, P. v. R.; Pople, J. A. *J. Am. Chem. Soc.* **1976**, *98*, 7498. (c) Clark, T.; Schleyer, P. v. R. *J. Chem. Soc., Chem. Commun.* **1979**, 883.

(6) Schleyer, P. v. R.; Clark, T.; Kos, A. J.; Spitznagle, G. W.; Rohde, C.; Arad, D.; Houk, K. N. *J. Am. Chem. Soc.* **1984**, *106*, 6467 and references cited therein.

(7) See, for example: (a) Still, W. C. *J. Am. Chem. Soc.* **1978**, *100*, 1481. (b) Still, W. C.; Sreekumar, C. *J. Am. Chem. Soc.* **1980**, *102*, 1201.

(8) Andersen, N. H.; McCrae, D. A.; Grotjahn, D. B.; Gabhe, S. Y.; Theodore, L. J.; Ippolito, R. M.; Sarkar, T. K. *Tetrahedron* **1981**, *37*, 4069.

(9) However, for studies directed at discounting this hypothesis, see: Reference 7.

(10) For recent work discussing the intermediacy of stannylate complexes, see: (a) Reich, H. J. *J. Am. Chem. Soc.* **1986**, *108*, 2101. (b) Reich, H. J.; Phillips, N. H.; Reich, I. L. *J. Am. Chem. Soc.* **1985**, *107*, 4101. (c) Kauffman, T.; Kriegusmann, R.; Altepeter, B.; Strinseifer, F. *Chem. Ber.* **1982**, *115*, 1810. (d) Meyer, N.; Seebach, D. *Chem. Ber.* **1980**, *113*, 1290.

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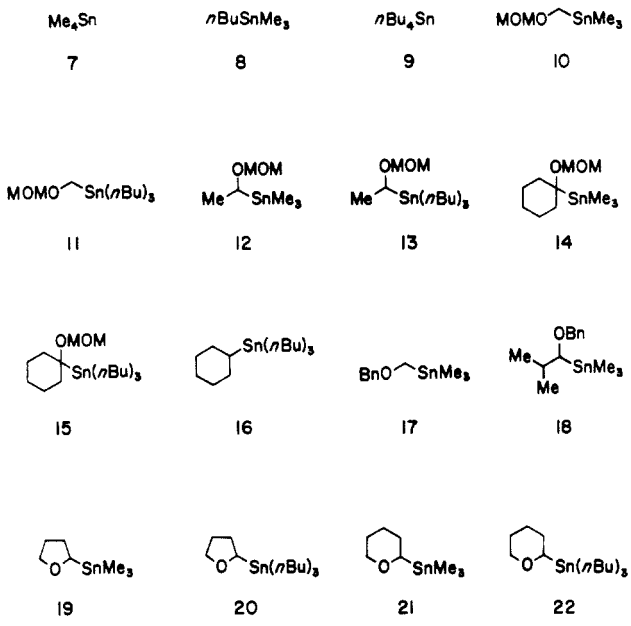


Figure 1. Organostannanes synthesized to examine the relative carbanionic stabilities of the stannyl ligands.

the mechanisms by which these α-alkoxy lithiocarbanion species undergo reaction, particularly processes involving alkylation and protonation with weak carbon acids, are complex and remain obscure.

Results and Discussion

Investigation of the Relative Thermodynamic Stabilities of Organolithium Species Generated via Tin–Lithium Exchange. The study of the thermodynamic properties of sp^3-hybridized organometallic species bearing oxygen substitution is complicated by the inherently low kinetic acidity of the parent carbon acid relative to carbon acids bearing third- and fourth-row substituents.[2a,3] One attractive solution to this problem is the use of metal–metal exchange (eq 2), which has been used successfully

$$R^1M^1 + R^2M^2 \rightleftharpoons R^2M^1 + R^1M^2 \qquad (2)$$

in previous studies to determine relative thermodynamic acidities.[3f] This equilibrium favors the association of the most stable carbanion (R^1 or R^2) with the most electropositive metal (M^1 or M^2). In the present study, we took advantage of the ready availability of α-alkoxy stannanes of type **1** to examine structural effects upon the tin–lithium exchange in eq 1.[7,11b] In this way, the relative stabilities of various carbanions could be ascertained by determining which radicals favored association with the more electropositive lithium metal.

A series of organostannanes (**7–16**) were synthesized via known methodology[7,12] for detailed spectroscopic and reaction product studies directed toward assigning the relative thermodynamic carbanionic stabilities of the stannyl ligands in these species and to semiquantitatively assess the relative energy differences between the organometallic species (Figure 1). Six additional organostannanes (**17–22**) were prepared to examine structural features of the α-alkoxyorganolithium species that could relate to the observed thermodynamic energy differences. The acetal-containing α-alkoxy stannanes were prepared either by addition of (trialkylstannyl)lithium to the corresponding carbonyl substrate and subsequent protection with chloromethyl methyl ether as demonstrated by Still[7b] (**11**, **13–15**) or by exchange of the tri-*n*-butylstannyl α-alkoxy substrate with *n*-BuLi and trapping of the corresponding lithiohydrocarbon with trimethyltin chloride. The ether-containing α-alkoxy stannanes (**17–22**) were synthesized by displacement of the corresponding α-alkoxyorgano halide by (trialkylstannyl)lithium.[7]

Low-temperature ^{1}H NMR (90-MHz) spectroscopy was the principal method chosen to study the tin–lithium exchange reaction described by eq 1. Initially, ^{1}H NMR spectra of *n*-butyllithium and methyllithium were recorded in THF-d_8 at room temperature (27 °C) and at −60 °C. Carbon centers possessing sizable degrees of carbanionic character, such as for organolithium species, are known to display marked upfield shifts for the attached protons. Organometallics having a higher percentage of covalent character, such as Me_4Sn, gave resonances at considerably lower field strengths.[13] The methylene protons α to lithium were observed as a triplet at −1.0 ppm for room temperature solutions of *n*-butyllithium and as a broad singlet having the same chemical shift value at −60 °C. The protons of methyllithium were observed as a sharp singlet near −2.0 ppm at room temperature and as a broad doublet (−2.0 ppm, J = 9 Hz) at −60 °C. This compares with 0.1 ppm for the ^{1}H resonance in Me_4Sn. The general procedure used to assess the transmetalation reaction consisted of equilibrating the appropriate stannane in THF-d_8 at −60 °C, followed by the addition of increasing amounts of selected alkyllithium reagents. When trimethyl-*n*-butyltin **8** was treated with *n*-butyllithium (1.0 equiv), a methyllithium peak appeared at −2.0 ppm having a ratio of one proton to every two associated with stannylmethyl resonances (eq 3). A second equivalent of *n*-butyllithium titrated a second methyl group from the tin center, as indicated by a corresponding increase in the area of the methyllithium peak; a peak corresponding to *n*-butyllithium was not observed under conditions that could detect <5% of the theoretical amount of *n*-butyllithium present. If the equilibrium relationship was approached alternatively (e.g., from *n*-Bu_2SnMe_2 + MeLi), an identical result was obtained. These results, coupled with various controls to insure that the exchange processes were operating under thermodynamic control, established that the thermodynamic relationship of eq 3 under the various conditions lies heavily in favor of the reaction pair to the right of the arrows–compatible with the known thermodynamic stability of methyllithium over *n*-butyllithium. In an identical manner, the low-temperature exchange processes of organostannanes **7–13** and **16** with methyllithium and *n*-butyllithium were investigated.

$$\underset{\mathbf{8}}{n\text{BuSnMe}_3} + n\text{BuLi} \rightleftharpoons \underset{\mathbf{23}}{n\text{Bu}_2\text{SnMe}_2} + \text{MeLi} \qquad (3)$$

In all cases involving the exchange of primary α-alkoxy stannanes **10** and **11** and secondary α-alkoxy stannanes **12** and **13**, the organolithium exchange products were observed directly by NMR spectroscopy, consistent with their existence as discrete species. Evidence in support of the predominant thermodynamic stability of lithium stannylate complexes,[8–10] such as **6**, und these reaction conditions was not obtained from our spect. scopic studies, although such species may well be involved as i erme-

(11) For recent utility of this exchange reaction, see: (a) Quintard, J. P.; Elissondo, B.; Pereyre, M. *J. Org. Chem.* **1983**, *48*, 1559. (b) McGarvey, G. J.; Kimura, M. *J. Org. Chem.* **1982**, *47*, 5420. (c) For early work on this exchange process, see: Seyferth, D. *J. Am. Chem. Soc.* **1964**, *86*, 883.

(12) (a) Gielen, M.; DePoorter, B.; Sciot, M. T.; Topart, *Bull. Soc. Chim. Belg.* **1973**, 271. (b) Bulten, E. J.; Gruter, H. F. M.; Martens, H. F. *J. Organomet. Chem.* **1976**, *117*, 329.

(13) (a) Dessy, R. E.; Kaplan, F.; Coe, G.; Salinger, R. H. *J. Am. Chem. Soc.* **1963**, *85*, 1191. (b) Dessy, R. E.; Kitching, W.; Psarras, T.; Salinger, R.; Chen, A.; Chivers, T. *J. Am. Chem. Soc.* **1966**, *88*, 460.

(14) The stereochemistry of these products was confirmed through protection (MOMCl, $PhNMe_2$) of the known 80:20 mixture of equatorial to axial alcohols resulting from $NaBH_4$ reduction of **31**.[15]

(15) Lansbury, P. T.; MacLeay, R. E. *J. Org. Chem.* **1963**, *28*, 1940.

(16) Cram, D. J. *Fundamentals of Carbanion Chemistry*; Academic: New York, 1965.

(17) Diastereomers **34a** and **34b** were independently prepared by treatment of ketone **31** with methyllithium to give a known 65:35 mixture of axial to equatorial alcohols[18] followed by protection (MOMCl, $PhNMe_2$).

(18) Ashby, E. C.; Laemmle, J. T. *Chem. Rev.* **1975**, *75*, 521.

(19) Kitching, W.; Olszowy, H.; Waugh, J.; Doddrell, D. *J. Org. Chem.* **1978**, *43*, 898.

(20) (a) Kuivila, H. G.; Considine, J. L.; Mynott, R. J.; Sarma, R. H. *J. Organomet. Chem.* **1973**, *55*, C11. (b) Doddrell, D.; Burfitt, I.; Kitching, W.; Bullpitt, M.; Lee, C.-H.; Mynott, R. J.; Considine, J. L.; Kuivila, H. G.; Sarma, R. H. *J. Am. Chem. Soc.* **1974**, *96*, 1640.

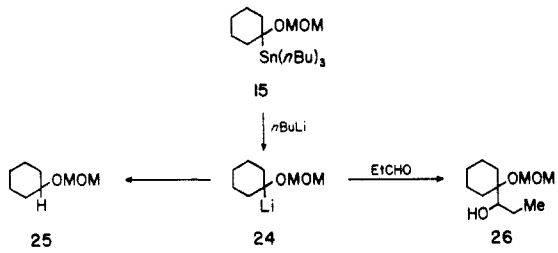


Figure 2.

diates in the exchange process with our NMR spectra representing a time average of the "free" and "ate" species [since small (<0.05 ppm) spectral changes would be undetectable].[10a,b]

The position of equilibria in the tin–lithium exchange processes described above was confirmed by low-temperature quench of the reactions with a proton source (methanol) and carbonyl electrophiles (propionaldehyde, benzaldehyde) followed by careful characterization of the products. In each instance, the product analysis of an exchange process precisely corroborated the result obtained via NMR spectroscopic analysis, indicating that both protonation and carbonyl addition occur under sufficient kinetic control so as to represent the thermodynamic equilibrium of the organolithium species (cf. ref 7).

Through the employment of such reaction product studies, data on the position of equilibria for the alkyllithium exchange reactions of tertiary α-alkoxy stannanes **14** and **15** could be obtained. Thus, in the reaction of (α-alkoxycyclohexyl)trimethylstannane (**14**) with *n*-butyllithium (3.0 equiv) in THF at −78 °C for 15 min, only (α-alkoxycyclohexyl)tri-*n*-butylstannane (**15**, 90%) could be isolated after quenching. However, when α-alkoxy stannane **15** was treated with *n*-butyllithium (1.1 equiv) in THF at −78 °C for 2 min, then quenched with methanol, (*O*-methoxymethyl)cyclohexanol (**25**, 95%) and tetra-*n*-butylstannane were obtained (Figure 2). These data suggested that in the tin–lithium exchange process, the tertiary α-alkoxyorganolithium species **24** was thermodynamically less preferred than methyllithium (>95:5) and more preferred than *n*-butyllithium (>95:5). When quenching of the α-alkoxyorganolithium species was attempted with propionaldehyde, only methoxymethyl-protected cyclohexanol (**25**) could be isolated (94%). The source of this premature protonation remains unclear; solutions of *n*-butyllithium were standardized prior to use, and THF was freshly distilled from sodium benzophenone ketyl. Great care was taken to ensure completely anhydrous conditions throughout the reaction. One possible explanation is the known instability of cyclic ethers to alkyllithium reagents or other strong bases. To test the possibility of incipient tin–lithium exchange, followed by solvent deprotonation, the reaction was conducted in THF-d_8 (99.5% D) at −78 °C with ^{1}H NMR analysis centering on the cyclohexyl proton adjacent to the protected alcohol. No deuterium incorporation (>90% ^{1}H) was observed, suggesting that either some other mechanism for protonation is operative or that a significant kinetic deuterium isotope effect must occur in a THF-mediated proton transfer. However, exchange of α-alkoxy stannane **15** with *n*-butyllithium (1.0 equiv) in DME at −78 °C for 2 min, followed by treatment with excess propionaldehyde, provided 1-propanol adduct **26** (85%) and confirmed the thermodynamic preference of α-alkoxy organolithium species **24** over *n*-butyllithium. Although *O*-(methoxymethyl)cyclohexanol (**25**, >10%) was additionally isolated, *O*-(methoxymethyl)cyclohexanol-containing stannanes (<5%) or 3-heptanol (<5%) were not detected.

The cumulative results of these exchange experiments on organostannanes **7–16** enabled the establishment of an order (Figure 3) for the relative stabilities of the organolithium species generated via tin–lithium exchange under the equilibrium conditions employed [THF (or DME for tertiary α-alkoxy stannane **15**) at −60 to −78 °C]. The position of equilibrium in each of the reaction pairs studied (as >95:5) allows the assessment of at least a 2 kcal/mol energy difference between the reaction pairs (in eq 1); if a significant portion of this energy difference can be ascribed to energy differences between the organolithium species (vide

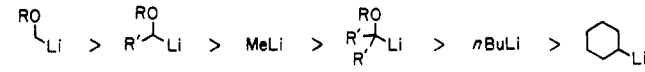
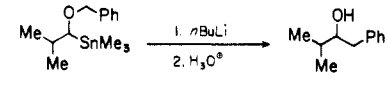


Figure 3. Relative stabilities of α-alkoxyorganolithium and alkyllithium reagents generated via tin–lithium exchange.

infra), an excess of approximately 1.5 pK_a units separates the organolithium species in Figure 3. The origins of the thermodynamic stabilities of the organolithium species in Figure 3 may be attributable to stabilization by a σ-inductive effect by the adjacent ether function, to an optimal orientation of the heteroatom lone pairs in order to enable three- or five-membered ring lithium chelation or to minimize π-conjugative destabilization, to differences in the aggregation status of the organolithium species, or to a combination of these effects.

In an attempt to dissect some of the specific structural and electronic contributions that could be operational in the promotion of lithium carbanion stability by the α-alkoxy function, organostannanes **17–22** were synthesized. Although the primary rationale for comparing the ether-based derivatives **17–22** relative to their acetal-based analogues **10–13** was to assess the potential significance of five-membered lithium chelation (**5**), clearly multiple factors may additionally contribute to the observed relative stabilization or destabilization, and complete differentiation of these interactive contributions may not be feasible. For example, the α-alkoxy moiety of the acetal system would be expected to exhibit a greater inductive effect relative to the other analogue, and the conformationally "fixed" lone pair orientations of the cyclic ether systems **19–22** would be anticipated to impact both on the postulated three-membered chelation (**4**) and on the minimization of destabilizing O lone pair–C–Li bond π-conjugative effects relative to their acyclic counterparts (**12**, **13**, and **18**). In addition, these organolithium species may aggregate in (THF or DME) solution, and the enthalpic and entropic contributions to the relative stabilities of each organometallic compound could vary substantially. Nonetheless, the results of the alkyllithium exchange reactions of α-alkoxy stannanes **17–22** proved enlightening. α-Alkoxy stannane **17** undergoes complete exchange at −60 °C with *n*-butyllithium or methyllithium (1.0 equiv) to generate exclusively (>95%) [α-(benzyloxy)methyl]lithium, as confirmed by both NMR spectroscopy and product analysis upon reaction with various electrophiles. In contrast, treatment of α-alkoxy stannane **18** under identical conditions led entirely to the Wittig rearrangement product **27**. Since rearrangement appeared

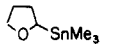
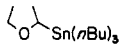
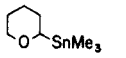
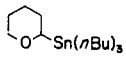


18 **27**

concomitant with Sn–Li exchange (on the NMR time scale), this substrate did not enable unambiguous assessment of the relative organolithium stabilities of the methyl and α-alkoxyalkyl ligands bound to tin. We focused our attention on the cyclic α-alkoxy stannanes **19–22** in order to address this issue.

Data for the Sn–Li exchange of α-alkoxy stannanes **19–22** and subsequent benzaldehyde quenching are compiled in Table I. Although exchange of the α-alkoxyalkyl ligand in **19** and **20** and **21** and **22** is substantially preferred over *n*-butyl (>95:5), only a moderate preference is observed over methyl (~3:1) statistically corrected for **21**, in dramatic contrast with the acetal analogue **12**. Although, as previously noted, multiple factors may be operative in the enhancement and depression of the thermodynamic stabilities of α-alkoxyalkyllithium species, the differences in the data (Table I) between stannanes **19** and **21** are intriguing and potentially informative. A priori the primary difference between **19** and **21** and their acyclic counterparts is the orientation of the O lone pairs relative to the carbon–lithium σ-bond; such stereoelectronic factors may play significant roles in α-alkoxyalkyllithium stability. Nonetheless, in every instance yet examined via tin–lithium exchange in a wide variety of solvents, an α-alkoxy substituent provides substantial stabilization to the derived organolithium species relative to hydrogen, independent of the ad-

Table I. Yields for the Exchange (*n*-BuLi) and Quench (PhCHO) of Alkoxy Stannanes **19–22**

stannane	no.	benzaldehyde condensation product,[a] % (diastereomeric ratio)	OH Ph Me	OH Ph Me
	**19**	47 (50:50)	13%	none
	**20**	71 (52:48)	none	none
	**21**	30 (52:48)	32%	none
	**22**	76 (51:49)	none	none

[a] Yields isolated products for exchange/quench of organostannanes **19**, **20**, and **22**. Yields for the exchange/quench of organostannane **21** were determined by GC analysis; details of the experimental and analytical procedures are presented in the Experimental Section.

ditional electronic or chelation influences introduced by the acetal function or of the stereoelectronic constraints imposed by the cyclic ether moiety. Such findings are consistent with the σ-inductive effect of the alkoxy moiety exhibiting the *predominant* stabilizing factor on an adjacent carbon–lithium bond, although stabilization by alternate α-alkoxy substituent dependent means is possible. These factors are considered below.

Throughout this discussion, our attention has been focused on the relative stabilities of the organolithium species generated via tin–lithium exchange. However, it is invalid to interpret the total energy difference of a lithium–metal exchange reaction in terms of only the ratio of the organolithium species without consideration of the effects of the exchange process on the organostannane compounds or of the effects that solvent might exert in coordinating to the organometallic species or promoting aggregate formation. The complete expression for the equilibrium constant of an exchange process of monomeric species in solvent(s) indicated earlier in eq 1 is illustrated. A more complex equation would

$$K = \frac{[R^2R^3C(OR^1)Li]\cdot S_a}{[R^5Li]\cdot S_b} \cdot \frac{[R^5SnR^4_3]\cdot S_c}{[R^2R^3C(OR^1)SnR^4_3]\cdot S_d}$$

be required to describe differences in the aggregation states of the organolithium species. Since thermodynamic data concerning α-substitution effects of oxygen substituents on carbon–tin bonds are unavailable, in all of the experiments detailed for organostannanes **7–16**, we undertook a series of equilibrium, competitive exchange processes in which we effectively "set" the ratio of the concentrations of the tin compounds equal to unity. In these experiments, we were able to detect by NMR spectroscopy a ratio of organolithium compounds of ~98:2. From the equilibria constants, and with proper adjustment of reagent concentrations, we could assign the relative acidity differences afforded some of these compounds primarily to energy differences between the organolithium species.

We propose that the principal factors influencing the relative thermodynamic stabilities of the organolithium species indicated in Figure 3 are stabilization by α-alkoxy substitution and destabilization by α-alkyl substituents of organolithium species. Our rationale for this proposal stems from the relative insensitivity of the thermodynamic acidity ranking to the nature of the alkyl substituents (R^2, R^3) at the organolithium site, the alkoxy protective group (R^1), or the solvent in the exchange reaction (refer to eq 1). Assuming the validity of this proposition for organolithium agent stability, conservative estimates of the destabilizing influence of alkyl substitution on sp^3-hybridized organolithium species can be placed at 3–4 kcal/mol and of the stabilization afforded by alkoxy substitution at about 5–6 kcal/mol.

Other factors may contribute to the relative stabilities of the organolithium species indicated in Table III as noted above. Prominent among these factors and undoubtedly relevant are the

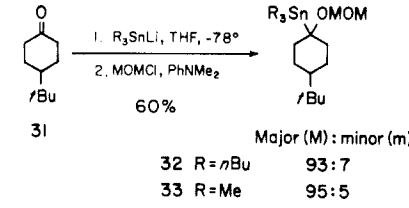


Figure 4.

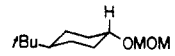
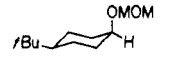
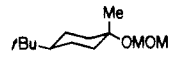
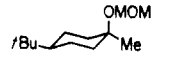
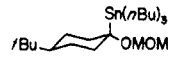
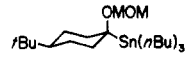
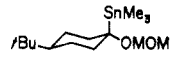
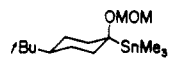
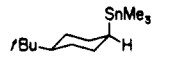
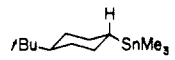
aggregation status of each organolithium species and level of solvent incorporation of each species. Clearly, if defined differences in the aggregation status (e.g., dimers, trimers, tetramers, etc.) or of the levels of solvent incorporation (e.g., solvent bound by alkyl-Li and by α-RO-alkyl-Li) could be attributed to α-alkoxy and α-alkyl substitution, either or both of these factors could be significant. In particular, the levels of solvent binding of each organolithium species may have substantial impact on the entropy contribution to the free energy of the system, as pointed out by a reviewer. We have not assessed the aggregation state of the organolithium species that we have studied here and can comment directly on these concerns. However, the contributions of these factors would be expected to depend in part on solvent and alkyl and α-alkoxy substitution. Since, over the limited solvent and substituent range that we have studied, we find no difference in the relative thermodynamic order of these organolithium species (Figure 3), we believe the primary factor to be intrinsic α-alkoxyl stabilization and α-alkyl destabilization of tetrahedral organolithium species.

Several features of the generation of α-alkoxyorganolithium species via tin–lithium exchange deserve mention. The process is subject to the thermodynamic considerations noted above and, for effective organometallic agent formation, to kinetic factors. The rate of exchange has a substantial solvent dependence (DME > THF > ether) and is strongly influenced by the size of the trialkylstannyl substituents (Me ≫ *n*-Bu ≫ cyclohexyl). Thus, under these conditions, (dialkylalkoxymethyl)lithium species can be conveniently generated only in DME. However, by utilizing the trimethylstannyl moiety, (phenylalkylalkoxymethyl)lithium species can be produced via tin–lithium exchange (e.g., **28** → **29**) in a variety of solvents (DME, THF, ether, vide infra). The ability to utilize the trimethylstannyl, rather than the tri-*n*-butylstannyl derivative, for the exchange process could be readily predicted through considerations of the thermodynamic stabilities of these species [e.g. **2** (R_2 = Me, R_3 = Ph) > Me].

Synthetic and Mechanistic Studies. Having established a hierarchy for organolithium agent stabilities that exposed the acidifying influence of α-oxygenation, we undertook studies to probe the mechanistic details and synthetic potential of trialkylstannane-mediated generation of α-alkoxyorganolithium species. With this in mind, we chose to explore the generation and reactions of the α-alkoxy organolithium reagents derived from the conformationally biased cyclic ketone 4-*tert*-butylcyclohexanone (**31**). As described previously, the ketone was treated with R_3SnLi (THF, −78 °C) to result in diastereomeric hydroxyl stannanes, which were protected without purification as their methoxymethyl derivatives providing the indicated mixtures of isomers **32M,m** and 33**M,m** (Figure 4). Spectral and chromatographic analyses of the intermediate hydroxy stannanes demonstrated that the isomeric ratios were unchanged following protection. Armed with stereochemically differentiated organostannanes, we initiated an investigation to determine the steric course of the tin–lithium exchange/alkylation sequence.

Preliminary insight into these events was gained through protonation of the organolithium intermediates derived by tin–lithium exchange of the separated tri-*n*-butylstannyl diastereomers (Figure 5). We noted initially the chemical shifts of the stannylmethyl carbons in which correspondingly higher shielding is observed for the equatorial stannanes (**33m** and **36b**) relative to the axial isomers (**33M** and **36a**) (Table II).

Table II. ^{13}C Chemical Shifts of Ring and Stannylmethyl Centers of Selected Stannanes and Derivatives

compound	no.	chemical shift, ppm C_1	C_2	C_3	C_4	$SnCH_3$
	**34a**[14]	76.11	33.15	25.63	47.27	
	**34b**[14]	70.81	31.06	21.55	47.05	
	**35a**[17]	76.64	38.00	24.36	47.71	
	**35b**[17]	73.93	37.37	22.30	47.39	
	**32M**	87.81	38.47	25.19	47.70	
	**32m**	80.93	36.99	22.07	48.06	
	**33M**	85.13	38.03	24.97	47.60	−8.13
	**33m**	76.90	35.34	21.93	48.11	−9.71
	**36a**[19]	27.80	31.06	26.78	48.57	−9.41
	**36b**[19]	25.26	31.72	29.91	48.53	−12.04

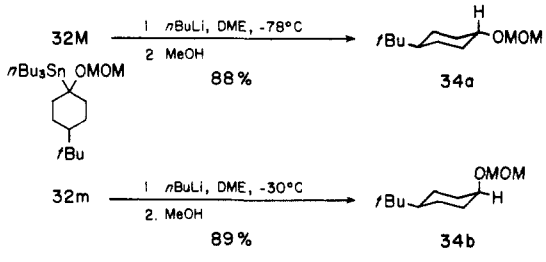


Figure 5.

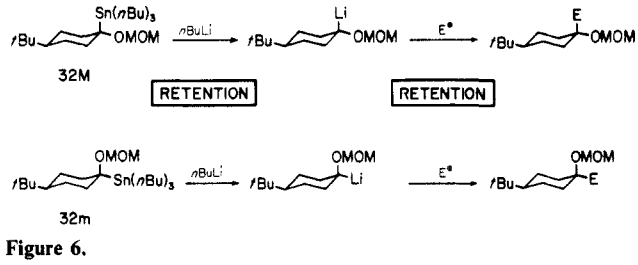


Figure 6.

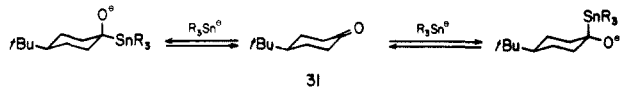
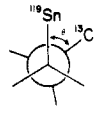


Figure 7.

Compelling evidence in support of these assignments for **32M,m** and **33M,m** was obtained through analysis of vicinal $^{119}Sn-^{13}C$ coupling of the form

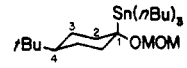
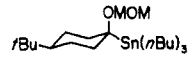
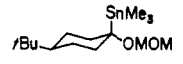
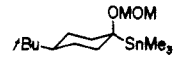
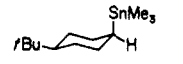
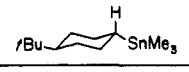


$$^3J = 30.4 - 7.6\cos\theta + 25.2\cos\theta$$

This equation is analogous to the Karplus equation[21] and similarly describes a curve having maxima at $\theta = 0, 180°$ and a minimum at $\theta \approx 90°$. The observed coupling constants and the calculated dihedral angles for compounds **32M,m**, **33M,m**, and **36a,b** are presented in Table III. The smaller coupling constants

(21) Karplus, M. *J. Am. Chem. Soc.* **1963**, *85*, 2870.

Table III. Vicinal $^{119}SnCC^{13}C$ Coupling Constants and Associated Dihedral Angles

compound	no.	^3J, Hz	θ, deg
	**32M**	<3	85
	**32m**	40.0	139
	**33M**	9.4	103
	**33m**	46.2	146
	**36a**[19]	12.0	107
	**36b**[19]	67.1	175

for the major isomers **32M** and **33M** clearly indicate an axial disposition of the trialkylstannyl group, consistent with the assignments made previously for **36a,b**.[19]

Armed with this data, the stereochemical course of events for Figure 5 can be confidently assigned to be retention/retention (Figure 6), confirming the previous conclusion.[7] In view of this configurational integrity, the sequence provides a synthetically useful method of stereospecifically replacing a trialkylstannyl group at a tetrahedral center.

The high levels of stereoselection in favor of axial addition of R_3SnLi to 4-*tert*-butylcyclohexanone (**31**) were unexpected and prompted us to further examine this condensation reaction. Since nucleophilic attack on cyclohexanones is kinetically favored in an equatorial sense,[18] we explored the possibility of reversibility in the stannyl anion addition (Figure 7). When *n*-Bu_3SnLi is condensed with ketone **31** in a less polar solvent, ether at −78 °C, a 55:45 mixture of tertiary alcohols was realized, now favoring the equatorial stannane. Furthermore, treatment of this mixture with a slight excess of *n*-butyllithium in THF at −78 °C quickly (<10 min) established the initially observed 93:7 mixture of axial to equatorial stannylation products. These results are consistent with a rapid equilibrium as in Figure 7 supplanting the kinetically

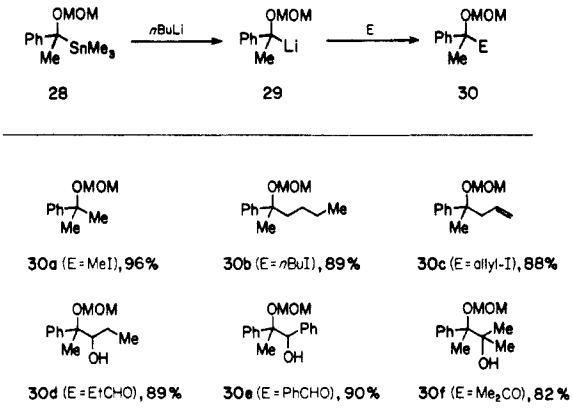


Figure 8.

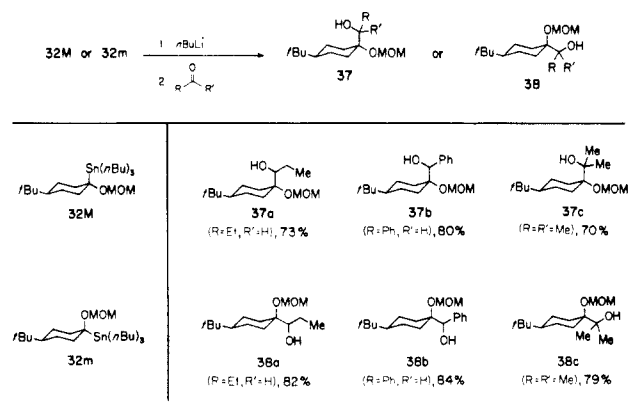


Figure 9.

Table IV. Addition of (Trialkylstannyl)lithium Reagents to 4-*tert*-Butylcyclohexanone

R	solvent	time, min	temp, °C	
n-Bu	THF	15	−78	93:7
n-Bu	THF	15	−40	93:7
Me	THF	15	−78	93:7
n-Bu	ether	5	−78	45:55
Me	ether	5	−78	45:55
n-Bu	ether	5	−100	25:75
n-Bu	pentane	30	−78 → 0	NR[b]
n-Bu	DME	15	−40	50:50

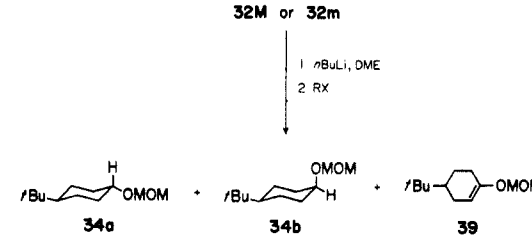
[a] Determined following protection of the alcohol (MOMCl, $PhNMe_2$). [b] No tin–lithium exchange was observed in this solvent.

regulated control in favor of equatorial attack. That the trialkylstannyl group would be preferred in the axial position is reasonable in light of the modest *A* values of 1.0–1.2 kcal/mol attributed to such R_3Sn groups.[22] It seems likely that the solvated lithium alkoxide possesses steric requirements sufficiently in excess of these values to establish the thermodynamic priorities observed. Table IV describes the effects of some changes in reaction conditions upon the axial to equatorial ratio. As shown, the highest level of kinetic control was realized in the condensation of *n*-Bu_3SnLi in ether at −100 °C (75% equatorial).

The availability of a wide range of tertiary α-alkoxy trialkylstannanes and strict stereochemical control by which tin–lithium exchange takes place confer unique synthetic utility to the derived α-alkoxyorganolithium species. We chose to explore this potential through a study of the reactions of the organolithium reagents derived from stannanes **32M**, **32m**, and **28** with a variety of alkyl halide and carbonyl electrophiles. An initial survey of the carbon–carbon bond forming reactions of organolithium species **29** was carried out with the result that efficient condensations were observed with a range of alkyl iodides and carbonyl compounds (Figure 8). Undoubtably, the stabilization of the phenyl ring and the α-alkoxy substituent contributed to lack of side reactions attributable to the highly basic nature of other tertiary organolithium species. Diols **30d** and **30e** were isolated as inseparable mixtures of diastereomers (65:35 and 68:32, respectively). Asymmetric induction by related α-alkoxy organometallic species has been noted previously in these laboratories,[11b] and no effort was made to ascertain the identity of these isomers.

Perhaps more interesting were the reactions of axial and equatorial stannanes **32M** and **32m**. Condensations with carbonyl electrophiles were once again found to proceed cleanly with no erosion of the configurational integrity at the tertiary stereocenter (Figure 9). The realization of exclusively axial products **37a–c** from stannane **32M** bears particular emphasis in view of the propensity for equatorial attack by carbon nucleophiles on conformationally biased cyclohexanones.[18,23] The slightly depressed yields for products derived from **32M** are probably attributable to the larger steric constraints placed upon axial substitution relative to the corresponding equatorial position. The isolated yields in Figure 9 further serve to demonstrate the remarkably nucleophilic nature of these agents as compared with the strongly basic properties of simple organolithium species devoid of α-oxygenation.[24]

Table V. Attempted Alkylations of the Organolithium Species Generated via Tin–Lithium Exchange of Stannanes **33M** and **32m**



RX	stannane	% 34a	% 34b	% 39
allyl-I	**32M**	44	18	38
	32m	21	32	47
n-Bu	**32M**	15	16	69
	32m	30	35	35
MeI	**32M**	14	27	59
	32m[a]	0	33	28
allyl-Br	**32M**	26	9	65
	32m	19	37	44
n-BuBr	**32M**	26	31	43
	32m	13	37	50
allyl-Cl	**32M**[b]	58	0	9
	32m	20	41	39
n-BuCl	**32M**	96	0	4
	32m	19	57	24

[a] 39% of the methylated product was observed. [b] 33% of 4-*tert*-butylcyclohexanone was observed.

The alkylation reactions of stannanes **32M** and **32m** with organohalides did not, however, parallel the results seen with **28**. In general, treatment of the derived tertiary organolithium compounds resulted in mixtures of protonated products **34a** and **34b** in addition to enol ether **39** (Table V). The composition of these product mixtures was found to be intimately tied to the identity of the organic halide employed, although no discernible trends are apparent. While further studies on the mechanism of these transformations are indicated, we speculate that halogen–metal exchange via a single-electron transfer mechanism may be operative to account for the formation of the enol ether **39** and the scrambling of the tertiary stereocenter in the generation of **34a** and **34b**. The generation of an incipient tertiary α-alkoxy radical is consistent with current mechanistic conclusions for halogen–

(22) (a) Kitching, W.; Doddrell, D.; Grutzner, J. B. *J. Organomet. Chem.* **1976**, *107*, C5. (b) Kitching, W.; Olszowy, H. A.; Harvey, K. *J. Org. Chem.* **1982**, *47*, 1893. (c) Moder, T. I.; Hsu, C. K.; Jensen, F. R. *J. Org. Chem.* **1980**, *45*, 1008. (d) Booth, H.; Everett, J. R. *J. Chem. Soc., Chem. Commun.* **1976**, 278.

(23) (a) Rei, M.-H. *J. Org. Chem.* **1979**, *44*, 2760 and referenced cited therein. (b) Wipke, T.; Gund, P. *J. Am. Chem. Soc.* **1976**, *98*, 8107. (c) Toromanoff, E. *Top. Stereochem.* **1967**, *2*, 157.

(24) Buhler, J. D. *J. Org. Chem.* **1973**, *38*, 904.

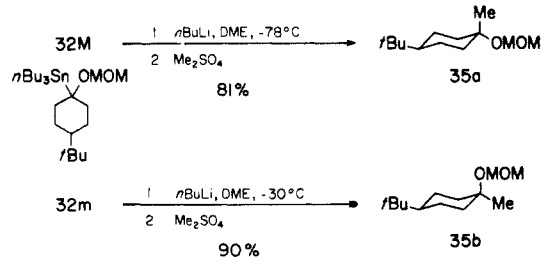


Figure 10.

metal exchange[25] and would account for the requisite decrease in the energy barrier to configurational inversions to result in the observed mixtures of **34a,b**.

Methylation of stannanes **32M** and **32m** became an efficient process when Me_2SO_4, an electrophilic alkylating reagent not susceptible to a single-electron transfer process (Figure 10), was employed. Once again, this sequence was found to proceed in a stereospecific manner with overall retention of configuration. With stereoselective access to axial stannane **32M** available, this route provides a convenient means to axially methylated materials such as **35a**, complementing existing methods of alkylating such ketones in equatorial fashion.[18]

Summary and Conclusion

The relative ease of the cleavage of some tin–carbon bonds upon treatment with alkyllithium reagents has been established through a series of comparative experiments. Since the lability of the tin ligand is dictated by thermodynamic considerations under the conditions employed, these results allow an assessment of the relative stability of the derived organolithium species. These studies demonstrated a high selectivity for cleavage of ligands possessing α-alkoxy substituents, which we propose to be indicative of the effective stabilizing influence of oxygen upon tetrahedral alkyllithium species, in agreement with recent theoretical findings. While the origin of this heteroatom stabilization is undoubtedly the result of several contributing factors, the present data implicate σ-inductive effects as playing a significant role in lowering the energy of these substituted organolithium species.

The synthetic potential of α-alkoxy stannanes is considerable as a means of forming functionalized carbon–carbon bonds with predictable stereo control at the carbon center bearing the trialkylstannyl group. Detailed NMR analysis of diastereomerically discrete trialkylstannyl adducts of 4-*tert*-butylcyclohexanone provided unambiguous evidence that the steric course of tin–lithium exchange takes place with retention at the alkoxy-bearing carbon. This is the first direct experimental evidence of this chemical event and supports previous conclusions addressing the overall replacement of the tin center by electrophiles with retention. In the course of these studies, it was found that the addition of (trialkylstannyl)lithium reagents to ketones is a reversible process, potentially allowing placement of the tin center in the most sterically demanding orientation with high selectivity. This reversibility may or may not play a role in condensations with aldehydes and awaits experimental verification. The attractive nucleophilic properties of α-alkoxyorganolithium reagents coupled with their stereospecific generation from stannyl precursors confer obvious synthetic utility to this class of reactive intermediates. It is expected that the results of this study will enhance the value of this important general method of preparing tetrahedral organolithium species and lays the groundwork for further investigations into the generation and use of organometallics bearing a wide variety of heteroatomic substitution.

Experimental Section

General Procedures. Thin-layer chromatograms were run on E. Merck glass plates precoated with silica gel 60 F-254 and visualized with either chromic acid or vanillin/sulfuric acid spray. Infrared spectra were recorded on a Perkin-Elmer Model 1430 ratio recording infrared spectrophotometer. ^{1}H NMR spectra were determined on a Varian Model EM-390 spectrometer at 90 MHz or a Nicolet NT-360 spectrometer with 1280/293B data system at 360 MHz. ^{13}C NMR spectra were determined on either a Japan Electron Optics Laboratory Model PFT-100 spectrometer with EC-100 data system at 25 MHz or a Nicolet NT-360 spectrometer at 90 MHz. Unless otherwise noted, chemical shifts are reported (δ) downfield from internal tetramethylsilane (^{1}H NMR) or referenced from the center peak of $CDCl_3$ at 77.00 ppm (^{13}C NMR). Hydroxyl protons (indicated O*H*) were confirmed by D_2O exchange. All reported ^{13}C spectra are proton decoupled. Mass spectra were recorded on a Finnigan MAT 4515 GC/MS/DS instrument utilizing both chemical ionization and electron impact ionization techniques. Microanalyses were performed by Atlantic Microlab, Inc., Atlanta, GA.

Column chromatographic separations were effected on Woelm silica 32-63 using a modified short/flash column technique. Deactivated silica gel was prepared by passing through one column volume of ethyl acetate. THF and DME were distilled under argon from sodium benzophenone ketyl prior to use. Reagent-grade acetone was distilled and stored over molecular sieves for 1 week prior to use. Reagent-grade benzaldehyde was distilled from calcium hydride immediately prior to use. Propionaldehyde and acetaldehyde were distilled immediately prior to use; all other reagents were used without further purification with the exception of allyl iodide, which was washed twice with saturated sodium thiosulfate solution and passed down a short column of basic alumina immediately prior to use. "Brine" refers to saturated sodium chloride solution. Reagents used in "excess" refers to at least a 5× molar factor based upon limiting reagent.

Methyllithium was purchased from Aldrich; *n*-butyllithium was purchased from Alfa Inorganics. Tetrahydrofuran-d_8 was purchased from Aldrich and used without further purification. Solutions of alkyllithium reagents in THF or THF-d_8 were prepared by solvent exchange and used immediately. All reactions were carried out under inert atmosphere (argon or nitrogen). Yields for the two-step synthesis of α-alkoxyorganostannanes from carbonyl compounds possessing α-hydrogens are not based upon recovered starting material. On the average, 20% of such carbonyl-containing starting materials are recovered unchanged upon final chromatography. Yields from exchange/addition reactions are not optimized. Organostannanes **7–9** and **16** were prepared according to literature procedures.[12]

Addition of (Trialkylstannyl)lithium Species to Selected Carbonyl Compounds and Protection of the Resulting Alcohols with Chloromethyl Methyl Ether. (a) General Procedure for the Synthesis of α-Alkoxy Trimethylstannyl Derivatives. (Trimethylstannyl)lithium (9.82 mmol) was prepared by the addition of *n*-butyllithium (9.82 mmol) to hexamethylditin (3.20 g, 9.80 mmol) in THF (25 mL) at 0 °C.[7a] This solution was cooled to −78 °C, and the desired substrate (8.0 mmol), dissolved in a minimum of THF, was added dropwise over 1 min. The yellow color faded but did not disappear totally. The reaction mixture was stirred for 15 min and then quenched with saturated ammonium chloride solution (10 mL). The mixture was poured into saturated ammonium chloride solution (20 mL) and extracted with petroleum ether (20 mL). The aqueous layer was back-extracted once with petroleum ether (20 mL), and the combined organic layers were dried over sodium sulfate, filtered, and concentrated in vacuo to give a cloudy white oil. This was immediately dissolved in methylene chloride (10 mL) and treated with chloromethyl methyl ether (20 mmol, 1.64 g) and *N,N*-dimethylaniline (1.5 mL) for 18 h at room temperature. The reaction mixture was poured into petroleum ether (10 mL) and washed successively with 0.5 N HCl (10 mL), water (10 mL), and saturated sodium bicarbonate solution (15 mL). Drying of the organic layer (sodium sulfate), filtration, and concentration in vacuo gave a yellow oil. The oil was chromatographed (10:1 silica gel, 0.5% ethyl acetate/99.5% petroleum ether) to afford the pure trimethylstannyl derivative as a colorless oil (60–95%).

***O*-(Methoxymethyl)-1-(trimethylstannyl)cyclohexanol (14) from cyclohexanone**: 84%; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.70 (2 H, s), 3.32 (3 H, s), 1.00–2.19 (10 H, m), 0.09 (9 H, s, $^2J(^{117/119}Sn-^1H)$ = 51.0 Hz); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 93.04, 79.11, 55.57, 35.33, 26.16, 21.74, −9.42; IR (NaCl, cm^{-1}) 2918, 2840 (w), 1441, 1390, 1149, 1130, 1089, 1037, 916, 758; MS (CI), *m/e* (relative intensity) 311 (2), 309 (2), 308 (1), 307 (6), 306 (3), 304 (3), 303 (4), 297 (20), 295 (15), 294 (12), 293 (100), 292 (38), 291 (77), 290 (32), 289 (50), 267 (7), 265 (5), 264 (3),

(25) (a) Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon: New York, 1974. (b) Wickham, G.; Olszowy, H. A.; Kitching, W. *J. Org. Chem.* **1982**, *47*, 3788. (c) Bailey, E. F.; Gagnier, R. P.; Patricia, J. J. *J. Org. Chem.* **1984**, *49*, 2098.

(26) (a) Gazizova, L. B.; Imashev, U. B.; Musavirov, R. S.; Kantor, E. A.; Zlotskii, S. S.; Kuzmichev, A. A.; Rakhmankulov, D. L. *Zh. Org. Khim., Engl. Ed.* **1981**, *17*(2), 226. (b) For additional characterization, this compound was prepared independently by the addition of chloromethyl methyl ether to cyclohexanol in the presence of *N,N*-dimethylaniline. See: Barot, B. C.; Pinnick, H. W. *J. Org. Chem.* **1981**, *46*, 2981.

263 (34), 262 (13), 261 (27), 260 (11), 259 (17), 169 (15), 167 (12), 166 (4), 165 (65), 164 (21), 163 (49), 162 (18), 161 (32), 99 (48); TLC (5 ethyl acetate/95% petroleum ether) R_f 0.66.

1-(Methoxymethoxy)-1-phenyl-1-(trimethylstannyl)ethane (28) from acetophenone: 53%; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 6.97–7.44 (5 H, m), 4.72 (2 H, dd, J = 18, 6 Hz), 3.43 (3 H, s), 1.83 (3 H, s, $^3J(^{117/119}Sn-^1H)$ = 54 Hz), 0.07 (9 H, s, $^2J(^{117/119}Sn-^1H)$ = 45 Hz); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 147.75, 128.14, 124.84, 123.91, 93.14, 79.74, 55.82, 23.44, −9.46; IR (NaCl, cm^{-1}) 2940, 2343 (w), 1595, 1489, 1440, 1153, 1082, 1025, 990, 912, 758, 694; MS (EI), m/e (relative intensity) 335 (17), 334 (11), 333 (30), 332 (14), 331 (79), 330 (42), 329 (100), 328 (58), 327 (95), 326 (42), 325 (46), 324 (16), 323 (18), 305 (4), 304 (4), 303 (8), 302 (6), 301 (27), 300 (14), 299 (35), 298 (20), 297 (33), 296 (14), 295 (16), 294 (4), 293 (5); TLF (5% ethyl acetate/95% petroleum ether) R_f 0.58. Anal. Calcd for $C_{13}H_{32}O_2Sn$: C, 47.46; H, 6.74. Found: C, 47.56; H, 6.77.

***trans*-4-*tert*-Butyl-*O*-(methoxymethyl)-1-(trimethylstannyl)cyclohexanol (33M) and *cis*-4-*tert*-Butyl-*O*-(methoxymethyl)-1-(trimethylstannyl)cyclohexanol (33m) from 4-*tert*-Butylcyclohexanone. 33M**: 59%; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.73 (2 H, s), 3.36 (3 H, s), 2.26 (2 H, br d, J = 13.5 Hz), 1.77 (2 H, br d, J = 10.7 Hz), 1.65 (1 H, dt, J = 2.8, 12.9 Hz), 0.85–1.71 (4 H, m), 0.85 (9 H, s), 0.15 (9 H, s, $^2J(^{117/119}Sn-^1H)$ = 49.2 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 92.58, 85.13, 55.32, 47.60, 38.03, 32.41, 27.67, 24.97 ($^3J(^{119}Sn-^{13}C)$ = 9.4 Hz), −8.13; IR (NaCl, cm^{-1}) 2930, 2340 (w), 1463, 1437, 1363, 1145, 1084, 1035, 916, 760; MS (CI), m/e (relative intensity) 367 (4), 366 (3), 365 (7), 364 (4), 363 (10), 362 (5), 361 (8), 360 (3), 359 (6), 351 (15), 350 (10), 349 (57), 348 (23), 347 (48), 346 (18), 345 (29), 171 (25), 169 (48), 167 (37), 165 (59), 164 (17), 163 (43), 162 (15), 161 (28), 155 (100); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.60. Anal. Calcd for $C_{15}H_{32}O_2Sn$: C, 49.62; H, 8.88. Found: C, 49.66; H, 8.98.

33m: 3%; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.55 (2 H, s), 3.29 (3 H, s), 2.13 (2 H, br d, J = 9 Hz), 1.08–1.75 (7 H, m), 0.80 (9 H, s), 0.00 (9 H, s, $^2J(^{117/119}Sn-^1H)$ = 48 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 93.17, 76.90, 55.67, 48.11, 35.34, 32.54, 27.44, 21.93 ($^3J(^{119}Sn-^{13}C)$ = 46.2 Hz), −9.71; IR (NaCl, cm^{-1}) 29.15, 2342 (w), 1475, 1462, 1437, 1360, 1134, 1068, 1036, 911, 755; MS (CI), m/e (relative intensity) 365 (5), 363 (10), 362 (6), 361 (21), 360 (8), 359 (15), 358 (6), 357 (8), 353 (21), 351 (15), 350 (15), 349 (100), 348 (42), 347 (84), 346 (37), 345 (59), 323 (12), 321 (12), 320 (5), 319 (62), 318 (25), 317 (51), 316 (21), 315 (35); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.61.

(b) General Procedure for the Synthesis of α-Alkoxy Tri-*n*-butylstannyl Derivatives. (Tri-*n*-butylstannyl)lithium was prepared from tri-*n*-butyltin hydride by the method of Still.[7a] A solution of (tri-*n*-butylstannyl)lithium (28.9 mmol) in THF (75 mL) was cooled to −40 °C, and the desired carbonyl substrate (26.1 mmol), dissolved in a minimum volume of THF, was added dropwise over 30 s. The reaction mixture was stirred at −40 °C for 15 min and then poured into a mixture of saturated ammonium chloride solution (50 mL) and petroleum ether (50 mL). The organic layer was washed once with brine (50 mL) and dried over sodium sulfate. Filtration, followed by solvent removal in vacuo, gave a clear colorless oil, which was dissolved immediately in methylene chloride (75 mL) and treated with chloromethyl methyl ether (10.3 g, 128 mmol) and *N,N*-dimethylaniline (7.0 mL) at room temperature for 16 h. The reaction mixture was poured into petroleum ether (100 mL) and washed successively with 75-mL portions of 0.5 N HCl, water, and saturated sodium bicarbonate. Drying of the organic layer over sodium sulfate, filtration, and solvent removal in vacuo gave a yellow oil (19.5 g), which was chromatographed (25:1 silica gel, 0.5% ethyl acetate/99.5% petroleum ether) to afford the pure tri-*n*-butylstannyl derivative (55–60%).

(Methoxymethoxy)(tri-*n*-butylstannyl)methane (11) from paraformaldehyde: 55%; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.47 (2 H, s), 3.71 (2 H, s, $^2J(^{117/119}Sn-^1H)$ = 15 Hz), 3.30 (3 H, s), 0.70–1.80 (27 H, m); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 99.44, 57.60, 54.91, 29.11, 27.30, 13.70, 8.90; IR (NaCl, cm^{-1}) 2905, 1460, 1139, 1089, 1032, 922, 658; MS (CI), m/e (relative intensity) 369 (0.4), 368 (0.1), 367 (0.3), 366 (0.3), 365 (1.6), 364 (0.7), 363 (1.3), 362 (0.5), 361 (0.9), 313 (19), 311 (15), 310 (12), 309 (100), 308 (38), 307 (84), 306 (84), 305 (58), 283 (8), 281 (6), 280 (4), 279 (42), 278 (16), 277 (33), 276 (13), 275 (21); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.61. Anal. Calcd for $C_{15}H_{34}O_2Sn$: C, 49.34; H, 9.39 Found: C, 49.58; H, 9.39.

1-(Methoxymethoxy)-1-(tri-*n*-butylstannyl)ethane (13) from acetaldehyde: 60%; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.66 (1 H, d, J = 6 Hz), 4.51 (1 H, d, J = 6 Hz), 4.08 (1 H, q, J = 6 Hz), 3.30 (3 H, s), 1.46 (3 H, d, J = 6 Hz), 1.07–1.91 (12 H, m), 0.88 (15 H, t, J = 6 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 95.47, 67.57, 54.81, 29.08, 27.36, 20.16, 13.46, 8.52; IR (NaCl, cm^{-1}) 2890, 1459, 1142, 1093, 1024, 916, 800; MS (CI), m/e (relative intensity) 383 (0.67), 381 (0.42), 379 (1.2), 378 (0.30), 377 (0.80), 376 (0.45), 375 (0.75), 327 (24), 325 (21), 323 (100), 322 (65), 321 (95), 320 (52), 319 (78), 295 (11), 293 (15), 291 (39), 290 (23), 289 (35), 288 (19), 287 (28), 239 (9), 237 (11), 235 (39), 234 (23), 233 (35), 232 (19), 231 (26); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.51.

***O*-(Methoxymethyl)-1-(tri-*n*-butylstannyl)cyclohexanol (15) from cyclohexanone**: 60%; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.59 (2 H, s), 3.33 (3 H, s), 0.69–2.32 (37 H, m); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 94.16, 82.66, 55.82, 36.74, 29.32, 27.67, 26.26, 21.94, 13.69, 9.71; IR (NaCl, cm^{-1}) 2909, 1460, 1440, 1372, 1149, 1131, 1030 (br), 915, 872, 661 (br); MS (CI), m/e (relative intensity) 435 (0.8), 434 (0.9), 433 (2.8), 432 (1.2), 431 (2.2), 430 (1), 429 (1.2), 381 (22), 379 (16), 378 (18), 377 (100), 376 (41), 375 (81), 374 (35), 373 (54), 295 (16), 293 (11), 292 (10), 291 (78), 290 (28), 289 (59), 288 (25), 287 (38); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.60.

***trans*-4-*tert*-Butyl-*O*-(methoxymethyl)-1-(tri-*n*-butylstannyl)cyclohexanol (32M) and *cis*-4-*tert*-Butyl-*O*-(methoxymethyl)-1-(tri-*n*-butylstannyl)cyclohexanol (32m) from 4-*tert*-Butylcyclohexanone. 32M**: 56%; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.73 (2 H, s), 3.36 (3 H, s), 2.25 (2 H, br d, J = 13.5 Hz), 1.76 (2 H, br d, J = 11.6 Hz), 1.67 (1 H, dt, J = 2.4, 13.0, 12.7 Hz), 1.44–1.54 (6 H, m), 1.33 (6 H, hextet, J = 7.3 Hz), 0.95–1.13 (4 H, m), 0.92 (6 H, t, J = 8.0 Hz), 0.90 (9 H, t, J = 7.3 Hz), 0.85 (9 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 92.73, 87.81, 55.24, 47.70, 38.47, 32.39, 29.22, 27.70, 27.66, 25.19 ($^3J(^{119}Sn-^{13}C)$ < 3 Hz), 13.62, 10.51; IR (NaCl, cm^{-1}) 2954, 1460, 1363, 1146, 1079, 1035, 1004, 918, 856, 660; MS (CI), m/e (relative intensity) 489 (M^+, tr), 437 (19), 435 (15), 434 (21), 433 (100), 432 (42), 431 (76), 436 (32), 429 (47), 295 (12), 293 (9), 292 (8), 291 (67), 290 (23), 289 (49), 288 (18), 287 (27); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.65. Anal. Calcd for $C_{24}H_{50}O_2Sn$: C, 58.91; H, 10.30. Found: C, 59.04; H, 10.32.

32m: 4%; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.66 (2 H, s), 3.41 (3 H, s), 2.22 (2 H, br d, J = 12 Hz), 1.38–1.64 (13 H, m), 1.26–1.38 (6 H, sextet, J = 7.4 Hz), 0.90 (15 H, t, J = 7.3 Hz), 0.84 (9 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 94.65, 80.93, 55.95, 48.06, 36.99, 32.59, 29.33, 27.67, 27.39, 22.07 ($^3J(^{119}Sn-^{13}C)$ = 40.0 Hz), 13.67, 9.48; IR (NaCl, cm^{-1}) 2900, 1460, 1361, 1133, 1089, 1033, 911, 860, 655; MS (CI), m/e (relative intensity) 449 (4), 447 (4), 446 (7), 445 (37), 444 (15), 443 (28), 442 (12), 441 (15), 437 (20), 435 (16), 434 (21), 433 (100), 432 (40), 431 (75), 430 (35), 429 (44), 295 (9), 293 (7), 292 (6), 291 (60), 290 (20), 289 (44), 288 (17), 287 (25); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.71. Anal. Calcd for $C_{24}H_{50}O_2Sn$: C, 58.91; H, 10.30. Found: C, 58.86; H, 10.31.

Procedures for the Synthesis of α-Alkoxyorganostannanes 10, 12, 17, and 18. (Methoxymethoxy)(trimethylstannyl)methane (10). (Methoxymethoxy)(tri-*n*-butylstannyl)methane (**11**; 100 mg, 0.274 mmol) was dissolved in THF (1.0 mL) and cooled to −40 °C. *n*-Butyllithium (0.301 mmol) was added to produce a pale yellow solution. After the mixture was stirred at −40 °C for 15 min, chlorotrimethylstannane (60.1 mg, 0.301 mmol) dissolved in a minimum of THF was added. After being stirred for 10 min, the reaction mixture was poured into a mixture of petroleum ether (5 mL) and saturated ammonium chloride solution (5 mL). After this mixture was shaken, the organic layer was separated and washed once with brine (5 mL), dried over sodium sulfate, filtered, and concentrated in vacuo to give a yellow oil. Preparative TLC (5% ethyl acetate/95% petroleum ether) afforded 56.9 mg (87%) pure **10** as a colorless oil.

10: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.52 (2 H, s), 3.71 (2 H, s, $^2J(^{117/119}Sn-^1H)$ = 18 Hz), 3.26 (3 H, s), 0.10 (9 H, s, $^2J^{117/119}Sn-^1H$) = 53 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 99.11, 58.56, 54.97, −10.45; IR (NaCl, cm^{-1}) 2951, 2914, 1450, 1139, 1090, 1035, 931; TLC (5% ethyl acetate/95% petroleum ether) R_f 0.45.

1-(Methoxymethoxy)-1-(trimethylstannyl)ethane (12). 1-(Methoxymethoxy)-1-(tri-*n*-butylstannyl)ethane (**13**; 100 mg, 0.264 mmol) was exchanged and quenched with chlorotrimethylstannane as described above for the synthesis of stannane **10**. Workup and preparative TLC (5% ethyl acetate/95% petroleum ether) afforded 36.7 mg (55%) of **12** as a colorless oil:

12: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.66 (1 H, d, J = 6.6 Hz), 4.57 (1 H, d, J = 6.6 Hz), 4.02 (1 H, q, J = 7.4 Hz), 3.34 (3 H, s), 1.47 (3 H, d, J = 7.4 Hz), 0.12 (9 H, S, $^2J(^{117/119}Sn-^1H)$ = 50.8 Hz); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 95.74, 67.71, 55.31, 19.81, −10.65; IR (NaCl, cm^{-1}) 2949, 2930, 1449, 1140, 1025, 917; TLC (5% ethyl acetate/95% petroleum ether) R_f 0.43.

(Benzyloxy)(trimethylstannyl)methane (17). (Trimethylstannyl)lithium (16.1 mmol) in THF (25 mL) was prepared as described above. This solution was maintained at 0 °C and bromomethyl benzyl ether (2.93 g, 14.6 mmol) was added dropwise over 1 min. The mixture was allowed to warm to room temperature where it was stirred for an additional 1 h. The reaction mixture was then quenched and proportionately worked up as described under the general procedure for the synthesis of α-alkoxy trimethylstannyl derivatives. The resulting yellow oil (9 g) was chro-

matographed (20:1 silica gel, 3.0% ethyl acetate/97% petroleum ether) to afford 4.17 g (91%) pure **17** as a colorless oil.

17: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.17 (5 H, s), 4.27 (2 H, s), 3.58 (2 H, s, $^2J(^{117/119}Sn-^1H)$ = 18 Hz), 0.06 (9 H, s, $^2J(^{117/119}Sn-^1H)$ = 38 Hz); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 138.67, 128.28, 127.55, 127.41, 76.98, 62.47, -10.29; IR (NaCl, cm^{-1}) 2966, 2834, 2352 (w), 1493, 1449, 1370, 1192, 1062, 763, 725; MS (CI) *m/e* (relative intensity) 289 (0.6), 287 (0.5), 286 (0.4), 285 (3), 284 (11), 283 (2.3), 282 (0.8), 281 (1.4), 275 (18), 273 (15), 272 (12), 271 (100), 270 (37), 269 (80), 268 (33), 267 (54), 213 (6), 211 (5), 210 (3), 209 (35), 208 (12), 207 (27), 206 (9), 205 (16), 91 (98); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.55.

1-(Benzyloxy)-2-methyl-1-(trimethylstannyl)propane (18). Isobutyraldehyde dibenzyl acetal (3.00 g, 11.1 mmol) was dissolved in methylene chloride (10 mL) and treated with acetyl chloride (10 mL) at room temperature for 2 h. All volatile materials were removed in vacuo, and the resulting oil was dissolved in a minimum of THF. The resulting solution was added dropwise over 1 min to a solution of (trimethylstannyl)lithium [12.0 mmol, prepared as described above in THF (25 mL) cooled to -78 °C]. After being stirred for 15 min, the reaction was quenched and proportionately worked up as described under the general procedure for the synthesis of (α-alkoxyalkyl)trimethylstannyl derivatives. The resulting pale yellow oil (3.2 g) was chromatographed (30:1 silica gel, 3.0% ethyl acetate/97% petroleum ether to afford 2.93 g (81%) pure stannane **18** as a colorless oil.

18: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.23 (5 H, s), 4.32 (2 H, s), 3.52 (1 H, d, J = 6 Hz, $^2J(^{117/119}Sn-^1H)$ = 45 Hz), 2.17 (1 H, octet, J = 6 Hz), 0.88 (6 H, d, J = 6 Hz), 0.12 (9 H, s, $^2J(^{117/119}Sn-^1H)$ = 51 Hz); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 138.91, 128.18, 127.60, 127.31, 84.79, 73.14, 32.42, 20.58, 20.00, -8.78; IR (NaCl, cm^{-1}) 2945, 2852, 2347 (w), 1494, 1450, 1377, 1059, 760, 690; MS (CI), *m/e* (relative intensity) 331 (0.5), 329 (1), 328 (0.5), 327 (3), 326 (1.5), 325 (2), 324 (0.8), 317 (18), 315 (14), 314 (12), 313 (82), 312 (34), 311 (68), 310 (28), 309 (47), 169 (13), 167 (11), 165 (66), 164 (27), 163 (100), 162 (18), 661 (32), 91 (58); TLC (10% ethyl acetate/90% petroleum ether) R_f 0.76.

General Procedure for the Synthesis of α-Alkoxyorganostannanes 19–22 from α-Chloro Cyclic Ethers. To a solution of (trialkylstannyl)-lithium (5.41 mmol, prepared as described above) in THF (11 mL) cooled to -78 °C was added the appropriate α-chloro cyclic ether (9.30 mmol). The resulting yellow solution was stirred at -78 °C for 1 h, then warmed to room temperature, and stirred for an additional 15 h. The reaction was diluted with water (10 mL) and extracted with ether (2 × 15 mL). The combined organic layers were dried (magnesium sulfate), filtered, and concentrated in vacuo. The resulting oil was chromatographed (10:1 silica gel, 2% ethyl acetate/98% petroleum ether) to afford the pure α-stannyl ether as a colorless oil in yields from 21 to 83%.

(2-Tetrahydrofuranyl)trimethylstannane (19) from 2-chlorotetrahydrofuran:[27] 83%; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 3.75 (2 H, m), 3.62 (1 H, m), 2.15 (1 H, m), 1.82 (3 H, m), 0.12 (9 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 72.14, 68.61, 30.68, 26.35, -11.19; IR (NaCl, cm^{-1}) 2980, 2930, 2880, 1460, 1450, 1200, 1045, 920, 775. Anal. Calcd for $C_7H_{16}OSn$: C, 35.79; H, 6.88. Found: C, 35.67; H, 6.93.

(2-Tetrahydrofuranyl)tri-*n*-butylstannane (20) from 2-chlorotetrahydrofuran: 59%; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 3.75 (2 H, m), 3.60 (1 H, m), 2.15 (1, H, m), 1.82 (3 H, m), 1.50 (5 H, m), 1.30 (7 H, m), 0.88 (15 H, m); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 72.25, 68.45 31.23, 29.23, 27.45, 26.47, 13.68, 8.47; IR (NaCl, cm^{-1}) 2930, 2900, 2840, 1450, 1065, 1020, 865; MS (CI), *m/e* (relative intensity) 361 (M + 1, 73), 360 (48), 359 (59), 305 (100), 303 (74), 301 (48), 291 (11), 71 (22). Anal. Calcd for $C_{16}H_{34}OSn$: C, 53.20; H, 9.51. Found: C, 53.44; H, 9.59.

(2-Tetrahydropyranyl)trimethylstannane (21) from 2-chlorotetrahydropyran:[27] 65%; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 3.85 (2 H, m), 3.39 (1 H, dt, J = 2.2, 11.1 Hz), 1.79 (2 H, m), 1.66 (2 H, m), 1.51 (2 H, m), 0.10 (9 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 74.94, 70.80, 31.55, 27.00, 25.34, -11.17; IR (NaCl, cm^{-1}) 2950, 2860, 1450, 1210, 1200, 1080, 1045, 1035, 920, 740. Anal. Calcd for $C_8H_{18}OSn$: C, 38.59; H, 7.30. Found: C, 38.55; H, 7.30.

(2-Tetrahydropyranyl)tri-*n*-butylstannane (22) from 2-chlorotetrahydropyran: 21%; ^{1}H NMR ($CDCl_3$, 360 MHz) δ 3.84 (2 H, m), 3.35 (1 H, dt, J = 11.1, 2.1 Hz), 1.61–1.92 (4 H, m), 1.50 (8 H, m), 1.32 (6 H, m), 0.89 (15 H, m); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 75.37, 70.86, 32.28, 29.18, 27.45, 27.16, 25.61, 13.71, 8.34; IR (NaCl, cm^{-1}) 2940, 2900, 2830, 1450, 1060, 1030, 1015, 815; MS (CI), *m/e* (relative intensity) 375 (M + 1, 80), 374 (57), 373 (64), 319 (100), 317 (80), 315 (52), 291 (14), 85 (37). Anal. Calcd for $C_{17}H_{36}OSn$: C, 54.41; H, 9.69 Found: C, 54.47; H, 9.70.

Low-Temperature ^{1}H NMR Exchange Experiments between Selected Organostannanes and Alkyllithium Reagents. (a) ^{1}H NMR Spectra of THF Solutions of *n*-Butyllithium and Methyllithium. The ^{1}H NMR spectrum of a solution of *n*-butyllithium in THF-d_8 was recorded at room temperature and at -60 °C. At room temperature (approximately 25 °C) a triplet was observed at -1.0 ppm (J = 9 Hz) corresponding to the protons adjacent to lithium. At -60 °C this signal remained at -1.0 ppm but appeared as a broad singlet. The protons of methyllithium were observed as a sharp singlet at -2.0 ppm at room temperature, and as a broad doublet at -60 °C (-2.0 ppm, J = 9 Hz). Spectra were referenced to THF.

(b) Representative Procedure for Exchange Reactions: Exchange of *n*-Butyltrimethyltin (8) with *n*-Butyllithium. *n*-Butyllithium (**8**) was dissolved in THF-d_8 (0.4 mL), injected into an NMR tube sealed with a rubber septum, and equilibrated in a variable temperature probe set at -60 °C. A spectrum was recorded that exhibited a singlet at 0.15 ppm, corresponding to the methyl protons adjacent to tin. The $^{117/119}Sn-^1H$-coupled satellites also were visible. Addition of approximately 1.0 equiv of *n*-butyllithium in THF-d_8 via syringe resulted in the appearance of a methyllithium peak at -2.0 ppm. The ratio of stannylmethyl to methyllithium protons was 2:1. Further addition of 1.0 equiv of *n*-butyllithium gave a signal ratio of 1:2. Excess *n*-butyllithium resulted in the total loss of stannylmethyl signals and the appearance of the broad *n*-butyllithium singlet at -1.0 ppm. The above procedure was repeated at room temperature with identical results.

(c) Exchange of 1-(benzyloxy)-2-methyl-1-(trimethylstannyl)propane (18) with *n*-Butyllithium. α-Alkoxyorganostannane (**18**) was subjected to low-temperature ^{1}H NMR analysis in THF-d_8 at -60 °C as described under the representative procedure. Addition of 0.5 equiv of *n*-butyllithium in THF-d_8 resulted in the appearance of signals corresponding to 3-methyl-1-phenyl-2-butanol. This rearrangement was confirmed independently by treatment of **18** (100 mg, 0.306 mmol) in THF (2.0 mL) at -78 °C with *n*-butyllithium (0.306 mmol). The yellow solution produced was stirred for 2 min and then quenched with cyclohexanone (30.0 mg, 0.306 mmol). The reaction mixtured was poured into saturated ammonium chloride solution (5 mL) and petroleum ether (10 mL). After this mixture was shaken for 1 min, the organic layer was separated and washed with brine (10 mL), then dried over sodium sulfate, filtered, and concentrated in vacuo to give a pale yellow oil (140 mg). Chromatography (30:1 silica gel, 10% ethyl acetate/90% petroleum ether) afforded 45.2 mg (90%) of a colorless oil identical in all respects with 3-methyl-1-phenyl-2-butanol (prepared separately via the addition of isopropylmagnesium bromide to phenylacetaldehyde) and unreacted cyclohexanone (25.1 mg).

Additional Exchange Experiments between Selected α-Alkoxyorganostannanes and *n*-Butyllithium. (a) Exchange of *O*-(Methoxymethyl)-1-(trimethylstannyl)cyclohexanol (14). α-Alkoxyorganostannane **14** (100 mg, 0.326 mmol) was dissolved in THF (1.0 mL) and cooled to -78 °C. *n*-Butyllithium (0.978 mmol) was added dropwise over 1 min. No color change was observed. After the mixture was stirred for 15 min, the reaction was quenched with saturated ammonium chloride solution (0.5 mL) producing much gas evolution. The reaction mixture was poured into water and extracted with petroleum ether (20 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated in vacuo to give a clear oil (110 g). Chromatography (10:1 silica gel, petroleum ether) afforded a colorless oil (127 mg, 90%), indistinguishable from *O*-(methoxymethyl)-1-(tri-*n*-butylstannyl)cyclohexanol (**15**) in all respects.

(b) Competitive Exchange of 1-(Methoxymethoxy)(tri-*n*-butylstannyl)methane (11) and 1-(Methoxymethoxy)-1-(tri-*n*-butylstannyl)-ethane (13) with *n*-Butyllithium. α-Alkoxyorganostannanes **11** (98.5 mg, 0.270 mmol) and **13** (106 mg, 0.270 mmol) were dissolved in DME (4.0 mL) and cooled to -78 °C. *n*-Butyllithium (0.270 mmol) was added dropwise over 1 min; a color change to pale yellow was noted. After being stirred for 5 min, the reaction mixture was quenched with excess methanol. Workup and chromatography, both as described for the exchange of *O*-(methoxymethyl)-1-(trimethylstannyl)cyclohexanol (**14**), afforded 93.1 mg of a colorless oil, indistinguishable from 1-(methoxymethoxy)-1-(tri-*n*-butylstannyl)ethane (**13**) in all respects.

(c) Attempted Exchange between Cyclohexyltri-*n*-butyltin (16) and *n*-Butyllithium. Cyclohexyltri-*n*-butyltin (**16**; 100 mg, 0.268 mmol) was dissolved in THF (2.0 mL) and cooled to -78 °C. *n*-Butyllithium (0.536 mmol) was added dropwise over 1 min. No color change was observed. After the mixture was stirred for 15 min, the reaction was quenched with saturated ammonium chloride solution (0.5 mL), producing much gas evolution. The mixture was processed and chromatographed as described above for the attempted exchange of α-alkoxy organostannane **14** to give 95.9 mg of a white oil, indistinguishable from cyclohexyl(tri-*n*-butyl)tin (**16**) in all respects.

Exchange of Tertiary α-Alkoxyorganostannanes with *n*-Butyllithium and Subsequent Quenching with Methanol and Dimethyl Sulfate. (a) Products from Methanol Addition. *O*-(Methoxymethyl)cyclohexanol

(27) Earl, R. A.; Townsend, L. B. *J. Heterocycl. Chem.* **1972**, *9*, 1141.

(25) from 15. α-Alkoxyorganostannane **15** (100 mg, 0.229 mmol) was dissolved in THF (5.0 mL) and cooled to −78 °C. *n*-Butyllithium (0.252 mmol) was added dropwise over 10 s, producing a pale yellow solution that became colorless after an additional 10 s. After 2 min, the reaction was quenched with excess methanol and then poured into saturated ammonium chloride solution (5 mL) and petroleum ether (10 mL). After this mixture was shaken for 1 min, the organic layer was separated and washed with brine (10 mL), dried over sodium sulfate, filtered, and concentrated in vacuo to give a colorless oil (80 mg). Chromatography (10:1 silica gel, 0.5% ethyl acetate/99.5% petroleum ether) afforded 31.6 mg (95%) pure *O*-(methoxymethyl)cyclohexanol (**25**), which exhibited ^{1}H and ^{13}C NMR data identical with the reported values.[26]

***trans*-4-*tert*-4-Butyl-*O*-(methoxymethyl)cyclohexanol (34a) from 32M.** α-Alkoxyorganostannane **32M** (100 mg, 0.204 mmol) was dissolved in DME (2.0 mL) and cooled to −78 °C. *n*-Butyllithium (0.210 mmol) was added dropwise over 10 s, producing a pale yellow solution. After the mixture was stirred for 2 min, the reaction was quenched with excess methanol and worked up as described for the synthesis of compound **25** to give a colorless oil (100 mg). Chromatography (10:1 silica gel, trace ethyl acetate/petroleum ether) afforded 40.8 mg (88%) of the pure protonated derivative **34a** (>98% as judged by 360-MHz ^{1}H NMR) as a colorless oil.

34a: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.63 (2 H, s), 3.42 (1 H, tt, J = 11.1, 4.3 Hz), 3.37 (3 H, s), 2.06 (2 H, br d), 1.78 (2 H, br d), 1.24 (2 H, q, J = 11.1 Hz), 0.97–1.12 (3 H, m), 0.85 (9 H, s); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 94.45, 76.11, 55.04, 47.27, 33.15, 32.23, 27.57, 25.63; IR (NaCl, cm^{-1}) 2916, 1448, 1360, 1143, 1103, 1033, 913; MS (CI), *m/e* (relative intensity) 201 (M + 1, 5.4), 200 (1), 199 (5), 169 (12), 153 (15), 139 (100); TLF (5% ethyl acetate/95% petroleum ether) R_f 0.47.

***cis*-4-*tert*-Butyl-*O*-(methoxymethyl)cyclohexanol (34b) from 32m.** α-Alkoxyorganostannane **32m** (100 mg, 0.204 mmol) was dissolved in DME (2.0 mL) and cooled to −30 °C. Exchange with *n*-butyllithium (0.210 mmol), followed by excess methanol quench and workup as described for the synthesis of compound **25**, gave a colorless oil. Chromatography (10:1 silica gel, trace ethyl acetate/petroleum ether) afforded 44 mg (89%) of the pure protonated derivative **34b** (>98% as judged by 360-MHz ^{1}H NMR) as a colorless oil.

34b: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.67 (2 H, s), 3.83 (1 H, m), 3.38 (3 H, s), 1.95 (2 H, br d), 1.54 (2 H, br d), 1.24–1.45 (5 H, m), 0.86 (9 H, s); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 94.45, 70.81, 55.14, 47.95, 32.57, 31.06, 27.52, 21.55; IR (NaCl, cm^{-1}) 2942, 1460, 1440, 1361, 1140, 1091, 1040, 914; MS (CI), *m/e* (relative intensity) 201 (M + 1, 6), 199 (6), 169 (15), 153 (5), 139 (100); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.50.

(b) Products from Dimethyl Sulfate Addition. *trans*-4-*tert*-Butyl-*O*-(methoxymethyl)-1-methylcyclohexanol (35a) from 32M. α-Alkoxyorganostannane **32M** (198 mg, 0.409 mmol) was dissolved in DME (4.0 mL) and cooled to −78 °C. *n*-Butyllithium (0.578 mmol) was added dropwise over 10 s, producing a pale yellow solution. After 2 min, the reaction was quenched with dimethyl sulfate (550 mg, 0.436 mmol) and worked up as described for the synthesis of compound **25** to give a colorless oil (220 mg). Chromatography (10:1 silica gel, 0.3% ethyl acetate/99.7% petroleum ether) afforded 71.0 mg (81%) of the pure methylated derivative **35a** as a colorless oil.

35a: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.73 (2 H, s), 3.33 (3 H, s), 0.96–2.00 (9 H, m), 1.24 (3 H, s), 0.86 (9 H, s); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 90.42, 76.64, 54.94, 47.71, 38.00, 32.18, 27.57, 24.36, 21.99; IR (NaCl, cm^{-1}) 2922, 1464, 1361, 1146, 1115, 1038, 961, 914; MS (CI), *m/e* (relative intensity) 215 (M + 1, 1.4), 214 (3.8), 215 (3.8), 137 (15), 97 (8); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.40. Anal. Calcd for $C_{13}H_{26}O_2$: C, 72.84; H, 12.23. Found: C, 72.96; H, 12.27.

***cis*-4-*tert*-Butyl-*O*-(methoxymethyl)-1-methylcyclohexanol (35b) from 32m.** α-Alkoxyorganostannane **32m** (300 mg, 0.614 mmol) was dissolved in DME (2.0 mL) and cooled to −30 °C. Exchange with *n*-butyllithium (0.742 mmol), followed by quenching and dimethyl sulfate (91.3 mg, 0.740 mmol) and workup as described for the synthesis of compound **25**, gave a colorless oil (270 mg). Chromatography (10:1 silica gel, 0.3% ethyl acetate/99.7% petroleum ether) afforded 118 mg (90%) of the pure methylated derivative **35b** as a colorless oil.

35b: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.66 (2 H, s), 3.36 (3 H, s), 1.88 (2 H, br d, J = 9 Hz), 0.96–1.63 (7 H, m), 1.14 3 H, s), 0.88 (9 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 90.65, 73.93, 55.26, 47.39, 37.37, 32.25, 27.45, 27.21, 22.30; IR (NaCl, cm^{-1}) 2960, 1440, 1363, 1147, 1088, 1033, 977, 917; MS (CI), *m/e* (relative intensity) 215 (M + 1, 0.3), 214 (1.3), 213 (1.6), 169 (16), 153 (100), 137 (15), 97 (10); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.48. Anal. Calcd for $C_{13}H_{26}O_2$: C, 72.84; H, 12.23. Found: C, 72.73; H, 12.27.

Exchange of Tertiary α-Alkoxyorganostannanes with *n*-Butyllithium and Subsequent Addition to Selected Carbonyl Compounds. (a) Attempted Synthesis of 1-(1-Hydroxypropyl)-*O*-(methoxymethyl)cyclohexanol (26) from 15 in THF. (*O*)-(Methoxymethyl)(tri-*n*-butylstannyl)cyclohexanol (**15**; 100 mg, 0.231 mmol) was dissolved in THF (5.0 mL) and cooled to −78 °C. *n*-Butyllithium (0.252 mmol) was added dropwise over 10 s, producing a pale yellow solution that became colorless after an additional 10 s. After the mixture was stirred for 2 min, the reaction was quenched with excess propionaldehyde and worked up as described for the synthesis of compound **25**. The resulting colorless oil was chromatographed (10:1 silica gel, 0.5% ethyl acetate/99.5% petroleum ether) to afford 30.2 mg (94%) of pure *O*-(methoxymethyl)cyclohexanol **25**, which exhibited ^{1}H and ^{13}C NMR data identical with the reported values.[26a]

(b) Synthesis of 1-(1-Hydroxypropyl)-*O*-(methoxymethyl)cyclohexanol (26) from 15 in DME. The above procedure was repeated substituting DME (2.0 mL) for THF. The pale yellow color resulting from *n*-butyllithium addition did not fade until the reaction was quenched with excess propionaldehyde (2 min at −78 °C). Workup and chromatography (10:1 silica gel, 2.5% ethyl acetate/97.5% petroleum ether), both as described above, afforded 39.7 mg (85%) of pure alcohol **26**.

26: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.68 (2 H, dd, J = 15 Hz), 3.42 (3 H, s), 3.23 (2 H, m, CHO*H*), 0.73–2.03 (15 H, m); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 90.76, 80.91, 77.61, 55.72, 30.29, 30.09, 25.92, 24.07, 21.50, 21.36, 11.55; IR (NaCl, cm^{-1}) 3440 (br), 2930, 2861, 1450, 1370, 1150, 1119, 1088, 1033, 981; MS (CI), *m/e* (relative intensity) 203 (M + 1, 15), 169 (26), 141 (100), 123 (90), 105 (41); TLC (25% ethyl acetate/75% petroleum ether) R_f 0.54.

(c) Further Addition Reactions. 2-(Methoxymethoxy)-2-phenyl-3-pentanol (30d) from 28. α-Alkoxyorganostannane **28** (300 mg, 1.22 mmol) was dissolved in DME (4.0 mL) and cooled to −78 °C. Exchange with *n*-butyllithium (1.35 mmol), followed by excess propionaldehyde quench and workup as described for the synthesis of alcohol **26**, gave a pale yellow oil. Chromatography (15:1 silica gel, 4% ethyl acetate/96% petroleum ether) afforded 242 mg (89%) of alcohol **30d** as an inseparable 67:33 mixture of diastereomers.

30d: ^{1}H NMR ($CDCl_3$, 90 MHz, major isomer) δ 7.02–7.53 (5 H, m), 4.55 (2 H, dd, J = 18, 12 Hz), 3.54 (1 H, m), 3.37 (3 H, s), 2.22 (1 H, d, J = 5 Hz, O*H*), 1.62 (3 H, s), 0.86–1.35 (5 H, m); ^{13}C NMR ($CDCl_3$, 90 MHz, major isomer) δ 142.72, 127.97, 127.15, 126.69, 92.04, 82.63, 80.11, 55.62, 23.93, 20.05, 11.14; ^{13}C NMR ($CDCl_3$, 90 MHz, minor isomer) δ 142.23, 128.06, 127.46, 126.90, 91.98, 83.31, 80.56, 55.62, 23.27, 16.57, 11.18; IR (NaCl, cm^{-1}) 3421, 2922, 2860, 1441, 1373, 1136, 1082, 1020, 758, 700; MS (EI), *m/e* (relative intensity) 224 (M^+, 0.15), 206 (2), 167 (2), 165 (100), 135 (22), 134 (38), 133 (33), 121 (100), 105 (32); TLC (25% ethyl acetate/75% petroleum ether) R_f 0.42.

1,2-Diphenyl-2-(methoxymethoxy)propanol (30e) from 28. α-Alkoxyorganostannane **28** (400 mg, 1.22 mmol) was dissolved in DME (4.0 mL) and cooled to −78 °C. Exchange with *n*-butyllithium (1.34 mmol), followed by benzaldehyde (155 mg, 1.46 mmol) quench and workup as described for the synthesis of alcohol **26**, gave a colorless oil. Chromatography (15:1 silica gel, 4% ethyl acetate/96% petroleum ether) afforded 299 mg (90%) of pure alcohol **30e** as an inseparable 70:30 mixture of diastereomers.

30e: ^{1}H NMR ($CDCl_3$, 360 MHz, minor isomer) δ 7.00–7.24 (8 H, m), 6.82 (2 H, d, J = 7.1 Hz), 4.86 (1 H, br s), 4.63 (2 H, dd, J = 28.0, 6.9 Hz), 3.45 (1 H, br d, J = 1.3 Hz, O*H*), 3.43 (3 H, s), 1.54 (3 H, s); ^{13}C NMR ($CDCl_3$ 90 MHz, major isomer) δ 141.73, 138.08, 127.96, 127.76, 127.54, 127.51, 127.45, 127.10, 92.34, 82.84, 81.69, 55.99, 16.33; IR (NaCl, cm^{-1}) 3448 (br), 2927, 1600, 1490, 1443, 1372, 1166, 1130, 1075, 1022, 915, 776, 695, 657; MS (EI), *m/e* (relative intensity) 163 (2), 164 (13), 165 (100), 135 (10), 134 (5), 133 (12), 123 (1), 122 (6), 121 (74), 77 (26); TLC (25% ethyl acetate/75% petroleum ether) R_f 0.45.

3-(Methoxymethoxy)-2-methyl-3-phenyl-2-butanol (30f) from 28. α-Alkoxyorganostannane **28** (200 mg, 0.608 mmol) was dissolved in DME (2.0 mL) and cooled to −78 °C. Exchange with *n*-butyllithium (0.700 mmol), followed by excess acetone quench and workup as described for the synthesis of alcohol **26**, gave a colorless oil. Chromatography (10:1 silica gel, 2.0% ethyl acetate/98% petroleum ether) afforded 122 mg (82%) of pure **30f** as a colorless oil.

30f: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.15–7.48 (5 H, m), 4.72 (2 H, s), 3.41 (3 H, s), 2.31 (1 H, s, O*H*), 1.68 (3 H, s), 1.21 (3 H, s), 1.06 (3 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 141.88, 127.84, 127.49, 127.03, 92.43, 85.14, 75.09, 55.72, 24.89, 24.60, 20.00; IR (NaCl, cm^{-1}) 3460 (br), 2960, 1440, 1367, 1153, 1110, 1021, 750, 699; MS (EI), *m/e* (relative intensity) 224 (2), 167 (3), 166 (13), 165 (50), 147 (8), 135 (8), 134 (9), 133 (13), 123 (1), 122 (7), 121 (100), 106 (3), 105 (21), 91 (6), 77 (13). TLF (25% ethyl acetate/75% petroleum ether) R_f 0.52. Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.69; H, 9.02.

***trans*-4-*tert*-Butyl-1-(1-hydroxypropyl)-*O*-(methoxymethyl)cyclohexanol (37a) from 32 M.** α-Alkoxystannane **32M** (100 mg, 0.204

mmol) was dissolved in DME (2.0 mL) and cooled to −78 °C. Exchange with *n*-butyllithium (0.210 mmol), followed by excess propionaldehyde quench and workup as described for the synthesis of alcohol **26**, gave a colorless oil. Chromatography (15:1 silica, gel, 2.5% ethyl acetate/97.5% petroleum ether) afforded 38.4 mg (73%) of pure alcohol **37a** as a colorless oil.

37a: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.74 (2 H, dd, J = 75.6, 7.2 Hz), 3.57 (1 H, dt, J = 3.0, 9.1 Hz), 3.40 (3 H, s), 2.70 (1 H, d, J = 9.1 Hz, O*H*), 2.36–2.42 (1 H, m), 1.92 (1 H, dq, J = 14.4, 3.2 Hz), 1.18–1.78 (9 H, m), 1.03 (3 H, t, J = 7.2 Hz), 0.85 (9 H, s); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 90.32, 80.76, 72.08, 55.43, 47.42, 34.22, 32.23, 30.87, 27.57, 23.88, 23.25, 11.16; IR (NaCl, cm^{-1}) 3433 (br), 2944, 2860, 1452, 1363, 1147, 1127, 1096, 1032, 979, 911; MS (CI), *m/e* (relative intensity) 259 (M + 1, 21), 225 (28), 197 (100), 179 (80), 161 (50); TLC (25% ethyl acetate/75% petroleum ether) R_f 0.57. Anal. Calcd for $C_{15}H_{30}O_3$: C, 69.72; H, 11.70. Found: C, 69.79; H, 11.75.

***trans*-4-*tert*-Butyl-1-(α-hydroxybenzyl)-*O*-(methoxymethyl)cyclohexanol (37b) from 32M.** α-Alkoxyorganostannane **32M** (300 mg, 0.614 mmol) was dissolved in DME (2.0 mL) and cooled to −78 °C. Exchange with *n*-butyllithium (0.675 mmol), followed by benzaldehyde (93.9 mg, 0.921 mmol) quench and workup as described for the synthesis of alcohol **26**, gave a colorless oil. Chromatography (10:1 deactivated silica gel, 2.5% ethyl acetate/97.5% petroleum ether) afforded 147 mg (80%) of pure alcohol **37b** as a colorless oil.

37b: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.30–7.37 (2 H, m), 7.16–7.30 (3 H, m), 4.74 (1 H, br d, J = 8.9 Hz), 4.68 (2 H, dd, J = 13.8, 7.2 Hz), 3.34 (1 H, br d, J = 8.9 Hz, O*H*), 3.29 (3 H, s), 2.42 (1 H, dq, J = 12.5, 3.0 Hz), 1.82 (1 H, d of quintets, J = 13.4, 3.2 Hz), 1.04–1.68 (7 H, m), 0.89 (9 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 140.96, 127.90, 127.61, 127.29, 90.50, 80.61, 73.96, 55.17, 47.17, 39.90, 32.16, 31.33, 27.46, 24.19, 23.89; IR (cm^{-1}) 3418 (br), 2943, 1448, 1364, 1142, 1091, 1026, 911, 716, 693; MS (CI), *m/e* (relative intensity) 200 (14), 199 (100), 169 (25), 155 (38), 107 (23); TLC (25% ethyl acetate/75% petroleum ether) R_f 0.59.

***trans*-4-*tert*-Butyl-1-(1-hydroxy-1-methylethyl)-*O*-(methoxymethyl)cyclohexanol (37c) from 32M.** α-Alkoxyorganostannane **32M** (200 mg, 0.409 mmol) was dissolved in DME (4.0 mL) and cooled to −78 °C. Exchange with *n*-butyllithium (0.422 mmol), followed by excess acetone quench and workup as described for the synthesis of alcohol **26**, gave a colorless oil. Chromatography (10:1 deactivated silica gel, 1.5% ethyl acetate/98.5% petroleum ether) gave 73.9 mg (70%) of pure alcohol **37c** as a colorless oil.

37c: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.67 (2 H, s), 3.55 (1 H, br s, O*H*), 3.36 (3 H, s), 1.03–2.07 (9 H, m), 1.20 (6 H, s), 0.84 (9 H, s); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 91.25, 83.92, 75.18, 55.57, 43.00, 32.91, 28.44, 27.37, 25.68, 22.04; IR (NaCl, cm^{-1}) 3455 (br), 2955, 1464, 1362, 1143, 1081, 1024, 911; MS (EI), *m/e* (relative intensity) 201 (1), 200 (12), 199 (100), 197 (6), 170 (5), 169 (39), 168 (23), 156 (6), 155 (54), 153 (27), 137 (13), 123 (9), 111 (11), 95 (11), 85 (16), 81 (20); TLC (25% ethyl acetate/75% petroleum ether) R_f 0.69. Anal. Calcd for $C_{15}H_{30}O_3$: C, 69.72; H, 11.70. Found: C, 69.48; H, 11.61.

***cis*-4-*tert*-Butyl-1-(1-hydroxypropyl)-*O*-(methoxymethyl)cyclohexanol (38a) from 32m.** α-Alkoxyorganostannane **32m** (301 mg, 0.614 mmol) was dissolved in DME (2.0 mL) and cooled to −30 °C. Exchange with *n*-butyllithium (0.713 mmol), followed by excess propionaldehyde quench and workup as described for the synthesis of alcohol **26**, gave a colorless oil. Chromatography (15:1 silica gel, 2.5% ethyl acetate/97.5% petroleum ether) afforded 131 mg (82%) of pure alcohol **38a** as a colorless oil.

38a: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.73 (2 H, dd, J = 34.6, 7.3 Hz), 3.45 (3 H, s), 3.35 (1 H, dd, J = 6.0, 0.6 Hz, O*H*), 3.18–3.27 (1 H, m), 1.84–2.04 (2 H, m), 1.44–1.61 (4 H, m), 1.09–1.40 (5 H, m), 1.03 (3 H, t, J = 7.3 Hz), 0.86 (9 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 90.74, 80.39, 78.27, 55.84, 47.74, 32.30, 30.26, 30.18, 27.42, 27.42, 24.16, 21.91, 21.81, 11.46; IR (NaCl, cm^{-1}) 3457 (br), 2944, 2845, 1449, 1361, 1138, 1084, 1027, 979; MS (CI), *m/e* (relative intensity) 259 (M + 1, 1), 225 (18), 199 (12), 198 (15), 197 (100), 195 (13), 179 (34); TLC (25% ethyl acetate/75% petroleum ether) R_f 0.62. Anal. Calcd for $C_{15}H_{30}O_3$: C, 69.72; H, 11.70. Found: C, 69.74; H, 11.75.

***cis*-4-*tert*-Butyl-1-(α-hydroxybenzyl)-*O*-(methoxymethyl)cyclohexanol (38b) from 32m.** α-Alkoxyorganostannane **32m** (100 mg, 0.205 mmol) was dissolved in DME (1.0 mL) and cooled to −30 °C. Exchange with *n*-butyllithium (0.222 mmol), followed by benzaldehyde (42.0 mg, 0.396 mmol) quench and proportional workup as described for the synthesis of alcohol **26**, gave a pale yellow oil. Chromatography (15:1 deactivated silica gel, 2.0% ethyl acetate/98% petroleum ether) afforded 51.3 mg (84%) of pure alcohol **38b** as a waxy solid.

38b: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.26–7.46 (5 H, m), 4.87 (2 H, dd, J = 17.8, 7.2 Hz), 4.62 (1 H, d, J = 2.6 Hz), 4.06 (1 H, d, J = 2.6 Hz, O*H*), 3.53 (3 H, s), 2.07 (1 H, dt, J = 10.6, 3.0 Hz), 1.89 (1 H, dq, J = 10.7, 3.0 Hz), 1.45–1.56 (2 H, m), 1.05–1.31 (5 H, m), 0.79 (9 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 140.29, 127.93, 127.59, 127.37, 91.02, 80.99, 79.48, 55.88, 47.38, 32.33, 31.67, 27.44, 21.99, 21.54; IR (NaCl, cm^{-1}) 3420 (br), 2936, 1600 (w), 1446, 1355, 1133, 1024, 918, 768, 697; MS (CI), *m/e* (relative intensity) 307 (M + 1, 47), 289 (11), 245 (100), 227 (15), 199 (20), 147 (65); TLC (25% ethyl acetate/75% petroleum ether) R_f 0.54.

***cis*-4-*tert*-Butyl-1-(1-hydroxy-1-methylethyl)-*O*-(methoxymethyl)cyclohexanol (38c) from 32m.** α-Alkoxyorganostannane **32m** (100 mg, 0.205 mmol) was dissolved in DME (1.0 mL) and cooled to −30 °C. Exchange with *n*-butyllithium (0.223 mmol), followed by excess acetone quench and workup as described for the synthesis of alcohol **26**, gave a colorless oil. Chromatography (15:1 deactivated silica gel, 2.5% ethyl acetate/97.5% petroleum ether) afforded 41.7 mg (79%) of pure alcohol **38c** as a colorless oil.

38c: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 4.77 (2 H, s), 4.16 (1 H, s, O*H*), 3.48 (3 H, s), 2.01 (2 H, br d, J = 12.9 Hz), 1.57 (2 H, br d, J = 13.4 Hz), 1.41 (2 H, dt, J = 2.5, 13.8 Hz), 1.19 (6 H, s), 1.14 (2 H, dq, J = 2.2, 12.7 Hz), 0.97 (1 H, tt, J = 12.0, 2.8 Hz), 0.84 (9 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 91.75, 83.65, 74.18, 55.92, 47.48, 32.33, 29.27, 27.49, 25.43, 22.23; IR (NaCl, cm^{-1}) 3446 (s), 2945, 1458, 1359, 1262, 1133, 1024, 913, 888; MS (CI), *m/e* (relative intensity) 259 (M + 1, 23), 241 (18), 225 (20), 211 (22), 197 (100), 179 (18); TLC (10% ethyl acetate/90% petroleum ether) R_f 0.36.

Exchange of Tertiary α-Alkoxyorganostannanes with *n*-Butyllithium and Subsequent Addition to Selected Alkyl Halides. (a) General Procedure for the Exchange of 1-(Methoxymethoxy)-1-phenyl-1-(trimethylstannyl)ethane (28) Followed by Alkyl Halide Addition. α-Alkoxyorganostannane **28** (200 mg, 0.608 mmol) was dissolved in DME (2.0 mL) and cooled to −78 °C. Exchange with *n*-butyllithium (0.850 mmol), followed by excess alkyl halide quench and workup as described for the synthesis of **25**, gave a colorless oil. A yellow precipitate was observed immediately after the addition of the alkyl halide. Chromatography (10:1 silica gel, petroleum ether) afforded the pure addition compound as a colorless oil.

***O*-(Methoxymethyl)-2-phenyl-2-propanol (30a) from iodomethane**: 96%; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.14–7.53 (5 H, m), 4.51 (2 H, s), 3.33 (3 H, s), 1.57 (6 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 146.30, 128.08, 126.88, 125.53, 92.24, 77.59, 55.30, 29.02; IR (NaCl, cm^{-1}) 2970, 1600 (w), 1492, 1443, 1379, 1361, 1256, 1136, 1083, 1027, 992, 915, 760, 696; MS (CI), *m/e* (relative intensity) 181 (M + 1, 2), 121 (11), 120 (12), 119 (100), 105 (7), 73 (5); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.48. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.02; H, 8.98.

***O*-(Methoxymethyl)-2-phenyl-2-hexanol (30b) from iodobutane**: 89%; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.07–7.53 (5 H, m), 4.50 (2 H, s), 3.35 (3 H, s), 1.76 (2 H, br t, J = 8 Hz), 1.60 (3 H, s), 0.64–1.44 (7 H, m); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 145.70, 127.94, 126.66, 125.92, 92.01, 80.12, 55.41, 43.49, 26.06, 24.23, 22.94, 13.90; IR (NaCl, cm^{-1}) 2933, 1490, 1445, 1372, 1303, 1211, 1139, 1027, (br), 911, 836, 760, 695; MS (CI), *m/e* (relative intensity) 161 (100), 145 (4), 119 (5), 105 (7); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.57.

***O*-(Methoxymethyl)-4-phenyl-1-penten-4-ol (30c) from allyl iodide**: 88%; ^{1}H NMR ($CDCl_3$, 90 MHz) δ 7.16–7.54 (5 H, m), 5.40–5.93 (1 H, m), 4.83–5.12 (2 H, m), 4.55 (2 H, s), 3.37 (3 H, s), 2.55 (2 H, d, J = 7 Hz), 1.61 (3 H, s); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 145.00, 133.90, 128.02, 126.95, 117.61, 92.06, 79.57, 55.48, 48.24, 24.02; IR (NaCl, cm^{-1}) 2915, 1630 (w), 1441, 1370, 1137, 1081, 1023, 913, 758, 969; MS (EI), *m/e* (relative intensity) 165 (100), 149 (74), 105 (23), 91 (15); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.52.

(b) General Procedure for the Exchange of *trans*-4-*tert*-Butyl-*O*-(methoxymethyl)-1-(tri-*n*-butylstannyl)cyclohexanol (32M) Followed by Alkyl Halide Quench. α-Alkoxyorganostannane **32M** (100 mg, 0.204 mmol) was dissolved in DME (5.0 mL) and cooled to −78 °C. Exchange with *n*-butyllithium (0.224 mmol), followed by excess alkyl halide quench and workup as described for the synthesis of compound **25**, gave the product mixture as a colorless oil. A precipitate was observed in all cases immediately upon addition of the alkyl halide. The crude oil was analyzed by ^{1}H NMR to determine product percentages (via integration of methylenedioxy and methoxy protons) and chromatographed to ascertain chemical yield and confirmation of assignments. Product profiles consisted of 4-*tert*-butylcyclohexanone (**31**), protonated adducts **34a** and **34b** [*trans*- and *cis*-4-*tert*-butyl-*O*-(methoxymethyl)cyclohexanol], and 4-*tert*-butyl-1-(methoxymethoxy)-1-cyclohexene (**39**). Product ratios are listed in Table V.

39: ^{1}H NMR ($CDCl_3$, 90 MHz) δ 4.85 (2 H, s), 4.83 (1 H, m), 3.36 (3 H, s), 1.58–2.22 (5 H, m), 1.03–1.47 (2 H, m), 0.87 (9 H, s); ^{13}C NMR ($CDCl_3$, 25 MHz) δ 152.55, 97.95, 93.24, 56.01, 44.12, 32.18, 28.49, 27.33, 24.80, 23.98; IR NaCl, cm^{-1}) 2946, 1670, 1465, 1361, 1212, 1155, 1070, 1047, 1019, 991, 946, 919, 797; MS (CI), *m/e* (relative

intensity) 200 (M + 2, 12), 199 (M + 1, 100), 183 (12), 169 (32), 155 (30), 107 (22), 95 (15), 83 (13); TLC (5% ethyl acetate/95% petroleum ether) R_f 0.58.

General Procedure for the Exchange of *cis*-4-*tert*-Butyl-*O*-(methoxymethyl)-1-(tri-*n*-butylstannyl)cyclohexanol (32m) Followed by Alkyl Halide Quench. α-Alkoxyorganostannane **32m** (100 mg, 0.204 mmol) was dissolved in DME (5.0 mL) and cooled to −30 °C. Exchange, quenching, workup and product analysis were identical with that described for stannane **32M** with the exceptions that precipitates were rarely formed upon alkyl halide addition, 4-*tert*-butylcyclohexanone was never observed in any product mixture, and quenching with iodomethane did provide some alkylated product [*cis*-4-*tert*-butyl-*O*-(methoxymethyl)-1-methylcyclohexanol (**35b**)]. Product ratios are listed in Table V.

Kinetic Addition of (Trialkylstannyl)lithium Species to 4-*tert*-Butylcyclohexanone and Protection of the Resulting Alcohols with Chloromethyl Methyl Ether. (a) General Procedure. Proportional reaction conditions and workup were identical with the general procedure for the synthesis of α-alkoxy trialkylstannyl derivatives (thermodynamic conditions) described above except addition was made at −100 °C (liquid nitrogen/CCl_4 bath) in diethyl ether. (Trialkylstannyl)lithium (0.720 mmol) was added to 4-*tert*-butylcyclohexanone (100 mg, 0.639 mmol), followed by protection of the resulting alcohols as their methoxymethyl derivatives and purification via chromatography.

(b) Equilibration of the Intermediate Alcohols Resulting from the Addition of (Tri-*n*-butylstannyl)lithium to 4-*tert*-Butylcyclohexanone under Kinetic Conditions. A crude 45:55 mixture of the alcohols [prepared by the addition of (tri-*n*-butylstannyl)lithium (0.720 mmol) to 4-*tert*-butylcyclohexanone (100 mg, 0.640 mmol) in ether at −78 °C] was dissolved in THF (2.0 mL) and cooled to −78 °C. *n*-Butyllithium (0.961 mmol) was added dropwise with stirring over 1 min. After the mixture was stirred for 10 min, the reaction was worked up as described previously. TLC analysis indicated the presence of an approximately 90:10 ratio of the alcohols. Protection as the methoxymethyl ethers, followed by high-field NMR analysis, revealed the identical 93:7 ratio of stannanes **32M** and **32m** as observed with the thermodynamic addition procedure.

(c) Other Addition Reactions Outlined in Table IV. The general procedures described above for kinetic (ether, pentane) and thermodynamic (THF, DME) addition of (trialkylstannyl)lithium reagents to 4-*tert*-butylcyclohexanone were used to complete Table IV. Variations between runs are due solely to differing solvents, reaction times, and temperatures. All chemical yields were 60–70% with the single exception of runs conducted in pentane,where no reaction was observed.

Exchange of Secondary α-Trialkylstannyl Cyclic Ethers with *n*-Butyllithium Followed by the Addition of Benzaldehyde. To a solution of the α-trialkylstannyl cyclic ether (0.398 mmol) dissolved in THF (1.5 mL) cooled to −78 °C was added *n*-butyllithium (0.410 mmol). After the mixture was stirred for 15 min, the reaction was quenched with benzaldehyde (0.610 mmol). After an additional 30 min of stirring at −78 °C, saturated ammonium chloride solution (2 mL) was added, and the mixture was permitted to warm to room temperature. The mixture was extracted with ether (2 × 5 mL), and the combined organic layers were dried (sodium sulfate), filtered, and concentrated in vacuo. Purification of the residue by chromatography (10:1 silica gel, 15% ethyl acetate/85% petroleum ether) afforded the designated products as oils.

Exchange of (2-Tetrahydrofuranyl)trimethylstannane (19). Stannane **19** was subjected to the general exchange and quenching procedure described above. Chromatography afforded 2-(α-hydroxybenzyl)tetrahydrofuran (47%) as an inseparable 50:50 mixture of diastereomers and 1-phenylethanol (13%, prepared independently by the sodium borohydride reduction of acetophenone). 2-(α-Hydroxybenzyl)tetrahydrofuran: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.30 (10 H, m), 4.95 (1 H, br s), 4.44 (1 H, dd, *J* = 7.5, 2.4 Hz), 3.79–4.33 (6 H, m), 2.94 (1 H, d, *J* = 2.6 Hz, O*H*), 2.46 (1 H, d, *J* = 2.3 Hz, O*H*), 1.63–2.00 (8 H, m); ^{13}C NMR ($CDCl_3$, 90 MHz) δ 140.58, 140.49, 128.28, 128.14, 127.84, 127.30, 126.89, 125.94, 83.39, 83.07, 77.35, 77.00, 76.90, 76.65, 73.92, 68.94, 68.34, 27.85, 25.96, 24.71; IR (NaCl, cm^{-1}) 3400 (br), 3050, 3020, 2960, 2930, 2850, 1490, 1190, 1050, 750, 690; MS (CI), *m/e* (relative intensity) 179 (M + 1, 0.01), 178 (0.03), 177 (0.08), 161 (100), 101 (33), 91 (0.07), 70 (39). Anal. Calcd for $C_{11}H_{24}O_2$: C, 74.12; H, 7.93. Found: C, 73.90; H, 7.97.

Exchange of (2-Tetrahydrofuranyl)tri-*n*-butylstannane (20). Stannane **20** was subjected to the general exchange and quenching procedure described above. Chromatography afforded 2-(α-hydroxybenzyl)tetrahydrofuran (71%) as an inseparable 52:48 mixture of diastereomers.

Exchange of (2-tetrahydropyranyl)trimethylstannane (21). Stannane **21** was subjected to the general exchange and quenching procedure described above. Chromatography afforded a yellow oil, which via GC analysis (DB5 glass capillary column, oven temperature of 110 °C, 1-phenylpentanol used as internal standard) consisted of a mixture of 2-(α-hydroxybenzyl)tetrahydropyran[28] (30%, 48:52 ratio of diastereomers) and 1-phenylethanol (32%). 2-(α-Hydroxybenzyl)tetrahydropyran: ^{1}H NMR ($CDCl_3$, 360 MHz) δ 7.25 (10 H, m), 4.84 (1 H, br t, *J* = 3.3 Hz), 4.44 (1 H, dd, *J* = 8.2, 0.9 Hz), 4.07 (2 H, m), 3.25–3.55 (4 H, m), 3.23 (1 H, d, *J* = 1.2 Hz, O*H*), 2.58 (1 H, d, *J* = 2.9 Hz, O*H*), 1.80 (2 H, m), 1.20–1.62 (10 H, m); IR (NaCl, cm^{-1}) 3430 (br), 2920, 2830, 1440, 1195, 1075, 1030, 750, 690.

Exchange of (2-Tetrahydropyranyl)tri-*n*-butylstannane (22). Stannane **22** was subjected to the general exchange and quenching procedure described above. Chromatography afforded 2-(α-hydroxybenzyl)tetrahydropyran (76%) as an inseparable 51:49 mixture of diastereomers.

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Registry No. 8, 1527-99-7; **10**, 89727-00-4; **11**, 100045-83-8; **12**, 89727-01-5; **13**, 110615-30-0; **14**, 89727-02-6; **15**, 89727-03-7; **16**, 40218-10-8; **17**, 110615-32-2; **18**, 110615-33-3; **19**, 110615-34-4; **20**, 110615-35-5; **21**, 110615-36-6; **22**, 110615-37-7; **23**, 1528-00-3; **25**, 42604-09-1; **26**, 110615-40-2; **27**, 705-58-8; **28**, 98877-58-8; **30a**, 24142-63-0; **30b**, 89726-96-5; **30c**, 89726-95-4; **30d** (isomer 1), 110615-41-3; **30d** (isomer 2), 110615-42-4; **30e** (isomer 1), 110637-06-4; **30e** (isomer 2), 110615-43-5; **30f**, 89726-94-3; **31**, 98-53-3; **32M**, 89726-83-0; **32m**, 89746-17-8; **33M**, 110615-31-1; **33m**, 110615-29-7; **34a**, 89726-87-4; **34b**, 89726-90-9; **35a**, 89726-88-5; **35b**, 89726-91-0; **37a/38a**, 110615-44-6; **37b/38b**, 110615-45-7; **37c**, 89726-86-3; **38c**, 110615-46-8; **39**, 89726-97-6; isobutylraldehyde dibenzyl acetal, 82053-19-8; [α-(benzyloxy)methyl]lithium, 71316-95-5; 2-(α-hydroxybenzyl)-tetrahydrofuran (isomer 1), 16765-46-1; 2-(α-hydroxybenzyl)tetrahydrofuran (isomer 2), 16765-45-0; 2-(α-hydroxybenzyl)tetrahydropyran (isomer 1), 110615-38-8; 2-(α-hydroxybenzyl)tetrahydropyran (isomer 2), 110615-39-9; 1-phenylethanol, 98-85-1; hexamethylditin, 661-69-8; (trimethylstannyl)lithium, 17946-71-3; cyclohexanone, 108-94-1; acetophenone, 98-86-2; (tri-*n*-butylstannyl)lithium, 4226-01-1; paraformaldehyde, 30525-89-4; acetaldehyde, 75-07-0; chlorotrimethylstannane, 1066-45-1; bromomethyl benzyl ether, 17690-16-3; 2-chlorotetrahydrofuran, 13369-70-5; 2-chlorotetrahydropyran, 3136-02-5; benzaldehyde, 100-52-7.

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