Oxidation and Reduction Reactions of Highly Functionalized Allyl Stannanes. Bicyclic and Tricyclic α-Stannylmethyl Enones Prepared via the Robinson Annulation Reaction of β′-Stannylethyl Vinyl Ketone

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Abstract: 5-(Tributylstannyl)-1-penten-3-one is prepared in 50% overall yield from the readily available 3-((triethylsilyl)-oxy)-1,4-pentadiene. Use of this reagent in the Robinson annulation reaction provides α-stannylmethyl enones in very good yields. Cerium-mediated 1,2 reduction followed by acylation affords the corresponding allylic acetate. Both classes of compounds undergo specific S_E2' oxidation with lead tetraacetate, mCPBA, and halogenating agents at the tertiary center of the allylic stannane to initially afford exocyclic olefins. Rearrangement of the allylic acetates and allylic halides subsequently provides the isomeric endocyclic enone bearing a functionalized methyl group. Further chemistry includes Birch reduction of an α-stannylmethyl enone to a saturated α-stannylmethyl ketone as well as application of the Robinson annulation strategy to a hydrophenanthrene system. Attempts to effect additional Robinson annulation reactions on substrates already bearing the tributylstannane moiety either fail or proceed in very poor yield.

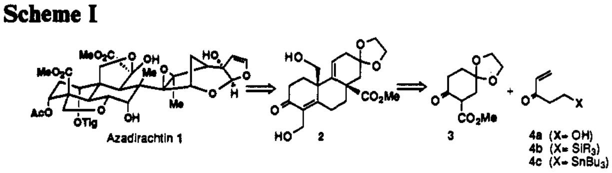
Introduction

In conjunction with our program to prepare highly oxygenated terpenoids (*cf.* azadirachtin (**1**),[1] Scheme I), we have reported the attempted application of β′-silylethyl vinyl ketone (**4b$_1$**) as a synthon for hydroxyethyl vinyl ketone (**4a**) in the Robinson annulation reaction.[2] Synthesis of β′-silylated ethyl vinyl ketone (EVK) reagents **4b$_{1-3}$** (Scheme II) is readily accomplished by metalation of silyl ether **5** by the method of the Oppolzer,[3] followed by treatment of the resultant anion with the appropriate chlorosilanes to provide dienylic silanes **6b$_{1-3}$** in 56–85% yield. Fluoride-mediated desilylation of **6b$_{1-3}$**, again using the method of Oppolzer,[3] smoothly provides the three reagents **4b$_{1-3}$**. Extension of this method by quenching of the dienylic anion from **5** with tributylstannyl chloride affords dienylic stannane **6c**, which can be uneventfully transformed to β′-stannylethyl enone **4c** using the same methodology (Scheme II).[4]

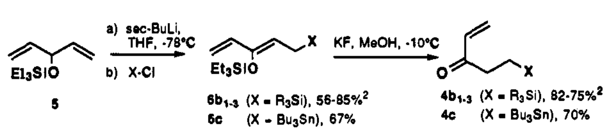
It rapidly became apparent that the β′-silylated EVK reagents **4b$_{1-3}$** were not especially well-suited for the Robinson annulation reaction. While monoannulation product **10b$_1$** could be isolated in 59% yield upon reaction of **4b$_1$** with β-ketoester **3**, the isolation of 25% yield of ester **9b$_1$** (after diazomethane treatment of acid **8b$_1$**) indicated that the initial Michael adduct **7b$_1$** had suffered hydroxide-mediated retro-Claisen reaction competitive to the aldol-dehydration process. Unfortunately, all attempts to employ **10b$_1$** (Scheme III) as substrate for a second annulation reaction using sodium methoxide in methanol at reflux in the presence of EVK did not give any of the desired tricyclic derivative **12b$_1$** but exclusively yielded **12H**. Control studies reveal that **12H** arose through the intermediacy of **10H**, protiodesilylation of allyl silane **10b$_1$** being faster than the second annulation reaction. Other conditions either led to no reaction (DBU or potassium *tert*-butoxide/*tert*-butyl alcohol/THF reflux) or provided mixtures of products devoid of the desired silyl compound **12b$_1$** (Scheme III).

Since desilylation of intermediate **10** results from attack of alkoxide (and/or water) at the silyl moiety, reagents **4b$_2$** and **4b$_3$** (Scheme III) were also tested in the annulation reaction. As can be seen from Table I, this modification has conferred greater stability characteristics upon the silyl moiety; unfortunately this comes at the expense of the intramolecular aldol-dehydration

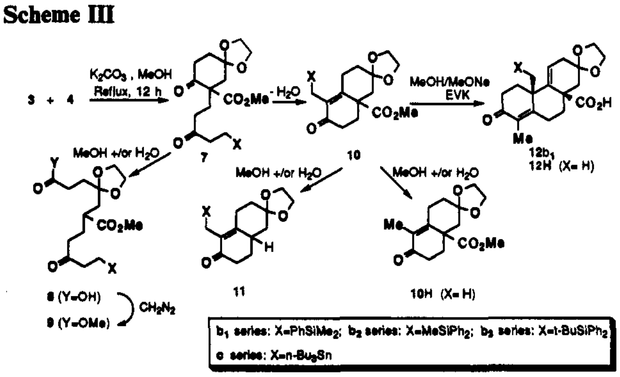
Scheme I



Scheme II



Scheme III



(1) For leading references see: (a) Kolb, H. C.; Ley, S. V.; Slawin, A. M. Z.; Williams, D. J. *J. Chem. Soc. Perkin Trans. 1* **1992**, 2735–2762. (b) Ley, S. V.; Lovell, H.; Williams, D. J. *J. Chem. Soc., Chem. Commun.* **1992**, 1304–1306. (c) Lallemand, J. Y.; Lejeune, J. *Tetrahedron Lett.* **1992**, *33*, 2977. (d) Chan, T. H.; Schwerdtfeger, A. E. *J. Org. Chem.* **1991**, *56*, 3294. (e) Anderson, J. C.; Ley, S. V.; Santafianos, D.; Sheppard, R. N. *Tetrahedron* **1991**, *47*, 6813–6850. (f) Blaney, W. M.; Simmonds, M. S. J.; Ley, S. V.; Anderson, J. C.; Toogood, P. L. *Entomol. Exp. Appl.* **1990**, *55*, 149–160.

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(4) The 70% yield represents reagent **4c**, which has been separated from 1-(tributylstannyl)-5-methoxy-3-pentanone, the Michael adduct of **4c** with methanol. In applications involving methanol and base, this adduct is in equilibrium with **4c**, and the "crude" mixture (usually containing ca. 20% of the Michael adduct) serves equally well as reagent.

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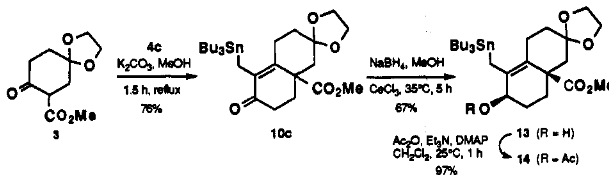
Table I. Reactions of β-Ketoester **3** with Reagents **4b**$_{1-3}$ and **4c**

SM	yield of **9** (%)	yield of **10** (%)	yield of **10H** (%)	yield of **11** (%)
4b$_1$	**9b**$_1$ 25	**10b**$_1$ 59	trace	trace
4b$_2$	**9b**$_2$ 30	**10b**$_2$ 41	5	5
4b$_3$	**9b**$_3$ 60	**10b**$_3$ trace	trace	22
4c	**9c** 3.3	**10c** 76	1.0	0

Scheme IV



step, which has slowed to the point where deacylation (to **11**) and retro-Claisen reactions (to **8**) have become the dominant processes.

Results and Discussion

Faced with the aforementioned constraints upon silyl reagent reactivity combined with hydrolytic instability, we elected to abandon the silicon-based reagents in favor of β'-stannylethyl reagent **4c**, since stannanes are known to be more resistant to hydrolytic cleavage than are silanes.[5] Synthesis of **4c** is readily accomplished by the Oppolzer technology as previously described in Scheme II.[3]

Reaction of β-ketoester **3** with reagent **4c** (1.05 equiv) with 2 equiv of potassium carbonate in methanol at reflux for 1.5 h afforded enone **10c** in 76% yield (Table I, Scheme IV).[6] Cerium-mediated borohydride reduction[7] of **10c** provided an 87:13 mixture of allylic alcohols which were separated by chromatography to provide β-alcohol **13** in 67% yield. Conversion of **13** to acetate **14** was uneventful (97%).

Table II details the results of subjecting bicyclic allyl stannanes **10c** and **14** to a series of S$_E$2' oxidation reactions (Scheme V). These substrates underwent successful oxidation with mCPBA,[8] Pb(OAc)$_4$,[9] Br$_2$,[10] and chloreal[11] while attempts at using MnO$_2$ (no reaction),[12] CuBr$_2$ in the presence of methanol or morpholine,[13,14] and ceric ammonium nitrate[15,16] were unsatisfactory.

As can be seen from Table II, the kinetic product in all cases appears to be the bridgehead oxidized olefin **15**. The ease of subsequent rearrangement of **15** to the thermodynamic endocyclic olefin **16** was a function of the substrate (enone versus allylic acetate) as well as the leaving group. For example, monitoring a solution of chloro enone **15d** in CDCl$_3$ revealed complete isomerization to endocyclic chloromethyl enone **16d** after 18 h at 25 °C. Presumably this is an acid-catalyzed process involving the intermediacy of enol **18**. Tertiary allylic acetate **15b** is also very prone to acid-catalyzed rearrangement to **16b**. In view of the differential leaving group ability of chloride and acetate, it was initially surprising that the rearrangement of **15b** proceeded with about equal facility to that of chloride **15d**. In order to explain the ease of this process, it is proposed that tertiary acetate **15b** undergoes rearrangement via dioxolenium ion **19** (Scheme VI). Alternatively, an acid-catalyzed (carbonyl-protonated) 3.3 sigmatropic rearrangement seems equally reasonable.[17] Consistent with the role of the carbonyl group in these rearrangements, it is noted that compounds **15h** and **15f** do not undergo rearrangement under comparable conditions (see Table II).

It was observed that reaction of **14** with 1 equivalent of mCPBA *in ether* smoothly affords tertiary alcohol **15e** in 75% yield (Scheme VII), while conducting this reaction in methylene chloride with 2.2 equiv of mCPBA provides epoxy alcohol **17** in 86% yield as the only detectable reaction product, consistent with the expectations of a directed epoxidation[18] process. Because of the considerable stability of the tertiary allylic alcohols, the peracid oxidation and the lead tetraacetate-isomerization reaction are complementary with respect to the regiochemical introduction of the oxygen functionality. This simple reaction sequence should see considerable synthetic application, since enones such as **15a–d** and **16a–d** are prized for their high S$_N$2' reactivity.[19] Moreover, stannyl-substituted allyl carboxylates related to **14** may serve as substrates for palladium-mediated trimethylenemethane annulation reactions.[20]

Initial investigations of extending this chemistry to the tricyclic series shown in Scheme VIII reveals several additional features. Treatment of bicyclic enone **10H** (Z = H, X = O)[2,21] with reagent

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(6) Analysis of the reaction residues provides the retro-Claisen product **9c** (3.3%), resulting from the initial Michael reaction adduct of **3** and **4c**, as well as 1% of the product resulting from destannylation of **10c**. See ref 2.
(7) Luche, J. L. *J. Am. Chem. Soc.* **1978**, *100*, 2226.
(8) (a) Bakale, R. P.; Scialdone, M. A.; Johnson, C. R. *J. Am. Chem. Soc.* **1990**, *112*, 6729. (b) Ueno, Y.; Sano, H.; Okawara, M. *Synthesis* **1980**, 1011. (c) Nishida, A.; Shibasaki, M.; Ikegami, S. *Tetrahedron Lett.* **1981**, *22*, 4819. (d) Shibasaki, M.; Suzuki, M.; Torisawa, Y.; Ikegami, S. *Chem. Lett.* **1983**, 1303. (e) Andrianome, M.; Häberle, K.; Delmond, B. *Tetrahedron* **1989**, *45*, 1079. (f) Hideg, K.; Sár, C.; Hankovszky, O. H.; Jerkovich, G. *Synthesis* **1991**, 616.
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(14) Evidence for significant formation of allylic ethers or allylic amines was not obtained in these reactions; allylic bromides **16c** (60%) and **16g** (30%) were obtained in the methanol reaction, while the allylic stannane starting materials were recovered in >85% yield in the presence of 50 equiv. morpholine after 10 hr at reflux in THF.
(15) Hanessian, S.; Léger, R. *J. Am. Chem. Soc.* **1992**, *114*, 3115.
(16) No aldehyde or dimethyl acetal was obtained. The only major products isolated from the reaction of **10c** and **14** with 10 equiv of ceric ammonium nitrate in methanol for 5 min at 25 °C were the destannylated endocyclic primary nitrite esters in 60% and 50% yields, respectively.
(17) It should be noted that palladium(II) catalysis of the 3.3 sigmatropic rearrangement has been previously observed (Overman, L. E.; Knoll, F. M. *Tetrahedron Lett.* **1979**, *79*, 321. Grieco, P. A.; Takigawa, T.; Bongers, S. L.; Tanaka, H. *J. Am. Chem. Soc.* **1980**, *102*, 7587).
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(19) For general references to the chemistry of exocyclic enones, see: (a) Nakahira, H.; Ryu, I.; Ikebe, M.; Oku, Y.; Ogawa, A.; Kamble, N.; Sonoda, N.; Murai, S. *J. Org. Chem.* **1992**, *57*, 17. (b) Tamura, R.; Watabe, K.-I.; Katayama, H.; Suzuki, H.; Yamamoto, Y. *J. Org. Chem.* **1990**, *55*, 408. (c) Schultz, A. G.; Taylor, R. E. *J. Am. Chem. Soc.* **1992**, *114*, 3937. (d) Review: Shono, T.; Matsumura, Y. *Yuki Gosei Kagaku Kyokaishi* **1981**, *39*, 358. For references to the S$_N$2' chemistry of enone-polarized allylic systems, see: (e) Tamura, R.; Watabe, K.-I.; Katayama, H.; Suzuki, H.; Yamamoto, Y. *J. Org. Chem.* **1990**, *55*, 408. (f) Tamura, R.; Tamai, S.; Suzuki, H. *Tetrahedron Lett.* **1989**, *30*, 2413. (g) Suzuki, M.; Kawagishi, T.; Noyori, R. *Tetrahedron Lett.* **1981**, *22*, 1809. (h) Takahashi, T.; Hori, K.; Tsuji, J. *Tetrahedron Lett.* **1981**, *22*, 119. (i) Cromwell, N. H.; Soriano, D. S.; Doomes, E. *J. Org. Chem.* **1980**, *45*, 4983. (j) Smith, A. B., III; Wexler, B. A.; Slade, J. S. *Tetrahedron Lett.* **1980**, *21*, 3237.
(20) (a) Trost, B. M.; King, S. A. *J. Am. Chem. Soc.* **1990**, *112*, 408. (b) Trost, B. M.; Nanninga, T. N. *J. Am. Chem. Soc.* **1985**, *107*, 1075.
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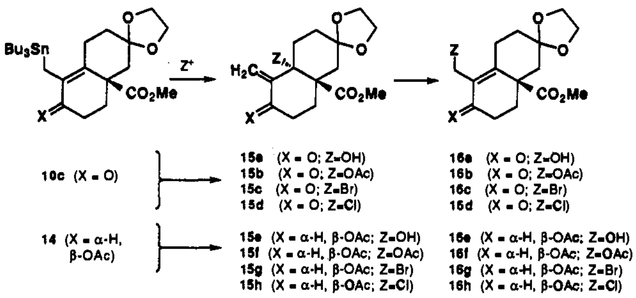
Table II. Oxidative Functionalization of Bicyclic α-Stannylmethyl Enone **10c** and Bicyclic α-Stannylmethyl Allyl Acetate **14**

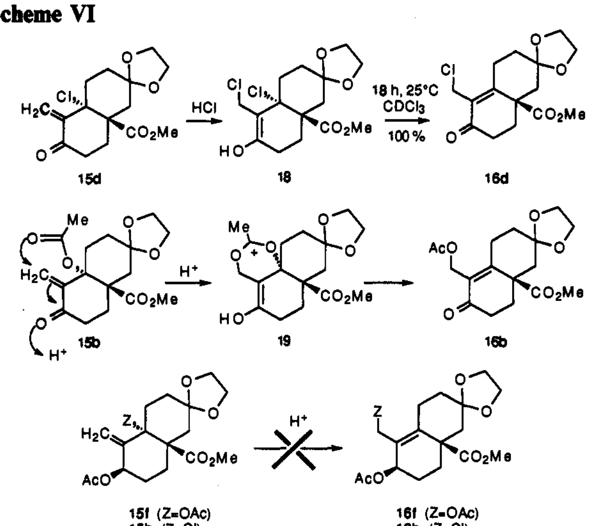
SM	reagents	conditions	ratio[a] 15 (% yield)	ratio[a] 16 (% yield)
10c	mCPBA (1.3 equiv)	CH_2Cl_2, 25 °C, 2.5 h	**15a**[b] >97 (80)	**16a** <3
10c	$Pb(OAc)_4$ (2 equiv)	CH_2Cl_2, 25 °C, 15 h	**15b**[b] ~4 (55)	**16b** ~1 (14)[c]
15b	PPTs (cat.) + HOAc (0.7 equiv)[d]	CH_2Cl_2, reflux, 3 h	**15b** <3 (0)	**16b** >97 (70)
10c	Br_2 (1 equiv)	*i*-PrOH, -50 °C, 10 min	**15c** ~90[e] (80)	**16c** ~10[e]
15c	none	C_6D_6, 25 °C, <30 min	**15c** <3 (0)	**16c** >97 (quant)
10c	chloreal (1 equiv)	*i*-PrOH, -30 °C, 30 min	**15d** >97 (89)	**16d** <3
15d	none	$CDCl_3$, 25 °C, 18 h	**15d** <3 (0)	**16d** >97 (quant)
14	mCPBA (1.1 equiv)	Et_2O, 25 °C, 7 h	**15e** >97 (75)	**16e** <3 (0)
14	$Pb(OAc)_4$ (2 equiv)	CH_2Cl_2, 25 °C, 40 h	**15f** >97 (82)	**16f** <3 (0)
15f	PPTs (cat.) + HOAc (0.7 equiv)	$ClCH_2CH_2Cl$, reflux, 12 h	**15f** >97 (97)	**16f** <3 (0)
14	Br_2 (1 equiv)	*i*-PrOH, 0 °C, 10 min	**15g** >97 (90)[f]	**16g** <3
15g	*n*-Bu_4NBr	THF, 40 min	**15g** <3 (0)	**16g** >97 (94)
14	chloreal (1 equiv)	*i*-PrOH, -30 °C, 30 min	**15h** >97 (81)	**16h** <3
15h	none	$CDCl_3$, 25 °C, 48 h	**15h** >97 (90)	**16h** <3

[a] Limit of detection by ^{1}H NMR. [b] Structure verified by X-ray (see supplementary material). [c] Produced by partial isomerization of **15b** under the reaction conditions. [d] Bu_3SnOAc and $Pb(OAc)_2$ do not effect the isomerization. HOAc alone is slower than in combination with PPTs. [e] Estimated from analytical TLC of the -50 °C reaction mixture. Isomerization of **15c** to **16c** is rapid even in acid-free C_6D_6. [f] **15g** is stable for 24 h in C_6D_6, but storage in commercial $CDCl_3$ for 1 day produces a mixture of starting material **15g** (28%), rearranged bromide **16g** (50%), and tertiary *chloride* **15h** (22%).

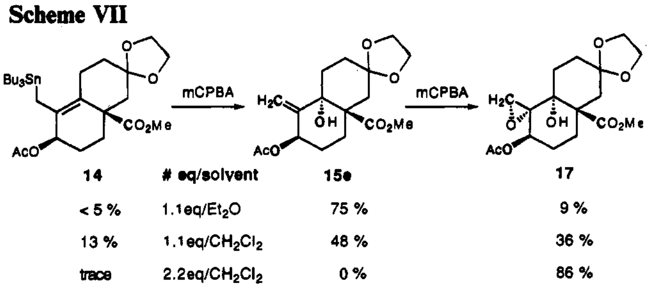
Scheme V



Scheme VI

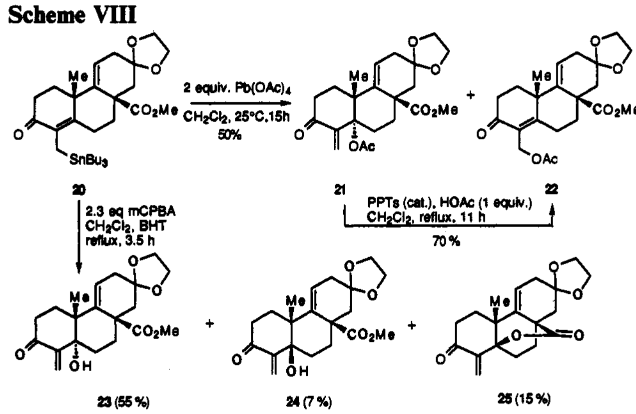


Scheme VII



4c in methanolic sodium methoxide at reflux for 20 h followed by esterification of the resulting carboxylic acid with diazomethane provides tricyclic enone **20** in 87% yield. Oxidation of **20** with lead tetraacetate provides a 4:1 mixture of exocyclic enone **21**

Scheme VIII

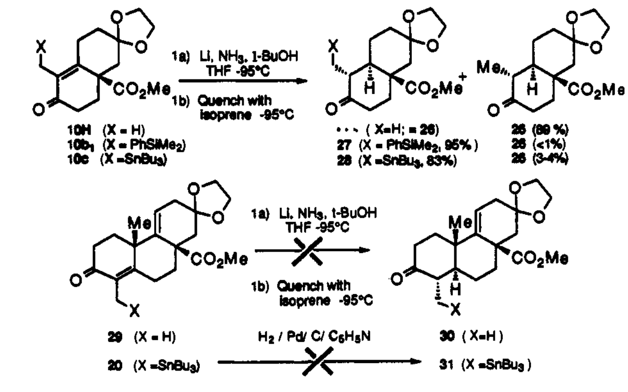


(50% yield, >95% α-acetate) which has undergone partial isomerization to the endocyclic isomer **22**. Completion of the isomerization can again be effected with the PPTs/HOAc system. By contrast to the **10c** to **15a** transformation, reaction of **20** with mCPBA in methylene chloride at reflux is quite slow and requires additional oxidant to complete the reaction even in the presence of the radical inhibitor BHT,[22] thereby producing, in addition to 12% recovered starting material, a mixture of products (**23–25**) resulting from oxygenation at both α- and β-faces of the substrate.

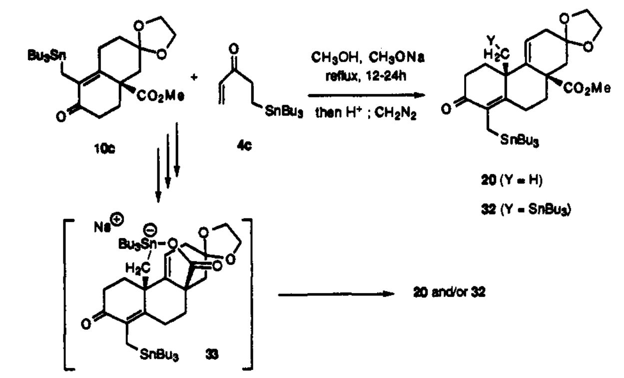
Previous experience with the dissolving-metal reduction of bicyclic enones **10H**[23] and **10b$_1$**[2] had revealed that it was possible to efficiently reduce the enone in the presence of the resident ester moiety. Especially striking is the observation that running the same reaction at -95 °C on the much more challenging α-stannylmethyl enone **10c** provides saturated ketone **28** with minimal production of ketone **26** by competitive reductive cleavage of the allylstannane moiety (Scheme IX). Application of this protocol on tricyclic α-stannylmethyl enone **20** was completely unrewarding, providing a complex product mixture which showed no evidence for generation of the target tricyclic ketone **31**. This mixture was devoid of ester functionality yet appeared to retain the tributylstannyl group. Consistent with the postulate of ester involvement as the unwanted reaction, it was also observed that attempted reduction of nonstannylated enone **29** also produced a similar product mixture, which again lacked the ester moiety. Therefore, the failure is likely not due to the presence of the tin function but rather due to intramolecular interaction of the incipient radical anion with the ester carbonyl group. While catalytic reduction of compounds related to **29** yields dihydro

(22) Kishi, B. Y.; Aratani, M.; Tanino, H.; Fukuyama, T.; Goto, T. *J. Chem. Soc., Chem. Commun.* **1972**, 64.
(23) Emeric, G. Ph.D. Thesis, Purdue University, 1991.

Scheme IX



Scheme X



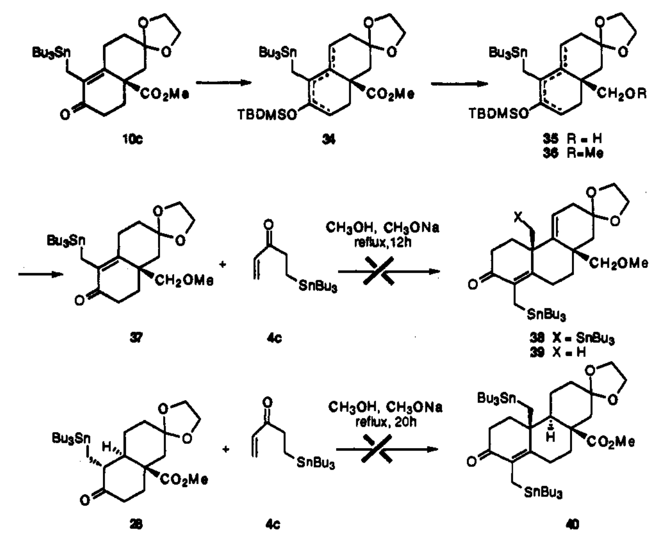
ketones such as **30**,[24] attempts to effect similar reduction (10% Pd/C, 25 °C, 36 h) of **20** simply serve to return the stannylated enone unchanged.

Attempts to utilize the annulation strategy for preparation of the target enone **2** were at best only partially successful. Heating **10c** in methanol for 12 h in the presence of sodium methoxide and 2.3 equiv of reagent **4c** provides, after diazomethane treatment, an 11% yield of the requisite bis-stannylated tricyclic enone **32** in addition to large amounts of starting bicyclic enone **10c** (Scheme X). Extending the reaction time to 24 h simply serves to consume tricyclic **32** with concomitant production of destannylated enone **29**, 80% of **10c** again being recovered. Control reactions serve to demonstrate that enone **10c** is not significantly converted to **10H** under these conditions; therefore, it appears that the internal carboxylate moiety may be responsible for the destannylation process (via **33**).

In an effort to avoid the carboxylate-mediated destannylation reaction, the axial ester moiety of **10c** was modified to a methoxymethyl group. This was accomplished by reaction with TBDMS-triflate and triethylamine in methylene chloride to provide a 98% yield of silyl dienyl ether **34** as a mixture of regioisomers which was not separated (Scheme XI). Subsequent reduction with LAH followed by alkylation of the neopentyl alcohol moiety of **35** with sodium hydride and methyl iodide afforded ether **36** in 70% yield for the two steps. Cleavage of the silyloxy protecting group was accomplished by reaction with tetrabutylammonium fluoride in THF, providing methoxymethyl enone **37** in 60% yield. Reaction of this material with reagent **4c** in methanolic methoxide for **12** h at reflux returned 70% of substrate **37**. Careful examination of the reaction residues failed to provide any evidence for formation of **38**, **39**, or destannylated **37**. In a final attempt to extend the scope of annulation with reagent **4c**, ketone **28** was recovered in >90% yield after being subjected to heating for 20 h in the standard basic medium.

In conclusion, it appears that while Robinson annulation reagent **4c** will provide excellent access to enones bearing the α-stannylmethyl moiety, the resultant stannylated enones are far more problematical with regard to serving as substrates for further annulation reactions, likely due to their substantial steric environment. Extension of those strategies employing the α-stannylmethyl enone should prove of considerable benefit for the concise synthesis of highly functionalized substrates.

Scheme XI



Experimental Section

General Methods. All reactions were performed under a positive pressure of argon in glassware which was washed with dilute aqueous sodium hydroxide prior to flame drying and which was equipped with rubber septa for the introduction of reagents via syringe. THF and ether were purified by distillation from sodium–benzophenone ketyl under argon in a standing still. Hexane and methylene chloride were maintained in standing stills over calcium hydride. All other recrystallization, chromatographic, and workup solvents were also distilled. Organolithium reagent was analyzed by titration of a solution of menthol in benzene containing 2,2′-bipyridyl as an indicator at room temperature under argon. Analytical thin-layer chromatography (TLC) was performed on silica gel 60 F-254 plates (EM). Flash silica gel chromatography (SGC) was carried out as described by Still.[25] All compounds reported have been analyzed by exact mass and appear homogeneous by ^{1}H and ^{13}C NMR. Proton NMR spectra were recorded on a General Electric QE-300 (300 MHz) and a Varian Gemini-200 (200 MHz) spectrometer. Carbon NMR spectra were recorded on a Varian Gemini 200 (50 MHz) spectrometer. Spectra were determined in chloroform-d_1 or benzene-d_6 as noted and are reported in parts per million (ppm) shifts from internal tetramethylsilane (0.00), chloroform (7.26), or benzene (7.15) standards. Splitting patterns are designated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad; OV, overlapping; and cm, complex multiplet. Carbon chemical shifts are reported (ppm) relative to the center line of the $CDCl_3$ triplet (77.0) and are denoted as "e" (none or two protons) or "o" (one or three protons), as determined from the APT pulse sequence. Compounds of >95% purity were characterized on a Finnigan 4000 mass spectrometer and a CEC 21 110 B high-resolution mass spectrometer with use of electron impact and chemical ionization, with the molecular ion designated as M. Infrared spectra were recorded on a Perkin-Elmer spectrophotometer. Microanalyses were performed by the Purdue Chemistry Department Microanalytical Laboratory. All silyl chlorides and tin chloride were purchased from Aldrich.

Phenyldimethylsilyl enone 4b$_1$. KF (Aldrich, 34.88 mg, 0.6 mmol) was added portionwise to a stirred solution of **6b$_1$**[2] (100 mg, 0.3 mmol) in methanol (5 mL) at −5 °C under Ar. The resulting solution was allowed to react for 3 h at 10 °C. The reaction mixture was then poured into water and extracted with CH_2Cl_2. The organic layer was washed with saturated NaCl solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give an oil, which was subjected to column chromatography on silica gel, using 5% EtOAc in hexane as eluent, to afford 49.1 mg (75%) of **4b$_1$**: IR (CCl_4) 1680, 1618 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.54–7.50 (2H, m), 7.39–7.34 (3H, m), 6.34 (1H, AB*X*, J = 18.5, 10.4 Hz, dd), 6.19 (1H, *A*BX, J = 18.5, 0.8 Hz, dd), 5.75 (1H, A*B*X, J = 10.4, 0.8 Hz, dd), 2.55 (2H, m), 1.07 (2H, m), 0.31 (6H, s);

(24) Hedstrand, D. M. Ph.D. Thesis, Purdue University, 1983.

(25) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 923.

^{13}C NMR (50 MHz, $CDCl_3$) δ 201.50 (e), 138.42 (e), 136.07 (o), 133.63 (o), 129.16 (o), 127.94 (o), 127.77 (e), 34.11 (e), 9.14 (e), −3.48 (o); MS (EI) *m/z* 218, 203, 135, 55; exact mass for $C_{13}H_{18}OSi$ (M) found 218.1108 (calcd 218.1127).

3-((Triethylsilyl)oxy)-5-(phenyldimethylsilyl)-1,3-pentadiene (6b$_1$). A 1.22 M solution of *sec*-BuLi (0.93 mL, 1.14 mmol) in cyclohexane was added dropwise to a stirred 1.5 M solution of triethylsilyl ether 5[3] (206 mg, 1.04 mmol) in dry THF at −78 °C under Ar. After 30 min at −78 °C, chlorodimethylphenylsilane (0.18 mL, 1.16 mmol) was added slowly to the deep-orange solution. After 10 min at −78 °C, the decolorized mixture was poured into saturated aqueous NH_4Cl solution. The organic layer was extracted with CH_2Cl_2. The CH_2Cl_2 solution was dried over Na_2SO_4 and evaporated in vacuo to leave a residue, which was chromatographed on silica gel, using hexane as eluent, to afford 307 mg (85%) of **6b$_1$**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.56–7.34 (5H, m), 6.18–6.09 (1H, *J* = 17, 11 Hz, dd), 5.20 (1H, *J* = 17 Hz, d), 4.88 (1H, *J* = 11.8 Hz, d), 4.79 (1H, t), 1.77 (2H, *J* = 8.4 Hz, d), 1.04–0.95 (9H, br t), 0.77–0.65 (6H, br q), 0.29 (6H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 149.25 (e), 139.59 (e), 136.42 (o), 134.09 (o), 129.48 (o), 128.29 (o), 111.76 (o), 110.44 (e), 78.04 (e), 77.41 (e), 76.77 (e), 15.86 (e), 7.05 (o), 5.85 (e), −2.93 (o); MS (EI) *m/z* 332, 135; exact mass for $C_{19}H_{32}OSi_2$ (M) found 332.1989 (calcd 332.1992).

Bicyclic α-Silylmethyl Enone 10b$_1$ and Retro-Claisen Product 9b$_1$. To β-ketoester 3[21e] (370 mg, 1.73 mmol) and K_2CO_3 (478 mg, 3.46 mmol) in methanol (20 mL) at reflux was slowly added enone **4b$_1$** (565 mg, 2.6 mmol) diluted in methanol (5 mL). The mixture was gently heated at reflux for 12 h. The resulting solution was cooled to room temperature, and the solvent was removed in vacuo. The oil was taken up in EtOAc (30 mL) and water (20 mL). The organic layer was separated and the solvent evaporated. The crude oil was purified by column chromatography (20% EtOAc in hexane), yielding the desired product **10b$_1$** (420 mg, 59%), along with a trace amount of **10H** and **11b$_1$**. The aqueous layer was acidified with 5% HCl to pH 3 and extracted with EtOAc, and the organic layer was evaporated to give a pale-yellow oil. The residue was reacted with excess diazomethane (prepared from Diazald) and then purified by column chromatography (20% EtOAc in hexane) to afford 200 mg of retro-Claisen product **9b$_1$** (25%). **10b$_1$**: IR (CCl_4) 1724, 1664, 1114 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48–7.45 (2H, m), 7.31–7.29 (3H, m), 3.98–3.78 (4H, m), 3.66 (3H, s), 2.45 (1H, m), 2.09 (2H, s), 1.33 (1H, m), 1.22–2.66 (8H, m), 0.26 (3H, s), 0.20 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 197.54 (e), 174.86 (e), 149.49 (e), 138.94 (e), 134.43 (e), 133.72 (o), 129.05 (o), 127.69 (o), 106.80 (o), 64.38 (e), 64.01 (e), 52.14 (o), 48.96 (e), 44.11 (e), 35.10 (e), 34.29 (e), 33.95 (e), 27.56 (e), 15.29 (e), −2.75 (o), −2.87 (o); MS (EI) *m/z* 414, 399, 355, 135; exact mass for $C_{23}H_{30}O_5Si$ (M) found 414.1863 (calcd 414.1863). **9b$_1$**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.5–7.32 (5H, m), 3.86 (4H, s), 3.64 (3H, s), 3.62 (3H, s), 2.36–1.67 (13H, remaining protons, m), 0.94 (2H, m), 0.25 (6H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 211.05 (e), 176.78 (e), 174.47 (e), 138.84 (e), 134.09 (o), 129.59 (o), 128.38 (o), 110.18 (e), 65.43 (e), 65.35 (e), 51.90 (o), 51.82 (o), 40.34 (o), 39.92 (e), 39.47 (e), 37.54 (e), 32.64 (e), 28.92 (e), 27.35 (e), 9.41 (e), −3.08 (o); MS (CI) *m/z* 465 (M + 1), 433, 387, 325, 281, 175, 159; exact mass for $C_{24}H_{36}O_7Si$ (M + 1) found 465.2299 (calcd 465.2309).

5-(Tributylstannyl)-1-penten-3-one (4c). KF (Aldrich, 92 mg, 2.3 mmol) was added portionwise to a stirred solution of stannylated silyl dienyl ether **6c** (866 mg, 1.76 mmol) in methanol (10 mL) at 0 °C under Ar. The resulting solution was allowed to react for 12 h at 10 °C. The reaction mixture was then poured into water and extracted with CH_2Cl_2. The organic layer was washed with saturated NaCl solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give an oil, which was subjected to column chromatography on silica gel, using 5% EtOAc in hexane as eluent, to afford 462 mg (70%) of **4c** and 107 mg (15%) of the Michael adduct of **4c**. **4c**: IR (CCl_4) 1702, 1682 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.4 (1H, AB*X*, *J* = 16.7, 10 Hz, dd), 6.3 (1H, *A*BX, *J* = 16.7, 1.8 Hz, dd), 5.75 (1H, A*B*X, *J* = 10, 1.8 Hz, dd), 2.75 (2H, t), 1.5–1.2 (15H, m), 0.9–0.76 (12H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 202.82 (e), 136.56 (o), 128.06 (e), 37.41 (e), 29.40 (e), 27.60 (e), 13.88 (o), 9.25 (e), 2.32 (e); MS (EI) *m/z* 375, 317, 291; exact mass for $C_{17}H_{34}OSn$ (M) found 371.1700 (calcd 371.1708).

3-((Triethylsilyl)oxy)-5-(tributylstannyl)-1,3-pentadiene (6c). A 1.22 M solution of *sec*-BuLi (2.25 mL, 2.75 mmol) in cyclohexane was added dropwise to a stirred 1.5 M solution of triethylsilyl ether **5** (496 mg, 2.5 mmol) in dry THF at −78 °C under Ar. After 30 min at −78 °C, chlorotributyltin (0.72 mL, 2.63 mmol) was added slowly to the deep-orange solution. After 1 h at −78 °C, the decolorized mixture was poured into saturated NH_4Cl solution. The organic layer was extracted with CH_2Cl_2. The CH_2Cl_2 solution was dried over Na_2SO_4 and evaporated in vacuo to leave a residue, which was chromatographed on silica gel, using hexane as eluent, to afford 856 mg (70%) of **6c**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 6.18–6.04 (1H, *J* = 17, 10.6 Hz, dd), 5.09 (1H, *J* = 17.2 Hz, d), 4.95 (1H, t), 4.76 (1H, *J* = 10.6 Hz, d), 1.76 (2H, *J* = 9.2 Hz, d), 1.53–0.65 (42H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 146.70 (e), 136.28 (o), 116.12 (o), 108.87 (e), 29.63 (e), 27.86 (e), 14.18 (o), 10.18 (e), 9.84 (e), 7.40 (o), 6.18 (e).

Bicyclic α-Stannylmethyl Enone 10c. To β-ketoester 3[21e] (598 mg, 2.79 mmol) and K_2CO_3 (848 mg, 2.93 mmol) in methanol (20 mL) at room temperature was slowly added enone **4c** (1.19 g, 2.93 mmol) diluted in methanol (5 mL). The mixture was gently heated at reflux for 1.5 h. The resulting solution was cooled to room temperature, and the solvent was removed in vacuo. The organic residue was diluted with EtOAc, and the organic layer was washed with saturated NaCl solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give a yellow oil, which was purified by column chromatography (20% EtOAc in hexane) to afford 1.2 g of desired product **10c** (76%) and 57 mg of retro-Claisen product **9c** (3.3%). **10c**: IR (CCl_4) 1732, 1668 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.02–3.9 (4H, m), 3.67 (3H, s), 2.83–2.74 (1H, m), 2.58–0.71 (38H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 198.43 (e), 175.64 (e) 146.41 (e), 137.85 (e), 107.49 (e), 64.92 (e), 64.58 (e), 52.64 (o), 49.32 (e), 44.97 (e), 35.78 (e), 34.82 (e), 29.30 (e), 27.64 (e), 27.31 (e), 13.91 (o), 10.21 (e), 9.24 (e); MS (EI) *m/z* (M + 1) 571, 513; exact mass for $C_{27}H_{46}O_5Sn$ (M) found 567.2434 (calcd 567.2445). Anal. Calcd for $C_{27}H_{46}O_5Sn$: C, 56.95; H, 8.14; Sn, 20.81. Found: C, 56.82; H, 8.39; Sn, 20.51.

Stannylated Allylic Acetate 14. Enone **10c** (138 mg, 0.24 mmol) was dissolved in a 0.4 M solution of $CeCl_3$ (65 mg, 0.24 mmol) in methanol. $NaBH_4$ (22 mg, 0.48 mmol) was then slowly added with stirring. After stirring for 5 h at 35 °C, the reaction was quenched by addition of 5% HCl (0.5 mL). The aqueous layer was extracted with EtOAc and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give an oil. NMR showed the ratio of β-alcohol to α-alcohol to be 87:13. The desired β-alcohol could be separated using column chromatography on silica gel using 20% EtOAc in hexane as eluent to afford 92 mg (67%) of **13**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.99–3.68 (5H, m), 3.67 (3H, s), 2.6–0.8 (39H, cm); MS (EI) *m/z* (M + 1) 573, 555, 541; exact mass for $C_{27}H_{47}O_5Sn$ (M) found 571.2581 (calcd 571.2598). The β-alcohol **13** could be easily protected (97%) by using standard acetylation conditions (Ac_2O, Et_3N, DMAP). **14**: IR (CCl_4) 1738 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.17 (1H, m), 3.99–3.86 (4H, m), 3.68 (3H, s), 2.5–2.41 (2H, m), 2.04 (3H, s), 2.01–0.75 (37H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 177.16 (e), 171.46 (e), 132.84 (e), 128.45 (e), 108.23 (e), 74.04 (o), 64.75 (e), 64.43 (e), 52.26 (o), 48.42 (e), 44.87 (e), 35.54 (e), 33.93 (e), 29.36 (e), 27.64 (e), 25.82 (e), 25.69 (e), 21.59 (o), 13.88 (o), 12.52 (e), 10.18 (e); MS (EI) *m/z* (M + 1) 615, 555, 497; exact mass for $C_{29}H_{50}O_6Sn$ (M + 1) found 613.2691 (calcd 613.2704).

Bicyclic Hydroxy Exocyclic Enone 15a. To a solution of enone **10c** (118 mg, 0.21 mmol) in CH_2Cl_2 was added portionwise 70% mCPBA (57 mg, 0.23 mmol) at room temperature. The resultant mixture was stirred under ambient temperature for 2 h. The reaction mixture was then poured into water. The organic layer was washed successively with saturated $NaHCO_3$ solution and saturated KF solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give an oil, which was subjected to column chromatography on silica gel using 30% EtOAc in hexane as eluent to afford 49.7 mg (80%) of **15a**: IR ($CDCl_3$) 3388, 1736, 1680 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.90 (1H, br s), 5.45 (1H, br s), 3.99–3.67 (4H, m), 3.65 (3H, s), 2.7–1.63 (10H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 201 (e), 174.89 (e), 150.94 (e), 118.91 (e), 108.35 (e), 72.54 (e), 64.78 (e), 64.56 (e), 51.92 (o), 51.44 (e), 38.72 (e), 37.22 (e), 30.50 (e), 30.08 (e), 29.54 (e); MS (EI) *m/z* (M + 1) 297, 279, 237; exact mass for $C_{15}H_{20}O_6$ (M + 1) found 297.1290 (calcd 297.1338); X-ray (supplementary material).

Bicyclic Hydroxy Exocyclic Allylic Acetate 15e. To a solution of enone **14** (57.9 mg, 0.095 mmol) in Et_2O was added 60% mCPBA (29 mg, 0.1 mmol) at 0 °C. The resultant mixture was stirred for 7 h at 0 °C. The reaction mixture was then poured into water. The organic layer was washed successively with saturated $NaHCO_3$ solution and KF solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give an oil, which was subjected to column chromatography on silica gel using 30% EtOAc in hexane as eluent to afford 24.6 mg (75%) of **15e** and 3.4 mg (9%) of **17**. **15e**: IR (CCl_4) 3460, 1742 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.70 (1H, m), 5.11 (1H, *J* = 2 Hz, d), 5.0 (1H, *J* = 2 Hz, d), 3.97–3.75 (4H, m), 3.61 (3H, s), 2.72 (1H, dt), 2.09 (3H, s), 2.2–1.21 (9H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 174.91 (e), 170.99 (e), 148.48 (e), 108.54 (e), 107.20 (e), 72.97 (e), 71.82 (o), 64.65 (e), 64.55 (e), 52.52 (e), 51.61 (o), 38.75 (e), 30.82 (e), 30.64 (e), 30.22 (e), 29.44 (e), 21.34 (o); MS (EI) m/z (M + 1) 341, 323, 281, 263; exact mass for $C_{17}H_{24}O_7$ (M + 1) found 341.1594 (calcd 341.1600).

Bicyclic Epoxy Alcohol 17. To a solution of enone **14** (70 mg, 0.114 mmol) in CH_2Cl_2 was added 70% mCPBA (62 mg, 0.25 mmol) at 0 °C. The resultant mixture was stirred for 2 h at 0 °C. The reaction mixture was then poured into water. The organic layer was washed successively with saturated $NaHCO_3$ and saturated KF solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give an oil, which was subjected to column chromatography on silica gel using 30% EtOAc in hexane as eluent to afford 34 mg (85%) of **17**: IR ($CDCl_3$) 3458, 1736 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.51 (1H, J = 12.2, 5.6 Hz, dd), 3.96–3.74 (4H, m), 3.65 (3H, s), 3.26 (1H, J = 4.4 Hz, d), 3.13 (1H, J = 4.4 Hz, d), 1.96 (3H, s), 2.13–1.2 (10H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 175.31 (e), 170.71 (e), 108.51 (e), 73.57 (e), 68.32 (o), 64.76 (e), 64.45 (e), 63.31 (e), 52.93 (e), 51.87 (e), 51.75 (o), 38.52 (e), 30.09 (e), 29.60 (e), 27.29 (e), 26.06 (e), 21.22 (o); MS (EI) m/z (M + 1) 357; exact mass for $C_{17}H_{24}O_8$ (M + 1) found 357.1538 (calcd 357.1549). Anal. Calcd for $C_{17}H_{24}O_8$: C, 57.30; H, 6.79. Found: C, 56.96; H, 6.85.

Bicyclic Acetoxy Exocyclic Enone 15b and Bicyclic Acetoxy Endocyclic Enone 16b. A mixture of enone **10c** (79 mg, 0.14 mmol) and lead tetraacetate (LTA) (124 mg, 0.28 mmol) in CH_2Cl_2 (5 mL) was stirred at room temperature under Ar for 15 h. After the reaction was quenched with saturated NH_4Cl solution, the organic layer was separated and washed with saturated KF solution. The solvent was dried over anhydrous Na_2SO_4 and evaporated to give an oil, which was purified by column chromatography (40% EtOAc in hexane) yielding the kinetic product **15b** (26 mg, 55%) and the thermodynamic product **16b** (6.6 mg, 14%). **15b**: ^1H NMR (200 MHz, $CDCl_3$) δ 6.23 (1H, J = 0.8 Hz, d), 5.77 (1H, J = 0.8 Hz, d), 4.02–3.7 (4H, m), 3.67 (3H, s), 3.23–3.16 (1H, m), 2.63–1.93 (7H, cm), 1.95 (3H, s), 1.7–1.6 (2H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 199.49 (e), 173.59 (e), 168.93 (e), 143.74 (e), 125.31 (e), 107.73 (e), 83.40 (e), 65.07 (e), 64.78 (e), 52.39 (e), 52.30 (o), 39.59 (e), 36.94 (e), 31.13 (e), 29.75 (e), 25.19 (e), 22.68 (o); MS (EI) m/z (M + 1) 339, 279; exact mass for $C_{17}H_{22}O_7$ (M + 1) found 339.1437 (calcd 339.1444); X-ray (supplementary material). **16b**: IR (CCl_4) 1734, 1676 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.92 (2H, br s), 4.04–3.85 (4H, m), 3.73 (3H, s), 3.0–2.9 (1H, m), 2.8–1.54 (9H, cm), 2.02 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 196.89 (e), 174.57 (e), 171.52 (e), 160.98 (e), 131.58 (e), 107.00 (e), 65.09 (e), 64.67 (e), 56.97 (e), 53.01 (o), 49.78 (e), 44.54 (e), 35.08 (e), 34.91 (e), 34.51 (e), 27.64 (e), 21.12 (o); MS (EI) m/z (M + 1) 339, 279; exact mass for $C_{17}H_{22}O_7$ (M + 1) found 339.1437 (calcd 339.1444).

Bicyclic Acetoxy Exocyclic Allylic Acetate 15f. A mixture of enone **14** (100 mg, 0.163 mmol) and LTA (144 mg, 0.32 mmol) in dry CH_2Cl_2 (5 mL) was stirred at room temperature under Ar for 40 h. After the reaction was quenched with saturated NH_4Cl solution, the organic layer was separated and washed with saturated KF solution. The solvent was dried over anhydrous Na_2SO_4 and evaporated to give an oil, which was purified by column chromatography (40% EtOAc in hexane) yielding the product **15f** (51 mg, 82%): IR (CCl_4) 1750 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.39 (1H, J = 2 Hz, d), 5.32 (1H, J = 2 Hz, d), 5.28–5.23 (1H, m), 3.97–3.75 (4H, m), 3.61 (3H, s), 3.02–2.9 (1H, m), 2.76–2.64 (1H, m), 2.17–1.89 (5H, m), 2.06 (3H, s), 2.04 (3H, s), 1.71–1.63 (2H, m), 1.3–1.1 (1H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.77 (e), 170.57 (e), 169.06 (e), 142.21 (e), 111.36 (e), 107.89 (e), 83.97 (e), 71.13 (o), 64.78 (e), 64.65 (e), 53.26 (e), 51.80 (o), 39.57 (e), 30.95 (e), 30.43 (e), 29.69 (e), 25.05 (e), 22.17 (o), 21.31 (o); MS (EI) m/z (M + 1) 383, 323, 263; exact mass for $C_{19}H_{26}O_8$ (M + 1) found 383.1698 (calcd 383.1706).

Bicyclic Bromo Endocyclic Enone 16c. Br_2 (23 mg, 0.145 mmol) in CCl_4 (0.5 mL) was added to a stirred solution of enone **10c** (83 mg, 0.145 mmol) in isopropyl alcohol (IPA) at −50 °C under Ar. The resulting solution was stirred for 10 min at −50 °C. The reaction mixture was then poured into water and extracted with CH_2Cl_2. The solvent was washed with saturated $NaHCO_3$ and KF solutions. The organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated to give an oil, which was subjected to column chromatography on silica gel using 30% EtOAc in hexane as eluent to afford 42 mg (80%) of **16c**: IR (CCl_4) 1732, 1678 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.26 (2H, br s), 4.02–3.82 (4H, m), 3.69 (3H, s), 2.94–2.89 (1H, m), 2.76–1.76 (8H, cm), 1.55 (1H, d); ^{13}C NMR (50 MHz, $CDCl_3$) δ 195.66 (e), 174.64 (e), 159.86 (e), 133.67 (e), 106.94 (e), 65.09 (e), 64.66 (e), 53.03 (o), 49.77 (e), 44.29 (e), 34.96 (e), 34.52 (e), 34.44 (e), 27.86 (e), 23.01 (e); MS (EI) m/z (M + 1) 359, 281; exact mass for $C_{15}H_{19}O_5Br$ (M + 1) found 358.0409 (calcd 358.0416).

Bicyclic Bromo Exocyclic Allylic Acetate 15g. Br_2 (22 mg, 0.137 mmol) in CCl_4 (0.5 mL) was added to a stirred solution of enone **14** (80 mg, 0.131 mmol) in IPA at 0 °C under Ar, and the solution was stirred for 1 min. The reaction mixture was then poured into water and extracted with CH_2Cl_2. The solvent was washed with saturated $NaHCO_3$ and KF solutions. The organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated to given an oil, which was subjected to column chromatography on silica gel using 30% EtOAc in hexane as eluent to afford 47.3 mg (90%) of **15g**: IR (CCl_4) 1740 cm^{-1}; ^1H NMR (200 MHz, C_6D_6) δ 6.49–6.41 (1H, m), 5.25 (1H, s), 5.24 (1H, s), 3.54–3.29 (4H, m), 3.28 (3H, s), 3.13–2.97 (1H, td), 2.70–2.54 (1H, td), 2.32–1.67 (7H, cm), 1.71 (3H, s), 1.45–1.29 (1H, m); ^{13}C NMR (50 MHz, C_6D_6) δ 171.08 (e), 169.52 (e), 147.71 (e), 108.12 (e), 107.29 (e), 80.44 (e), 71.81 (o), 64.74 (e), 64.57 (e), 54.34 (e), 51.71 (o), 41.36 (e), 34.40 (e), 33.97 (e), 33.64 (e), 29.62 (e), 20.97 (o); MS (EI) m/z (M + 1) 403, 361, 345, 323, 265; exact mass for $C_{17}H_{23}O_6Br$ (M + 1) found 403.0743 (calcd 403.0756).

Bicyclic Bromo Endocyclic Allylic Acetate 16g. To a solution of bromide **15g** (21 mg, 0.052 mmol) in THF was added TBAB (16.7 mg, 0.052 mmol) at room temperature. The resultant mixture was stirred under ambient temperature for 1 h. The reaction mixture was then poured into water. The aqueous layer was extracted twice with Et_2O, and the organic solvent was evaporated to give an oil, which was subjected to column chromatography on silica gel using 30% EtOAc in hexane as eluent to afford 19.7 mg (94%) of **16g**: IR (CCl_4) 1734 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.50 (1H, m), 4.23 (1H, J = 10.4 Hz, d), 3.99–3.86 (5H, m), 3.67 (3H, s), 2.7–2.73 (1H, m), 2.6–2.37 (2H, m), 2.05 (3H, s), 2.04–1.47 (7H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 176.13 (e), 171.40 (e), 142.77 (e), 129.76 (e), 107.84 (e), 69.64 (o), 64.93 (e), 64.49 (e), 52.48 (o), 48.79 (e), 43.70 (e), 35.64 (e), 32.35 (e), 28.96 (e), 26.10 (e), 25.30 (e), 21.44 (o); MS (CI) m/z (M + 1 − HOAc) 345, 323, 265; exact mass for $C_{17}H_{23}O_6Br$ (M + 1 − HOAc) found 343.0535 (calcd 343.0545). Anal. Calcd for $C_{17}H_{23}O_6Br$: C, 50.63; H, 5.74; Br, 19.81. Found: C, 50.32; H, 5.70; Br, 19.50.

Bicyclic Chloro Endocyclic Enone 16d. Chloreal (13.55 mg, 0.058 mmol) was added portionwise to a stirred solution of enone **10c** (30 mg, 0.0531 mmol) in IPA at −30 °C. The resultant solution was stirred for 30 min at −30 °C. The reaction mixture was then poured into water and extracted with Et_2O. The solvent was washed with saturated $NaHCO_3$ and KF solutions. The organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated to give an oil, which was subjected to column chromatography on silica gel using 25% EtOAc in hexane as eluent to afford 14 mg (88%) of **15d**. After some time later either in $CDCl_3$ or C_6D_6, the product was converted to the thermodynamic product **16d**: IR (CCl_4) 1732, 1678 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 4.4 (2H, q), 4.04–3.8 (4H, m), 3.72 (3H, s), 3.03–1.54 (10H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 195.65 (e), 174.38 (e), 160.21 (e), 133.58 (e), 106.99 (e), 65.25 (e), 64.83 (e), 53.21 (o), 49.95 (e), 44.63 (e), 35.94 (e), 35.29 (e), 34.96 (e), 34.71 (e), 28.05 (e); MS (EI) m/z (M) 314, 279, 255; exact mass for $C_{15}H_{19}O_5Cl$ (M) found 314.0918 (calcd 314.0921).

Bicyclic Chloro Exocyclic Acetate 15h. Chloreal (6.97 mg, 0.028 mmol) was added portionwise to a stirred solution of enone **14** (15.6 mg, 0.0251 mmol) in IPA at −30 °C. The resultant solution was stirred for 30 min at −30 °C. The reaction mixture was then poured into water and extracted with Et_2O. The solvent was washed with saturated $NaHCO_3$ and KF solutions. The organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated to given an oil, which was subjected to column chromatography on silica gel using 25% EtOAc in hexane as eluent to afford 7.3 mg (81%) of **15h**: IR (CCl_4) 1742 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 5.94–5.85 (1H, m), 5.23 (1H, J = 2 Hz, d), 5.183 (1H, J = 2.2 Hz, d), 3.98–3.75 (4H, m), 3.63 (3H, s), 3.05–2.87 (1H, m), 2.4–1.2 (9H, cm), 2.10 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 173.57 (e), 170.65 (e), 146.44 (e), 107.92 (e), 71.02 (o), 64.76 (e), 64.63 (e), 53.71 (e), 52.04 (o), 39.52 (e), 32.45 (e), 31.64 (e), 31.49 (e), 29.01 (e), 21.31 (o); MS (EI) m/z (M + 1) 359, 323, 299, 265; exact mass for $C_{17}H_{23}O_6Cl$ (M) found 359.1253 (calcd 359.1261).

Tricyclic α-Stannylmethyl Enone 20. To 10 mL of methanol was slowly added freshly cut sodium metal (54 mg, 2.35 mmol). After the sodium had completely reacted, enone **10H** (300 mg, 1.07 mmol) was added, and the yellowish solution was heated to reflux. Stannyl enone **4c** (441 mg, 1.18 mmol) was added dropwise over 12 h. Heating at reflux was continued for 8 more hours. The resulting solution was cooled to room temperature, and the solvent was removed in vacuo. The aqueous layer was separated, acidified with 5% HCl to pH 3, and extracted with EtOAc, and the organic layer was evaporated to give a pale-yellow oil. This residue was methylated with excess diazomethane (prepared from diazald) and then purified by column chromatography (15% EtOAc in hexane) to afford

594 mg (87%) of **20**: IR (CCl_4) 1720, 1664, 1560 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.74 (1H, t), 3.95–3.87 (4H, m), 3.70 (3H, s), 2.6–0.7 (41H, cm), 1.4 (3H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 198.49 (e), 177.36 (e), 155.69 (e), 142.83 (e), 134.10 (e), 122.90 (o), 107.04 (e), 64.90 (e), 64.43 (e), 52.21 (o), 48.13 (e), 44.21 (e), 41.47 (e), 37.23 (e), 35.25 (e), 34.50 (e), 34.05 (e), 29.28 (e), 27.60 (e), 26.67 (o), 25.99 (e), 13.86 (o), 10.14 (e), 8.81 (e); MS (EI) m/z (M + 1) 637, 579; exact mass for $C_{32}H_{52}O_5Sn$ (M) found 633.2910 (calcd 633.2914).

Tricyclic Exocyclic Acetoxy Enone 21 and Tricyclic Endocyclic Acetoxy Enone 22. A mixture of enone **20** (93 mg, 0.146 mmol) and LTA (148 mg, 0.29 mmol) in dry CH_2Cl_2 was stirred at room temperature under Ar for 15 h. After the reaction was quenched with saturated NH_4Cl solution, the organic layer was separated and washed with saturated KF solution. The solvent was dried over anhydrous Na_2SO_4 and evaporated to give an oil, which was purified by column chromatography (40% EtOAc in hexane) yielding the kinetic product **21** (23 mg, 39%) and the thermodynamic product **22** (6 mg, 11%). **21**: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.804 (1H, t), 4.82 (2H, s), 3.95–3.87 (4H, m), 3.71 (3H, s), 1.99 (3H, s), 1.42 (3H, s), 2.59–1.60 (12H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 197.29 (e), 177.02 (e), 171.58 (e), 170.26 (e), 142.08 (e), 128.05 (e), 124.02 (o), 106.82 (e), 64.99 (e), 64.54 (e), 57.30 (e), 52.39 (o), 48.55 (e), 44.19 (e), 42.07 (e), 37.24 (e), 35.05 (e), 34.95 (e), 33.95 (e), 27.19 (o), 26.17 (e), 21.15 (o); MS (EI) m/z (M + 1) 405, 345; exact mass for $C_{22}H_{28}O_7$ (M) found 404.1826 (calcd 404.1835). **22**: IR (CCl_4) 1736, 1670 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.96 (1H, br s), 5.76 (1H, t), 5.45 (1H, br s), 3.94–3.70 (4H, m), 3.66 (3H, s), 2.9–2.8 (1H, m), 1.89 (3H, s), 1.04 (3H, s), 2.6–1.5 (11H, m); ^{13}C NMR (50 MHz, $CDCl_3$) δ 202.27 (e), 177.55 (e), 169.79 (e), 145.80 (e), 140.08 (e), 124.25 (o), 122.95 (e), 107.17 (e), 87.09 (e), 64.92 (e), 64.41 (e), 52.32 (o), 48.04 (e), 44.98 (e), 44.05 (e), 36.60 (e), 36.17 (e), 31.30 (e), 30.33 (e), 23.06 (e), 21.99 (o), 21.64 (o); MS (EI) m/z (M + 1) 405, 345; exact mass for $C_{22}H_{28}O_7$ (M) found 404.1831 (calcd 404.1835).

Tricyclic Exocyclic Hydroxy Enone 23. To a solution of enone **20** (51 mg, 0.08 mmol) in CH_2Cl_2 was added 70% mCPBA (47 mg, 0.184 mmol) in the presence of 5% 2,6-di-*tert*-butyl-4-methylphenol (BHT) at 0 °C. The resultant mixture was stirred for 4 h at reflux. The reaction mixture was then poured into water. The organic layer was washed with saturated $NaHCO_3$ and saturated KF successively. The solvent was evaporated, and the resulting residue was subjected to column chromatography on silica gel using 30% EtOAc in hexane as eluent to afford 18 mg of a mixture of **23** and **24** (62%, 88:12), 4 mg of **25** (15%), and 6 mg (12%) of starting material **20**. **23** and **24** (88:12): IR (CCl_4) 3460, 1720, 1700 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.82 (1H, t), 5.79 (1H, br s), 5.29 (1H, br s), 3.94–3.90 (4H, br s), 3.66 (3H, s), 1.02 (3H, s), 2.7–1.2 (12H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 203.52 (e), 177.55 (e), 150.37 (e), 140.22 (e), 125.73 (o), 119.61 (e), 107.37 (e), 77.48 (e), 64.93 (e), 64.58 (e), 52.33 (o), 48.29 (e), 44.32 (e), 44.24 (e), 36.41 (e), 36.20 (e), 30.51 (e), 30.22 (e), 28.10 (e), 21.59 (o); MS (CI) m/z (M + 1) 361, 345; exact mass for $C_{20}H_{26}O_6$ (M + 1) found 362.1722 (calcd 362.1729).

Dihydro β-Tributylstannyl Ketone 28. Into a 50-mL three-neck flask equipped with a mechanical stirrer, dry-ice condenser, and gas inlet tube, cooled in a dry-ice/acetone bath, was condensed 10 mL of ammonia. Lithium wire (47 mg, 6.76 mmol) was added, and the solution was stirred for 1 h at that temperature to ensure complete dissolution of the metal. Liquid nitrogen was added to the cold bath to further cool the flask to between −90 and −95 °C. A solution of 385 mg (0.676 mmol) of enone **10c** and 55 mg of *t*-BuOH in THF was added via syringe. The reaction was maintained at this temperature for 1 h. Addition of isoprene to quench excess electrons at −78 °C, followed by addition of NH_4Cl solid, gave a clear solution. Removal of the condenser allowed the evaporation of the ammonia under a slow stream of Ar. The residue was dissolved in ether, washed several times with water, and dried with Na_2SO_4, and the solvent was removed in vacuo. The resulting oil was subjected to column chromatography on silica gel using 20% EtOAc in hexane as eluent to afford 319 mg (83%) of **28**: IR (CCl_4) 1736, 1706 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.99–3.79 (4H, m), 3.72 (3H, s), 3.5–3.35 (1H, m), 2.48–0.5 (40H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 213.40 (e), 175.53 (e), 108.33 (e), 64.71 (e), 52.38 (o), 51.77 (o), 49.45 (o), 47.95 (e), 44.88 (e), 38.72 (e), 38.11 (e), 35.55 (e), 29.45 (e), 27.68 (e), 24.40 (e), 13.92 (o), 10.41 (e), 7.4 (e); MS (EI) m/z (M + 1) 573, 515; exact mass for $C_{27}H_{48}O_5Sn$ (M + 1) found 569.2590 (calcd 569.2601). Anal. Calcd for $C_{27}H_{48}O_5Sn$: C, 56.75; H, 8.47; Sn, 20.78. Found: C, 56.95; H, 8.84; Sn, 20.48.

Tricyclic Distannane 32. To 3 mL of methanol was slowly added freshly cut sodium metal (4.3 mg, 0.182 mmol). After the sodium had completely reacted, enone **10c** (52 mg, 0.09 mmol) was added, and the yellowish solution was heated to reflux. Stannyl enone **4c** (78.5 mg, 0.2 mmol) was added dropwise over 4 h. Heating at reflux was continued for 8 more hours. The resulting solution was cooled to room temperature, and the solvent was removed in vacuo. The aqueous layer was separated, acidified with 5% HCl to pH 3, and extracted with EtOAc, and the organic layer was evaporated to give a pale-yellow oil. This residue was methylated with excess diazomethane (prepared from diazald) and then purified by column chromatography (15% EtOAc in hexane) to afford 10 mg (11%) of **32** and starting material **10c** (>75%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.8 (1H, t), 3.9–4.0 (4H, m), 3.7 (3H, s), 3.35 (1H, q), 2.7–0.7 (remaining H, cm); MS (CI) m/z (M + 1) 925, 637, 579; exact mass for $C_{44}H_{78}O_5Sn_2$ (M) found 919.3934 (calcd 919.3970).

Bicyclic Methoxymethyl Stannane 37. To enone **10c** (103 mg, 0.18 mmol) in 5 mL of CH_2Cl_2 at 0 °C was added triethylamine (10% of solvent) followed by TBDMSOTf (0.045 mL, 0.198 mmol) dropwise. After 2 h, TLC showed no starting material left. The mixture was poured into 10 mL of saturated $NaHCO_3$ solution and extracted twice with 5 mL of CH_2Cl_2. The organic layer was dried over anhydrous Na_2SO_4. The solvent was evaporated to give an oil, which was subjected to column chromatography on silica gel using 10% EtOAc in hexane as eluent to afford 120 mg (98%) of the two-regioisomeric product **34**. To silyl enol ether (120 mg, 0.175 mmol) in THF at 0 °C was added an excess of LAH, and the reaction mixture was slowly warmed to room temperature over 8 h. The reaction mixture was then cooled back to 0 °C, and Gaubler's salt was added until a white precipitate formed. The solid was filtered off and washed with THF. Concentration in vacuo allowed the isolation of the desired alcohol **35**. The crude mixture containing alcohol **35** was dissolved in 5 mL of THF and cooled to 0 °C. Excess NaH (Aldrich) was added to the solution. After 10 min, methyl iodide (Malinckrodt, excess) was added and the reaction mixture warmed to room temperature. TLC showed the reaction to be complete after 30 min. After 3 h, the reaction mixture was cooled back to 0 °C, and the reaction was quenched with saturated NH_4Cl solution. The aqueous phase was extracted three times with ether, and the combined organic layer was dried with $MgSO_4$, filtered, and concentrated. Column chromatography (5% EtOAc in hexane) allowed isolation of the two-regioisomeric product **36** (84 mg, 70%). Major isomer: ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.3 (1H, t), 4.05-3.8 (4H, m), 3.55 (1H, d), 3.3 (3H, s), 3.25 (1H, d), 2.6–0.7 (remaining H, cm), 0.15 (6H, s). Tetra-*n*-butylammonium fluoride (TBAF) (Aldrich, 0.11 mL, 0.11 mmol) in THF was added to a solution of **36** (70 mg, 0.11 mmol) in THF at 0 °C. The resulting solution was allowed to react for 1 h at 0 °C. The reaction mixture was then poured into water and extracted with CH_2Cl_2. The organic layer was washed with saturated NaCl solution and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give an oil, which was subjected to column chromatography on silica gel, using 20% EtOAc in hexane as eluent, to afford 36.5 mg of **37** (60%): ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.05–3.9 (4H, m), 3.63 (1H, J = 9.2 Hz, d), 3.33 (1H, J = 9.3, 0.8 Hz, OV, dd), 3.327 (3H, s), 2.8–0.64 (39H, cm); ^{13}C NMR (50 MHz, $CDCl_3$) δ 199.32 (e), 149.93 (e), 137.50 (e), 108.31 (e), 73.47 (e), 64.66 (e), 64.15 (e), 59.15 (o), 42.07 (e), 41.47 (e), 34.61 (e), 33.75 (e), 32.65 (e), 29.32 (e), 27.65 (e), 26.29 (e), 13.67 (o), 10.13 (e), 9.16 (e); MS (CI) m/z (M + 1) 557, 499; exact mass for $C_{27}H_{48}O_4Sn$ (M) found 555.2636 (calcd 555.2649).

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Supplementary Material Available: ^{1}H and ^{13}C NMR of all new compounds as well as X-ray crystal structures and tables of crystal data, bond distances and angles, torsion angles, atomic multiplicities, and anisotropic temperature factors for compounds **15a** and **15b** (81 pages); tables of observed and calculated structure factors for **15a** and **15b** (16 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS. Ordering information is available on any current masthead page.