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INTRAMOLECULAR PALLADIUM(0)-CATALYZED COUPLING OF ENOL TRIFLATE AND VINYLSTANNANE FUNCTIONS. NEW ANNULATION SEQUENCES LEADING TO BICYCLIC DIENE SYSTEMS

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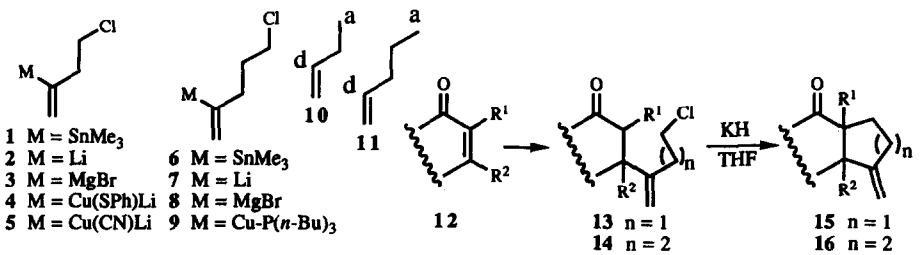
ABSTRACT - A new, concise annulation method leading to the efficient production of structurally novel bicyclic dienes has been developed. The individual synthetic steps that constitute this method, as outlined in general terms in Scheme 1, involve (a) the alkylation of (functionalized) carbonyl compounds with ω-iodo-2-trimethylstannyl-1-alkenes (17 → 21), (b) the conversion of the alkylation products into the corresponding enol trifluoromethanesulfonates (triflates) (21 → 22), and (c) the palladium(0)-catalyzed intramolecular coupling of the enol triflate-vinylstannanes to provide the dienes (22 → 23). The generality of the method is demonstrated by the synthesis of functionalized bicyclo[4.3.0]nonane (61, 62, 65, 66), bicyclo[4.4.0]decane (63, 64, 67, 68, 71), bicyclo[5.3.0]decane (70), and bicyclo[5.4.0]undecane (69) derivatives.

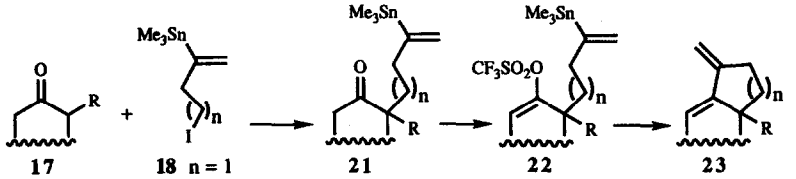
INTRODUCTION

Recent reports form this laboratory have demonstrated that 4-chloro-2-trimethylstannyl-1-butene (1)[1-3] and 5-chloro-2-trimethylstannyl-1-pentene (6)[1,4-6] are effective precursors of a series of novel bifunctional reagents (e.g. 2-5 derived from 1 and 7-9 obtained from 6) that serve as versatile synthetic equivalents to the 1-butene d^2,a^4- and 1-pentene d^2,a^5-synthons[7] 10 and 11, respectively. Indeed, reagents 3-5 can readily be employed to effect synthetically useful methylenecyclopentane annulation sequences represented in general terms by 12 → 15.[2,3,8] In similar fashion, reagents 8 and 9 efficiently transform α,β-unsaturated ketones 12 into the corresponding methylenecyclohexane annulation products 16.[4-6]



In the annulation processes mentioned above, the (potential) donor center of each of the compounds 1 and 6 was deployed first, while the acceptor site was used subsequently. Thus, transmetalation (MeLi, THF, -78°C) of 1 and 6 provides the lithio species 2 and 7, which can then be transformed into reagents 3-5, 8, or 9. Appropriate conjugate additions to the enones 12 (involving reagents 3-5, 8, or 9) provide the chloro ketones 13 or 14, which can then be transformed into the annulation products 15 or 16 via intramolecular alkylation reactions.

It was envisaged that if the order of deployment of the donor and acceptor sites of substances structurally related to 1 and 6 were to be reversed from that discussed above, versatile and potentially useful chemistry quite different from that outlined above could be accomplished. In particular, we wished to develop new annulation sequences that would result in the formation of novel dienes of general structure 23. Thus, we envisaged carrying out sequences of reactions outlined in general terms in Scheme 1. Alkylation of functionalized or substituted ketones 17 with the ω-iodo-2-trimethylstannyl-1-alkenes 18-20, followed by conversion of the resultant products 21 into the corresponding enol trifluoromethanesulfonates (triflates) 22, would set the stage for intramolecular versions of a versatile coupling method developed by Stille and co-workers.[9,10] Thus, treatment of the intermediates 22 with a palladium(0) catalyst should effect bond formation between the alkenyl carbon atoms containing the Me_3Sn and OSO_2CF_3 moieties to produce the dienes 23. We report in this paper the details of our studies[11] leading to the efficient synthesis of a variety of structurally interesting dienes of general structure 23.

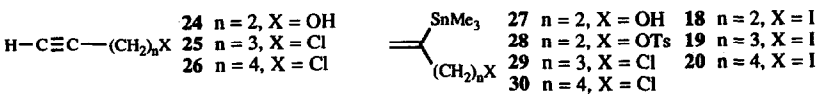


17 **18** n = 1, **19** n = 2, **20** n = 3 **21** **22** **23**

Scheme 1

RESULTS AND DISCUSSION

(a) Preparation of the ω-Iodo-2-trimethylstannyl-1-alkenes 18-20. Reaction of commercially available 3-butyn-1-ol (24) (Chart 1) with $Me_3SnCu{\cdot}Me_2S$[12] under conditions very similar to those reported earlier,[2] afforded the vinylstannane alcohol 27.[1] In similar fashion, using reaction conditions modified[13] somewhat from those described previously,[1] the chloro alkynes 25 (commercially available) and 26[14] were transformed efficiently into 29 and 30, respectively. Treatment of the p-toluenesulfonate 28, readily derived from the alcohol 27, with NaI in N,N-dimethylformamide at 60-70°C provided the required iodo compound 18. Reaction of the chlorides 29 and 30 with NaI in refluxing acetone afforded the iodides 19 and 20, respectively, in excellent yields.



24 n = 2, X = OH; **25** n = 3, X = Cl; **26** n = 4, X = Cl

27 n = 2, X = OH; **28** n = 2, X = OTs; **29** n = 3, X = Cl; **30** n = 4, X = Cl

18 n = 2, X = I; **19** n = 3, X = I; **20** n = 4, X = I

Chart 1

(b) Alkylations Employing the Iodides 18-20. Alkylation[15] of the N,N-dimethylhydrazone 32 (readily derived from the commercially available keto ketal 31) with the iodides 18 and 19, followed by immediate cleavage[15] of the hydrazone function, produced the ketones 33 and 35 in overall yields of 65 and 70%, respectively (see Chart 2).

Methylation of 33 and 35 via the procedure reported by Kuwajima et al.[16] produced significant amounts of the starting materials (~40%) in addition to poor yields of the desired products 34 (34%) and 36 (43%), respectively. However, methylation of 33 under conditions ($KOCMe_3$, Me_3COH-THF; MeI) that would cause rapid equilibration between the two possible enolate anions provided the α,α-disubstituted ketone 34 in 78% yield. In similar fashion, the conversion of 35 into 36 was accomplished in 66% yield and the ketone 37 was obtained (46%) by alkylation of 2-methylcyclohexanone with the iodide 19.

The substituted β-keto esters 43-47 (Chart 2) were produced by alkylation of the potassium enolates of the β-keto esters 38-42[17] with 5-iodo-2-trimethylstannyl-1-pentene (19) in refluxing THF. Similarly, the substrate 38 could be alkylated with the iodide 20 to provide 48. The yields of 43-48 from these transformations ranged from 57-92%.

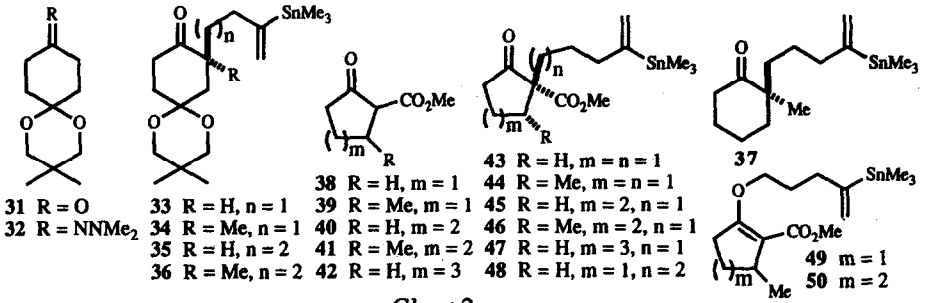


Chart 2

Two points regarding the reactions leading to the β-keto esters 44 and 46 deserve explicit mention. Firstly, alkylation of 39 and 41 with the iodide 19 provided, in each case, a mixture of C- and O-alkylation products. Thus, 39 produced 44 and 49 in a ratio of 96:4, while alkylation of 41 afforded a mixture of 46 and 50 (3:1). The formation of O-alkylation products was not observed in the alkylation reactions involving the β-keto esters 38, 40, and 42. Secondly, in connection with stereochemistry, a single C-alkylated diastereomer was obtained from the alkylation of each of the substrates 39 and 41. Not unexpectedly, the iodide 19 approaches the enolate anion of each of these substances from the less hindered face, opposite to the adjacent secondary methyl group.

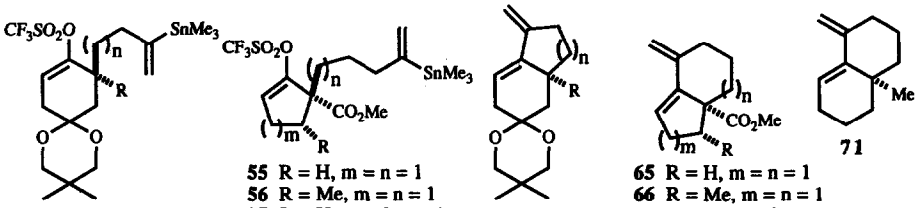
Each of the alkylation products 33-37 and 43-48 displayed IR and ^1H NMR spectra in full accord with the structural formulas shown in Chart 2. The presence of the vinylstannane moiety was, in each case, indicated by the appropriate resonances (δ ~0.1, 9 H, Me_3Sn, $^2J_{Sn-H} \approx 54$ Hz; δ 5.1-5.7, 2 H, alkenyl protons) in the ^1H NMR spectrum.

(c) Preparation of Bicyclic Dienes (Annulation Products). Completion of the initially envisaged annulation sequences required the conversion of the ketones 33-37 and 43-48 (Chart 2) into the corresponding enol triflates, followed, in each case, by the key intramolecular palladium(0)-catalyzed coupling process.

The useful method reported by McMurry and Scott[22] was employed to acquire the enol triflates **51-60** (see Chart 3 and Table 1) from the corresponding ketone substrates (**33-36**; **43-48**). For example, successive treatment of a solution of LDA in THF (-48°C) with the ketone **43** (THF solution) and *N*-phenyltrifluoromethylsulfonimide ($PhN(SO_2CF_3)_2$, *solid*), followed by warming of the reaction mixture to room temperature, provided, after column chromatography of the crude product, the enol triflate **55** in 64% yield (Table 1, entry 5). The IR spectrum of **55** showed absorptions due to the ester function (1740 cm^{-1}) and the sulfonate moiety (1425, 1145 cm^{-1}), while the ^1H NMR spectrum displayed three olefinic proton signals at δ 5.15, 5.65, and 5.78.

The enol triflates **51-60** were, in each case, purified by column chromatography on *silica gel*. However, although compounds **51-54** could also be distilled, the thermal lability of substances **55-60** precluded the further purification of these materials by distillation. Nevertheless, ^1H NMR analyses of the chromatographically purified products indicated that they were of sufficient purity (>95%) to be used for the ring closure step. Furthermore, the spectral properties of **51-60** were, in each case, in agreement with the assigned structure.

When small samples taken from a refluxing solution (THF) of compound **55** containing 0.05 equivalents of $(Ph_3P)_4Pd$ were purified and analyzed by GLC analyses, it was established that a single product was produced in 11 h. This product was isolated in 82% yield and was shown to be the expected diene **65** (Table 1, entry 5).



51 R = H, n = 1
52 R = Me, n = 1
53 R = H, n = 2
54 R = Me, n = 2

55 R = H, m = n = 1
56 R = Me, m = n = 1
57 R = H, m = 2, n = 1
58 R = Me, m = 2, n = 1
59 R = H, m = 3, n = 1
60 R = H, m = 1, n = 2

61 R = H, n = 1
62 R = Me, n = 1
63 R = H, n = 2
64 R = Me, n = 2

65 R = H, m = n = 1
66 R = Me, m = n = 1
67 R = H, m = 2, n = 1
68 R = Me, m = 2, n = 1
69 R = H, m = 3, n = 1
70 R = H, m = 1, n = 2

Chart 3

The generality of this key ring closure reaction was demonstrated by converting the vinylstannane-enol triflates **51-54** and **56-60** into the corresponding bicyclic dienes **61-64** and **66-70**. The results are summarized in Table 1.

The cyclizations of **51-53** (Table 1, entries 1-3) were conveniently carried out in THF at room temperature, while those of **54** and **56-60** (entries 4,6-10) were accomplished in refluxing THF, as described above for **55**. In each case, the progress of the cyclization could be followed conveniently by GLC analyses and, in each of 9 out of 10 cases, a single bicyclic ketone was produced. Only the ring closure of **59**, to produce the bicyclo[5.4.0]undecane derivative **69**, was not entirely clean. In this case, the product (85% yield) consisted of a mixture containing ~85% of the diene **69** and small amounts of other (uncharacterized) products that appeared to be dienes isomeric with **69**. Careful chromatography of this mixture on silver nitrate-impregnated silica gel furnished a small

Table 1. Preparation of the Bicyclic Dienes 61-71

Entry	Substrate	Enol triflate[a] (yield, %)[b]	Diene[a]	Reaction conditions for ring closure[c] (reaction time, h)	Yield, %[d]
1	33	51 (73)	61	A (0.25)	85
				B (1)	83
2	34	52 (72)	62	A (0.25)	83
3	35	53 (76)	63	A (0.25)	84
				B (8)	80
4	36	54 (70)	64	C (0.25)	86
5	43	55 (64)	65	C (11)	82
				D (15)	58
				E (4)	84
6	44	56 (62)	66	C (9)	82
7	45	57 (71)	67	C (3)	90
				F	72
8	46	58 (84)	68	C (19)	86
9	47	59 (63)	69	C (3)	85[e]
10	48	60 (63)	70	C (23)	50
11	37	-	71	F	55

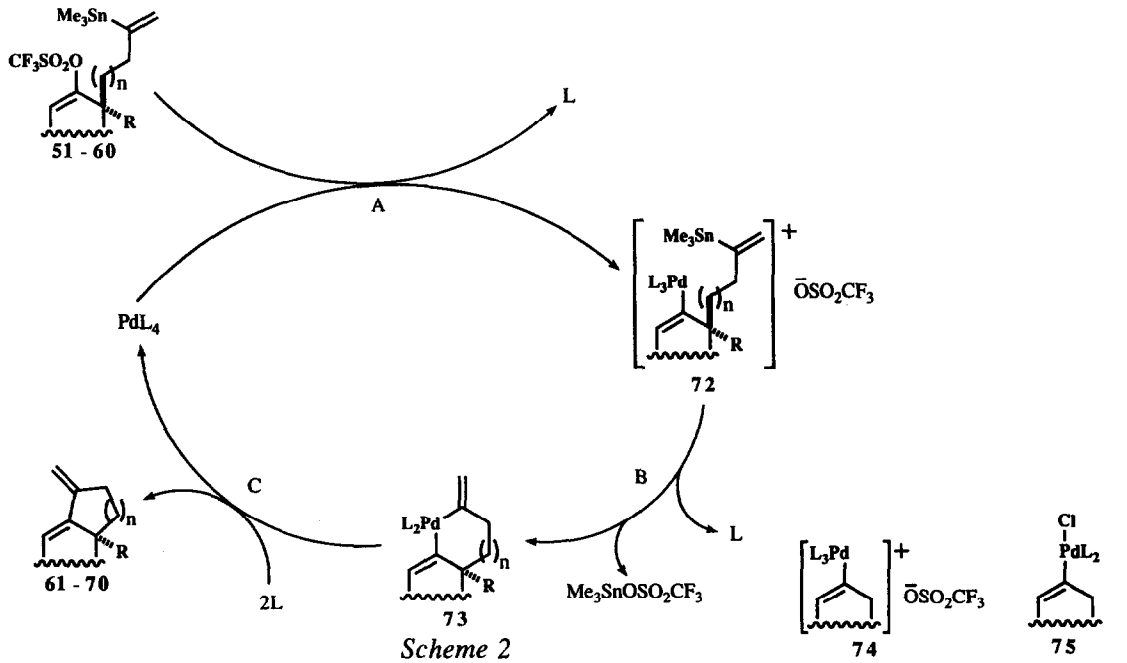
[a] The structural formulas of these materials are listed in Chart 3. [b] Yield of chromatographically purified product. The enol triflates 51-54 were also distilled. [c] In each case, 5 mol % of $(Ph_3P)_4Pd$ was employed. A: THF, room temperature. B: THF, LiCl (10-15 equivalents), room temperature. C: THF, reflux. D: THF, LiCl (15 equivalents), reflux. E: MeCN, reflux. F: "one-pot" conversion of substrate into diene (see text). [d] Yield of purified, distilled product. [e] This product consisted of a mixture of dienes which, on the basis of analysis by GLC, contained ~85% of the diene 69.

sample of pure 69. In terms of efficiency, all but one of the cyclization reactions proceeded in excellent yield (≥82%). However, ring closure of 60 provided 70 in only mediocre yield (50%). Presumably, this cyclization is less efficient because it involves the production of a seven-membered carbocycle, which must be preceded by the formation of an eight-membered palladocycle (vide infra). The difficulties associated with forming eight-membered rings are well known.

With respect to the cyclization reactions summarized in Table 1, several additional points deserve mention. It had been demonstrated[9] that the success of the intermolecular palladium(0)-catalyzed coupling of enol triflates with vinylstannanes depends upon the presence of LiCl in the reaction mixture. However, in our intramolecular reactions, LiCl is not required for the successful formation of the bicyclic dienes 61-71. In fact, the presence of LiCl appeared to decrease the rate of the intramolecular coupling process. For

example, the preparation of the diene **63** from **53** was accomplished in 15 min at room temperature, while, in the presence of 15 equivalents of LiCl but under otherwise identical reaction conditions, the same transformation required 8 h (Table 1, entry 3). Similar (although less dramatic) results were observed in the preparation of the dienes **61** and **65** (Table 1, entries 1 and 5).

The success of the ring closures in the absence of LiCl is, no doubt, due to the intramolecular nature of the processes. Presumably, the internal coupling reactions of compounds **51-60** take place via a catalytic cycle that may be outlined in general terms as shown in Scheme 2. A similar pathway has been proposed[9] for the intermolecular cross-coupling of vinylstannanes with enol triflates. However, in these cases, the intermediate palladium(II) species corresponding to **72** (Scheme 2) (i.e. **74**) is, apparently, unstable and the palladium catalyst is transformed into an uncharacterized, catalytically ineffective complex.[9] Thus, **74** does not participate in a <u>bimolecular</u> transmetalation step with a vinylstannane. This problem is overcome by addition of LiCl, which results in the production of the palladium(II) complex **75**, a species that is sufficiently stable to participate in the catalytic cycle.



Scheme 2

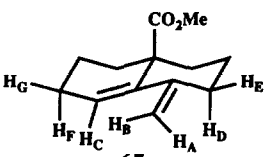
In the intramolecular coupling sequence shown in Scheme 2, the internal transmetalation reaction (step B) would be expected to proceed at a much higher rate than the corresponding bimolecular reaction in an intermolecular coupling process.[23] Thus, the "inherent instability" of **72** does not interfere with the overall process and **72** is readily converted, via internal transmetalation, into the palladocycle **73**. Subsequent reductive elimination from this cis-bis(organo)-palladium(II) species would provide the bicyclic dienes **61-70** (Scheme 2, step C).

The cyclizations of the enol triflates 51-54 (Table 1, entries 1-4), leading to dienes (61-64) possessing an angular proton or a methyl group, are more facile than those involving the substrates 55-60 (entries 5-10), which form dienes with an angular CO_2Me function. It is not immediately clear why the presence of the methoxycarbonyl group in 55-60 should retard the rate of ring closure. Perhaps, if step A in Scheme 2 is the rate-limiting reaction,[23] it is the electron-withdrawing nature of the CO_2Me group that slows down the rate of oxidative addition of Pd(0) to the adjacent carbon-oxygen bond of the enol triflate function.

Although the palladium(0)-catalyzed cyclizations occur well in THF as solvent, the reactions appear to be faster in MeCN (Table 1, entry 5). This observation was confirmed by work done subsequently in our laboratory.[24]

It was thought that the efficiency of the overall annulation sequences might be improved if the last two steps (enol triflate formation and palladium(0)-catalyzed ring closure) were to be combined in a one-pot procedure. The isolation and purification of the (potentially) unstable enol triflates would thus be avoided. In the event, the ketone 45 was converted into the enol triflate 57 in the normal manner. To the resultant THF solution (no workup) was added 3 mol % of $(Ph_3P)_4Pd$ and the solution was refluxed for 5 h. Analysis (GLC) indicated that the diene 67 had been produced cleanly. Product isolation and purification produced 67 in 72% yield (Table 1, entry 7). The same overall transformation via a two-pot process provided the diene 67 in 64% yield from 45. In a similar one-pot procedure, the ketone 37 was converted into the diene 71 in 55% yield (Table 1, entry 11).

Each of the structurally interesting bicyclic dienes 61-71 gave spectra in full accord with the structural formulas indicated in Chart 3. Of particular note were the olefinic proton resonances in the ^1H NMR spectra of these substances. For example, the ^1H NMR spectrum of the diene 67 displayed three olefinic proton signals at δ 4.64 (t, H_A, $J_{AB} = J_{AD} = 2.5$ Hz), 4.92 (t, H_B, $J_{AB} = J_{BD} = 2.5$ Hz), and 5.86 (t, H_C, $J_{CF} = J_{CG} = 4$ Hz). In a NOE difference experiment, irradiation at δ 5.86 (H_C) caused signal enhancement at δ 4.92 (H_B). A similar pattern for the chemical shifts of the olefinic protons was observed for all the conjugated dienes listed in Chart 3. In general, the exocyclic methylene protons of these compounds give rise to signals between δ 4.6 and 5.2, while the olefinic ring protons resonate between δ 5.4 and 6.0.



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CONCLUSION

It is evident from the work outlined above that the preparation of structurally novel bicyclic dienes of general structure 23 (see Scheme 1) can readily be accomplished via chemical transformations that are easily performed and are generally efficient. It is important to note explicitly that a variety of diversely functionalized derivatives of

bicyclo[4.3.0]nonane (61, 62, 65, 66), bicyclo[4.4.0]decane (63, 64, 67, 68, 71), bicyclo[5.3.0]decane (70), and bicyclo[5.4.0]undecane (69) can be conveniently accessed via this chemistry. Clearly, the intramolecular palladium(0)-catalyzed coupling of the enol triflate and vinylstannane moieties in 22 (Scheme 1) is the key step of this new annulation sequence (17 → 23). In this sense, the elegant and important investigations of Stille and co-workers[9] served as an informative prelude to our studies. Future publications from this laboratory will deal with the use of our annulation method for the preparation of conjugated dienes more highly functionalized than 23 and with the use of these dienes as key intermediates in the total synthesis of natural products.

EXPERIMENTAL

General Information. Distillation temperatures, which refer to bulb-to-bulb (Kugelrohr) distillations, are uncorrected. ^1H and ^{13}C NMR spectra were recorded on $CDCl_3$ solutions. Carbon chemical shifts are given relative to that of $CDCl_3$ (δ 77.0). Proton signal positions for compounds containing the Me_3Sn group are given relative to the signal for $CHCl_3$ (δ 7.25). The tin-proton coupling constants (J_{Sn-H}) are given as an average of the ^{117}Sn and ^{119}Sn values. For compounds containing the Me_3Sn function, high resolution molecular mass measurements were determined on the (M^+-Me) fragment[25] and are based on ^{120}Sn. GLC analyses were performed on instruments equipped with 25 m x 0.21 mm fused silica columns coated with cross-linked SE-54. TLC analyses were carried out with commercial aluminum-backed silica gel plates (E. Merck, Type 5554). Flash chromatography[26] was done with 230-400 mesh silica gel (E. Merck).

Note: All compounds for which high resolution mass measurements are given exhibited, unless otherwise noted, clean ^1H NMR spectra and showed essentially one spot on TLC analyses and (or) one peak on GLC analysis.

Note: All reactions, unless otherwise noted, were carried out under an atmosphere of dry argon using oven- or flame-dried glassware.

5-Chloro-2-trimethylstannyl-1-pentene (29). To a cold (-78°C), stirred solution of $Me_3SnCu{\cdot}Me_2S$[12] (19 mmol) in 180 mL of dry THF was added a solution of 1.5 g (14.6 mmol) of 5-chloro-1-pentyne (25) in 20 mL of dry THF. The dark red mixture was stirred at -78°C for 6 h and then glacial HOAc (2 mL), aqueous NH_4Cl-NH_4OH (pH 8) (70 mL), MeOH (70 mL) and Et_2O (50 mL) were added sequentially. The mixture was allowed to warm to room temperature, was opened to the air, and then was stirred vigorously until the aqueous layer was deep blue. The phases were separated and the aqueous layer was extracted with Et_2O (2 x 50 mL). The combined organic solution was washed with aqueous NH_4Cl-NH_4OH (pH 8) until the washings were colorless and then was dried ($MgSO_4$). Removal of the solvent, followed by column chromatography of the remaining oil on silica gel (240 g, petroleum ether), provided a liquid that, upon distillation (85-95°C (15 Torr)), gave 2.54 g (65%) of the chloro stannane 29. This colorless oil exhibited spectra identical with those reported previously.[1]

6-Chloro-2-trimethylstannyl-1-hexene (30). Using a procedure identical with that described above, 6-chloro-1-hexyne (26)[14] (1.7 g, 14.6 mmol) was converted into the chloro stannane 30. Distillation (110-115°C (15 Torr)) of the liquid derived from column chromatography of the crude product provided 2.96 g (72%) of 30, a colorless oil that displayed spectra identical with those recorded earlier.[1]

4-Iodo-2-trimethylstannyl-1-butene (18). To a cold (0°C), stirred solution of the alcohol 27 (3.67 g, 15.6 mmol) in dry CH_2Cl_2 (20 mL) were added 4-*N*,*N*-dimethylaminopyridine (2.10 g, 17.2 mmol) and *p*-toluenesulfonyl chloride (3.28 g, 17.2 mmol) and the solution was stirred overnight at room temperature. Water (50 mL) was added and the organic phase was separated, dried ($MgSO_4$), and concentrated. A solution of the residual material and NaI (3.10 g, 20.7 mmol) in dry *N*,*N*-dimethylformamide (10 mL) was heated at 60-70°C for 1 h. The

cooled mixture was poured into water (50 mL) and the mixture was extracted with Et_2O (4 x 20 mL). The combined extracts were washed with brine (5 x 10 mL), dried ($MgSO_4$), and concentrated. Distillation (50-55°C (0.1 Torr)) of the residual liquid afforded 3.30 g (70%) of the iodide **18** as a colorless oil: IR (neat) 1165, 920, 770 cm^{-1}; ^1H NMR (400 MHz) δ 0.18 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 2.80-2.86 (m, 2 H, $^3J_{Sn-H}$ = 46 Hz), 3.18 (t, 2 H, J = 8 Hz), 5.30 (m, 1 H, $^3J_{Sn-H}$ = 68 Hz), 5.72 (m, 1 H, $^3J_{Sn-H}$ = 144 Hz). Exact Mass calcd. for $C_6H_{12}ISn$ (M^+-Me) 330.9005, found 330.9042.

5-Iodo-2-trimethylstannyl-1-pentene (19). A stirred solution of the chloride **29** (2.20 g, 8.24 mmol) and NaI (8.65 g, 57.7 mmol) in acetone (30 mL) was refluxed for 24 h. The acetone was removed under reduced pressure and to the resulting residue was added Et_2O (60 mL) and water (30 mL). The organic phase was separated and the aqueous phase was extracted with Et_2O (3 x 30 mL). The combined extracts were dried ($MgSO_4$) and concentrated, and the remaining oil was distilled (95-110°C (0.8 Torr)) to provide 2.61 g (88%) of the iodide **19** as a colorless liquid: IR (neat) 1225, 915, 760 cm^{-1}; ^1H NMR (80 MHz) δ 0.20 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.7-2.15 (m, 2 H), 2.25-2.55 (m, 2 H), 3.20 (t, 2 H, J = 7 Hz), 5.23 (dt, 1 H, J = 2.5, 1 Hz, $^3J_{Sn-H}$ = 74 Hz), 5.73 (dt, 1 H, J = 2.5, 1.3 Hz, $^3J_{Sn-H}$ = 152 Hz). Exact Mass calcd. for $C_7H_{14}ISn$ (M^+-Me) 344.9162, found 344.9168.

6-Iodo-2-trimethylstannyl-1-hexene (20). Following a procedure identical with that described above, the chloride **30** (2.90 g, 10.3 mmol) was converted into the iodide **20**. Distillation (60-70°C (0.1 Torr)) of the crude oil afforded 3.18 g (84%) of **20** as a colorless liquid: IR (film) 1210, 915, 765 cm^{-1}; ^1H NMR (80 MHz) δ 0.16 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.30-2.05 (m, 4 H), 2.29 (br t, 2 H, J = 7 Hz, $^3J_{Sn-H}$ = 50 Hz), 3.18 (t, 2 H, J = 6.5 Hz), 5.15 (br s, 1 H, $^3J_{Sn-H}$ = 72 Hz), 5.65 (dt, 1 H, J = 2.5, 1 Hz, $^3J_{Sn-H}$ = 150 Hz). Exact Mass calcd. for $C_8H_{16}ISn$ (M^+-Me) 358.9319, found 358.9307.

Preparation of the *N,N*-Dimethylhydrazone **32**. A stirred solution of the commercially available keto ketal **31** (19.5 g, 98.3 mmol) and H_2N-NMe_2 (9.0 mL, 1.2 equivalents) in dry benzene was refluxed for 2 h under a Dean-Stark water trap. The resulting solution was dried ($MgSO_4$) and concentrated, and the remaining oil was distilled (105-120°C (0.03 Torr)) to provide 23.5 g (99%) of **32** as a white crystalline solid: mp 45-46°C; IR (KBr) 2773, 1640 cm^{-1}; ^1H NMR (80 MHz) δ 0.99, 1.05 (s, s, 3 H each), 1.83-2.15 (m, 4 H), 2.20-2.75 (m, 4 H), 2.49 (s, 6 H), 3.56 (s, 4 H). Exact Mass calcd. for $C_{13}H_{24}N_2O_2$ 240.1837, found 240.1835.

Preparation of the Keto Ketal **33**. To a cold (0°C), stirred solution of LDA (3 mmol) in dry THF (5 mL) was added a solution of the hydrazone **32** (603 mg, 2.5 mmol) in THF (2 mL). The solution was stirred for 90 min at 0°C and then was cooled to -78°C. A solution of the iodide **18** (1.035 g, 3 mmol) in 1 mL of dry THF was added dropwise. The mixture was stirred for 30 min at -78°C and for 2 h at room temperature and then saturated aqueous ammonium chloride (5 mL) was added. The mixture was extracted with CH_2Cl_2 (6 x 5 mL) and the combined extracts were dried ($MgSO_4$) and concentrated. The remaining dark red oil was immediately dissolved in a mixture of THF, water, and pH 7 phosphate buffer (8:2:2.4, 50 mL total) and to the resulting mixture was added $NaIO_4$ (1.05 g, 5 mmol). The mixture was stirred for 12 h at room temperature and then was suction filtered. To the filtrate was added Et_2O (40 mL) and the organic phase was separated, dried ($MgSO_4$) and concentrated. Subjection of the crude red oil to flash chromatography on silica gel (70 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (160-165°C (0.1 Torr)) of the resulting oil, provided 675 mg (65%) of **33** as a colorless oil: IR (neat) 1710, 780 cm^{-1}; ^1H NMR (400 MHz) δ 0.16 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.01, 1.02 (s, s, 3 H each), 1.21-1.32 (m, 1 H), 1.50 (t, 1 H, J = 12 Hz), 1.74-1.84 (m, 1 H), 1.86-1.99 (m, 1 H), 2.20-2.35 (m, 3 H), 3.45-3.65 (m, 4 H), 3.55, 3.56 (s, s, 2 H each), 5.16 (dt, 1 H, J = 2.8, 1.3 Hz, $^3J_{Sn-H}$ = 71 Hz), 5.66 (dt, 1 H, J = 2.8, 1.4 Hz, $^3J_{Sn-H}$ = 150 Hz). Exact Mass calcd. for $C_{17}H_{29}O_3Sn$ (M^+-Me) 401.1139, found 401.1140.

Preparation of the Keto Ketal **35**. Following a procedure identical with that described above, the hydrazone **32** (584 mg, 2.43 mmol) was alkylated with the iodide **19** (1.50 g, 4.16 mmol). Subjection of the crude product to flash chromatography on silica gel (70 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (165-170°C (0.1 Torr)) of the resulting liquid, provided 730 mg (70%) of **35** as a colorless oil: IR (neat) 1720, 780 cm^{-1}; ^1H NMR (400 MHz) δ 0.14 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.01, 1.03 (s, s, 3 H each), 1.12-1.27 (m, 1 H), 1.31-1.44 (m, 2 H), 1.45-1.57 (t, 1 H, J = 13 Hz), 1.71-1.85 (m, 2 H), 2.20-2.35 (m,

3 H), 2.45-2.65 (m, 4 H), 3.52-3.58 (m, 4 H), 5.14 (d, 1 H, J = 2 Hz, $^3J_{Sn-H}$ = 71 Hz), 5.65 (br s, 1 H, $^3J_{Sn-H}$ = 151 Hz). Exact Mass calcd. for $C_{18}H_{31}O_3Sn$ (M^+-Me) 415.1295, found 415.1302.

Preparation of the Keto Ketal 34. To a cold (0°C), stirred solution of $KOBu^t$ (15 mg, 0.13 mmol) in dry THF (2.5 mL) and dry Bu^tOH (1 mL) was added, dropwise, a solution of the keto ketal 33 (37.6 mg, 0.09 mmol) in dry THF (0.5 mL). The solution was stirred for 5 min, MeI (7 μL, 1.4 mmol) was added and the solution was warmed to room temperature. After 1 h at this temperature, saturated aqueous NH_4Cl (10 mL) and Et_2O (10 mL) were added. The organic phase was separated, dried ($MgSO_4$) and concentrated. Distillation (166-172°C (0.1 Torr)) of the remaining liquid provided 30.3 mg (78%) of 34 as a colorless oil: IR (neat) 1720, 790 cm^{-1}; ^1H NMR (400 MHz) δ 0.15 (s, 9 H, $^2J_{Sn-H}$ = 51 Hz), 1.00, 1.01, 1.13 (s, s, s, 3 H each), 1.50-1.60 (m, 1 H), 1.75-1.92 (m, 2 H) 2.00-2.09 (m, 2 H), 2.18-2.30 (m, 3 H), 2.38-2.46 (m, 1 H), 2.49-2.59 (m, 1 H), 3.48-3.58 (m, 4 H), 5.12 (d, 1 H, J = 3 Hz, $^3J_{Sn-H}$ = 69 Hz), 5.74 (d, 1 H, J = 3 Hz, $^3J_{Sn-H}$ = 153 Hz). Exact Mass calcd. for $C_{18}H_{31}O_3Sn$ (M^+-Me) 415.1295, found 415.1277.

Preparation of the Keto Ketal 36. Following a procedure identical with that outlined above, the keto ketal 35 (505 mg, 1.18 mmol) was alkylated with MeI. Subjection of the crude product to flash chromatography on silica gel (70 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (165-171°C (0.1 Torr)) of the resulting oil, provided 344 mg (66%) of 36 as a colorless oil: IR (neat) 1720, 790 cm^{-1}; ^1H NMR (400 MHz) δ 0.14 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 0.98, 1.02, 1.10 (s, s, s, 3 H each), 1.12-1.24 (m, 1 H), 1.30-1.40 (m, 1 H), 1.42-1.52 (dt, 1 H, J = 4, 13 Hz), 1.60-1.72 (dt, 1 H, J = 4, 13 Hz), 1.85-1.93 (m, 1 H), 2.00-2.30 (m, 5 H), 2.38-2.45 (m, 2 H), 3.45-3.61 (m, 4 H), 5.13 (d, 1 H, J = 3 Hz, $^3J_{Sn-H}$ = 69 Hz), 5.63 (d, 1 H, J = 3 Hz, $^3J_{Sn-H}$ = 153 Hz). Exact Mass calcd. for $C_{19}H_{33}O_3Sn$ (M^+-Me) 429.1452, found 429.1463.

Preparation of the Ketone 37. Following a procedure identical with that described above, 2-methylcyclohexanone (0.31 mL, 2.55 mmol) was alkylated with the iodide 19 (1.0 g, 2.8 mmol) in 10 mL of dry THF. Subjection of the crude oil to flash chromatography on silica gel (50 g, 1:20 Et_2O-petroleum ether), followed by distillation (100-110°C (0.03 Torr)) of the resulting oil, provided 399 mg (46%) of 37 as a colorless oil: IR (neat) 1708, 769 cm^{-1}; ^1H NMR (400 MHz) δ 0.13 (s, 9 H, $^2J_{Sn-H}$ = 54 Hz), 1.04 (s, 3 H), 1.30-2.50 (m, 14 H), 5.14 (m, 1 H, $^3J_{Sn-H}$ = 71 Hz), 5.64 (m, 1 H, $^3J_{Sn-H}$ = 150 Hz). Exact Mass calcd. for $C_{14}H_{25}OSn$ (M^+-Me) 329.0927, found 329.0927.

General Procedure for the Alkylation of β-Keto Esters. To a well stirred suspension of potassium hydride (1.1 equivalents) in dry THF (3 mL per mmol of β-keto ester) at room temperature was added, dropwise, a solution of the appropriate β-keto ester (1 equivalent) in dry THF (1 mL per mmol). The resulting mixture was stirred at room temperature for 30-45 min, and then the appropriate alkyl halide (1.1 equivalents) was added as a solution in dry THF (1 mL per mmol). The reaction mixture was heated to reflux and after the reaction was determined to have reached completion (by GLC and (or) TLC analyses), the mixture was cooled to room temperature and concentrated. Direct chromatography of the resulting mixture, followed by distillation of the crude product thus obtained, provided the desired alkylated β-keto ester.

Preparation of the β-Keto Ester 43. Following the general procedure, the β-keto ester 38 (200 mg, 1.41 mmol) was alkylated with the iodide 19 (355 mg, 1.55 mmol). The reaction mixture was refluxed for 8 h. Flash chromatography of the crude material on silica gel (27 g, 1:25 ethyl acetate-petroleum ether), followed by distillation (135-140°C (0.8 Torr)) of the resulting oil, provided 314 mg (60%) of 43 as a colorless oil: IR (neat) 1750, 1720, 1165, 770 cm^{-1}; ^1H NMR (400 MHz) δ 0.09 (s, 9 H, $^2J_{Sn-H}$ = 54 Hz), 1.20-1.45 (m, 2 H), 1.51 (dt, 1 H, J = 4.5, 9 Hz), 1.80-2.00 (m, 4 H), 2.10-2.55 (m, 5 H), 3.66 (s, 3 H), 5.10 (m, 1 H, $^3J_{Sn-H}$ = 72 Hz), 5.59 (m, 1 H, $^3J_{Sn-H}$ = 152 Hz). Exact Mass calcd. for $C_{14}H_{23}O_3Sn$ (M^+-Me) 359.0669, found 359.0667.

Preparation of the β-Keto Ester 44. Following the general procedure, the β-keto ester 39[18] (90 mg, 0.577 mmol) was alkylated with the iodide 19 (228 mg, 0.63 mmol). The reaction mixture was refluxed for 8 h. Medium pressure chromatography of the crude material on

silica gel (18 g, 1:25 ethyl acetate-petroleum ether), followed by distillation (135-140°C (0.8 Torr)) of the resulting oil, provided 127 mg (57%) of a mixture of 44 and 49 in a ratio of 96:4 (by GLC), respectively. A small amount of pure 44, a colorless oil, was obtained by drip column chromatography of this material on silica gel (18 g, 1:25 ethyl acetate-petroleum ether). Compound 44 exhibited: IR (neat) 1750, 1725, 1230, 1165, 770 cm^{-1}; ^1H NMR (400 MHz) δ 0.09 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.01 (d, 3 H, J = 7.5 Hz), 1.19 (m, 1 H), 1.49 (m, 1 H), 1.63-1.85 (m, 3 H), 1.98-2.33 (m, 5 H), 2.50 (ddd, 1 H, J = 1.5, 8, 18 Hz), 3.63 (s, 3 H), 5.11 (dt, 1 H, J = 2.8, 1.3 Hz, $^3J_{Sn-H}$ = 72 Hz), 5.61 (dt, 1 H, J = 2.8, 1.4 Hz, $^3J_{Sn-H}$ = 152 Hz). Exact Mass calcd. for $C_{15}H_{25}O_3Sn$ (M^+-Me) 373.0825, found 373.0829.

Preparation of the β-keto Ester 45. Following the general procedure, the β-keto ester 40[19] (1.09 g, 6.97 mmol) was alkylated with the iodide 19 (3.00 g, 8.4 mmol). The reaction mixture was refluxed for 16 h. Flash chromatography of the crude material on silica gel (100 g, 1:20 Et_2O-petroleum ether), followed by distillation: (115-120°C (0.1 Torr)) of the resulting oil, provided 2.45 g (91%) of 45 as a colorless oil: IR (neat) 1710, 1200, 770 cm^{-1}; ^1H NMR (400 MHz) δ 0.09 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.15-1.78 (m, 7 H), 1.83 (ddd, 1 H, J = 4.5, 11.5, 13 Hz), 1.97 (m, 1 H), 2.17-2.32 (m, 2 H), 2.35-2.44 (m, 2 H), 2.48 (m, 1 H), 3.68 (s, 3 H), 5.10 (dt, 1 H, J = 2.5, 1 Hz, $^3J_{Sn-H}$ = 72 Hz), 5.60 (dt, 1 H, J = 2.5, 1.5 Hz, $^3J_{Sn-H}$ = 152 Hz). Exact Mass calcd. for $C_{15}H_{25}O_3Sn$ (M^+-Me) 373.0825, found 373.0824.

Preparation of the β-Keto Ester 46. Following the general procedure, the β-keto ester 41[20] (130 mg, 0.765 mmol) was alkylated with the iodide 19 (302 mg, 0.84 mmol). The reaction mixture was refluxed for 16 h. Flash chromatography of the crude material on silica gel (27 g, 1:25 ethyl acetate-petroleum ether), followed by distillation (132-138°C (0.8 Torr)) of the resulting liquid, provided 163 mg (57%) of a mixture of 46 and 50, in a ratio of 3:1 (by ^1H NMR), respectively. This mixture, a colorless oil which proved to be inseparable by chromatography on silica gel, exhibited: IR (neat) 1710, 1195, 770 cm^{-1}; ^1H NMR (400 MHz) δ 0.13, 0.14 (s, s, ratio ~3:1, 9 H, $^2J_{Sn-H}$ = 53 Hz each), 1.00, 1.13 (d, d, ratio ~1:3, 3 H, J = 7.2 Hz each), 1.16-2.77 (m, 13 H), 3.68, 3.72 (s, s, ratio ~3:1, 3 H), 3.77 (t, ^{3}-OCH_2 of enol ether, J = 6 Hz), 5.13, 5.16 (dt, dt, ratio ~3:1, 1 H, J = 2.8, 1.3 Hz each, $^3J_{Sn-H}$ = 72 Hz each), 5.65 (m, 1 H, $^3J_{Sn-H}$ = 152 Hz). Exact Mass calcd. for $C_{16}H_{27}O_3Sn$ (M^+-Me) 387.0982, found 387.0980.

Preparation of the β-Keto Ester 47. Following the general procedure, the β-keto ester 42[21] (129 mg, 0.76 mmol) was alkylated with the iodide 19 (300 mg, 0.84 mmol). The reaction mixture was refluxed for 6.5 h. Flash chromatography of the crude material on silica gel (27 g, 1:14 ethyl acetate-petroleum ether), followed by distillation (150-155°C (0.8 Torr)) of the resulting liquid, provided 280 mg (92%) of 47 as a colorless oil: IR (neat) 1735, 1710, 1230, 1150, 770 cm^{-1}; ^1H NMR (400 MHz) δ 0.09 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.23-1.77 (m, 11 H), 1.93 (m, 1 H), 2.07-2.31 (m, 2 H), 2.45 (m, 1 H), 2.58 (m, 1 H), 3.69 (s, 3 H), 5.11 (dt, 1 H, J = 2.8, 1.2 Hz, $^3J_{Sn-H}$ = 71 Hz), 5.61 (dt, 1 H, J = 2.8, 1.4 Hz, $^3J_{Sn-H}$ = 151 Hz). Exact Mass calcd. for $C_{16}H_{27}O_3Sn$ (M^+-Me) 387.0982, found 387.0977.

Preparation of the β-Keto Ester 48. Following the general procedure, the β-keto ester 38 (200 mg, 1.41 mmol) was alkylated with the iodide 20 (577 mg, 1.55 mmol). The reaction mixture was refluxed for 9 h. Flash chromatography of the crude mixture on silica gel (30 g, 1:30 ethyl acetate-petroleum ether), followed by distillation (145-148°C (0.6 Torr)) of the resulting liquid, provided 340 mg (63%) of 48 as a colorless oil: IR (neat) 1748, 1719, 1225, 1155, 768 cm^{-1}; ^1H NMR (400 MHz) δ 0.11 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.10-1.40 (m, 4 H), 1.54 (ddd, 1 H, J = 4.5, 11.5, 13.5 Hz), 1.80-2.05 (m, 4 H), 2.28-2.32 (m, 3 H), 2.38 (m, 1 H), 2.53 (m, 1 H), 3.68 (s, 3 H), 5.11 (dt, 1 H, J = 2.8, 1.2 Hz, $^3J_{Sn-H}$ = 72 Hz), 5.61 (dt, 1 H, J = 2.8, 1.4 Hz, $^3J_{Sn-H}$ = 152 Hz). Exact Mass calcd. for $C_{15}H_{25}O_3Sn$ (M^+-Me) 373.0825, found 373.0824.

General Procedure for the Preparation of Bicyclic Dienes via the Corresponding (Isolated) Enol Triflate Intermediates. To a cold (-48°C to 0°C), stirred solution of LDA (1.1-2.0 equivalents) in dry THF (1-1.3 mL per 0.1 mmol of β-keto ester or ketone) was added, dropwise, a solution of the appropriate β-keto ester or ketone (1 equivalent) in dry THF (1-2 mL per 0.3 mmol). The resulting solution was stirred at the specified temperature for 1 h. $PhN(SO_2CF_3)_2$ (1.17-2.0 equivalents) was added as a finely ground solid and the

resulting yellow solution was warmed to room temperature over a period of 30 min. The solvent was removed under reduced pressure and the residual oil was subjected to flash chromatography. The enol triflate was characterized and then was used as soon as possible in the subsequent reaction.. If storage was required, the enol triflate was stored in a freezer under an argon atmosphere.

To a stirred solution of the appropriate enol triflate (1 equivalent) in dry THF or CH_3CN (5 mL per 0.1 mmol) at room temperature was added $Pd(PPh_3)_4$ (5 mol %) as a solid. If necessary, the resulting solution was heated to reflux. When the reaction was determined to have reached completion (by GLC and/or TLC analyses), the mixture was cooled to room temperature and concentrated. The residual oil was subjected to flash chromatography and distillation of the oil thus obtained provided the expected diene.

Preparation of the Diene 61. Following the general procedure, employing 0.46 mmol of LDA in dry THF (-40°C) and 0.49 mmol of $PhN(SO_2CF_3)_2$, the ketone 33 (160 mg, 0.386 mmol) was converted into the enol triflate 51. Flash chromatography of the crude product on silica gel (30 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (163-170°C (0.1 Torr)) of the resulting liquid, provided 154 mg (73%) of 51 as a colorless oil: IR (neat) 1220, 780 cm^{-1}; ^1H NMR (270 MHz) δ 0.16 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 0.98, 0.99 (s, s, 3 H each) 1.40-1.65 (m, 3 H), 1.70-1.90 (m, 1 H), 2.10-2.80 (m, 5 H), 3.40-3.60 (m, 4 H), 5.19 (br s, 1 H, $^3J_{Sn-H}$ = 68 Hz), 5.62 (br t, 1 H, J = 4 Hz), 5.69 (br s, 1 H, $^3J_{Sn-H}$ = 148 Hz). Exact Mass calcd. for $C_{18}H_{28}F_3O_5SSn$ (M^+-Me) 533.0631, found 533.0607.

Following the general procedure, compound 51 (92.0 mg, 0.164 mmol) was converted into the diene 61, using dry THF as solvent, in 15 min at room temperature. Flash chromatography of the crude oil on silica gel (18 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (110-119°C (0.1 Torr)) of the resulting oil, provided 32.7 mg (85%) of 61 as a colorless oil: IR (neat) 1120 cm^{-1}; ^1H NMR (400 MHz) δ 0.97, 1.03 (s, s, 3 H each), 1.10-1.30 (m, 2 H), 1.97 (dt, 1 H, J = 12, 7 Hz), 2.24-2.34 (m, 1 H), 2.35-2.60 (m, 3 H), 2.61-2.68 (ddd, 1 H, J = 1.5, 4, 13 Hz), 2.69-2.78 (m, 1 H), 3.44-3.70 (m, 4 H), 4.80 (m, 1 H), 5.23 (m, 1 H), 5.83 (m, 1 H). Exact Mass calcd. for $C_{15}H_{22}O_2$ 234.1621, found 234.1620.

Preparation of the Diene 62. Following the general procedure, employing 0.93 mmol of LDA in dry THF (0°C) and 0.93 mmol of $PhN(SO_2CF_3)_2$, the ketone 34 (200 mg, 0.466 mmol) was converted into the enol triflate 52. Flash chromatography of the crude mixture on silica gel (30 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (183-190°C (0.1 Torr)) of the resulting liquid, afforded 185 mg (72%) of 52 as a colorless oil: IR (neat) 1220, 780 cm^{-1}; ^1H NMR (400 MHz) δ 0.15 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 0.96, 1.01, 1.25 (s, s, s, 3 H each), 1.42-1.52 (m, 1 H), 1.56-1.66 (m, 1 H), 1.94 (d, 1 H, J = 14 Hz), 2.11 (dd, 1 H, J = 2, 14 Hz), 2.15-2.35 (m, 2 H), 2.46 (dd, 1 H, J = 4, 16 Hz), 2.62 (ddd, 1 H, J = 2.6, 16 Hz), 3.42-3.56 (m, 4 H), 5.14 (d, 1 H, J = 3 Hz, $^3J_{Sn-H}$ = 69 Hz), 5.60 (dd, 1 H, J = 4, 6 Hz), 5.68 (d, 1 H, J = 3 Hz, $^3J_{Sn-H}$ = 151 Hz). Exact Mass calcd. for $C_{19}H_{30}F_3O_5SSn$ (M^+-Me) 547.0788, found 547.0789.

Following the general procedure, compound 52 (15 mg, 0.027 mmol) was converted into the diene 62, using THF as solvent, in 15 min at room temperature. Flash chromatography of the crude product on silica gel (5 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (80-85°C (0.1 Torr)) of the resulting liquid, produced 5.4 mg (83%) of 62 as a colorless oil: IR (neat) 1280 cm^{-1}; ^1H NMR (400 MHz) δ 0.9, 1.07, 1.09 (s, s, s, 3 H each), 1.35-1.45 (m, 2 H), 1.68 (dd, 1 H, J = 8, 12 Hz), 2.36-2.48 (m, 2 H), 2.50-2.70 (m, 3 H), 3.40-3.50 (m, 2 H), 3.60-3.66 (m, 2 H), 4.80 (br s, 1 H), 5.27 (br s, 1 H), 5.74 (t, 1 H, J = 3.5 Hz). Exact Mass calcd. for $C_{16}H_{24}O_2$ 248.1777, found 248.1780.

Preparation of the Diene 63. Following the general procedure, employing 0.78 mmol of LDA in dry THF (-40°C) and 0.78 mmol of $PhN(SO_2CF_3)_2$, the ketone 35 (223 mg, 0.52 mmol) was converted into the enol triflate 53. Flash chromatography of the crude material on silica gel (30 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (171-173°C (0.1 Torr)) of the resulting liquid, provided 222 mg (76%) of 53 as a colorless oil: IR (neat) 1690, 1220, 780 cm^{-1}; ^1H NMR (270 MHz) δ 0.19 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 0.98, 1.02 (s, s, 3 H each), 1.22-1.81 (m, 6H), 2.15-2.50 (m, 3 H), 2.61-2.83 (m, 2 H), 3.46-3.62 (m, 4 H), 5.18 (br s, 1 H, $^3J_{Sn-H}$ = 71 Hz), 5.40-5.64 (m, 1 H), 5.67 (br s, 1 H, $^3J_{Sn-H}$ = 153 Hz). Exact Mass calcd. for $C_{19}H_{30}F_3O_5SSn$ (M^+-Me) 547.0788, found 547.0801.

Following the general procedure, substance 53 (92.0 mg, 0.164 mmol) was converted into the diene 63, using THF as solvent, in 15 min at room temperature. Flash chromatography of the crude oil on silica gel (18 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (95-97°C (0.1 Torr)) of the resulting liquid, yielded 34.2 mg (84%) of 63 as a colorless oil: IR (neat) 1120 cm^{-1}; ^1H NMR (400 MHz) δ 0.92, 1.04 (s, s, 3 H each), 1.12-1.37 (m, 2 H), 1.38-1.52 (m, 1 H), 1.80-1.92 (m, 2 H), 2.04-2.16 (m, 1 H), 2.18-2.33 (m, 2 H), 2.34-2.50 (m, 2 H), 2.52-2.63 (m, 1 H), 3.44-3.60 (m, 3 H), 3.65 (d, 1 H, J = 11.2 Hz), 4.60 (t, 1 H, J = 1.7 Hz), 4.90 (t, 1 H, J = 1.7 Hz), 5.60 (m, 1 H). Exact Mass calcd. for $C_{16}H_{24}O_2$ 248.1777, found 248.1781.

Preparation of the Diene 64. Following the general procedure, employing 0.40 mmol of LDA in dry THF (0°C) and 0.40 mmol of $PhN(SO_2CF_3)_2$, compound 36 (118 mg, 0.27 mmol) was converted into the enol triflate 54. Flash chromatography of the crude mixture on silica gel (27 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (183-190°C (0.1 Torr)) of the resulting liquid, provided 109 mg (70%) of 54 as a colorless oil: IR (neat) 1220, 780 cm^{-1}; ^1H NMR (400 MHz) δ 0.14 (s, 9 H, $^2J_{Sn-H}$ = 50 Hz), 0.93, 1.03, 1.22 (s, s, s, 3 H each), 1.30-1.55 (m, 4 H), 1.87 (d, 1 H, J = 14 Hz), 2.12 (dd, 1 H, J = 2.5, 14 Hz), 2.20-2.35 (m, 2 H), 2.42 (dd, 1 H, J = 3, 17.5 Hz), 2.63 (ddd, 1 H, J = 2.5, 5.5, 17.5 Hz), 3.40-3.60 (m, 4 H), 5.15 (d, 1 H, J = 3 Hz, $^3J_{Sn-H}$ = 70 Hz), 5.59 (dd, 1 H, J = 3, 5.5 Hz), 5.65 (d, 1 H, J = 3 Hz, $^3J_{Sn-H}$ = 150 Hz). Exact Mass calcd. for $C_{20}H_{32}F_3O_5SSn$ (M^+-Me) 561.0945, found 561.0945.

Following the general procedure, compound 54 (50 mg, 0.09 mmol) was converted into the diene 64, using THF as solvent, in 15 min at reflux. Flash chromatography of the crude product on silica gel (5 g, 1:9 ethyl acetate-petroleum ether), followed by distillation (89-92°C (0.1 Torr)) of the resulting liquid, provided 20.2 mg (86%) of 64 as a colorless oil: IR (neat) 1300 cm^{-1}; ^1H NMR (400 MHz) δ 0.88, 1.08, 1.10 (s, s, s, 3 H each), 1.38-1.50 (m, 2 H), 1.52-1.67 (m, 2 H), 1.74 (tq, 1 H, J = 4, 14 Hz), 2.02-2.15 (m, 1 H), 2.30-2.40 (m, 3 H), 3.38-3.45 (m, 2 H), 3.48 (ddd, 1 H, J = 3, 6, 17 Hz), 3.60 (d, 1 H, J = 12 Hz), 3.68 (d, 1 H, J = 12 Hz), 4.63 (t, 1 H, J = 2 Hz), 4.80 (t, 1 H, J = 2 Hz), 5.42 (dd, 1 H, J = 4, 6 Hz). Exact Mass calcd. for $C_{17}H_{26}O_2$ 262.1934, found 262.1941.

Preparation of the Diene 65. Following the general procedure, employing 0.33 mmol of LDA in dry THF (-48°C) and 0.35 mmol of $PhN(SO_2CF_3)_2$, the ketone 43 (110 mg, 0.295 mmol) was converted into the enol triflate 55. Flash chromatography of the crude material on silica gel (27 g, 1:25 ethyl acetate-petroleum ether) gave 95 mg (64%) of 55 as a colorless oil: IR (film) 1740, 1650, 1425, 1215, 1145, 770 cm^{-1}; ^1H NMR (80 MHz) δ 0.18 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.10-2.75 (m, 10 H), 3.75 (s, 3 H), 5.15 (dt, 1 H, J = 2.8, 1.3 Hz, $^3J_{Sn-H}$ = 72 Hz), 5.65 (dt, 1 H, J = 2.8, 1.4 Hz, $^3J_{Sn-H}$ = 152 Hz), 5.78 (br s, 1 H, $w_{1/2}$ = 5 Hz). Exact Mass calcd. for $C_{15}H_{22}F_3O_5SSn$ (M^+-Me) 491.0162, found 491.0140.

Following the general procedure, compound 55 (87 mg, 0.17 mmol) was converted into the diene 65, using THF as solvent, in 11 h at reflux. Flash chromatography of the crude oil on silica gel (18 g, 1:25 ethyl acetate-petroleum ether), followed by distillation (65-68°C (0.8 Torr)) of the resulting liquid, produced 27 mg (82%) of 65 as a colorless oil: IR (neat) 1725, 1632, 895 cm^{-1}; ^1H NMR (400 MHz) δ 1.32 (dt, 1 H, J = 3.5, 13.5 Hz), 1.51 (tq, 1 H, J = 3.5, 13.5 Hz), 1.75 (m, 1 H), 1.83 (dt, 1 H, J = 13, 9 Hz), 2.09 (m, 1 H), 2.29-2.47 (m, 4 H), 2.49 (br d, 1 H, J = 13.5 Hz), 3.65 (s, 3 H), 4.75 (t, 1 H, J = 2 Hz), 5.05 (t, 1 H, J = 2 Hz), 5.84 (t, 1 H, J = 2 Hz). Exact Mass calcd. for $C_{12}H_{16}O_2$ 192.1151, found 192.1152.

In a separate experiment, substrate 55 was converted into the diene 65 in 84% yield in 4 h in refluxing CH_3CN.

Preparation of the Diene 66. Following the general procedure, employing 0.33 mmol of LDA in dry THF (-48°C) and 0.36 mmol of $PhN(SO_2CF_3)_2$, the ketone 44 (114 mg, 0.295 mmol) was converted into the enol triflate 56. Flash chromatography of the crude material on silica gel (27 g, 1:25 ethyl acetate-petroleum ether) provided 95 mg (62%) of 56 as a colorless oil: IR (neat) 1730, 1650, 1420, 1210, 1138, 765 cm^{-1}; ^1H NMR (80 MHz) δ 0.16 (s, 9 h, $^2J_{Sn-H}$ = 53 Hz), 1.00 (d, 3 H, J = 6.5 Hz), 1.25-2.75 (m, 9 H), 3.73 (s, 3 H), 5.15 (m, 1 H, $^3J_{Sn-H}$ = 72 Hz), 5.66 (dt, 1 H, J = 2.8, 1.4 Hz, $^3J_{Sn-H}$ = 152 Hz), 5.80 (m, 1 H). Exact

Mass calcd. for $C_{16}H_{24}F_3O_5SSn$ (M^+-Me) 505.0318, found 505.0335.

Following the general procedure, substrate **56** (85 mg, 0.16 mmol) was converted into the diene **66**, using THF as solvent, in 9 h at reflux. Flash chromatography of the crude oil on silica gel (18 g, 1:30 ethyl acetate-petroleum ether), followed by distillation (68-70°C (0.8 Torr)) of the resulting oil, gave 28 mg (82%) of **66** as a colorless oil: IR (neat) 1720, 1620, 890 cm^{-1}; ^1H NMR (400 MHz) δ 0.98 (d, 3 H, J = 7 Hz), 1.16 (dt, 1 H, J = 3.5, 13 Hz), 1.46 (ddq, 1 H, J = 3.5, 3.5, 13 Hz), 1.77 (m, 1 H), 2.08 (m, 1 H), 2.11 (ddd, 1 H, J = 1.9, 10, 15.5 Hz), 2.23-2.60 (m, 2 H), 2.43 (ddd, 1 H, J = 3, 7.5, 15.5 Hz), 2.60 (br d, 1 H, J = 13 Hz),3.65 (s, 3 H), 4.71 (t, 1 H, J = 2.5 Hz), 5.03 (t, 1 H, J = 2.5 Hz), 5.87 (dd, 1 H, J = 2, 3 Hz). Exact Mass calcd. for $C_{13}H_{18}O_2$ 206.1307, found 206.1300.

Preparation of the Diene **67**. Following the general procedure, using 5.1 mmol of LDA in dry THF (-48°C) and 5.35 mmol of $PhN(SO_2CF_3)_2$, the ketone **45** (1.32 g, 3.41 mmol) was converted into the enol triflate **57**. Flash chromatography of the crude material on silica gel (180 g, 1:20 ethyl acetate-petroleum ether) afforded 1.24 g (71%) of **57** as a colorless oil: IR (neat) 1735, 1415, 1210, 1142, 770 cm^{-1}; ^1H NMR (80 MHz) δ 0.18 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 0.90-2.50 (m, 12 H), 3.75 (s, 3 H), 5.15 (dt, 1 H, J = 2.8, 1.3 Hz, $^3J_{Sn-H}$ = 72 Hz), 5.65 (dt, 1 H, J = 2.8, 1.3 Hz, $^3J_{Sn-H}$ = 152 Hz), 5.87 (t, 1 H, J = 4 Hz). Exact Mass calcd. for $C_{16}H_{24}F_3O_5SSn$ (M^+-Me) 505.0318, found 505.0350.

Following the general procedure, compound **57** (1.20 g, 2.31 mmol) was converted into the diene **67**, using THF as solvent, in 3 h at reflux. Flash chromatography of the crude oil on silica gel (180 g, 1:25 ethyl acetate-petroleum ether), followed by distillation (75-85°C (0.8 Torr)) of the resulting liquid, provided 428 mg (90%) of **67** as a colorless oil: IR (neat) 1720, 895 cm^{-1}; ^1H NMR (400 MHz) δ 1.25-1.50 (m, 4 H), 1.56-1.78 (m, 2 H), 2.05-2.20 (m, 4 H), 2.29-2.40 (m, 2 H), 3.66 (s, 3 H), 4.64 (t, 1 H, J = 2.5 Hz), 4.92 (t, 1 H, J = 2.5 Hz), 5.86 (t, 1 H, J = 4 Hz); in a NOE difference experiment, irradiation at δ 5.86 caused signal enhancement at δ 4.92; ^{13}C NMR (75.3 MHz) δ 19.3, 23.7, 25.9, 34.9, 35.6, 37.5, 49.1, 51.8, 108.8, 123.8, 139.3, 148.2, 176.2. Exact Mass calcd. for $C_{13}H_{18}O_2$ 206.1307, found 206.1306.

Preparation of the Diene **68**. Following the general procedure, employing 0.3 mmol of LDA in dry THF (-48°C) and 0.32 mmol of $PhN(SO_2CF_3)_2$, a 3:1 mixture of the ketone **46** and the enol ether **50** (100 mg, 0.25 mmol) was converted into a mixture of the enol triflate **58** and uncharacterized material derived from enol ether **50**. Flash chromatography of the crude mixture on silica gel (27 g, 1:25 ethyl acetate-petroleum ether) provided 89 mg (84% based on amount of **46** in the starting material mixture) of **58** as a colorless oil: IR (neat) 1735, 1675, 1415, 1210, 1145, 770 cm^{-1}; ^1H NMR (80 MHz) δ 0.18 (s, 9 H, $^2J_{Sn_3H}$ = 53 Hz), 0.95 (d, 3 H, J = 6.5 Hz), 1.10-2.50 (m, 11 Hz), 3.72 (s, 3 H), 5.16 (m, 1 H, $^3J_{Sn-H}$ = 71 Hz), 5.66 (dt, 1 H, J = 2.8, 1.4 Hz, $^3J_{Sn-H}$ = 151 Hz), 6.00 (t, 1 H, J = 4 Hz). Exact Mass calcd. for $C_{16}H_{26}F_3O_5SSn$ (M^+-Me) 519.0475, found 519.0439.

Following the general procedure, substrate **58** (89 mg, 0.167 mmol) was converted into the diene **68**, using THF as solvent, in 19 h at reflux. Flash chromatography of the crude oil on silica gel (10 g, 1:25 ethyl acetate-petroleum ether), followed by distillation (74-76°C (0.8 Torr)) of the resulting liquid, afforded 32 mg (86%) of **68** as a colorless oil: IR (neat) 1720, 1620, 890 cm^{-1}; ^1H NMR (400 MHz) δ 0.91 (d, 3 H, J = 6.5 Hz), 1.14 (dt, 1 H, J = 4, 13.5 Hz), 1.42-1.62 (m, 4 H), 1.76 (m, 1 H), 2.06 (dtt, 1 H, J = 5, 2.5, 13.5 Hz), 2.15 (m, 2 H), 2.30 (dddd, 1 H, J = 2.5, 2.5, 4, 13.5 Hz), 2.63 (dddd, 1 H, J = 2.5, 2.5, 2.5, 13.5 Hz), 3.64 (s, 3 H), 4.60 (t, 1 H, J = 2.5 Hz), 4.81 (t, 1 H, J = 2.5 Hz), 5.84 (br t, 1 H, J = 4 Hz). Exact Mass calcd. for $C_{14}H_{20}O_2$ 220.1464, found 220.1455.

Preparation of the Diene **69**. Following the general procedure, using 2.0 mmol of LDA in THF (-48°C) and 2.1 mmol of $PhN(SO_2CF_3)_2$, the ketone **47** (534 mg, 1.33 mmol) was converted into the enol triflate **59**. Flash chromatography of the crude material on silica gel (70 g, 1:25 ethyl acetate-petroleum ether) gave 447 mg (63%) of **59** as a colorless oil: IR (neat) 1733, 1660, 1410, 1215, 1140, 770 cm^{-1}; ^1H NMR (80 MHz) δ 0.18 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.00-2.45 (m, 14 H), 3.75 (s, 3 H), 5.16 (dt, 1 H, J = 2.8, 1.3 Hz, $^3J_{Sn-H}$ = 72 Hz), 5.66 (dt, 1 H, J = 2.8, 1.4 Hz, $^3J_{Sn-H}$ = 152 Hz), 6.00 (t, 1 H, J = 6.5 Hz). Exact Mass calcd. for $C_{17}H_{26}F_3O_5SSn$ (M^+-Me) 519.0475, found 519.0475.

Following the general procedure, compound **59** (101 mg, 0.190 mmol) was converted into the diene **69**, using THF as solvent, in 3 h at reflux. Flash chromatography of the crude product on silica gel (18 g, 1:25 ethyl acetate-petroleum ether), followed by distillation (80-82°C (0.6 Torr)) of the resulting liquid, produced 35 mg (85%) of a mixture containing (GLC analysis) ~85% of the diene **69**, along with minor amounts of three other components that appeared to be dienes isomeric with **69**. This mixture was subjected to drip column chromatography on silver nitrate impregnated silica gel (12 g, 1:30 ethyl acetate-petroleum ether). A small amount of pure **69** was obtained and this oil exhibited: IR (neat) 1720, 1615, 895 cm^{-1}; ^1H NMR (400 MHz) δ 1.39 (m, 1 H), 1.49-1.80 (m, 6 H), 1.87-1.96 (m, 2 H), 2.05-2.08 (m, 4 H), 2.33 (m, 1 H), 3.74 (s, 3 H), 4.63 (t, 1 H, J = 2.2 Hz), 4.89 (t, 1 H, J = 2.2 Hz), 5.98 (dd, 1 H, J = 4.8, 7.5 Hz). Exact Mass calcd. for $C_{14}H_{20}O_2$ 220.1464, found 220.1463.

Preparation of the Diene **70**. Following the general procedure, employing 1.0 mmol of LDA in dry THF (-48°C) and 1.1 mmol of $PhN(SO_2CF_3)_2$, the ketone **48** (260 mg, 0.672 mmol) was converted into the enol triflate **60**. Flash chromatography of the crude material on silica gel (40 g, 1:30 ethyl acetate-petroleum ether) gave 220 mg (63%) of **60** as a colorless oil: IR (neat) 1730, 1643, 1420, 1220, 1140, 768 cm^{-1}; ^1H NMR (80 MHz) δ 0.14 (s, 9 H, $^2J_{Sn-H}$ = 53 Hz), 1.10-2.70 (m, 12 H), 3.71 (s, 3 H), 5.13 (dt, 1 H, J = 2.8, 1.3 Hz, $^3J_{Sn-H}$ = 72 Hz), 5.63 (dt, 1 h, J = 2.8, 1.4 Hz, $^3J_{Sn-H}$ = 152 Hz), 5.75 (br s, 1 H). Exact Mass calcd. for $C_{16}H_{24}F_3O_5SSn$ (M^+-Me) 505.0318, found 505.0319.

Following the general procedure, substrate **60** (100 mg, 0.193 mmol) was converted into the diene **70**, using THF as solvent, in 23 h at reflux. Flash chromatography of the crude oil on silica gel (20 g, 1:30 ethyl acetate-petroleum ether), followed by distillation (69-73°C (0.6 Torr)) of the resulting liquid, provided 20 mg (50%) of **70** as a colorless oil: IR (neat) 1724, 1610, 890 cm^{-1}; ^1H NMR (400 MHz) δ 1.14-1.53 (m, 3 H), 1.73-1.88 (m, 2 H), 1.92 (ddd, 1 H, J = 4, 8, 12 Hz), 2.06 (br t, 1 H, J = 13.5 Hz), 2.20-2.48 (m, 5 H), 3.70 (s, 3 H), 4.73 (br s, 1 H), 5.18 (br s, 1 H), 6.00(t, 1 H, J = 4.5 Hz). Exact Mass calcd. for $C_{13}H_{18}O_2$ 206.1307, found 206.1307.

"One-Pot" Preparation of the Diene **71**. To a cold (-78°C), stirred solution of LDA (1.7 mmol) in dry THF (12 mL) was added dry HMPA (2.3 mmol). The resulting pale yellow solution was stirred for 10 min at -78°C and for 10 min at 0°C. After the solution had been recooled to -78°C, a solution of the ketone **37** (390 mg, 1.14 mmol) in dry THF (5 mL) was added dropwise. The resulting mixture was stirred for 10 min at -78°C and then was warmed to 0°C and stirred at this temperature for 1 h. $PhN(SO_2CF_3)_2$ (1.79 mmol) was added as a solid and the resulting yellow solution was stirred at room temperature for 30 min. $(Ph_3P)_4Pd$ (3 mol %) was added as a solid and the resulting solution was refluxed for 30 min, cooled to room temperature and concentrated. Medium pressure chromatography of the crude oil on silica gel (70 g, petroleum ether), followed by distillation (50-70°C (15 Torr)) of the residual oil, provided 101 mg (55%) of **71** as a colorless oil: IR (neat) 1628, 887, 817 cm^{-1}; ^1H NMR (300 MHz) δ 0.98 (s, 3 H), 1.25-2.15 (m, 11 H), 2.35 (d of quintets, 1 H, J = 12, 2 Hz), 4.58 (t, 1 H, J = 2.5 Hz), 4.74 (t, 1 H, J = 2.5 Hz), 5.56 (dd, 1 H, J = 3, 4.5 Hz). Exact Mass calcd. for $C_{12}H_{18}$ 162.1409, found 162.1402.

"One-Pot" Preparation of the Diene **67**. Following a procedure identical with that outlined above, the ketone **45** (1.81 g, 4.68 mmol) was converted into the diene **67**. After addition of $(Ph_3P)_4Pd$, the reaction mixture was refluxed for 5 h. Flash chromatography of the crude product on silica gel (180 g, 1:20 Et_2O-petroleum ether), followed by distillation (75-78°C (0.8 Torr)) of the resultant liquid, afforded 693.8 mg (72%) of **67** as a colorless oil. This material exhibited spectra (IR, ^1H NMR) that were identical with the same compound prepared earlier (*vide supra*).

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