Diastereo- and Enantioselective Synthesis of Allenylcarbinols through S_E2' Addition of Transient Nonracemic Propargylic Stannanes to Aldehydes

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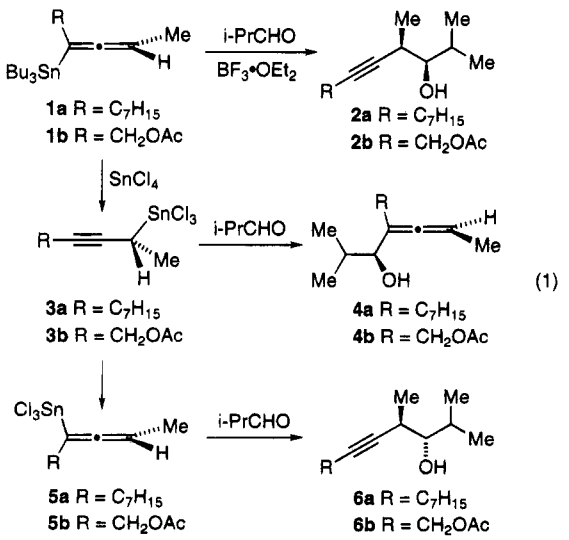
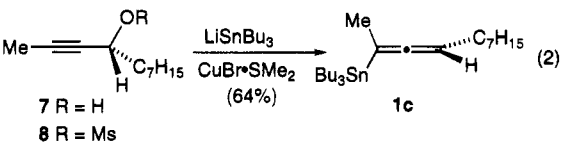
The nonracemic allenylstannane **1c** was prepared by S_N2' displacement of mesylate **8** with Bu_3SnLi–$CuBr{\cdot}SMe_2$. Treatment of this stannane with $BuSnCl_3$ followed by addition of isobutyraldehyde at −40 °C afforded the *syn* allenylcarbinol **4c** in nearly 80% yield. The nonracemic aldehydes (*S*)- and (*R*)-**16** were similarly converted to the adducts **17** and **18** in high yield with good to excellent diastereoselectivity. Best results were obtained when hexane was employed as the solvent. A reaction pathway is proposed to account for the steric preference of these additions. The allenylcarbinols were converted stereospecifically to the *cis*-2,5-dihydrofurans **23**–**25** upon treatment with catalytic $AgNO_3$ in acetone.

During the course of studies on the Lewis acid-promoted addition of nonracemic allenylstannanes **1a** and **1b** to aldehydes as a route to *syn* and *anti* homopropargylic alcohol adducts **2a/b** and **6a/b**, possible intermediates for the synthesis of polypropionate natural products, we noted an interesting divergence in reaction outcome as a function of Lewis acid and experimental protocol.[1] With $BF_3{\cdot}OEt_2$ as the Lewis acid, the *syn* homopropargylic alcohol adducts **2a/b** were obtained from isobutyraldehyde in high yield. When $SnCl_4$ was employed as the Lewis acid, the *anti* adducts **6a/b** or the allenylcarbinols **4a/b**, or both, were formed depending on reaction conditions. Thus, admixture of stannane **1a** or **1b** with $SnCl_4$ followed by immediate addition of the aldehyde favored the formation of allenylcarbinols **4a** or **4b**. If, on the other hand, addition of the aldehyde was delayed for several minutes, then the homopropargylic alcohol adducts **6a** or **6b** were favored (eq 1).



On the basis of our analysis of stereochemistry, we proposed the sequence depicted in eq 1 whereby the addition of $SnCl_4$ to stannane **1** leads to the transient propargylic S_E' adduct **3**, which isomerizes to allene **5** on standing. In the case of propargylic stannane **3a**, the isomerization is rapid. Unless the aldehyde is added within a few seconds after the $SnCl_4$, little of the allenylcarbinol **4a** is produced. Isomerization of the transient acetoxymethyl propargylic stannane **3b** is much slower, requiring several hours. Possibly, internal chelation is reponsible for this rate retardation.[1]

We have previously shown that allenylcarbinols such as **4a** and **4b** undergo stereospecific cyclization to 2,5-dihydrofurans in the presence of catalytic $AgNO_3$ or $AgBF_4$.[2] Because of the importance of such compounds and their dihydro derivatives as subunits of acetogenin[3] and polyether[4] natural products, we felt it would be worthwhile to further study the *in situ* formation of nonracemic propargylic stannanes such as **3** and their addition to aldehydes. In consideration of the aforementioned applications, we conducted these studies with allenic stannane **1c**, obtained analogously to **1a** and **1b** by S_N2' displacement of the nonracemic propargylic mesylate **8** with a Gilman cuprate reagent derived from Bu_3SnLi (eq 2).[1]



Admixture of stannane **1c** with $SnCl_4$ at −78 °C followed by rapid addition of isobutyraldehyde led to a mixture of allenylcarbinols **4c** and **9** along with the related homopropargylic alcohol **10** (eq 3). Evidently, isomerization of the (presumed) intermediate propargyl reagent must be fairly rapid in this system.

Hoping to decrease the rate of this isomerization, we substituted Bu_2SnCl_2 for $SnCl_4$. This modification had the desired effect, giving rise to the allenylcarbinol

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(1) Marshall, J. A.; Perkins, J. *J. Org. Chem.* **1994**, *59*, 3509. Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1992**, *57*, 1242.

(2) Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1991**, *56*, 4913. Marshall, J. A.; Pinney, K. G. *J. Org. Chem.* **1993**, *58*, 7180.

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(4) Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309.

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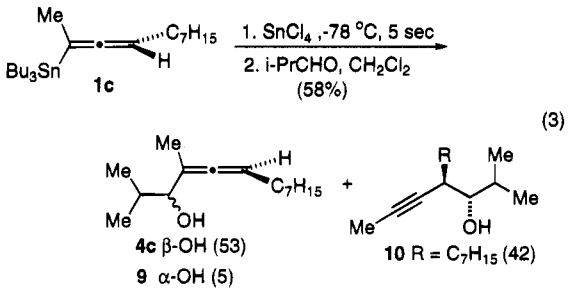


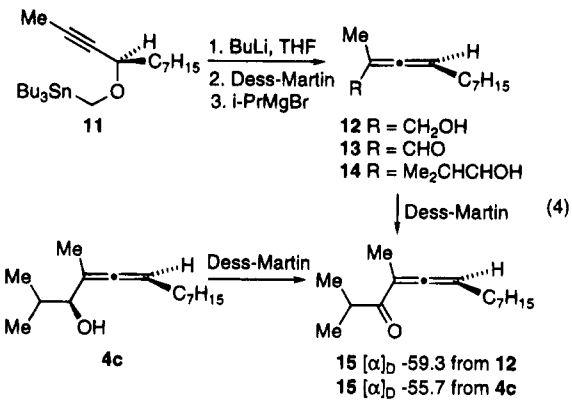
(3)

exclusively. However, the reaction proved impractical, requiring 3–4 days at −78 to −30 °C for completion.

It therefore seemed logical to examine $BuSnCl_3$.[5] Although we found that the addition was still relatively slow at −78 °C, satisfactory results could be achieved at that temperature after prolonged reaction times (Table 1, entries 1, 3, 4).

In this way, allenylcarbinol **4c** could be obtained in nearly 70% yield as an 86:14 mixture of *syn* and *anti* adducts **4c** and **9** (entry 4). None of the homopropargylic alcohol **10** could be detected by GC. At higher reaction temperatures (entry 2), diastereoselectivity was considerably diminished. When both transmetalation and the subsequent addition were performed at −40 °C, adduct **4c** was obtained in 72% yield, with less than 10% of the *anti* isomer **9** after a 5 h reaction time (entry 6).

The absolute configuration of the carbinol center of adduct **4c** was assigned by analogy to **4a/4b** and confirmed through ^1H NMR analysis of the (*R*)- and (*S*)-*O*-methyl mandelates.[6] The allenyl configuration could also be assigned by analogy. Additional support was obtained by the correlation outlined in eq 4. Thus, Still [2,3]Wittig



(4)

rearrangement[7] of the (tributylstannyl)methyl ether **11** derived from alcohol **7** led to allenylmethanol **12**.[1] Oxidation with the Dess–Martin periodinane reagent[8] and addition of *i*-PrMgBr to the derived aldehyde **13** afforded alcohol **14** as a *ca.* 1:1 mixture of diastereomers. This mixture was oxidized to ketone **15** of the indicated rotation. The same ketone, of comparable rotation, was secured through oxidation of alcohol **4c**, thus confirming the allene configuration of **4c**.

It was of interest to examine the addition of the transient propargylstannane reagent from **1c** and $BuSnCl_3$ to an α-chiral aldehyde as a test for possible double stereodifferentiation. With a view toward applications

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(6) *Cf.* Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. G.; Balkovec, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. D. *J. Org. Chem.* **1986**, *51*, 2370.
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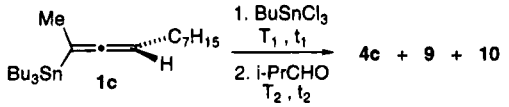
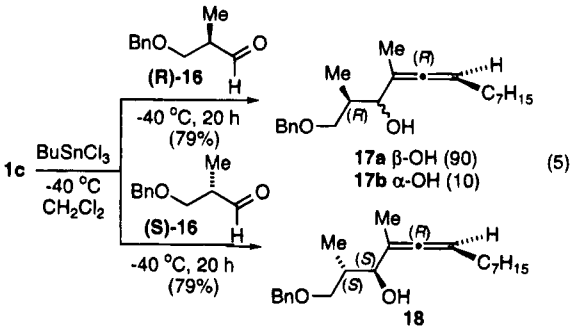
Table 1. $BuSnCl_3$-Promoted Additions to Isobutyraldehyde



entry	T_1, °C	t_1, h	T_2, °C	t_2, h	yield, %	4c:9	4c/9:10
1	−78	1	−78	2	44	94:6	>99:1
2	−78	1	−78–0	5	88	61:39	99:1
3	−78	1	−78	10	55	93:7	>99:1
4	−78	1	−78	24	69	86:14	>99:1
5	−40	0.2	−40	2	56	91:9	>99:1
6	−40	0.3	−40	5	72	92:8	>99:1

in the polyether area,[4] we selected aldehydes (*R*)- and (*S*)-**16** for these studies. Preequilibration of stannane **1c** in CH_2Cl_2 with $BuSnCl_3$ at −40 °C for 2 h followed by addition of aldehyde (*R*)-**16** and stirring for an additional 20 h led to allenylcarbinol **17a** and **17b** (90:10) in high yield along with a significant amount of byproduct **18** (20–30%) from the epimerized aldehyde (*S*)-**16**. When aldehyde (*S*)-**16** was subjected to the same protocol, the diastereomeric allenylcarbinol **18** was secured along with 20–30% of the adduct **17a** arising from aldehyde (*R*)-**16** (eq 5). In each case, the ee of the starting aldehyde was



(5)

determined to be >90% by ^1H NMR analysis of the Mosher ester derivative of the derived alcohol. Suspecting that adventitious HCl was responsible for the apparent partial racemization of aldehydes (*R*)- and (*S*)-**16**, we conducted the additions in hexane. Remarkably, both reactions were complete within 4 h at 0 °C with virtually no contamination by products arising from aldehyde epimerization. Under these conditions, aldehyde (*R*)-**16** yielded a 9:1 (corrected for the ee of stannane **1c**) mixture of *syn,syn* and *anti,anti* adducts **17a** and **17b**, whereas (*S*)-**16** gave only the *anti,syn* adduct **18**, after correction for the small amount of byproducts resulting from enantiomeric contaminants in the stannane and aldehyde reactants. Thus (*R*)-**16** would appear to be mismatched and (*S*)-**16** matched with the $BuSnCl_3$ allene adduct (**3c**) of stannane **1c**.

The stereochemistry at C-2 in the alcohol adducts **17** and **18** follows from the absolute configuration of the starting aldehydes (*R*)- and (*S*)-**16**. The allene stereochemistry can be assigned by analogy. The configuration of the carbinol center can be deduced from diagnostic chemical shifts in the ^1H NMR spectra of the (*R*)- and (*S*)-*O*-methyl mandelates **19** (from **17a**) and **20** (from **18**) as depicted in Figure 1.[6] Analysis of these spectra also provides confirmation of the allene stereochemistry.

Since both enantiomeric aldehydes (*R*)- and (*S*)-**16** afford mainly or exclusively the (*S*) propargylic alcohol products, we conclude that the reactions are reagent rather than substrate controlled. A pathway for the

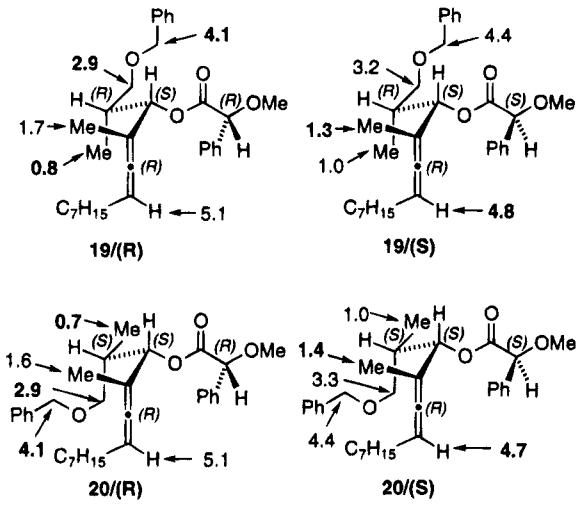


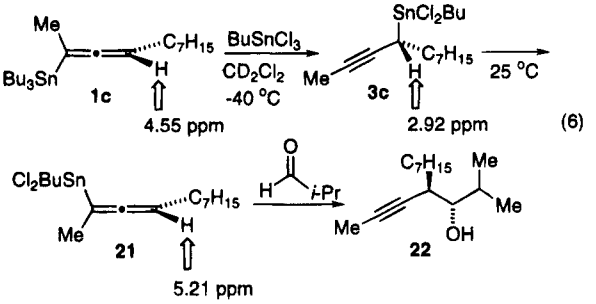
Figure 1. Diagnostic chemical shift differences for *O*-methyl mandelates. Boldface numbers indicate shielded proton signals.

sequence is proposed in Figure 2. We assume that transmetalation of allenylstannane **1c** follows an *anti* S_E2' course leading to the transient propargylic stannane **3c**. In view of the Lewis acidity of the Sn atom in such a species, it seems likely that the subsequent aldehyde addition step involves a *syn* S_E2' transition state, as pictured. As might be expected, the α-position of an aldehyde such as **16** exerts a relatively modest influence on diastereoselectivity in these additions.[9]

If diastereoselectivity were solely the result of Cram–Felkin–Ahn control, aldehyde (*R*)-**16** would be matched with stannane **3c** leading to adduct **17a** via transition state **B**. Presumably, this is the pathway through which **17a** is actually formed. However, the exclusive formation of the *anti* adduct **18** from aldehyde (*S*)-**16** suggests that chelation control may also be operative and, in this case, supersedes Cram control. Presumably the additional electropositive Sn moiety present in **A** comes from a slight excess of $BuSnCl_3$ or from the Bu_3SnCl formed in the transmetalaltion step leading to **3c**.

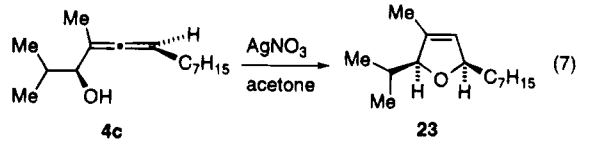
The chelation transition state **C** for aldehyde (*R*)-**16** leading to the minor adduct **17b** is evidently disfavored. This arrangement requires the near eclipsing of the adjacent C_7H_{15} and Cl substituents of the propargylstannane **3c**. In **B** these groups are staggered. We presume that the Cl and carbonyl O adopt apical orientations on the 5-coordinate tin atom.[10]

Experimental support for the transmetalation segment of the foregoing scenario was provided by a ^1H NMR study. Accordingly, when stannane **1c** in CD_2Cl_2 at −40 °C was treated with a slight excess of $BuSnCl_3$, the signal at 4.55 ppm for the allenic proton of **1c** was replaced within 1 min by a signal at 2.92 ppm, attributable to the propargylic proton of stannane **3c**, plus a signal at 2.66 ppm arising from the α-CH_2 protons of the excess $BuSnCl_3$. The spectrum was unchanged over 2 h at −40 °C. When the sample was warmed to 25 °C, a new signal attributable to the allenic proton of stannane **21** appeared at 5.21 ppm over a period of 5 h.[11] Concomitantly, the signal at 2.92 ppm diminished in proportion until an apparent equilibrium was reached favoring **21** by *ca.* 10:1 or better. Addition of isobutyraldehyde to this sample led to the propargylic alcohol **22** along with a small amount of allenylcarbinol **4c**.



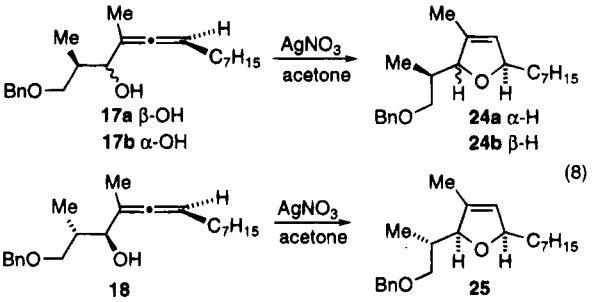
(6)

In the second phase of these studies, we examined the conversion of allenylcarbinols **4c**, **17**, and **18** to the corresponding *cis*-2,5-dihydrofurans by treatment with $AgNO_3$ in acetone.[2] These cyclizations proceeded smoothly and stereospecifically as judged by the ^1H NMR spectra of the products. Thus, allenylcarbinol **4c**, contaminated with 8% of the *anti* epimer, afforded a like mixture of the *cis*-2,5-dihydrofuran **23** and its *anti* epimer after exposure to $AgNO_3$ for 2 h (eq 7).



(7)

The 90:10 mixture of allenylcarbinols **17a** and **17b** was converted to 2,5-dihydrofurans **24a** and **24b**, whereas **18** gave only **25** after correction for the inseparable diastereomeric allenylcarbinol impurities arising from enantiomeric contaminants in the allenylstannane and aldehyde starting materials (eq 8).



(8)

These experiments confirm the potential of this methodology for the synthesis of polyether natural products. Additional studies along these lines will be reported in due course.

Experimental Section[12]

(*S*)-2-(Tri-*n*-butylstannyl)-2,3-undecadiene (1c). To a solution of alcohol **7** (1.50 g, 8.90 mmol, 96% ee) in CH_2Cl_2 (35 mL) at −78 °C was added triethylamine (3.00 mL, 18.0 mmol) with stirring. After 5 min, methanesulfonyl chloride (1.33 mL,

(9) Such is the case with chiral allylboronates and boranes. *Cf.* Roush, W. R.; Palkowitz, A. D.; Palmer, M. A. J. *J. Org. Chem.* **1987**, *52*, 316. Brown, H. C.; Bhat, K. S.; Randad, R. S. *J. Org. Chem.* **1987**, *52*, 319.

(10) Jastrzebski, J. T. B. H.; Van Koten, G. *Adv. Organomet. Chem.* **1993**, *35*, 241.

(11) For a related study with allylic stannanes and $SnCl_4$, see: Naruta, Y.; Nishigaichi, Y.; Maruyama, K. *Tetrahedron* **1989**, *45*, 1067.

(12) The ^1H (at 400 MHz) and ^{13}C (at 100.6 MHz) NMR spectra were recorded in $CDCl_3$. For typical experimental protocols, see: Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1991**, *56*, 960.

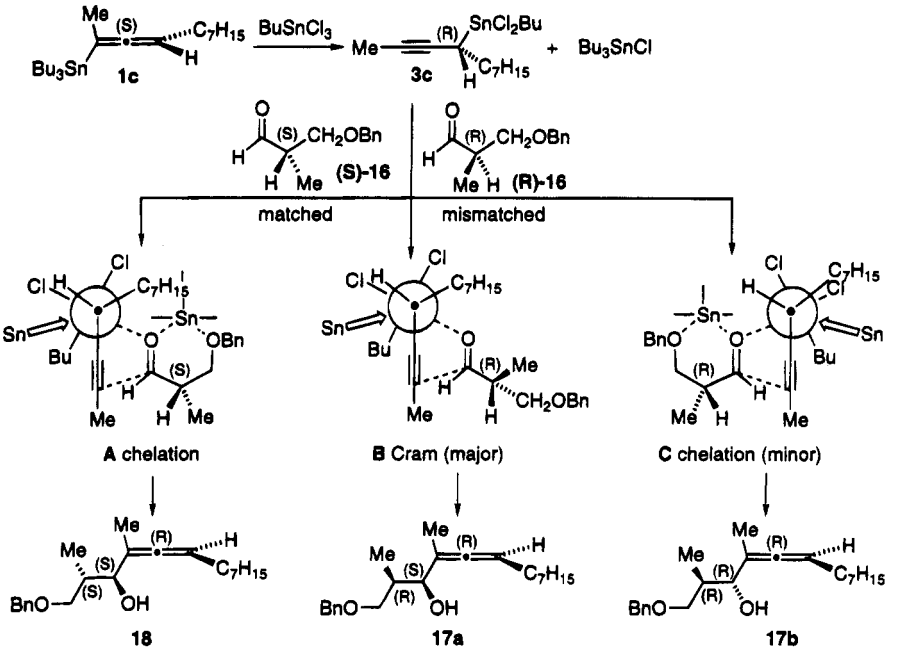


Figure 2. Reaction pathway for the formation of transient propargylic stannane **3c** and its addition to aldehydes (*S*)-**16** and (*R*)-**16**. The Newman segment in A-C projects the propargylic Sn-C bond.

17.2 mmol) was added, and the resulting solution was stirred for 1 h (TLC assays show product and starting material spots to be coincidental at 30% Et_2O in hexane). The mixture was quenched with saturated aqueous $NaHCO_3$ solution, extracted with Et_2O, dried over Na_2SO_4, and concentrated under reduced pressure to yield mesylate **8** as a light yellow oil that was used without further purification.

To a solution of diisopropylamine (1.63 mL, 11.6 mmol) in THF (35 mL) at 0 °C was added *n*-BuLi (4.45 mL, 11.1 mmol, 2.5 M in hexane). After 5 min, *n*-Bu_3SnH (3.00 mL, 11.1 mmol) was added, and after 25 min, the mixture was cooled to −78 °C. To this was added $CuBr{\cdot}SMe_2$ (2.30 g, 11.1 mmol) in one portion with stirring. After 35 min, a solution of mesylate **8** in THF (5 mL) was added; the mixture was stirred for 15 min and then poured into a rapidly stirring 9:1 mixture of saturated aqueous NH_4Cl/concd NH_4OH solution (50 mL) and extracted with Et_2O. The ether extract was washed with additional portions of aqueous NH_4Cl/NH_3 solution until the layers became colorless. The organic extract was then dried over $MgSO_4$ and concentrated under reduced pressure to give a light yellow oil. Purification by flash column chromatography on deactivated silica gel (Et_3N) afforded allenylstannane **1c** (3.89 g, 99%) as a colorless oil contaminated with hexabutylditin. Further purification by treatment with AgOAc (1.5 equiv) in THF at rt gave 2.50 g (64%) of pure material (>99% according to GC analysis): IR (film) 1933 cm^{-1}; ^1H NMR δ 4.57−4.53 (m, 1H), 1.91−1.84 (m, 2H), 1.78 (d, J = 2.9 Hz, 3H), 1.60−1.40 (m, 8H), 1.40−1.20 (m, 20H), 0.88 (t, J = 8.2 Hz, 3H), 0.87 (t, J = 7.3 Hz, 9H); ^{13}C NMR δ 202.8, 87.6, 81.2, 31.9, 30.0, 29.2, 29.2, 29.0, 27.3, 22.7, 19.2, 14.1, 13.7, 9.9; $[\alpha]^{23}_D$ 82.7 (*c* 1.59, $CHCl_3$).

(3*S*,5*R*)-2,4-Dimethyl-4,5-tridecadien-3-ol (4c). To a solution of allenylstannane **1c** (50.0 mg, 0.113 mmol) in CH_2Cl_2 (2 mL) at −40 °C was added *n*-butyltin trichloride (20 μL, 0.113 mmol) with stirring. After 20 min, a solution of isobutyraldehyde (0.128 mL, 0.141 mmol) in CH_2Cl_2 (0.2 mL) was added. The solution was stirred at −40 °C for 5 h and then saturated aqueous NH_4Cl solution was added. Upon being warmed to rt, the mixture was extracted with Et_2O and dried over Na_2SO_4. To this was added triethylamine (~2 mL), and after being stirred for 10 min, the slurry was filtered through a pad of Celite and the filtrate was concentrated to give a yellow oil. Purification by flash column chromatography gave alcohol **4c** (18 mg, 72%) as a clear oil: IR (film) 3422, 1946, 1728 cm^{-1}; ^1H NMR δ 5.24 (dq, J = 9.3, 2.8 Hz, 1H), 3.70 (dd, J = 5.3, 2.3 Hz, 1H), 1.98 (apparent q, J = 6.9, 2H), 1.82−72 (m, 1H), 1.65 (d, J = 2.9 Hz, 3H), 1.53 (d, J = 5.3, 1H), 1.40−1.20 (m, 10H), 0.95 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.7 Hz, 3H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR δ 199.7, 102.5, 94.1, 31.8, 31.2, 29.3, 29.2, 29.1, 29.0, 22.6, 19.6, 16.3, 15.4, 14.1. Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.08; H, 12.55.

(*R*)-(−)-2-Undecyn-4-ol (7). To a solution of DMSO (5.60 mL, 71.4 mmol) in CH_2Cl_2 at −78 °C was slowly added oxalyl chloride (4.54 mL, 35.8 mmol) with stirring. After 15 min, a solution of 2-undecyn-4-ol[13] (5.00 g, 29.8 mmol) in CH_2Cl_2 (20 mL) was added followed by slow addition of triethylamine (21.7 mL). The resulting cloudy, white mixture was stirred for 30 min with monitoring by TLC. When the reaction was judged complete, water was added and the mixture was allowed to warm to rt and extracted with Et_2O. The combined extracts were washed with 10% aqueous HCl, saturated aqueous $NaHCO_3$, and brine. The extracts were dried over $MgSO_4$ and concentrated under reduced pressure, affording a light yellow oil. Purification by flash column chromatography (20% Et_2O in hexane) gave 2-undecyn-4-one (4.00 g, 80%) as a light yellow oil: IR (film) 2222, 1679 cm^{-1}; ^1H NMR δ 2.47 (t, J = 7.6 Hz, 2H), 1.97 (t, J = 0.70 Hz, 3H), 1.65−1.55 (m, 2H), 1.36−1.15 (m, 8H), 0.84 (t, J = 6.7 Hz, 3H); ^{13}C NMR δ 188.4, 89.7, 80.2, 45.4, 43.9, 31.6, 28.9, 28.9, 24.0, 22.6, 22.1, 14.0, 3.96. Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.55; H, 10.93.

To a stirring solution of Chirald (9.18 g, 32.4 mmol) in Et_2O (500 mL) at 0 °C was added fresh lithium aluminum hydride (14.4 mL, 1.0 M in THF, 14.4 mmol) dropwise. Upon completion of the addition the solution was cooled to −78 °C to give a white slurry. If stirring ceased or became difficult, excess Et_2O (~200 mL) was added. To the vigorously stirring slurry was added a solution of 2-undecyn-4-one (2.00 g, 12.0 mmol) in Et_2O (50 mL) over 100 min. It is important to maintain slow addition with vigorous stirring. The progress of the reaction was monitored by TLC. After 2 h, 10% aqueous HCl was added, and the reaction mixture was allowed to warm to rt. Then additional 10% aqueous HCl was added until the mixture became clear. The mixture was extracted with Et_2O and washed with saturated aqueous $NaHCO_3$ and brine. The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to give alcohol **7** (2.00 g, 99%) as a light yellow oil. This product, judged to be pure on the basis of its ^1H NMR spectrum, was used directly. An analytical sample was prepared by flash column chromatography

(13) Baudin, J.-B.; Bkouche-Waksman, I.; Julia, S. A.; Pascard, C.; Wang, Y. *Tetrahedron* **1991**, *47*, 3353.

(30% Et_2O in hexane): IR (film) 3358, 2237 cm^{-1}; ^1H NMR δ 4.24 (ddq, J = 6.6, 4.5, 2.1 Hz, 1H), 2.31 (s, 1H), 1.77 (d, J = 2.1 Hz, 1H), 1.65–1.52 (m, 2H), 1.37–1.25 (m, 2H), 1.25–1.12 (m, 10H), 0.81 (t, J = 6.7 Hz, 3H); ^{13}C NMR δ 80.6, 80.6, 62.6, 38.1, 31.8, 29.2, 29.2, 25.2, 22.6, 14.0, 3.40; $[\alpha]^{23}_D$ −1.35 (c 1.41, $CHCl_3$). Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.54; H, 11.94.

The *O*-methyl mandelate derivative was prepared as follows. To a solution of alcohol **7** in CH_2Cl_2 (2 mL) at rt was added 1,3-dicyclohexylcarbodiimide (37 mg, 0.018 mmol), 4-(*N*, *N*-dimethylamino)pyridine (11.0 mg, 0.009 mmol), and (*R*)-methoxyphenylacetic acid (30.0 mg, 0.018 mmol). The reaction was monitored by TLC and was judged complete after 15 min. The reaction mixture was concentrated and purified by flash column chromatography (30% Et_2O in hexane) to give a clear oil. GC analysis showed two peaks of 98:2 ratio, indicating an *ee* of 96%: ^1H NMR δ 7.45–7.42 (m, 2H), 7.40–7.28 (m, 3H), 5.34 (ddq, J = 6.7, 4.5, 2.1 Hz, 1H), 4.76 (s, 1H), 3.41 (s, 3H), 1.73 (d, J = 2.1 Hz, 3H), 1.73–1.63 (m, 2H), 1.34–1.22 (m, 10H), 0.86 (t, J = 6.8 Hz, 3H); ^{13}C NMR δ 169.9, 135.9, 128.6, 128.5, 127.2, 82.8, 82.0, 76.1, 65.5, 57.4, 34.9, 31.7, 29.1, 29.0, 24.9, 22.6, 14.0, 2.49. Anal. Calcd for $C_{20}H_{28}O_3$: C, 75.91; H, 8.92. Found: C, 75.95; H, 8.96.

(*R*)-4-[(Tri-*n*-butylstannyl)methoxy]-2-undecyne (11). To a slurry of NaH (113.0 mg, 4.69 mmol) in dry DMSO (5 mL) at rt was added alcohol **7** (657 mg, 3.91 mmol) with evolution of H_2. After 10 min, (iodomethyl)tri-*n*-butylstannane[14] (2.02 g, 4.69 mmol) was added, and the resulting mixture was stirred overnight. The mixture was then diluted with aqueous HCl, and the aqueous layer was extracted with Et_2O. The organic extract was dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash column chromatography gave the ether **11** (1.55 g, 84%) as a clear oil: IR (film) 2239 cm^{-1}; ^1H NMR δ 3.98 (d, J = 10.2 Hz, 1H), 3.76–3.59 (m, 1H), 3.56 (d, J = 10.2 Hz, 1H), 1.84 (d, J = 2.0 Hz, 3H), 1.67–1.50 (m, 2H), 1.50–1.40 (m, 6H), 1.38–1.10 (m, 22H), 0.876 (t, J = 8.2 Hz, 3H), 0.871 (t, J = 7.3 Hz, 9H); ^{13}C NMR δ 80.9, 79.1, 74.0, 59.2, 36.0, 31.8, 29.4, 29.2, 29.1, 27.5, 25.4, 22.7, 14.0, 13.7, 9.04, 3.57; $[\alpha]^{23}_D$ 34.0 (c 0.69, $CHCl_3$).

(*R*)-2-Methyl-2,3-undecadien-1-ol (12). To a solution of ether **11** (0.658 g, 1.39 mmol) in THF (10 mL) at −78 °C was slowly added *n*-BuLi (0.61 mL, 2.5 M in hexane, 1.53 mmol), with stirring. After 12 h, the reaction was quenched with saturated aqueous NH_4Cl, extracted with Et_2O, dried over Na_2SO_4, and concentrated to give a yellow oil. Purification by flash column chromatography (30% Et_2O in hexane) gave allenylcarbinol **12** (0.148 g, 58%) as a clear oil: IR (film) 3320, 1967 cm^{-1}; ^1H NMR δ 5.21 (ddq, J = 9.4, 5.9, 2.9 Hz, 1H), 3.80 (m, 2H), 1.95 (q, J = 6.8 Hz, 2H), 1.80 (t, J = 1.4 Hz, 1H) 1.66 (d, J = 2.7 Hz, 3H), 1.40–1.00 (m, 10H), 0.84 (t, J = 6.6 Hz, 3H); ^{13}C NMR δ 199.3, 100.3, 94.1, 63.9, 62.6, 31.8, 29.2, 29.2, 29.1, 25.6, 15.7, 14.0. Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 78.81; H, 12.07.

(*R*)-2-Methyl-2,3-undecadienal (13). To a solution of alcohol **12** (0.423 g, 2.32 mmol) in CH_2Cl_2 (5 mL) at rt was added 1,1,1-triacetoxy-1,1-dihydro-1,2-benzodooxol-3(1*H*)-one[8] (1.48 g, 3.48 mmol) with stirring. After 20 min, the mixture was filtered through a pad of silica gel. Purification by flash column chromatography gave aldehyde **13** (257 mg, 80%) as a yellow oil: IR (film) 1946, 1684 cm^{-1}; ^1H NMR δ 9.49 (s, 1H), 5.64 (dq, J = 6.9, 3.1 Hz, 1H), 2.13 (q, J = 7.2, 2H), 1.74 (d, J = 2.6, 3H), 1.50–1.10 (m, 10H), 0.86 (t, J = 6.4, 3H); ^{13}C NMR δ 218.5, 192.9, 106.4, 95.6, 31.8, 29.0, 28.9, 27.9, 22.6, 14.0, 10.9.

(5*R*,3*R*)- and (5*R*,3*S*)-2,4-Dimethyl-4,5-tridecadien-3-ol (14). To a stirring mixture of magnesium turnings (0.127 g, 5.22 mmol) in Et_2O (1 mL) at rt was added dropwise 2-bromopropane (0.49 mL, 5.22 mmol). The mixture was allowed to reflux (external heating was applied when necessary) until the magnesium dissolved. The solution was added dropwise to aldehyde **13** (0.200 g, 1.11 mmol) in Et_2O (10 mL) at −78 °C with stirring. After 20 min, the solution was allowed to warm to 0 °C. Upon completion of the reaction (as determined by TLC) 10% aqueous HCl was added. The mixture was extracted with Et_2O, dried over Na_2SO_4, and concentrated to give a yellow oil. Purification by flash column chromatography gave alcohol **14**, a mixture of diastereomers (162 mg, 65%), as a clear oil: IR (film) 3422, 1946, 1728 cm^{-1}; ^1H NMR δ 5.24 (dq, J = 9.3, 2.8 Hz, 1H), 3.70 (dd, J = 5.3, 2.3 Hz, 1H), 1.98 (apparent q, J = 6.9, 2H), 1.82–72 (m, 1H), 1.65 (d, J = 2.9 Hz, 3H), 1.53 (d, J = 5.3, 1H), 1.40–1.20 (m, 10H), 0.95 (d, J = 6.8 Hz, 3H), 0.88 (d, J = 6.7 Hz, 3H), 0.86 (t, J = 6.6 Hz, 3H); ^{13}C NMR δ 199.7, 102.5, 94.1, 31.8, 31.2, 29.3, 29.2, 29.1, 29.0, 22.6, 19.6, 16.3, 15.4, 14.1. Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.19; H, 12.50.

(*R*)-2,4-Dimethyl-4,5-tridecadien-3-one (15). A. From Alcohol 4c. The procedure described for aldehyde **13** was employed with alcohol **4c** (0.100 g, 0.446 mmol) to afford ketone **15** (60 mg, 61%) as a clear oil: IR (film) 1946, 1679 cm^{-1}; ^1H NMR δ 5.42–5.47 (m, 1H), 3.26 (hept, J = 6.9 Hz, 1H), 2.11 (apparent q, J = 8.0, 2H), 1.73 (d, J = 2.7 Hz, 3H), 1.47–1.39 (m, 2H), 1.33–1.25 (m, 8H), 1.03 (d, J = 2.3 Hz, 3H), 1.01 (d, J = 2.3 Hz, 3H), 0.85 (t, J = 6.6 Hz, 3H); ^{13}C NMR δ 211.5, 206.1, 102.8, 94.2, 35.8, 31.8, 29.1, 29.0, 28.2, 22.6, 19.5, 19.4, 14.0, 13.8; $[\alpha]^{23}_D$ −55.7 (c 0.10, $CHCl_3$). Anal. Calcd for $C_{15}H_{26}O$: C, 81.02; H, 11.79. Found: C, 81.15; H, 11.73.

B. From Alcohol 14. The procedure described for aldehyde **13** was followed, affording ketone **15** (36.0 mg, 60%) as a clear oil: $[\alpha]^{23}_D$ −59.3 (c 1.19, $CHCl_3$).

(2*R*,3*S*,5*R*)-1-(Benzyloxy)-2,4-dimethyl-4,5-tridecadien-3-ol (17a). To a solution of allenylstannane **1c** (50.0 mg, 0.113 mmol, 90% ee) in hexane (1 mL) at −40 °C was added *n*-$BuSnCl_3$ (20 μL, 0.113 mmol) with stirring. After 1 h, a solution of aldehyde (*R*)-**16** (19.5 mg, 0.110 mmol, ee 94%) in hexane (0.2 mL) was added. The solution was allowed to stir at −40 °C for 5 min and then warmed to 0 °C. After 4 h, saturated aqueous NH_4Cl was added, and the mixture was extracted with Et_2O and dried over Na_2SO_4. To this was added triethylamine (~2 mL), and after beng stirred for 10 min, the slurry was filtered through a pad of Celite and the filtrate was concentrated to give a yellow oil. Purification by flash column chromatography afforded 25.0 mg (67%) of an 84:8:8 mixture of alcohol **17a**, diastereomeric alcohols **18** (from (*S*)-**16**) and *ent*-**18** (from *ent*-**1c**)), and *anti* adduct **17b** as a clear oil: IR (film) 3462, 1964 cm^{-1}; ^1H NMR δ 7.33–7.25 (m, 5H), 5.31–5.29 (m, 1H), 4.51 (dd, J = 12.0, 4.8 Hz, 2H), 4.15–4.10 (m, 1H), 3.56 (dd, J = 6.7, 2.2 Hz, 1H), 3.45 (dd, J = 5.8, 3.2 Hz, 1H), 3.25 (d, J = 3.4 Hz, 1H), 2.03–1.94 (m, 3H), 1.65 (d, J = 2.9 Hz, 3H), 1.40–1.15 (m, 10H), 0.87 (d, J = 7.0 Hz, 3H), 0.87 (t, J = 7.2 Hz, 3H); ^{13}C NMR δ 199.3, 138.5, 128.6, 127.6, 127.5, 102.3, 95.1, 73.9, 73.3, 72.1, 36.3, 31.8, 29.3, 29.2, 29.1, 29.0, 22.6, 16.0, 14.1, 10.1. Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 80.06; H, 10.35.

(2*S*,3*S*,5*R*)-1-(Benzyloxy)-2,4-dimethyl-4,5-tridecadien-3-ol (18). The above procedure was followed with allenylstannane **1c** (50.0 mg, 0.113 mmol) in hexane (1 mL) at −40 °C, *n*-$BuSnCl_3$ (20 μL, 0.113 mmol) and a solution of aldehyde (*S*)-**16** (19.5 mg, 0.110 mmol) in hexane (0.2 mL) yielding a yellow oil. Purification by flash column chromatography afforded 24.5 mg (66%) of a 94:6 mixture of alcohol **18** and diastereomers **17a** (from (*R*)-**16**) and *ent*-**17a** (from *ent*-**1c**) as a clear oil: IR (film) 3462, 1964 cm^{-1}; ^1H NMR δ 7.35–7.25 (m, 5H), 5.08–5.09 (m, 1H), 4.5 (s, 2H), 3.93 (dd, J = 7.6, 2.7 Hz, 1H), 3.60 (dd, J = 9.1, 4.6 Hz, 1H), 3.50 (dd, J = 9.1, 7.0 Hz, 1H), 3.26 (d, J = 3.4 Hz, 1H), 2.05–1.90 (m, 3H), 1.66 (d, J = 2.9 Hz, 3H), 1.40–1.10 (m, 10H), 0.89 (d, J = 7.0 Hz, 3H), 0.86 (t, J = 7.0 Hz, 3H); ^{13}C NMR δ 201.5, 137.9, 128.4, 127.7, 127.6, 100.9, 91.9, 78.1, 74.5, 73.5, 36.7, 31.9, 29.4, 29.2, 29.1, 22.7, 14.5, 14.3, 14.1. Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 79.86; H, 10.42.

The *O*-methyl mandelates **19** and **20** were prepared as described for alcohol **4c**. Diagnostic ^1H NMR signals:

19/(*R*): δ 5.15–5.05 (m, 1H), 4.11 (s, 1H), 2.91 (dd, J = 9.0, 7.2 Hz, 1H), 1.61 (d, J = 2.8 Hz, 3H).

19/(*S*): δ 4.85–4.80 (m, 1H), 4.37 (d, J = 4.0 Hz, 1H), 3.24 (dd, J = 9.0, 7.2 Hz, 1H), 1.33 (d, J = 2.9 Hz, 3H).

20/(*R*): δ 5.15–5.05 (m, 1H), 4.15 (d, J = 4.0 Hz, 1H), 2.83 (dd, J = 9.0, 7.2 Hz, 1H), 1.60 (d, J = 2.8 Hz, 3H).

(14) Seitz, D. E.; Carroll, J. J.; Cartaya M., C. P.; Lee, S.-H.; Zapata, A. *Synthetic Commun.* **1983**, *13*, 129.

20/(S): δ 4.80–4.70 (m, 1H), 4.39 (s, 1H), 3.25 (dd, *J* = 9.0, 7.2 Hz, 1H), 1.40 (d, *J* = 2.9 Hz, 3H).

(2S,5R)-2-Isopropyl-3-methyl-5-heptyl-2,5-dihydrofuran (23). To a stirring solution of alcohol **4c** (33.0 mg, 0.147 mmol) in acetone (2 mL) at rt was added $AgNO_3$ (3.50 mg, 0.0295 mmol). The mixture was stirred protected from light for 2 h, whereupon the reaction was judged complete by TLC and the solvent was distilled under reduced pressure. Purification of the residue by flash column chromatography gave the dihydrofuran **23** (25.0 mg, 78%) as a clear oil: ^{1}H NMR δ 5.41 (d, *J* = 1.8 Hz, 1H), 4.61–4.59 (br m, 1H), 4.49–4.46 (br m, 1H), 1.77 (dhept, *J* = 6.9, 2.4 Hz, 1H), 1.62 (dd, *J* = 2.8, 1.6 Hz, 3H), 1.50–1.47 (m, 2H), 1.20–1.30 (m, 10H), 1.00 (d, *J* = 6.9 Hz, 3H), 0.86 (t, *J* = 6.7 Hz, 3H), 0.74 (d, *J* = 6.8 Hz, 3H); ^{13}C NMR δ 137.4, 125.3, 91.6, 84.7, 36.6, 31.8, 30.0, 29.7, 29.2, 25.8, 22.6, 19.8, 15.3, 14.1, 12.7. Anal. Calcd for $C_{15}H_{28}O$: C, 80.29; H, 12.58. Found: C, 80.36; H, 12.50.

(2S,5R)-2-[(S)-1-Methyl-2-(benzyloxy)ethyl]-3-methyl-5-heptyl-2,5-dihydrofuran (24a). The procedure described for dihydrofuran **23** was followed with allenylcarbinol **17a/17b** (35.0 mg, 0.106 mmol of a 90:10 mixture) affording dihydrofuran **24a**, contaminated with diastereomers **24b** and **25**/*ent*-**25** (30.0 mg, 86% of an 82:8:10 mixture), as a clear oil: ^{1}H NMR δ 7.35–7.24 (m, 5H) , 5.43 (d, *J* = 1.6 Hz, 1H), 4.77–4.70 (m, 1H), 4.63–4.60 (m, 1H), 4.57 (d, *J* = 12.0 Hz, 1H), 4.58 (d, *J* = 12.0 Hz, 1H), 3.55 (dd, *J* = 8.9, 7.2 Hz, 1H), 3.39 (dd, *J* = 8.9, 7.2 Hz, 1H), 1.98 (dq, *J* = 7.0, 1.9 Hz, 1H), 1.62 (d, *J* = 1.1 Hz, 3H), 1.50–1.20 (t, *J* = 6.6 Hz, 12H), 0.87 (t, *J* = 6.6 Hz, 3H), 0.75 (d, *J* = 6.9 Hz, 3H); ^{13}C NMR δ 138.7, 136.8, 128.3, 127.6, 127.4, 125.4, 87.1, 85.1, 73.9, 73.2, 36.5, 35.4, 31.8, 29.7, 29.3, 25.9, 22.7, 14.1, 12.4, 10.3. Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 79.92; H, 10.38.

(2S,5R)-2-[(R)-1-Methyl-2-(benzyloxy)ethyl]-3-methyl-5-heptyl-2,5-dihydrofuran (25). The procedure described for dihydrofuran **23** was followed with allenylcarbinol **18** (60.0 mg, 0.181 mmol) affording dihydrofuran **25**, contaminated with diastereomers **24a**/*ent*-**24a** (55.0 mg, 92% of a 90:10 mixture), as a clear oil: ^{1}H NMR δ 7.35–7.24 (m, 5H), 5.39 (d, *J* = 1.8 Hz, 1H), 4.60–4.48 (m, 2H), 4.45 (d, *J* = 1.6 Hz, 2H), 3.45 (dd, *J* = 9.30, 5.0 Hz, 1H), 3.26 (dd, *J* = 9.2, 8.2 Hz, 1H), 2.07–2.00 (m, 1H), 1.67 (d, *J* = 1.0 Hz, 3H), 1.50–1.30 (m, 2H), 1.30–1.15 (m, 10H), 1.10 (d, *J* = 7.0 Hz, 3H), 0.87 (t, *J* = 6.5 Hz, 3H); ^{13}C NMR δ 138.7, 137.3, 128.3, 127.5, 127.4, 125.3, 89.7, 84.7, 73.1, 71.8, 36.6, 36.1, 31.8, 29.7, 29.3, 25.8, 22.7, 15.5, 14.1, 12.9. Anal. Calcd for $C_{22}H_{34}O_2$: C, 79.95; H, 10.37. Found: C, 79.68; H, 10.42.

^{1}H NMR Study. An NMR tube was purged with N_2 and then charged with allenylstannane **1c** (10.0 mg, 0.0227 mmol) and degassed CD_2Cl_2 (1.0 mL). The ^{1}H NMR (500 MHz) spectrum of this sample was recorded at −40 °C. The cold sample was then treated with *n*-$BuSnCl_3$ (4.0 μL, 0.0239 mmol) and spectra were recorded at 1, 30, and 120 min. After 2 h, the sample was allowed to warm to rt, and ^{1}H NMR spectra were recorded at 1, 2, 5, 9, and 15 h. After 48 h, the sample was treated with isobutyraldehyde (1.1 equiv). After 3 h, the reaction was quenched and the product, homopropargylic alcohol **22**, was isolated. Analysis by GC and ^{1}H NMR showed only a trace amount of allenyl alcohol **4c**.

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Supporting Information Available: ^{1}H NMR spectra for key intermediates and products; stacked plots of **1c** → **3c** (Figure 1) and **3c** → **21** (Figure 2) (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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