over magnesium sulfate, filtered, and concentrated in vacuo to give 120 mg of crude **30** and benzyloxazolidinone. Flash chromatography (50:1 hexane–EtOAc) gave 52 mg (95%) of pure **30**: ^{1}H NMR ($CDCl_3$) δ 7.29–7.39 (m, 5), 5.10 (s, 2, CH_2Ph), 4.92 (s, 1, =CHH), 4.74 (s, 1, =CHH), 2.34 (t, 2, J = 7.7, CH_2CO), 2.25 (m, 1, $CHCH_3$), 1.75 (ddt, 1, J = 7.3, 13.7, 7.6, C*H*HCH), 1.74 (ddt, 1, J = 7.4, 13.7, 7.6, CH*H*CH), 1.04 (d, 3, J = 6.8), 1.02 (s, 9); ^{13}C NMR ($CDCl_3$) δ 173.7, 163.1, 136.1, 128.5, 128.3, 128.2, 105.2, 66.1, 36.6, 33.4 (2 C), 32.7, 28.8, 23.6; IR (neat) 1740 cm^{-1}; $[\alpha]_D$ −16.6° (c 0.247, $CHCl_3$).

Benzyl 5-Oxo-4,6,6-trimethylheptanoate (31).[23] A solution of 40 mg (0.14 mmol) of **30** in 3 mL of CH_2Cl_2 was cooled to −78 °C, and O_3 was passed through the solution for 1 min. The reaction was quenched by 1.4 equiv of dimethyl sulfide, and the solution was stirred at 25 °C for 30 min. The solution was diluted with 2 mL of water and extracted twice with CH_2Cl_2. The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give 42 mg of crude **31**. Flash chromatography (50:1 hexane–EtOAc) gave 34 mg (85%) of pure **31**: ^{1}H NMR ($CDCl_3$) δ 7.30–7.39 (m, 5), 5.11 (s, 2, CH_2Ph), 3.05 (br sext, 1, J = 7.0, $CHCH_3$), 2.30 (t, 1, J = 7.5, CHHCO), 2.29 (t, 1, J = 7.3, CHHCO), 1.94 (dddd, 1, J = 7.3, 7.5, 7.1, 14.0, CHHCH), 1.68 (dddd, 1, J = 7.3, 7.5, 7.1, 14.0, CHHCH), 1.10 (s, 9), 1.04 (d, 3, J = 6.8); ^{13}C NMR ($CDCl_3$) δ 173.0, 135.8, 128.5, 128.3, 128.2, 66.2, 44.6, 38.4, 31.8, 28.8, 26.0, 18.2; IR (neat) 1740, 1705 cm^{-1}; $[\alpha]_D$ −18.8° (c 0.268, $CHCl_3$); $[\theta]$ +397° at 285 nm.

(*S*)-*sec*-Butyl *tert*-Butyl Ketone (32). *t*-BuLi (2.0 equiv) was added dropwise during 20 min to a solution of (*S*)-(+)-2-methylbutyric acid (0.5 mL, 4.5 mmol, 98% pure) in 10 mL of anhydrous ether at 0 °C. The mixture was stirred overnight, and the reaction mixture was hydrolyzed by pouring it slowly into 15 mL of water. The organic phase was separated, and the aqueous layer was extracted twice with 15 mL of ether. The combined organic layers were washed with brine, dried ($MgSO_4$), and concentrated in vacuo to give 0.6 g of crude **32** as a clear yellow liquid. Distillation of the crude product at 20 Torr gave 0.35 g (45%) of ketone **32**, bp 60–65 °C: ^{1}H NMR δ 2.91 (br sext, 1, J = 7.0), 1.62 (m, 1), 1.33 (m, 1), 1.15 (s, 9), 1.03 (d, 3, J = 6.7), 0.84 (t, 3, J = 7.4); $[\alpha]_D$ +27.7° (c 0.132, $CHCl_3$); $[\alpha]_D$ −29.6° for the *R* enantiomer,[27] $[\theta]$ +280° at 308 nm.

Registry No. **1b**, 90719-30-5; **4**, 109299-92-5; **5**, 134178-33-9; **6**, 134178-34-0; **7**, 134178-35-1; **9**, 134178-36-2; **10**, 134178-37-3; **12**, 134178-38-4; **13**, 134178-39-5; **14** (isomer 1), 134178-40-8; **14** (isomer 2), 134178-41-9; **15**, 134178-42-0; **16**, 134178-43-1; **18**, 134178-44-2; **19**, 134178-45-3; **20**, 134178-46-4; **21**, 2043-21-2; **22**, 134178-47-5; **23**, 134178-48-6; **24**, 134178-49-7; **25**, 134178-50-0; **26**, 90719-27-0; **27a**, 134178-51-1; **27b**, 134178-52-2; **28**, 134178-53-3; **29**, 134178-54-4; **30**, 134178-55-5; **31**, 134178-56-6; **32**, 134178-57-7; Me_2AlCl, 1184-58-3; methylenecyclopentane, 1528-30-9; isobutylene, 115-11-7; 2-ethyl-1-butene, 760-21-4; allyltrimethylsilane, 762-72-1; ethylidenecyclohexane, 1003-64-1; (*E*)-3,4,4-trimethyl-2-pentene, 39761-57-4; 1-methylcycloheptene, 1453-25-4; (*S*)-(+)-2-methylbutyric acid, 1730-91-2.

Supplementary Material Available: Experimental details for the ene reactions of the achiral oxazolidinones **4** and **21** (3 pages). Ordering information is given on any current masthead page.

(27) Brown, H. C.; Srebnik, M.; Bakshi, R. K.; Cole, T. E. *J. Am. Chem. Soc.* **1987**, *109*, 5420.

Synthesis of Enantioenriched α-Hydroxy-α-allenylacetic Acids by [2,3] Wittig Rearrangement of α-(Propargyloxy)acetates

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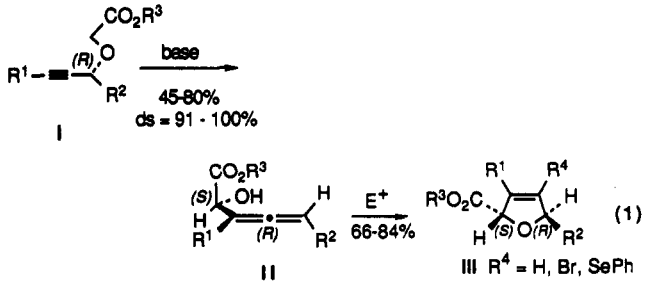
Optically active (*R*)-(propargyloxy)acetic esters **5**, available in ca. 90% ee through reduction of alkynones **2** with Chirald–$LiAlH_4$ followed by alkylation with chloroacetic acid and esterification with CH_2N_2, undergo highly stereoselective [2,3] rearrangement upon treatment with LDA in THF at −78 °C followed by Cp_2ZrCl_2 to afford α(*S*)-hydroxy-β(*R*)-allenic esters **7** with complete transfer of chirality and >90% diastereoselectivity. Upon treatment with TESOTf in Et_3N the (*R*)-(propargyloxy)acetic esters **5** afford the diastereomeric α-(*R*)-hydroxy-β-(*R*)-allenic esters **8** stereoselectively. Both hydroxy esters **7** and **8** cyclize stereospecifically to *trans*- and *cis*-2,5-dihydrofurans **13–15** and **17–19** upon treatment with $AgNO_3$–$CaCO_3$, PhSeCl, or NBS.

We recently showed that enantioenriched α-hydroxy-α-allenylacetic acids II can be readily prepared by [2,3] Wittig rearrangement of chiral α-(propargyloxy)acetates (eq 1).[1] The reaction proceeds with excellent diastereoselectivity, especially when Cp_2ZrCl_2 is added to chelate the ether and carboxylic groupings.[2] Cyclization of the allenyl alcohol products II is readily effected with $AgNO_3$, NBS, or PhSeCl to give the tri- or tetrasubstituted 2,5-dihydrofurans III stereospecifically.[3] Such furans are of interest as subunits of various natural products.[4]



(1)

Propargylic [2,3] rearrangements differ from their allylic counterparts in that the chiral sense of the sp^3 carbinyl center is faithfully transferred to the allenyl moiety of the product as a consequence of a rigid five-center transition state (A in Figure 1.)[1] In contrast, the stereogenicity of analogous allylic ether rearrangements, though generally high, depends upon conformational, and to some extent,

(1) Marshall, J. A.; Robinson, E. D.; Zapata, A. *J. Org. Chem.* **1989**, *54*, 5854.

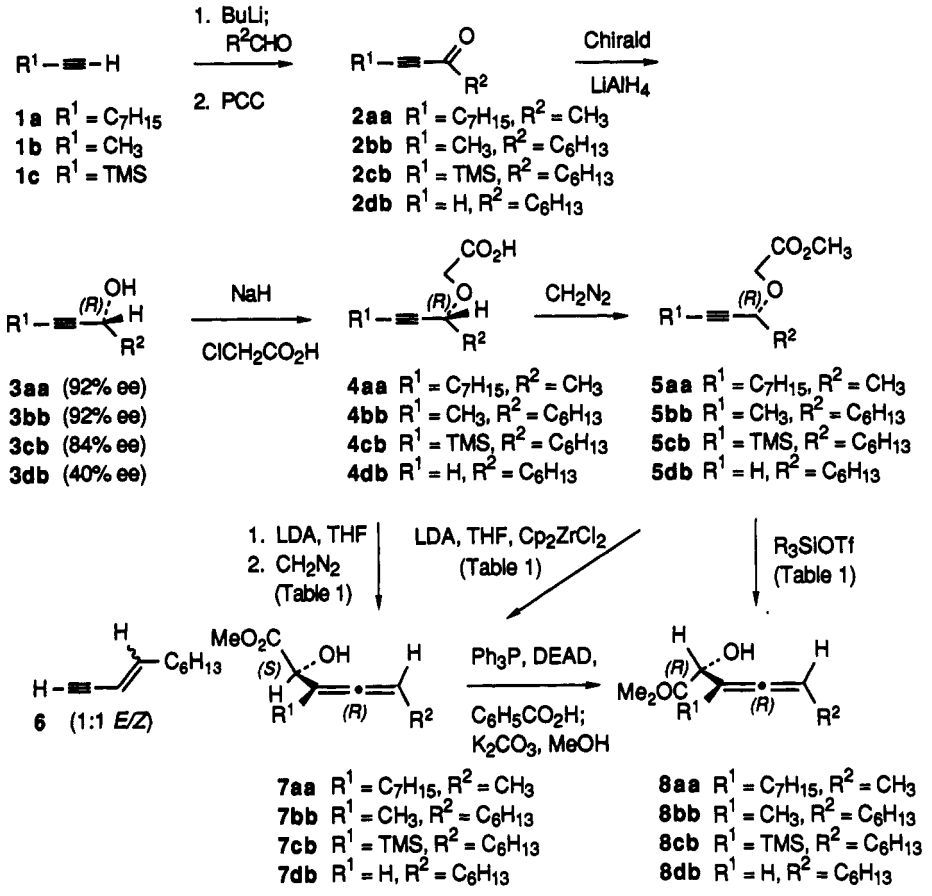
(2) Cf: Kuroda, S.; Sakaguchi, S.; Ikegami, S.; Harramoto, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1988**, *29*, 4763. Uchikawa, M.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 4581.

(3) For a preliminary account, see: Marshall, J. A.; Wang, X.-j. *J. Org. Chem.* **1990**, *55*, 2995.

(4) Cf: Boivin, T. L. B. *Tetrahedron* **1987**, *43*, 3309. Mulholland, R. L., Jr.; Chamberlin, A. R. *J. Org. Chem.* **1988**, *53*, 1082. Perron, F.; Albizati, K. F. *Chem. Rev.* **1989**, *89*, 1617.

0022-3263/91/1956-4913$02.50/0

Scheme I



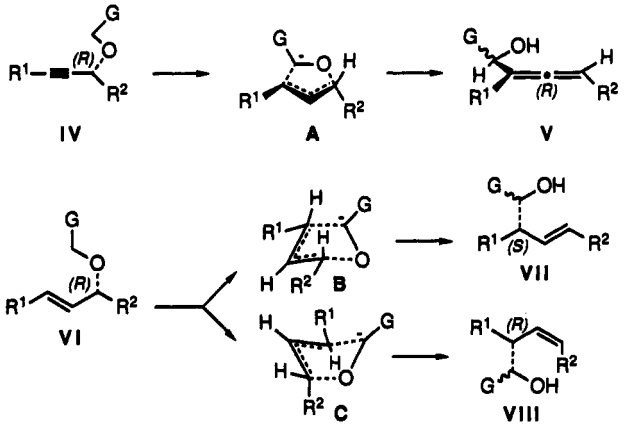
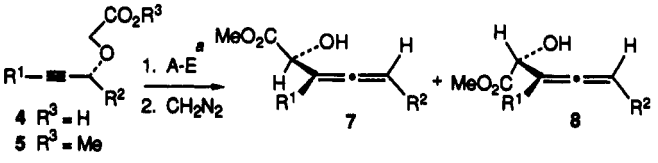


Figure 1. Comparative transition-state geometries for [2,3] rearrangements of propargylic and allylic ethers.

electronic preferences in envelope-like transition states (B vs C in Figure 1).[5] Prior to our work only a few examples of propargylic ether rearrangements were known.[6] Hence, it was of interest to examine additional systems and conditions in order to define the scope of this potentially valuable synthetic methodology.

The propargylic ethers **4** and **5** employed in these studies were prepared as outlined in Scheme I. Reduction of the acetylenic ketones **2** with Chirald[7]–$LiAlH_4$ gave (*R*)-propargylic alcohols **3** of 80–>90% ee according to ^1H NMR analysis of the *O*-methyl mandelate derivatives.[8] It is worth noting that reduction of acetylenic ketone **2db** by this methodology gave alcohol **3db** of only 40% ee. The functionally equivalent TMS acetylenic ketone **2cb**, on the

Table I. [2,3] Wittig Rearrangements of (Propargyloxy)acetic Acid Derivatives



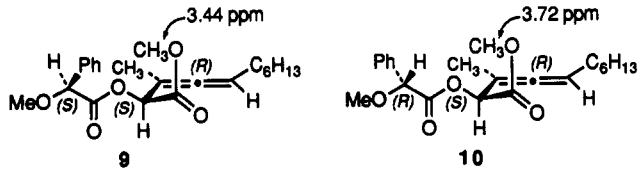
entry	ether	R^1	R^2	R^3	conditions	yield	7:8
1	**4aa**	C_7H_{15}	CH_3	H	A	80	93:7
2	**4bb**	CH_3	C_6H_{13}	H	A	48[b]	91:9
3	**5aa**	C_7H_{15}	CH_3	CH_3	B	57	100:0
4	**5bb**	CH_3	C_6H_{13}	CH_3	B	45[c]	100:0
5	**5db**	H	C_6H_{13}	CH_3	B	0[d]	
6	**5aa**	C_7H_{15}	CH_3	CH_3	C	93	23:77
7	**5bb**	CH_3	C_6H_{13}	CH_3	C	90	32:68
8	**5db**	H	C_6H_{13}	CH_3	C	91	20:80
9	**5cb**	TMS	C_6H_{13}	CH_3	C	71	28:72
10	**5aa**	C_7H_{15}	CH_3	CH_3	D	96	10:90
11	**5bb**	CH_3	C_6H_{13}	CH_3	D	94	10:90
12	**4aa**	C_7H_{15}	CH_3	H	D	90	10:90
13	**5aa**	C_7H_{15}	CH_3	CH_3	E	8[e]	10:90

[a] Key: A = LDA, THF −78 °C; CH_2N_2; B = LDA, THF, −78 °C, Cp_2ZrCl_2; C = TMSOTf, Et_3N, CH_2Cl_2; D = TESOTf, Et_3N, CH_2Cl_2; E = TBSOTf, Et_3N, CH_2Cl_2. [b] 46% elimination. [c] 5% elimination. [d] Total decomposition of starting material. [e] 88% starting material after 12 h.

(5) Nakai, T.; Mikami, K. *Chem. Rev.* **1986**, *86*, 885. Wu, Y-D., Houk, K. N.; Marshall, J. A. *J. Org. Chem.* **1990**, *55*, 1421.
(6) Huche, M.; Cresson, P. *Tetrahedron Lett.* **1975**, 367. Cazes, B.; Julia, S. *Synth. Commun.* **1977**, *7*, 273. Schollkopf, V.; Fellenberger, K.; Rizk, M. *Liebigs Ann. Chem.* **1970**, *734*, 106.
(7) Aldrich Chemical Co. Chirald is a trade name for Darvon alcohol. Cf.: Yamaguchi, S.; Mosher, H. S. *J. Org. Chem.* **1973**, *38*, 1870.
(8) Trost, B. M.; Belletire, J. L.; Godleski, S.; McDougal, P. D.; Balkovic, J. M.; Baldwin, J. J.; Christy, M. E.; Ponticello, G. S.; Varga, S. L.; Springer, J. D. *J. Org. Chem.* **1986**, *51*, 2370. Dale, J. A.; Mosher, H. S. *J. Am. Chem. Soc.* **1973**, *95*, 512.

other hand, yielded alcohol **3cb** of >80% ee. Williamson etherification with chloroacetic acid afforded the ethers **4** in nearly quantitative yield.

Treatment of the (propargyloxy)acetic acids **4aa** and **4bb** with 2.5 equiv of LDA in THF at −78 °C for several hours followed by esterification with CH_2N_2 led to the allenic hydroxy esters **7aa** and **7bb** in moderate to high yield (Table I, entries 1 and 2). GC analysis indicated a 93:7 mixture of stereoisomers in the former case and a 91:9 mixture in the latter. The configuration of the allene follows from the concerted nature of the [2,3] rearrangement (Figure 1).[1,5] The carbinyl configuration was established from chemical shift differences of the carbomethoxy protons in the ^1H NMR spectrum of the *O*-methyl mandelate derivs. **9** and **10**.[8]



9 **10**

The yield of [2,3] rearrangement product **7bb** was low because of a competing elimination reaction leading to the enyne **6** (1:1 mixture of *E* and *Z* isomers). Evidently, deprotonation of the acetylenic CH_3 grouping is competitive with enolate formation. A related elimination product was not observed from ether **4aa**.

In an effort to minimize this elimination reaction and improve diastereoselectivity, we examined [2,3] rearrangement of the ester derivatives **5**. Allyloxy analogues of ester **5** have been found to undergo highly stereoselective rearrangement upon conversion to their zirconium enolates.[2] Treatment of ether ester **5aa** with LDA at −78 °C followed by Cp_2ZrCl_2 led to the rearranged allenic alcohol **7aa** as the sole isolable product in 57% yield (Table I, entry 3). Analogous treatment of **5bb** afforded allenic alcohol **7bb** (45%) along with a small amount (5%) of elimination product **6** (Table I, entry 4).

[2,3] Rearrangements of acids **4** or their esters **5** could also be effected with TMSOTf and Et_3N along the lines reported by Mikami et al. for (allyloxy)acetates.[9] Interestingly, the major diastereomer produced in these reactions was different from that of the base-promoted rearrangements (Table I, entries 6–9). Diastereoselectivity could be increased to 90:10 by use of TESOTf (Table I, entries 10–12). Use of the bulkier silylating agent, TBSOTf, led to no further improvement in diastereoselectivity and had the disadvantage of slow reaction rates (Table I, entry 13).

The use of TESOTf to effect [2,3] rearrangement in these systems offers several advantages over the base-promoted reactions. Thus, elimination products such as **6** are not produced in the Si reactions. Furthermore, terminal alkynes can be employed (Table I, entry 8). Such alkynes decompose upon treatment with strong base (Table I, entry 5).

The stereochemistry of allenols **8** was established through analysis of the ^1H NMR spectra of the *O*-methyl mandelates and on mechanistic grounds as noted for allenols **7**.[8] Conversion of **7** to **8** could be effected by Mitsunobu inversion with benzoic acid followed by methanolysis.[10]

The stereochemical trends in the foregoing rearrangements can be understood from transition-state considerations, as illustrated in Figure 2. It has been established that zirconium enolates of α-alkoxy esters form chelated structures such as D or E.[2] Steric interactions between the endo Cp grouping and R^2 disfavor E relative to D leading to a predominance of **7** in such rearrangements. In the case of the acids **4** the $ZrCp_2$ and R^3 groupings would be replaced by solvated lithium ions.

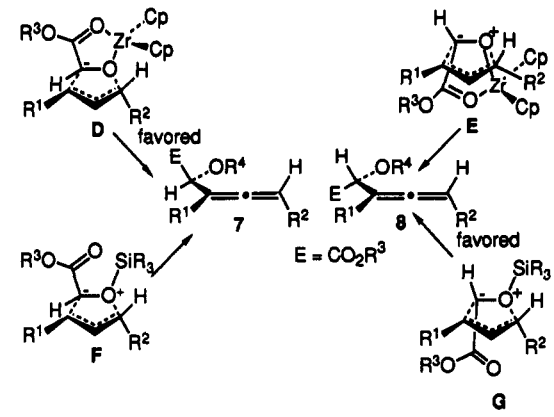
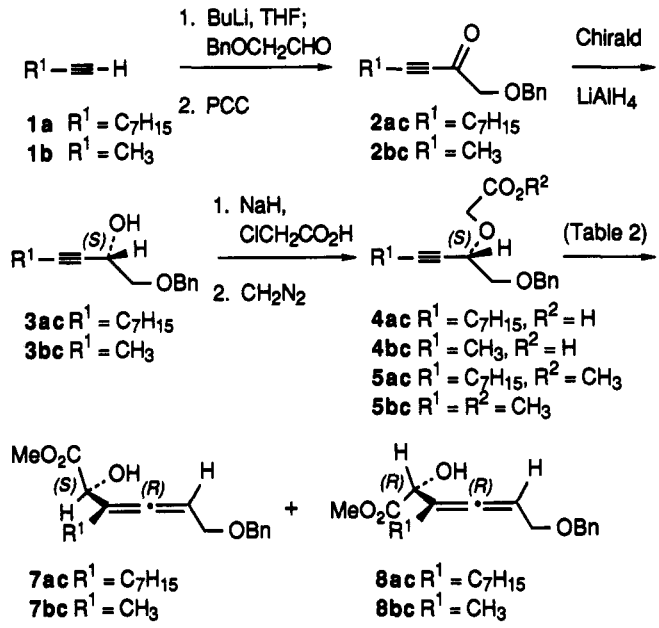


Figure 2. Transition states for [2,3] rearrangements of (propargyloxy)acetates leading to diastereomeric allenols **7** and **8** (R^4 = $ZrCp_2Cl$ or SiR_3).

Scheme II

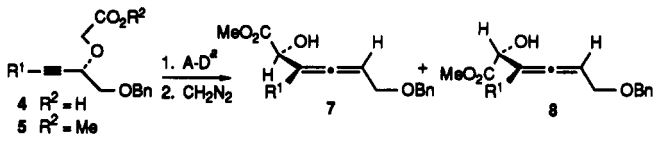


The silyl triflate promoted rearrangements are thought to proceed by oxonium ylide species such as F or G.[9] Here intermediate F, analogous to D, does not benefit from chelation but experiences steric repulsion between the carboxylic and silyl groupings. Thus, reaction by way of transition state G is favored. As expected, increasing the steric bulk of the silyl substituents enhances stereoselectivity and decreases reaction rate. Presumably, steric interactions between R^2 and SiR_3 retard oxonium salt formation with bulky silyl groups.

With a view toward the eventual synthesis of polyether natural products, we tested the applicability of this methodology to the benzyloxy ethers **4ac**, **5ac**, and especially **5bc**, prepared as shown in Scheme II. Surprisingly, the rearrangements were markedly less selective than the analogous alkyl systems. Thus, acid **4ac** gave rise to a 60:40 mixture of allenols **7** and **8** in only 21% yield (Table II, entry 1). The derived ester **5ac** failed to rearrange under conditions previously employed for esters **5aa** and

(9) Mikami, K.; Takahashi, O.; Tabei, T.; Nakai, T. *Tetrahedron Lett.* **1986**, *27*, 4511.
(10) Mitsunobu, O. *Synthesis* **1981**, 1.

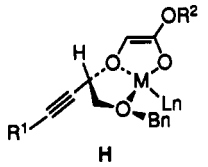
Table II. [2,3] Wittig Rearrangements of Carboxymethyl 1-(Benzyloxy)-3-alkyn-2-yl Ethers



entry	ether	R^1	R^2	conditions[a]	yield	7:8
1	**4ac**	C_7H_{15}	H	A	21	60:40
2	**5ac**	C_7H_{15}	CH_3	B	0[b]	
3	**5ac**	C_7H_{15}	CH_3	D	67	33:67
4	**5bc**	CH_3	CH_3	C	95	45:55
5	**5bc**	CH_3	CH_3	D	88	33:67

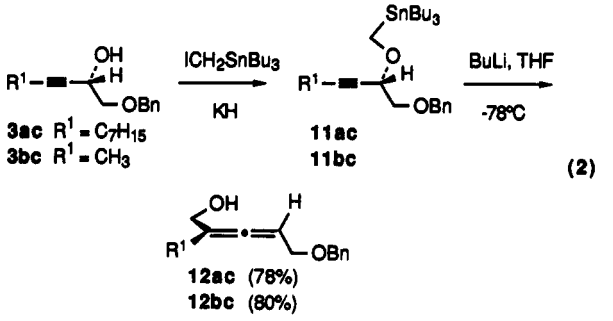
[a] Key: A = LDA, THF, −78 °C; B = LDA, THF, −78 °C, Cp_2ZrCl_2; C = TMSOTf, Et_3N; D = TESOTf, Et_3N. [b] Starting material and decomposition products recovered after 18 h at −20 °C.

5bb. Although silyl-promoted rearrangements proceeded more readily, the stereoselectivity was a modest 1:2, at best (Table II, entries 3–5). Presumably, complexation of Li, $ZrCp_2$, and R_3Si cations with the benzylic ether oxygen is responsible for the contrasting behavior of ethers **4ac**, **5ac**, and **5bc** and **4aa**, **4bb**, **5aa**, and **5bb**. In the base-promoted reactions a tridentate complex such as H could prevent proper alignment of the enolate carbon with the triple bond. We can offer no rationale for the poor selectivity of the silyl-promoted rearrangements.



H

A possible alternative route to allene-1,5-diols through Still–Wittig rearrangement of the stannylmethyl ethers 11 was briefly examined (eq 2).[11] Both **11ac** and **11bc** readily

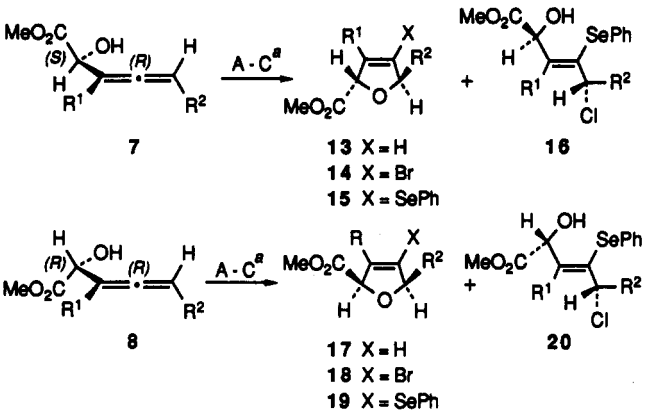


(2)

rearranged upon treatment with BuL in THF at −78 °C. We have previously shown that such rearrangements proceed by a concerted pathway and stereochemistry is assigned accordingly.[1] We are currently investigating methodology for the stereoselective elaboration of allenols such as **12bc** to potential polyether precursors.

In the final stage of this preliminary study, we examined cyclizations of the various allenols **7** and **8** to the corresponding 2,5-dihydrofurans **13** and **17** (Table III). With $AgNO_3$–$CaCO_3$ in aqueous acetone, allenols **7aa** and **7bb** and their diastereoisomers **8aa** and **8bb** underwent smooth and stereospecific cyclization to the dihydrofurans **13aa**, **13bb**, **17aa**, and **17bb** (Table III, entries 1–4).[12] Cyclization could also be induced with NBS (entries 5 and 6)

Table III. Electrophile-Induced Cyclizations of Allenols to 2,5-Dihydrofurans



entry	allenol	R^1	R^2	conditions[a]	yield	X
1	**7aa**	C_7H_{15}	CH_3	A	84	H
2	**7bb**	CH_3	C_6H_{13}	A		H
3	**8aa**	C_7H_{15}	CH_3	A	84	H
4	**8bb**	CH_3	C_6H_{13}	A		H
5	**7aa**	C_7H_{15}	CH_3	B	66	Br
6	**8aa**	C_7H_{15}	CH_3	B	64	Br
7	**7aa**	C_7H_{15}	CH_3	C	66	SePh[b]
8	**8aa**	C_7H_{15}	CH_3	C	62	SePh[c]

[a] Key: A = $AgNO_3$, $CaCO_3$, Me_2CO–H_2O; B = NBS, CH_2Cl_2; C = PhSeCl, CH_2Cl_2. [b] 17% of **16** was also isolated. [c] 17% of **20** was also isolated.

or PhSeCl (entries 7 and 8). In the latter cases, the byproducts **16** and **20** were formed.[13,14] These are presumed to arise from attack on the allenic double bond syn to the side chain OH, and the stereochemistry is assigned accordingly.

Experimental Section

The apparatus and methods described by Kramer, Midland, and Levy[15] were used to maintain an Ar or N_2 atmosphere in the reaction flask. Anhydrous solvents were obtained by distillation from benzophenone ketyl (diethyl ether, THF), P_2O_5 (CH_2Cl_2), CaH_2 (HMPA), or sodium (benzene, toluene). ^1H NMR samples were prepared as dilute solutions in $CDCl_3$. Glass-capillary gas chromatography was performed on a Superox 4 25M column. Analytical thin-layer chromatography (TLC) on plates precoated with E. Merck silica gel 60 F254 of 0.25-mm thickness was used to monitor reactions. E. Merck silica gel 60 (230–400 ASTM mesh) was employed for column chromatography according to the procedure of Still, Kahn, and Mitra.[16]

Representative Experimental Procedures. 3-Undecyn-2-one (2aa). To a solution of 5.00 g (40.3 mmol) of 1-nonyne (**1a**) in 150 mL of THF was slowly added 15.9 mL (44.3 mmol) of 2.78 M *n*-BuLi at −78 °C. The resulting mixture was stirred for 1 h. To the mixture was added 3.68 g (80.0 mmol) of acetaldehyde. The resulting mixture was warmed to rt and stirred for another 1 h and then neutralized with 10% HCl and extracted with ether. The organic layer was washed with saturated aqueous $NaHCO_3$ and brine and then dried over $MgSO_4$. After removal of solvent, the residue was distilled at reduced pressure to give 6.19 g (92%) of 3-undecyn-2-ol, racemic **3aa**.

A solution of 6.19 g (36.8 mmol) of 3-undecyn-2-ol and 15.85 g (73.5 mmol) of PCC in 100 mL of CH_2Cl_2 was stirred at rt for 18 h, and then 10 g of Florisil was added to the reaction mixture.[17]

(11) Still, W. C.; Mitra, A. *J. Am. Chem. Soc.* **1978**, *100*, 1927.
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(15) Brown, H. C. *Organic Synthesis via Boranes*; Wiley: New York, 1975; pp 191–202.
(16) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

The mixture was stirred for 15 min and filtered through silica gel, eluting with ether. Evaporation of the solvent gave a yellow oil, which was purified by chromatography on silica gel (hexane–ether (6:1)) to afford 5.44 g (89%) of ketone **2aa** as a colorless oil: IR (film) ν 2932, 2859, 2210, 1678, 1467, 1358, 1229 cm^{-1}; ^1H NMR (300 MHz) δ 2.32 (t, J = 7.1 Hz, 2 H, propargylic), 2.29 (s, 3 H, $COCH_3$), 1.60–1.50 (m, 2 H, H-6), 1.36–2.05 (m, 8 H, $(CH_2)_4$), 0.86 (t, J = 6.8 Hz, 3 H, CH_2CH_3).

(*R*)-3-Undecyn-2-ol (3aa). To a suspension of 3.1 mL (3.1 mmol) of 1 M $LiAlH_4$ in 75 mL of ether was added dropwise a solution of 1.95 g (6.9 mmol) of (*R*)-Chirald in 15 mL of ether at 0 °C. The mixture was cooled to −78 °C. A solution of 424 mg (2.6 mmol) of 3-undecyn-2-one (**2aa**) in 15 mL of ether was added to the mixture over 2 h. The resulting mixture was stirred at −78 °C for 5 h and quenched with 10% HCl. The layers were separated, and the aqueous layer was extracted with ether. The combined extracts were washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, filtered, and concentrated. The residue was then chromatographed on silica gel (hexane–ether (4:1)) to afford 417 mg (97%) of (*R*)-3-undecyn-2-ol (**3aa**): $[\alpha]_D$ +18.7° ($CHCl_3$, c 2.37); IR (film) ν 3363, 2930, 2859, 2247, 1457, 1156, 1078 cm^{-1}; ^1H NMR (300 MHz) δ 4.50–4.46 (m, 1 H, $HOCHCH_3$), 2.16 (dt, J = 1.9, 7.1 Hz, 2 H, propargylic H), 1.82–1.80 (m, 1 H, OH), 1.49–1.38 (m, 2 H, H-6), 1.40 (d, J = 6.5 Hz, 3 H, $OCHCH_3$), 1.33–1.25 (m, 8 H, $(CH_2)_4$), 0.86 (t, J = 6.7 Hz, 3 H, CH_2CH_3); MS m/e 167 (2, M − H), 151 (19), 109 (70), 95 (100). The ee of this alcohol was found to be 92% by ^1H NMR analysis of the (*R*)-*O*-methyl mandelate derivative.

2-[((*R*)-1-Methyl-2-nonynyl)oxy]acetic Acid (4aa). To a suspension of 184 mg (7.7 mmol) of NaH in 5 mL of THF was added a solution of 359 mg (2.1 mmol) of *R* alcohol **3aa** in 4 mL of THF at 0 °C, and the mixture was stirred at 0 °C for 30 min. A solution of 302 mg (3.2 mmol) of chloroacetic acid in 5 mL of THF was added dropwise to the mixture at 0 °C. The resulting mixture was refluxed for 18 h and acidified with 10% HCl and then extracted with ether. The extracts were dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane–ether (4:1), then ether) to give 444 mg (92%) of acid **4aa**: $[\alpha]_D$ +91.5° ($CHCl_3$, c 1.99); IR (film) ν 3600–3500, 2240, 1735, 1216, 1125 cm^{-1}; ^1H NMR (300 MHz) δ 4.38–4.33 (m, 1 H, $OCHCH_3$), 4.30, 4.17 (J = 16.9 Hz, AB, 2 H, OCH_2CO_2H), 2.18 (dt, J = 1.7, 7.1 Hz, 2 H, propargylic H), 1.50–1.40 (m, 2 H, H-6), 1.45 (d, J = 6.5 Hz, 3 H, $OCHCH_3$), 1.40–1.31 (m, 8 H, $(CH_2)_4$), 0.86 (t, J = 6.6 Hz, 3 H, CH_2CH_3); HRMS calcd for $C_{13}H_{22}O_3NH_4$ 244.1917, found 244.1913.

Methyl 2-[((*R*)-1-Methyl-2-nonynyl)oxy]acetate (5aa). A solution of 500 mg (2.21 mmol) of acid **4aa** in 10 mL of ether was treated with excess CH_2N_2. The excess CH_2N_2 was destroyed by acetic acid, and then the mixture was washed with saturated aqueous $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on silica gel (hexane–ether (8:1)) to afford 501 mg (94%) of ester **5aa**: $[\alpha]_D$ +92.8° ($CHCl_3$, c 1.68); IR (film) ν 2928, 2240, 1759, 1438, 1208, 1130 cm^{-1}; ^1H NMR (300 MHz) δ 4.34 (m, 1 H, $OCHCH_3$), 4.26, 4.17 (J = 16.4 Hz, AB, 2 H, OCH_2CO_2Me), 3.74 (s, 3 H, CO_2CH_3), 2.18 (dt, J = 2.0, 7.0 Hz, 2 H, propargylic), 1.50–1.43 (m, 2 H, H-6), 1.45 (d, J = 6.6 Hz, 3 H, $OCHCH_3$), 1.40–1.26 (m, 8 H, $(CH_2)_4$), 0.86 (t, J = 6.8 Hz, 3 H, CH_2CH_3); HRMS calcd for $C_{14}H_{23}O_3$ (M − H) 239.1647, found 239.1651. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.97; H, 10.06. Found: C, 70.00; H, 10.08.

Methyl (2*S*,4*R*)-2-Hydroxy-3-heptyl-3,4-hexadienecarboxylate (7aa). A. From Acid 4aa. To a solution of 0.65 mL (4.5 mmol) of diisopropylamine in 5 mL of THF was added 1.5 mL (4.2 mmol) of 2.78 M *n*-BuLi at 0 °C. The mixture was stirred at 0 °C for 30 min and cooled to −78 °C. To the mixture was added dropwise 380 mg (1.7 mmol) of acid **4aa** in 5 mL of THF. The reaction mixture was stirred at −78 °C for 1 h, acidified with 10% HCl, and extracted with ether. The extracts were dried over $MgSO_4$ and concentrated. The residue was directly used for esterification without purification.

To a solution of the above crude oil in 10 mL of ether was added excess CH_2N_2 in 10 mL of ether. The reaction mixture was stirred at rt until the TLC showed no trace of the starting material. The excess CH_2N_2 was destroyed by acetic acid. Concentration of the mixture and chromatography of the crude product on silica gel (hexane–ether (4:1)) afforded 320 mg (80%) of **7aa** as an oil, a 93:7 mixture of diastereomers according to GC analysis: $[\alpha]_D$ +33.8° ($CHCl_3$, c 2.13); IR (film) ν 3500, 1967, 1745, 1215, 1078 cm^{-1}; ^1H NMR (500 MHz) δ 5.31–5.27 (m, 1 H, vinyl H), 4.53 (b s, 1 H, $HOCHCO_2Me$), 3.75 (s, 5 H, CO_2CH_3), 2.84 (b s, 1 H, OH), 2.06–1.89 (m, 2 H, vinyl CH_2), 1.64 (d, J = 7.1 Hz, 3 H, CH_3), 1.40–1.23 (m, 10 H, $(CH_2)_5$), 0.85 (t, J = 7.0 Hz, 3 H, CH_2CH_3); HRMS calcd for $C_{14}H_{24}O_3$ 240.1725, found 244.1717. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.97; H, 10.06. Found: C, 70.02; H, 10.11.

The (*R*)-*O*-methyl mandelate derivatives were separated into a major and minor fraction by chromatography on silica gel. The CO_2Me peak appeared at 3.72 ppm for the major diastereomer and 3.44 ppm for the minor in accord with their assignments as *RSR* and *RRR*, respectively. The minor mandelate, *RRR*, contained a nearly equal amount of the *RRS* diastereomer arising from the (*S*)-allene derived from the *S* contaminant of alcohol **3aa**.

B. From Ester 5aa. To a solution of 0.07 mL (0.499 mmol) of diisopropylamine in 2 mL of THF was added 0.16 mL (0.458 mmol) of 2.82 M *n*-BuLi at 0 °C. The mixture was stirred at 0 °C for 30 min and then cooled to −78 °C. To the mixture was added 100 mg (0.416 mmol) of ester **5aa** in 2 mL of THF with stirring at −78 °C, and after 30 min, 182 mg (0.624 mmol) of Cp_2ZrCl_2 in 2.5 mL of THF was added. The resulting mixture was stirred at −78 °C for 30 min, allowed to stand at −20 °C for 18 h, and then quenched with 10% HCl and extracted with ether. The ether layer was dried over $MgSO_4$ and concentrated. The residue was chromatographed on silica gel (hexane–ether (6:1)) to afford 59 mg (59%) of allenic alcohol **7aa** as a single isomer according to GC analysis: $[\alpha]_D$ +43.5° ($CHCl_3$, c 1.70).

Methyl (2*R*,4*R*)-2-Hydroxy-3-heptyl-3,4-hexadienecarboxylate (8aa). A. From Alcohol 7aa. To a solution of 218 mg (0.83 mmol) of Ph_3P and 200 mg (0.83 mmol) of allenyl alcohol **7aa** (93:7 mixture of diastereomers) in 2 mL of ether was added a mixture of 107 mg (0.83 mmol) of benzoic acid and 0.13 mL (0.83 mmol) of diethyl azodicarboxylate in 3 mL of ether. The mixture was stirred at room temperature overnight, and then it was filtered through a short column of silica gel with hexane–ether (8:1) to yield the crude benzoate. This product was dissolved in 5 mL of methanol and treated with 117 mg (0.85 mmol) of K_2CO_3 at room temperature for 6 h. The mixture was quenched with water and extracted with ether. The extracts were washed with brine, dried over $MgSO_4$, and concentrated. The residue was chromatographed on silica gel (hexane–ether (4:1)) to give 160 mg (80%) of alcohol **8aa** as a 93:7 mixture of diastereomers according to GC analysis: $[\alpha]_D$ −66.1° ($CHCl_3$, c 3.48); IR (film) ν 3500, 1967, 1745, 1215, 1078, cm^{-1}; ^1H NMR (500 MHz) δ 5.31–5.27 (m, 1 H, vinyl H), 4.53 (b s, 1 H, $HOCHOCO_2Me$), 3.76 (s, 3 H, CO_2CH_3), 2.83 (d, J = 7.9 Hz, 1 H, OH), 2.06–1.89 (m, 2 H, vinyl CH_2), 1.65 (d, J = 7.1 Hz, 3 H, CH_3), 1.40–1.23 (m, 10 H, $(CH_2)_5$), 0.85 (t, J = 7.0 Hz, 3 H, CH_2CH_3). Anal. Calcd for $C_{14}H_{24}O_3$: C, 68.99; H, 9.80. Found: C, 68.88; H, 9.82.

When the above reaction was repeated on a pure sample of hydroxy ester **7aa**, the obtained alcohol **8aa** was a single isomer: $[\alpha]_D$ −80.7° ($CHCl_3$, c 1.34).

B. From Ester 5aa with TESOTf. To a mixture of 88 mg (0.37 mmol) of propargyloxy ester **5aa** and 0.06 mL (0.43 mmol) of Et_3N in 5 mL of CH_2Cl_2 was added 0.10 mL (0.44 mmol) of TESOTf at 0 °C. The resulting mixture was refluxed for 16 h, and then 1.32 mL (1.32 mmol) of 1.0 M Bu_4NF in THF was added. The mixture was stirred for 30 min and diluted with ether. The ether layer was washed with saturated $NaHCO_3$, dried over $MgSO_4$, and concentrated. The residue was chromatographed on silica gel (hexane–ether (4:1)) to give 84 mg (96%) of allenic alcohol **8aa** as a 90:10 mixture of diastereomers according to GC analysis: $[\alpha]_D$ −59.7° ($CHCl_3$, c 1.44).

(*S*)-*O*-Methyl Mandelates of Allenyl Alcohol 7aa (9 and 10). To a mixture of 37 mg (0.15 mmol) of alcohol **7aa** (93:7 mixture of diastereomers) and 38 mg (0.23 mmol) of (*S*)-α-methoxyphenylacetic acid in 5 mL of CH_2Cl_2 were added 47 mg (0.23 mmol) of DCC and a catalytic amount of DMAP.[8] The mixture was stirred at room temperature for 3 h and then evaporated to dryness. The residue was chromatographed on silica gel (hexane–ether (4:1)) to afford 45 mg (80%) of *S,S,R* ester **9**

(17) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.

as a single isomer: IR (film) 1750, 1440, 1200, 1170, 1105 cm^{-1}; ^1H NMR (300 MHz) 7.48–7.34 (m, 5 H, ArH), 5.43 (d, J = 1.7 Hz, 1 H, CO_2CHCO_2Me), 5.26 (m, 1 H, vinyl H), 4.85 (s, 1 H, $MeOCHCO_2$), 3.59 (s, 3 H, CO_2Me), 3.47 (s, 3 H, OMe), 1.92 (m, 2 H, vinyl CH_2), 1.64 (d, J = 7.1 Hz, 3 H, vinyl CH_3), 1.40–1.26 (m, 8 H, $(CH_2)_4$), 0.87 (t, J = 6.8 Hz, 3 H, CH_2CH_3); HRMS calcd for $C_{23}H_{32}O_5$ 338.2248, found 338.2250. Anal. Calcd for $C_{23}H_{32}O_5$: C, 71.11; H, 8.30. Found: C, 71.21; H, 8.34.

Continued elution yielded 4.5 mg (8%) of *S,R,R* and *S,R,S* ester **10** as a 50:50 mixture: IR (film) 1750, 1440, 1200, 1170, 1105 cm^{-1}; ^1H NMR (300 MHz) 7.46–7.32 (m, 5 H, ArH), 5.42 (d, J = 1.6 Hz, 1 H, CO_2CHCO_2Me), 5.22 (m, 1 H, vinyl H), 4.89 (s, 1 H, $MeOCHCO_2$), 3.71 (s, 3 H, CO_2Me), 3.43 (s, 3 H, OMe), 1.71 (m, 2 H, vinyl CH_2), 1.64 (d, J = 7.1 Hz, 3 H, vinyl CH_3), 1.40–1.26 (m, 8 H, $(CH_2)_4$), 0.86 (t, J = 6.8 Hz, 3 H, CH_2CH_3). The isomer peaks could be seen at: 5.39 (d, J = 1.6 Hz, 1 H, CO_2CHCO_2Me), 1.61 (d, J = 7.1 Hz, 3 H, vinyl CH_3). Anal. Calcd for $C_{23}H_{32}O_5$: C, 71.11; H, 8.30. Found: C, 71.15; H, 8.32.

(*R*)-1-(Benzyloxy)-2-[(tributylstannyl)oxy]-3-undecyne (11ac). To a suspension of 257 mg (1.61 mmol) of KH (25% in oil, washed by hexane) in 4 mL of THF–HMPA (2:1) was added 290 mg (1.07 mmol) of alcohol **3ac** in 2 mL of THF. After 15 min, 553 mg (1.28 mmol) of ICH_2SnBu_3 was added. The mixture was stirred at rt overnight and then quenched with dilute HCl and extracted with ether. The ether layer was washed with brine and dried over $MgSO_4$. After removal of the solvent, the residue was chromatographed on silica gel (hexane–ether (5:1)) to afford 525 mg (85%) of propargylic ether **11ac**: $[\alpha]_D$ +12.9° ($CHCl_3$, c 1.06); IR (film) ν 2233, 1455, 1073, 733, 696 cm^{-1}; ^1H NMR (300 MHz) δ 7.33–7.24 (m, 5 H, ArH), 4.62, 4.55 (AB, J = 12.3 Hz, 2 H, OCH_2Ar), 4.08 (m, 1 H, propargylic CH), 4.02, 3.64 (AB, J = 10.1 Hz, 2 H, OCH_2SnBu_3), 3.56 (d, J = 5.7 Hz, 2 H, $CHCH_2OBn$), 2.20 (dt, J = 2.0, 6.9 Hz, 2 H, propargylic CH_2), 1.54–0.84 (m, 27 H, $(C_4H_9)_3Sn$); HRMS calcd for $C_{31}H_{54}O_2Sn$ (M – Bu) 517.2437, found 517.2439. Anal. Calcd for $C_{31}H_{54}O_2Sn$: C, 64.48; H, 9.43. Found: C, 64.66; H, 9.46.

(*R*)-2-Methyl-5-(benzyloxy)-2,3-pentadien-1-ol (12ac). To a solution of 70 mg (0.14 mmol) of propargylic ether **11ac** in 2 mL of THF was added dropwise 0.05 mL (0.15 mmol) of 2.9M *n*-BuLi at −78 °C. The reaction mixture was stirred at −78 °C for 1.5 h and then quenched with aqueous NH_4Cl and 10% HCl and extracted with ether. The ether layer was dried over $MgSO_4$ and concentrated. The residue was purified by chromatography on silica gel (hexane–ether (2:1)) to afford 23 mg (80%) of allenic alcohol **12ac**: $[\alpha]_D$ +1.7° ($CHCl_3$, c 0.90); IR (film) ν 3394, 1968, 1073, 738, cm^{-1}; ^1H NMR (300 MHz) δ 7.34–7.24 (m, 5 H, ArH), 5.40–5.35 (m, 1 H, vinyl H), 4.53 (s, 2 H, OCH_2Ar), 4.03 (d, J = 6.5 Hz, vinyl CH_2OBn), 4.01 (m, 2 H, vinyl CH_2OH, overlap with vinyl CH_2OBn), 1.73 (d, J = 2.9 Hz, 3 H, vinyl CH_3); HRMS calcd for $C_{19}H_{28}O_2$ 288.2089, found 288.2090. Anal. Calcd for $C_{19}H_{28}O_2$: C, 79.12; H, 9.78. Found: C, 79.35; H, 9.77.

(2*S*,5*R*)-5-Methyl-3-heptyl-2-(methoxycarbonyl)-2,5-dihydrofuran (13aa). A mixture of 25 mg (0.104 mmol) of allenic alcohol **7aa**, 4 mg (0.024 mmol) of $AgNO_3$, and 8 mg (0.080 mmol) of $CaCO_3$ in 1 mL of 3:2 acetone–water was stirred in the dark at room temperature for 48 h. The product was taken up in ether, and the ether layer was washed with water, dried over $MgSO_4$, and concentrated. Column chromatography of the residue on silica gel (hexane–ether (8:1)) afforded 21 mg (84%) of dihydrofuran **13aa** as a single product: $[\alpha]_D$ −161.7° ($CHCl_3$, c 1.05); IR (film) ν 1750, 1740, 1355, 1195, 1110 cm^{-1}; ^1H NMR (300 MHz) 5.52 (s, 1 H, vinyl H), 5.13–5.00 (m, 1 H, H-5), 5.10 (s, 1 H, H-2, overlap with H-5), 3.72 (d, J = 1.0 Hz, 3 H, CO_2CH_3), 2.06 (t, J = 7.5 Hz, 2 H, vinyl CH_2), 1.49–1.24 (m, 10 H, $(CH_2)_5$), 1.25 (d, J = 5.3 Hz, 3 H, CH_3), 0.86 (t, J = 6.4 Hz, 3 H, CH_2CH_3); HRMS calcd for $C_{14}H_{24}O_3$ 240.1725, found 240.1721. Anal. Calcd for $C_{14}H_{24}O_3$: C, 69.97; H, 10.06. Found: C, 70.05; H, 10.06.

(2*S*,5*R*)-5-Methyl-4-bromo-3-heptyl-2-(methoxycarbonyl)-2,5-dihydrofuran (14aa). To a solution of 33 mg (0.137mmol) of allenic alcohol **7aa** in 1 mL of CH_2Cl_2 was added 25 mg (0.140 mmol) of NBS. The resulting mixture was stirred at rt overnight and then evaporated to dryness. The residue was directly chromatographed on silica gel (hexane–ether (10:1)) to give 29 mg (66%) of dihydrofuran **14aa** as a single isomer: $[\alpha]_D$ −113.0° ($CHCl_3$, c 1.05); IR (film) ν 1755, 1740, 1664, 1265, 1197, 1115 cm^{-1}; ^1H NMR (300 MHz) δ 5.08 (s, 1 H, H-2), 5.06 (m, 1 H, H-5), 3.74 (s, 3 H, CO_2CH_3), 2.38–2.00 (m, 2 H, vinyl CH_2), 1.54–1.28 (m, 10 H, $(CH_2)_5$), 1.36 (d, J = Hz, 3 H, CH_3), 0.87 (t, J = 6.9 Hz, 3 H, CH_2CH_3); MS m/e 318 (5), 316 (4), 275 (10), 259 (100), 180 (25). Anal. Calcd for $C_{14}H_{23}O_3Br$: C, 52.67; H, 7.26. Found: C, 52.51; H, 7.25.

(2*S*,5*R*)-5-Methyl-4-(phenylselenyl)-3-heptyl-2-(methoxycarbonyl)-2,5-dihydrofuran (15aa). To a solution of 35 mg (0.146 mmol) of allenic alcohol **7aa** in 5 mL of CH_2Cl_2 was added dropwise a solution of 29 mg (0.153 mmol) of PhSeCl in 3 mL of CH_2Cl_2. The reaction mixture was stirred at rt for 5 min and then poured into water. The mixture was extracted with ether. The ether layer was dried over $MgSO_4$ and concentrated. The residue was carefully chromatographed on silica gel (hexane–ether (10:1)) to afford 38 mg (66%) of dihydrofuran **15aa** as a pure isomer: $[\alpha]_D$ −189.8° ($CHCl_3$, c 1.55); IR (film) ν 1755, 1740, 1578, 1438, 1173, 1115 cm^{-1}; ^1H NMR (300 MHz) δ 7.37–7.21 (m, 5 H, ArH), 5.25 (d, J = 5.2 Hz, 1 H, H-2), 5.04 (m, 1 H, H-5), 3.77 (s, 3 H, CO_2CH_3), 2.50–2.10 (m, 2 H, vinyl CH_2), 1.53–1.24 (m, 10 H, $(CH_2)_5$), 1.25 (d, J = 6.4 Hz, 3 H, CH_3), 0.86 (t, J = 7.0 Hz, 3 H, CH_2CH_3); HRMS calcd for $C_{20}H_{28}O_3Se$ 396.1204, found 396.1197. Anal. Calcd for $C_{20}H_{28}O_3Se$: C, 60.75; H, 7.14. Found: C, 60.67; H, 7.15.

Continued elution afforded 11 mg (17%) of allylic alcohol **16**: IR (film) ν 3499, 1734, 1709, 1580, 1227, 1087 cm^{-1}; ^1H NMR (300 MHz) δ 7.42–7.14 (m, 5 H, ArH), 5.78 (d, J = 4.1 Hz, 1 H, $HOCHCO_2Me$), 5.22 (q, J = 6.6 Hz, 1 H, $ClCHCH_3$), 3.71 (s, 3 H, CO_2CH_3), 3.21 (d, J = 4.1 Hz, 1 H, OH), 2.46–2.10 (m, 2 H, vinyl CH_2), 1.65–1.27 (m, 10 H, $(CH_2)_5$), 1.55 (d, J = 6.6 Hz, 3 H, CH_3), 0.87 (t, J = 6.9 Hz, 3 H, CH_2CH_3); HRMS calcd for $C_{20}H_{29}ClO_3Se$ 432.0970, found 432.0959. Anal. Calcd for $C_{20}H_{29}ClO_3Se$: C, 55.62; H, 6.77. Found: C, 55.80; H, 6.81.

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Supplementary Material Available: Experimental procedures for **2bb**, **2cb**, **2ac**, **3cb**, **3db**, **3ac**, **3bc**, **4bb**, **4ac**, **4bc**, **5bb**, **5cb**, **5db**, **5ac**, **5bc**, **7bb**, **7ac**, **8aa**, **8bb**, **8cb**, **8db**, **8ac**, **8bc**, **11bc**, **12bc**, **13bb**, **14bb**, **15bb**, **17aa**, **18aa**, and **19aa** (18 pages). Ordering information is given on any current masthead page.