ester is esterified, additional resonances attributable to the *RR,SS* diastereomer are observed: δ 6.65 (br d, J = 8), 3.8 (m), 3.56 (s).

(3*RS*,3a*RS*,7*SR*,7a*SR*)-Hexahydro-7-iodo-3-[[(1,1-dimethylethoxy)carbonyl]amino]benzofuran-2(3*H*)-one (16). A mixture of 100 mg (0.39 mmol) of cyclohexenylglycine derivative **15d**-*e*, 109 mg (0.43 mmol) of iodine, and 143 mg (0.86 mmol) of KI in 3 mL of saturated $NaHCO_3$ and 3 mL of ether was stirred for 12 h at 21 °C in the dark. The layers were separated, and the organic phase was washed with saturated $Na_2S_2O_3$, water, and brine, dried ($MgSO_4$), filtered, and evaporated to give 115 mg (78% yield) of iodo lactone **16**. A sample was purified for analysis by preparative TLC: IR 3475, 2950, 1790, 1710, 1510 cm^{-1}; ^1H NMR δ 5.1 (br d, 1, J = 8.5), 4.69 (dd, 1, J = 7.5, 9.7), 4.52 (dd, 1, J = 12, 8.5), 3.96 (ddd, J = 4, 10, 13), 2.65–2.4 (m, 2), 2.18–1.4 (m, 6), 1.48 (s, 9); ^{13}C NMR δ 140.4, 83.4, 50.4, 43.4, 36.6, 28.2, 27.0, 23.3, 22.4. Anal. Calcd for $C_{13}H_{19}NO_4I$: C, 40.96; H, 5.29; N, 3.67; I, 33.29. Found: C, 40.68; H, 5.31; N, 3.50; I, 33.0.

(3*RS*,3a*RS*,7*SR*,7a*SR*)-3-(Benzoylamino)hexahydro-7-iodo-3-methylbenzofuran-2(3*H*)-one (17). A mixture of 250 mg (0.92 mmol) of cyclohexenylalanine derivative **15e**-*e*, 255 mg (1.0 mmol) of iodine, and 1 g (6.1 mmol) of KI in 5 mL of saturated $NaHCO_3$ and 10 mL of ether was stirred for 30 min at 21 °C in the dark. A workup similar to that described above afforded 80 mg (22% yield) of iodo lactone **17**. Recrystallization from benzene gave analytically pure material: mp 174.5–176 °C; IR 3440, 2950, 1780, 1660, 1600, 1500 cm^{-1}; ^1H NMR δ 7.8–7.6 (m, 2), 7.6–7.2 (m, 3), 6.58 (br s, 1), 4.97 (br s, 1, $\Delta\nu_{1/2}$ < 10 Hz), 4.87 (br s, 1, $\Delta\nu_{1/2}$ < 10 Hz), 3.41 (ddd, 1, J = 3.8, 6.0, 12.3), 2.0–1.25 (m, 7), 1.67 (s, 3); ^{13}C NMR δ 133.5, 131.9, 128.6, 80.8, 63.3, 41.3, 29.1, 26.6, 22.6, 19.5, 19.4. Anal. Calcd for $C_{16}H_{18}NO_3I$: C, 48.14; H, 4.54; N, 3.51; I, 31.79. Found: C, 48.05; H, 4.57; N, 3.42; I, 31.66.

Acknowledgment. Support for this research was provided by the National Institutes of Health (Grant No. CA-16616).

Registry No. 1a, 82634-92-2; **1b**, 82706-21-6; **1c**, 82706-22-7; **1d**, 82706-23-8; **1e**, 82706-24-9; **1f**, 82706-25-0; **2a**-t, 82634-94-4; **2a**-e, 82634-95-5; **2b**-t, 82706-26-1; **2b**-e, 82706-72-7; **2c**-t, 82706-27-2; **2c**-e, 82706-73-8; **2d**-t, 82706-28-3; **2d**-e, 82706-74-9; **2e**-t, 82706-29-4; **2e**-e, 82706-69-2; **4**, 82706-30-7; **6**, 82706-31-8; **7**, 82706-32-9; **8a**, 82706-33-0; **8b**, 82706-34-1; **8c**, 82706-35-2; **8d**, 82706-36-3; **9a**-t, 82706-37-4; unblocked **9a**-t·TFA, 82706-66-9; **9a**-e, 82706-75-0; unblocked **9a**-e·TFA, 82706-68-1; (*RS,SR*)-**9b** (R^1 = PhCO, H; R^2 = R^3 = Me; R^4 = H), 82706-38-5; (*RR,SS*)-**9b** (R^1 = PhCO, H; R^2 = R^3 = Me; R^4 = H), 82706-39-6; (*RS,SR*)-**9b** (R^1 = phthaloyl; R^2 = R^3 = Me; R^4 = H), 82706-40-9; (*RR,SS*)-9b (R^1 = phthaloyl; R^2 = R^3 = Me; R^4 = H), 82706-41-0; (*RS,SR*)-**10**-t, 82706-42-1; (*RR,SS*)-**10**-e, 82706-70-5; **11**-t, 82706-43-2; **12a**, 82634-92-2; **12b**, 82706-44-3; **12c**, 82740-44-1; **12d**, 53777-91-6; **12e**, 82731-47-3; **12f**, 82706-45-4; **12g**, 82706-46-5; **13b**, 82706-47-6; **13d**, 82706-48-7; **13e**, 82706-49-8; **13f**, 82706-50-1; **13g**, 82706-51-2; **14a**, 82300-72-9; **14b**, 82706-52-3; **14c**, 82300-74-1; **14d**, 82706-53-4; **14e**, 82706-54-5; **14f**, 58400-62-7; **15a**, 82706-55-6; **15b**, 82706-56-7; **15c**, 82706-57-8; **15d**-e, 62090-89-5; **15d**-t, 82706-71-6; **16**, 82706-58-9; **17**, 82706-59-0; *N*-(*tert*-butoxycarbonyl)glycine, 4530-20-5; *trans*-crotyl *N*-benzoylalaninate, 82706-64-7; (*RS,RS*)-methyl 2-benzoylamino-3-phenyl-4-pentenoate, 82706-60-3; methyl (*RR,SS*)-2-benzoylamino-3-phenyl-4-pentenoate, 82706-61-4; 4-(2-cyclohexenyl)-4-methyl-2-phenyl-5(4*H*)-oxazolone, 82706-63-6; 4-(1-ethenyl)-1,5-dimethyl-4-hexenyl)-4-methyl-2-phenyl-5(4*H*)-oxazolone, 82706-62-5.

Ester-Enolate Claisen Rearrangement of Lactic Acid Derivatives

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The ester–enolate Claisen rearrangement of a number of allylic esters of α-hydroxy acids and O-protected derivatives was studied. Crotyl lactate (**1b**), for example, is converted to the enediolate, silylated, and rearranged to afford the *RS,SR* and *RR,SS* diastereomers **2b** and **3b** in 30% yield and a ratio of 4:1; rearrangement of the benzyl ether of crotyl lactate shows a similar stereospecificity but higher yield. The enediolate derived from crotyl mandelate is rearranged without silylation to provide the phenyl analogues **2c** and **3c** in 59% yield and 12:1 stereoselectivity. Only modest variation in stereoselectivity is seen on varying the solvent or conditions. On the assumption that the Claisen rearrangements proceed via the chairlike transition state, the *E* stereochemistry is shown to be the preferred geometry of the alkoxy enediolate and dialkoxy enolate intermediates.

The preceding paper[1] presents the results of our study of the Ireland–Claisen rearrangement[2] as a method for the stereocontrolled construction of α-amino acid derivatives. In this report, we discuss its extension to the synthesis of α-hydroxy and α-alkoxy acids. Although there have been isolated examples in cyclic systems of the application of the ester–enolate rearrangement procedure to allylic esters of α-alkoxy carboxylic acids,[3] no systematic study of this variant has been undertaken. Nor has the possibility of applying the procedure to the unprotected α-hydroxy analogues been reported.[4] For these reasons, we studied the rearrangement of a variety of acyclic O-protected and -unprotected allylic lactate, glycolate, and mandelate esters. Although our results indicate that the utility of the ester–enolate Claisen rearrangement of such derivatives is often limited by either modest stereoselectivity or low yields, we were able to deduce the preferred stereochemistry of dialkoxy enolate or alkoxy enediolate formation for a variety of derivatives.

Rearrangement Yield and Stereoselectivity

The ester–enolate Claisen rearrangement was studied most thoroughly with use of the crotyl esters of lactic acid (**1b**) and its *O*-benzyl derivative (**1a**). With use of lithium isopropylcyclohexylamide (LICA) as the base,[5,6] these es-

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(2) (a) R. E. Ireland, R. H. Mueller, and A. K. Willard, *J. Am. Chem. Soc.*, **98**, 2868 (1976); (b) R. E. Ireland and C. S. Wilcox, Jr., *Tetrahedron Lett.*, 2839 (1977).

(3) (a) J. K. Whitesell and A. M. Helbling, *J. Org. Chem.*, **45**, 4135 (1980); (b) J. K. Whitesell and A. M. Helbling, *J. Chem. Soc., Chem. Commun.*, 594 (1977); (c) J. K. Whitesell, R. S. Matthews, and A. M. Helbling, *J. Org. Chem.*, **43**, 784 (1978); (d) R. E. Ireland, S. Thaisrivongs, N. Vanier, and C. S. Wilcox, *Ibid.*, **45**, 48 (1980); (e) R. E. Ireland, S. Thaisrivongs, and C. S. Wilcox, *J. Am. Chem. Soc.*, **102**, 1155 (1980).

(4) While this work was in progress, Professor D. E. Bergbreiter and Professor M. Newcomb, Department of Chemistry, Texas A & M University, informed us of their independent observation of the Claisen rearrangement of the enediolate of crotyl mandelate.

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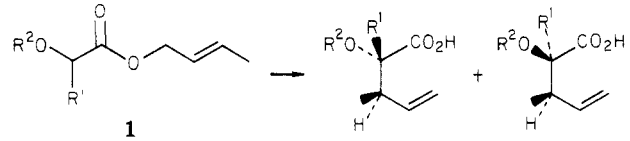
Table I

entry	substrate	conditions[a]	yield,[b] %	ratio of 2/3[c]
1	1a	standard	67	3
2	1a	20% HMPA/THF	60	1.5
3	1a	hexane	67	2
4	1a	0.9 equiv of base, 0 °C for 5 min before silylation	25	2
5	1b	standard	30	4
6	1b	20% HMPA/THF	28	3.5
7	1b	1 equiv of $MgCl_2$ added with ester	20	>10
8	1c	standard	50	0.8
9	1c	without silylation	59	12
10	1d	standard	38	1.4
11	4	standard	69	2[d]

[a] "Standard" conditions involve addition of ester to 1.1 equiv (2.25 equiv for α-hydroxy esters) of LICA in THF at −75 °C, followed 30 min later (60–75 min for α-hydroxy esters) by 1 equiv of Me_3SiCl/equiv of LICA used, warming to 21 °C, reflux for 1 h, and silyl ester cleavage with acidic methanol. Variations in solvent, base, or procedure are indicated. Note: with the exception of entry 9, all cases involve rearrangement of a silylated enol derivative. [b] Isolated yield. [c] Determined by ^{13}C NMR. [d] The product was 5; the stereochemistry was not proven.

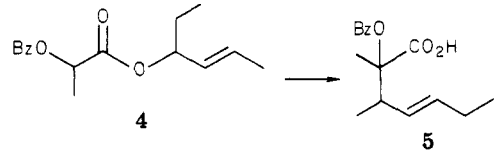
ters require significantly longer enolate generation times than is necessary for propionate esters[2a] or α-acylamido esters.[1] The best conditions found for rearrangement of the benzyl ether **1a**, for example, involve addition of the ester to a solution of LICA in THF at −78 °C followed 30 min later by trimethylsilyl chloride and slow warming to reflux (70 °C; "standard conditions"). Hydrolysis of the silyl ester with acidic methanol affords a 67% yield of rearranged product as a 3:1 mixture of diastereomers **2a** and **3a** (entry 1, Table I). Application of this process to



1 2 3

a, R^1 = Me, R^2 = $PhCH_2$; b, R^1 = Me, R^2 = H; c, R^1 = Ph, R^2 = H; d, R^1 = H, R^2 = H

the secondary allylic ester **4** affords a 69% yield of rearranged material as a 2:1 mixture of diastereomers **5** (entry 11).



4 5

For the free hydroxy ester **1b**, formation of the enediolate intermediate is even slower than for the benzyl ether: a reaction time at −78 °C of 1 h before addition of trimethylsilyl chloride and warming appears to be optimal, affording a 30% yield of **2b** and **3b** (4:1 isomer ratio, entry 5). Ciochetto, Bergbreiter, and Newcomb[7] indicate that higher temperatures may be required before deprotonation of ethyl lactate under similar conditions takes place. It is conceivable, therefore, that deprotonation and concomitant silylation of the lactate esters are occurring as the mixture warms up in the presence of the silylating agent. However, if the crotyl lactate (**1b**)/base solution is brought to −23 °C before addition of the silylating agent, the yield is not improved.

Although we found fluctuations in the degree of stereoselectivity of the overall rearrangement process, no reversal was seen on going from THF to 20% HMPA/THF, as is known for acyclic allylic propionates[2a] (compare entries 1 with 2 and 5 with 6). On the other hand, inclusion of 1 equiv of $MgCl_2$ with the solution of crotyl lactate (**1b**) during addition to the base improves the stereoselectivity of enediolate formation, although not the yield (entry 7). In an attempt to facilitate thermodynamic control over the enolization geometry, a solution of the enolate of **1a**, made with a deficiency of base, was brought to 0 °C for 5 min before silylation and rearrangement (entry 4). However, a significant decrease in yield was observed with no improvement in stereoselectivity.

The more stabilized enediolate derived from crotyl mandelate (**1c**) is readily formed and rearranges in as good yield and stereoselectivity as the unsilylated dianion itself (entries 8 and 9). In contrast, rearrangement of this ester under the standard conditions is nonstereoselective. Not unexpectedly, attempted rearrangement of the enediolate derived from crotyl lactate without silylation[2a] affords a very poor yield of product (<15%).

Three esters of glycolic acid were investigated: the allyl, crotyl, and cinnamyl derivatives, although for these esters only the free hydroxyl compounds were studied. Only for the crotyl derivative **1d** was any rearranged product obtained, and in that case only in poor yield and stereoselectivity (entry 10). In their study of alkylation of enediolates derived from α-hydroxy esters, Ciochetto, Bergbreiter, and Newcomb[7] found that ethyl glycolate fails to undergo the reaction, whereas ethyl lactate and ethyl mandelate give good yields.

We were unable to generalize these rearrangements to any useful extent. In addition to the unsuccessful attempts delineated above, allyl lactate, allyl mandelate, the *tert*-butyl ether or the methyl carbonate of crotyl lactate, and the benzyl ether of (*E*)-5-methyl-2,4-hexadienyl lactate failed to give the desired rearrangement products under the standard conditions. Interestingly, the *tert*-butyldimethylsilyl ether and the benzoate of crotyl lactate (1; R^1 = Me, R^2 = *t*-$BuMe_2Si$ and PhCO, respectively) afford rearranged products in which diastereomer **3** predominates (4:1 and 2.5:1 ratios, respectively). The low yields (<20%) of these particular examples, however, detract from their importance.

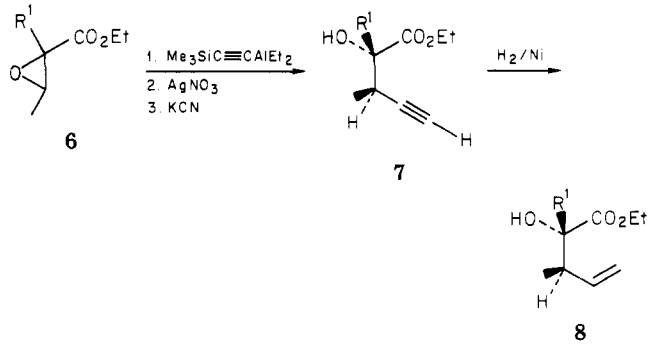
The major side reaction in these processes appeared to be ester cleavage: in the case of attempted rearrangement of (*E*)-5-methyl-2,4-hexadienyl lactate, for example, the alcohol was isolated by preparative TLC as the major identifiable product. This mode of decomposition presumably involves formation of a ketene intermediate.[8] The increased prevalance of this side reaction with the enediolates is perhaps not surprising in view of the enolate-destabilizing effect the ionized α-hydroxyl is expected to have.[3a]

Stereochemical Assignments

Lactate Rearrangement Products 2a and 2b. Two independent proofs of stereochemistry for the lactate re-

(5) M. W. Rathke and A. Lindert, *J. Am. Chem. Soc.*, **93**, 2318 (1971).
(6) Our initial experiments gave higher yields with LICA instead of lithium diisopropylamide as base and with trimethylsilyl chloride instead of *tert*-butyldimethylsilyl chloride; hence we used this combination throughout.
(7) L. J. Ciochetto, D. E. Bergbreiter, and M. Newcomb, *J. Org. Chem.* **42**, 2948 (1977).
(8) D. F. Sullivan, R. P. Woodbury, and M. W. Rathke, *J. Org. Chem.*, **42**, 2038 (1977).

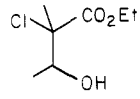
Scheme I[a]



6 7 8

[a] a, R^1 = Me; b, R^1 = H.

arrangement products were devised. Reaction of diethyl[(trimethylsilyl)ethynyl)]alane (prepared from diethylchloroalane and the lithium acetylide) with ethyl epoxytiglate (**6a**; see Scheme I) afforded predominantly the chlorohydrin **9**. Although formation of this side



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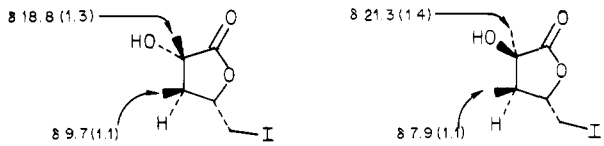
product was never completely suppressed, use of a 2:1 ratio of lithium acetylide to diethylchloroalane in preparation of the aluminum reagent afforded a 1.4:1 mixture of the desired acetylene and chlorohydrin **9**. Desilylation[9] and partial hydrogenation over P-2 nickel[10] was accompanied by some overreduction, providing a 3:1 mixture of pentenoate **8a** and the saturated analogue, which was separable by preparative VPC. The Claisen rearrangement products **2a**/**3a** and **2b**/**3b** were correlated with **8a** by debenzylation (Na/NH_3) and esterification.

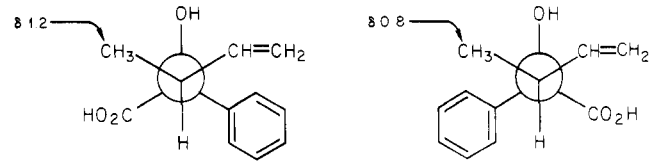
The stereostructures of the hydroxy acids **2b** and **3b** were independently determined by conversion of a 2:1 mixture to the iodolactones **10** and **11** using iodine in



10 11

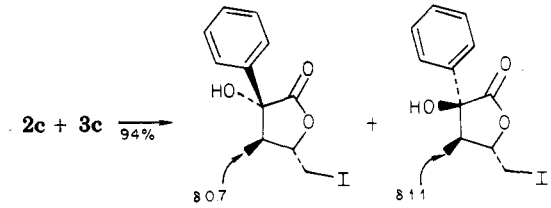
acetonitrile.[11] This procedure is highly selective for the thermodynamically favored product, so essentially only the two β,γ-trans lactones **10** and **11** were obtained, in 72% yield. The methyl resonances in the ^{13}C NMR spectrum were assigned on the basis of their chemical shifts and by correlation with the proton resonances by off-resonance decoupling techniques;[12] the observed values of the carbon (and proton) chemical shifts are indicated in structures **10** and **11**. The upfield ^{13}C shift of the α-methyl group in the major isomer **10** clearly indicates its cis relationship with the β-methyl group and confirms the *RS,SR* stereochemistry of **2b**.[13]

Mandelate Rearrangement Products 2c and 3c. ^1H NMR analysis of the hydroxy acids **2c** and **3c** suggested



2c 3c

that their stereostructures should be assigned as shown. The conformations depicted were chosen to minimize steric interactions. The upfield ^1H NMR shift of the methyl resonance of the minor product of rearrangement (**3c**) indicates that it lies within the shielding cone of the anisotropic phenyl group,[14] as expected for the structure depicted. Firmer evidence was obtained from the conformationally fixed iodo lactones **12** and **13**. Cyclization reverses the methyl–phenyl relationship and therefore the relative chemical shifts of the methyl groups.



12 13

Glycolate Rearrangement Product 2d. An authentic sample of ethyl (*RS,SR*)-2-hydroxy-3-methyl-4-pentenoate (**8a**) was prepared analogously to the lactate-derived compound (see Scheme I) by starting with ethyl epoxycrotonate.[11] This material proved to be identical with the major isomer obtained on esterification (3% HCl/ethanol) of the mixture of **2d** and **3d** obtained from rearrangement.

Stereochemistry of Dialkoxy Enolate and Alkoxy Enediolate Formation. That the Claisen rearrangement of acyclic systems takes place via a chairlike transition state has been affirmed many times.[15] Indeed, this generalization is often used as evidence in the elucidation of stereochemical details of other processes.[16] Although a number of examples of Claisen rearrangements which prefer a boatlike transition state have recently been discovered,[17] these cases are confined to cyclic systems exclusively. The predominance of isomer **2** in all but two of the rearrangements discussed in this report is strong evidence for preferential formation of the *E* enolates **14** or *E* enediolates **15**, in which the α-oxygen substituent (alkoxy or oxy anion) is cis to the enolate oxygen. This assignment of enediolate stereochemistry in particular is opposite that expected intuitively on electrostatic grounds and inferred by Bergbreiter, Newcomb, and co-workers from the results of their "polarity reversed" Prelog reaction.[18]

Our results suggest that the stereochemistry of enolization is controlled by counterion chelation for these α-

(9) H. M. Schmidt and J. F. Arens, *Recl. Trav. Chim. Pays-Bas*, **86**, 1138 (1967).
(10) C. A. Brown and U. K. Ahuja, *J. Org. Chem.*, **38**, 2226 (1973); *J. Chem. Soc., Chem. Commun.*, 553 (1973).
(11) P. A. Bartlett and J. Myerson, *J. Am. Chem. Soc.*, **100**, 3950 (1978).
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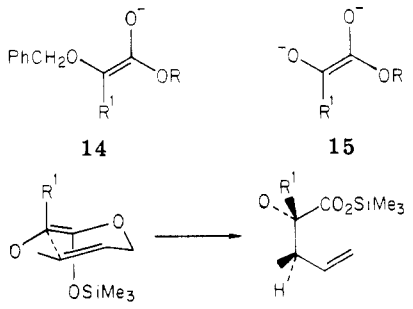

14 15

oxygenated esters, as it appears to be for the α-acylamido derivatives described in the preceding paper as well. The increase in stereoselectivity for crotyl lactate rearrangement in the presence of magnesium directly supports this interpretation. The increasing selectivity on going from crotyl glycolate to lactate to mandelate is consistent with a steric influence as well.[2]

Experimental Section

Unless otherwise indicated, infrared spectra were recorded with neat films on a Perkin-Elmer Model 710 spectrophotometer. ^1H NMR spectra were recorded on a Varian Associates Model T-60 or EM-390 instrument; chemical shifts are reported in parts per million on the δ scale relative to internal tetramethylsilane. Data are presented as follows: chemical shift (multiplicity, number of protons, coupling constants). Unless otherwise noted, the NMR solvent was $CDCl_3$. ^{13}C NMR spectra were acquired on a Nicolet TT23 instrument (25.14 MHz). Chemical shifts are reported in parts per million on the δ scale, referenced to the $CDCl_3$ solvent as 77.0 ppm relative to tetramethylsilane. Preparative VPC was performed on a Varian Model A-90 gas chromatograph by using helium as the carrier gas and 6 ft × 0.25 in. columns packed with either 10% or 30% SE-30 on 100–120-mesh Gas-Chrom Q. Noncrystalline compounds were purified for analysis by preparative VPC. Distillations were bulb-to-bulb distillations with a Büchi Kugelrohr oven at the temperature and pressure indicated. Microanalyses were performed by the Microanalytical Laboratory of the College of Chemistry, University of California, Berkeley.

(*E*)-2-Butenyl 2-(Phenylmethoxy)propanoate (1a). Condensation of 2-(phenylmethoxy)propanoyl chloride[19] with (*E*)-2-buten-1-ol with pyridine in $CHCl_3$ afforded the ester **1a**: bp 140 °C (4 torr); IR 2950, 1740, 1680 cm^{-1}; ^1H NMR (CCl_4) δ 1.4 (d, 3, J = 7 Hz), 1.8 (d, 3, J = 5 Hz), 4.0 (q, 1, J = 7 Hz), 4.6 (m, 4), 5.8 (m, 2), 7.3 (br s, 5). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.77; H, 7.58.

(*E*)-2-Butenyl 2-Hydroxypropanoate (1b). This was prepared by the method of Olah et al.[20] in 43% yield after distillation [150 °C (0.1 torr)]: IR 3350, 2950, 1730, 1680 cm^{-1}; ^1H NMR δ 1.7 (d, 6), 3.1 (s, 1), 4.3 (q, 1), 4.6 (d, 2), 5.6 (m, 2). Anal. Calcd for $C_7H_{12}O_3$: C, 58.32; H, 8.39. Found: C, 58.11; H, 8.17.

(*E*)-2-Butenyl 2-Hydroxy-2-phenylacetate (1c). In a similar manner, **1c** was prepared in 86% yield: mp 46–47 °C after recrystallization from ether/hexane: IR ($CDCl_3$) 3525, 3000, 1720, 1680, 1610 cm^{-1}; ^1H NMR δ 1.6 (d, 3), 3.8 (d, 1), 4.5 (dd, 2), 5.1 (d, 1), 5.5 (m, 2), 7.3 (m, 5). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.73; H, 6.84.

(*E*)-2-Butenyl 2-Hydroxyacetate (1d). A solution of the potassium salt of (*E*)-2-buten-1-ol was prepared from 20 mmol of KH, 20 mmol of the alcohol, and 40 mL of THF. This solution was cooled to 0 °C, and 1.75 g (20 mmol) of 1,3-dioxolan-4-one[21] was added, keeping the temperature below 5 °C. After an additional 4 min, the mixture was partitioned between saturated $NaHCO_3$ and ether, and the organic layer was dried and evaporated to give 0.91 g (35% yield) of the ester **1d** after distillation [100 °C (0.1 torr)]: IR 3450, 2950, 1740, 1680 cm^{-1}; ^1H NMR 1.8 (d, 3), 3.7 (s, 1), 4.3 (s, 2), 4.7 (d, 2), 5.8 (m, 2). Anal. Calcd for $C_6H_{10}O_3$: C, 55.37; H, 7.74. Found: C, 55.52; H, 7.59.

2,3-Dimethyl-2-(phenylmethoxy)-4-pentenoic Acids 2a and 3a. General Procedure for Ester–Enolate Claisen Rearrangements. A solution of 66 mmol of lithium isopropylcyclohexylamide in 135 mL of dry THF was prepared from the amine and 1.6 M butyllithium in hexane and kept at −75 °C for 15 min. (*E*)-2-Butenyl 2-(phenylmethoxy)propanoate (**1a**; 15.2 g, 65 mmol) was added slowly, and the solution was stirred at −75 °C for 30 min. Trimethylsilyl chloride (8.4 mL, 66 mmol) was added, the cooling bath was removed, and the mixture was allowed to warm to 21 °C over 15 min and then heated at reflux for 1 h. The silyl moieties were hydrolyzed by adding 6 mL of 10% methanolic HCl overnight. The mixture was partitioned between ether and 1 N KOH, and the aqueous layer was acidified and extracted with $CHCl_3$. After the mixture was dried and evaporated, the residue was chromatographed (silica/ethyl acetate) to give 10.2 g (67% yield) of oily product as a mixture (3:1 ratio) of diastereomers: mp 57–59 °C; IR 3000, 1710, 1640 cm^{-1}; ^1H NMR δ 1.1 (d, 3), 1.4 (s, 3), 2.6 (m, 1), 4.6 (s, 2), 5.1 (m, 2), 5.8 (m, 1), 7.3 (s, 5), 11.4 (s, 1); ^{13}C NMR for major (*RS,SR*) diastereomer **2a** δ 14.6 (q), 18.0 (q), 46.3 (d), 66.4 (t), 82.0 (s), 116.4 (t), 127.1 (d), 128.0 (d)(overlap), 138.3 (d), 138.5 (s), 179.6 (s); for minor (RR,SS) diastereomer **3a** δ 14.0 (q), 18.0 (q), 45.9 (d), 66.4 (t), 82.4 (s), 115.5 (t), 127.1 (d), 128.0 (d) (overlap), 138.5 (s), 138.8 (d), 179.1 (s). Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.66. Found: C, 71.56; H, 7.66.

2-Hydroxy-2,3-dimethyl-4-pentenoic Acids 2b and 3b. This synthesis was performed as described for the general procedure, except that an enolate generation time of 1.25 h was allowed before trimethylsilyl chloride was added. A 30% yield of a 4:1 mixture of diastereomers was obtained as a 3.3:1 mixture of diastereomers: IR 1720, 1640 cm^{-1}; ^1H NMR δ 1.03 (major) and 1.06 (minor) (diastereomeric d, 3), 1.4 (s, 3), 2.5 (m, 1), 5.1 (m, 2), 5.8 (m, 1), 7.5 (br s, 2); ^{13}C NMR for major (*RS,SR*) diastereomer **2b** δ 15.1, 24.0, 46.0, 76.6, 117.2, 137.9, 180.5; for minor (*RR,SS*) diastereomer **3b** δ 13.4, 23.2, 45.8, 76.6, 116.5, 138.6, 180.4. For analytical purposes, this material was characterized as the methyl ester (CH_3I, K_2CO_3): IR 3550, 2975, 1730, 1640 cm^{-1}; ^1H NMR δ 1.0 (d, 3, J = 7 Hz), 1.4 (s, 3), 2.5 (m, 1), 3.2 (br s, 1), 3.8 (s, 3), 5.1 (m, 2), 5.7 (m, 1). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.57; H, 8.71.

2-Hydroxy-3-methyl-2-phenyl-4-pentenoic Acids 2c and 3c. This synthesis was performed as described above but with the omission of trimethylsilyl chloride and gave a 59% yield of a 12:1 mixture of diastereomers: IR 3550, 3000, 1710, 1640 cm^{-1}; ^1H NMR δ 0.8 (minor) and 1.2 (major) (diastereomeric d, 3), 3.2 (m, 1), 4.9–5.2 (m, 2), 5.4–6.0 (m, 1), 7.2 (m, 3), 7.6 (m, 2); ^{13}C NMR for major (*RR,SS*) diastereomer **2c** δ 14.6, 44.9, 80.3, 116.1, 125.9, 127.8, 127.9, 137.5, 140.4, 177.4; for minor (*RS,SR*) diastereomer **3c** δ 13.2, 45.5, 80.5, 116.5, 125.9, 127.3, 127.8, 138.5, 139.8, 177.6. Crystallization of the mixture from CH_2Cl_2/hexane gave the *RR,SS* diastereomer **2c**, mp 115.5–117 °C. Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.88; H, 6.84. Found: C, 69.68; H, 6.77.

2-Hydroxy-3-methyl-4-pentenoic Acids 2d and 3d. Obtained by the standard procedure in 38% yield as a 1.4:1 mixture of diastereomers: IR 3300, 2950, 1710, 1640 cm^{-1}; ^1H NMR δ 1.1 and 1.2 (diastereomeric d, 3, J = 7 Hz), 2.7 (m, 1), 4.2 (m, 1), 5.1 (m, 2), 5.8 (m, 1), 7.1 (br s, 2); ^{13}C NMR for major (*RS,SR*) diastereomer **2d** δ 13.3, 41.1, 73.7, 115.7, 139.0, 177.4; for minor (RR,SS) diastereomer **3d** δ 16.1, 41.4, 74.2, 116.6, 137.2, 177.6. Characterized as the ethyl ester (3% HCl/ethanol): IR 3475, 2950, 1730, 1640 cm^{-1}; ^1H NMR δ 1.0 (d, 3), 1.3 (t, 3), 2.7 (m, 1), 4.1 (m, 1), 4.2 (q, 2), 5.0 (m, 2), 5.7 (m, 1). Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.84; H, 8.78.

(*E*)-1-Ethyl-2-butenyl 2-(Phenylmethoxy)propanoate (4). In a similar manner to the crotyl ester **1a**, the secondary ester **4** was prepared in 48% yield after distillation [118 °C (0.1 torr)]: IR 2950, 1740, 1680, 1600 cm^{-1}; ^1H NMR δ 0.9 (t, 3), 1.25 (m, 5), 1.75 (d, 3, J = 6 Hz), 4.0 (q, 1, J = 7 Hz), 4.6 (ABq, 2, J = 12 Hz), 5.2 (m, 1), 5.5 (m, 2), 7.3 (s, 5). Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 73.05; H, 8.28.

(*E*)-2,3-Dimethyl-2-(phenylmethoxy)-4-heptenoic Acid (5). By the standard rearrangement procedure, a 69% yield of **5** as a 2:1 mixture of diastereomers was obtained after distillation [150 °C (0.1 torr)]: IR 3000, 1710 cm^{-1}; ^1H NMR δ 0.9 (t, 3), 1.2 (d, 3), 1.4 (s, 3), 1.6–2.8 (m, 3), 4.5 (s, 2), 5.4 (m, 2), 7.2 (br s, 5); ^{13}C

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NMR for the major diastereomer δ 13.7, 15.1, 17.8, 25.5, 45.2, 66.6, 82.7, 127.2, 128.1 (overlap), 128.8, 134.5, 138.7, 180.0; for the minor diastereomer δ 13.7, 14.8, 18.4, 25.5, 45.2, 66.5, 82.6, 127.2, 128.1 (overlap), 129.4, 133.6, 138.7, 179.2. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.25; H, 8.45. Found: C, 72.90; H, 8.26.

Ethyl (*RS,SR*)-2-Hydroxy-3-methyl-5-(trimethylsilyl)-4-pentynoate. To a solution of 0.3 mL of a 77% solution in THF (1.5 mmol) of (trimethylsilyl)acetylene[22] in 1 mL of toluene at 0 °C was added 0.62 mL of a 1.61 M solution (1 mmol) of butyllithium in hexane. After 10 min, 0.59 mL of a 1.70 M solution (1 mmol) of diethylaluminum chloride in toluene was added, and the mixture was stirred at 0 °C for 30 min (LiCl precipitates). A solution of 65 mg (0.5 mmol) of ethyl *trans*-2,3-epoxybutanoate in 0.25 mL of toluene was added, and stirring was continued at 21 °C for 2.5 h. The mixture was partitioned between ether and 1 N HCl, and the organic layer was washed with water, dried, and evaporated to give 86 mg (76% yield) of the pentynoate as an oil: IR 3450, 3000, 2175, 1740 cm^{-1}; ^1H NMR δ 0.2 (s, 9), 1.2 (d, 3), 1.3 (t, 3), 3.0 (m, 1), 3.4 (br s, 1), 4.2 (m, 3). Anal. Calcd for $C_{11}H_{20}O_3Si$: C, 57.85; H, 8.83. Found: C, 57.62; H, 8.66.

Ethyl (*RS,SR*)-2-Hydroxy-2,3-dimethyl-5-(trimethylsilyl)-4-pentynoate. In a similar manner, the epoxide of ethyl tiglate was converted to the title compound in 27% yield after purification by preparative VPC (150 °C/30% SE-30): IR 3525, 3000, 2175, 1730 cm^{-1}; ^1H NMR δ 0.1 (s, 9), 1.2 (d, 3), 1.35 (t, 3), 1.5 (s, 3), 2.9 (m, 1), 3.2 (br s, 1), 4.3 (q, 2). Anal. Calcd for $C_{12}H_{22}O_3Si$: C, 59.46; H, 9.15. Found: C, 59.38; H, 8.92.

Ethyl (*RS,SR*)-2-Hydroxy-3-methyl-4-pentynoate (7b). The (trimethylsilyl)alkyne was treated sequentially with ethanolic $AgNO_3$ and KCN according to the method of Schmidt and Arens[9] to give a 66% yield of the product **7b** after distillation [150 °C (0.1 torr)]: IR 3550, 2975, 2125, 1720 cm^{-1}; ^1H NMR δ 1.3 (d, 3), 1.35 (t, 3), 2.2 (d, 1, J = 2 Hz), 3.0 (m, 1), 3.3 (br d, 1), 4.3 (q, 3). Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.11; H, 7.59.

Ethyl (*RS,SR*)-2-Hydroxy-2,3-dimethyl-4-pentynoate (7a). This was obtained in an analogous manner: 61% yield; IR 3525, 3325, 2900, 2125, 1725 cm^{-1}; ^1H NMR δ 1.15 (d, 3), 1.3 (t, 3), 1.55 (s, 3), 2.15 (d, 1, J = 2 Hz), 2.85 (dq, 1, J = 2, 7 Hz), 3.3 (br s, 1), 4.25 (q, 2). Anal. Calcd for $C_9H_{14}O_3$: C, 69.51; H, 8.29. Found: C, 63.59; H, 8.19.

Ethyl (*RS,SR*)-2-Hydroxy-3-methyl-4-pentenoate (8b). A suspension of P-2 Ni catalyst[10] was prepared from 0.1 mmol of $Ni(OAc)_2$ in 1.6 mL of 95% ethanol and used to hydrogenate 1.1 mmol of alkyne **7b** under 1 atm of H_2 at 21 °C for 18 h. After filtration and evaporation a 1:1 mixture of the alkenoate **8b** and the saturated ester was obtained. Pure alkenoate was obtained by preparative VPC (130 °C/30% SE-30): IR 3475, 2950, 1730, 1640 cm^{-1}; ^1H NMR δ 1.0 (d, 3), 1.3 (t, 3), 2.6 (m, 2), 4.1 (d, 1), 4.2 (q, 2), 5.0 (m, 2), 5.7 (m, 1); ^{13}C NMR δ 13.5, 14.1, 41.6, 61.4, 73.8, 115.2, 139.4, 174.0. Anal. Calcd for $C_8H_{14}O_3$: C, 60.74; H, 8.92. Found: C, 60.84; H, 8.78.

A mixture containing the *RR,SS* diastereomer, prepared by esterification (3% ethanolic HCl) of the product from Claisen rearrangement, showed additional resonances in the ^{13}C NMR at δ 16.1, 41.8, 74.2, 116.1, and 137.7.

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Ethyl (*RS,SR*)-2-Hydroxy-2,3-dimethyl-4-pentenoate (8a). In a similar manner, a 3:1 mixture of alkenoate **8a** and the corresponding alkanoate was obtained from alkynoate **7a**. Pure alkenoate was obtained by preparative VPC (150 °C/30% SE-30): IR 3550, 3000, 1720, 1640 cm^{-1}; ^1H NMR δ 1.0 (d, 3), 1.35 (t, 3), 1.4 (s, 3), 2.5 (m, 1), 4.25 (q, 2), 5.0 (m, 2), 5.7 (m, 1); ^{13}C NMR δ 14.1, 15.1, 24.1; 46.2, 61.7, 76.1, 116.5, 138.5, 176.9. Anal. Calcd for $C_9H_{16}O_3$: C, 62.77; H, 9.36. Found: C, 62.77; H, 9.16.

A mixture containing the *RR,SS* diastereomer (from esterification of Claisen rearrangement product) showed additional resonances in the ^{13}C NMR at δ 13.4, 23.4, 46.1, 116.5, 138.5.

3-Hydroxy-5-(iodomethyl)-3,4-dimethyl-4,5-dihydro-2(3*H*)-furanones 10 and 11. A mixture of 288 mg (2 mmol) of a 2:1 mixture of **2b** and **3b** and 1.02 g (4 mmol) of I_2 in 7 mL of acetonitrile was stirred at 21 °C for 18 h. After diluting with ether, the solution was washed with aqueous $Na_2S_2O_3$, saturated $NaHCO_3$, dried and evaporated to give 390 mg of the iodo lactones **10** and **11**. Recrystallization of the crude product from ether/hexane gave a pure sample of the major diastereomer **10**: mp 87–88.5 °C; IR ($CDCl_3$) 3475, 3000, 1780 cm^{-1}; ^1H NMR δ 1.1 (d, 3), 1.3 (s, 3), 2.4 (m, 1), 3.4 (AB of ABX, 2), 3.6 (s, 1), 3.8 (ddd, 1); ^{13}C NMR 4.9(t), 9.7(q), 18.8(q), 46.4(d), 75.4(s), 80.9(d), 178.4(s). Anal. Calcd for $C_7H_{11}O_3I$: C, 31.13; H, 4.10; I, 46.99. Found: C, 31.47; H, 4.22; I, 46.58.

The mixture of diastereomers showed additional resonances in the ^1H NMR at δ 1.4 (s, 3) and 2.0 (m, 1) and in the ^{13}C NMR at δ 5.7 (t), 7.9 (q), 21.3 (q), 46.7 (d), 74.3 (s), 81.5 (d), and 176.8 (s).

3-Hydroxy-5-(iodomethyl)-4-methyl-3-phenyl-4,5-dihydro-2(3*H*)-furanone 12 and 13. In a similar manner, a 5:1 mixture of **2c** and **3c** was converted to the iodo lactones **12** and **13** in 94% yield. Recrystallization from ether/hexane gave a pure sample of the major (3*RS*,4*RS*,5*SR*) diastereomer **12**: mp 102–103 °C; IR 3425, 2975, 1770 cm^{-1}; ^1H NMR δ 0.7 (d, 3, J = 7 Hz), 2.6 (dq, 1, J = 10, 7 Hz), 3.1 (s, 1), 3.4 (AB of ABMX, 2), 3.8 (M of ABMX, 1), 7.5 (br s, 5). Anal. Calcd for $C_{12}H_{13}O_3I$: C, 43.40; H, 3.94; I, 38.21. Found: C, 43.53; H, 4.08; I, 38.36.

The mixture of diastereomers showed additional resonances in the ^1H NMR for the 3*RS*,4*SR*,5*RS* isomer **13** at δ 1.1 (d, 3), 2.8 (dq, 1), and 4.5 (dt, 1) and for a third, minor isomer (assigned the 3*RS*,4*SR*,5*SR* configuration) at δ 1.05 (d, 3), 2.3 (dq, 1), and 4.1 (m, 1).

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Registry No. **1a**, 82731-55-3; **1b**, 82731-56-4; **1c**, 82731-57-5; **1d**, 82731-58-6; **2a**, 82731-59-7; **2b**, 82731-60-0; **2b** methyl ester, 82731-81-5; **2c**, 82731-61-1; **2d**, 82731-62-2; **2d** ethyl ester, 71249-94-0; **3a**, 82731-63-3; **3b**, 82731-64-4; **3b** methyl ester, 82731-82-6; **3c**, 82731-65-5; **3d**, 82731-66-6; **3d** ethyl ester, 71215-26-4; **4**, 82731-67-7; **5** (isomer 1), 82731-68-8; **5** (isomer 2), 82731-80-4; **6a**, 82731-69-9; **6b**, 82769-14-0; **7a**, 82731-70-2; **7a** 5-$SiMe_3$, 82731-78-0; **7b**, 82731-71-3; **7b** 5-$SiMe_3$, 82731-77-9; **8a**, 82731-72-4; **8b**, 71249-94-0; **10**, 82731-73-5; **11**, 82731-74-6; **12**, 82731-75-7; **13**, 82731-76-8; 2-(phenylmethoxy)propanoyl chloride, 74406-96-5; 1,3-dioxolan-4-one, 4158-81-0; (*E*)-2-buten-1-ol, 504-61-0; diethyl[(trimethylsilyl)ethynyl]alane, 82731-79-1.