Diastereoselective Coupling Reaction of Activated Cyclic Ketene Ortho Ester with Aldehydes Promoted by Lewis Acid Catalyst

Chan-Mo Yu,* Ha-Soon Choi, Jeon-Koo Lee, and Sook-Kyung Yoon

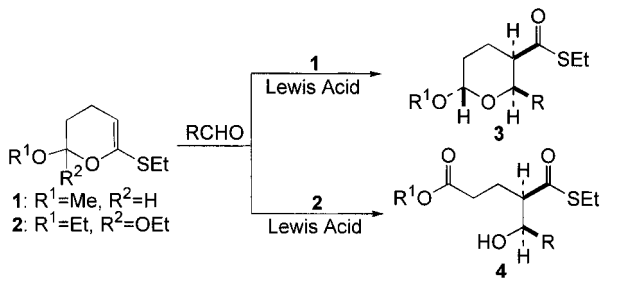
Department of Chemistry, Sung Kyun Kwan University, Suwon 440-746, Korea

Received May 1, 1997

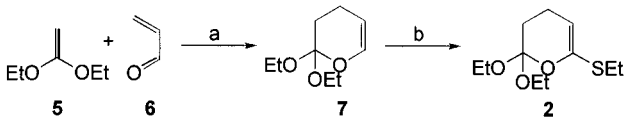
The development of new synthetic methodologies for achieving stereocontrol via catalytic process in the construction of acyclic systems is an important objective in current organic chemistry.[1] Significant advances in diastereocontrol have been made in the formation of β-hydroxy esters through the aldol reaction. The aldolates of rich stereochemical complexity are definitive structural features in a wide variety of useful substances.[2] Effective methods have been developed in recent years for accessing these structures, the majority of which involve the construction of this system through carbon−carbon bond formation *via* addition of enolate or ketene acetal to the carbonyl functionalities.[3] The design of synthetic methods to effect functionalized enolate or equivalent addition to aldehydes would expand the scope of the aldol process. We recently reported the diastereoselective synthesis of highly functionalized tetrahydropyrans **3** from the reaction of dihydropyran **1** with aldehydes mediated by a Lewis acid catalyst.[4] The efficiency of this transformation concerning diastereocontrolled catalytic processes has encouraged us to apply the extension of this method to more versatile systems. We report herein our discovery of a broadly useful method for assembling aldol products of glutarates **4** from the reaction of 2,2-diethoxy-6-(ethylthio)-3,4-dihydro-2*H*-pyran (**2**) with aldehydes in the presence of Lewis acid catalyst as depicted in Scheme 1. This unique and highly stereocontrolled transformation involves the diastereoselective generation of a carbon−carbon bond and introduction of an ester functionality from hydrolysis of the ortho ester intermediate. The method described herein is successful with a variety of aldehydes and affords products in high yields with useful levels of diastereoselectivity.

The starting point of this investigation was the availability of compound **2**; this was prepared in quantity by a two-step sequence, purified by distillation, and is stable to storage. The hetero-Diels−Alder reaction of **5** with acrolein (**6**) in the presence of 2,6-di-*tert*-butylphenol (0.5 mol %) at 180 °C for 2 h in a sealed tube afforded adduct **7** in 74% yield.[5] Subsequent treatment of **7** with a mixture of *n*-BuLi and *t*-BuOK[6] in the presence of TMEDA in pentane at −78 to −20 °C for 1 h followed by reaction with diethyl disulfide at −78 °C for 4 h afforded 6-(ethylthio)-2,2-diethoxy-2*H*-dihydropyran (**2**) in 81% yield (Scheme 2). The stage was thus set for the coupling reaction of **2** with aldehydes mediated by a Lewis acid catalyst.

Scheme 1



Scheme 2[a]



[a] (a) 2,6-Di-*tert*-butylphenol (0.5 mol %), 180 °C, 2h, sealed tube; (b) (i) *n*-BuLi, *t*-BuOK, TMEDA, −78 to −20 °C, pentane. (ii) EtSSEt, Et_2O.

Preliminary studies on the reaction of **2** with benzaldehyde indicated that the conversion to the corresponding product could be realized with a variety of Lewis acids such as $BF_3{\cdot}OEt_2$, $TiCl_4$, and $SnCl_4$. Especially encouraging was the utilization of $SnCl_4$ as a catalyst; reaction of **2** with aldehydes in the presence of $SnCl_4$ occurred readily at −78 °C.[7] After exploring several reaction conditions, we found that the addition of $SnCl_4$ to the mixture of **2** and aldehyde in CH_2Cl_2 always resulted in the best chemical yields and stereoselectivities. Under optimal conditions, the addition reaction was performed by addition of $SnCl_4$ to a solution of **2** and benzaldehyde in CH_2Cl_2 at −78 °C. After 4 h at −78 °C, the reaction mixture was quenched with 0.5 N aqueous HCl at −78 °C followed by workup and silica gel chromatography to afford inseparable *threo*-**9a** and *erythro*-**10a** in a ratio of 91:9 as judged by ^{1}H NMR.[8] The results obtained with various aldehydes are summarized in Table 1.

The stereochemistry of the major component **9** in each case was determined on the basis of the vicinal coupling patterns in the ^{1}H NMR spectra. The *erythro*−*threo* stereochemical assignments in β-hydroxy esters are often based on the magnitude of vicinal coupling constants resulting from intramolecular hydrogen bonding.[9] The larger coupling constant (7.43 Hz at δ 4.84) obtained from the spectrum of **9a** (R = Ph) clearly indicated *threo*

(1) For general discussions, see: (a) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307. (b) Ager, D. J.; East, M. B. *Asymmetric Synthetic Methodology*; CRC: New York, 1996.

(2) For example, see: Norcross, R. D.; Paterson, I. *Chem. Rev.* **1995**, *95*, 2041.

(3) For reviews, see: (a) Heathcock, C. H. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, U.K., 1991; Vol. 2, p 133. (b) Kim, B. M.; Williams, S. F.; Masamune, S. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, U.K., 1991; Vol. 2, p 239. (c) Paterson, I. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon Press: Oxford, U.K., 1991; Vol. 2, p 301. (d) Heathcock, C. H. In *Modern Synthetic Methods*; Scheffold, R., Ed.; VCH: Basel, Swiss, 1992; p 1.

(4) Yu, C.-M.; Jung, W.-H.; Choi, H.-S.; Lee, J.; Lee, J.-K. *Tetrahedron Lett.* **1995**, *36*, 8255.

(5) Boeckman, R. K., Jr.; Brunza, K. J. *Tetrahedron* **1981**, *37*, 3997.

(6) (a) Schlosser, M. *Pure Appl. Chem.* **1988**, *60*, 1627. (b) Schlosser, M. In *Organometallics in Synthesis*; Schlosser, M., Ed.; John Wiley & Son: New York, 1994, p 1.

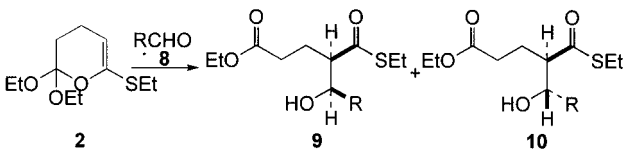
(7) This Lewis acid is superior to others. For example, the reaction which employed $BF_3{\cdot}OEt_2$ required the use of stoichiometric amounts of Lewis acid, presumably due to complexation of Lewis acid with product, and gave only yields in the range of 50%.

(8) We tried to isolate intermediate **15** under various neutral or basic conditions, but unsuccessfully. The major component was always **9** along with several minor components. However, after mild acidic workup, **9** was cleanly obtainable.

(9) Evans, D. A.; Nelson, J. V.; Taber, T. R. In *Topics in Stereochemistry*, Alliger, N. L., Eliel, E. L., Wilson, S. H., Eds.; Wiley: New York, 1982; Vol. 13, p 1.

S0022-3263(97)00774-3 CCC: $14.00

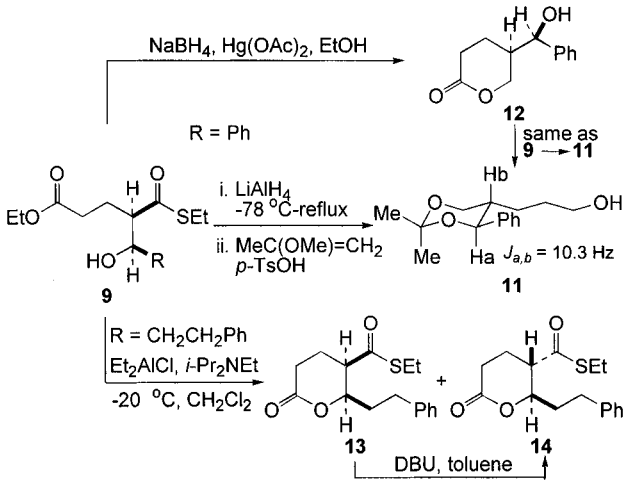
Table 1. Addition of 2 to Aldehydes Mediated by $SnCl_4$ Catalyst[a]



entry	RCHO (**8**)	product	**9**:**10**[b]	yield, %[c]
1	Ph	**a**	91:9	93
2	$PhCH_2CH_2$	**b**	92:8	89
3	n-C_6H_{13}	**c**	88:12	83
4	Me_2CH	**d**	85:15	85
5	Me_2CHCH_2	**e**	89:11	78
6	$CH_3CH{=}CH$	**f**	77:23	71

[a] All reactions were carried out at −78 °C for 4 h in the presence of 10 mol % of $SnCl_4$ in CH_2Cl_2. [b] Determined by the analysis of ^1H NMR spectra of crude products. [c] Yields refer to isolated and purified products.

Scheme 3



configuration, whereas a doublet coupling of 5.34 Hz at δ 4.96 of minor component **10a** implied it to be *erythro*. However, the magnitude of the coupling constant in β-hydroxy esters hinges on the subtle conformational interplay between intramolecular hydrogen bonding and gauche interactions. To clarify any uncertainty, we converted **9** to the conformationally fixed 1,3-dioxane **11** to support the stereochemical assignment. The dioxane **11**, easily prepared from ester **9a**, has a 1,2-diaxial relationship between vicinal protons, as demonstrated by coupling constant of 10.3 Hz at δ 4.48. This study clearly indicates that the major components of these transformations have *threo* stereochemical relationships.

The coupling products **9** are readily amenable for further conversion to useful synthetic intermediates, as demonstrated by the functional group transformations in Scheme 3. For example, the structurally interesting lactone **12** was obtained from **9a** by the chemoselective reduction of the thioester in 91% isolated yield ($NaBH_4$, $Hg(OAc)_2$, EtOH, 0−23 °C, 4 h and 40 °C for 1 h). Surprisingly, we encountered unexpected difficulties for the lactonization of **9** from the methods listed in the literature.[10] Indeed, we were delighted to find that the reaction of **9b** (92:8 mixture) with Et_2AlCl in the presence of i-Pr_2NEt in CH_2Cl_2 at −20 °C for 2 h and then 20 °C

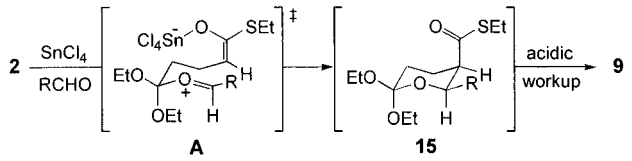


Figure 1. A plausible reaction pathway for C−C bond formation.

for 4 h resulted in the formation of a mixture of **13** and **14** (82%, 87:13) with a diminished diastereomeric ratio presumably due to partial epimerization of **13** to **14** during the process. The mixture was allowed to stand for 5 h at 40 °C with DBU in toluene to give **14** in somewhat lower yield (54%).

Although the exact mechanistic aspects of this transformation have not been rigorously elucidated, the following pathway could be a probable stereochemical route on the basis of product population. Reaction of cyclic ketene ortho ester **2** initiated by $SnCl_4$ results in cleavage of the activated C−O bond in the ortho ester to simultaneously form an intermediate with retention of enolate geometry. C−C bond formation between zwitterionic species and aldehyde can occur in the following plausible way pictured in Figure 1: addition of aldehyde to **2** to form an oxocarbenium intermediate[11] followed by an intramolecular aldol process. Consequently, transition state **A** provides the stereoselectivities for the conversion of **2** with aldehyde in forming the *threo* compound **15** as a major component.

In summary, this paper describes a new methodology for the diastereoselective synthesis of aldol products of glutarates in a very general and efficient way which promises to be widely useful. We believe that the products can serve as synthetic intermediates for the synthesis of valuable substances by selective functional group transformations. Further studies including synthetic application and extension of this method into enantiomeric pathways are in progress.

Experimental Section

All reagents were obtained from the Aldrich Chemical Co. and used without further purification, unless indicated otherwise. *N*,*N*,*N*′,*N*′-Tetramethylethylenediamine (TMEDA) was distilled from CaH_2, and stored over 4 Å molecular sieves. Tetrahydrofuran (THF) was dried by refluxing over sodium and benzophenone until permanently purple and distilled prior to use. Diethyl ether was also distilled from Na/benzophenone ketyl prior to use. Dichloromethane was distilled from CaH_2 prior to use. Pentane was distilled from P_2O_5 prior to use. All reactions were run in oven- or flame-dried glassware under an atmosphere of nitrogen. Purification was conducted by flash column chromatography on silica gel, eluting with a mixture of hexane and ethyl acetate, unless otherwise stated.

2,2-Diethoxy-6-(ethylthio)-2*H*-dihydropyran (2). A flame-dried flask containing *t*-BuOK (5.40 g, 48 mmol) was evacuated and carefully purged with nitrogen three times and then charged with dry pentane (30 mL) followed by TMEDA (7.25 mL, 48 mmol). The solution was cooled to −78 °C in a dry ice−acetone bath, and a solution of *n*-BuLi (20 mL, 2.41 M in hexane) was added over 30 min while the temperature was kept below −50 °C. After stirring for 20 min at −78 °C, freshly distilled 2,2-diethoxy-2*H*-dihydropyran (**7**, 6.90 g, 40 mmol) in pentane (10 mL) was added in 20 min. After −78 °C for 20 min, the cooling bath was replaced by a dry ice−CCl_4 bath and the temperature was allowed to rise to −20 °C. The temperature was maintained for 15 min, then stirring was continued for 15 min at −20 °C during which time a fine suspension in a light brown solution was formed. Precooled diethyl ether (−78 °C, 30 mL) was added via cannula at −20 °C, after which the mixture was cooled to −78 °C. Diethyl disulfide (5.0 g, 40 mmol) was then added dropwise with vigorous stirring. After stirring for 4 h at −78 °C, water (10 mL) was added to the white suspension. The organic layer was washed with water (ca. 30 mL, 3×). The

(10) Larock, R. L. *Comprehensive Organic Transformations*, VCH: New York, 1989, p 94.

(11) Oxocarbenium intermediates in organic synthesis, see: (a) Molander, G. A.; Eastwood, P. R. *J. Org. Chem.* **1996**, *61*, 1910. (b) Petasis, N. A.; Lu, S.-P. *J. Am. Chem. Soc.* **1995**, *117*, 6394. (c) Paquette, L. A.; Branan, B. M.; Friedrich, D.; Edmondson, S. D.; Rogers, R. D. *J. Am. Chem. Soc.* **1994**, *116*, 506.

original aqueous layer and the washings were combined and subsequently extracted with pentane (ca. 50 mL, 1×). After drying of the combined organic solution over anhydrous Na_2SO_4, the solvents were removed under reduced pressure. Careful distillation under reduced pressure afforded **2** (7.53 g, 33 mmol, 81%) as a colorless liquid: TLC, R_f 0.59 (4:1 hexane/EtOAc); bp 62−63 °C (3 mmHg); FT-IR (neat) 3054, 1635, 1446, 1358 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$, distilled from CaH_2 prior to use) δ 1.23 (t, J = 6.3 Hz, 6H), 1.30 (t, J = 7.4 Hz, 3H), 1.91 (t, J = 6.8 Hz, 2H), 2.13−2.23 (m, 2H), 2.75 (q, J = 7.4 Hz, 2H), 3.60−3.78 (m, 4H), 5.15 (t, J = 4.2 Hz, 1H); EIMS m/z (relative intensity) 232 (M^+, 14.8), 187 (20.2), 171 (19.1), 145 (37.6), 116 (100), 87 (59.0). Anal. Calcd for $C_{11}H_{20}O_3S$: C, 56.86; H, 8.68; S, 13.80. Found: C, 56.84; H, 9.07; S, 13.65.

(4*R,5*R**)-Ethyl 4-[(Ethylthio)carbonyl]-5-hydroxy-5-phenylpentanoate (9a): General Procedure.** A flame-dried flask containing 2,2-diethoxy-6-(ethylthio)-2*H*-dihydropyran (**2**, 0.83 g, 3.57 mmol) was evacuated and purged with nitrogen three times and then charged with freshly distilled CH_2Cl_2 (12 mL). The solution was cooled to −78 °C in a dry ice−acetone bath, and benzaldehyde (0.35 g, 3.25 mmol) was added. To the resulting solution was added dropwise a solution of $SnCl_4$ in CH_2Cl_2 (0.5 M, 0.65 mL, 0.325 mmol) with a gas-tight syringe. The reaction was monitored by TLC. The reaction was allowed to proceed for 4 h at −78 °C and then quenched by addition of 0.5 N HCl (10 mL) at −78 °C. The aqueous layer was extracted with ether (3×). The combined organic extracts were washed with saturated aqueous $NaHCO_3$ (1×), water (1×), brine (1×), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Final purification was effected by column chromatography (SiO_2, 25% EtOAc in hexane) to afford **9a** along with an inseparable minor diastereomer **10a** (0.94 g, 3.02 mmol, 93%) as a colorless liquid; the diastereomeric ratio was 91:9 as judged by the analysis of ^1H NMR of crude products: TLC, R_f 0.29 (3:1 hexane/EtOAc); FT-IR (neat) 3495 (br), 1739, 1680 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.13−1.25 (m, 6H), 1.63−1.76 (m, 1H), 1.85−1.97 (m, 1H), 2.24−2.32 (m, 2H), 2.72 (d, J = 5.48 Hz, 1H), 2.89 (q, J = 7.46 Hz, 2H), 2.97−3.05 (m, 1H), 4.09 (q, J = 7.13 Hz, 2H), 4.84 (dd, J = 7.43, 5.51 Hz, 1H), 7.27−7.61 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.2, 14.5, 23.6, 25.1, 31.4, 59.8, 60.5, 75.7, 126.4, 128.2, 128.6, 141.5, 172.5, 202.6; EIMS m/z (relative intensity) 310 (M^+, 8.3 × 10^{-1}), 249 (16.5), 132 (63.9), 185, (52.3), 143 (100), 115 (87.0), 105 (87.0), 77 (91.4). Anal. Calcd for $C_{16}H_{22}O_4S$: C, 61.91; H, 7.14; S, 10.33. Found: C, 62.05; H, 7.30; S, 10.36.

(4*S,5*S**)-2,2-Dimethyl-5-(3′-hydroxypropyl)-3-phenyl-1,3-dioxane (11).** To a stirred suspension of $LiAlH_4$ (0.34 g, 8.9 mmol) in THF (10 mL) at −78 °C was added **9a** (0.55 g, 1.8 mmol) in THF (2 mL) over a period of 10 min. After 1 h, the reaction mixture was allowed to warm to 20 °C. The temperature was maintained for 30 min, then stirring was continued for 4 h at 67 °C under reflux condition. Diethyl ether (20 mL) was added, after which the mixture was cooled to 20 °C. The reaction mixture was sequentially treated with water (0.5 mL) and 15% aqueous NaOH (1 mL). The resulting suspension was stirred vigorously for 30 min and filtered. The collected filtrate was dried over anhydrous $MgSO_4$ and then filtered through a sintered-glass funnel containing silica gel (ca. 3 cm). Removal of the solvents under reduced pressure gave the corresponding triol (0.32 g, 1.5 mmol, 86%), which was used without further purification: TLC, R_f 0.19 (3:2 EtOAc/hexane); FT-IR (neat) 3343 (br) cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.15−1.97 (m, 5H), 2.82−3.38 (br s, 3H), 3.48−3.86 (m, 4H), 4.76 (d, J = 6.48 Hz, 1H), 7.21−7.40 (m, 5H); EIMS m/z (relative intensity) 192 ($M^+ - H_2O$, 3.2), 174 (4.8), 163 (5.2), 145 (4.9), 108 (17.1), 86 (19.2), 68 (100). This triol (0.15 g, 0.71 mmol) was dissolved in benzene (5 mL) along with 2,2-dimethoxypropane (0.11 g, 1.05 mmol) and *p*-TsOH (3 mg, 0.016 mmol). The resulting solution was heated at reflux under a Soxhlet extractor containing freshly conditioned 4 Å molecular sieves for 3 h. Anhydrous K_2CO_3 (20 mg) was added to the cooled reaction mixture which was stirred at room temperature for 2 h, filtered, and concentrated under reduced pressure. Purification of crude product by flash column chromatography (SiO_2, 50% EtOAc in hexane) provided **11** (0.145 g, 0.58 mmol, 81%) as a colorless oil: TLC, R_f 0.46 (2:1 hexane/EtOAc); FT-IR (neat) 3416 (br), 1264 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 0.97−1.28 (m, 4H), 1.41−1.51 (m, 1H), 1.48 (s, 3H), 1.55 (s, 3H), 1.85−1.97 (m, 1H), 3.45−3.55 (m, 2H), 3.75 (dd, J = 11.4, 11.4 Hz, 1H), 3.98 (dd, J = 5.0, 11.4 Hz, 1H), 4.48 (d, J = 10.3 Hz, 1H), 7.31−7.62 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 19.1, 24.0, 29.4, 29.8, 40.5, 62.6, 64.8, 77.9, 127.7, 128.2, 128.4, 140.3; EIMS m/z (relative intensity) 250 (M^+, 1.4), 232 (29.8), 191 (82.6), 173 (72.0), 128 (100), 104 (88). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.92; H, 8.86. Found: C, 72.12; H, 9.06.

(5*R)-5-[(1*R**)-1-Hydroxy-1-phenylmethyl]-3,4,5,6-tetrahydro-2*H*-pyran-2-one (12).** A gray suspension of **9a** (0.24 g, 0.77 mmol) and mercury acetate (0.25 g, 0.77 mmol) in distilled ethanol (10 mL) was cooled to 0 °C, and sodium borohydride (0.12 g, 3.1 mmol) was added in small portions. After 30 min, the resulting pale yellow solution was warmed to 20 °C, stirred for 3 h, and warmed to 40 °C in oil bath. After 1 h, the mixture was cooled to room temperature and then poured into a separatory funnel and extracted with ether (3 × 20 mL). The combined organic extracts were washed with 10% aqueous HCl (1×), saturated aqueous $NaHCO_3$ (1×), water (1×), and brine (1×), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of crude product by flash column chromatography (SiO_2, 50% EtOAc in hexane) provided **12** (0.145 g, 0.70 mmol, 91%) as a colorless oil: TLC, R_f 0.19 (2:1 hexane/EtOAc); FT-IR (neat) 3425, 1731, 1266 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.44−1.72 (m, 2H), 1.98 (d, J = 2.79 Hz, 1H), 2.22−2.63 (m, 3H), 4.33−4.42 (m, 1H), 4.51−4.65 (m, 2H), 7.21−7.48 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 22.1, 28.7, 39.7, 70.5, 75.5, 126.5, 128.5, 128.8, 142.0, 171.8; EIMS m/z (relative intensity) 206 (M^+, 1.4), 106 (10.7), 100 (100), 99 (85.4), 82 (8.1). Anal. Calcd for $C_{12}H_{14}O_3$: C, 69.84; H, 6.81. Found: C, 69.89; H, 6.84.

(5*S,6*R**)-5-[(Ethylthio)carbonyl]-6-(2-phenylethyl)-3,4,5,6-tetrahydro-2*H*-pyran-2-one (13) and (5*S**,6*R**)-5-[(Ethylthio)carbonyl]-6-(2-phenylethyl)-3,4,5,6-tetrahydro-2*H*-pyran-2-one (14).** To a solution of **9b** (92:8 diastereomeric mixture, 0.125 g, 0.37 mmol) and diisopropylamine (0.053 g, 0.41 mmol) in CH_2Cl_2 (5 mL) was added diethylaluminum chloride (1.8 M in toluene, 0.21 mL, 0.37 mmol). The reaction mixture was stirred at −20 °C for 3 h and allowed to warm slowly to room temperature. After 3 h, the mixture poured into a separatory funnel and extracted with ether (2×). The combined organic extracts were washed with cold saturated aqueous $NaHCO_3$ (1×), water (1×), and brine (1×), dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure. Purification of crude products by flash column chromatography (SiO_2, 25% EtOAc in hexane) provided separable **13** and **14** (0.080 g, 0.274 mmol, 82%) as a colorless oil; diastereomeric ratio was turned out 87:13 as judged by the analysis of ^1H NMR of crude products.

13: TLC, R_f 0.26 (2:1 hexane/EtOAc); FT-IR (neat) 1740, 1678 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.25 (t, J = 7.41, 3H), 1.84−2.20 (m, 4H), 2.57−3.06 (m, 7H), 4.40 (ddd, J = 9.57, 3.77, 3.77, 1H), 7.18−7.34 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.5, 21.7, 23.6, 27.2 31.5, 34.0, 49.0, 78.5, 126.2, 128.4, 128.4, 128.5, 140.5, 170.2, 197.8; EIMS m/z (relative intensity) 292 (M^+, 8.4), 231 (42.0), 185 (23.8), 178 (21.3), 142 (25.2), 117 (68.4), 104 (67.0), 103 (51.0), 97 (54.1), 91 (51.6), 56 (100). Anal. Calcd for $C_{16}H_{20}O_3S$: C, 65.77; H, 6.89; S, 10.97. Found: C, 65.45; H, 6.79: S, 10.66.

14: TLC, R_f 0.45 (2:1 hexane/EtOAc); FT-IR (neat) 1739, 1678 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.26 (t, J = 7.40 Hz, 3H), 1.93−2.20 (m, 4H), 2.54−2.97 (m, 7H), 4.52 (ddd, J = 9.87, 7.40, 3.77 Hz, 1H), 7.17−7.33 (m, 5H); ^{13}C NMR (50 MHz, $CDCl_3$) δ 14.4, 23.6, 23.9, 28.5, 30.9, 35.9, 52.2, 79.2, 126.1, 128.4, 128.5, 140.8, 170.5, 199.1; EIMS m/z (relative intensity) 292 (M^+, 7.2), 231 (45.9), 213 (40.3), 185 (44.6), 178 (27.9), 91 (46.9), 56 (100). Anal. Calcd for $C_{16}H_{20}O_3S$: C, 65.77; H, 6.89; S, 10.97. Found: C, 65.38; H, 6.85; S, 10.65.

Acknowledgment. Generous financial support of this research by grants from the Ministry of Education (BSRI 96-3420) and the Korea Science and Engineering Foundation (KOSEF 94-0501-08-01-3) are gratefully acknowledged.

Supporting Information Available: Analytical data for compounds **9b**−**f** and ^1H NMR spectra for compounds **2**, **9a**−**f**, and **11**−**14** (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.

JO9707747