Orthoester-Dependent Alcoholysis of Lactones. Facile Preparation of 4-Alkoxybutanoates and 5-Alkoxypentanoates

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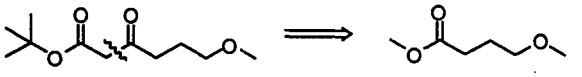
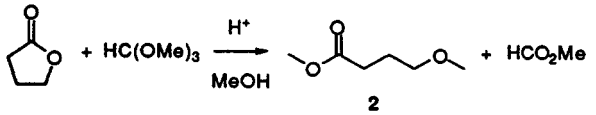
The 4-alkoxybutanoyl and 5-alkoxypentanoyl moieties have seen considerable use in the design and synthesis of biologically active molecules, including antibiotics,[1] prostaglandins[2] and prostaglandin antagonists, analgesics,[3] bronchodilators,[4] antiarrhythmics,[5] and flavorants.[6] We required β-keto ester **1**, which could be prepared by Claisen



1 **2**

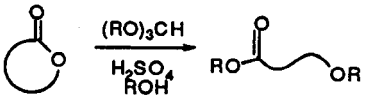
condensation of *tert*-butyl acetate with methyl 4-methoxybutanoate (**2**). Although numerous syntheses of **2** exist in the literature,[7] the most commonly used is the classical route of Reppe:[8] basic hydrolysis of butyrolactone followed by permethylation with dimethyl sulfate. Unfortunately, this procedure is both difficult and low yielding. We required a more practical route to **2** and disclose here a simple, efficient synthesis from readily available starting materials. The generality of the reaction, the rate accelerating effect of orthoesters, and mechanistic studies are also reported.

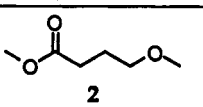
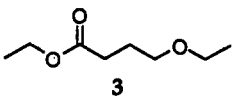
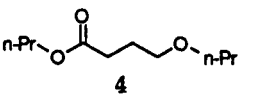
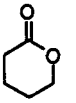
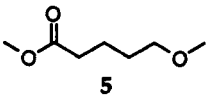
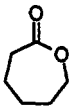
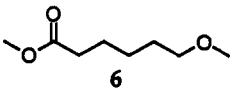
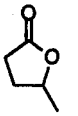
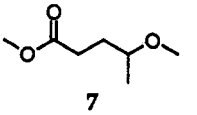
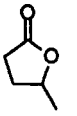
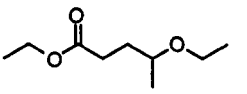
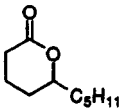
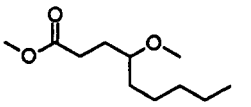
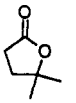
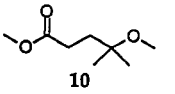
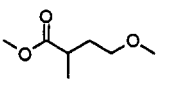
Treatment of a solution of butyrolactone and trimethyl orthoformate in dry methanol with a catalytic amount (2–10 mol %) of acid generates methyl 4-methoxybutanoate (**2**) according to eq 1. Heating overnight at 50 °C followed by distillation of the reaction mixture affords



2

Table 1. One-Step Synthesis of Ester–Ethers from Lactones



lactone	R	product	yield (%)
	Me	 **2**	86
	Et	 **3**	83
	n-Pr	 **4**	92
	Me	 **5**	92
	Me	 **6**	61
	Me	 **7**	95
	Et	 **8**	82
	Me	 **9**	94
	Me	 **10**	88
	Me	 **11**	95

the desired product in 85% yield. Strong acids with nonnucleophilic counterions—sulfuric, methanesulfonic, trifluoromethanesulfonic, and perchloric—are effective catalysts. Hydrochloric acid is consumed by the formation of alkyl chlorides, and the desired reaction does not go to completion.

As shown in Table 1, this procedure was applied to the synthesis of a variety of ester–ethers. Reactions were generally allowed to proceed overnight, although most were complete in 3–8 h depending on the amount of acid catalyst added; 1.5–2.0 equiv of orthoformate was used. Other primary alcohol derivatives are available using the appropriate orthoester and solvent. (Secondary orthoesters are not readily available.) Both five- and six-membered lactones are transformed in excellent yields. In these examples the reaction is extremely clean and high yielding. For some less volatile products (**5**, **9**, and **11**), the crude material obtained after workup gave satisfactory elemental

(1) Brickner, S. J.; Gaikema, J. J.; Zurenko, G. E.; Greenfield, L. J.; Manninen, P.R.; Ulanowicz, D. A. *J. Antibiot.* **1992**, *45*, 213. Archer, S.; Perianayagam, C. *J. Med. Chem.* **1979**, *22*, 306.

(2) Schaaf, T. K.; Bindra, J. S.; Johnson, M. R. US Patent 3984424, 1976. Monkhouse, D. US Patent 3851052, 1972. Johnson, M. R.; Hess, H. J. E. German Patent 2327813, 1973.

(3) Mueller, R. A. U.S. Patent 4559337, 1985.

(4) Regnier, G.; Guillonneau, C.; Duhault, J.; Boulanger, M. French Patent 2531085, 1984.

(5) Cavazza, C.; De Witt, P.; Tinti, M. O.; Quaresima, E. French Patent 2483407, 1981.

(6) Yoshida, T.; Koyama, Y.; Tokoro, K.; Morishita, I.; Anma, M.; Ito, T. Japanese Patent 53148598.

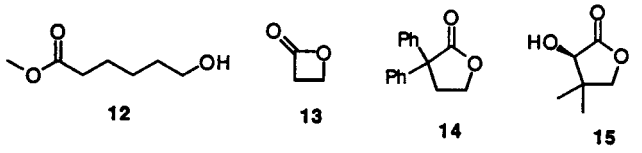
(7) 4-Methoxybutyric acid derivatives have also been prepared from the Grignard reagent and carbon dioxide (Wirz, B.; Kueng, W. *J. Labelled Compd. Radiopharm.* **1983**, *20*, 635); by hydrolysis of the appropriate malonic ester (Bogatskii, A. V.; Glinskaya, L. Y.; Kamalov, G. L. *Zh. Org. Khim.* **1971**, *7*, 2538) or nitrile (Palomaa, K. *Chem. Ber.* **1931**, *64*, 800); by oxidation of 4-methoxybutanol (Djerassi, C.; Sheehan, M.; Spangler, R. J.; Ikeda, M. *J. Org. Chem.* **1971**, *36*, 1796) or 1,4-dimethoxybutane (Smith, A. B., III; Scarborough, R. M., Jr. *Synth. Commun.* **1980**, *10*, 205); by metal-catalyzed carbonylation (Fuchigama, T.; Urata, H. Japanese Patent 03197441, 1991. Urata, H.; Maekawa, H.; Takahashi, S.; Fuchikami, T. *J. Org. Chem.* **1991**, *56*, 4320). These methods use expensive starting materials and/or are low yielding. Methyl 5-methoxypentanoate has also been prepared by a radical coupling method (Giese, B.; Heuck, K. *Tetrahedron Lett.* **1980**, *21*, 1829) and by nonselective oxidation of the 1,5-diol (Kirmse, W.; Jansen, U. *Chem. Ber.* **1985**, *118*, 2607).

(8) Reppe, v. W.; Mitarbeitern, M. *Liebigs Ann. Chem.* **1956**, *596*, 191.

0022-3263/94/1959-2253$04.50/0

analysis results without purification. Primary, secondary, and tertiary ethers (2, 7, and 10) were readily prepared from the corresponding lactones by this method. In these last cases, the relative rates of reaction were quite similar, varying by less than 50%.

The seven-membered ϵ-caprolactone is rapidly opened to the hydroxy ester 12 under the reaction conditions, however, formation of the ester–ether 6 is slow. After 48 h, 6 was isolated in 61% yield after chromatography to remove unreacted hydroxy ester. β-Propiolactone (13) was also subjected to the reaction conditions. The desired product is formed very slowly, and decomposition products eventually dominate the reaction mixture. Two sterically hindered substrates, 2,2-diphenyl-γ-butyrolactone (14) and pantolactone (15), also produced only trace amounts of product.



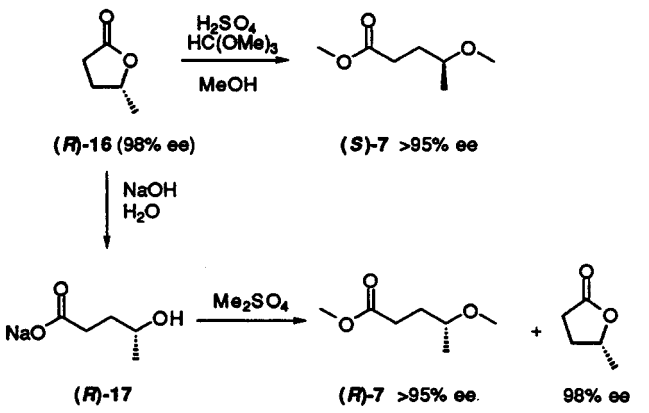
12 13 14 15

Other orthoesters including trimethyl orthoacetate, orthobutanoate, and orthobenzoate and tetramethyl orthocarbonate can be used; however, the reaction proceeds to less than 50% conversion even when a large excess is supplied (*vide infra*). Benzaldehyde dimethyl acetal, 2,2-dimethoxypropane, and DMF dimethyl acetal do not generate product.

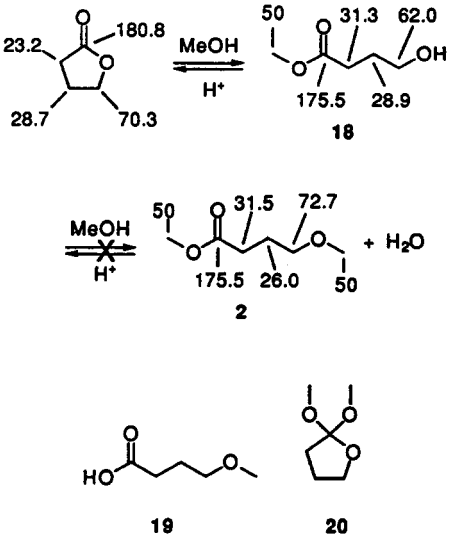
Although a 92% yield of *n*-propyl 4-propoxybutanoate (4) was obtained by the usual protocol, *n*-propyl orthoformate is not available in quantity. Molecular sieves were explored as an alternative dehydrating agent.[9] However, the reaction did not proceed under the usual conditions (50 °C). It could be forced to completion only after refluxing (105 °C) for 48 h through a pad of 3A sieves.[10] A 74% yield was obtained. This result was surprising in view of the potent dehydrating ability of molecular sieves and raised questions concerning the mechanism of the process. The mode of formation of the ether linkage was of particular interest.

The stereochemistry of ether formation was established by converting optically active γ-valerolactone to 7. The starting material, (*R*)-16, was prepared[11] from methyl levulinate by asymmetric hydrogenation with a Ru(II)–BINAP catalyst.[12] An optically active reference sample of 7 was prepared by saponifying lactone (*R*)-16 as shown in Scheme 1. Treatment of the sodium salt (*R*)-17 with dimethyl sulfate provided a 1:5 mixture of ester–ether and lactone. Chiral NMR shift reagent studies showed that the ester–ether 7 possessed greater than 95% enantiomeric excess and that no epimerization of recovered lactone had occurred. Since dimethyl sulfate alkylation does not affect the stereogenic center, the reference material must be of the *R* configuration. Lactone (*R*)-16 was then subjected to the standard reaction conditions. Chiral shift studies showed that the *S* enantiomer had been produced in greater than 95% excess. Therefore, lactone alcoholysis proceeds stereospecifically with inversion of configuration at the γ carbon.

Scheme 1



Scheme 2. Carbon Chemical Shifts of Observed Species



Another mechanistic clue was gained during attempts to establish the equilibrium position of the reaction as shown in Scheme 2. Treatment of butyrolactone in dry methanol (<50 μg/mL water) with 5 mol % sulfuric acid at 50 °C provided a 1.5:1 mixture of hydroxy ester 18 and starting lactone. However, no ester–ether 2 could be observed by NMR or GC analyses. The carbon chemical shifts shown in Scheme 2 confirm the identity of 18 and show that the observed species are not ether–acid 19 nor orthoester 20. In particular, the chemical shift of δ 62.0 for the γ carbon confirms the presence of a primary alcohol function.

Surprisingly, acidification of a mixture of ester–ether 2 and methanol failed to produce any lactone or hydroxy ester even when water was used as a 10% cosolvent. An experiment in which 2 was formed under the usual reaction conditions and then water was added also did not yield any starting lactone. The γ-valerolactone, δ-valerolactone, and ϵ-caprolactone systems behaved identically. Even the tertiary ether 10 and the corresponding lactone fail to equilibrate. In a similar experiment, treatment of 4 with methanol, trimethyl orthoformate, and acid caused exchange of the ester groups only, yielding methyl 4-propoxybutanoate.

These results can only be explained if the orthoester is more than a simple water scavenger. Instead, it must play

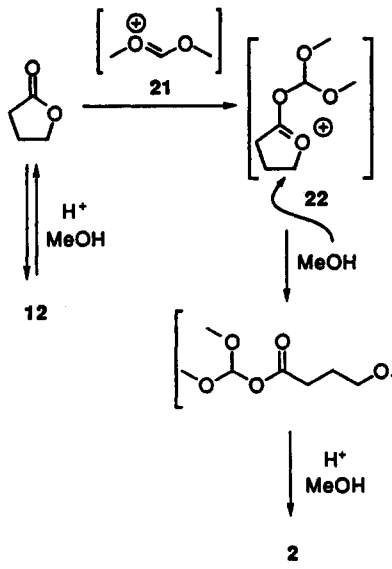
(9) The dehydrating agent must be selective for water in the presence of alcoholic solvent.

(10) Several attempts to prepare the benzyl analog by analogous methods failed owing to the competing formation of dibenzyl ether.

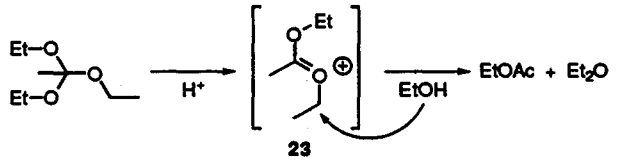
(11) Ohkuma, T.; Kitamura, M.; Noyori, R. *Tetrahedron Lett.* **1990**, *31*, 5509.

(12) King, S. A.; Thompson, A. S.; King, A. O.; Verhoeven, T. R. *J. Org. Chem.* **1992**, *57*, 6689.

Scheme 3



Scheme 4



a direct role in the overall transformation. A mechanism which is consistent with the results presented here is proposed in Scheme 3. The transformation of butyrolactone to **2** is used as an example.

While the reaction conditions bear resemblance to the classical acid catalyzed conversion of alcohols to ethers,[13] they are clearly much milder. The requirement for stereospecific inversion together with the slow rates of conversion of β-propiolactone and ϵ-caprolactone (which are rapidly opened to the hydroxy acid) indicate that nucleophilic attack takes place on an activated lactone-like intermediate. Although protic acid is capable of inducing lactone opening by attack of methanol at the carbonyl, the action of another species is required to induce nucleophilic ring opening at the γ carbon. That species must be derived from the orthoester. Protic acid causes ionization of orthoester to the stabilized carbocation **21**,[14] which can be considered a Lewis acid. Complexation of **21** with the lactone might provide an activated intermediate **22** which would suffer ring opening by attack of solvent at the γ-carbon to provide the products after solvolysis.

Attempts to directly establish the viability of this hypothesis by generating similar Lewis acids *in situ* failed. For instance, neither trityl alcohol/sulfuric acid nor methyl formate/sulfuric acid induced the equilibration shown in Scheme 2. Therefore, to gain insight into the reactivity of the proposed intermediate, an analogous species was examined. The carbocation **23** illustrated in Scheme 4, which is derived from acid-catalyzed ionization of triethyl orthoacetate, is structurally similar to the complexed lactone **22**. When triethyl orthoacetate was treated with catalytic acid in ethanol at 30 °C for 1 h, it was completely converted to diethyl ether (an ether) and ethyl acetate (an ester). Thus, the known intermediate **23** displays the reactivity proposed for **22** in Scheme 3. Decomposition of orthoacetate by the process shown in Scheme 4 is more than 1000 times faster than that of orthoformate. This is probably due to the more favorable reaction of **21** (relative to **23**) and the alcoholic solvent to regenerate orthoester.

Conclusion. In the presence of alcohol, acid, and an orthoformate, five- and six-membered lactones are cleanly converted to ester–ethers. The reaction is general and proceeds under mild conditions only in the presence of the orthoester. The critical ether linkage is formed by an S_N2-like opening of an activated intermediate formed by combination of the lactone and the orthoester-derived carbocation **21**.

Experimental Section

General. Methanol, ethanol, propanol, and all lactones were dried over 4A molecular sieves prior to use. Orthoesters and sulfuric acid were used as received. All reactions were performed under a nitrogen atmosphere.

General Procedure for the Synthesis of Ester–Ethers. Sulfuric acid (0.02–0.10 equiv) was added to a stirred 1 M solution of the orthoformate (1.5–2.0 equiv) and lactone (1 equiv) in the appropriate alcohol as solvent. The mixture was heated 3–8 h at 50 °C and cooled to room temperature. The solvent was removed *in vacuo*, and the concentrate was partitioned between ethyl acetate and saturated sodium bicarbonate solution. The organic layer was separated and concentrated. The residue was distilled or chromatographed to provide the product in pure form.

Methyl 4-Methoxybutanoate (2). Sulfuric acid (0.25 mL, 4.5 mmol) was added to a stirred solution of butyrolactone (10.0 mL, 11.2 g, 130 mmol), trimethyl orthoformate (27 mL, 26.5 g, 250 mmol), and methanol (52 mL). The mixture was heated at 50 °C for 12 h. At this time GC analysis showed no butyrolactone remained. Distillation of the reaction mixture provided 14.7 g (86%) of **2**: bp 103–104 °C/100 mmHg; GC retention time (25 m DB-5 column; 50–200 °C, 10 °C/min) 6.29; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 3.65 (s, 3H), 3.38 (t, J = 6.2 Hz, 2H), 3.30 (s, 3H), 2.38 (t, J = 7.4 Hz, 2H), 1.87 (quint, J = 7.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.8, 71.4, 58.4, 51.4, 30.6, 24.8. Anal. Calcd for $C_7H_{14}O_3$: C, 54.53; H, 9.15. Found: C, 54.56; H, 9.51.

Ethyl 4-ethoxybutanoate (3): bp 74 °C/12 mmHg; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.11 (q, J = 7.2 Hz, 2 H), 3.45 (t, J = 7.2 Hz, 2 H), 3.43 (t, J = 7.1 Hz, 2 H), 2.38 (t, J = 7.4 Hz, 2 H), 1.88 (quint, J = 7.0 Hz, 2 H), 1.24 (t, J = 7.1 Hz, 2 H), 1.17 (t, J = 7.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 173.5, 69.4, 66.1, 60.2, 31.1, 25.1, 15.1, 14.2. Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 60.25; H, 10.45.

Methyl 5-methoxypentanoate (5): bp 85 °C/8mm; ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.64 (s, 3H), 3.35 (t, J = 6.3 Hz, 2H), 3.29 (s, 3H), 2.32 (t, J = 7.1 Hz, 2H), 1.62 (m, 4H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 173.9, 72.2, 58.5, 51.4, 33.7, 29.0, 21.6. Anal. Calcd for $C_7H_{14}O_3$: C, 57.51; H, 9.65. Found: C, 57.17; H, 10.01.

Methyl 6-Methoxyhexanoate (6). ϵ-Caprolactone (4.52 g, 40 mmol), trimethyl orthoformate (8.4 g, 8.8 mL), sulfuric acid (0.20 mL), and methanol (40 mL) were heated for 24 h. More trimethyl orthoformate (8.8 mL) was added, and the mixture was heated a further 24 h. The reaction was stopped and worked up. Methyl 6-hydroxyhexanoate (1.75 g, 30%) and the desired product (3.84 g, 61%) were isolated by flash chromatography (90:10 hexane/ethyl acetate): ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.65 (s, 3H), 3.36 (t, J = 6.5 Hz, 2H), 3.31 (s, 3H), 2.31 (t, J = 7.4 Hz, 2H), 1.6 (m, 4H), 1.4 (m, 2H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 174.1, 72.5, 58.5, 51.4, 34.0, 29.3, 25.7, 24.7. Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 59.78; H, 10.32.

Methyl 4-methoxypentanoate (7): bp 88 °C/39 mmHg; ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.64 (s, 3H), 3.31 (m, 1H), 3.27 (s, 3H), 2.37 (t, J = 7.3 Hz, 2H), 1.77 (m, 2H), 1.11 (d, J = 6.2 Hz, 3H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 174.2, 75.7, 56.0, 51.4, 31.3, 30.0,

(13) March, J. *Advanced Organic Chemistry*, 3rd ed.; John Wiley and Sons, Inc.: New York, 1985; pp 344–5.
(14) Cordes, E. H. Orthoesters. In Patai, S. *Chemistry of Carboxylic Acid Derivatives*; Wiley: New York, 1982; pp 623–667.

18.8. Anal. Calcd for $C_7H_{14}O_3$: C, 57.71; H, 9.65. Found: C, 57.72; H, 10.00.

Ethyl 4-Ethoxypentanoate (8). (±)-γ-Valerolactone (10.0 g, 100 mmol), trimethyl orthoformate (15.9 g, 16.4 mL, 150 mmol), sulfuric acid (0.10 mL) and ethanol (100 mL) were heated 24 h. After workup and concentration, 14.30 g (82 %) of the product was isolated by distillation: bp 71–73 °C/9 mmHg; ^{1}H NMR (250 MHz, $CDCl_3$) δ 4.11 (q, J = 7.2 Hz, 2 H), 3.45 (t, J = 7.2 Hz, 2 H), 3.43 (t, J = 7.1 Hz, 2 H), 2.38 (t, J = 7.4 Hz, 2 H), 1.88 (quint, J = 7.0 Hz, 2 H), 1.24 (t, J = 7.1 Hz, 2 H), 1.17 (t, J = 7.0 Hz, 2 H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 173.4, 74.0, 63.7, 60.2, 31.6, 30.4, 19.6, 15.5, 14.2. Anal. Calcd for $C_9H_{18}O_3$: C, 62.04; H, 10.41. Found: C, 61.68; H, 10.60.

Methyl 5-methoxydecanoate (9): ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.66 (s, 3H), 3.31 (s, 3H), 3.13 (quint, J = 5.6 Hz, 1H), 2.32 (t, J = 7.3 Hz, 2H), 1.7 (m, 2H), 1.6–1.2 (m, 10H), 0.88 (br t, 3H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 174.0, 80.5, 56.4, 51.4, 34.1, 33.2, 32.8, 32.0, 24.8, 22.6, 20.8, 14.0; HRMS calcd for $C_{12}H_{24}O_3$ 215.1648, found 215.1645. Anal. Calcd for $C_{12}H_{24}O_3$: C, 66.63; H, 11.18. Found: C, 67.01; H, 11.55.

Methyl 4-Methoxy-4-methylpentanoate (10). 4,4-Dimethyl-γ-butyrolactone (940 mg, 8.25 mmol), trimethyl orthoformate (2.1 g, 2.2 mmol, 20 mmol), sulfuric acid (50 μL), and methanol (10 mL) were heated at 50 °C overnight. After workup the product was isolated by flash chromatography with 95:5 hexane/EtOAc to give 1.16 g (88%) of **10**: ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.65 (s, 3H), 3.15 (s, 3H), 2.35 (t, J = 8.1 Hz, 2H), 1.80 (t, J = 8.1 Hz, 2H), 1.14 (s, 6H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 174.5, 73.6, 51.5, 49.2, 34.4, 28.7, 24.8. Anal. Calcd for $C_8H_{16}O_3$: C, 59.98; H, 10.07. Found: C, 59.90; H, 10.35.

Methyl 4-Methoxy-2-methylbutanoate (11). 2-Methyl-γ-butyractone (2.00 g, 20 mmol), trimethyl orthoformate (4.2 g, 4.4 mL, 40 mmol), sulfuric acid (50 μL), and methanol (20 mL) were heated at 50 °C overnight. After workup, concentration provided 2.77 g (95%) of **11** in analytically pure form: ^{1}H NMR (250 MHz, $CDCl_3$) δ 3.64 (s, 3H), 3.35 (t, J = 6.0 Hz, 2H), 3.28 (s, 3H), 2.57 (sextet, J = 7.1 Hz, 1H), 1.92 (m, 2H), 1.62 (m, 2H), 1.14 (d, J = 7.0 Hz, 3H); ^{13}C NMR ($CDCl_3$, 63 MHz) δ 176.9, 70.3, 58.5, 51.5, 36.3, 33.4, 17.1. Anal. Calcd for $C_7H_{14}O_3$: C, 57.71; H, 9.65. Found: C, 57.34; H, 9.89.

***n*-Propyl 4-*n*-propoxybutanoate (4) (Use of Molecular Sieves as Dehydrating Agent).** Sulfuric acid (0.50 mL, 9.0 mmol) was added to a stirred solution of butyrolactone (10.0 mL, 11.2 g, 130 mmol) and 1-propanol (52 mL). The mixture was heated at reflux under an addition funnel filled with 4A molecular sieves (20 g). After 24 h, ^{1}H NMR showed the reaction to be 80% complete, and the sieves were recharged. After an additional 24 h the reaction was complete. The mixture was poured into ethyl acetate (160 mL) and washed with saturated NaCl solution (80 mL). After concentration, the mixture was distilled to give 20.6 g (74%) of the title compound: bp 85–89 °C/3 mmHg; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.00 (t, J = 6.7 Hz, 2H), 3.41 (t, J = 6.2 Hz, 2H), 3.38 (t, J = 6.7 Hz, 2H), 2.38 (t, J = 7.4 Hz, 2H), 1.87 (quint, J = 7.0 Hz, 2 H), 1.60 (m, 4H), 0.91 (t, J = 7.6 Hz, 3H), 0.88 (t, J = 7.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 173.7, 72.6, 69.6, 65.9, 31.1, 25.1, 22.9, 22.0, 10.6, 10.4.

5(*R*)-γ-Valerolactone [(*R*)-16]. A mixture of methyl levulinate (10.0 g, 77 mmol), methanol (10 mL), and concentrated HCl (0.4 mL) was deoxygenated with bubbling nitrogen for 2 min. $[RuCl_2(BINAP)]\cdot NEt_3$ (50 mg) was added and the mixture placed in a standard Parr shaker apparatus. After evacuating and flushing with nitrogen three times, the mixture was evacuated and exposed to 40 psi hydrogen pressure at 40 °C for 48 h. The solvent was removed in vacuo to give the product (9.90g, 99% yield) which was identical to a commercially available (Aldrich) racemic sample by ^{1}H NMR. The optical purity was shown to be 99:1 by obtaining the proton NMR spectrum of the product (1 μL) and (*S*)-(+)-2,2,2-trifluro-1-(9-anthryl)ethanol (27 mg) in $CDCl_3$. Peak assignments were made by spiking with a sample of the racemate.

Methyl 4(*R*)-Methoxypentanoate [(*R*)-7]. Optically active valerolactone [(*R*)-16] (1.00 g, 10 mmol) was heated at 50 °C for 24 h with 2 N NaOH (5 mL). The mixture was cooled and concentrated *in vacuo* to give a wet gray solid which was stirred overnight with dimethyl sulfate (2.0 mL). The resulting suspension was extracted with hexane (10 mL), and the hexane layer was concentrated to give 220 mg of a 3:1 mixture of starting lactone and product. The product was determined to be >95:5 *R*/*S* by dissolving 10 mg in $CDCl_3$ and adding 30 mg of tris[3-[(heptafluoropropyl)hydroxymethylene]-(+)-camphorato]europium(III) and recording the proton NMR spectrum.

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Supplementary Material Available: Additional experimental details and characterization (2 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.