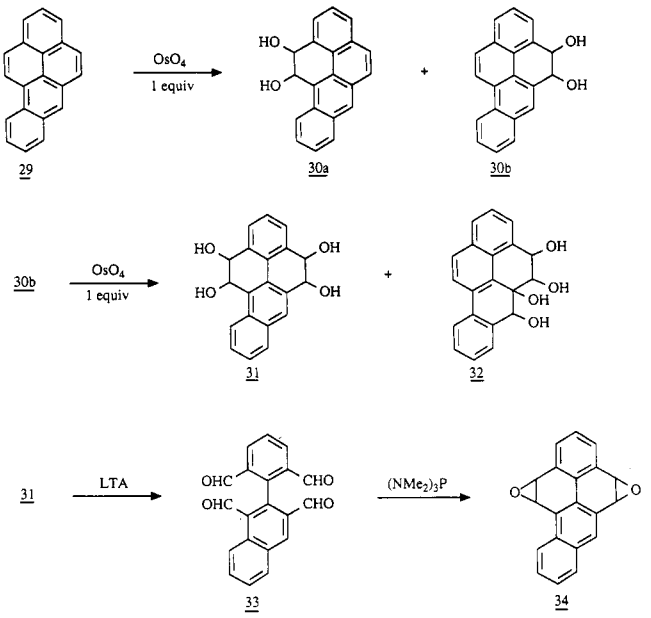
Scheme XII. Synthesis of the "K-Region" Diepoxide, 4,5:11,12-Diepoxy-4,5,11,12-tetrahydrobenzo[*a*]pyrene



32. Treatment of **31** with LTA using the first-selectivity conditions gives the tetraaldehyde **33**, which is the precursor of the desired diepoxide, **34**.

V. Conclusion

A reaction module that treats the chemistry of organic and inorganic oxidants has recently been incorporated into the CAMEO program. Clearly, the development of this module is a difficult undertaking, considering the current state of knowledge in the area. Nevertheless, its implementation has been successfully carried out by employing a technique that analyzes the problem in terms of the nature of the reagent, the interactive effects of reaction conditions, and traditional structure–reactivity correlations. Selectivity for the potential reactive sites is dealt with by using reactivity tables derived from extensive empirical analyses of product distributions as well as mechanistic and kinetic data. Fortunately, the evaluation of products is simplified by the constancy of oxidative transformations for most reagents. Consequently, mechanistic analyses have been confined to reactive sites that undergo more than one possible transformation. Grand reaction schemes that establish structure–pathway correlations have been utilized to assess competitions among viable reaction paths. For the mechanistically less well defined reactions, empirical rules have been employed to evaluate multistep transformations.

So far, the oxidation module has been shown to make reliable predictions for a wide range of reactions. However, significant extensions and refinements are anticipated as more information, especially mechanistic data, becomes available.

Acknowledgment. Gratitude is expressed to the National Science Foundation for support of this work. The assistance of Dr. Pascal Metivier is also gratefully acknowledged.

Preparation of Optically Active 2-Furylcarbinols by Kinetic Resolution Using the Sharpless Reagent and Their Application in Organic Synthesis

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The kinetic resolution of 2-furylcarbinols **1** by the Sharpless reagent proceeds highly efficiently, thus providing a general method for the synthesis of homochiral **1**. The reaction can be applied to compounds **1** possessing various types of substituents, although compound **1d**, which has a sterically demanding tertiary alkyl group, is a poor substrate. The kinetic resolution of 3-furylcarbinol **3** also proceeds efficiently. Various homochiral **1** thus obtained have been successfully converted into α-alkoxy acids **4** by oxidative cleavage of the furan ring after protection of the hydroxyl group. The compound (*R*)-**1b** has been converted into the naturally occurring γ-lactone **5**.

After the discovery of the highly efficient kinetic resolution of secondary allylic alcohols by asymmetric epoxidation using *tert*-butyl hydroperoxide (TBHP) in the presence of chiral titanium/tartrate catalyst,[1] Sharpless has pointed out that this asymmetric oxidation reaction is applicable to the kinetic resolution of other substrates, that possess a hydroxyl group for coordination to the metal center, and a proximate locus capable of accepting an oxygen atom. On the basis of this idea, several substrates were investigated, and it was revealed that β-hydroxy amines[2] are good substrates, while β-hydroxy sulfides[3] and α-acetylenic alcohols[3] are poor substrates.

2-Furylcarbinols **1** can be oxidized to 2*H*-pyran-3-(6*H*)-ones **2** by TBHP in the presence of an early transition metal catalyst (eq 1),[4] and we were, therefore, interested in the possibility of the kinetic resolution of **1** using the Sharpless reagent. Herein we describe our finding that the kinetic resolution proceeds highly efficiently, thus pro-

(1) (a) Martin, V. S.; Woodard, S. S.; Katsuki, T.; Yamada, Y.; Ikeda, M.; Sharpless, K. B. *J. Am. Chem. Soc.* **1981**, *103*, 6237. (b) Gao, Y.; Hanson, R. M.; Klunder, J. M.; Ko, S. Y.; Masamune, H.; Sharpless, K. B. *Ibid.* **1987**, *109*, 5765.

(2) Miyano, S.; Lu, L. D.-L.; Viti, S. M.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 4350.

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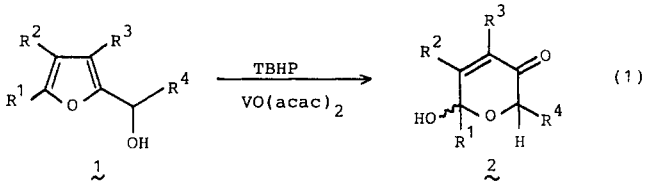
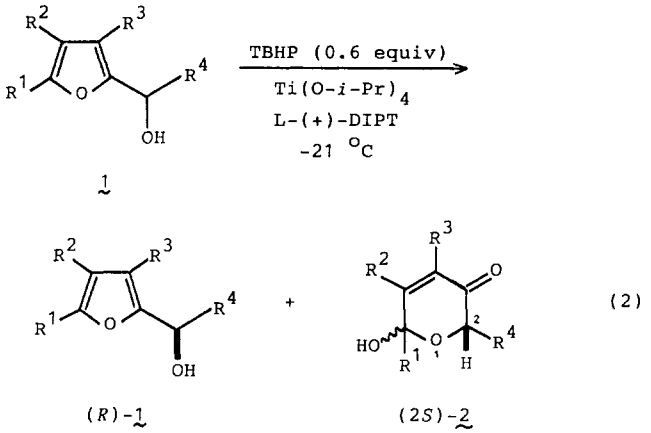


(1)

viding a general method for the synthesis of homochiral **1** (eq 2).[5,6]



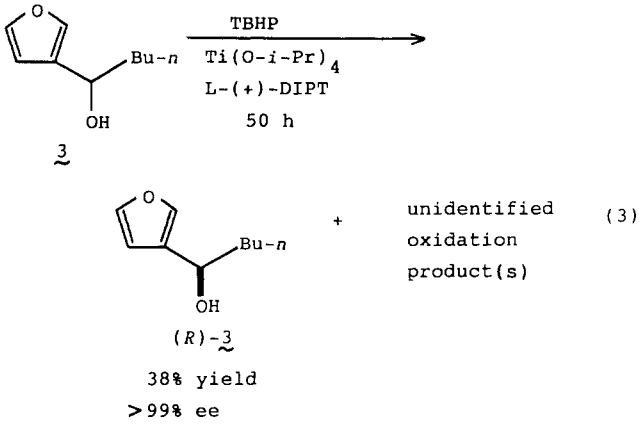
(2)

Table I summarizes the results of the kinetic resolution of 12 different types of **1**, including benzofurylcarbinol. It can be seen from Table I that highly efficient kinetic resolution occurs in every case except for **1d**, which has a sterically demanding tertiary alkyl group, by using either a catalytic (20 mol %) or a stoichiometric amount of Ti(O-*i*-Pr)$_4$/L-(+)-diisopropyl tartrate (L-(+)-DIPT).

In these reactions, when L-(+)-DIPT is used, the slow-reacting enantiomer is always that shown in eq 2, i.e., when the hydroxyl group is up, the furan ring is on the left. Thus, this system adds another example of the feature of predictability to the parent process for the kinetic resolution of allylic alcohols.[10] Noteworthy also is the fact that although 2-furylcarbinols **1i**, **1j**, and **1k** have another site for accepting an oxygen atom, the kinetic resolution occurs in every case via oxidation of the furan ring, suggesting that the rate of oxidation of the furan ring is far faster than that of the other site.[11]

In all cases except for **1l**, 2-furylcarbinols (*R*)-**1** can be readily separated from oxidation products (2*S*)-**2** and L-(+)-DIPT by column chromatography on silica gel because of their quite different R_f values.[12] However, the isolation of (*R*)-**1** can be carried out more conveniently by treating the crude reaction mixture with aqueous NaOH, which resulted not only in hydrolysis of L-(+)-DIPT into water-soluble tartaric acid[1] but also in decomposition of **2** into unidentified but highly water soluble compound(s).[13] The yields reported in Table I are those obtained after this alkaline treatment. Isolation of **1l**, however, was difficult because of identical chromatographic mobility with L-(+)-DIPT; moreover, it had an alkali-sensitive ester function. We, thus, used (*R*)-**1l** for the next reaction without separating it from L-(+)-DIPT (vide infra).

We also found that the kinetic resolution of 3-furylcarbinol proceeds efficiently under the same reaction conditions. Thus, the kinetic resolution of **3** using 20 mol % of Ti(O-*i*-Pr)$_4$/L-(+)-DIPT afforded (*R*)-**3** in 38% yield (based on racemic **3**) with >99% ee (eq 3). In this case, however, we could not identify the oxidation product(s).



(3)

As described above, the present method for the preparation of chiral **1** is operationally simple and highly efficient and can be applied to a wide range of substrates. Furthermore, racemic **1** can be readily prepared in large quantity from furfural and organometallic reagents or 2-furyllithium and aldehydes. Optically active compounds **1** have thus become readily available asymmetric starting materials; hence, we have been making a great deal of effort to utilize **1** in organic synthesis.[14] Described next is the transformation of **1** into homochiral α-alkoxy acids **4** and the synthesis of the naturally occurring γ-lactone **5** from (*R*)-**1b**.

Homochiral α-alkoxy acids are useful intermediates for organic synthesis.[15] Procedures currently available for their preparation include chemical methods,[16-21] fermen-

(5) Preliminary report: Kobayashi, Y.; Kusakabe, M.; Kitano, Y.; Sato, F. *J. Org. Chem.* **1988**, *53*, 1586.

(6) Much effort has been directed to the preparation of optically active 2-furylcarbinols: (a) Duveen, D. I.; Kenyon, J. *J. Chem. Soc.* **1936**, 621. (b) Červinka, O.; Bělovský, O.; Korálová, L. *Z. Chem.* **1969**, *9*, 448. (c) Horton, D.; Meshreki, M. H. *Carbohydr. Res.* **1975**, *40*, 345. (d) Martin, S. F.; Gluchowski, C.; Campbell, C. L.; Chapman, R. C. *J. Org. Chem.* **1984**, *49*, 2512. (e) Martin, S. F.; Guinn, D. E. *Ibid.* **1987**, *52*, 5588. (f) Suzuki, K.; Yuki, Y.; Mukaiyama, T. *Chem. Lett.* **1981**, 1529. (g) Pikul, S.; Raczko, J.; Ankner, K.; Jurczak, J. *J. Am. Chem. Soc.* **1987**, *109*, 3981. (h) Brown, J. M.; Cutting, I. *J. Chem. Soc., Chem. Commun.* **1985**, 578. (i) Achmatowicz, O. In *Organic Synthesis Today and Tommorow*; Trost, B. M., Hutchinson, C. R., Eds.; Pergamon Press: 1981; pp 307–318. (j) Achmatowicz, O., Jr.; Bielski, R. *Carbohydr. Res.* **1977**, *55*, 165. (k) Drueckhammer, D. G.; Barbas, C. F., III; Nozaki, K.; Wong, C.-H.; Wood, C. Y.; Ciufolini, M. A. *J. Org. Chem.* **1988**, *53*, 1607. (l) Ziffer, H.; Kawai, K.; Kasai, M.; Imuta, M.; Froussios, C. *Ibid.* **1983**, *48*, 3017. (m) Akita, H.; Furuichi, A.; Koshiji, H.; Horikoshi, K.; Oishi, T. *Chem. Pharm. Bull.* **1984**, *32*, 1333. (n) Ziegler, F. E.; Wester, R. T. *Tetrahedron Lett.* **1984**, *25*, 617. (o) DeShong, P.; Lin, M.-T.; Perez, J. J. *Ibid.* **1986**, *27*, 2091. (p) Mori, K.; Kisida, H. *Tetrahedron* **1986**, *42*, 5281. (q) Brown, H. C.; Cho, B. T.; Park, W. S. *J. Org. Chem.* **1988**, *53*, 1231.

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(10) Thus far, no exception has been reported; cf ref 2 and 3.

(11) The products resulting from the oxidation of the olefinic or acetylenic moieties were detected neither on TLC nor on the ^{1}H NMR spectra of the crude reaction mixture.

(12) The oxidation products (2*S*)-**2** and L-(+)-DIPT have similar R_f values on TLC (except for **2l**). We thus made no effort to isolate (2*S*)-**2**.

(13) After this workup, the organic layer contains only remaining **1**.

(14) 2-Furylcarbinols **1** have been frequently utilized as starting materials in organic synthesis: (a) ref 6d–f,i,j,n–p. (b) Piancatelli, G.; Scettri, A.; Barbadoro, S. *Tetrahedron Lett.* **1976**, 3555. (c) Piancatelli, G.; Scettri, A. *Ibid.* **1977**, 1131. (d) DeShong, P.; Ramesh, S.; Elango, V.; Perez, J. J. *J. Am. Chem. Soc.* **1985**, *107*, 5219. (e) DeShong, P.; Waltermire, R. E.; Ammon, H. L. *Ibid.* **1988**, *110*, 1901. (f) Mase, T.; Sodeoka, M.; Shibasaki, M. *Tetrahedron Lett.* **1984**, *25*, 5087. (g) Bromidge, S. M.; Sammes, P. G.; Street, L. J. *J. Chem. Soc., Perkin Trans. 1* **1985**, 1725. (h) Achmatowicz, O., Jr.; Grynkiewicz, G.; Szechner, B. *Tetrahedron* **1976**, *32*, 1051. (i) Akita, H.; Koshiji, H.; Furuichi, A.; Horikoshi, K.; Oishi, T. *Chem. Pharm. Bull.* **1984**, *32*, 1242.

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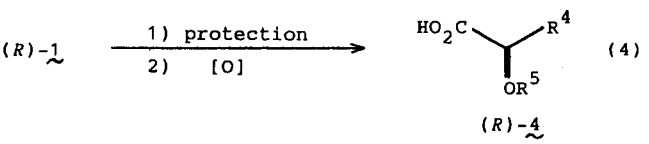
Table I. Kinetic Resolution of 1 Using TBHP, Ti(O-*i*-Pr)$_4$, and L-(+)-DIPT[a]

	substrate 1						slow-reacting enantiomer (*R*)-1[c]	
	R^1	R^2	R^3	R^4	method[b]	time, h	yield,[d] %	% ee
a	H	H	H	Me	A	12	33	>95[e]
b	H	H	H	*n*-Am	A	14	38[f]	>95[g]
					B	25	42	>95[g]
c	H	H	H	*i*-Pr	B	25	39	>95[g]
d	H	H	H	*t*-Bu	B	40	41	6[g,h]
e	H	H	H	Ph	A	48	38	>99[i]
f	Me	H	H	*n*-Am	A	6	40	>95[g]
g	H	H	Me	*n*-Am	B	4	39	>95[g]
h			H	Me	A	45	43	>99[g]
i	H	H	H	HC=CH$_2$	B	24	38	>95[j,k]
j	H	H	H	CH$_2$CH=CH$_2$	B	36	42	>95[g,l]
k	H	H	H	C≡CSiMe$_3$	B	20	38	88[m]
l	H	H	H	CH$_2$CO$_2$Et	A	22	40[n]	>95[g,o]

[a] The oxidation products **2** were obtained in the kinetic resolution of **1a–g**, **1j**, and **1l** in the range of 44–58% yield (based on ^{1}H NMR analysis of the crude reaction mixture), while in the cases of **1h**, **1i**, and **1k**, the corresponding **2** were detected neither on the crude ^{1}H NMR nor on TLC. [b] Method A: The reaction was carried out by using TBHP (0.6 equiv), Ti(O-*i*-Pr)$_4$ (0.2 equiv), and L-(+)-DIPT (0.24 equiv) in CH_2Cl_2 at −21 °C in the presence of 4A molecular sieves. Method B: The reaction was carried out by using TBHP (0.6 equiv), Ti(O-*i*-Pr)$_4$ (1 equiv), and L-(+)-DIPT (1.2 equiv) in CH_2Cl_2 at −21 °C. [c] Unless otherwise noted, absolute configurations were proven by correlation with the corresponding (*R*)-α-hydroxy acids[7] by the following sequence: (1) Ac_2O, C_5H_5N; (2) $NaIO_4$, $RuCl_3 \cdot 3H_2O$ (cat.), $CCl_4/CH_3CN/H_2O$ (2:2:3); (3) K_2CO_3, MeOH/H_2O (4:1). [d] Unless otherwise noted, isolated yields based on racemic **1** after alkaline treatment (see text). [e] Determined by ^{1}H NMR analysis of the corresponding acetate in the presence of (−)-Pr(dppm)$_3$. [f] Without alkaline treatment, the isolated yield was 41%. [g] Determined by ^{1}H NMR analysis of the corresponding MTPA ester. [h] Absolute configuration was not determined. [i] Determined by HPLC analysis of the corresponding benzoate by using Chiralpak OT (+) (Daicel Chemical Industries, Ltd.). [j] Determined by ^{1}H NMR analysis of the MTPA ester of (*R*)-1-(2-furyl)propan-1-ol obtained from (*R*)-**1i** by hydrogenation (H_2, Pd/C). [k] Absolute configuration was proven by correlation with (*R*)-α-acetoxybutanoic acid[8] by the following sequence: (1) H_2, Pd/C; (2) Ac_2O, C_5H_5N; (3) $NaIO_4$, $RuCl_3 \cdot 3H_2O$. [l] Absolute configuration was proven by correlation with (*R*)-α-hydroxypentanoic acid[9] by the following sequence: (1) H_2, Pd/C; (2–4) the same as 1–3 in the footnote *c*. [m] Absolute configuration was proven by correlation with (*R*)-1-(2-furyl)propan-1-ol (see footnote *j*) by the following sequence: (1) *n*-Bu$_4$NF; (2) H_2, Pd/C. (*R*)-1-(2-Furyl)propan-1-ol thus obtained was converted into the corresponding MTPA ester to determine the optical purity. [n] In this case, the alkaline treatment was omitted. The yield was determined by ^{1}H NMR analysis of the crude reaction mixture. [o] Absolute configuration was proven by correlation with (*R*)-1-(2-furyl)propan-1-ol (see footnote *j*) by the following sequence: (1) $LiAlH_4$; (2) TsCl, C_5H_5N; (3) $LiAlH_4$.

tation,[22] and enzymatic catalysis.[23] Among them, two recently reported procedures, which utilize enzymatic reduction of α-keto acids using L-lactate dehydrogenase,[23a] and Ti(O-*i*-Pr)$_4$-mediated ring opening of homochiral 2,3-epoxy alcohols (prepared by the Sharpless asymmetric epoxidation reaction of allyl alcohols) by benzoic acid, followed by oxidative cleavage of the resulting 1,2-diol unit,[21] seem to be the most attractive methods for the preparation of this class of compounds in large quantity.

The furan ring can be converted into a carboxylic acid by ozonolysis[24] or by oxidation using $RuO_4/NaIO_4$.[25,26] It is evident that the combination of the present kinetic resolution of 2-furylcarbinols (eq 2) and oxidative cleavage of the furan ring after protection of the hydroxyl group (eq 4) provides another general and practical method for



(4)

Table II. The Synthesis of α-Alkoxy Acids (*R*)-4 from (*R*)-1[a]

	substrate (*R*)-1:[b] R^4	protecting group:[c] R^5	product (*R*)-4:[d] % yield[e]
a	Me	TBS	85
b	*n*-Am	TBS	71
		Bn	77
		Ac	89, 86[f]
c	*i*-Pr	TBS	76
e	Ph	TBS	79
		Ac	83[f]
l	CH$_2$CO$_2$Et	TBS	77

[a] Unless otherwise noted, the oxidative cleavage of the furan ring was effected by ozonolysis. [b] R^1 = R^2 = R^3 = H. [c] TBS = *tert*-butyldimethylsilyl; Bn = benzyl; Ac = acetyl. [d] All the products obtained were confirmed to be >99% ee by ^{1}H NMR analysis of the MTPA ester of methyl α-hydroxy carboxylates obtained from (*R*)-**4** by (1) deprotection and (2) esterification (CH_2N_2). [e] Overall isolated yields for two steps. [f] The oxidative cleavage of the furan ring was carried out by using $RuO_4/NaIO_4$.

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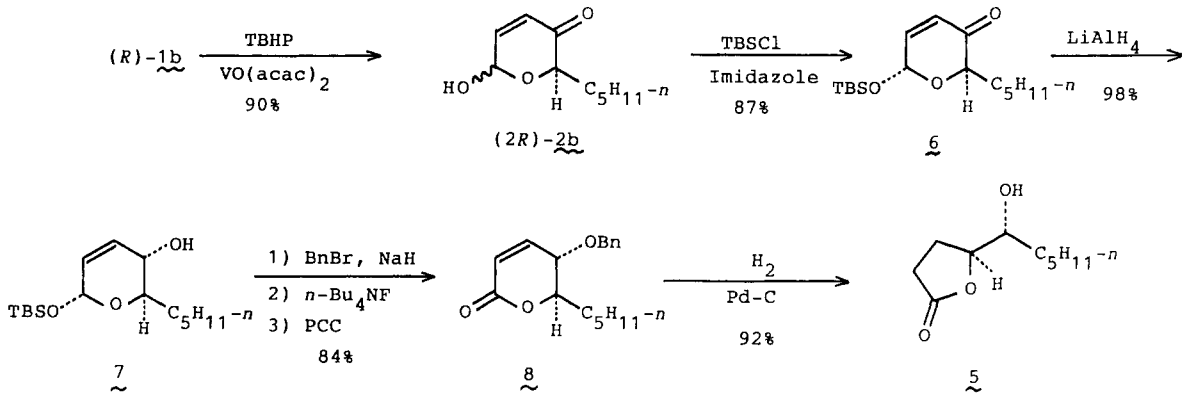
(26) This transformation has been used in natural product synthesis. For example, see: (a) Reference 14i. (b) Danishefsky, S.; Maring, C. *J. Am. Chem. Soc.* **1985**, *107*, 7762. (c) Danishefsky, S. J.; DeNinno, M. P.; Chen, S. *Ibid.* **1988**, *110*, 3929.

Scheme I



the synthesis of homochiral α-alkoxy acids. Table II, which summarizes the results of the conversion of (*R*)-**1** into (*R*)-**4**, shows that regardless of the protecting group (R^5) the desired products **4** were obtained in excellent yields without loss of stereochemical integrity. Thus, various homochiral α-alkoxy acids **4** were prepared from racemic **1** in 56–75% yields via three steps (kinetic resolution, protection of the hydroxyl group, and oxidative cleavage of the furan ring).

As described before, oxidation of **1** into **2** proceeds essentially quantitatively (eq 1).[27] Thus, the present kinetic resolution reaction provides a very efficient method for the preparation of various optically active **2** that are also recognized as important synthetic intermediates.[28] We next describe the synthesis of the naturally occurring γ-lactone **5**, isolated from *Streptomyces griseus*,[29] from (*R*)-**1b** via (2*R*)-**2b** (Scheme I).[30] Oxidation of (*R*)-**1b** by TBHP in the presence of a catalytic amount of $VO(acac)_2$ afforded the pyranone (2*R*)-**2b** in 90% yield as a mixture (ca 3:1) of α- and β-anomers.[31,32] Protection of the anomeric hydroxyl function with a *tert*-butyldimethylsilyl group resulted in the exclusive formation of the α-anomer **6** in 87% yield.[33] Compound **6** was stereospecifically reduced by $LiAlH_4$[34] to **7** in 98% yield. Conversion into **8** occurred in 84% overall yield by the following sequence: (1) protection of the hydroxyl group as the benzyl ether, (2) deprotection of the anomeric hydroxyl group by *n*-Bu_4NF, and (3) PCC oxidation. Finally, catalytic hydrogenation[30a] of **8** afforded the γ-lactone **5** in 92% yield. The spectral data and optical rotation of **5** are in good accord with values reported in the literature: $[\alpha]^{25}_D$ +10.9° (*c* 1.42, CCl_4) (lit.[30a] $[\alpha]_D$ +11.0° (*c* 1.37, CCl_4)).

In summary, the kinetic resolution of 2-furylcarbinols **1** by the Sharpless reagent proceeds highly efficiently, thus providing direct access to a variety of homochiral **1**. The utility of the present reaction was illustrated by the synthesis of various homochiral α-alkoxy acids **4** and the naturally occurring γ-lactone **5**. Further investigation on the utilization of homochiral **1** is being continued in our laboratory.[35]

Experimental Section

General. ^1H NMR spectra were measured either on a Hitachi R-40 (90 MHz) or JEOL FX-90Q (90 MHz) spectrometer, whereas ^{13}C NMR spectra were recorded on a JEOL FX-90Q spectrometer. Both ^1H and ^{13}C NMR spectra were obtained with CCl_4 or $CDCl_3$ as a solvent, and values are reported in ppm (δ) downfield from tetramethylsilane or residual $CHCl_3$ as an internal standard unless otherwise noted. Signal patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br s, broad singlet. Infrared (IR) spectra were measured on a JASCO A-100 spectrometer. Optical rotations were measured on a YANACO OR-50 polarimeter using a 20-cm^3-capacity (0.5-dm path length) cell. Elemental analyses were performed by the Research Laboratory of Resources Utilization, Tokyo Institute of Technology.

Materials. Oxygen- and water-sensitive reactions were carried out under an argon atmosphere. Methylene chloride was freshly distilled from calcium hydride. Tetrahydrofuran and ether were freshly distilled from sodium benzophenone ketyl. Titanium isopropoxide and L-(+)-DIPT were distilled under high vacuum and stored under an argon atmosphere before use. A stock solution of TBHP in CH_2Cl_2 was prepared and stored as described by Sharpless.[1b]

Racemic 1-(2-furyl)ethanol (**1a**), 1-(2-furyl)hexan-1-ol (**1b**), 1-(2-furyl)-2-methylpropan-1-ol (**1c**), 2-furylbenzyl alcohol (**1e**), 1-(2-furyl)-2-propen-1-ol (**1i**), and 1-(2-furyl)-3-buten-1-ol (**1j**) were prepared from furfural and the corresponding Grignard reagents.[36] 1-(2-Furyl)-2,2-dimethylpropan-1-ol (**1d**) was prepared from furfural and *t*-BuLi. 1-[2-(5-Methylfuryl)]hexan-1-ol (**1f**) was prepared from hexanal and the lithium anion prepared from 2-methylfuran and *n*-BuLi. 1-[2-(3-Methylfuryl)]hexan-1-ol (**1g**) was prepared from methyl 3-methyl-2-furoate[37] by the following reactions: (1) *i*-Bu_2AlH; (2) PCC; (3) *n*-AmMgBr. 1-(Benzofuran-2-yl)ethanol (**1h**) was prepared from benzofuran-2-yl methyl ketone (Aldrich Chemical Co.) by reduction with $NaBH_4$. 1-(2-Furyl)-3-(trimethylsilyl)-2-propyn-1-ol (**1k**) was prepared from furfural and the lithium anion prepared from (trimethylsilyl)-acetylene[38] and *n*-BuLi. Ethyl 3-(2-furyl)-3-hydroxypropionate

(27) Oxidation of **1** into **2** can also be carried out by other oxidants such as MCPBA, PCC, NBS, and Br_2/MeOH. See: Georgiadis, M. P.; Couladouros, E. A. *J. Org. Chem.* **1986**, *51*, 2725 and references cited therein.

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(30) For previous reports on the synthesis of **5**, see: (a) Stamatatos, L.; Sinay, P.; Pougny, J.-R. *Tetrahedron* **1984**, *40*, 1713. (b) Cooper, R. D.; Jigajinni, V. B.; Wightman, R. H. *Tetrahedron Lett.* **1984**, *25*, 5215.

(31) The compound (2*R*)-**2b** can also be prepared by the kinetic resolution of **1b** using D-(−)-DIPT as a chiral source (eq 2). However, in this case, it is necessary to stop the reaction at a low conversion stage to obtain (2*R*)-**2b** with high optical purity.

(32) Similarly, 2-furylcarbinols **1a**, **1c**, **1e–g**, and **1l** could be converted into the corresponding pyranones **2** in the range of 84–93% yields (see Experimental Section). However, the oxidation of **1h**, **1i**, and **1k** resulted in the formation of complex mixtures.

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(34) Fraser-Reid, B.; McLean, A.; Usherwood, E. W.; Yunker, M. *Can. J. Chem.* **1970**, *48*, 2877. Koga, K.; Yamada, S.; Yoh, M.; Mizoguchi, T. *Carbohydr. Res.* **1974**, *36*, C9.

(35) Recently, the synthesis of (5*R*,6*S*)-6-acetoxy-5-hexadecanolide, the major component of the oviposition attractant pheromone, using the kinetic resolution of **1** has been reported: Kametani, T.; Tsubuki, M.; Tatsuzaki, Y.; Honda, T. *Heterocycles* **1988**, *27*, 2107.

(36) Amouroux, R.; Chastrette, F.; Chastrette, M. *J. Heterocycl. Chem.* **1981**, *18*, 565.

(37) Burness, D. M. *Organic Syntheses*; Wiley: New York, 1963; Collect. Vol. IV, p 649.

(**11**) was prepared according to the reported procedure.[39] 1-(3-Furyl)pentan-1-ol (**3**) was prepared from 3-furaldehyde and *n*-BuMgBr.

In order to determine the optical purity, in some cases, the alcoholic products were converted into MTPA esters according to Mosher's procedures by using (*S*)- or (*R*)-MTPACl. A chiral shift reagent (−)-Pr(dppm)$_3$ (Daiichi Pure Chemicals Co., Ltd.) was also employed for determining the optical purity of the products after conversion into the corresponding acetates. High-performance liquid chromatography (HPLC) analysis was carried out on a NSP-800-9DX (Nihon Seimitsu Kagaku Co., Ltd.) instrument with a chiral column (Chiralpak OT (+), Daicel Chemical Industries, Ltd.) and a Shodex RI SE-51 detector (Showa Denko Co., Ltd.) for determining the optical purity of the products after conversion into the corresponding benzoates.

General Procedure for the Kinetic Resolution of 1 and 3. Method A. Kinetic Resolution with a Catalytic Amount of Ti(O-*i*-Pr)$_4$/L-(+)-DIPT. The preparation of (*R*)-1-(2-furyl)hexan-1-ol (**1b**) is described as an illustrative case. To a mixture of crushed 4A molecular sieves (5 g) and 0.2 equiv of Ti(O-*i*-Pr)$_4$ (7.35 mL, 24.7 mmol) in CH_2Cl_2 (100 mL) was added 0.24 equiv of L-(+)-DIPT (6.23 mL, 29.6 mmol) at −21 °C. The mixture was stirred for 10 min at −21 °C and cooled to −30 °C. Racemic **1b** (20.7 g, 123 mmol) dissolved in CH_2Cl_2 (20 mL) was added, and the mixture was stirred between −30 °C and −20 °C for 30 min. The mixture was again cooled to −30 °C, and 0.6 equiv of TBHP (17.0 mL, 74.0 mmol, 4.35 M in CH_2Cl_2) was slowly added. After stirring for 14 h at −21 °C, Me_2S (5.43 mL, 74.0 mmol) was slowly added and the mixture was stirred for 30 min at −21 °C. To this mixture were added 10% aqueous tartaric acid (5 mL), Et_2O (100 mL), and NaF (30 g), and the resulting mixture was vigorously stirred for 2 h at room temperature. The white precipitate was filtered off through a pad of Celite with ether (100 mL). The filtrate was concentrated to give an oil, which was dissolved in ether (200 mL) and treated with NaOH (3 N, 100 mL) for 30 min at 0 °C with vigorous stirring. The organic layer was washed with brine, dried ($MgSO_4$), and concentrated to give an oil, which was passed through a short silica gel column to afford (*R*)-**1b** (7.94 g, 38%, >95% ee determined by ^{1}H NMR analysis of the derived MTPA ester): $[\alpha]^{25}_D$ +13.8° (*c* 1.07, $CHCl_3$); IR (neat) 3350, 1140, 1005, 725 cm^{-1}; ^{1}H NMR (CCl_4, D_2O) δ 0.7–1.9 (m, 11 H), 4.45 (t, *J* = 7.3 Hz, 1 H), 6.05 (d, *J* = 3.6 Hz, 1 H), 6.16 (dd, *J* = 1.8, 3.6 Hz, 1 H), 7.19 (br s, 1 H). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.40; H, 9.71.

Method B. Kinetic Resolution with a Stoichiometric Amount of Ti(O-*i*-Pr)$_4$/L-(+)-DIPT. The preparation of (*R*)-1-(2-furyl)-2-methylpropan-1-ol (**1c**) is described as an illustrative case. To a solution of Ti(O-*i*-Pr)$_4$ (4.04 mL, 13.6 mmol) in CH_2Cl_2 (60 mL) was added L-(+)-DIPT (3.42 mL, 16.3 mmol) at −21 °C. After 10 min, the solution was cooled to −30 °C and racemic **1c** (1.90 g, 13.6 mmol) dissolved in CH_2Cl_2 (3 mL) was slowly added. After 30 min, TBHP (2.18 mL, 8.13 mmol, 3.73 M in CH_2Cl_2) was added, and the solution was stirred for 25 h at −21 °C. Workup as described above afforded (*R*)-**1c** (743 mg, 39%, >95% ee determined by ^{1}H NMR analysis of the derived MTPA ester): $[\alpha]^{25}_D$ +18.1° (*c* 1.04, $CHCl_3$); IR (neat) 3360, 1000, 720 cm^{-1}; ^{1}H NMR (CCl_4, D_2O) δ 0.76 and 0.88 (2 d, *J* = 6.6 Hz, 6 H), 1.70–2.15 (m, 1 H), 4.17 (d, *J* = 7.0 Hz, 1 H), 6.05 (d, *J* = 3.6 Hz, 1 H), 6.16 (dd, *J* = 1.8, 3.6 Hz, 1 H), 7.20 (br s, 1 H). Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.08; H, 8.85.

(*R*)-1-(2-Furyl)ethanol (1a). The kinetic resolution of racemic **1a** (7.05 g, 62.9 mmol) was run according to method A using Ti(O-*i*-Pr)$_4$ (3.75 mL, 12.6 mmol), L-(+)-DIPT (3.18 mL, 15.1 mmol), 4A molecular sieves (2 g), TBHP (6.63 mL, 37.8 mmol, 5.70 M in CH_2Cl_2), and CH_2Cl_2 (70 mL) to afford (*R*)-**1a** (2.35 g, 33%, >95% ee determined by ^{1}H NMR analysis of the derived acetate in the presence of (−)-Pr(dppm)$_3$): $[\alpha]^{25}_D$ +20.8° (*c* 1.27, $CHCl_3$); IR (neat) 3340, 1060, 730 cm^{-1}; ^{1}H NMR (CCl_4) δ 1.37 (d, *J* = 6.6 Hz, 3 H), 3.26–3.75 (br s, 1 H), 4.65 (q, *J* = 6.6 Hz, 1 H), 6.03 (d, *J* = 3.6 Hz, 1 H), 6.15 (dd, *J* = 1.9, 3.6 Hz, 1 H), 7.18 (br s, 1 H). Anal. Calcd for $C_6H_8O_2$: C, 64.27; H, 7.19. Found: C, 64.25; H, 7.34.

(*R*)-2-Furylbenzyl Alcohol (1e). The kinetic resolution of racemic **1e** (11.0 g, 63.3 mmol) was run according to method A using Ti(O-*i*-Pr)$_4$ (5.65 mL, 19.0 mmol), L-(+)-DIPT (4.79 mL, 22.8 mmol), 4A molecular sieves (3 g), TBHP (11.7 mL, 37.9 mmol, 3.24 M in CH_2Cl_2), and CH_2Cl_2 (50 mL) to afford (*R*)-**1e** (4.23 g, 38%, >99% ee determined by HPLC analysis of the derived benzoate): $[\alpha]^{25}_D$ +6.9° (*c* 1.13, $CHCl_3$); IR (neat) 3350, 1000, 725, 690 cm^{-1}; ^{1}H NMR (CCl_4, D_2O) δ 5.43 (s, 1 H), 5.85 (d, *J* = 3.6 Hz, 1 H), 6.06 (dd, *J* = 1.9, 3.6 Hz, 1 H), 7.02–7.26 (m, 6 H). Anal. Calcd for $C_{11}H_{10}O_2$: C, 75.85; H, 5.79. Found: C, 75.59; H, 5.86.

(*R*)-1-[2-(5-Methylfuryl)]hexan-1-ol (1f). The kinetic resolution of racemic **1f** (2.85 g, 15.6 mmol) was run according to method A using Ti(O-*i*-Pr)$_4$ (0.93 mL, 3.13 mmol), L-(+)-DIPT (0.79 mL, 3.8 mmol), 4A molecular sieves (600 mg), TBHP (2.16 mL, 9.38 mmol, 4.35 M in CH_2Cl_2), and CH_2Cl_2 (15 mL) to afford (*R*)-**1f** (1.15 g, 40%, >95% ee determined by ^{1}H NMR analysis of the derived MTPA ester): $[\alpha]^{25}_D$ +7.8° (*c* 1.01, $CHCl_3$); IR (neat) 3350, 1015, 780 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.7–1.9 (m, 11 H), 2.19 (s, 3 H), 2.78 (br s, 1 H), 4.39 (t, *J* = 6.6 Hz, 1 H), 5.72 and 5.90 (2 d, *J* = 3.0 Hz, 2 H). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.97; H, 10.72.

(*R*)-1-[2-(3-Methylfuryl)]hexan-1-ol (1g). The kinetic resolution of racemic **1g** (439 mg, 2.41 mmol) was run according to method B using Ti(O-*i*-Pr)$_4$ (0.72 mL, 2.4 mmol), L-(+)-DIPT (0.61 mL, 2.9 mmol), TBHP (0.37 mL, 1.5 mmol, 3.9 M in CH_2Cl_2), and CH_2Cl_2 (12 mL) to afford (*R*)-**1g** (171 mg, 39%, >95% ee determined by ^{1}H NMR analysis of the derived MTPA ester): $[\alpha]^{25}_D$ +8.89° (*c* 1.10, $CHCl_3$); IR (neat) 3330, 1450, 1010, 730 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.7–2.0 (m, 11 H), 1.92 (s, 3 H), 2.60 (br s, 1 H), 4.40 (t, *J* = 7.4 Hz, 1 H), 5.95 and 7.03 (2 d, *J* = 1.8 Hz, 2 H). Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.26; H, 10.39.

(*R*)-1-(Benzofuran-2-yl)ethanol (1h). The kinetic resolution of racemic **1h** (1.42 g, 8.79 mmol) was run according to method A using Ti(O-*i*-Pr)$_4$ (0.53 mL, 1.8 mmol), L-(+)-DIPT (0.44 mL, 2.1 mmol), 4A molecular sieves (400 mg), TBHP (1.85 mL, 5.27 mmol, 2.85 M in CH_2Cl_2), and CH_2Cl_2 (8 mL) to afford (*R*)-**1h** (609 mg, 43%, >99% ee determined by ^{1}H NMR analysis of the derived MTPA ester): $[\alpha]^{25}_D$ +19.9° (*c* 1.21, $CHCl_3$); IR (neat) 3320, 1455, 1250, 1080, 740 cm^{-1}; ^{1}H NMR (CCl_4, D_2O) δ 1.42 (d, *J* = 6.3 Hz, 3 H), 4.74 (q, *J* = 6.3 Hz, 1 H), 6.31 (s, 1 H), 6.93–7.40 (m, 4 H). Anal. Calcd for $C_{10}H_{10}O_2$: C, 74.06; H, 6.21. Found: C, 74.14; H, 6.17.

(*R*)-1-(2-Furyl)-2-propen-1-ol (1i). The kinetic resolution of racemic **1i** (3.05 g, 24.6 mmol) was run according to method B using Ti(O-*i*-Pr)$_4$ (7.3 mL, 24.6 mmol), L-(+)-DIPT (6.2 mL, 29.5 mmol), TBHP (5.2 mL, 14.8 mmol, 2.85 M in CH_2Cl_2), and CH_2Cl_2 (113 mL) to afford (*R*)-**1i** (1.15 g, 38%, >95% ee determined by ^{1}H NMR analysis of the MTPA ester of 1-(2-furyl)-propan-1-ol obtained from (*R*)-**1i** by hydrogenation (H_2, Pd/C)): $[\alpha]^{25}_D$ −1.74° (*c* 2.41, $CHCl_3$); IR (neat) 3330, 1145, 990, 730 cm^{-1}; ^{1}H NMR (CCl_4) δ 3.73 (br s, 1 H), 4.85–5.38 (m, 3 H), 5.69–6.23 (m, 3 H), 7.18 (br s, 1 H). Anal. Calcd for $C_7H_8O_2$: C, 67.73; H, 6.50. Found: C, 67.54; H, 6.59.

(*R*)-1-(2-Furyl)-3-buten-1-ol (1j). The kinetic resolution of racemic **1j** (1.64 g, 11.9 mmol) was run according to method B using Ti(O-*i*-Pr)$_4$ (3.54 mL, 11.9 mmol), L-(+)-DIPT (3.00 mL, 14.3 mmol), TBHP (2.04 mL, 7.14 mmol, 3.50 M in CH_2Cl_2), and CH_2Cl_2 (56 mL) to afford (*R*)-**1j** (0.68 g, 42%, >95% ee determined by ^{1}H NMR analysis of the derived MTPA ester): $[\alpha]^{25}_D$ +39.9° (*c* 1.54, $CHCl_3$); spectral data (IR, ^{1}H NMR) are identical with those reported for the racemic compound.[40]

(*R*)-1-(2-Furyl)-3-(trimethylsilyl)-2-propyn-1-ol (1k). The kinetic resolution of racemic **1k** (1.57 g, 8.1 mmol) was run according to method B using Ti(O-*i*-Pr)$_4$ (2.4 mL, 8.1 mmol), L-(+)-DIPT (2.0 mL, 9.7 mmol), TBHP (4.25 mL, 12.1 mmol, 2.85 M in CH_2Cl_2), and CH_2Cl_2 (40 mL) to afford (*R*)-**1k** (0.60 g, 38%, 88% ee determined by ^{1}H NMR analysis of the MTPA ester of 1-(2-furyl)propan-1-ol obtained from (*R*)-**1k** by (1) protiodesilylation (*n*-Bu_4NF) and (2) hydrogenation (H_2, Pd/C)): $[\alpha]^{25}_D$ −16.5° (*c* 1.65, $CHCl_3$); IR (neat) 3350, 1250, 1040, 1010, 844 cm^{-1}; ^{1}H NMR (CCl_4, benzene as an internal standard) δ 0.05 (s, 9 H), 3.12 (br s, 1 H), 5.20–5.40 (m, 1 H), 6.18–6.40 (m, 2 H), 7.37 (br

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s, 1 H). Anal. Calcd for $C_{10}H_{14}O_2Si$: C, 61.82; H, 7.26. Found: C, 61.17; H, 7.43.

Ethyl (*R*)-3-(2-Furyl)-3-hydroxypropionate (1l). The kinetic resolution of racemic **1l** (2.14 g, 11.7 mmol) was run according to method A using Ti(O-*i*-Pr)$_4$ (0.69 mL, 2.3 mmol), L-(+)-DIPT (0.59 mL, 2.8 mmol), 4A molecular sieves (500 mg), TBHP (2.45 mL, 6.99 mmol, 2.85 M in CH_2Cl_2), and CH_2Cl_2 (11 mL). The alkaline treatment was omitted in this case. Purification of the crude products by column chromatography on silica gel afforded (*R*)-**1l** and L-(+)-DIPT as an inseparable mixture (1.41 g) and (2*S*)-**2l** (1.21 g, 52%). The yield of (*R*)-**1l** is estimated to be 40% based on ^{1}H NMR analysis of the mixture. The optical purity of (*R*)-**1l** was determined to be >95% ee by ^{1}H NMR analysis of the derived MTPA ester. The compound (*R*)-**1l** thus obtained was used for the synthesis of (*R*)-**4l** and (2*R*)-**2l** without further purification.

(*R*)-1-(3-Furyl)pentan-1-ol (3). The kinetic resolution of racemic **3** (770 mg, 5.00 mmol) was run according to method A using Ti(O-*i*-Pr)$_4$ (0.30 mL, 1.00 mmol), L-(+)-DIPT (0.25 mL, 1.20 mmol), TBHP (0.89 mL, 3.0 mmol, 3.37 M in CH_2Cl_2), and CH_2Cl_2 (5 mL) to afford (*R*)-**3** (293 mg, 38%, >99% ee determined by ^{1}H NMR analysis of the derived MTPA ester): $[\alpha]^{25}_D$ +16.2° (*c* 1.08, $CHCl_3$); IR (neat) 3340, 1020, 785 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.7–1.9 (m, 9 H), 3.20 (br s, 1 H), 4.39 (t, *J* = 6.3 Hz, 1 H), 6.19 (br s, 1 H), 7.12–7.30 (m, 2 H). Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 69.87; H, 9.15.

(*R*)-2-[(*tert*-Butyldimethylsilyl)oxy]propanoic Acid (4a, R^5 = *tert*-Butyldimethylsilyl (TBS)). A solution of (*R*)-**1a** (1.18 g, 10.5 mmol), imidazole (1.08 g, 15.8 mmol), and *tert*-butyldimethylsilyl chloride (1.90 g, 12.6 mmol) in DMF (5 mL) was stirred at room temperature for 2 h and poured into a mixture of hexane (10 mL) and brine (10 mL). The organic layer was separated, and the aqueous layer was extracted with hexane (10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give a crude oil, which was purified by column chromatography on silica gel to afford the silyl ether of (*R*)-**1a** (2.14 g, 89%): $[\alpha]^{25}_D$ +42.5° (*c* 1.04, $CHCl_3$); IR (neat) 1250, 1100, 830 cm^{-1}; ^{1}H NMR (CCl_4, CH_2Cl_2 as an internal standard) δ –0.02 (s, 6 H), 0.77 (s, 9 H), 1.33 (d, *J* = 6.3 Hz, 3 H), 4.65 (q, *J* = 6.3 Hz, 1 H), 5.89 (d, *J* = 3.5 Hz, 1 H), 6.02 (dd, *J* = 2.0, 3.5 Hz, 1 H), 7.04 (br s, 1 H). Anal. Calcd for $C_{12}H_{22}O_2Si$: C, 63.67; H, 9.79. Found: C, 63.42; H, 9.61.

The solution of the above silyl ether of (*R*)-**1a** (1.41 g, 6.21 mmol) in MeOH (8 mL) was cooled to –78 °C, and ozone was passed at a rate of gentle bubbling for 2 h. Argon was bubbled at –78 °C for 5 min to remove excess ozone. The solution was allowed to warm to room temperature and concentrated to give a crude oil, which was purified by column chromatography on silica gel to afford (*R*)-**4a** (R^5 = TBS) (1.21 g, 95%): $[\alpha]^{25}_D$ –3.7° (*c* 1.13, $CHCl_3$); IR (neat) 3100, 1720, 1250, 1145 cm^{-1}; ^{1}H NMR (CCl_4, CH_2Cl_2 as an internal standard) δ –0.05 (s, 6 H), 0.73 (s, 9 H), 1.24 (d, *J* = 6.6 Hz, 3 H), 4.06 (q, *J* = 6.6 Hz, 1 H), 8.46 (br s, 1 H). Anal. Calcd for $C_9H_{20}O_3Si$: C, 52.90; H, 9.86. Found: C, 52.85; H, 10.12.

(*R*)-2-[(*tert*-Butyldimethylsilyl)oxy]heptanoic Acid (4b, R^5 = TBS). The acid (*R*)-**4b** (R^5 = TBS) was prepared from (*R*)-**1b** in 71% overall yield by the same procedure as described for the preparation of (*R*)-**4a** (R^5 = TBS): $[\alpha]^{25}_D$ +5.74° (*c* 1.01, $CHCl_3$); IR (neat) 3020, 1710, 1245, 1140 cm^{-1}; ^{1}H NMR (CCl_4, CH_2Cl_2 as an internal standard) δ –0.06 (s, 6 H), 0.6–1.7 (m, 11 H), 0.74 (s, 9 H), 3.95 (t, *J* = 6.0 Hz, 1 H), 10.82 (br s, 1 H). Anal. Calcd for $C_{13}H_{28}O_3Si$: C, 59.95; H, 10.84. Found: C, 60.40; H, 10.98.

(*R*)-2-(Benzyloxy)heptanoic Acid (4b, R^5 = Bn). To a mixture of (*R*)-**1b** (1.56 g, 9.29 mmol) and oil-free NaH (579 mg, 12.1 mmol) in THF (6 mL) was added benzyl bromide (1.33 mL, 11.1 mmol) at room temperature. The mixture was stirred for 1 h and poured into saturated aqueous $NaHCO_3$ (5 mL). The organic layer was separated, and the aqueous layer was extracted with hexane (5 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give a crude oil, which was purified by column chromatography on silica gel to afford the benzyl ether of (*R*)-**1b** (2.11 g, 88%): $[\alpha]^{25}_D$ +97.5° (*c* 1.12, $CHCl_3$); IR (neat) 1460, 1070, 735, 700 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.7–2.0 (m, 11 H), 4.02–4.45 (m, 3 H), 6.05 (d, *J* = 3.5 Hz, 1 H), 6.12 (dd, *J* = 2.0, 3.5 Hz, 1 H), 6.90–7.23 (m, 6 H). Anal. Calcd for $C_{17}H_{22}O_2$: C, 79.03; H, 8.58. Found: C, 79.28; H, 8.80.

The above benzyl ether of (*R*)-**1b** (688 mg, 2.67 mmol) was ozonolyzed as described for the preparation of (*R*)-**4a** (R^5 = TBS) to afford (*R*)-**4b** (R^5 = Bn) (549 mg, 87%): $[\alpha]^{25}_D$ +40.5° (*c* 1.01, $CHCl_3$); IR (neat) 3030, 1710 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.7–1.9 (m, 11 H), 3.80 (t, *J* = 6.0 Hz, 1 H), 4.27 and 4.64 (2 d, *J* = 12.0 Hz, 2 H), 7.21 (br s, 5 H). Anal. Calcd for $C_{14}H_{20}O_3$: C, 71.16; H, 8.53. Found: C, 71.42; H, 8.79.

(*R*)-2-Acetoxyheptanoic Acid (4b, R^5 = Ac). A mixture of (*R*)-**1b** (1.41 g, 8.37 mmol), acetic anhydride (0.95 mL, 10 mmol), and dry pyridine (5 mL) was stirred at room temperature for 12 h. Saturated aqueous $NaHCO_3$ (5 mL) was added, and the mixture was extracted with hexane (2 × 5 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give the crude acetate of (*R*)-**1b**, which was ozonolyzed as described for the preparation of (*R*)-**4a** (R^5 = TBS) to afford (*R*)-**4b** (R^5 = Ac) (1.41 g, 89%): $[\alpha]^{25}_D$ +21.8° (*c* 1.11, $CHCl_3$); IR (neat) 3150, 1720, 1220 cm^{-1}; ^{1}H NMR (CCl_4) δ 0.7–1.8 (m, 11 H), 1.98 (s, 3 H), 4.84 (t, *J* = 6.0 Hz, 1 H), 10.54 (br s, 1 H). Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.55; H, 8.97.

(*R*)-2-[(*tert*-Butyldimethylsilyl)oxy]-3-methylbutanoic Acid (4c, R^5 = TBS). The acid (*R*)-**4c** (R^5 = TBS) was prepared from (*R*)-**1c** in 76% overall yield by the same procedure as described for the preparation of (*R*)-**4a** (R^5 = TBS): $[\alpha]^{25}_D$ +21.1° (*c* 1.03, $CHCl_3$); IR (neat) 3020, 1715, 1250, 840 cm^{-1}; ^{1}H NMR (CCl_4, CH_2Cl_2 as an internal standard) δ –0.07 (s, 6 H), 0.76 and 0.83 (2 d, *J* = 6.7 Hz, 6 H), 0.77 (s, 9 H), 1.76–2.10 (m, 1 H), 3.77 (d, *J* = 3.9 Hz, 1 H), 11.15 (br s, 1 H). Anal. Calcd for $C_{11}H_{24}O_3Si$: C, 56.85; H, 10.41. Found: C, 56.69; H, 10.38.

(*R*)-[(*tert*-Butyldimethylsilyl)oxy]phenylacetic Acid (4e, R^5 = TBS). The acid (*R*)-**4e** (R^5 = TBS) was prepared from (*R*)-**1e** in 79% overall yield by the same procedure as described for the preparation of (*R*)-**4a** (R^5 = TBS): $[\alpha]^{25}_D$ –78.1° (*c* 1.03, $CHCl_3$); IR (neat) 3030, 1710, 1250, 1120 cm^{-1}; ^{1}H NMR (CCl_4, CH_2Cl_2 as an internal standard) δ 0.00 (s, 6 H), 0.88 (s, 9 H), 5.12 (s, 1 H), 7.07–7.43 (m, 5 H), 10.58 (br s, 1 H). Anal. Calcd for $C_{14}H_{22}O_3Si$: C, 63.12; H, 8.32. Found: C, 63.22; H, 8.34.

(*R*)-Acetoxyphenylacetic Acid (4e, R^5 = Ac). The alcohol (*R*)-**1e** (1.18 g, 6.79 mmol) was acetylated by the same procedure as described for the preparation of (*R*)-**4b** (R^5 = Ac). This acetate was dissolved in $CCl_4/CH_3CN/H_2O$ (2:2:3, 70 mL). To this mixture were added $NaIO_4$ (11.6 g, 54.3 mmol) and $RuCl_3 \cdot 3H_2O$ (35.5 mg, 0.136 mmol) at room temperature, and the mixture was vigorously stirred for 1 h at room temperature. The white precipitate was filtered off through a pad of Celite with AcOEt (50 mL). The organic layer was separated, and the aqueous layer was extracted with AcOEt (2 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give a crude oil, which was purified by column chromatography on silica gel to afford (*R*)-**4e** (R^5 = Ac) (1.09 g, 83%): $[\alpha]^{25}_D$ –154° (*c* 1.01, $CHCl_3$); IR (neat) 3020, 1720, 1220 cm^{-1}; ^{1}H NMR (CCl_4) δ 2.00 (s, 3 H), 5.74 (s, 1 H), 7.06–7.40 (m, 5 H), 11.29 (br s, 1 H). Anal. Calcd for $C_{10}H_{10}O_4$: C, 61.85; H, 5.19. Found: C, 61.93; H, 5.25.

(*R*)-2-[(*tert*-Butyldimethylsilyl)oxy]succinic Acid 4-Ethyl Ester (4l, R^5 = TBS). The monoester (*R*)-**4l** (R^5 = TBS) was prepared from (*R*)-**1l** in 77% overall yield by the same procedure as described for the preparation of (*R*)-**4a** (R^5 = TBS): $[\alpha]^{25}_D$ +21.6° (*c* 1.00, $CHCl_3$); IR (neat) 3110, 1720, 1260, 1140 cm^{-1}; ^{1}H NMR (CCl_4, CH_2Cl_2 as an internal standard) δ –0.06 (s, 6 H), 0.70 (s, 9 H), 1.08 (t, *J* = 7.4 Hz, 3 H), 2.46 (dd, *J* = 7.4, 15.6 Hz, 1 H), 2.50 (dd, *J* = 5.0, 15.6 Hz, 1 H), 3.89 (q, *J* = 7.4 Hz, 2 H), 4.38 (dd, *J* = 5.0, 7.4 Hz, 1 H), 10.73 (br s, 1 H). Anal. Calcd for $C_{12}H_{24}O_5Si$: C, 52.15; H, 8.75. Found: C, 52.40; H, 8.98.

The Synthesis of (2*R*)-2*H*-Pyran-3(6*H*)-one 2 from (*R*)-1. This reaction was carried out by using the reported procedure[4] with a slight modification. The synthesis of (2*R*)-**2b** is described as an illustrative case. To a solution of (*R*)-**1b** (545 mg, 3.24 mmol) in CH_2Cl_2 (10 mL) were added TBHP (1.30 mL, 4.87 mmol, 3.73 M in CH_2Cl_2) and VO(acac)$_2$ (8.6 mg, 0.032 mmol) at 0 °C. The solution was stirred for 14 h at 0 °C, and Me_2S (0.36 mL, 4.9 mmol) was added at 0 °C. After stirring for 30 min at 0 °C, saturated aqueous $NaHCO_3$ (10 mL) was added. The organic layer was separated, and the aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give a crude oil, which was purified by column chromatography on silica gel to afford (2*R*)-**2b** as an inseparable

mixture (ca 3:1) of α- and β-anomers (535 mg, 90%): IR (neat) 3370, 1670 cm^{-1}; ^1H NMR ($CDCl_3$, D_2O) δ 0.6–1.9 (m, 11 H), 3.81–4.00 (m, 0.24 H), 4.38 (dd, J = 4.8, 6.9 Hz, 0.76 H), 5.45 (d, J = 3.6 Hz, 1 H), 5.93 (d, J = 9.9 Hz, 0.76 H), 5.97 (dd, J = 2.1, 9.9 Hz, 0.24 H), 6.75 (dd, J = 3.6, 10.5 Hz, 1 H). Anal. Calcd for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.39; H, 8.71.

(2*R*)-2a: 88% yield from (*R*)-**1a**; spectral data (IR, ^1H NMR) are identical with those reported for the racemic compound.[41]

(2*R*)-2c: 85% yield from (*R*)-**1c**; IR (neat) 3370, 1665, 1020 cm^{-1}; ^1H NMR ($CDCl_3$, D_2O) δ 0.73 and 0.87 (2 d, J = 6.6 Hz, 6 H), 1.94–2.48 (m, 1 H), 3.66–3.81 (m, 0.25 H), 4.19 (d, J = 3.0 Hz, 0.75 H), 5.46 (d, J = 3.6 Hz, 1 H), 5.89 (d, J = 10.8 Hz, 0.75 H), 5.93 (dd, J = 1.8, 10.8 Hz, 0.25 H), 6.75 (dd, J = 3.6, 10.8 Hz, 1 H). Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74. Found: C, 61.16; H, 8.10.

(2*R*)-2e:[4] 88% yield from (*R*)-**1e**; IR (neat) 3360, 1670, 740, 690 cm^{-1}; ^1H NMR ($CDCl_3$, D_2O, acetone as an internal standard) δ 4.86 (d, J = 1.8 Hz, 0.3 H), 5.42 (s, 0.7 H), 5.48 (d, J = 3.6 Hz, 1 H), 5.99 (d, J = 11.2 Hz, 0.7 H), 6.03 (dd, J = 1.6, 11.2 Hz, 0.3 H), 6.76 (dd, J = 3.6, 11.2 Hz, 1 H), 7.21 (br s, 5 H).

(2*R*)-2f: 93% yield from (*R*)-**1f**; IR (neat) 3380, 1670, 1000 cm^{-1}; ^1H NMR ($CDCl_3$) δ 0.7–1.9 (m, 11 H), 1.50 (s, 3 H), 3.52 (br s, 1 H), 4.03 (dd, J = 4.8, 6.4 Hz, 0.2 H), 4.36 (dd, J = 7.7, 4.1 Hz, 0.8 H), 5.85 (d, J = 10.8 Hz, 1 H), 6.68 (d, J = 10.8 Hz, 0.8 H), 6.73 (d, J = 10.8 Hz, 0.2 H). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.27; H, 9.33.

(2*R*)-2g: 93% yield from (*R*)-**1g**; IR (neat) 3390, 1670, 1015 cm^{-1}; ^1H NMR ($CDCl_3$, D_2O) δ 0.7–1.9 (m, 11 H), 1.71 (s, 3 H), 3.90 (dd, J = 3.6, 7.2 Hz, 0.27 H), 4.40 (dd, J = 4.5, 6.9 Hz, 0.73 H), 5.38–5.56 (m, 1 H), 6.45–6.61 (m, 1 H). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.25; H, 9.39.

(2*R*)-2l: 84% yield from (*R*)-**1l**; IR (neat) 3380, 1680 cm^{-1}; ^1H NMR ($CDCl_3$, D_2O) δ 1.01 (t, J = 7.5 Hz, 3 H), 2.48 (dd, J = 7.2, 16.8 Hz, 0.77 H), 2.51 (dd, J = 7.2, 16.8 Hz, 0.23 H), 2.66 (dd, J = 4.8, 16.8 Hz, 0.77 H), 2.69 (dd, J = 4.8, 16.8 Hz, 0.23 H), 3.89 (q, J = 7.5 Hz, 2 H), 4.21–4.40 (m, 0.23 H), 4.71 (dd, J = 4.8, 7.2 Hz, 0.77 H), 5.32 (d, J = 3.7 Hz, 0.77 H), 5.38–5.51 (m, 0.23 H), 5.84 (d, J = 10.8 Hz, 0.77 H), 5.88 (dd, J = 10.8, 1.8 Hz, 0.23 H), 6.69 (dd, J = 3.7, 10.8 Hz, 1 H). Anal. Calcd for $C_9H_{12}O_5$: C, 54.00; H, 6.04. Found: C, 53.56; H, 6.18.

The Synthesis of the γ-Lactone 5. A solution of (2*R*)-**2b** (854 mg, 4.65 mmol), imidazole (474 mg, 6.97 mmol), and *tert*-butyldimethylsilyl chloride (906 mg, 6.04 mmol) in DMF (30 mL) was stirred for 1 h at 0 °C. Saturated aqueous $NaHCO_3$ (30 mL) was added, and the mixture was extracted with hexane (2 × 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give crude **6** (1.21 g, 87%), which was used without further purification. A pure sample was obtained by column chromatography on silica gel: ^1H NMR (CCl_4, CH_2Cl_2 as an internal standard) δ 0.03 (s, 6 H), 0.62–1.90 (m, 11 H), 0.75 (s, 9 H), 4.13 (dd, J = 4.8, 7.8 Hz, 1 H), 5.22 (d, J = 3.0 Hz, 1 H), 5.66 (d, J = 9.6 Hz, 1 H), 6.43 (dd, J = 3.0, 9.6 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 196.9, 145.8, 126.2, 87.9, 74.1, 31.7, 29.7, 25.7, 24.8, 22.5, 18.1, 14.0, −4.5, −5.3.

To a solution of **6** (1.21 g, 4.06 mmol) in ether (40 mL) was added $LiAlH_4$ (155 mg, 4.06 mmol) at −60 °C. After 30 min, H_2O (0.3 mL, 16 mmol) and NaF (686 mg, 16.3 mmol) were added, and the mixture was vigorously stirred for 1 h at room temperature. The white precipitate was filtered off through a pad of Celite with ether (20 mL). The filtrate was concentrated to give crude **7** (1.19 g, 98%), which was used without further purification. A pure sample was obtained by column chromatography on silica gel: ^1H NMR (CCl_4, D_2O, benzene as an internal standard) δ 0.09 (s, 6 H), 0.7–1.9 (m, 11 H), 0.84 (s, 9 H), 3.26–3.72 (m, 2 H), 5.03–5.14 (m, 1 H), 5.34–5.55 (m, 1 H), 5.63 (d, J = 10.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 131.8, 129.1, 89.0, 71.7, 68.1, 32.1, 31.9, 25.7, 25.2, 22.6, 18.1, 14.0, −4.3, −5.3.

To a solution of **7** (1.19 g, 3.98 mmol) in THF/DMF (4:1, 25 mL) were added oil-free NaH (292 mg, 6.09 mmol) and benzyl bromide (0.63 mL, 5.3 mmol) at 0 °C. The mixture was stirred for 30 min at room temperature, and saturated aqueous NH_4Cl (20 mL) was added. The organic layer was separated, and the aqueous layer was extracted with hexane (2 × 10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give the crude benzyl ether of **7** (1.49 g, 96%), which was used without further purification. A pure sample was obtained by column chromatography on silica gel: ^1H NMR (CCl_4, CH_2Cl_2 as an internal standard) δ 0.11 (s, 6 H), 0.7–1.9 (m, 11 H), 0.87 (s, 9 H), 3.40–3.85 (m, 2 H), 4.36–4.48 (2 d, J = 11.4 Hz, 2 H), 5.07–5.17 (m, 1 H), 5.41–5.63 (m, 1 H), 5.79 (d, J = 11.2 Hz, 1 H), 7.11 (br s, 5 H).

To a solution of the above benzyl ether of **7** (1.49 g, 3.82 mmol) in THF (20 mL) was added *n*-Bu_4NF (6.84 mL, 4.58 mmol, 0.67 M in THF) at 0 °C. The solution was stirred for 10 min, and then saturated aqueous NH_4Cl (10 mL) was added. The organic layer was separated, and the aqueous layer was extracted with ether (10 mL). The combined organic layers were dried ($MgSO_4$) and concentrated to give the crude hemiacetal (980 mg, 93%), which was used without further purification. A pure sample was obtained by column chromatography on silica gel: ^1H NMR (CCl_4, D_2O) δ 0.6–1.9 (m, 11 H), 3.23–3.96 (m, 2 H), 4.21–4.55 (m, 2 H), 5.04–5.15 (m, 1 H), 5.49–5.93 (m, 2 H), 7.17 (br s, 5 H).

To a mixture of PCC (1.21 g, 5.61 mmol), sodium acetate (900 mg, 11.0 mmol), and 4A molecular sieves (300 mg) in dry CH_2Cl_2 (20 mL) was added the above hemiacetal (516 mg, 1.87 mmol) dissolved in CH_2Cl_2 (2 mL) at room temperature. The mixture was vigorously stirred for 1 h and diluted with ether (20 mL). The resulting black precipitate was filtered off through a pad of Celite with ether (10 mL). The filtrate was concentrated to give crude **8** (482 mg, 94%), which was used without further purification. A pure sample was obtained by column chromatography on silica gel: ^1H NMR (CCl_4) δ 0.7–1.9 (m, 11 H), 3.83 (dt, J = 9.2, 2.3 Hz, 1 H), 3.96–4.22 (m, 1 H), 4.43 and 4.53 (2 d, J = 12.6 Hz, 2 H), 5.72 (dd, J = 1.6, 10.8 Hz, 1 H), 6.67 (dd, J = 2.4, 10.8 Hz, 1 H), 7.13 (br s, 5 H).

A mixture of **8** (405 mg, 1.48 mmol) and 10% Pd/C in MeOH (10 mL) was vigorously stirred under a hydrogen atmosphere for 18 h at room temperature. The mixture was filtered off through a pad of Celite with ether (10 mL). The filtrate was concentrated to give a crude oil, which was purified by column chromatography on silica gel to afford **5** (254 mg, 92%): $[\alpha]^{25}_D$ +10.9° (*c* 1.42, CCl_4) (lit.[30a] $[\alpha]_D$ +11.0° (*c* 1.37, CCl_4)). The spectral data (^1H NMR and IR) of **5** were in good accord with values reported in the literature.[30a] Anal. Calcd for $C_{10}H_{18}O_3$: C, 64.49; H, 9.74. Found: C, 64.48; H, 9.71.

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Registry No. **1a**, 106565-48-4; (*R*)-**1a**, 27948-61-4; (*R*)-**1a** (silyl ether deriv), 119619-33-9; **1b**, 113509-45-8; (*R*)-**1b**, 113565-48-3; (*R*)-**1b** (benzyl ether deriv), 119619-34-0; (*R*)-**1b** (acetate deriv), 119619-35-1; **1c**, 113509-46-9; (*R*)-**1c**, 113565-49-4; **1d**, 113509-47-0; (*R*)-**1d**, 113565-50-7; **1e**, 60907-91-7; (*R*)-**1e**, 113565-51-8; (*R*)-**1e** (acetate deriv), 113565-51-8; **1f**, 113509-48-1; (*R*)-**1f**, 113565-52-9; **1g**, 119619-36-2; (*R*)-**1g**, 119678-65-8; **1h**, 119619-37-3; (*R*)-**1h**, 119678-66-9; **1i**, 119619-38-4; (*R*)-**1i**, 119678-67-0; **1j**, 119619-39-5; (*R*)-**1j**, 119678-68-1; **1k**, 119619-40-8; (*R*)-**1k**, 119678-69-2; **1l**, 119619-41-9; (*R*)-**1l**, 119678-70-5; **2a**, 41728-14-7; (2*R*)-**2b** (isomer 1), 119678-71-6; (2*R*)-**2b** (isomer 2), 119678-72-7; **2c**, 74425-88-0; **2d**, 113509-50-5; **2e**, 36169-68-3; **2f**, 113509-51-6; **2g**, 119619-42-0; **2j**, 74426-00-9; **2l**, 119619-43-1; **3**, 119619-44-2; (*R*)-**3**, 119678-73-8; **4a** (R^5 = TBS), 119619-45-3; **4b** (R^5 = TBX), 119619-46-4; **4b** (R^5 = Bn), 117682-99-2; **4b** (R^5 = Ac), 78672-88-5; **4c** (R^5 = TBX), 119619-47-5; **4e** (R^5 = TBX), 119619-48-6; **4e** (R^5 = Ac), 51019-43-3; **4l** (R^5 = TBX), 119619-49-7; **5**, 92470-98-9; **6**, 119619-50-0; **7**, 119619-51-1; **7** (benzyl ether deriv), 119619-52-2; **8**, 119619-53-3; **8** (hydroxy deriv), 119619-54-4; L-(+)-DIPT, 2217-15-4; $Ti(O\text{-}i\text{-}Pr)_4$, 13421-84-6; furfural, 98-01-1; hexanal, 66-25-1; 2-methylfuran, 534-22-5; methyl 3-methyl-2-furoate, 6141-57-7; benzofuran-2-yl methyl ketone, 1646-26-0; (trimethylsilyl)acetylene, 1066-54-2; (*R*)-1-(2-furyl)propan-1-ol, 119619-55-5; (*R*)-α-acetoxybutanoic acid, 3347-89-5; (*R*)-α-hydroxypentanoic acid, 24809-83-4; 3-furaldehyde, 498-60-2.

(41) Achmatowicz, O., Jr.; Bukowski, P.; Szechner, B.; Zwierzchowska, Z.; Zamojski, A. *Tetrahedron* **1971**, 1973.