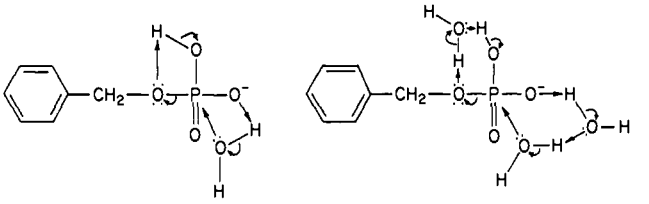
tiomeric ratio of the alcohol (to 70% *R* ee) would be expected if the reaction were to be a displacement reaction (S_N2) involving solvent attack at the benzyl carbon atom. We found a 20% *R* ee in [α-^{2}H]benzyl alcohol following hydrolysis in 1 M perchloric acid solution, which may be interpreted to mean that the benzyl phosphate ester is subjected to hydrolysis by an A-1 (S_N1) mechanism involving carbocation formation. The configuration of the product formed during reaction in 1 M $HClO_4$ at 75 °C is consistent with 70% racemization and 30% inversion.

The hydrolysis of benzyl phosphate in the region $1.3 < pH < 2.0$ is effected through concurrent C–O and P–O bond fission. As the pH is raised, progressively more ester P–O bond scission is observed with the transition half-way complete between pH 1.9–2.0. When chiral benzyl phosphate was hydrolyzed at a pH (1.9) where fission of the C–O bond and of the P–O bond were approximately equivalent, the isolated [α-^{2}H]benzyl alcohol had ee 30% *S*. An ee of 25% *S* may be calculated for a reaction with equivalent concurrent C–O and P–O bond fission. This calculation is based on the assumption that the reactions for scission of the C–O bond and of the P–O bond are independent and that the mechanism for C–O bond fission is A-1 (S_N1) involving 70% racemization and 30% inversion. This calculation is well within the experimental error and agrees with the experimentally measured value. This result implies that the bond cleavage reactions are independent and the mechanisms are preserved. The change in the scissile bond is quite dramatic, with the transition taking place within ±0.4 pH units of the pK_{a_1} (1.6) for the ester.

Thus, the experimental observations regarding the hydrolysis reactions of benzyl phosphate are accommodated in the following mechanisms. An A-1 (S_N1) mechanism—formation of a benzyl carbocation—operates in the hydrolysis of the neutral species and is accompanied by C–O bond scission. Formation of the conjugate acid of the neutral ester species in strongly acidic solution only enhances the reactivity of the benzyl group and renders the phosphate ester susceptible to hydrolysis by this mechanism. The hydrolysis mechanism involving C–O bond cleavage continues to be favored as the pH of the acidic solution passes through the pK_{a_1} of the benzyl phosphate ester. However, the monoanion of the ester undergoes hydrolysis by another mechanism. For the monoanion of benzyl phosphate, the hydrolysis reaction resulting in scission of the P–O bond proceeds by an intramolecular concerted general acid–general base mechanistic pathway. The same properties that enable the benzyl group to form a relatively stable carbocation and that facilitate its participation in displacement reactions also make the oxygen atom in the ester more basic, as does the formation of the monoanion of the phosphate ester, and thus the benzyl phosphate is subject to hydrolysis by this mechanism. Intramolecular concerted general acid–general base hydrolysis thus proceeds by the intramolecular proton transfer from the phosphate ester monoanion to the ester oxygen concerted with the phosphate ester monoanion-catalyzed attack by the solvent, water:



Hydrolysis by this mechanism is consistent with a proposed preassociative mechanistic pathway which results in inversion at the phosphorus atom.[11]

Acknowledgment. This investigation was supported by USPHS Grant GM 27003 from the National Institute of General Medical Sciences and by NIH Grant RR 01077 from the Division of Research Resources. We thank Prof. M. Mark Midland of the University of California, Riverside, for the kind gift of (*S*)-(+)-[α-^{2}H]benzyl alcohol.

Acyclic Stereoselection. 23. Lactaldehyde Enolate Equivalents†[1]

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Contribution from the Department of Chemistry, University of California, Berkeley, California 94720. *Received June 4, 1984*

Abstract: A number of lactate esters have been synthesized and stereochemistry of the reactions of their enolates with aldehydes examined. Dioxolanones **3** and **4** and oxazolanone **10** show low stereoselectivity (Table I). Methyl esters of various O-alkylated lactic acids (**17–19**) show generally higher stereoselectivity (Table II). Of these reagents, the best is methyl 2-methoxypropanoate (**17**), which shows exceedingly high selectivity with aliphatic aldehydes that are branched at C-2. For example, it gives a single adduct with isobutyraldehyde and pivalaldehyde and shows comparable simple diastereoselectivity with the chiral aldehydes **29** and **30**. Hindered aryl esters of *O*-benzyllactic acid (**37–39**) show complex behavior (Table III), with the sense and magnitude of stereoselectivity clearly being associated with the steric bulk of the aryl group (Table IV). The most useful member of this series of compounds is 2,6-di-*tert*-butyl-4-methylphenyl (butylated hydroxytoluene, BHT) *O*-benzyllactate (**39**), which gives only one isomer in its reactions with isobutyraldehyde and benzaldehyde. Ester **39** also shows useful stereoselectivity with chiral, β,γ-unsaturated aldehydes (**73** and **76**). The stereoselectivities observed in this study may be understood in terms of the transition-state models presented in Figure 2. It is argued on the basis of circumstantial evidence that the lactate esters give enolates of the *Z* configuration (eq 8 and 15). As shown in Figure 2, it is proposed that the dihedral angle between the carbonyl and enolate double bonds is approximately 90° and that the two stereoisomers in each case arise from transition states A and B. When the R″ group is small (methyl), then transition state A is preferred, leading to the sense of stereoselectivity shown by esters **17–19**. However, when R″ is large (BHT), transition state B predominates. The DMP and DIPP esters show intermediate behavior. The studies reported in this paper are the first that demonstrate aldol stereoselectivity with fully substituted enolates.

In previous papers in this series[3] we have outlined a strategy for the synthesis of macrolides and other polyketide natural products wherein the crucial carbon–carbon bond constructions would be made by stereoselective aldol addition reactions. In fact, an elegant synthesis of 6-deoxyerythronolide B (**1**), proceeding

† Dedicated to the memory of R. V. Stevens, 1941–1984.

(1) For part 22, see: Heathcock, C. H.; Kiyooka, S.-I.; Blumenkopf, T. A. *J. Org. Chem.*, in press.

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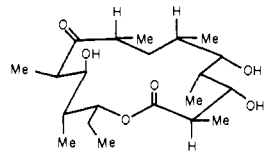

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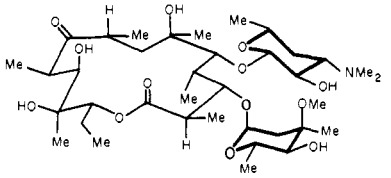
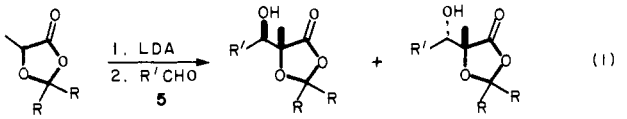


2

along very much these same lines, has been reported by Masamune and co-workers.[4] To apply this strategy to the synthesis of erythromycin A (**2**), we must face the problem of the tertiary hydroxyl groups at C-6 and C-12. In this paper, we report the results of an extensive investigation of the stereochemistry of addition of the enolates of *O*-alkyllactic acid esters to aldehydes.[5]

We began our study by investigating the dioxolanones **3** and **4**[6] and the oxazolanone **10**.[7] Each of these lactic acid derivatives was deprotonated with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) and allowed to react at −78 °C with various aldehydes (eq 1 and 2). Stereostructures of compounds **6–9** were



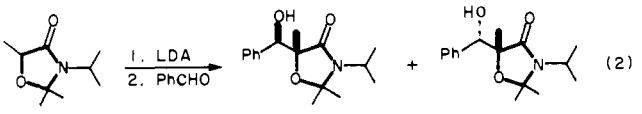
(1)

3: R = H
4: R = Me

6: R = H
8: R = Me

7: R = H
9: R = Me

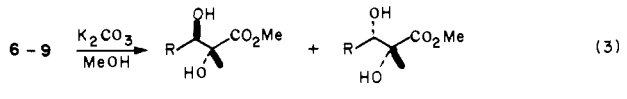
b: R′ = Et, c: R′ = *i*-Pr, d: R′ = *t*-Bu, e: R′ = Ph



(2)

10 11 12

elucidated in several ways. Treatment of the dioxolanone addition products with K_2CO_3 in methanol gave α,β-dihydroxy esters **13** and **14** (eq 3). Ester **13b**, obtained from aldol **8b**, was hydrolyzed



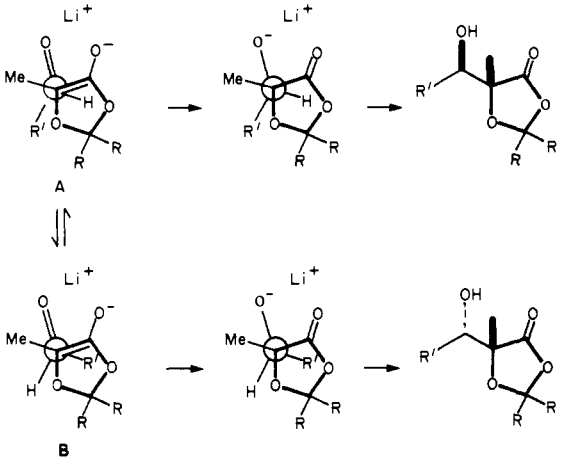
(3)

b: R = Et, c: R = *i*-Pr, d: R = *t*-Bu, e: R = Ph

to the known acid.[8] Dihydroxy ester **13e** was converted into the

Table I. Stereochemistry of the Reactions of the Enolates of Compounds **3**, **4**, and **10** with Aldehydes (eq 1)

entry	substrate	aldehyde	yield, %	products	ratio
1	**3**	**5b**	67	**6b,7b**	50:50
2	**3**	**5e**	85	**6e,7e**	67:33
3	**4**	**5b**	80	**8b,9b**	70:30
4	**4**	**5c**	79	**8c,9c**	70:30
5	**4**	**5d**	74	**8d,9d**	70:30
6	**4**	**5e**	72	**8e,9e**	75:25
7	**10**	**5e**	100	**11,12**	75:25

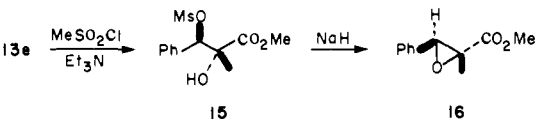


A

B

Figure 1. Reaction of dioxolanones **3** and **4** with aldehydes.

secondary mesylate **15**, which was cyclized by treatment with NaH to obtain the known glycidic ester **16** (eq 4).[9] To guard against



(4)

15 16

the possibility that the ring-closure reaction might have occurred by a carbocation mechanism, and simply delivered the more stable glycidic ester, the identical sequence of eq 4 was performed with isomer **14e**, to obtain the diastereomeric glycidic ester. Dihydroxy esters **8c/9c** and **8d/9d** were assigned stereostructures on the basis of their ^{13}C NMR spectra[10] and by analogy to those of **8b/9b** and **8e/9e**. The products from oxazolanone **10** were assigned on the basis of a single-crystal X-ray of the major isomer, **11**.[11]

The results obtained in this study are summarized in Table I. As will be seen from examination of the table, dioxolanone **4** shows slightly greater stereoselectivity than does **3**, although in neither case is the selectivity particularly attractive, from a preparative point of view. In the one example investigated, oxazolanone **10** showed the same stereoselectivity as the analogous dioxolanone (entries 6 and 7). Subsequent to the completion of this phase of our investigation,[12] Fräter and Seebach reported the preparation and alkylation of several analogous dioxolanones.[13,14]

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(3) (a) Buse, C. T.; Heathcock, C. H. *J. Am. Chem. Soc.* **1977**, *99*, 2337. (b) Heathcock, C. H.; Buse, C. T.; Kleschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066.

(4) Masumune, S.; Hirama, M.; Mori, S.; Ali, S. A.; Garvey, D. S. *J. Am. Chem. Soc.* **1981**, *103*, 1568.

(5) For a preliminary account, see: Heathcock, C. H.; Hagen, J. P.; Jarvi, E. T.; Pirrung, M. C.; Young, S. D. *J. Am. Chem. Soc.* **1981**, *103*, 4972.

(6) Farines, M.; Soulier, J. *Bull. Soc. Chim. Fr.* **1970**, 332.

(7) Aoyama, H.; Hasegawa, T.; Watabe, M.; Shiriashi, H.; Omote, Y. *J. Org. Chem.* **1978**, *43*, 419.

(8) (a) Bergel'son, L. D.; Dyatloritskaya, E. V.; Tichy, M.; Voronkova, V. V. *Izv. Akad. Nauk. SSSR, Ser. Khim.* **1962**, 1612. (b) See also: Masamune, S.; Kim, C. V.; Wilson, K. E.; Spessand, G. O.; Georghiou, P. E.; Bates, G. E. *J. Am. Chem. Soc.* **1975**, *97*, 3512. Masamune, S.; Yamamoto, H.; Kamata, S.; Fukuzawa, A. *J. Am. Chem. Soc.* **1975**, *97*, 3513.

(9) (a) Roux-Schmitt, M. C.; Seyden-Penne, J.; Wolfe, S. *Tetrahedron* **1972**, *28*, 4965. (b) Valoente, V. R.; Wolfhagen, J. L. *J. Org. Chem.* **1966**, *31*, 2509.

(10) Heathcock, C. H.; Pirrung, M. C.; Sohn, J. E. *J. Org. Chem.* **1979**, *44*, 4294.

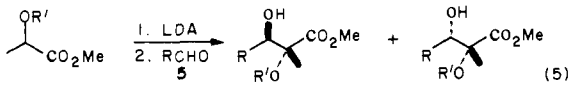
(11) See paragraph at end of paper regarding supplementary material.

(12) Pirrung, M. C. Ph.D. Dissertation, University of California, Berkeley, 1981.

(13) (a) Fráter, G.; Müller, U.; Günther, W. *Tetrahedron Lett.* **1981**, *22*, 4221. (b) Seebach, D.; Näf, R. *Helv. Chim. Acta* **1981**, *64*, 2704.

A proposal that explains the observed stereoselectivity of dioxolanones **3** and **4** is depicted in Figure 1. It is supposed that reaction occurs through the conventional Zimmerman–Traxler transition state[15-17] with the hydrogen of the aldehyde, rather than the R′ group, over the face of the dioxolanone ring (conformation A). The topography of the reaction transition state is therefore similar to that observed in the reactions of cyclohexanone and cyclopentanone enolates, and the same sense of diastereoselectivity is, in fact, observed.[16] The rather feeble stereoselectivity that is observed can be ascribed to the fact that the R′ group in the alternative conformation (B) interacts only with an oxygen atom, rather than with a methylene group, as it would in the reaction with cycloalkanone enolates. The slightly greater selectivity of the acetonide **4**, relative to the formaldehyde derivative **3**, is probably due to the additional steric discrimination that is provided by the geminal methyl substituents. That the effect is not greater is probably due to the previously postulated "right-angle" geometry of the aldol transition state.[3b,17,18] Thus, the R′ group in conformation B is not really very close to the R group.

We next turned our attention to a series of ethers of methyl lactate. Methyl 2-methoxypropanoate (**17**) was prepared by Fischer esterification of the known 2-methoxypropanoic acid.[19] Methyl 2-(benzyloxy)propanoate (**18**) was prepared by the procedure of Malone and Meyers.[20] Methyl 2-((2′-methoxyethoxy)methoxy)propanoate (**19**) was prepared by protection of ethyl lactate with (2-methoxyethoxy)methyl chloride,[21] followed by transesterification with K_2CO_3 in methanol. The preformed lithium enolates of esters **17–19** were allowed to react with a series of aldehydes (eq 5). Results are presented in Table II.



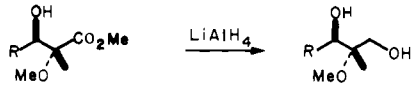
17: R′ = Me; **18**: R′ = CH_2Ph; **19**: R′ = $CH_2OCH_2CH_2OMe$ (MEM)

20: R′ = Me; **22**: R′ = CH_2Ph; **24**: R′ = MEM

21: R′ = Me; **23**: R′ = CH_2Ph; **25**: R′ = MEM

b: R = Et, c: R = *i*-Pr, d: *t*-Bu, e: R = Ph

Aldol **20c**, the only detectable product from the reaction of ester **17** with isobutyraldehyde and aldol **20e**, the major product obtained in the reaction of **17** with benzaldehyde, were reduced by lithium aluminum hydride to the corresponding diols **26c** and **26e**.



20 **26**

c: R = *i*-Pr, e: R = Ph

These two diols were shown to be different from diastereomers

(14) In the Seebach and Näf paper, the reactions of a dioxolanone prepared from lactic acid and pivalaldehyde with acetaldehyde, pivalaldehyde, and benzaldehyde are reported. In each case, two of the four possible diastereomers are formed. The stereoselectivity in these reactions is reported as "% distereoselectivity", presumably referring to the percent of the major isomer produced, with the values ranging from 83% to 85%. It is implied in ref 13b that the two diastereomers result from attack on the two diastereotopic faces of the dioxolanone enolate and that both therefore have the same relative configuration at the two centers created in the aldol addition. This interpretation is at obvious variance with the results reported in this paper.

(15) Zimmerman, H.; Traxler, M. *J. Am. Chem. Soc.* **1957**, *79*, 1920.

(16) For a detailed discussion of the application of the Zimmerman–Traxler postulate to various enolate addition reactions, see: Heathcock, C. H. "Asymmetric Organic Reactions"; Morrison, J. D., Ed.; Academic Press: New York, 1984; Chapter 2.

(17) Fellmann, P.; Dubois, J. E. *Tetrahedron* **1978**, *34*, 1349.

(18) Briefly, the "right-angle" postulate has been advanced to account for the fact that, within a stereoisomeric pair of ketone or ester enolates, the *Z* isomer often shows greater intrinsic stereoselectivity than the *E* isomer.

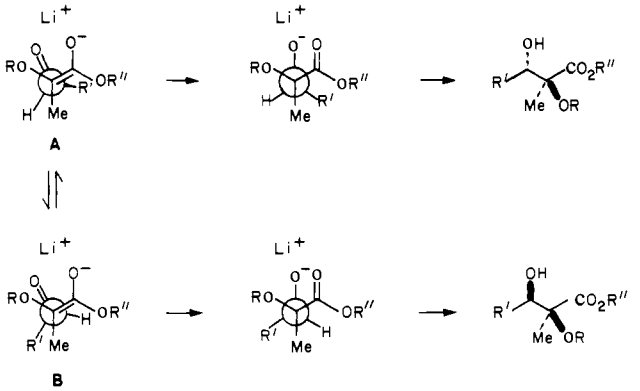
(19) (a) Oki, M.; Hirota, M. *Bull. Chem. Soc. Jpn.* **1963**, *36*, 290. (b) Petrov, A.; Gantseva, B.; Kiselva, O. *Zh. Obsch. Khim.* **1953**, *23*, 737.

(20) Malone, G.; Meyers, A. *J. Org. Chem.* **1974**, *39*, 623.

(21) Corey, E. J.; Gras, J.; Ulrich, P. *Tetrahedron Lett.* **1976**, 809.

Table II. Stereochemistry of the Reactions of the Enolates of Esters **17–19** with Aldehydes (eq 5)

entry	ester	aldehyde	yield, %	products	ratio
1	**17**	**5b**	99	**20b,21b**	70:30
2	**17**	**5c**	98	**20c,21c**	>97:3
3	**17**	**5d**	84	**20d,21d**	>97:3
4	**17**	**5e**	85	**20e,21e**	75:25
5	**18**	**5b**	87	**22b,23b**	70:30
6	**18**	**5c**	85	**22c,23c**	70:30
7	**18**	**5d**	80	**22d,23d**	70:30
8	**18**	**5e**	100	**22e,23e**	70:30
9	**19**	**5b**	60	**24b,25b**	82:18
10	**19**	**5c**	83	**24c,25c**	85:15
11	**19**	**5d**	73	**24d,25d**	88:12
12	**19**	**5e**	95	**24e,25e**	85:15

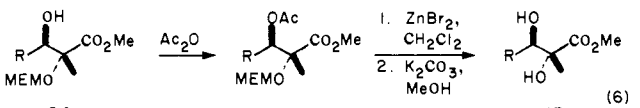


A ⇌ **B**

Figure 2. Reaction of α-alkoxy esters with aldehydes.

of rigorously defined relative configuration (vide infra). Structures are assigned to **20b/21b** and **20d/21d** by analogy.

Acetylation of the free secondary hydroxyl of compounds **24b** and **24c** gave the corresponding acetates, which were deprotected by successive treatment with $ZnBr_2$ and methanolic K_2CO_3 (eq 6).[21,22] In both cases studied, the major aldol gave an α,β-di-

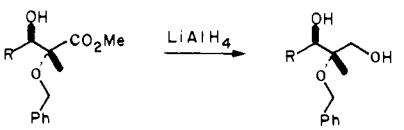


24 **13**

b: R = Et, c: R = *i*-Pr

hydroxy acid identical with that obtained from the analogous dioxolanone aldol (eq 3). Since ester **13b** has been converted to the known Bergel'son's acid (vide supra), the stereostructures of **24b/25b** are secure. Because ester **19** gives similar ratios with all four aldehydes, the products **24c/25c**, **24d/25d**, and **24e/25e** are assigned by analogy.

Esters **22c** and **22e**, the major products from the reactions of **18** with isobutyraldehyde and benzaldehyde, respectively, were reduced with lithium aluminum hydride to the corresponding diols (eq 7). The major diol from the **22c/23c** mixture (**27c**) and the



22 **27**

c: R = *i*-Pr e: R = Ph

diol (**27e**) obtained from the reduction of **22e** were each shown to be *different* from a stereoisomer of rigorously determined relative configuration (vide infra). Since ester **18** gives 70:30 ratios with all of the aldehydes studied (Table II, entries 5–8), it seems

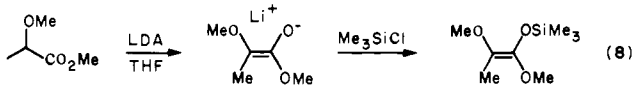
(22) Attempts to remove the MEM group in the presence of the unprotected secondary alcohol leads to the formation of a dioxolane, which is resistant to further hydrolysis.

Table III. Stereochemistry of the Reactions of the Enolates of Esters **37–39** with Aldehydes (eq 11)

entry	ester	aldehyde	yield, %	products	ratio
1	**37**	**5a**	65	**40a,41a**	64:36
2	**37**	**5b**	50	**40b,41b**	78:22
3	**37**	**5c**	77	**40c,41c**	83:17
4	**37**	**5d**	30	**40d,41d**	<3:97
5	**37**	**5e**	65	**40e,41e**	25:75
6	**38**	**5c**	73	**42c,43c**	33:67
7	**38**	**5e**	75	**42e,43e**	10:90
8	**39**	**5a**	88	**44a,45a**	25:75
9	**39**	**5b**	57	**44b,45b**	17:83
10	**39**	**5c**	89	**44c,45c**	<3:97
11	**39**	**5d**	0		
12	**39**	**5e**	62	**44e,45e**	<3:97

safe to assume the stereostructures assigned to **22b/23b** and **22d/23d**. One further argument that may be advanced in favor of the assigned stereostructures is the regularity that is observed in their ^{13}C NMR chemical shifts.[10]

Treatment of the lithium enolate of ester **17** with chlorotrimethylsilane provides two enol silanes in a ratio of about 12:1. Although we have no direct evidence with regard to the stereostructures of these compounds, we believe the major isomer has structure **28** (eq 8). This assignment is made on the basis of the



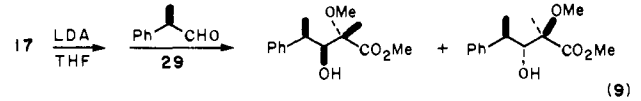
(8)

17 **28**

following arguments. First, it is not unreasonable to propose that the intermediate enolate profits from internal coordination of its lithium cation by the methoxy group. Second, the suggested *Z* configuration[23] of the enolate nicely agrees with a mechanistic rationale to be presented shortly.

The transition states that are proposed for the reactions of the enolates derived from esters **17–19** are depicted in Figure 2 (R″ = Me). Because of the previously mentioned distortion in the Zimmerman–Traxler transition states,[3b,17] conformation A is favored over conformation B. It follows from the transition-state hypothesis put fourth in Figure 2 that stereoselectivity should decrease if esters other than methyl are employed. Indeed, we shall see that this is precisely the case.

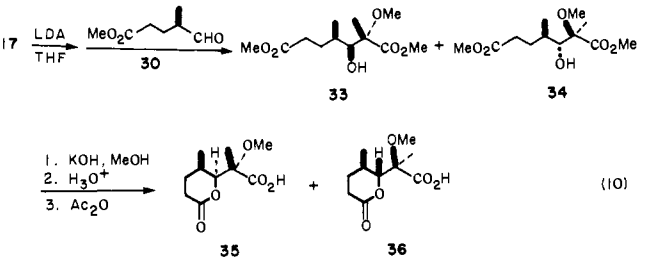
Ester **17** shows exceedingly high diastereoselectivity in its reactions with isobutyraldehyde and pivalaldehyde (Table II, entries 2 and 3). To further probe the behavior of ester **17**, we examined its reactions with 2-phenylpropanal (**29**) and the chiral ester aldehyde **30**. With aldehyde **29**, a mixture of two aldols were produced in a ratio of 80:20 (eq 9). Because of the high simple



(9)

31 **32**

diastereoselectivity shown by ester **17** with α-branched aldehydes, we assume that both **31** and **32** have the configuration 2*SR*,3*RS*; the 4:1 ratio is a typical Cram/anti-Cram ratio for this aldehyde. With ester **30** two adducts were formed (**33** and **34**), in a ratio of 75:25. The mixture of **33** and **34** was saponified and the resulting mixture of diacids lactonized by treatment with acetic anhydride. The resulting lactonic acids (**35** and **36**) were separated chromatographically (eq 10). The C-4,C-5 H–H coupling constants observed for the two valerolactones (J = 8 and J = 3 Hz, respectively) clearly show that the isomers stem from reaction at the two diastereotopic faces of **30** and that they therefore probably

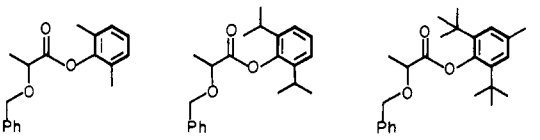


(10)

33 **34** **35** **36**

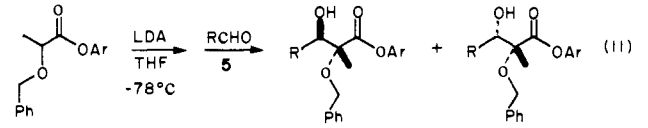
have the same relative configuration at the two newly created stereocenters.

Because of the high stereoselectivity that we had observed with esters of hindered phenols,[24] we prepared esters **37–39** (2,6-di-



37 **38** **39**

methylphenyl (DMP) *O*-benzyllactate, 2,6-diisopropylphenyl (DIPP) *O*-benzyllactate, and 2,6-di-*tert*-butyl-4-methylphenyl *O*-benzyllactate, respectively). Esters **37–39** were converted into their enolates by treatment with LDA in THF at −78 °C, and the resulting solutions were then treated with various aldehydes (eq 11). The results of this study are summarized in Table III.



(11)

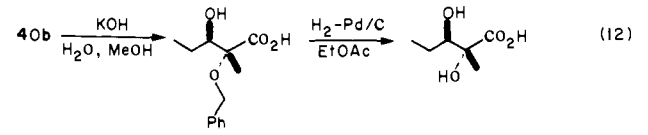
37: Ar = DMP
38: Ar = DIPP
39: Ar = BHT

40: Ar = DMP
42: Ar = DIPP
44: Ar = BHT

41: Ar = DMP
43: Ar = DIPP
45: Ar = BHT

a: R = CH_2=CH, **b**: R = Et, **c**: R = *i*-Pr, **d**: R = *t*-Bu, **e**: R = Ph

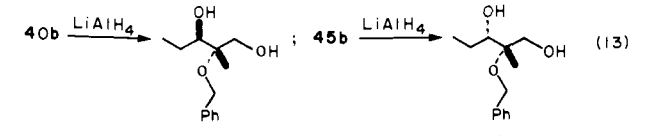
The stereostructures of the aldols listed in Table III rest on several solid pieces of evidence. First, aldols **40a/41a** were hydrogenated to give aldols **40b/41b**, thus linking these series. Saponification of ester **40b**, the major product from the reaction of **37** with propanal, provided a crystalline hydroxy acid, **46**, which was hydrogenolyzed to Bergel'son's acid **47** (eq 12). Second,



(12)

46 **47**

lithium aluminum hydride reduction of ester **40b** provided the crystalline diol **48**, mp 42–44 °C. This compound was clearly different from the diol produced by lithium aluminum hydride reduction of ester **45b**, the major product produced in the reaction of 2,6-di-*tert*-butyl-4-methylphenyl *O*-benzyllactate (**39**) with propanal; the latter diol, mp 60–63 °C, is therefore **49** (eq 13).



(13)

48 **49**

Finally, the aldol mixture **44a/45a** was hydrogenated to **44b/45b**, thus completing the link in this series.

The structures of the sole crystalline products from the reactions of 2,6-di-*tert*-butyl-4-methylphenyl *O*-benzyllactate with iso-

(23) From the suggestion of Evans, in sequence rule assignments involving ester enolates priority is given to the alkoxide oxygen, regardless of the metal with which it is formally associated: Evans, D. A. "Asymmetric Organic Reactions"; Morrison, J. D., Ed.; Academic Press: New York, 1984; Vol. 3, Chapter 1.

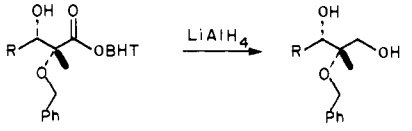
(24) (a) Pirrung, M. C.; Heathcock, C. H. *J. Org. Chem.* **1980**, *45*, 1727. (b) Heathcock, C. H.; Pirrung, M. C.; Montgomery, S. H.; Lampe, J. *Tetrahedron* **1981**, *37*, 4087.

Table IV. Ratios of Diastereomeric Aldols Produced in the Reactions of *O*-Benzyllactic Acid Esters with Various Aldehydes (eq 5 and 11)[a]

ester	aldehyde			
	EtCHO	*i*-PrCHO	*t*-BuCHO	PhCHO
18	70:30	70:30	70:30	70:30
37	78:22	83:17	<3:97	25:75
38		33:67		10:90
39	17:83	<3:97		<3:97

[a] For each entry, the ratio of diastereomers given would result from transition states A and B, respectively, in Figure 2.

butyraldehyde and benzaldehyde, **45c** and **45e**, respectively, were established by single-crystal X-ray analysis.[11] Lithium aluminum hydride reduction of **45c** provided diol **50** (eq 14). The 33:67



(14)

45c: R = *i*-Pr
45e: R = Ph

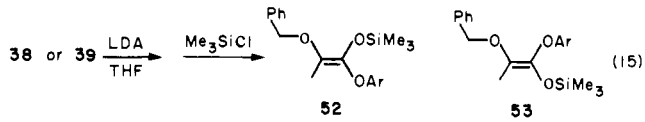
50: R = *i*-Pr
51: R = Ph

mixture of aldols produced from the reaction of 2,6-diisopropylphenyl *O*-benzyllactate and isobutyraldehyde was separated chromatographically, and the two isomers were reduced separately by lithium aluminum hydride. The major isomer (**43c**) gave diol **50**. The minor isomer (**42c**) provided diol **27c**, previously obtained from aldol **22c**. Diol **27c** was also produced from reduction of the major isomer (**40c**) formed in the reaction of 2,6-dimethylphenyl *O*-benzyllactate with isobutyraldehyde.

Reduction of **45e** provided diol **51** (eq 14). The same diol was also produced from the reduction of the major isomers (**41e** and **43e**) formed in the reactions of 2,6-dimethylphenyl *O*-benzyllactate and 2,6-diisopropylphenyl *O*-benzyllactate with benzaldehyde (Table III, entries 4 and 7). These correlations rigorously establish the stereostructures of all of the benzaldehyde adducts, including those (**22e**/**23e**) obtained from ester **18**. Thus, of all the aldols summarized in eq 11 and Table III, all except **41d** are rigorously identified either by correlation with Bergel'son's acid or with **45c** or **45e**, for which X-ray structures have been obtained.

The stereoselectivities summarized in Table III can be understood in terms of Figure 2. Thus, as the size of R″ increases (Me, DMP, DIPP, BHT), there is a regular decrease in the fraction of reaction proceeding through transition state A. The results are summarized in Table IV.

Of course, the arguments just advanced are based on the tacit assumption that the enolates derived from esters **37**–**39** have the *Z* configuration, as shown in Figure 2. As in the case of the esters previously discussed, we have no firm evidence that this is the case. However, there is circumstantial evidence in support of this assumption. Silylation of the enolate derived from 2,6-diisopropylphenyl *O*-benzyllactate provides two enol silanes, assigned structures **52a** and **53a**, in a ratio of 94:6. Similar treatment of 2,6-di-*tert*-4-methylphenyl *O*-benzyllactate gives a single, crystalline enol silane, presumed to have the structure **52b** (eq 15).



(15)

52 **53**

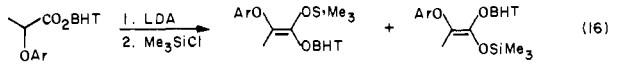
a: Ar = DIPP, b: Ar = BHT

Unfortunately, we were unable to obtain crystals of this compound that were suitable for X-ray analysis.

To probe the basic hypothesis that the *Z* enolate configuration results from chelation of the lithium cation by the α-alkoxy group, we prepared the phenoxy esters **54** and **55**. If chelation of the lithium cation is an important factor in determining the stereostructure of the enolate, then one would expect that both **54** and **55** might give less *Z* enolate than the alkoxy esters discussed heretofore. Indeed, such is the case. With ester **54** the ratio of enol silanes is 78:22 and with **55** it is 91:9 (eq 16).

Table V. Stereochemistry of the Reactions of the Enolates of Esters **54** and **55** with Aldehydes (eq 17)

entry	ester	aldehyde	yield, %	products	ratio
1	**54**	**5c**	83	**60c,61c**	33:67
2	**54**	**5e**	83	**60e,61e**	50:50
3	**55**	**5c**	62	**62c,63c**	10:90
4	**55**	**5e**	81	**62e,63e**	<5:95



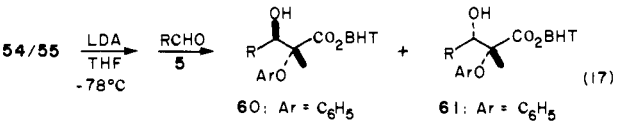
(16)

54: Ar = C_6H_5
55: Ar = *p*-$MeOC_6H_4$

56: Ar = C_6H_5
58: Ar = *p*-$MeOC_6H_4$

57: Ar = C_6H_5
59: Ar = *p*-$MeOC_6H_4$

The enolates derived from esters **54** and **55** were also added to isobutyraldehyde and benzaldehyde (eq 17). The results are



(17)

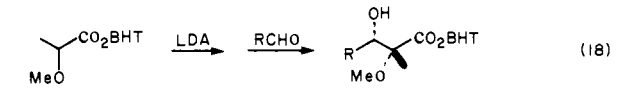
60: Ar = C_6H_5
62: Ar = *p*-$MeOC_6H_4$

61: Ar = C_6H_5
63: Ar = *p*-$MeOC_6H_4$

c: R = *i*-Pr e: R = Ph

summarized in Table V. Ester **55** is almost as stereoselective as the other BHT esters studied. Not surprisingly, ester **54** is considerably less selective.

As we showed earlier in the paper, methyl 2-methoxypropanoate (**17**) is an excellent reagent for the synthesis of α-methoxy β-hydroxy esters such as **20**, particularly with aldehydes that are branched at C-2 (eq 5, 9, and 10). The transition-state arguments that we have presented suggest that the BHT ester of 2-methoxypropanoic acid should show equally high selectivity, but in the complementary sense. Thus, we prepared ester **64** and studied its reactions with benzaldehyde and isobutyraldehyde (eq 18). In

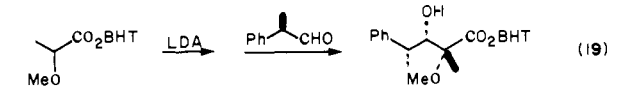


(18)

64

65: R = *i*-Pr
66: R = Ph

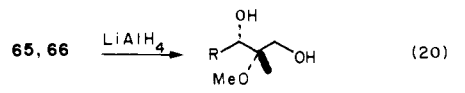
both cases, a single, crystalline adduct was produced. With the chiral aldehyde 2-phenylpropanal, a single crystalline product, assigned structure **67**, was also produced (eq 19)!



(19)

64 **67**

The stereostructures of the products produced from benzaldehyde and isobutyraldehyde were elucidated by single-crystal X-ray analysis.[11] Lithium aluminum hydride reduction of aldols **65** and **66** provides diols **68** and **69** (eq 20). Both **68** and **69** were



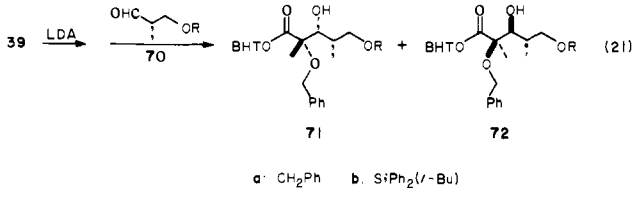
(20)

68: R = Ph
69: R = *i*-Pr

found to be different from the diols produced by reduction of the major products (**21c** and **21e**) of the reactions of methyl 2-methoxypropanoate (**17**) with isobutyraldehyde and benzaldehyde, respectively (eq 5, Table III, entries 2 and 5).

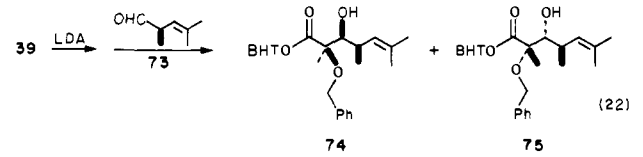
Earlier in this paper, we have reported the reactions of several lactate esters with chiral aldehydes. As we have seen, diastereofacial preferences vary from modest (eq 9 and 10) to outstanding (eq 19). To further examine this question, we carried out the reactions of 2,6-di-*tert*-butyl-4-methylphenyl *O*-benzyllactate (**39**) with several chiral aldehydes.

With the β-alkoxy aldehydes **70a** and **70b**, ester **39** gives a 50:50 ratio of two isomeric aldols, presumed to be **71** and **72** (eq 21).

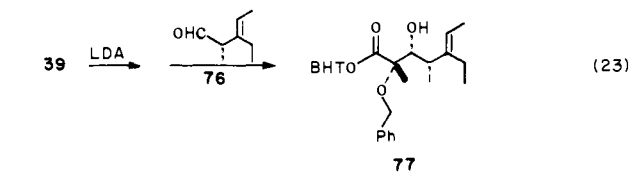


a: CH_2Ph b: $SiPh_2(t\text{-}Bu)$

Somewhat better results were obtained with chiral, α,β-unsaturated aldehydes. The reaction of **39** with the racemic aldehyde **73**[25] provides two aldols in a ratio of 71:29 (eq 22). Because of the



high stereoselectivity shown by ester **39** in its reactions with all other aldehydes studied, we assume that these two isomers are the Cram and anti-Cram products **74** and **75**. Even better results are obtained in the reaction of **39** with aldehyde **76**;[25] a single diastereomeric aldol is produced in 70% yield (eq 23). On the



basis of the normal stereoselectivity of ester **39**, we have assigned structure **77** to this material.

In summary, our goal of finding diastereoselective lactaldehyde enolate surrogates has been achieved. The most useful reagents are methyl ester **17** and the BHT esters **39** and **64**, which show complementary stereochemical behavior. Finally, it will be noted that the relative stereochemistry of the three stereocenters in aldols **74** and **77** is the same as that seen in the C-4,C-6 and C-10,C-12 regions of erythromycin A (**2**). Further applications of this chemistry to the synthesis of this material are under investigation.

Experimental Section[26]

General Procedure for Aldol Additions with Compounds 3, 4, and 10. To a solution of LDA (prepared from 0.77 mL of diisopropylamine and 3.65 mL of a 1.50 M solution of *n*-BuLi in hexane) in 10 mL of THF at −70 °C was added 5 mmol of the enolate precursor. Liquid substrates were added neat by syringe and solid substrates were added as solutions in 2 mL of THF. During the addition, the internal temperature was maintained below −68 °C. After stirring at low temperature for 30–60 min, 5 mmol of aldehyde was added by syringe. After a reaction time of from 15 s to 15 min, the reaction was quenched by the addition of 5 mL of either saturated NH_4Cl or saturated $NaHCO_3$ solution. After warming the quenched reaction mixture to room temperature, the layers were separated and the aqueous phase was extracted with ether (3 × 15 mL). The combined organic phases were washed with water, 1% HCl, and brine. When nonvolatile aldehydes were used, washing with $NaHSO_3$ and water was also performed. The resulting ethereal solution was dried over $MgSO_4$. After filtration, the solvents were removed with a rotary evaporator.

(5*RS*,1′*RS*)- and (5*RS*,1′*SR*)-5-Methyl-5-(1′-hydroxypropyl)-1,3-dioxolan-4-ones (6b and 7b). The standard aldol procedure was followed (with care being taken to maintain the temperature below −70 °C during the addition of the lactone) to provide in 67% yield a 1:1 mixture of diastereomers: IR 3450, 1780 cm^{-1}; ^1H NMR δ 1.03 (br t, 3, J = 7 Hz), 1.37 (s, 3, first diastereomer), 1.43 (s, 3, second diastereomer), 3.6–3.9 (m, 1), 4.90 (br, 1), 5.43 (s, 1), 5.51 (s, 1); preparative GLC (10 ft × $^1/_4$ in., 8% Carbowax, 210 °C) furnished the analytical sample. Anal. C, H.

(5*RS*,1′*RS*)- and (5*RS*,1′*SR*)-5-Methyl-5-(phenylhydroxymethyl)-1,3-dioxolan-4-ones (6e and 7e). The general aldol procedure was followed, with care being taken to maintain the temperature of the solution below −70 °C during the addition of **3**, to give in 85% yield a 2:1 mixture of diastereomers, which were separated by chromatography on silica gel (1:9 ether/benzene): IR 3400, 1780, 1690 cm^{-1}.

Compound **6e**: ^1H NMR δ 1.35 (s, 3), 4.15 (s, 1), 4.73 (s, 1), 5.00 (s, 1), 5.20 (s, 1), 7.23 (s, 5); R_f 0.30. Anal. C, H.

Compound **7e**: ^1H NMR δ 1.08 (s, 3), 4.15 (s, 1), 4.69 (s, 1), 5.32 (s, 1), 5.52 (s, 1), 7.18 (s, 5); R_f 0.25; mp (from hexane/EtOAc) 100–102 °C.

(5*RS*,1′*RS*)- and (5*RS*,1′*SR*)-2,2,5-Trimethyl-5-(1′-hydroxypropyl)-1,3-dioxolan-4-ones (8b and 9b). The standard aldol procedure was followed (with care being taken to maintain the temperature below −70 °C during the addition of **4**) to provide in 75–85% yield a 70:30 mixture of diastereomers: IR 3500, 1780 cm^{-1}; preparative GLC (10 ft × $^1/_4$, in., 8% Carbowax, 130 °C) afforded the analytical sample. Anal. C, H.

Compound **8b**: ^1H NMR δ 1.03 (br t, 3, J = 7 Hz), 1.50 (s, 3), 1.60 (s, 6), 3.47 (br t, 1, J = 7 Hz), 5.00 (br, 1).

Compound **9b**: ^1H NMR δ 1.03 (br t, 3, J = 7 Hz), 1.40 (s, 3), 1.60 (s, 6), 3.47 (br t, 1, J = 7 Hz), 5.00 (br, 1).

(5*RS*,1′*RS*)- and (5*RS*,1′*SR*)-2,2,5-Trimethyl-5-(1′-hydroxy-2′-methylpropyl)-1,3-dioxolan-4-ones (8c and 9c). The standard aldol procedure provided in 79% yield a 70:30 mixture of diastereomers: IR 3500, 1790 cm^{-1}; preparative GLC (10 ft × $^1/_4$ in., 8% Carbowax, 180 °C) afforded the analytical sample. Anal. C, H.

Compound **8c**: ^1H NMR δ 1.05 (d, 6, J = 7 Hz), 1.53 (s, 3), 1.63 (s, 6), 2.80 (br, 1), 3.40 (d, 1, J = 7 Hz).

Compound **9c**: ^1H NMR δ 1.02 (d, 6, J = 7 Hz), 1.43 (s, 3), 1.63 (s, 6), 2.80 (br, 1), 3.45 (d, 1, J = 7 Hz).

(5*RS*,1′*RS*)- and (5*RS*,1′*SR*)-2,2,5-Trimethyl-5-(1′-hydroxy-2′,2′-dimethylpropyl)-1,3-dioxolan-4-ones (8d and 9d). The standard aldol procedure provided in 65–83% yield a 70:30 mixture of diastereomers: IR 3550, 1780 cm^{-1}, preparative GLC (10 ft × $^1/_4$ in., 8% Carbowax, 210 °C) furnished the analytical sample. Anal. C, H.

Compound **8d**: ^1H NMR δ 1.10 (s, 9), 1.56 (s, 3), 1.60 (s, 6), 3.37 (s, 1).

Compound **9d**: ^1H NMR, δ 1.10 (s, 9), 1.51 (s, 3), 1.60 (s, 6), 3.29 (s, 1).

(5*RS*,1′*RS*)- and (5*RS*,1′*SR*)-2,2,5-Trimethyl-5-(phenylhydroxymethyl)-1,3-dioxolan-4-ones (8e and 9e). The general procedure was followed, with care being taken to maintain the temperature below −70 °C during the addition of **4** to provide in 72% yield a 3:1 mixture of diastereomers.

The major isomer, **8e**, was obtained in a pure state by crystallization: mp (from heptane) 124–125 °C; IR 3470, 1780 cm^{-1}; ^1H NMR δ 1.20 (s, 3), 1.50 (s, 6), 2.80 (s, 1), 4.80 (s, 1), 7.26 (s, 5). Anal. C, H.

The oily minor isomer, **9e**, showed the following ^1H NMR spectrum: δ 1.06 (s, 3), 1.67 (s, 6), 3.53 (s, 1), 4.70 (s, 1), 7.33 (s, 5).

(*RS*)-2,5,5-Trimethyl-3-isopropyl-1,3-oxazolidin-4-one (10). In a 50-mL, three-necked, round-bottomed flask, flame dried and kept under N_2, was placed 311 mg (8.42 mmol) of a 65% suspension of NaH. The NaH was washed with toluene (3 × 5 mL) then covered with 15 mL of toluene. 2,2,5-Trimethyl-1,3-oxazolidin-4-one (1.002 g, 7.76 mmol; readily available by the literature procedure[29]) in 12 mL of toluene was added dropwise, and the mixture was heated at reflux for 3 **h**. After cooling to room temperature, 10 mL of DMF was added, followed by 10 mL of 2-iodopropane (100 mmol). After stirring at room temperature for 2 days, the reaction mixture was poured into ice water and extracted with $CHCl_3$. Washing with 1% HCl, drying ($MgSO_4$), and removal of solvents under reduced pressure provided the crude product, which was transferred to the top of a 150-g silica gel column and eluted with 70% ether/hexane to afford **10** (R_f 0.49). Distillation (Kugelrohr, 90 °C (1 torr)) gave 255 mg (19%) of a solid having spectral data consistent with those previously reported.[29]

(5*RS*,1′*RS*)- and (5*RS*,1′*SR*)-2,2,5-Trimethyl-3-isopropyl-5-(phenylhydroxymethyl)-1,3-oxazolidin-4-ones (11 and 12). The standard

(25) The syntheses of aldehydes **70** and **73** will be communicated separately in connection with a further extension of this project.

(26) Unless otherwise stated, the solvent for both ^1H and ^{13}C NMR spectra was $CDCl_3$. Significant ^1H NMR data are tabulated in the following order: multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), number of protons, coupling constant(s) in hertz. ^{13}C NMR data are listed separately for each isomer; for those samples containing mixtures of diastereomers, the resonances for all carbons of the minor isomers were not always discernible. "Flash chromatography" refers to the procedure of Still, Kahn, and Mitra.[27] All $LiAlH_4$ reductions were worked up by the procedure described by Fieser and Fieser (*n*, *n*, 3*n*).[28] For other general experimental details, see ref 1.

(27) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

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procedure provided a 75:25 mixture of diastereomers **11** and **12** in quantitative yield. The mixture slowly crystallized from hexanes to form easily separable crystals of needles (pure **11**, mp 85 °C) and prisms (a 1:1 mixture of **11** and **12**, mp 109.5–110 °C): IR ($CHCl_3$) 3450, 1680 cm^{-1}.

Compound **11**: ^1H NMR δ 1.23 (s, 3), 1.36 (d, 3, J = 6.9 Hz), 1.38 (s, 6), 1.41 (s, 3), 1.42 (d, 3, J = 7.1 Hz), 3.28 (septet, 1, J = 7.0 Hz), 3.66 (d, 1, J = 2.6 Hz), 4.85 (d, 1, J = 2.7 Hz), 7.30 (m, 5). Anal. C, H.

Compound **12**: ^1H NMR δ 0.95 (s, 3), 1.34–1.46 (m, 12), 3.23 (septet, 1, J = 7.0 Hz), 3.72 (d, 1, J = 8.4 Hz), 4.64 (d, 1, J = 8.4 Hz), 7.30 (m, 5).

General Procedure for Methanolysis of Dioxolanone Aldols. Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-Methyl-2,3-dihydroxybenzenepropanoates (13e and 14e). A mixture of 2 mmol of the 75:25 mixture of dioxolanone aldols **8e** and **9e** and 30 mg of K_2CO_3 in 30 mL of CH_3OH was kept for 3 h at room temperature. The solution was filtered and the solvents were removed under reduced pressure to obtain 95–100% of the known[30] dihydroxy esters.

Compound **13e**: ^1H NMR δ 1.17 (s, 3), 3.83 (s, 3), 4.83 (s, 2), 4.85 (s, 1), 7.33 (s, 5); ^{13}C NMR: 22.4, 52.2, 77.9, 127.9, 128.0, 175.0.

Compound **14e**: ^1H NMR δ 1.47 (s, 3), 3.53 (s, 3), 4.00 (s, 2), 4.70 (s, 1), 7.17 (s, 5); ^{13}C NMR 21.9, 52.7, 77.6, 127.8, 176.2.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-Methyl-2,3-dihydroxypentanoates (13b and 14b). The general methanolysis procedure was followed with **8b**/**9b** to provide in 97% yield a 70:30 mixture of diastereomers.

The major isomer, **13b**, was spectrally identical with the known compound:[8] ^1H NMR δ 1.00 (br t, 3, J = 7 Hz), 1.47 (s, 3), 3.00 (br s, 2), 3.47 (br t, 1, J = 7 Hz), 3.80 (s, 3); ^{13}C NMR, δ 10.6, 22.3, 24.6, 52.3, 77.8, 175.8.

Compound **14b**: ^1H NMR δ 1.00 (br t, 3, J = 7 Hz), 1.33 (s, 3), 3.40 (br s, 2), 3.47 (br t, 1, J = 7 Hz), 3.80 (s, 3); ^{13}C NMR δ 10.2, 21.3, 22.9, 52.4, 77.7, 176.7.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2,4-Dimethyl-2,3-dihydroxypentanoates (13c and 14c). The general methanolysis procedure was followed with **8c**/**9c** to provide a 70:30 mixture of diastereomers in quantitative yield: IR 3450, 1730 cm^{-1}; preparative GLC (10 ft × 1/4 in., 8% Carbowax, 180 °C) furnished the analytical sample. Anal. C, H.

Compound **13c**: ^1H NMR δ 0.94 (d, 6, J = 7 Hz), 1.50 (s, 3), 3.43 (d, 1, J = 7 Hz), 3.77 (s, 3); ^{13}C NMR 16.8, 21.0, 24.0, 30.3, 52.2, 79.2, 176.3.

Compound **14c**: ^1H NMR δ 0.98 (d, 6, J = 7 Hz), 1.40 (s, 3), 3.43 (d, 1, J = 7 Hz), 3.72 (s, 3); ^{13}C NMR δ 15.7, 21.4, 22.0, 28.2, 52.5, 78.3, 176.9.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2,4,4-Trimethyl-2,3-dihydroxypentanoates (13d and 14d). The general methanolysis procedure was followed with **8d**/**9d** to provide a 70:30 mixture of diastereomers in quantitative yield: IR 3500, 1730 cm^{-1}.

Compound **13d**: mp (from hexane) 97.5–98.5 °C; ^1H NMR δ 1.00 (s, 9), 1.53 (s, 3), 3.20 (br, 2), 3.50 (s, 1), 3.73 (s, 3); ^{13}C NMR δ 26.3, 27.0, 52.3, 81.6, 177.2. Anal. C, H.

Compound **14d**: ^1H NMR δ 1.08 (s, 9), 1.51 (s, 9), 3.20 (br, 2), 3.50 (s, 1), 3.75 (s, 3); ^{13}C NMR δ 24.6, 27.6, 52.8, 77.0, 177.2.

Methyl (2*RS*,3*SR*)- and (2*RS*,3*RS*)-2-Methyl-3-phenylglycidate (16). Dihydroxy ester **13e** (2 mmol) was dissolved in 10 mL of pyridine, and methanesulfonyl chloride (3.5 mmol) was added. After it stood overnight, the reaction mixture was poured into ice water (50 mL), stirred for 1 h, and extracted with ether (2 × 50 mL). The organic phases were combined and washed with saturated $CuSO_4$ solution (10 mL portions) until complexation with pyridine was not evident and were then washed with saturated $NaHCO_3$ (20 mL). Drying ($MgSO_4$), filtration, and removal of solvents under reduced pressure gave mesylate **15** as a light yellow oil (95% yield): IR 3375, 1740 cm^{-1}; ^1H NMR δ 1.57 (s, 3), 2.73 (s, 3), 3.67 (s, 3), 5.63 (s, 1), 7.33 (s, 5).

The crude mesylate (534 mg, 1.85 mmol) was dissolved in 15 mL of dry ether. This solution was added to a flask containing 115 mg of a 65% suspension of NaH in mineral oil, which had been washed with ether (3 × 5 mL) and covered with 15 mL of ether. After standing overnight, the reaction mixture was poured into 50 mL of saturated NH_4Cl, and the layers were separated. The aqueous layer was extracted with ether (3 × 50 mL), the organic phases were dried over K_2CO_3, and the solvent was removed under reduced pressure to give **16** (60–85% from **13e**).

A similar reaction was carried out with diastereomer **14e** to obtain the diastereomeric mesylate: ^1H NMR δ 1.27 (s, 3), 2.67 (s, 3), 3.90 (s, 3), 5.67 (s, 1), 7.36 (s, 5). This mesylate was converted into the diastereomeric glycidic ester in a manner identical with that just described. The two glycidic esters exhibited spectral properties consistent with those previously reported for these compounds.[9]

Methyl (*RS*)-2-Methoxypropanoate (17). 2-Methoxypropanoic acid (12.0 g, 115 mmol, prepared in 94% yield by the literature procedure[18]) was dissolved in 180 mL of CH_3OH and 2 drops of H_2SO_4 were added. The solution was refluxed through a Soxhlet extractor containing 3-Å molecular sieves for 24 h. Most of the solvent was removed by distillation, and the residue was dissolved in ether. The organic phase was washed with saturated $NaHCO_3$ and NaCl, dried, filtered, and carefully evaporated. Distillation (Kugelrohr, 100 °C, 18 torr) gave 6.10 g of the known ester.[19b]

Methyl (*RS*)-2-[(2′-Methoxyethoxy)methoxy]propanoate (19). To a solution of (2-methoxyethoxy)methyl chloride[21] (6 mL, 55.4 mmol) in 20 mL of CH_2Cl_2 was added diisopropylethylamine (10 mL, 57.5 mmol) at 0 °C. Ethyl lactate (5 mL, 44 mmol, purified by washing with $NaHCO_3$ and fractional distillation) was added, and the mixture was allowed to stand overnight. The reaction mixture was diluted with water, the layers were separated, and the aqueous phase was extracted with CH_2Cl_2 (2 × 30 mL). Washing with $NaHCO_3$ (50 mL), 1% HCl (50 mL), and NaCl (50 mL), drying ($MgSO_4$), filtration, and removal of solvents under reduced pressure gave a crude material, which was dissolved in 100 mL of MeOH, to which was added 100 mg of K_2CO_3. After the mixture stood overnight, the CH_3OH was removed under reduced pressure and the residue partitioned between saturated NH_4Cl and ether. Separation, extraction of the aqueous phase with ether, and drying of the combined organics ($MgSO_4$) gave a solution which was evaporated and distilled (160 °C, Kugelrohr, 137 torr) to give 4.54 g (54%) of the desired ester: IR 1745 cm^{-1}; ^1H NMR δ 1.46 (d, 3, J = 7 Hz), 3.46 (s, 3), 3.5–3.7 (m, 4), 3.77 (s, 3), 4.33 (q, 3, J = 7 Hz), 4.80 (s, 2). Anal. C, H.

General Procedure for Aldol Additions with Methyl 2-Methoxypropanoate (17). To a solution of LDA (1.88 mmol, prepared from 0.27 mL of diisopropylamine and 1.25 mL of a 1.50 M solution of *n*-BuLi) in 10 mL of THF was added methyl 2-methoxypropanoate (0.18 mL, 1.66 mmol) at −70 °C. After stirring the solution for 30 min at low temperature, the aldehyde (1.66 mmol) was added, followed by 5 mL of saturated NH_4Cl. The solution was warmed to room temperature, the layers were separated, and the aqueous phase was extracted with ether (2 × 10 mL). Washing with 1% HCl and NaCl, drying, filtration, and removal of solvents under reduced pressure gave the crude product.

General Procedure for Aldol Additions with Methyl 2-(Benzyloxy)propanoate (18). To a solution of LDA (2.25 mmol, prepared from 0.34 mL of diisopropylamine and 1.50 mL of a 1.50 M solution of *n*-BuLi) in 10 mL of THF was added the known methyl 2-(benzyloxy)propanoate[31] (0.30 mL, 2.07 mmol) at −70 °C. After the mixture was stirred for 30 min at −70 °C, an aldehyde (2.10 mmol) was added, and the solution was stirred 1 min and then quenched with saturated NH_4Cl. The solution was allowed to stir while warming to room temperature, the layers were separated, and the organic phase was extracted with ether (2 × 15 mL). The combined organic phases were washed with 1% HCl and NaCl (10 mL), dried ($MgSO_4$), and filtered and the solvents removed under reduced pressure.

General Procedure for Aldol Additions with Methyl 2-[(2′-methoxyethoxy)methoxy]propanoate (19). To a solution of LDA (1.71 mmol, prepared from 0.24 mL of diisopropylamine and 1.14 mL of a 1.50 M solution of *n*-BuLi) in 10 mL of THF was added **19** (0.20 mL, 1.54 mmol) at −70 °C. After stirring the solution for 30 min, the aldehyde (1.54 mmol) was added and the solution was stirred for 5 min and then quenched by the addition of 5 mL of saturated NH_4Cl solution. The layers were separated, and the aqueous phase was extracted with ether (2 × 15 mL). The combined organic phases were washed with 1% HCl and NaCl (10 mL), dried ($MgSO_4$), and filtered, and the solvents were removed under reduced pressure.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-Methyl-2-methoxy-3-hydroxypentanoates (20b and 21b). The aldol was obtained in 99% yield as 70:30 mixture of diastereomers: IR 3500, 1735 cm^{-1}; preparative GLC (10 ft × 1/4 in., 8% Carbowax, 110 °C) gave the analytical sample. Anal. C, H.

Compound **20b**: ^1H NMR δ 1.00 (br t, 3, J = 7 Hz), 1.40 (s, 3), 2.5 (br, 1), 3.30 (s, 3), 3.73 (s, 3); ^{13}C NMR δ 10.5, 16.1, 24.0, 51.6, 52.0, 77.2, 82.8, 173.4.

Compound **21b**: ^1H NMR δ 1.00 (br t, 3, J = 7 Hz), 1.32 (s, 3), 2.5 (br, 1), 3.30 (s, 3), 3.73 (s, 3); ^{13}C NMR, δ 10.5, 15.0, 23.8, 50.0, 51.6, 77.4, 83.2, 173.4.

Methyl (2*RS*,3*RS*)-2,4-Dimethyl-2-methoxy-3-hydroxypentanoate

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(**20c**). The aldol was obtained in 98% yield as a single isomer: IR 3500, 1735 cm^{-1}; ^1H NMR δ 0.94 (d, 3, J = 7 Hz), 1.00 (d, 3, J = 7 Hz), 1.50 (s, 3), 2.50 (br d, 1, J = 11 Hz), 3.34 (s, 3), 3.50 (m, 1), 3.73 (s, 3); ^{13}C NMR δ 16.9, 17.2, 21.2, 29.9, 51.4, 51.7, 79.7, 83.0, 173.5; preparative GLC (10 ft × $^1/_4$ in., 8% Carbowax, 120 °C) gave the analytical sample. Anal. C, H.

Methyl (2*RS*,3*RS*)-2,4,4-Trimethyl-2-methoxy-3-hydroxypentanoate (20d). The aldol was obtained as a single isomer in 84% yield: IR 3500, 1740 cm^{-1}; ^1H NMR δ 1.00 (s, 9), 1.53 (s, 3), 2.70 (br s, 1), 3.33 (s, 3), 3.60 (br d, 1), 3.70 (s, 3); preparative GLC (10 ft × $^1/_4$ in., 8% Carbowax, 110 °C) gave the analytical sample. Anal. Anal. C, H.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-Methoxy-2-methyl-3-hydroxybenzenepropanoates (20e and 21e). The aldol was obtained in 85% yield as a 3:1 mixture of diastereomers which could be separated by column chromatography (10% ether/benzene): IR 3500, 1738 cm^{-1}.

Compound **20e**: ^1H NMR δ 1.30 (s, 3), 3.23 (s, 3), 3.66 (s, 3), 4.80 (s, 1), 723 (s, 5); ^{13}C NMR δ 15.6, 51.4, 51.9, 77.7, 83.3, 127.4, 127.5, 172.5. Anal. C, H.

Compound **21e**: ^1H NMR δ 1.23 (s, 3), 3.30 (s, 3), 3.73 (s, 3), 4.83 (s, 1), 7.33 (s, 5); ^{13}C NMR δ 14.9, 51.4, 52.1, 78.2, 83.6, 127.4, 127.5, 172.5.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-Methyl-2-(benzyloxy)-3-hydroxypentanoates (22b and 23b). The aldol was obtained in 87% yield as a 70:30 mixture of distereomers: IR 3550, 1735 cm^{-1}; preparative GLC (10 ft × $^1/_4$ in., 8% Carbowax, 130 °C) gave the analytical sample. Anal. C, H.

Compound **22b**: ^1H NMR δ 0.97 (br t, 3, J = 7 Hz), 1.50 (s, 3), 2.42 (br s, 1), 3.53 (s, 3), 4.47 (br s, 2), 7.20 (s, 5); ^{13}C NMR δ 10.6, 17.0, 24.0, 51.6, 66.7, 77.2, 82.9, 127.3, 128.0 138.3, 173.4.

Compound **23b**: ^1H NMR δ 0.97 (br t, 3, J = 7 Hz), 1.43 (s, 3), 2.42 (br s, 1), 3.53 (s, 3), 4.47 (br s, 2), 7.20 (s, 5); ^{13}C NMR δ 10.6, 16.2, 23.7, 51.6, 66.7, 77.6, 83.4, 127.3, 128.0, 138.3, 173.4.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2,4-Dimethyl-2-(benzyloxy)-3-hydroxypentanoates (22c and 23c). The aldol was obtained in 85% yield as a 70:30 mixture of diastereomers: IR 3350, 1735 cm^{-1}. Anal. C, H.

Compound **22c**: ^1H NMR δ 0.97 (d, 3, J = 7 Hz), 1.00 (d, 3, J = 7 Hz), 1.58 (s, 3), 2.60 (br s, 1), 3.67 (s, 3), 4.42 (s, 2), 7.15 (s, 5); ^{13}C NMR δ 16.9, 18.3, 21.4, 30.0, 51.5, 66.6, 79.8, 83.1, 127.3, 128.0, 138.3, 173.6.

Compound **23c**: ^1H NMR δ 0.97 (d, 3, J = 7 Hz), 1.00 (d, 3, J = 7 Hz), 1.48 (s, 3), 2.60 (br s, 1), 3.67 (s, 3), 4.49 (s, 2), 7.15 (s, 5); ^{13}C NMR δ 16.5, 18.3, 20.9, 28.9, 51.5, 66.6, 79.8, 83.1, 127.3, 128.0, 138.3, 173.6.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2,4,4-Trimethyl-2-(benzyloxy)-3-hydroxypentanoates (22d and 23d). Aldol addition under the standard conditions gave a mixture of starting ester and two adducts in a ratio of 1:1.3:2.9 (70:30 diastereomer ratio, 80% condensation). The mixture was separated by chromatography on silica gel using 1:3 ether/hexane (respective R_f's, 0.34, 0.28, and 0.19). IR 3550, 1740 cm^{-1}.

Compound **22d**: ^1H NMR δ 1.00 (s, 9), 1.63 (s, 3), 2.5 (br d, 1), 3.70 (s, 3), 4.53 (2, AB, J = 12 Hz, ν_{AB} = 17.5),[32] 7.30 (br s, 5). ^{13}C NMR δ 20.7, 27.2, 36.1, 51.3, 66.6, 82.4, 83.0, 127.2, 127.4, 128.0, 174.1. Anal. C, H.

Compound **23d**: ^1H NMR δ 1.00 (s, 9), 1.56 (s, 3), 2.8 (br d, 1), 3.70 (s, 3), 4.43 (s, 2), 7.26 (s, 5); ^{13}C NMR δ 17.2, 27.2, 35.2, 51.6, 66.1, 82.1, 83.7, 127.3, 127.4, 128.0, 173.8.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-Methyl-2-(benzyloxy)-3-hydroxylbenzenepropanoates (22e and 23e). Aldol addition under standard conditions gave in quantitative yield a 70:30 mixture of diastereomers, from which the major isomer (**22e**) slowly crystallized (mp 88–89 °C, from hexane): IR 3500, 1740 cm^{-1}.

Compound **22e**: ^1H NMR δ 1.45 (s, 3), 2.8, (br s, 1), 3.60 (s, 3), 4.43 (s, 2), 4.80 (s, 1), 7.23 (s, 5); ^{13}C NMR δ 16.0, 51.5, 66.7, 77.8, 83.4, 127.4, 127.5, 128.0, 172.6. Anal. C, H.

Compound **23e**: ^1H NMR δ 1.32 (s, 3), 3.2 (br s, 1), 3.67 (s, 3), 4.46 (s, 2), 4.83 (s, 1), 7.23 (s, 5); ^{13}C NMR δ 16.5, 51.7, 67.0, 78.4, 83.7, 127.4, 127.5, 128.0, 173.0.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-Methyl-2-[(2′-methoxyethoxy)methoxy]-3-hydroxypentanoates (24b and 25b). The aldol was obtained in 60% yield as an 82:18 mixture of diastereomers: IR 3450, 1735 cm^{-1}; preparative GLC (10 ft × $^1/_4$ in., 8% Carbowax, 130 °C) gave the analytical sample. Anal. C, H.

Compound **24b**: ^1H NMR δ 1.00 (br t, 3, J = 7 Hz), 1.50 (s, 3), 3.38 (s, 3), 3.75 (s, 3), 4.87 (2, AB, J = 12 Hz, ν_{AB} = 10.6);[32] ^{13}C NMR δ 10.6, 16.4, 24.1, 51.7, 58.5, 67.5, 71.5, 77.1, 91.4, 173.4.

Compound **25b**: ^1H NMR δ 1.00 (br t, 3, J = 7 Hz), 1.40 (s, 3), 3.38 (s, 3), 3.75 (s, 3), 4.87 (s, 2); ^{13}C NMR δ 10.9, 16.2, 23.7, 50.0, 58.5, 67.5, 71.5, 77.1, 91.4, 173.4.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2,4-Dimethyl-2-[(2′-methoxyethoxy)methoxy]-3-hydroxypentanoates (24c and 25c). The aldol was obtained in 83% yield as a 85:15 mixture of diastereomers: IR 3450, 1740 cm^{-1}; preparative GLC (10 ft × $^1/_4$ in., 8% Carbowax, 130 °C) gave the analytical sample. Anal. C, H.

Compound **24c**: ^1H NMR δ 1.00 (d, 6, J = 7 Hz), 1.58 (s, 3), 3.37 (s, 3), 3.72 (s, 3), 4.80 (br s, 2); ^{13}C NMR δ 17.2, 18.3, 20.9, 30.0, 51.4, 58.3, 67.5, 71.5, 79.5, 91.2, 173.6.

Compound **25c**: ^1H NMR δ 1.00 (d, 6, J = 7 Hz), 1.48 (s, 3), 3.37 (s, 3), 3.72 (s, 3), 4.80 (br s, 2); ^{13}C NMR δ 16.6, 18.3, 19.7, 28.7, 51.4, 58.3, 67.5, 71.5, 79.5, 91.2, 173.6.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2,4,4-Trimethyl-2-[(2′-methoxyethoxy)methoxy]-3-hydroxypentanoates (24d and 25d). The aldol was obtained in 73% yield as an 88:12 mixture of diastereomers: IR 3460, 1735 cm^{-1}; preparative GLC (10 ft × $^1/_4$ in., 8% SE-30, 150 °C) gave the analytical sample. Anal. C, H.

Compound **24d**: ^1H NMR δ 1.00 (s, 9), 1.62 (s, 3), 3.40 (s, 3), 3.70 (s, 3), 4.87 (br s, 2). ^{13}C NMR δ 21.0, 27.1, 51.5, 58.5, 67.7, 71.8, 81.9, 91.3, 174.6.

Compound **25d**: ^1H NMR δ 0.93 (s, 9), 1.55 (s, 3), 3.40 (s, 3), 3.70 (s, 3), 4.87 (br s, 2). ^{13}C NMR δ 17.8, 27.1, 51.5, 58.5, 67.7, 71.8, 83.0, 91.3, 174.6.

Methyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-Methyl-2-[(2′-methoxyethoxy)methoxy]-3-hydroxybenzenepropanoates (24e and 25e). The aldol was obtained in 95% yield as a 85:15 mixture of diastereomers: IR 3450, 1735, 1700, 1600 cm^{-1}; column chromatography utilizing 1:1 ether/hexane gave the analytical sample (R_f 0.12). Anal. C, H.

Compound **24e**: ^1H NMR δ 1.78 (s, 3), 3.33 (s, 3), 3.63 (s, 3), 4.90 (m, 3), 7.25 (s, 5); ^{13}C NMR δ 16.5, 51.7, 58.5, 67.5, 71.5, 77.4, 91.3, 127.4, 127.5, 173.0.

Compound **25e**: ^1H NMR δ 1.33 (s, 3), 3.33 (s, 3), 3.63 (s, 3), 4.90 (m, 3), 7.25 (s, 5); ^{13}C NMR δ 16.3, 51.7, 58.5, 67.5, 71.5, 77.8, 81.6, 127.4, 127.5, 173.0.

Proof of the Stereostructure of Aldol Adducts 24b and 24c. The acetylated aldol was produced by one of two procedures.

(1) Compound **24c**: Acetic anhydride (1.54 mmol) was added to the aldol reaction mixture prior to quenching. Normal workup gave the acetoxy ester (92% yield).

(2) Compound **24b**: The hydroxy ester was treated with 2 equiv of acetic anhydride in pyridine overnight. Aqueous workup gave the acetoxy ester (74% yield).

The acetoxy ester (0.915 mmol) was dissolved in 10 mL of CH_2Cl_2 and anhydrous $ZnBr_2$ (1.03 g, 4.57 mmol) was added. After stirring overnight, the reaction mixture was diluted with H_2O, separated, and extracted with CH_2Cl_2. The organic phases were washed with $NaHCO_3$ and NaCl, and these aqueous phases were back-extracted with ether. Drying of the combined organic phases followed by removal of solvents under reduced pressure gave the α-hydroxy ester (100%). This ester was dissolved in MeOH, and a small crystal of K_2CO_3 was added. After it stood overnight, the solution was filtered and the solvent removed under reduced pressure. The dihydroxy ester produced (100% yield) was compared with authentic samples by ^{13}C NMR spectroscopy. The product resulting from aldol **24c** (via **26c**) was almost completely dihydroxy ester **13c**. However, the product resulting from aldol **24b** was a 2:1 mixture of dihydroxy ester **13b** and its diastereomer. The reduced ratio may result from fractionation in the acylation step.

(*Z*)-1-(Trimethylsilyloxy)-1,2-dimethoxypropene (28). To a solution of LDA (5.34 mmol) in 12 mL of THF at −78 °C was added a solution of 551 mg (4.67 mmol) of ester **17** in 5 mL of THF. After the mixture was stirred for 3 min, 0.70 mL (5.52 mmol) of chlorotrimethylsilane was added. The solution was warmed to room temperature over 30 min, and the solvents were removed under reduced pressure. The resulting residue was taken up in ether and filtered to remove the LiCl. Removal of the ether under reduced pressure gave 628 mg (70%) of ketene acetal as an approximate 12:1 mixture of diastereomers. This material is relatively unstable and decomposes upon attempted distillation at 40 °C with a Kugelrohr apparatus (bath temperature 0.125 torr). Spectra were obtained with crude material, obtained directly from the foregoing procedure. IR (mixture of diastereomers) 1230, 855 cm^{-1}.

Major diastereomer: ^1H NMR δ 0.23 (s, 9), 1.71 (s, 3), 3.40 (s, 3), 3.43 (s, 3); ^{13}C NMR δ −0.1, 11.3, 56.0, 56.5, 121.4, 146.3.

Minor diastereomer: ^1H NMR δ 0.12 (s, 9), 1.71 (s, 3), 3.40 (s, 3), 3.48 (s, 3); ^{13}C NMR δ −0.2, 12.3, 57.2, 57.7, 122.6, 147.4.

Methyl (2*SR*,3*SR*,4*RS*)- and (2*RS*,3*RS*,4*RS*)-3-Hydroxy-2-methoxy-2-methyl-4-phenylpentanoate (31 and 32). The aldol was obtained in 99% yield as an 80:20 mixture of Cram and anti-Cram products which were not resolved by analytical HPLC (2:3 CH_2Cl_2/pentane): IR 3500,

(32) Two-spin (AB) patterns are reported in the convention of: Jackman, L. M.; Sternhell, S. "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry", 2nd ed.; Pergamon Press: New York, 1969; p 129.

1740, 1605 cm^{-1}; preparative GLC (10 ft × $^1/_4$ in., 8% Carbowax, 180 °C) gave the analytical sample. Anal. C, H. Magnetic resonance data were obtained on the mixture of isomers.

Compound **31**: ^1H NMR δ 1.26 (d, 3, J = 7 Hz), 1.40 (s, 3), 3.00 (m, 1), 3.17 (br s, 1), 3.30 (s, 3), 3.43 (s, 3), 3.88 (d, 1, J = 6 Hz), 7.16 (s, 5); ^{13}C NMR δ 17.5, 18.2, 41.1, 51.4, 52.0, 79.3, 82.6, 126.0, 126.2, 127.1, 127.3, 127.7, 128.0, 173.0.

Compound **32**: ^1H NMR δ 1.27 (d, 3, J = 7 Hz), 1.40 (s, 3), 3.00 (m, 1), 3.17 (br s, 1), 3.22 (s, 3), 3.37 (s, 3), 3.98 (d, 1, J = 6 Hz), 7.16 (s, 5); ^{13}C NMR δ 16.0, 18.2, 40.9, 51.4, 52.0, 79.3, 82.6, 126.0, 126.2, 127.1, 127.3, 127.7, 128.0, 173.0.

Methyl (2*SR*,3*SR*,4*RS*)- and (2*RS*,3*RS*,4*RS*)-2,4-Dimethyl-3-hydroxy-2-methoxyheptanedioate Lactones (35 and 36). Aldol addition to produce the mixture of hydroxy diesters proceeded in 88% yield. Analysis by ^{13}C NMR showed this was a 3:1 mixture of diastereomeric products (**33** and **34**).

Compound **33**: ^1H NMR δ 1.48 (s, 3), 3.33 (s, 3), 3.66 (s, 3), 3.75 (s, 3); ^{13}C NMR δ 13.3, 17.1, 30.7, 31.3, 34.0, 51.0, 51.5, 51.8, 77.4, 173.3, 173.8.

Compound **34**: ^{13}C NMR δ 14.9, 17.9, 26.8, 27.9, 34.6, 51.0, 51.5, 51.8, 78.9, 173.3, 173.8.

The crude mixture of aldols was treated with 1 equiv of KOH in 10 mL of 1:1 H_2O/MeOH for 1 h. The solvent was removed under reduced pressure, the residue was partitioned between water and ether, and the layers were separated. The aqueous layer was acidified and extracted with ether. Washing with saturated aqueous NaCl, drying, filtration, and removal of solvents under reduced pressure gave the crude hydroxy acid, which was treated with 5 equiv of acetic anhydride, with heating under vacuum, for 1 h. The resulting product was partitioned between ether and saturated aqueous $NaHCO_3$ and allowed to stand overnight. Separation of layers, drying, filtration, and removal of solvents under reduced pressure gave the lactones (50%), which were separated by column chromatography (1:1 ether/hexane): IR 1740 cm^{-1}.

Compound **35**: R_f 0.17; ^1H NMR δ 1.04 (d, 3, J = 7 Hz), 1.53 (s, 3), 2.30 (m, 2), 3.30 (s, 3), 3.77 (s, 3), 4.67 (d, 1, J = 3 Hz); MS, 231 (m + 1), 199, 171, 139, 118, 113, 103, 85; HRMS, calcd for $C_{11}H_{18}O_5$ 230.1154, found 230.1158.

Compound **36**: R_f 0.22; ^1H NMR δ 1.02 (d, 3, J = 7 Hz), 1.58 (s, 3), 2.30 (m, 2), 3.33 (s, 3), 3.77 (s, 3), 4.23 (d, 1, J = 8 Hz); MS, 231 (m + 1), 199, 171, 139, 118, 113, 103, 85.

2′,6′-Dimethylphenyl (*RS*)-2-(Benzyloxy)propanoate (37). To 215 mg (1.76 mmol) of 2,6-dimethylphenol in 2 mL of THF was added at −78 °C 1.07 mL (1.6 mmol) of a 1.5 M solution of *n*-BuLi in hexane. After 5 min, 0.32 g (1.6 mmol) of 2-(benzyloxy)propanoyl chloride was added. After 5 min the mixture was allowed to warm to room temperature and was poured into 1 M KOH. The aqueous phase was extracted with ether, and the ether extract was washed with 1 M HCl and brine. The ether phase was dried over $MgSO_4$, filtered, and concentrated to give 0.48 g of an oil. Purification by TLC (SiO_2, eluant, 1:9 ether/hexane, R_f 0.26) gave the analytical sample (237 mg, 52%): IR 1760 cm^{-1}; ^1H NMR δ 1.60 (d, 3, J = 7 Hz), 2.13 (s, 6), 4.27 (q, 1, J = 7 Hz), 4.45 (d, 1, J = 11 Hz), 4.75 (d, 1, J = 4 Hz), 7.00 (s, 3), 7.27 (m, 5); HRMS, calcd for $C_{18}H_{20}O_3$ 284.1412, found 284.1415.

2′,6′-Diisopropylphenyl (*RS*)-2-(Benzyloxy)propanoate (38). To a solution of 6.24 g (35.0 mmol, 6.49 mL) of 2,6-diisopropylphenol in 50 mL of THF under argon, cooled to −70 °C, was slowly added 35.0 mmol (22.2 mL of a 1.58 M solution in hexanes) of *n*-BuLi. After the mixture was stirred for 5 min at −70 °C, 2-(benzyloxy)propanoyl chloride (35.0 mmol, 6.95 g) was added dropwise. The mixture was allowed to gradually warm to room temperature and was stirred for 15 h. The reaction mixture was diluted with an equal volume of ether and washed with 10% aqueous NaOH (3 × 50 mL) and brine (1 × 50 mL). This solution was dried ($MgSO_4$), filtered, and concentrated under reduced pressure, to give 11.90 g of crude **38**, which was purified by HPLC with 1:19 ether/hexanes as the eluant to give 7.17 g (60%) of pure **38**: IR 1760 cm^{-1}; ^1H NMR δ 1.15 (d, 12 H, J = 7 Hz), 1.60 (d, 3, J = 7 Hz), 2.85 (septet, 2, J = 7 Hz), 4.25 (q, 1, J = 7 Hz), 4.55 (2, AB, J = 12 Hz, ν_{AB} = 26),[32] 7.00 (s, 3), 7.25 (br s, 5). Anal. C, H.

2′,6′-Di-*tert*-butyl-4′-methylphenyl (*RS*)-2-(Benzyloxy)propanoate (39). To 15.65 g (71 mmol) of butylated hydroxytoluene (BHT) in 75 mL of THF was added under N_2 at −78 °C 46.5 mL (69.7 mmol) of a 1.5 M solution of *n*-BuLi in hexane. The solution was briefly warmed to 0 °C and then cooled again to −78 °C. The 2-(benzyloxy)propanoyl chloride[36] (13.18 g, 66.4 mmol) was then added by motor driven syringe over 25 min. The mixture was stirred at −78 °C for 3 h, allowed to warm overnight to room temperature, then poured into saturated aqueous $NaHCO_3$, washed with H_2O and brine, and dried over $MgSO_4$. Filtration and solvent removal (first at aspirator pressure, then with a vacuum pump) gave 26.5 g of oil. Excess BHT was removed by distillation to give a forerun (3.16 g, 67–70 °C/0.075 torr) which was a mixture of BHT, product **39**, and a residue (21.26 g, 84%) pure **39** by ^1H NMR. Purification by HPLC (SiO_2, 2% ether/hexane, R_f 0.20) gave analytically pure material: IR 1755, 1600 cm^{-1}; ^1H NMR δ 1.31 (s, 18), 1.60 (d, 3, J = 7 Hz), 2.27 (s, 3), 4.20 (q, 1, J = 7 Hz), 4.55 (d, 1, J = 12 Hz), 4.83 (d, 1, J = 12 Hz), 7.03 (s, 2), 7.25 (m, 5). Anal. C, H.

General Procedure for Aldol Additions with Esters 37–39. Into a three-necked, 25-mL round-bottomed flask equipped with a stirring bar, N_2 inlet, septum, and low-temperature thermometer were placed 5.0 mL of THF and 0.42 mL of diisopropylamine (304 mg, 3.0 mmol). The solution was cooled to 0 °C and 2.8 mmol of *n*-BuLi (1.87 mL of a 1.50 M solution in hexanes) was added in one portion. The resulting LDA solution was cooled to −78 °C and 2.0 mmol of the ester was added neat, dropwise. After 1 h at −78 °C, 2.0 mmol of the aldehyde was added, and the resulting mixture was stirred for 20 min. Reaction was quenched by addition of saturated aqueous $NaHCO_3$ (1.0 mL), and the mixture was allowed to warm to room temperature with stirring. The layers were separated and the aqueous phase was extracted with ether. The combined ether fractions were washed with cold 1% HCl, saturated aqueous $NaHCO_3$, and brine. The crude product was obtained by drying over $MgSO_4$, filtration, and removal of the solvent with a rotary evaporator.

2′,6′-Dimethylphenyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-(Benzyloxy)-3-hydroxy-2-methylpent-4-enoates (40a and 41a). The foregoing general procedure was followed, with the exception that 2.4 mmol of LDA in 3.0 mL of THF, 2.0 mmol (0.568 g) of **37**, and 0.16 mL (2.4 mmol) of acrolein were used. The crude product (0.620 g) was analyzed by TLC (1:4 ether/hexane), which showed a spot for 2,6-dimethylphenol and two barely resolved product spots (R_f 0.26). ^{13}C NMR of the crude product indicated a 1.8:1 mixture of aldols **40a** and **41a**. The mixture of aldols was separated from 2,6-dimethylphenol by column chromatography (1:9 ether/hexanes); 445 mg (65%) of product was obtained as a clear oil: IR 3550–3400, 1750 cm^{-1}; ^1H NMR δ 1.65 (s, 3), 2.15 (s, 6), 2.80 (m, 1), 4.4–4.8 (m, 3), 5.20 (m, 1), 5.35 (m, 1), 5.95 (ddd, 1, J = 6, 10 17 Hz), 6.95 (s, 3), 7.30 (m, 5); ^{13}C NMR (**40a**) δ 16.4, 16.6, 17.0, 18.7, 66.8, 76.5, 77.8, 83.0, 117.6, 125.8, 127.3, 128.1, 128.6, 130.0, 135.2, 135.5, 138.1, 148.1, 170.3; ^{13}C NMR (**41a**) δ 67.1, 82.6, 118.3, 138.3, 170.5. Anal. C, H.

2′,6′-Dimethylphenyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-(Benzyloxy)-3-hydroxy-2-methylpentanoates (40b and 41b). The general procedure was followed with the exception that 3.3 mmol of LDA in 4.5 mL of THF, 0.852 g (3 mmol) of **37**, and 0.24 mL (3.3 mmol) of propionaldehyde (distilled from $CaSO_4$) was added. The crude product (0.855 g) was shown by ^{13}C NMR to be a mixture of aldols **40b** and **41b** in ratio of 3.5:1. Analysis by TLC (1:4 ether/hexane) indicated **37** (R_f 0.48), 2,6-dimethylphenol (R_f 0.36), **41b** (R_f 0.31, minor), and **40b** (R_f 0.24, major). Separation by HPLC (1:19 ether/hexane) afforded 100 mg of **37**, 34 mg of 2,6-dimethylphenol, 125 mg of **41b**, and 448 mg of **40b** (50% yield of aldols): IR 3500, 1740 cm^{-1}.

Compound **40b**: ^1H NMR δ 1.10 (t, 3, J = 7 Hz), 1.70 (m, 2), 1.75 (s, 3), 2.15 (s, 6), 2.43 (d, 1, J = 8 Hz), 3.83 (td, 1, J = 3, 9 Hz), 4.60 (d, 1, J = 11 Hz), 4.82 (d, 1, J = 11 Hz), 7.03 (s, 3), 7.15 (m, 5); ^{13}C NMR δ 10.7, 16.6, 17.5, 24.4, 66.9, 77.6, 83.5, 125.8, 127.4, 128.1, 128.7, 129.9, 138.3, 148.1, 170.9. Anal. C, H.

Compound **41b**: ^1H NMR δ 1.08 (t, 3, J = 7 Hz), 1.60 (m, 2), 1.66 (s, 3), 2.15 (s, 6), 2.33 (d, 1, J = 8 Hz), 3.88 (td, 1, J = 3, 9 Hz), 4.62 (d, 1, J = 10 Hz), 4.82 (d, 1, J = 10 Hz), 7.03 (s, 3), 7.15 (m, 5); ^{13}C NMR δ 10.5, 16.5, 17.7, 23.8, 66.7, 77.8, 83.2, 126.0, 126.8, 127.5, 128.1, 128.6, 130.0, 170.9. Anal. C, H.

Compounds **40b**/**41b** were also obtained by catalytic hydrogenation of **40a**/**41a**. A mixture of 410 mg of a 1.8:1 mixture of **40a** and **41a**, 200 mg of 5% Pd/C, and 4 mL of EtOAc took up 31 mL of hydrogen (120% of the calculated amount) in 20 min. The mixture was filtered and the filtrate was evaporated to afford 325 mg (80%) of an oil. The ^{13}C NMR spectrum of this material showed it to be a 1.8:1 mixture of **40b** and **41b**.

2′,6′-Dimethylphenyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-(Benzyloxy)-2,4-dimethyl-3-hydroxypentanoates (40c and 41c). The general procedure was followed to obtain 550 mg (77%) of a 5:1 mixture of aldols **40c** and **41c** (^{13}C NMR). An analytical sample was prepared by HPLC with 1:9 ether/hexanes as eluant. The ^{13}C NMR spectrum of this material showed it to be a 9:1 mixture of the two aldols: IR 3550, 1750 cm^{-1}; ^1H NMR δ 0.90 (d, 3, J = 4 Hz), 1.00 (d, 3, J = 4 Hz), 1.70 (s, 3), 2.10 (s, 6), 2.20 (d, 1, J = 11 Hz), 3.70 (dd, 1, J = 3, 11 Hz), 4.60 (2, AB,

(33) Feldmann, L.; Fischer, H. O. L. *Arch. Biochem.* **1947**, *14*, 117.
(34) Heathcock, C. H.; Young, S. D.; Hagen, J. P.; Pirrung, M. C.; White, C. T.; VanDerveer, D. *J. Org. Chem.* **1980**, *45*, 3846.
(35) The syntheses of these aldehydes will be reported later as part of a continuation of this project.

(36) The aldehyde **73** used contained about 10% of the conjugated isomer (^1H NMR spectroscopy).

J = 12 Hz, ν_{AB} = 25.3),[32] 6.95 (s, 3), 7.20 (m, 5); ^{13}C NMR δ 16.7, 16.9, 18.7, 22.1, 30.3, 67.1, 79.4, 125.9, 127.5, 128.2, 129.9, 130.4, 138.3, 171.1. Anal. C, H.

2′,6′-Dimethylphenyl (2*RS*,3*SR*)-2-(Benzyloxy)-3-hydroxy-2,4,4-trimethylpentanoate (41d). The general procedure was followed except that 2.3 mmol of LDA in 3 mL of THF, 426 mg (1.5 mmol) of **37** in 1 mL of THF, and 0.27 mL (2.5 mmol) of pivalaldehyde were employed. The crude product (555 mg) was shown by ^{13}C NMR spectroscopy to be a mixture of 2,6-dimethylphenol and **41d**; no **37** was detected. Compound **41d** (165 mg, 30%) was isolated by column chromatography (1:9 ether/hexane). The aldol was recrystallized from pentane/ether to given analytically pure material: mp 84–85 °C; IR (KBr) 3500, 1710 cm^{-1}; ^{1}H NMR δ 1.10 (s, 9), 1.75 (s, 3), 2.10 (s, 6), 3.85 (d, 1, J = 7 Hz), 4.60 (m, 2), 7.00 (s, 3), 7.30 (m, 5); ^{13}C NMR δ 17.0, 18.2, 28.0, 66.9, 80.7, 85.2, 125.9, 127.4, 128.2, 128.9, 130.2, 138.3, 170.7. Anal. C, H.

2′,6′-Dimethylphenyl (3*RS*,2*RS*)- and (3*RS*,2*SR*)-2-(Benzyloxy)-3-hydroxy-2-methyl-3-benzenepropanoates (40e and 41e). By use of the general procedure, a 1:3 mixture of aldols **40e** and **41** was obtained in 65% yield. Two recrystallizations from 1:9 ether/hexanes gave a pure sample of aldol **41e**: mp 84–85 °C; IR (KBr) 3550, 3460, 1760 cm^{-1}.

Compound **41e**: ^{1}H NMR δ 1.40 (s, 3), 2.15 (s, 6), 3.30 (d, 1, J = 8 Hz), 4.60 (2, AB, J = 12 Hz, ν_{AB} = 29.7),[35] 5.05 (d, 1, J = 8 Hz), 7.00 (s, 3), 7.25 (m, 5); ^{13}C NMR δ 16.1, 22.5, 66.8, 78.7, 82.7, 125.7, 126.3, 127.6, 127.8, 128.0, 128.3, 128.5, 130.0, 138.1, 138.8, 147.9, 170.7. Anal. C, H.

Compound **40e**: ^{1}H NMR δ 1.60 (s, 3), 2.00 (s, 6), 2.80 (d, 1, J = 4 Hz), 4.65 (2, AB, J = 12 Hz, ν_{AB} = 18.7),[32] 5.10 (d, 1, J = 6 Hz), 6.95 (s, 3); ^{13}C NMR δ 15.3, 22.5, 66.3, 76.3, 83.2, 125.7, 126.3, 127.6, 127.8, 128.0, 128.3, 128.5, 130.0, 130.5, 138.1, 138.8, 147.9, 170.7.

2′,6′-Diisopropylphenyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-(Benzyloxy)-2,4-dimethyl-3-hydroxypentanoates (42c and 43c). By the general procedure, the mixture of aldols **42c** and **43c** was prepared in 73% yield of a 5-mmol scale. The aldols were separated by preparative HPLC with 1:14 ether/hexanes as eluant to give pure **42c** (22%) and **43c** (51%).

Compound **42c**: IR 3500, 1750 cm^{-1}; ^{1}H NMR δ 1.03 (d, 3, J = 7 Hz), 1.08 (d, 3, J = 7 Hz), 1.19 (s, 12, J = 7 Hz), 1.86 (s, 3), 2.08 (m, 1), 2.28 (d, 1, J = 9 Hz), 2.95 (m, 2), 3.84 (dd, 1, J = 2, 9 Hz), 4.70 (2, AB, J = 10 Hz, ν_{AB} = 34.2),[32] 7.30 (m, 8); ^{13}C NMR δ 16.8, 18.6, 22.2, 23.3, 27.2, 30.2, 66.9, 79.3, 84.5, 123.9, 126.7, 127.5, 128.2, 138.2, 140.3, 172.0. Anal. C, H.

Compound **43c**: IR 3550, 1755 cm^{-1}; ^{1}H NMR δ 0.99 (d, 3, J = 7 Hz), 1.09 (d, 3, J = 7 Hz), 1.21 (d, 12, J = 6.5 Hz), 1.75 (s, 3), 2.10 (m, 1), 2.61 (d, 1, J = 11 Hz), 3.05 (m, 2), 3.93 (dd, 1, J = 2, 11 Hz), 4.70 (2, AB, J = 10 Hz, ν_{AB} = 39.8),[32] 7.30 (m, 8); ^{13}C NMR δ 16.1, 18.6, 22.3, 23.3, 27.0, 28.6, 66.9, 79.5, 123.8, 126.5, 127.5, 127.8, 128.2, 138.1, 140.5, 145.5, 172.0. Anal. C, H.

2′,6′-Diisopropylphenyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-(Benzyloxy)-3-hydroxy-2-methyl-3-benzenepropanoates (42e and 43e). The general procedure was followed on a 2.0-mmol scale to obtain a 1:10 mixture of aldols **42e** and **43e** in 75% yield. The mixture was not separated. IR 3550, 1755 cm^{-1}; ^{1}H NMR δ [1.10 (d, 12, J = 7 Hz), minor], 1.20 (d, 12, J = 7 Hz), 1.54 (s, 3) [1.70 (s, 3), minor], 3.03 (br m, 2), 3.44 (d, 1, J = 9 Hz), 4.60 (2, AB, J = 10.5 Hz, ν_{AB} = 21.6),[32] 5.14 (d, 1, J = 9 Hz), [5.21 (d, 1, J = 5.5 Hz), minor], 7.35 (m, 13); ^{13}C NMR δ 16.2, 18.9, 23.1, 27.0, 128.7, 129.2, 129.4, 138.1, 140.4, 145.4, 171.6. Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-(Benzyloxy)-3-hydroxy-2-methylpent-4-enoates (44a and 45a). The general procedure was employed except that 4.5 mmol of LDA in 6.5 mL of THF, 574 mg (1.5 mmol) of **39**, and 0.30 mL (4.5 mmol) of acrolein were used. The crude product (643 mg) was seen by ^{13}C NMR spectroscopy to be a 3:1 mixture of aldols **45a** and **44a**. The mixture of aldols, 583 mg (88%), was isolated by column chromatography (1:3 ether/hexanes): IR 3500, 1740 cm^{-1}. Anal. C, H. When the experiment was carried out with 1 equiv of LDA and 1 equiv of aldehyde, a 3:1 mixture of aldols was obtained in 50% yield.

Compound **45a**: ^{1}H NMR δ 1.30 (s, 9), 1.37 (s, 9), 1.73 (s, 3), 2.33 (s, 3), 3.08 (d, 1, J = 8 Hz), 4.55 (m, 1), 4.81 (d, 1, J = 11 Hz), 4.99 (d, 1, J = 11 Hz), 5.27–5.47 (m, 2), 6.13 (ddd, 1, J = 6, 10, 17 Hz), 7.15 (s, 2), 7.30–7.39 (m, 5); ^{13}C NMR δ 15.9, 23.1, 35.0, 66.0, 74.0, 81.3, 117.2, 126.8, 126.9, 127.2, 127.3, 134.3, 135.6, 138.1, 142.3, 146.1, 172.2.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*SR*)- and (2*RS*,3*RS*)-2-(Benzyloxy)-3-hydroxy-2-methylpentanoates (45b and 44b). The general procedure was followed except that 3.65 mmol of LDA in 4.5 mL of THF, 1.15 g (3.0 mmol) of **39** in 3 mL of THF, and 0.38 mL (5.3 mmol) of propionaldehyde were used. The crude product (1.18 g) was subjected to column chromatography, to obtain 440 mg of **39** and 772 mg of a 5:1 mixture of aldols **45b** and **44b**: IR 3550, 1740 cm^{-1}. Anal. C, H.

Compound **44b**: ^{1}H NMR δ 1.06 (t, 3, J = 7 Hz), 1.31 (s, 18), 1.56 (m, 1), 1.75 (s, 3), 1.92 (m, 2), 2.32 (s, 3), 2.67 (d, 1, J = 8 Hz), 3.90 (ddd, 1, J = 2, 8, 10 Hz), 4.81 (d, 1, J = 11 Hz), 4.97 (d, 1, J = 11 Hz), 7.15 (s, 2), 7.27–7.39 (m, 5); ^{13}C NMR δ 14.0, 15.9, 21.1, 23.3, 35.1, 66.3, 76.8, 81.8, 126.9, 127.0, 127.3, 128.1, 134.4, 142.3, 146.0, 173.3.

Compound **45b**: ^{1}H NMR δ 1.06 (t, 3, J = 7 Hz), 1.34 (s, 9), 1.37 (s, 9), 1.56 (m, 1), 1.77 (s, 3), 2.32 (s, 3), 2.67 (d, 1, J = 7.6 Hz), 3.90 (ddd, 1, J = 2, 8, 10 Hz), 4.74 (d, 1, J = 11 Hz), 4.99 (d, 1, J = 11 Hz), 7.15 (s, 2), 7.27–7.39 (m, 5); ^{13}C NMR δ 10.9, 18.0, 21.1, 24.2, 31.4, 66.3, 76.8, 82.2, 126.9, 127.3, 128.1, 138.2, 142.1, 146.0, 173.3.

Compounds **44b**/**45b** were also obtained by catalytic hydrogenation of aldols **44a**/**45a**. A mixture of 520 mg (1.19 mmol) of a 3:1 mixture of **45a** and **44a**, 150 mg of 5% Pd/C, and 4 mL of EtOAc took up 35 mL of hydrogen over a period of 1 h. Filtration and evaporation of the filtrate afforded 427 mg (80%) of product, shown by ^{13}C NMR spectroscopy to be a 3:1 mixture of **45b** and **44b**.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*SR*)-2-(Benzyloxy)-2,4-dimethyl-3-hydroxypentanoate (45c). By use of the general procedure on a 5.0-mmol scale, aldol **45c** was obtained in 89% yield, after chromatographic purification. An analytical sample, mp 68–70 °C, was obtained by recrystallization from pentane containing 1% ether. Crystals suitable for single-crystal X-ray analysis were obtained by evaporative crystallization from toluene. It was found that toluene intercalates into the crystal lattice: IR (Nujol) 3560, 1750 cm^{-1}; ^{1}H NMR δ 0.94 (d, 3, J = 7 Hz), 1.07 (d, 3, J = 7 Hz), 1.36 (s, 9), 1.38 (s, 9), 1.80 (s, 3), 2.32 (s, 3), 2.74 (d, 1, J = 10 Hz), 4.08 (dd, 1, J = 2.3, 10 Hz), 4.80 (2, AB, J = 10 Hz, ν_{AB} = 67.3),[32] 7.16 (s, 2), 7.34 (m, 5); ^{13}C NMR δ 15.9, 19.0, 21.3, 22.3, 28.8, 31.4, 31.7, 35.3, 66.5, 77.6, 82.2, 127.6, 128.0, 128.3, 134.7, 142.4. Anal. Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*SR*)-2-(Benzyloxy)-3-hydroxy-2-methyl-3-benzenepropanoate (45e). The general procedure was followed to obtain aldol 45e in 63% yield. Crystals suitable for single-crystal X-ray analysis, mp 137–138 °C, were obtained by recrystallization from 1:9 ether/hexanes: IR (Nujol) 3540, 1760 cm^{-1}; ^{1}H NMR δ 1.35 (s, 18), 1.50 (s, 3), 2.27 (s, 3), 3.45 (d, 1, J = 8 Hz), 4.65 (2, AB, J = 10 Hz, ν_{AB} = 31.5),[32] 5.15 (d, 1, J = 8 Hz), 7.10 (s, 2), 7.25 (m, 5); ^{13}C NMR δ 19.5, 21.0, 31.1, 31.3, 35.0, 66.6, 82.1, 126.8, 127.0, 127.4, 127.5, 127.7, 128.0, 128.4. Anal. C, H.

(2*RS*,3*RS*)-2-(Benzyloxy)-3-hydroxy-2-methylpentanoic Acid (46). A mixture of 1.113 g (3.25 mmol) of **40b**, 1.10 g (20 mmol) of KOH, 20 mL of CH_3OH, and 5 mL of water was stirred for 45 min at room temperature. Solid CO_2 was added to bring the solution to pH 8. The mixture was partitioned between water and ether, the layers were separated, and the aqueous layer was acidified with concentrated HCl. The resulting mixture was extracted with ether (2 × 50 mL). The ether layer was dried and evaporated to obtain 425 mg (58%) of acid **46**: mp 103–104 °C; IR (KBr) 3300, 3000–2400, 1695 cm^{-1}; ^{1}H NMR δ 1.05 (t, 3, J = 7 Hz), 1.40 (m, 2), 1.51 (s, 3), 3.63 (dd, 1, J = 3, 9 Hz), 4.45 (s, 2), 6.3 (br, 2), 7.25 (s, 5). Anal. C, H.

(2*RS*,3*RS*)-2,3-Dihydroxy-2-methylpentanoic Acid (47). A mixture of 400 mg of **46**, 206 mg of 10% Pd/C, and 10 mL of EtOAc was stirred under an atmosphere of hydrogen; 54 mL of hydrogen was taken up in a period of 18 h. Filtration and evaporation of the filtrate afforded 225 mg (90%) of acid **47**, mp 141–142 °C. Two recrystallizations yielded 100 mg, mp 149–150 °C. The material was identified as Bergel'son's acid[8] by mixture melting point with an authentic specimen from another source[34] (mp 149–150 °C).

General Procedure for Lithium Aluminum Hydride Reductions of Aldols. To a solution of $LiAlH_4$ in dry THF or ether was added a solution of aldol in the same solvent. The mixture was stirred at room temperature or heated at reflux for an appropriate period of time, then quenched, and worked up in the standard manner[28] to obtain the crude product.

(2*SR*,3*RS*)-2,4-Dimethyl-2-methoxy-1,3-pentanediol (26c). The general procedure was followed with 25.8 mg (0.68 mmol) of $LiAlH_4$ in 2 mL of ether and 86.1 mg (0.45 mmol) of aldol **20c** in 3 mL of ether. The mixture was kept at room temperature for 30 min, then quenched in the normal manner, and worked up to obtain a crude product that was subjected to flash chromatography using 2:3 EtOAc/hexanes as eluant to obtain 60.1 mg (82%) of diol as a colorless oil: ^{1}H NMR δ 1.02 (d, 3, J = 6.6 Hz), 1.03 (d, 3, J = 6.7 Hz), 1.09 (s, 3), 1.86 (d septet, 1, J = 4.4, 6.6 Hz), 2.70 (br s, 2), 3.30 (s, 3), 3.47 (d, 1, J = 4.2 Hz), 3.62 (d, 1, J = 11.9 Hz), 3.73 (d, 1, J = 11.9 Hz). Anal. C, H.

(1*RS*,2*SR*)-2-Methoxy-2-methyl-1-phenyl-1,3-propanediol (26e). The reduction of 61.7 mg (0.275 mmol) of aldol **20e** in 2 mL of ether was carried out with 15.7 mg (0.41 mmol) of $LiAlH_4$ in 2 mL of ether. After 15 min at room temperature, the reaction was quenched and worked up to obtain 42.6 mg of product (78%). The analytical sample (38.2 mg) was obtained by chromatography on 5 g of silica gel using 3:7 EtOAc/hexanes as eluant: ^{1}H NMR δ 1.00 (s, 3), 2.57 (dd, 1, J = 5.2, 6.8 Hz), 3.30 (d, 1, J = 3.1 Hz), 3.37 (s, 3), 3.48 (dd, 1, J = 6.0, 12.0 Hz), 3.72 (dd, 1, J = 5.0, 12.0 Hz), 4.84 (d, 1, J = 2.9 Hz), 7.38, (m,

5); ^{13}C NMR 15.6, 49.6, 64.5, 77.5, 127.5, 127.8. Anal. C, H.

(1*RS*,2*SR*)-2-(Benzyloxy)-2-methyl-1-phenyl-1,3-propanediol (27e). The general procedure for reductions was followed with 11.4 mg (0.30 mmol) of $LiAlH_4$ in 1.5 mL of ether and 60 mg (0.20 mmol) of a 95:5 mixture of aldols **22e** and **23e** (obtained by chromatography of the 70:30 mixture, vide supra, on silica gel) in 1.5 mL of ether. The reduction was allowed to proceed for 1 h at room temperature and was then quenched and worked up as usual to obtain a crude product. This material was chromatographed on 5 g of silica gel using 2:3 EtOAc/hexanes as eluant, which gave 40.1 mg (73%) of diol **23e** as a colorless oil: ^{1}H NMR (**27e**) δ 1.12 (s, 3), 2.65 (br m, 1), 3.36 (br s, 1), 3.58, (dd, 1, J = 6.0, 12.1 Hz), 3.75 (dd, 1, J = 4.9, 12.0 Hz), 4.57 (dd, 2, J = 10.8, 15.6 Hz), 4.91 (d, 1, J = 2.6 Hz), 7.35 (m, 10). Anal. C, H.

(2*SR*,3*RS*)-2-(Benzyloxy)-2-methylpentane-1,3-diol (48). The general procedure was followed with 80 mg (2.1 mmol) of $LiAlH_4$ in 15 mL of THF and 203 mg (0.93 mmol) of aldol **40b** in 5 mL THF. The mixture was heated at reflux for 140 min, then quenched, and worked up in the standard manner to obtain 118 mg (58%) of crude material. Diol **48** (64 mg, 48%) was separated from the 2,6-dimethylphenol by chromatography on silica gel. Trituration with pentane afforded an analytical sample: mp 42–44 °C; ^{1}H NMR δ 1.08 (t, 3, J = 7 Hz), 1.15 (s, 3), 1.42–1.68 (s, 2), 7.29–7.37 (m, 5); ^{13}C NMR δ 10.9, 15.6, 15.7, 17.7, 23.8, 63.8, 64.7, 76.8, 79.0, 119.7, 127.2, 128.0, 128.2. Anal. C, H.

(2*SR*,3*SR*)-2-(Benzyloxy)-2-methylpentane-1,3-diol (49). The general procedure was followed with 175 mg (4.6 mmol) of $LiAlH_4$ in 20 mL of THF and 580 mg (1.3 mmol) of a 5:1 mixture of aldols **45b** and **44b**. The mixture was heated at reflux for 1.5 h, then worked up in the standard manner to obtain a 4:1 mixture of diols in 74% yield. The ^{13}C NMR spectrum of this mixture showed the minor product to be diol **48** (vide supra). The mixture of diols, 193 mg (65%), was isolated by chromatography on silica (eluted with hexane to collect BHT, then ether to obtain **48**/**49**). A sample was recrystallized from pentane/ether to give a pure sample of the major isomer (**49**): mp 60–63 °C; ^{1}H NMR δ 1.04 (t, 3, J = 7 Hz), 1.18 (s, 3), 1.4–1.7 (m, 2), 2.36 (d, 1, J = 6 Hz), 2.54 (t, 1, J = 6 Hz), 3.63 (m, 1), 3.80 (dd, 1, J = 5, 12 Hz), 4.55 (s, 2), 7.28–7.36 (m, 5); ^{13}C NMR δ 11.0, 16.4, 24.3, 64.5, 65.8, 77.6, 79.4, 127.5, 128.5. Anal. C, H.

(2*SR*,3*SR*)-2,4-Dimethyl-2-(benzyloxy)pentane-1,3-diol (50) and (2*SR*,3*RS*)-2,4-Dimethyl-2-(benzyloxy)pentane-1,3-diol (27c). A. From aldol 45c: The general procedure was followed with 100 mg (2.64 mmol) of lithium aluminum hydride in 5 mL of THF and 100 mg (0.22 mmol) of aldol **45c** in 5 mL of THF. The reaction solution was heated at reflux for 13 h. The crude product was chromatographed on a 1-mm silica gel preparative TLC plate using 3% CH_3OH in $CHCl_3$ as eluant to obtain 25 mg (48%) of diol **50**: mp 24–25 °C; ^{1}H NMR δ 0.97 (d, 3, J = 7 Hz), 1.02 (d, 3, J = 7 Hz), 1.22 (s, 3), 1.87 (m, 1), 2.60 (d, 1, J = 9 Hz), 3.06 (dd, 1, J = 7 Hz), 3.60 (m, 2), 3.90 (m, 1), 4.58 (2, AB, J = 11 Hz, ν_{AB} = 69.0),[32] 7.31 (s, 5). Anal. C, H.

B. From aldol 43c: The general procedure was carried out with 50 mg (1.33 mmol) of $LiAlH_4$ in 2 mL of THF and 50 mg (0.12 mmol) of aldol **43c** in 3 mL of THF, at room temperature for 14 h, to obtain a crude product, which was purified by preparative TLC with 3% CH_3OH in $CHCl_3$ as eluant, to give 27 mg (94%) of diol **50**. This material was identical by ^{1}H NMR with the sample obtained from aldol **45c**.

C. From aldol 42c: The standard reduction procedure was carried out with 50 mg (1.33 mmol) of $LiAlH_4$ in 2 mL of THF and 50 mg (0.12 mmol) of **42c** in 3 mL of THF at room temperature for 12 h, to obtain a crude product which was purified by preparative TLC using 3% CH_3OH in $CHCl_3$ as eluant to obtain 23 mg (80%) of pure diol **27c**: ^{1}H NMR δ 1.03 (d, 3, J = 4 Hz), 1.06 (d, 3, J = 4 Hz), 1.22 (s, 3), 1.89 (m, 1), 2.66 (m, 2), 3.58 (m, 1), 3.75 (m, 2), 4.55 (s, 2), 7.34 (m, 5). Anal. C, H.

D. From aldols 40c/41c: The standard reduction procedure was carried out with 50 g (133 mmol) of $LiAlH_4$ in 2 mL of THF and 50 mg (0.14 mmol) of a 1:9 mixture of aldols **40c** and **41c** in 3 mL of THF, at room temperature for 13 h. The crude product was chromatographed on a 1-mm silica gel preparative TLC plate with 3% CH_3OH in $CHCl_3$ as the eluant to obtain 25 mg (75%) of a 1:9 mixture of diols **50** and **27c**, identified by ^{1}H NMR spectroscopy.

E. From aldols 22b/23b: The general reduction procedure was carried out with 28.5 mg (0.75 mmol) of $LiAlH_4$ in 1.5 mL of ether and 133.1 mg (0.50 mmol) of a 70:30 mixture of aldols **22b** and **23b** in 2 mL of ether. The mixture was stirred at 0 °C for a 30-min period then warmed to room temperature. After standard workup, diols **27c** and **50** were obtained in a ratio of 70:30.

(1*SR*,2*SR*)-2-(Benzyloxy)-2-methyl-1-phenylpropane-1,3-diol (51). A. From aldol 45e: The standard procedure was followed with 61 mg (1.6 mmol) of $LiAlH_4$ in 3 mL of THF and 78 mg (0.16 mmol) of aldol **45e**, at reflux for 12 h. The crude product was purified by preparative TLC with 3% CH_3OH in $CHCl_3$ as eluant to obtain 29 mg (67%) of diol **51**: ^{1}H NMR δ 1.05 (s, 3), 2.25 (br s, 1), 3.02 (br s, 1), 3.60 (m, 2), 4.57 (s, 2), 4.95 (s, 1), 7.40 (m, 10); ^{13}C NMR δ 14.9, 64.3, 64.5, 77.0, 80.0, 125.3, 127.3, 127.4, 127.6, 128.2, 138.5, 139.5, 151.3. Anal. C, H.

B. From aldols 42e/43e: The general procedure was followed with 190 mg (5.0 mmol) of $LiAlH_4$ in 10.0 mL of THF and 558 mg (1.25 mmol) of a 1:10 mixture of aldols **42e** and **43e** in 5.0 mL of THF. The mixture was heated at reflux for 34 h, then quenched, and worked up as usual. The residue was chromatographed on 25 g of silica gel with 1% CH_3OH in $CHCl_3$ as eluant to give 278 mg (82%) of diol **51** containing a small amount of the minor diol derived from aldol **42e**.

C. From aldol 41e: The general procedure was employed with 141 mg (3.7 mmol) of $LiAlH_4$ in 5 mL of THF and 415 mg (1.06 mmol) of **41e** in 2.5 mL of THF. The mixture was heated at reflux for 80 min, then quenched and worked up as usual to obtain 298 mg of product (70%). The ^{1}H NMR and ^{13}C NMR spectra of this material were identical with those of diol **51** prepared in parts A and B.

(*Z*)- and (*E*)-2-(Benzyloxy)-1-(2′,6′-diisopropylphenoxy)-1-((trimethylsilyl)oxy)propene (52a and 53a). A solution of 1.0 mmol of LDA was prepared from 0.168 mL (1.20 mmol) of diisopropyamine and 0.64 mL of 1.56 M *n*-BuLi in hexane (1.0 mmol) in 1 mL of THF. After cooling the LDA solution to −78 °C, a solution of 165.3 mg (0.486 mmol) of ester **38** in 0.5 mL of THF (0.5 mL of THF was used to rinse the syringe) was slowly added. The reaction mixture was stirred at −78 °C for 1 h, and 0.127 mL (1.0 mmol) of trimethylchlorosilane was added slowly. The mixture was stirred at −78 °C for another 10 min and then allowed to come to room temperature over a period of 45 min; the reaction mixture was then partitioned between petroleum ether and ice water. The petroleum ether layer was washed with saturated $NaHCO_3$ solution and with brine and evaporated with a rotary evaporator (after addition of some EtOAc). The residue was dissolved in petroleum ether, filtered, and evaporated again (rotary evaporator followed by a 1-torr vacuum) to give crude 200.7 mg (100%) of a slightly yellow oil. The ^{1}H NMR spectrum showed a **52a**:**53a** ratio of 94:6 and about 13% of starting ester. Flash chromatography on 9 g of silica gel (KG 60, 230–400 mesh, 3 × 3 cm) with 98:2 petroleum ether/ether gave 136.7 mg (68.2%) of a 94:6 mixture of **52a** and **53a**, R_f 0.46, as a colorless oil: IR 1710, 1590 cm^{-1}; ^{1}H NMR (**52a**) δ −0.16 (s, 9), 1.20 (d, 12, J = 6.9 Hz), 1.95 (s, 3), 3.26 (septet, 2, J = 6.9 Hz), 4.71 (s, 2), 7.08 (s, 3), 7.38 (m, 5). A few signals from the minor isomer **53a** were discernible: δ 0.04 (s, 9), 1.82 (s, 3), 4.32 (s, 2). Anal. C, H.

(*Z*)-2-(Benzyloxy)-1-(4′-methyl-2′,6′-di-*tert*-butylphenoxy)-1-((trimethylsilyl)oxy)propene (52b). To a solution of 0.168 mL (1.20 mmol) of diisopropylamine and 0.083 mL (0.60 mmol) of triethylamine in 1 mL of THF at 0 °C was added 0.64 mL of *n*-BuLi in hexane (1.56 *M*, 1.0 mmol). The solution was stirred at room temperature for 15 min and a solution 211 mg (0.522 mmol) of ester **39** in 1 mL of THF was added slowly at −78 °C (an additional 1 mL of THF was used to rinse the syringe). The reaction mixture was stirred at −78 °C for 1 h and 0.19 mL (1.50 mmol) of trimethylchlorosilane was added. After an additional hour at −78 °C, the reaction mixture was allowed to come to room temperature over a period of 2 h. The mixture was partitioned between petroleum ether and ice water, the petroleum ether layer was washed twice with saturated $NaHCO_3$ solution and once with brine, and the solvents were evaporated with a rotary evaporator (after addition of some EtOAc). The residue was dissolved in a small amount of petroleum ether, filtered, and evaporated again (rotary evaporator followed by a 1-torr vacuum) to give 245.5 mg (98%) of a slightly yellow oil. The ^{1}H NMR spectrum of this material showed that no starting material was left and indicated the presence of only one alkene isomer. The crude product was chromatographed on 11 g of silica gel (KG 60, 230–400 mesh, 4 × 3 cm) with 98:2 petroleum ether/ether to give 182.3 mg (73%) of a colorless oil, which solidified in the refrigerator: mp 70–71 °C; IR 1710, 1600 cm^{-1}; ^{1}H NMR δ −0.16 (s, 9), 1.36 (s, 18), 1.99 (s, 3), 2.28 (s, 3), 4.67 (s, 2), 6.99 (s, 2), 7.25–7.40 (m, 5). Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (*RS*)-2-Phenoxypropanoate (54). To a slurry of 0.327 mmol of NaH (15.7 g of 50% dispersion in oil) in a mixture of 80 mL of THF and 15 mL of HMPT at 0 °C was added dropwise a solution of 20 g (0.130 mmol) of 2-bromopropanoic acid in 50 mL of THF. To this sodium salt solution was added a solution of 12.28 g (0.130 mmol) of phenol in 70 mL of THF; during the addition, the temperature rose to 50 °C. After it was stirred overnight at room temperature, the reaction mixture was diluted with hexane and the excess NaH was destroyed by addition of water. The 2-phenoxypropanoic acid sodium salt was extracted with water; the aqueous phase was extracted with ether to remove the mineral oil. The pH was adjusted to 1 by addition of 85% H_3PO_4, and the 2-phenoxypropanoic acid was extracted with ether. The combined ether extracts were washed with brine, dried ($MgSO_4$), filtered, and concentrated with a rotary evaporator to give 17.5 g (81%) of a crystalline white solid, which still contained some phenol.

Recrystallization from hot benzene gave 15.15 g (70%) of a white solid, mp 112–115 °C.

To 6.5 mL (10.75 g, 90.4 mmol) of $SOCl_2$ and a few drops of DMF was added 10 g (60.2 mmol) of 2-phenoxypropanoic acid and the resulting mixture was heated at reflux until gas evolution ceased (about 1 h). Excess $SOCl_2$ was removed at aspirator pressure and the residue was distilled (short path, 0.1 torr) to give 10.66 g (96%) of a nearly colorless oil.

To a solution of 4-methyl-2,6-di-*tert*-butylphenol (12.71 g, 57.8 mmol) in 50 mL of THF at 0 °C was added a 1.5 M solution of *n*-butyllithium in hexane. The resulting mixture was stirred for 15 min and a solution of 10.6 g (57.8 mmol) of 2-phenoxypropanoic acid chloride in 20 mL of THF was added slowly. The cooling bath was removed and the reaction mixture was stirred overnight. The mixture was poured into ice water and partitioned between ether and water. The ether layer was washed with 2 N NaOH and brine, dried ($MgSO_4$), filtered, and concentrated with a rotary evaporator to give a yellow oil. This material was chromatographed on silica gel to obtain 8.02 g (38%) of a thick yellow oil: IR 1720 cm^{-1}; ^1H NMR δ 1.28 (s, 9), 1.32 (s, 9), 1.76 (d, 3, J = 6.5 Hz), 2.31 (s, 3), 5.13 (d, 1, J = 6.5 Hz), 6.97–7.34 (m, 7).

4-Methyl-2,6-di-*tert*-butylphenyl 2-(4′-Methoxyphenoxy)propanoate (55). To a slurry of 0.327 mmol of NaH (15.7 g of 50% dispersion in oil) in a mixture of 130 mL of THF and 20 mL of HMPT at 0 °C was added a solution of 162 g (0.13 mmol) of 4-methoxyphenol in 30 mL of THF. 2-Bromopropanoic acid (20.0 g, 0.13 mmol) as added, neat, dropwise, and the resulting mixture was stirred overnight at 60 °C. The excess NaH was destroyed by addition of water and the reaction mixture was diluted with ether. The 2-(4′-methoxyphenoxy)propanoic acid sodium salt was extracted with water and the water layer was washed with hexane to remove the mineral oil. The aqueous phase was acidified with 85% H_3PO_4 (pH 1–2) and the reaction product was extracted with ether. The ether layer was washed with brine, dried ($MgSO_4$), filtered and concentrated with a rotary evaporator to give 21.12 g (82%) of a slowly crystallizing yellow oil. This material is nearly pure and may be used without further purification.

To 11.63 mL (19.21 g, 161.7 mmol) of $SOCl_2$ and a few drops of DMF was added 21.12 g (107.8 mmol) of 2-(4′-methoxyphenoxy)-propanoic acid. After refluxing for 1 h, the excess $SOCl_2$ was removed at aspirator pressure and the residue was distilled (short path, 0.2 torr, bp 98–100 °C) to give 13.66 g (69%) of a yellow oil. To a solution of 4-methyl-2,6-di-*tert*-butylphenol (14.04 g, 63.7 mmol in 60 mL of THF at −78 °C) was added a 1.5 M solution of *n*-BuLi in hexane. 2-(4′-Methoxyphenoxy)propanoic acid chloride (13.66 g, 63.7 mmol) was dropped in slowly, neat. The cooling bath was removed and the reaction mixture was poured onto a mixture of ice and 2 N NaOH and partitioned between ether and the aqueous phase. The ether layer was washed with brine, dried ($MgSO_4$), filtered, and concentrated with a rotary evaporator to give 26.7 g (100%) of a yellow oil. This oil was chromatographed on silica gel to obtain 11.41 g (45%) of the product: R_f 0.35; IR 1720 cm^{-1}; ^1H NMR δ 1.29 (s, 9), 1.31 (s, 9), 1.73 (d, 3, J = 7 Hz), 2.31 (s, 3), 3.75 (s, 3), 4.97, (d, 1, J = 7 Hz), 6.79–7.23 (m, 6).

(*Z*)- and (*E*)-1-(4′-Methyl-2′,6′-di-*tert*-butylphenoxy)-2-phenoxy-1-((trimethylsilyl)oxy)propene (56 and 57). To a solution of 0.21 mL (0.152 g, 1.5 mmol) of diisopropylamine in 3 mL of dry THF at 0 °C was added 1 mL of a 1.5 M *n*-BuLi in hexane. The resulting solution was stirred for 5 min and then cooled to −78 °C. A solution of 0.368 g (1 mmol) of ester **54** in 1 mL of THF was added and the mixture was stirred for 1 h. Chlorotrimethylsilane (0.14 mL, 0.152 g, 1.5 mmol) was added, neat, in one portion. After 10 min, the cooling bath was removed, and the solution was allowed to warm to room temperature. The reaction mixture was concentrated with a rotary evaporator to give a yellow oil, which was distilled using a Kugelrohr apparatus (bp 130–150 °C (0.01 torr)) to obtain 0.384 g (94%) of product. This material still contained **54** and was subjected to flash chromatography to obtain 0.181 g (41%) of analytically pure material: IR 2950, 2900, 1720, 1480, 1420, 1281, 1100, 900 cm^{-1}; ^1H NMR (**57**) δ 1.55 (s, 18), 2.10 (s, 3), 2.5 (s, 3), 7.27–7.56 (m, 7); (**56**) δ 1.62 (s, 18), 2.22 (s, 3), 2.48 (s, 3), 7.27–7.56 (m, 7). Anal. C, H.

(*Z*)- and (*E*)-1-(4′-Methyl-2′,6′-di-*tert*-butylphenoxy)-1-(4″-methoxyphenoxy)-1-((trimethylsilyl)oxy)propene (58 and 59). To a solution of 0.420 mL (0.304 g, 3.0 mL) of diisopropylamine in 3 mL of THF at 0 °C was added 2.0 mL of a 1.5 M solution of *n*-BuLi in hexane. The resulting solution was stirred for 5 min and then cooled to −78 °C. A solution of 0.796 g (2.0 mmol) of ester **55** in 1 mL of THF was slowly added, and the mixture was stirred for 1 h. Chlorotrimethylsilane (0.4 mL, 0.337 g, 3.1 mmol) was added, neat, in one portion. After 10 min the cooling bath was removed and the solution was allowed to warm to room temperature. The mixture was partitioned between ice water and hexanes. The hexane layer was washed with $NaHCO_3$ and brine, dried (Na_2SO_4), filtered, and concentrated with a rotary evaporator to give 0.98 g (100%) of a yellow oil which contained small amounts of impurities and some starting material. An analytical sample was prepared by flash chromatography: IR 1710 cm^{-1}; ^1H NMR (**59**) δ 1.53 (s, 18), 1.87 (s, 3), 2.25 (s, 3), 3.98 (s, 3), 7.05–7.45 (m, 6); **58** δ 1.61 (s, 18), 2.17 (s, 3), 2.49 (s, 3), 3.98 (s, 3), 7.05–7.45 (m, 6). Anal. C, H. The **58**/**59** ratio was determined by ^1H NMR spectroscopy to be 11:1.

General Procedure for Aldol Additions with Esters 54 and 55. To a solution of 3.3 mmol of diisopropylamine in 3 mL of THF at 0 °C was added 2 mL of a 1.5 M solution of *n*-BuLi in hexane. The resulting solution was stirred for 5 min and was then cooled to −78 °C. A solution of 3.0 mmol of ester **54** or **55** in THF was added, and the mixture was stirred for 1 h. Isobutyraldehyde or benzaldehyde (6.0 mmol) was added, neat. The mixture was stirred for 30 min and quenched by addition of 1 mL of saturated NH_4Cl solution. After it was warmed to room temperature the mixture was partioned between ether and ice water. The ether layer was washed with 1% aqueous H_2SO_4, saturated $NaHCO_3$, and brine and was dried over Na_2SO_4, filtered, and concentrated with a rotary evaporator to give the crude product.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2,4-Dimethyl-3-hydroxy-2-phenoxyhexanoate (60c and 61c). The general procedure was followed with ester **54** and isobutyraldehyde to obtain 1.1 g (83%) of a yellow oil, a 2:1 mixture of **61c** and **60c**. A sample was chromatographed on silica gel to obtain 0.070 g of **60c** and 0.180 g of **61c**.

Compound **60c**: ^1H NMR δ 1.05–1.06 (m, 6), 1.34 (s, 9), 1.37 (s, 9), 1.65 (s, 3), 2.33 (s, 3), 3.09, (d, 1, J = 6 Hz), 4.10 (m, 1), 7.16–7.30 (m, 7); ^{13}C NMR δ 16.7, 18.8, 20.7, 22.9, 29.0, 31.6, 35.3, 78.3, 79.0, 86.3, 124.4, 127.3, 129.0, 134.8, 142.7, 154.5. Anal. C, H.

Compound **61c**: ^1H NMR δ 1.12 (d, 3, J = 7 Hz), 1.16 (d, 3, J = 7 Hz), 1.25 (s, 9), 1.34 (s, 9), 1.73 (s, 3), 2.31 (s, 3), 2.90 (d, 1, J = 10 Hz), 3.97–4.03 (m, 1), 7.09–7.26 (m, 7); ^{13}C NMR δ 17.1, 18.8, 21.2, 23.2, 28.8, 31.6, 35.2, 78.2, 86.3, 124.0, 127.1, 128.9, 134.7, 142.2, 154.5. Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2-Methyl-3-hydroxy-2-phenoxy-3-benzenepropanoate (60e and 61e). The general procedure was followed with ester **54** and benzaldehyde to obtain 1.40 g (100%) of a yellow oil. Flash chromatography of this residue gave 0.615 g of aldol **61e** and 0.570 of aldol **60e**, total yield, 1.183 g (83%).

Compound **60e**: IR 3550, 1740, 1610 cm^{-1}; ^1H NMR δ 1.25 (s, 9), 1.35 (s, 9), 1.55 (s, 3), 2.35 (s, 3), 3.70 (d, 1, J = 10 Hz), 5.35 (d, 1, J = 10 Hz), 7.0–7.6 (m, 14); ^{13}C NMR δ 21.2, 31.4, 31.7, 35.2, 78.0, 85.8, 124.5, 127.3, 127.8, 128.1, 128.8, 134.7, 139.2, 142.5, 154.3, 172.9.

Compound **61e**: IR 3550, 1720, 1600 cm^{-1}; ^1H NMR δ 1.25 (s, 9), 1.45 (s, 12), 2.35 (s, 3), 4.35 (d, 1, J = 5 Hz), 5.38 (d, 1, J = 5 Hz), 6.45–7.63 (m, 12); ^{13}C NMR δ 16.6, 21.3, 31.6, 35.4, 75.7, 76.8, 78.2, 84.8, 124.4, 127.4, 127.7, 128.1, 128.7, 129.4, 135.1, 138.5, 142.7, 154.4, 176.4. Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*RS*)- and (2*RS*,3*SR*)-2,4-Dimethyl-3-hydroxy-2-(4″-methoxyphenoxy)hexanoate (62c and 63c). The general procedure was followed with ester **55** and isobutyraldehyde to obtain 1.32 g (92%) of a yellow oil, which was was chromatographed to obtain 774 mg of **63c** and 92 mg of **62c**; the total yield was 61.5% of the theoretical.

Compound **62c**: ^1H NMR δ 0.75–0.96 (m, 1), 0.99–1.03 (m, 3), 1.25 (s, 9), 1.29 (s, 9), 1.52 (s, 3), 2.24 (s, 3), 3.03–3.06 (m, 1), 3.68 (s, 3), 3.85–3.89 (m, 1), 6.69–7.18 (m, 6).

Compound **63c**: IR 3550, 1740 cm^{-1}; ^1H NMR δ 0.91–0.98 (m, 1), 1.04 (d, 2, J = 7 Hz), 1.16 (d, 2, J = 6 Hz), 1.23 (s, 9), 1.64 (s, 3), 2.31 (s, 3), 2.88 (d, 1, J = 10 Hz), 3.77 (s, 3), 4.0 (dd, J = 3, 10 Hz), 6.74–6.79 (m, 2), 7.13–7.19 (m, 2), 7.20–7.23 (m, 2); ^{13}C NMR δ 16.6, 20.4, 21.2, 31.5, 55.4, 78.7, 86.0, 125.3, 127.2, 134.6, 142.3, 147.5, 156.4, 172.7. Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*SR*)-3-Hydroxy-2-methyl-2-(4″-methoxyphenoxy)-3-benzenepropanoate (63e). The general procedure was followed with ester **55** and benzaldehyde to obtain 1.00 g (100%) of a yellow oil. This material was chromatographed (flash) to obtain 0.822 g (82%) of aldol **63e**, mp 68–71 °C, and 0.050 g of the starting material: IR 3550, 1740, 1590 cm^{-1}; ^1H NMR δ 1.26 (s, 9), 1.36 (s, 3), 2.33 (s, 3), 3.65 (d, 1, J = 9 Hz), 3.73 (s, 3), 5.31 (d, 1, J = 9 Hz), 6.94–7.65 (m, 11); ^{13}C NMR δ 21.2, 31.5, 31.6, 35.3, 55.5, 78.0, 85.7, 114.0, 125.4, 127.2, 127.4, 128.1, 128.8, 134.8, 139.3, 142.5, 147.7, 173.0. Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (*RS*)-2-Methoxypropanoate (64). To a solution of 3.91 g (17.74 mmol) of 4-methyl-2,6-di-*tert*-butylphenol in 30 mL of THF was added 17.85 mmol of *n*-BuLi (11.90 mL of a 1.50 M hexane solution) at −70 °C. After 15 min, 2.501 g (20.4 mmol) of 2-methoxypropanoyl chloride[29] was added and the reaction mixture was warmed to room temperature and stirred overnight. The reaction was quenched with saturated NH_4Cl, the layers were separated, and the aqueous phases were extracted with ether. The combined organic layers

were washed with water, $NaHCO_3$, water, and brine, dried ($MgSO_4$), filtered, and evaporated. The residue was filtered through silica, purified by preparative HLPC (4% ether/hexane, R_f 0.13), and distilled (Kugelrohr, 140 °C (0.6 torr)) to give 2.77 g (51%) of a white solid: mp 42–43.5 °C; IR 1770, 1755, 1600 cm^{-1}; ^1H NMR δ 1.00 (s, 18), 1.56 (d, 3, J = 7 Hz), 2.27 (s, 3), 3.50 (s, 3), 4.06 (q, 1, J = 7 Hz), 7.00 (s, 2); MS, 57 (5.79), 59 (8.23), 205 (5.65), 220 (5.14), 306 (0.02). Anal. C, H.

General Procedure for Aldol Addition of Ester 64 with Aldehydes. To a solution of LDA in 7 mL of THF at −70 °C was added 313 mg (1.02 mmol) of ester **64** in 3 mL of THF. After stirring the solution at −70 °C for 1 h, 1.08 mmol of an aldehyde was added, and the mixture was stirred for 15 min and then quenched with saturated NH_4Cl solution. Workup consisted of warming to room temperature, separation of the layers, and ether extraction. The combined organic phases were washed with water, $NaHSO_3$, water, 1% HCl, and brine, dried ($MgSO_4$), filtered, and concentrated with a rotary evaporator.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*SR*)-2,4-Dimethyl-3-hydroxy-2-methoxypentanoate (65). The aldol was obtained in 84% yield after preparative HPLC using 1:9 ether/hexane (R_f 0.29). This material crystallized and was recrystallized from hexane: mp 80 °C; IR 3570, 1745, 1600 cm^{-1}; ^1H NMR δ 0.92 (d, 3, J = 7 Hz), 1.08 (d, 3, J = 7 Hz), 1.03 (s, 18), 1.63 (s, 3), 2.30 (s, 3), 2.63 (d, 1, J = 9 Hz), 3.50 (s, 3), 4.0 (dd, 1, J = 9, 3 Hz), 7.10 (s, 2); ^{13}C NMR δ 15.6, 17.9, 21.2, 22.1, 28.6, 31.3, 35.1, 51.6, 77.4, 82.1, 127.1, 134.5, 142.3. Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenol (2*RS*,3*SR*)-3-Hydroxy-2-methoxy-2-methylbenzenepropanoate (66). The aldol was obtained as crystals in a 91% crude yield. The crude crystals were recrystallized from hexane: mp 114–115 °C; IR 3640, 1740, 1700 cm^{-1}; ^1H NMR δ 1.30 (s, 9), 1.35 (s, 9), 1.45 (s, 3), 2.27 (s, 3), 3.38 (d, 1, J = 8 Hz), 3.50 (s, 3), 5.11 (d, 1, J = 8 Hz), 7.10 (s, 2), 7.25 (m, 5); ^{13}C NMR δ 18.6, 21.3, 31.4, 35.2, 52.4, 77.2, 81.9, 127.1, 127.2, 127.9, 128.7. Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*SR*,4*RS*)-2,4-Dimethyl-3-hydroxy-2-methoxybenzenebutanoate (67). The crystalline aldol, mp 83.5–84.5 °C, was obtained in 59% yield after preparative HPLC using 1:9 ether/hexane (R_f 0.23) as a single compound of greater than 97% isomeric purity, as judged by ^1H and ^{13}C NMR spectroscopy: IR 3550, 1740, 1600 cm^{-1}; ^1H NMR δ (s, 9), 1.03 (s, 9), 1.60 (s, 3), 2.27 (s, 3), 2.83 (d, 1, J = 9 Hz), 3.47 (s, 3), 4.27 (dd, 1, J = 9, 4 Hz), 7.05 (s, 2), 7.20 (s, 5); ^{13}C NMR δ 16.6, 18.6, 21.2, 31.3, 31.4, 35.2, 40.3, 51.8, 77.8, 82.6, 125.9, 127.1, 127.2, 127.4, 127.6, 128.3, 128.4, 134.6, 142.4, 147.2.

(2*SR*,3*SR*)-2-Methoxy-2-methyl-1-phenyl-1,3-propanediol (68). The general procedure for reductions (vide supra) was followed with 50 mg (1.32 mmol) of $LiAlH_4$ in 2 mL of THF and 181 mg (0.44 mmol) of aldol **66** in 1.5 mL of THF. The reaction mixture was heated at reflux overnight and then quenced and worked up in the normal manner to obtain a residue that was purified by column chromatography (1:1 ether/hexane, R_f 0.08) to obtain 86 mg (100%) of a solid. This material was recrystallized from hexane to give material with mp 117–119 °C: ^1H NMR δ 0.93 (s, 3), 2.80 (d, 1, J = 2 Hz), 3.33 (s, 3), 3.50 (m, 2), 4.80 (d, 1, J = 2 Hz), 7.20 (m, 5); ^{13}C NMR δ 13.9, 50.0, 63.6, 76.7, 127.5, 127.8. Anal. C, H.

(2*SR*,3*SR*)-2,4-Dimethyl-2-methoxy-1,3-pentanediol (69). The general reduction pressure was followed with 45.6 mg (1.20 mmol) of $LiAlH_4$ in 2 mL of THF and a solution of 151.6 mg (0.40 mmol) of aldol **65** in 2 mL of THF; the mixture was refluxed for an 18-h period. After the normal workup, there was obtained 151 mg (100%) of a mixture of diol **69** and BHT. Chromatography on 5 g of silica gel with hexanes to remove the BHT, followed by 2:3 EtOAc/hexanes as eluant, gave 52.1 mg (80%) of diol **69** as white needles: mp 61–62.5 °C; ^1H NMR δ 0.94 (d, 3, J = 6.8 Hz), 1.02 (d, 3, J = 6.9 Hz), 1.09 (s, 3), 1.92 (d septet, 1, J = 2.8, 6.8 Hz), 2.52 (d, 1, J = 8.1 Hz), 2.86 (dd, 1, J = 4.3, 7.0 Hz), 3.30 (s, 3), 3.52 (dd, 1, J = 2.8, 8.1 Hz), 3.54 (dd, 1, J = 4.3, 11.9 Hz), 3.77 (dd, 1, J = 7.0, 11.9 Hz). Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*S*,3*R*,4*S*)- and (2*R*,3*S*,4*S*)-2,5-Bis(benzyloxy)-2,4-dimethyl-3-hydroxypentanoates (71a and 72a). Standard aldol addition with 278 mg (0.728 mmol) of ester **39** and 0.175 mL (0.728 mmol) of aldehyde **70a**[35] gave 410 mg of an oil. Purification by preparative TLC (SiO_2, eluant 1:6 ether/hexane, R_f 0.2) gave 250 mg (61%) of a 1:1 mixture of aldols (analysis by ^{13}C and ^1H NMR): IR 3500, 1740, 1595, 1400, 1210, 1170, 1065 cm^{-1}; ^1H NMR δ 0.95 (d, 3, J = 7 Hz), 1.30 (m, 1), 1.37 (s, 9), 1.80 (s, 3), 2.28 (s, 3), 2.65 (d, 1, J = 9 Hz), 3.2–3.6 (m, 2), 4.0–5.0 (m, 5), 7.10 (s, 2), 7.25 (m, 10); ^{13}C NMR δ 10.7, 17.5, 19.1, 21.2, 31.3, 31.6, 34.1, 34.4, 35.1, 66.4, 72.0, 72.3, 72.8, 73.0, 74.1, 78.4, 82.6, 82.9, 126.7, 127.0, 127.3, 127.4, 127.9, 128.1, 128.6, 134.5, 137.9, 138.1, 138.4, 138.5, 142.3, 142.5, 146.5, 172.8, 173.1. Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*S*,3*R*,4*S*)- and (2*R*,3*S*,4*S*)-2-Benzyloxy-3,5-dihydroxy-2,4-dimethylpentanoates 5-*tert*-Butyldiphenylsilyl) Ethers (71b and 72b). Standard aldol addition of BHT ester **39** (304 mg, 0.796 mmol) and aldehyde **70b**[35] (260 mg, 0.796 mmol) gave 589 mg of an oil. Purification by preparative TLC (SiO_2, eluant 1:19 EtOAc/hexane) gave 389 mg (69%) of a mixture of aldols (R_f 0.26, 0.22) in a 1:1 ratio: IR 3500, 1740, 1590 cm^{-1}; ^1H NMR δ 1.03 (m, 3), 1.03 (s, 9), 1.32 (s, 18), 1.58 (s, 3/2), 1.73 (s, 3/2), 2.20 (m, 1), 2.25 (s, 3), 2.65 (d, 1/2, J = 9 Hz), 2.98 (d, 1/2, J = 8 Hz), 3.3–4.1 (m, 2), 4.25–4.95 (m, 3), 7.03 (br s, 4) 7.23 (m, 9), 7.55 (m, 4); ^{13}C NMR δ 10.3, 15.1, 16.8, 18.9, 19.1, 19.5, 21.1, 26.9, 31.4, 31.5, 35.2, 36.7, 65.5, 66.4, 66.5, 67.5, 73.0, 78.1, 82.8, 127.1, 127.5, 127.8, 128.1, 128.7, 128.8, 129.5, 133.6, 133.7, 133.9, 134.5, 135.1, 135.5, 137.7, 138.1, 142.3, 142.6, 172.8, 173.2. Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*SR*,4*RS*)- and (2*SR*,3*RS*,4*RS*)-2-(Benzyloxy)-3-hydroxy-2,4,6-trimethylhept-5-enoate (74 and 75). The standard aldol addition procedure was followed with 1.1 mmol of LDA in 1 mL of THF and 405 mg (1.06 mmol) of ester **39** in 1.5 mL of THF. After 45 min at −78 °C, 133 mg (1.19 mmol) of aldehyde **73**[35,36] was added neat (0.5 mL of THF was used to rinse the syringe). After 20 min at −78 °C, the reaction was quenched by addition of 3 mL of saturated NH_4Cl solution. The normal workup provided 483 mg of the crude aldol, which showed a ratio **74**:**75** = 2.5:1 (^1H NMR). This mixture was separated on 33 g of silica gel (KG 60, 230–400 mesh, 12 × 3 cm) with 95:5 petroleum ether/ether as eluant to give 58.6 mg (11%) of pure **75**, 99.8 mg (19%) of a mixture of **74** and **75**, 129.5 mg (25%) of pure **74**, 46.4 mg (8.8%) of a mixture of **74**, the aldol product from **39**, and the α,β-unsaturated isomer of **73**, and 32.8 mg (6.3%) of the pure latter product, of undefined stereostructure.

Compound **74**, obtained as a viscous, colorless oil: R_f 0.09; IR 3550, 1740, 1600 cm^{-1}; ^1H NMR δ 1.01 (d, 3, J = 6.9 Hz), 1.36 (s, 9), 1.37 (s, 9), 1.61 (s, 3), 1.68 (s, 3), 1.80 (s, 3), 2.32 (s, 3), 2.82 (d, 1, J = 9.9 Hz), 2.88 (m, 1), 4.08 (dd, 1, J = 9.9, 4.0 Hz), 4.68 (d, 1, J = 10.3 Hz), 4.95 (d, 1, J = 10 Hz), 5.26 (dm, 1, J = 9 Hz), 7.15 (s, 2), 7.36 (m, 5). Anal. C, H.

Compound **75**, obtained as a viscous, colorless oil: R_f 0.10; IR 3550, 1740, 1600 cm^{-1}; ^1H NMR δ 1.09 (d, 3, J = 6.9 Hz), 1.35 (s, 9), 1.37 (s, 9), 1.63 (s, 3), 1.65 (s, 3), 1.71 (s, 3), 2.32 (s, 3), 2.86 (d, 1, J = 8.4 Hz), 2.90 (m, 1), 4.14 (dd, 1, J = 8.4, 2.3 Hz), 4.61 (d, 1, J = 10.3 Hz), 4.91 (d, 1, J = 10.2 Hz), 5.32 (d, 1, J = 9 Hz), 7.15 (s, 2), 7.34 (m, 5). Anal. C, H.

(*E*)- or (*Z*)-4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*RS*,3*SR*)-2-(benzyloxy)-3-hydroxy-2,4,6-trimethylhept-4-enoate, obtained as a colorless, viscous oil: R_f 0.07; IR 3550, 1740, 1600 cm^{-1}; ^1H NMR δ 0.99 (d, 6, J = 6.4 Hz), 1.38 (s, 9), 1.40 (s, 9), 1.64 (s, 3), 1.69 (s, 3), 2.33 (s, 3), 2.60 (m, 1), 3.33 (d, 1, J = 9.8 Hz), 4.56 (d, 1, J = 9.5 Hz), 4.60 (d, 1, J = 9.8 Hz), 4.88 (d, 1, J = 10.0 Hz), 5.27 (d, 1, J = 8.9 Hz), 7.16 (s, 2), 7.36 (m, 5). Anal. C, H.

4′-Methyl-2′,6′-di-*tert*-butylphenyl (2*S*,3*R*,4*S*)-(*E*)-2-(Benzyloxy)-2,4-dimethyl-5-ethyl-3-hydroxyhept-5-enoate (77). A solution of 4.06 mmol of LDA in 2.5 mL of THF was prepared in the normal manner. The solution was cooled to −78 °C, and 1.56 g (4.08 mmol) of ester **39** in 2.5 mL of THF (1.0 mL of THF was used to rinse the syringe) was slowly added. After 45 min, 390 mg (3.09 mmol) of neat aldehyde **76**[35] was added (1.0 mL of THF was used to rinse the syringe). The reaction mixture was stirred at −78 °C for 20 min, then quenched with 5 mL of saturated NH_4Cl solution and worked up in the normal manner to obtain 1.91 g of crude product. This material was chromatographed on 100 g of silica gel (KG 60, 230–400 mesh, 12 × 5 cm) with 95:5 petroleum ether/ether to give, after separation of ester **39**, 1.100 g (70%) of pure aldol **77** as a viscous, colorless oil, R_f 0.13, and 86 mg (0.017 mmol) 5.5%, of a mixture of **77** and another isomer (ratio 1:1.2) (most likely a double-bond isomer).

Compound **77**: IR 3560, 1750, 1590 cm^{-1}; ^1H NMR δ 1.03 (t, 3, J = 7.3 Hz), 1.06 (d, 3, J = 7.1 Hz), 1.36 (s, 9), 1.37 (s, 9), 1.62 (dm, 3, J = 6.8 Hz), 1.82 (s, 3), 2.12 (q, 2, J = 7.3 Hz), 2.32 (s, 3), 2.85 (s, 1, J = 10.1 Hz), 3.25 (m, 1), 4.15 (dd, 1, J = 4.2, 10.2 Hz), 4.67 (d, 1, J = 10.5 Hz), 4.92 (d, 1, J = 10.4 Hz), 5.16 (q, 1, J = 6.8 Hz), 7.15 (s, 2), 7.33 (m, 5). Anal. C, H.

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Registry No. *dl*-**3**, 92935-40-5; *dl*-**4**, 74262-60-5; **5a**, 123-38-6; **5b**, 78-84-2; **5c**, 630-19-3; **5d**, 100-52-7; DL-**6b**, 92817-18-0; *dl*-**6e**, 92817-19-1; DL-**7b**, 92817-20-4; *dl*-**7e**, 92817-21-5; DL-**8b**, 74262-61-6; DL-**8c**, 92817-22-6; DL-**8d**, 92817-23-7; *dl*-**8e**, 92817-24-8; DL-**9b**, 74262-62-7; DL-**9c**, 92817-25-9; DL-**9d**, 92817-26-0; *dl*-**9e**, 92900-50-0; *dl*-**10**, 92844-

10-5; *dl*-**11**, 92817-27-1; *dl*-**12**, 92817-28-2; DL-**13b**, 92998-31-7; DL-**13c**, 92935-41-6; DL-**13d**, 92935-42-7; *dl*-**13e**, 92817-29-3; DL-**14b**, 92998-32-8; DL-**14c**, 92935-43-8; DL-**14d**, 92935-44-9; *dl*-**14e**, 92817-30-6; *dl*-**14e** (mesylate), 92817-97-5; *dl*-**15**, 92817-31-7; *dl*-**16**, 92817-32-8; *dl*-**17**, 92935-45-0; *dl*-**18**, 41921-90-8; *dl*-**19**, 92935-46-1; DL-**20b**, 92935-47-2; DL-**20c**, 92935-48-3; DL-**20d**, 92935-49-4; *dl*-**20e**, 92817-33-9; DL-**21b**, 92935-50-7; *dl*-**21e**, 92817-34-0; DL-**22b**, 92998-33-9; DL-**22c**, 92935-51-8; DL-**22d**, 92935-52-9; *dl*-**22e**, 92844-11-6; DL-**23b**, 92936-87-3; DL-**23c**, 92935-53-0; DL-**23d**, 92935-54-1; *dl*-**23e**, 92817-35-1; DL-**24b**, 92935-55-2; DL-**24b** (β-acetate), 92817-99-7; DL-**24b** (α-hydroxy, β-acetate), 92818-01-4; DL-**24c**, 92935-56-3; DL-**24c** (β-acetate), 92817-98-6; DL-**24c** (α-hydroxy, β-acetate), 92818-00-3; DL-**24d**, 92935-57-4; *dl*-**24e**, 92817-36-2; DL-**25b**, 92935-58-5; DL-**25c**, 92935-59-6; DL-**25d**, 92935-60-9; *dl*-**25e**, 92817-37-3; DL-**26c**, 92817-59-9; *dl*-**26e**, 92817-60-2; DL-**27c**, 92817-64-6; *dl*-**27e**, 92844-12-7; **28**, 92817-38-4; (*E*)-**28**, 92818-02-5; *dl*-**29**, 34713-70-7; *dl*-**30**, 64869-28-9; *dl*-**31**, 92935-61-0; *dl*-**32**, 92935-62-1; DL-**33**, 78957-60-5; DL-**33** (7-monoacid), 92818-03-6; DL-**34**, 79026-94-1; DL-**34** (7-monoacid), 92818-04-7; DL-**35**, 92817-39-5; DL-**36**, 92817-40-8; *dl*-**37**, 92817-41-9; *dl*-**38**, 92817-42-0; *dl*-**39**, 92817-43-1; DL-**40a**, 92817-44-2; DL-**40b**, 92817-45-3; DL-**40c**, 92817-46-4; *dl*-**40e**, 92817-47-5; DL-**41a**, 92817-48-6; DL-**41b**, 92817-49-7; DL-**41c**, 92817-50-0; DL-**41d**, 92817-51-1; *dl*-**41e**, 92817-52-2; DL-**42c**, 92817-53-3; *dl*-**42e**, 92817-54-4; DL-**43c**, 92817-55-5; *dl*-**43e**, 92817-56-6; DL-**44a**, 92935-63-2; DL-**44b**, 92935-64-3; DL-**45a**, 92935-65-4; DL-**45b**, 92935-66-5; DL-**45c**, 92935-67-6; *dl*-**45e**, 92817-57-7; DL-**46**, 92817-58-8; DL-**47**, 56709-62-7; DL-**48**, 92817-61-3; DL-**49**, 92817-62-4; DL-**50**, 92817-63-5; *dl*-**51**, 92817-65-7; **52a**, 92817-66-8; **52b**, 92817-67-9; **53a**, 92817-68-0; *dl*-**54**, 92817-69-1; *dl*-**55**, 92817-70-4; **56**, 92817-71-5; **57**, 92817-72-6; **58**, 92817-73-7; **59**, 92817-74-8; DL-**60c**, 92817-75-9; *dl*-**60e**, 92817-76-0; DL-**61c**, 92817-77-1; *dl*-**61e**, 92817-78-2; DL-**62c**, 92817-79-3; DL-**63c**, 92817-80-6; *dl*-**63e**, 92817-81-7; *dl*-**64**, 92817-82-8; DL-**65**, 92817-83-9; *dl*-**66**, 92817-84-0; *dl*-**67**, 92817-85-1; *dl*-**68**, 92817-86-2; DL-**69**, 92817-87-3; **70a**, 79027-28-4; **70b**, 92817-88-4; **71a**, 92817-89-5; **71b**, 92817-90-8; **72a**, 92817-91-9; **72b**, 92817-92-0; *dl*-**73**, 92817-93-1; *dl*-**74**, 92817-94-2; *dl*-**74** ((*E*)-Δ^4 isomer), 92818-06-9; *dl*-**74** ((*Z*)-Δ^4 isomer), 92818-07-0; *dl*-**75**, 92935-68-7; **76**, 92817-95-3; **77**, 92817-96-4; MEMCl, 3970-21-6; DMP, 576-26-1; DIPP, 2078-54-8; BHT, 128-37-0; *i*-PrI, 75-30-9; $MeSO_2Cl$, 124-63-0; *dl*-$CH_3CH(OH)CO_2Et$, 2676-33-7; Ac_2O, 108-24-7; Me_3SiCl, 75-77-4; *dl*-$CH_3CH(OCH_2Ph)COCl$, 74406-96-5; CH_2=$CHCHO$, 107-02-8; *dl*-$CH_3CHBrCO_2H$, 10327-08-9; *dl*-$CH_3CHBrCO_2Na$, 56985-74-1; PhOH, 108-95-2; *dl*-$CH_3CH(OPh)CO_2H$, 1912-21-6; *dl*-$CH_3CH(OMe)COCl$, 23943-97-7; *dl*-$CH_3CH(OPh)COCl$, 84771-76-6; 4-$MeOC_6H_4OH$, 150-76-5; *dl*-$CH_3CH(OC_6H_4$-4-$OMe)CO_2H$, 4276-73-7; *dl*-$CH_3CH(OC_6H_4$-4-$OMe)COCl$, 92818-05-8; 2,2,5-trimethyloxazolidin-4-one, 92935-69-8.

Supplementary Material Available: Experimental details containing stereoscopic ORTEP plots, positional thermal parameters of non-hydrogen atoms, bond lengths, bond angles, and torsion angles for compounds **11**, **45c**, **45e**, **65**, and **66** (36 pages). Ordering information is given on any current masthead page.

Stereochemical Studies of Dioxetane Formation with Hindered Olefins

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Abstract: Two stereoisomeric di-*tert*-butylbis(bicyclo[3.3.1]non-9-ylidenes) (*anti*-**2** and *syn*-**2**) and related hindered olefins were synthesized, and their reactivities and stereochemistries in various dioxetane formations were evaluated. Whereas the singlet oxygenation of a series of three closely related olefins, **1**, **3**, and **4**, gave the corresponding dioxetanes in almost the same reactivity, in the electrode-catalyzed oxygenation the relative reactivities of the three olefins decreased in a ratio 1:0.74:0.06. The singlet oxygenation and 9,10-dicyanoanthracene-sensitized photooxygenation of **2** occurred stereospecifically to yield three stereoisomeric dioxetanes (*cis,trans*-**12**, *cis,cis*-**12**, and *trans,trans*-**12**), while the electrode-catalyzed oxygenation was nonstereospecific. Conclusions dealing with the mechanistic aspects of these reactions are presented and references are made to their possible usefulness in the elucidation of transition-state geometries.

In recent years it has become apparent that several oxygenation reactions do not involve singlet oxygen ($^1O_2$). Dioxetane and endoperoxide, once thought to be products characteristic of a singlet oxygen reaction, were also produced by electron-transfer photooxygenation. Foote[1a-e] first suggested that 9,10-dicyanoanthracene(DCA) sensitizes oxygenation of polyaryl olefins through the intervention of a superoxide anion and the radical cation of substrates to form dioxetanes which finally decompose to carbonyl compounds reminiscent of the singlet oxygen reaction. Subsequently, Barton,[2a-c] Tang,[2e] and Landis[2f] proposed a new route to nonsinglet oxygenation, in which the cation radical of dienes reacts with triplet oxygen and propagates a chain oxidation to form endoperoxide. Examples are trityl cation-photosensitized or Barton's reagent-catalyzed oxygenation of dienes such as ergosteryl acetate and the photosensitized oxygenation of azines. More recently, Nelsen[2g] and Clennan[2h] have reported that the cation radical of adamantylideneadamantane (**1**) could react with triplet oxygen to afford dioxetane.

These observations suggest a number of experiments, especially using sterically hindered olefins such as **1**, in order to elucidate

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