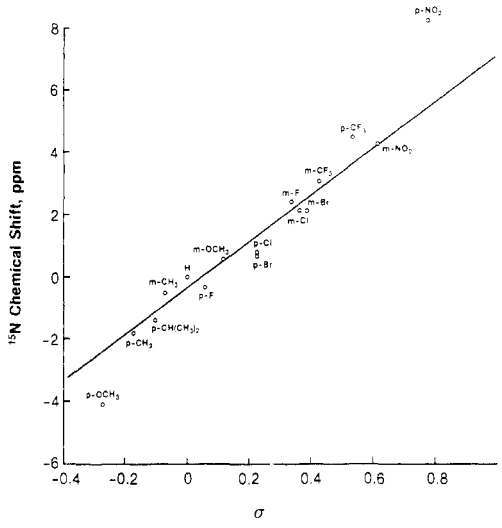

Figure 3. Correlation of the chemical shift of the methyl carbon of NMA's with the Hammett constant, σ; correlation coefficient = 0.954.

produce an upfield shift for that carbon. Alternatively, these small shift differences can be attributed to substituent field effects, as has been proposed to explain the anomalous shift effects in the proton spectra of benzal imines.[14]

The foregoing discussion of the chemical shifts suggests that the NMR properties of the nitrosamine moiety are largely dictated by the unique features of that functional group. These data also suggest that while nitrosamines have to be considered as resonance hybrids, the importance of the two principal canonical forms can be manipulated by appropriate substitution. Various chemical properties, such as the acidity of the α-hydrogens,[15,16] and various biological reactions, such as enzymatic N-demethylation,[9] ought to be influenced by that effect.

Acknowledgment. Research sponsored by the National Cancer Institute, DHHS, under contract No. N01-CO-23909 with Litton Bionetics, Inc. The contents of this publication do not necessarily reflect the views or policies of the Department of Health and Human Services, nor does mention of trade names, commercial products, or organizations imply endorsement by the U.S. Government.

Registry No. 4-Methoxy-*N*-nitroso-*N*-methylaniline, 940-11-4; 4-methyl-*N*-nitroso-*N*-methylaniline, 937-24-6; 4-isopropyl-*N*-nitroso-*N*-methylaniline, 79073-95-3; 3-methyl-*N*-nitroso-*N*-methylaniline, 17485-25-5; *N*-nitroso-*N*-methylaniline, 614-00-6; 4-fluoro-*N*-nitroso-*N*-methylaniline, 937-25-7; 3-methoxy-*N*-nitroso-*N*-methylaniline, 18559-18-7; 4-chloro-*N*-nitroso-*N*-methylaniline, 1007-19-8; 4-bromo-*N*-nitroso-*N*-methylaniline, 937-23-5; 3-fluoro-*N*-nitroso-*N*-methylaniline, 1978-26-3; 3-chloro-*N*-nitroso-*N*-methylaniline, 4243-20-3; 3-bromo-*N*-nitroso-*N*-methylaniline, 17405-06-0; 3-(trifluoromethyl)-*N*-nitroso-*N*-methylaniline, 79073-93-1; 4-(trifluoromethyl)-*N*-nitroso-*N*-methylaniline, 91385-14-7; 3-nitro-*N*-nitroso-*N*-methylaniline, 18600-50-5; 4-nitro-*N*-nitroso-*N*-methylaniline, 943-41-9.

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High Diastereoface Selection in an Ester Enolate Addition to α-Alkoxy Aldehydes: Stereoselective Synthesis of α-Methylene-β-hydroxy-γ-alkoxy Esters[1]

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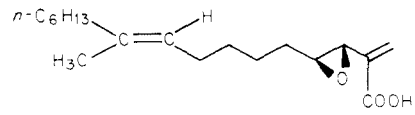
The aldol-type condensation of β-(dimethylamino)propionates **3** and **4** with a series of α-alkoxy aldehydes proceeds with unprecedented high stereoselectivity (up to 24:1) to give anti α-methylene-β-hydroxy-γ-alkoxy esters. The best results were obtained when the reaction was carried out in diethyl ether and the ester enolate was allowed to equilibrate to the thermodynamically more stable geometric isomer.

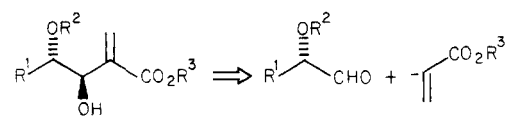
During the course of our studies directed toward the total synthesis of the antibiotic conocandin (**1**),[2] we became



1

interested in developing a method for the stereoselective synthesis of anti[3] (threo)[4] esters of general formula **2**.[5] We thought that the most straightforward way to achieve this goal was an aldol-type condensation between a chiral α-alkoxy aldehyde and a synthetic equivalent of acrylate α-anion (Scheme I).

Scheme I



2

Actually optically pure α-alkoxy aldehydes are easily available in a multigram scale by stereoselective reduction of optically active α-(*p*-tolylsulfinyl)-α-(*p*-tolylthio) ketones.[6] Moreover, condensation of simple metal enolates

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(5) In this paper we use the nomenclature proposed by Masamune:[3] drawing the carbon backbone in a "zig-zag" fashion, the isomer projecting the two substituents either toward or away from the viewer has been defined syn and anti the other one.

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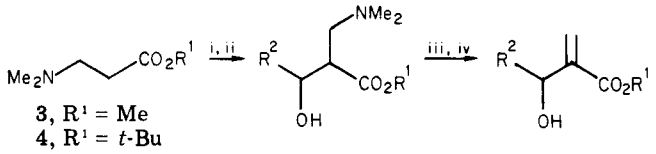
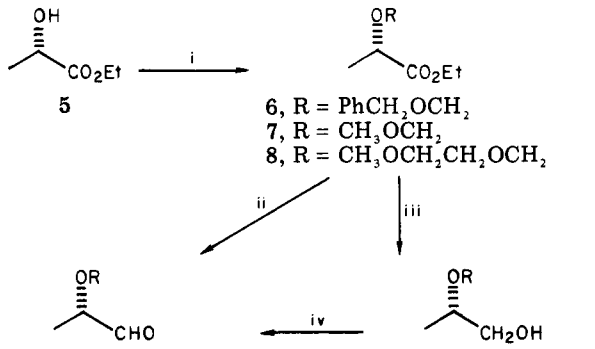
Scheme II[a]



3, R^1 = Me
4, R^1 = *t*-Bu

[a] Reagents: (i) LDA, THF; (ii) R^2CHO, -78 °C; (iii) MeI, MeOH, -15 °C, 20 h; (iv) DBU, acetone, room temperature, 5 h.

Scheme III[a]



5

6, R = $PhCH_2OCH_2$
7, R = CH_3OCH_2
8, R = $CH_3OCH_2CH_2OCH_2$

11, R = $PhCH_2OCH_2$
12, R = CH_3OCH_2
13, R = $CH_3OCH_2CH_2OCH_2$

9, R = $PhCH_2OCH_2$
10, R = CH_3OCH_2

[a] Reagents: (i) RCl, $EtN(i\text{-}Pr)_2$, CH_2Cl_2; (ii) DIBAH, *n*-hexane, -90 °C; (iii) $LiAlH_4$, Et_2O, room temperature; (iv) $CrO_3 \cdot Py_2$, CH_2Cl_2.

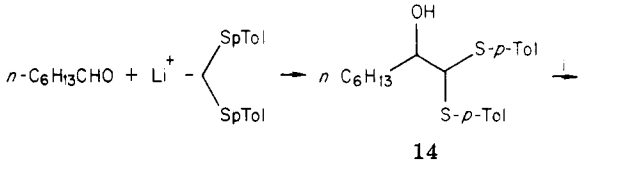
with α-alkoxy aldehydes is known to give predominantly anti adducts,[7,8] although with moderate diastereoface selectivity.

Several metal enolates have been used as synthetic equivalents of acrylate anion in reaction with alkyl halides[9,10] and aldehydes.[11,12] Out of them we chose Helquist's method[10] that involves the reaction of the lithium enolates of β-(dimethylamino)propionates **3** and **4** with electrophiles, followed by N-methylation and base-catalyzed elimination of the resulting quaternary ammonium salt (Scheme II). Although these synthons (which can be very easily prepared from acrylate esters and dimethylamine)[13] had been previously used only in alkylation reactions, preliminary experiments with simple aliphatic aldehydes[14] proved their feasibility also in aldol-type reactions, provided that milder conditions than those described[10] for the methylation–elimination steps were used.

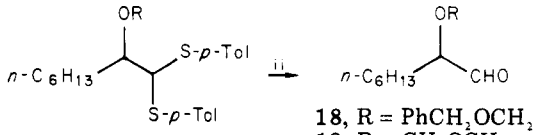
Results and Discussion

In order to carefully assess the stereochemical course of the condensation, we changed several parameters, that is the ester group (R^3 in **2**), the aliphatic residue (R^1), the protective group at the OH (R^2), and last but not least the enolization conditions.

Scheme IV[a]



14

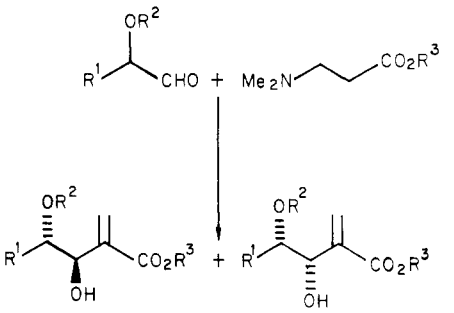


15, R = $PhCH_2OCH_2$
16, R = CH_3OCH_2
17, R = CH_3

18, R = $PhCH_2OCH_2$
19, R = CH_3OCH_2
20, R = CH_3

[a] Reagents: (i) for **15** and **16** RCl, $EtN(i\text{-}Pr)_2$, NaI, CH_2Cl_2, and for **17** NaH, CH_3I, DMF; (ii) for **18** and **19** HgO, $BF_3 \cdot Et_2O$, THF, H_2O, and for **20** $NaHCO_3$, I_2, THF, H_2O.

Scheme V



21, R^1 = Me, R^2 = $PhCH_2OCH_2$, R^3 = Me, **22**
23, R^1 = Me, R^2 = $PhCH_2OCH_2$, R^3 = *t*-Bu, **24**
25, R^1 = Me, R^2 = CH_3OCH_2, R^3 = Me, **26**
27, R^1 = Me, R^2 = CH_3OCH_2, R^3 = *t*-Bu, **28**
29, R^1 = Me, R^2 = $CH_3OCH_2CH_2OCH_2$, R^3 = Me, **30**
31, R^1 = *n*-C_6H_{13}, R^2 = $PhCH_2OCH_2$, R^3 = *t*-Bu, **32**
33, R^1 = *n*-C_6H_{13}, R^2 = CH_3OCH_2, R^3 = Me, **34**
35, R^1 = *n*-C_6H_{13}, R^2 = CH_3OCH_2, R^3 = *t*-Bu, **36**
37, R^1 = *n*-C_6H_{13}, R^2 = Me, R^3 = *t*-Bu, **38**

For this purpose we synthesized two series of α-alkoxy aldehydes **11–13** and **18–20**. O-Protected lactaldehydes **11–13** were prepared in optically active form[15] starting from easily available (-)-(*S*)-ethyl lactate via the O-protected lactates **6–8**[16] (Scheme III). Esters **6–8** were reduced ($LiAlH_4$) to the alcohols and reoxidized with Collins' reagent[17] or directly transformed into the aldehyde using diisobutylaluminium hydride (DIBAH) at low temperature.[18] This last reaction showed a very high chemoselectivity for all tested α-alkoxy esters. Since other similar results recently appeared in the literature,[19] this selective reduction is probably of general application for such substrates.

α-Alkoxy octaldehydes **18–20** were prepared in racemic form from the "masked" α-hydroxy aldehyde **14**, obtained in quantitative yield by condensation of *n*-heptanal with the "formyl anion equivalent" lithium bis(*p*-tolylthio)-methane (Scheme IV). O-Methylation of **14** was realized in a quantitative yield by using NaH/Me I in dimethylformamide (DMF), while methoxymethyl- and (benzyl-

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Table I. Asymmetric Induction in the Condensations between Aldehydes 11–13 and 18–20 and Esters 3 and 4 Preparing the Enolate at −78 °C in THF with LDA[a]

entry	aldehyde	ester	anti:syn ratio[b]	yield,[c] %
1	11	3	65:35	55
2	11	4	80:20	68
3	12	3	77:23	42
4	12	4	83:17	47
5	13	3	65:35	52
6	18	4	79:21	72
7	19	3	73:27	60
8	19	4	82:18	69
9	20	4	80:20	71

[a] Metalation time: 1 h. [b] Determined by GLC except for entry 6 which was determined by ^{1}H NMR. [c] Overall yield of anti and syn compounds after chromatography.

oxy)methyl-protected compounds **16** and **15** were obtained in good yields (96% and 80%) by using the chloro ether, $(i\text{-Pr})_2$NEt,[16] and 1 equiv of anhydrous NaI.[20] Finally, hydrolysis of the thioacetal was performed with $NaHCO_3/I_2$ for the methylated compound **17**[21] (85%) and with HgO and $BF_3\cdot Et_2O$ for **15** and **16**[22] (77 and 83%).

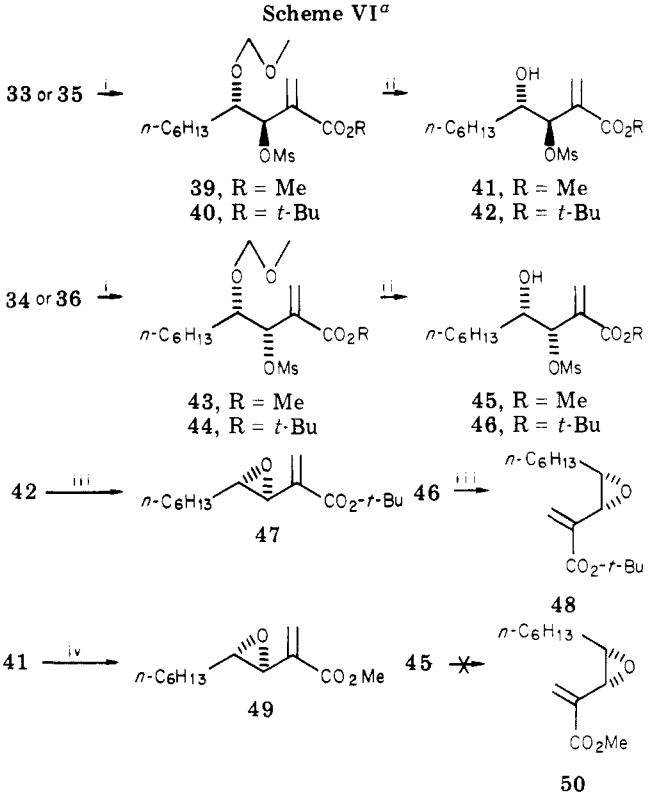
First of all we carried out the condensation of these aldehydes with β-(dimethylamino)propionates **3** and **4** (Scheme V) by using the following procedure: metalation at −78 °C in THF with lithium diisopropylamide (LDA) and condensation at the same temperature for 5 min. The products of the aldol-type reactions were not isolated and were immediately subjected to the methylation-elimination procedure to give mixtures of anti and syn α-methylene-β-hydroxy-γ-alkoxy esters **21–38**. The diastereomeric ratios were determined by GLC on the crude products and confirmed by ^{1}H NMR (200 MHz) on the chromatographed diastereomeric mixtures (see Table I).

O-Silylated aldehydes could not be used because the t-BuPh$_2$Si protecting group was extensively cleaved during the Hofmann elimination step, even operating at low temperatures (−30 °C).

The anti configuration of α-methylene esters **33** and **35** was undoubtedly proved by their transformation into epoxides **49** and **47** (Scheme VI), which were assigned as trans by their characteristic 3,4 proton vicinal coupling constants (2.1 Hz). On the contrary the syn compound **36** gave the *cis*-epoxide **48** with a coupling constant of 4.6 Hz.

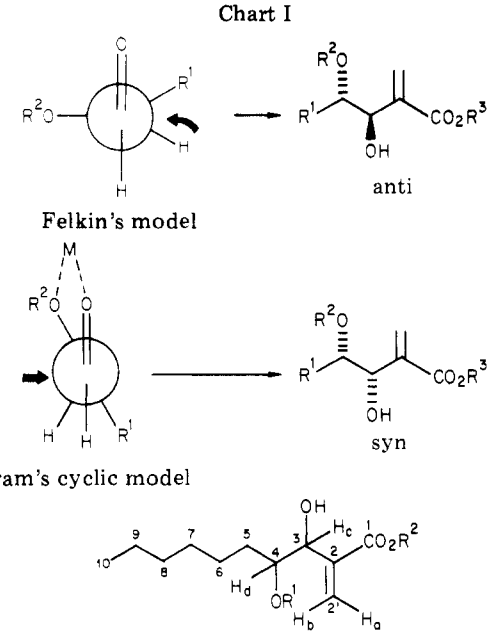
The epoxide ring closure of **41**, **42**, **45**, and **46** was rather difficult. While many attempted procedures (NaH, KH, or CaH_2 in DMF, Me_2SO, or THF; Ph_3CLi in THF; K_2CO_3 in MeOH or MeOH/H_2O; NaOH in MeOH or MeOH/H_2O) failed or gave poor yields, under phase-transfer conditions (40% n-Bu$_4$NOH, CH_2Cl_2),[23] *tert*-butyl esters **42** and **46** could be cyclized in good yield (70–75%) to the respective epoxides. Unfortunately these conditions affected competitive ester hydrolysis when the methyl esters **41** and **45** were employed. Eventually *trans*-epoxide **49** was obtained in 50% yield by using milder conditions (10% n-Bu$_4$NOH, CH_2Cl_2) and very short reaction time (1–2 min), but all attempts to isolate the cis isomer **50** remained unsuccessful. The configuration of the remaining products was assigned by very clear shifts in the ^{13}C and ^{1}H NMR spectra which were very regular all along the series of studied compounds.[24]

Scheme VI[a]



[a] Reagents: (i) MsCl, Et_3N, CH_2Cl_2; (ii) HCl, H_2O, THF; (iii) 40% n-Bu$_4$NOH, CH_2Cl_2; (iv) 10% n-Bu$_4$NOH, CH_2Cl_2.

Chart I



Regarding the stereochemical results reported in Table I, it is interesting to observe the following features: (1) Anti compounds are always preferred. (2) An increase in the steric hindrance of the ester group (R^3) leads to higher stereoselectivities (cf. entry 1 and 2, 3 and 4, and 7 and 8). (3) Although the methoxymethyl group gave the best results, the influence of the protective group does not seem to be very relevant. (4) Very little differences were found passing from the lactaldehydes to α-alkoxy octaldehydes (cf. entries 2 and 6, 3 and 7, and 4 and 8).

The quite general preference for the anti isomer can be explained (see Chart I) assuming that the Felkin's model

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Table II. Asymmetric Induction in the Condensations between Aldehydes 19 and 20 and Ester 4 on Varying the Metalation Conditions[a]

entry	aldehyde	metalation conditions	solvent	anti:syn ratio[b]
1	19	KDA[c]/−78 °C/1 h	THF	55:45
2	19	MgBrDA[d]/ −78 → 0 °C/2 h	THF	73:27
3	19	LDA/−78 °C/1 h	THF	82:18
4	19	LDA/HMPT[e]/ −78 °C/1 h	THF/HMPT	63:37
5	19	LDA/−78 °C/1 h	THF/HMPT[f]	67:33
6	20	LDA/−78 °C/1 h	THF	80:20
7	20	LDA/−30 °C/1 h	THF	87:13
8	20	LDA/0 °C/1 h	THF	88:12
9	20	LDA/−78 → 0 °C/1 h	THF	86:14
10	20	LDA/−30 °C/1 h	Et_2O	92:8
11	20	LDA/0 °C/1 h	Et_2O	93:7
12	20	LDA/0 °C/4 h	Et_2O	96:4
13	20	LDA/0 °C/ $ZrCp_2Cl_2$[g]/2 h	THF	76:24

[a] Condensations were always performed at −78 °C for 5 min. [b] Determined by GLC. [c] KDA = potassium diisopropylamide. [d] MgBrDA = magnesium diisopropylamide, prepared from diisopropylamine and EtMgBr. [e] HMPT = hexamethylphosphoric triamide; 3.75 equiv added before metalation. [f] 3.75 equiv added just before condensation. [g] $ZrCp_2Cl_2$ = bis(cyclopentadienyl)zirconium dichloride.

for asymmetric induction[25] is followed and the alkoxy group plays the role of "large" group. This means that chelation between the metal and the alkoxy oxygen occurs only at a little extent, and the Cram's cyclic model,[26] predicting the syn compound as the major product, is not operating. This explanation was already proposed by Heathcock[7] who also found that diastereoface selection was increased by using protecting groups containing an acetal moiety, such as the (benzyloxy)methyl group. This behavior has been explained on the basis of the reduced basicity of the α-oxygen, caused by the inductive effect of the second oxygen, which disfavors a chelated transition state.

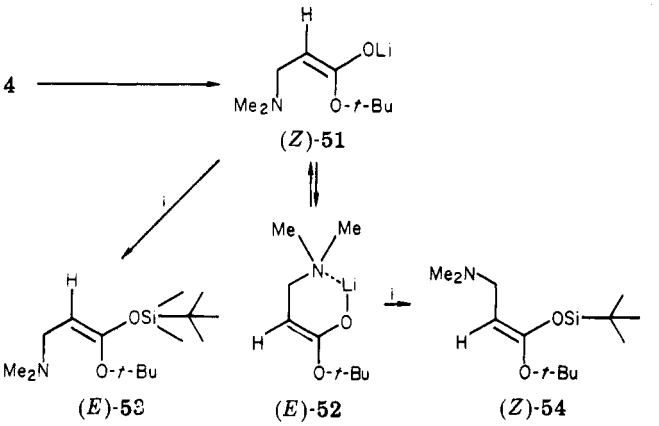
Our results do not seem to agree with the interpretation since, for example, α-methoxy aldehyde **20** gave approximately the same anti–syn ratio as α-(benzyloxy)methoxy aldehyde **18** (entries 6 and 9). It is worth noting that methoxymethyl and methyl protective groups gave the best results.

In order to improve the observed moderate selectivity (ca. 4:1), we changed other factors, like temperature of metalation, counterion, and solvent. The results, listed in Table II show that these parameters have a dramatic influence on the asymmetric induction.

The most interesting points are (1) an increase of the anti:syn ratio when the enolate is formed at higher temperatures and (2) an increase of the stereoselectivity passing from more to less dissociating conditions (i.e., K^+/HMPT vs. Li^+/Et_2O).

One possible explanation may involve an equilibration between the two geometric isomers of the ester enolate (see Scheme VII). It is well-known that esters tend to give the *Z*-enolate (in our case **51**) on kinetic deprotonation with lithium dialkylamides.[27] On heating **51** could equilibrate to the *E*-enolate **52** which is likely to be more stable because of lithium coordination by the dimethylamino group. If the *E*-enolate **52** is more "anti-selective" than its isomer **51**, this equilibration can justify the increased ratio on raising the metalation temperature. This assumption is quite logical considering that a tight intramolecular coordination of lithium in the enolate makes more difficult an intermolecular metal coordination in the transition state following Cram's cyclic model (Chart I). Similarly Masamune has recently observed that intramolecular chelation in the starting enolate strongly disfavors intermolecular chelation during an aldol condensation.[28] This effect, moreover, is expected to be larger in ether than in THF, which could effectively compete with the NMe_2 for coordination sites at lithium.[29]

Scheme VII[a]



[a] Reagents: (i) *t*-$BuMe_2SiCl$, HMPT.

In order to prove the actual existence of this equilibration we quenched the enolates with *tert*-butyldimethylsilyl chloride (TBDMSCl) according to the procedure by Rathke[30] and Ireland[27] to give a mixture of two isomeric silylketene acetals A and B. The A:B ratio, which was 67:33[31] carrying out the deprotonation with LDA at −78 °C in THF, reversed to 14:86 operating in ether at 0 °C for 4 h. Unfortunately we were not able to assign unambigously the *E* or *Z*[32] configurations **53** and **54** to these silylketene acetals. Actually a spectroscopic method to assess stereostructures of this class of compounds is still lacking.[27,33] So we were only able to prove the existence of an equilibration between the two isomeric enolates, but not its direction. Anyway, the mechanism proposed in Scheme VII seems the most probable on the basis of the known preference for *Z*-enolates in kinetic deprotonations by LDA and of the supposed greater stability of *E* isomer **52** in ether solutions.

Conclusion

The high level of asymmetric induction reached in the aldol-type condensation with α-alkoxy aldehydes (24:1) is

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unprecedented and is probably due to the presence in the ester molecule of a β-dimethylamino group. Since optically pure α-alkoxy aldehydes are easily obtained either from natural compounds or via an asymmetric synthesis[6] and since α-methylene-β-hydroxy-γ-alkoxy esters possess several functionalties which can be further elaborated, this stereoselective condensation can be utilized as a key step in the transformation of simple chiral building blocks into more complex natural products.

Experimental Section

^1H NMR spectra were recorded with Varian XL-200 or Bruker WP-80, while ^{13}C NMR spectra were recorded with a Varian XL-100 instruments in the FT mode with tetramethylsilane as internal standard. IR spectra were recorded with a Perkin-Elmer 457 spectrophotometer. Optical rotations were measured in 1-dm cells of 1-mL capacity by using a Perkin-Elmer 141 polarimeter. Mass spectra were recorded with a Varian MAT 112 spectrometer. Elemental analyses were performed with a Perkin-Elmer 240 instrument. Silica gel 60 F_{254} plates (Merck) were used for both analytic and preparative TLC; 70–230 mesh or 270–400 mesh (for "flash chromatography"[34]) silica gel (Merck) or 60–100 mesh Florisil (BDH) was used for column chromatography. GLC analyses were performed on a Carlo-Erba FRACTOVAP 2400 V with a SE-30 10% (3 m) column (for all diastereomeric mixtures except **35**/**36**) or on a Dani 3900 with a capillary OV-1 column (for **35**/**36**) by using a Hewlett-Packard 3390 A integrator. Organic extracts were dried over Na_2SO_4 and filtered before removal of the solvent under reduced pressure. "Dry" solvents were distilled under dry N_2 just before use: diethyl ether and tetrahydrofuran (THF) were distilled from sodium metal in the presence of benzophenone as indicator, *n*-hexane from sodium metal, methanol from magnesium methoxide, CH_2Cl_2, dimethylformamide (DMF), hexamethylphosphoric triamide (HMPT), diisopropylamine, and triethylamine from CaH_2, and acetone from K_2CO_3. All reactions employing "dry" solvents were run under a nitrogen (from liquid N_2) atmosphere. For numbering of carbons and protons in NMR spectra see the general formula **55**.

(*S*)-(−)-Ethyl 2-[(Benzyloxy)methoxy]propanoate (6). A solution of (*S*)-(−)-ethyl lactate **5** (19.5 mL, 0.165 mol) in anhydrous CH_2Cl_2 (100 mL) was treated at 0 °C with chloromethyl benzyl ether (27 mL, 0.19 mol) and diisopropylethylamine (44 mL, 0.24 mol). The solution was stirred overnight at room temperature and then evaporated under reduced pressure to give an oil which was purified by silica gel chromatography (*n*-hexane/ether) to give pure **6** as a colorless liquid (22.6 g, 56%). Anal. Found: C, 65.8; H, 7.9. $C_{13}H_{18}O_4$ requires: c, 65.51; H, 7.62. $[\alpha]_D$ −45.3° (*c* 1.7, 95% ethanol) [lit.[14] −48.3 (*c* 1.73, ethanol)]; ν_{max} ($CHCl_3$) 1740 (C=O), 1270 (acetal), 1175 and 1120 (ester), 905 cm^{-1} (acetal); ^1H NMR δ (80 MHz, $CDCl_3$) 1.24 (3 H, t, *J* = 8 Hz, CH_3CH_2), 1.45 (3 H, d, *J* = 8 Hz, CH_3CH), 4.18 (2 H, q, *J* = 8 Hz, CH_2CH_3), 4.30 (1 H, q, *J* = 8 Hz, $CHCH_3$), 4.65 (2 H, s, CH_2Ph), 4.85 (2 H, s, OCH_2O), 7.33 (5 H, s, Ph*H*).

(*S*)-(−)-Ethyl 2-(Methoxymethoxy)propanoate (7). A solution of (*S*)-(−)-ethyl lactate **5** (9.6 mL, 0.0845 mol) in anhydrous CH_2Cl_2 (120 mL) was treated at 0 °C with freshly distilled chloromethyl methyl ether (10.9 mL, 130 mmol) and diisopropylethylamine (33 mL, 190 mmol), stirred overnight, and then quenched with diluted HCl to pH 1–2. After extraction with CH_2Cl_2 and washing with water to neutrality, the organic phase was distilled (179–181 °C) to give **7** as a colorless liquid (12.45 g, 91%). Anal. Found: C, 51.7; H 8.7. $C_7H_{14}O_4$ requires: C, 51.84; H, 8.7. $[\alpha]_D$ −84.0° (*c* 1.6, $CHCl_3$); ν_{max} ($CHCl_3$) 1735 (C=O), 1270 (acetal), 1160 and 1120 (ester), 915 (acetal); ^1H NMR δ (80 MHz, $CDCl_3$) 1.28 (3 H, t, *J* = 7 Hz, CH_3CH_2), 1.43 (3 H, d, *J* = 7 Hz, CH_3CH), 3.40 (3 H, s, CH_3O), 4.20 (3 H, q, *J* = 7 Hz, $CHCH_3$ and CH_2CH_3), 4.70 (2 H, s, OCH_2O); MS, *m*/*z* 161 ($M^+ - 1$, 0.35), 131 (10.7), 118 (11.0), 103 (14.5), 102 (12.6), 89 (100), 88 (72.4), 59 (40.0).

(*S*)-(−)-Ethyl 2-[(2-Methoxyethoxy)methoxy]propanoate (8). This compound was prepared from (*S*)-(−)-ethyl lactate and (methoxyethoxy)methyl chloromethyl ether (MEM-Cl) with the same procedure employed for **7**. Distillation under reduced pressure [120–122 °C (20 mmHg)] gave **8** as a colorless liquid (78%). Anal. Found: C, 52.0; H, 8.65. $C_9H_{18}O_5$ requires: C, 52.41; H, 8.80. $[\alpha]_D$ −64.0° (*c* 1, $CHCl_3$); ν_{max} 1740 (C=O), 1180–1100 and 910 cm^{-1} (acetal); ^1H NMR δ (80 MHz, $CDCl_3$) 1.29 (3 H, t, *J* = 7 Hz, CH_3CH_2), 1.43 (3 H, d, *J* = 8 Hz, CH_3CH), 3.38 (3 H, s, OCH_3), 3.40–3.93 (4 H, m, CH_2CH_2), 4.20 (2 H, q, *J* = 7 Hz, CH_2CH_3), 4.25 (1 H, q, *J* = 8 Hz, $CHCH_3$), 4.81 (2 H, s, OCH_2O); MS, *m*/*z* 131 ($M^+ - 75$, 11.8), 89 (100), 59 (98), 45 (35.3).

(*S*)-(+)-2-[(Benzyloxy)methoxy]propan-1-ol (9). To a suspension of $LiAlH_4$ (3.8 g, 100 mmol) in anhydrous tetrahydrofuran (THF) (100 mL) was added dropwise a solution of **6** (22.4 g, 94 mmol) in the same solvent (150 mL). After 10 min the reaction was complete. The mixture was treated sequentially with ethyl acetate (7.7 mL, 100 mmol) and 10% aqueous KOH (22.5 mL) and then stirred for 30 min. The precipitate was filtered off and washed with ether, and the filtrate evaporated under reduced pressure to give pure **9** as a liquid (18.2 g, 99%). Anal. Found: C, 67.6; H, 8.35. $C_{11}H_{16}O_3$ requires: C, 67.30; H,. 8.22. $[\alpha]_D$ +2.71° (*c* 1.9, 95% ethanol); ν_{max} ($CHCl_3$) 3660–3440 (OH), 1160 and 1140 (acetal), 1030 (C–OH), 900 cm^{-1} (acetal); ^1H NMR δ (80 MHz, $CDCl_3$) 1.18 (3 H, d, *J* = 7 Hz, CH_3CH), 2.70 (1 H, broad s, OH), 3.51 (2 H, d, *J* = 6 Hz, CH_2OH), 3.69 (1 H, dt, *J* = 7, 6 Hz, $CHCH_3$), 4.67 (2 H, s, CH_2Ph), 4.85 (2 H, s, OCH_2O), 7.38 (5 H, s, Ph*H*); MS, *m*/*z* 166 ($M^+ - 30$, 2.7), 165 (3.8), 152 (2.7), 151 (2.2), 135 (13.1), 120 (25.7), 108 (21.9), 107 (24.8), 92 (43.8), 91 (100), 77 (11.0).

(*S*)-(+)-2-(Methoxymethoxy)propan-1-ol (10). This compound was prepared from **7** (3.95 g, 24.4 mmol) as described for **9** in 98% yield (2.87 g). Anal. Found: C, 49.6; H, 10.2. $C_5H_{12}O_3$ requires: C, 49.98; H, 10.07. $[\alpha]_D$ +18.7° (*c* 1.7, $CHCl_3$); ν_{max} ($CHCl_3$) 3680–3440 (OH), 1260 (acetal), 1030 (C–OH), 860 cm^{-1} (acetal); ^1H NMR δ (80 MHz, $CDCl_3$) 1.17 (3 H, d, *J* = 7 Hz, CH_3CH), 2.16 (1 H, s, OH), 3.43 (3 H, s, CH_3O), 3.46 (2 H, d, *J* = 6 Hz, CH_2OH), 3.43–3.97 (1 H, m, $CHCH_3$), 4.72 (2 H, s, OCH_2O); MS, *m*/*z* 90 ($M^+ - 30$, 65.4), 89 (29.0), 77 (71.8), 58 (38.5), 43 (100).

(*S*)-(−)-2-[(Benzyloxy)methoxy]propan-1-al (11). (i) From 9. A solution of **10** (2 g, 10 mmol) in anhydrous CH_2Cl_2 (50 mL) was added to a solution of Collins' reagent[17] (16 g, 42.5 mmol) in the same solvent (150 mL) at 0 °C. After 30 min the mixture was filtered through a silica gel column (30 g) eluted with ether to give, after evaporation under reduced pressure to dryness, **11** as a colorless liquid (1.68 g, 86%). **(ii) From 6.** A solution of **6** (2.84 g, 11.90 mmol) in anhydrous *n*-hexane (45 mL) was treated at −90 °C with a solution of 20% diisobutylaluminium hydride in *n*-hexane (12.1 mL, 12.1 mmol). After 10 min the reaction was quenched with saturated aqueous NH_4Cl, diluted with ether, and filtered through a Celite cake. The organic phase was separated and evaporated under reduced pressure to give a crude product which was purified by "flash" chromatography[34] (*n*-hexane/AcOEt) (2.26 g, 80%). Anal. Found: C, 67.75; H, 7.35. $C_{11}H_{14}O_3$ requires: C, 68.00; H, 7.27. $[\alpha]_D$ −13.4° (*c* 1.6, $CHCl_3$); ν_{max} ($CHCl_3$) 2720 (O=C—H), 1730 (C=O), 1190, 1170, and 900 cm^{-1} (acetal); ^1H NMR δ (80 MHz, $CDCl_3$) 1.23 (3 H, d, *J* = 7 Hz, CH_3CH), 4.05 (1 H, dq, *J* = 7, 1.4 Hz, CH–O), 4.60 (2 H, s, CH_2Ph), 4.78 (2 H, s, OCH_2O), 7.30 (5 H, s, Ph*H*), 9.63 (1 H, d, *J* = 1.4 Hz, O=C—H); MS, *m*/*z* 194 (M^+, 0.04), 165 (4.3), 164 (5.4), 135 (28.6), 120 (9.8), 107 (27.7), 92 (35.7), 91 (100), 77 (9.8).

(*S*)-(−)-2-(Methoxymethoxy)propan-1-al (12). It was prepared as already described for **11** either by Collins' oxidation of **10** or by diisobutylaluminium hydride reduction of ester **7**. In both cases the crude product was purified by distillation [bp 90 °C (23 mmHg)] to give pure **12** in 45% and 38% yield, respectively. Anal. Found: C, 50.6; H, 8.25. $C_5H_{10}O_3$ requires: C, 50.83; H, 8.53. $[\alpha]_D$ −12.6° (*c* 1.6, $CHCl_3$); ν_{max} ($CHCl_3$) 2720 (O=C—H), 1730 (C=O), 1240, 1030, and 915 (acetal); ^1H NMR δ (80 MHz, $CDCl_3$) 1.37 (3 H, d, *J* = 7.2 Hz, CH_3CH), 3.40 (3 H, s, CH_3O), 4.03 (1 H, dq, *J* = 7.2, 1.4 Hz, $CHCH_3$), 4.73 (2 H, s, OCH_2O), 9.67 (1 H, d, *J* = 1.4 H—C=O); MS, *m*/*z* 117 ($M^+ - 1$, 1.0), 103 (1.2), 89 (100), 87 (14.7), 74 (3.1), 61 (11.8), 59 (24.3), 58 (16.2), 57 (47.3).

(*S*)-(−)-2-[(2-Methoxyethoxy)methoxy]propan-1-al (13). It was prepared, as described for **11**, by diisobutylaluminium hydride reduction of ester **8** (4.2 g, 20.4 mmol) to give a crude product which was purified by "flash" chromatography[34] (ether/acetone 95:5) (1.9 g, 46%). Anal. Found: C, 51.3; H, 8.8.

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$C_7H_{14}O_4$ requires: C, 51.84; H, 8.70. $[\alpha]_D$ - 12.1° (c 1.0, $CHCl_3$); ν_{max} ($CHCl_3$) 2800 (O=C—H), 1735 cm^{-1} (C=O); ^1H NMR δ (80 MHz, $CDCl_3$) 1.30 (3 H, d, J = 6 Hz, CH_3CH), 3.40 (1 H, s, OCH_3), 3.40–3.90 (4 H, m, CH_2CH_2), 4.10 (1 H, dq, J = 6, 2 Hz, $CHCH_3$), 4.81 (2 H, s, OCH_2O), 9.70 (1 H, d, J = 2 Hz, O=C—H); MS, m/z 162 (M^+, 0.17), 161 (0.25), 133 (5.1), 131 (5.5), 105 (14.7), 103 (14.0), 89 (83.0), 87 (52.1), 73 (26.1), 59 (100), 57 (62.3), 45 (70.1).

1,1-Bis(*p*-tolylthio)octan-2-ol (14). To a solution of bis(*p*-tolylthio)methane[35] (38.7 g, 0.149 mmol) in anhydrous tetrahydrofuran (300 mL) was slowly added at 0 °C a 1.63 N solution of *n*-butyllithium in *n*-hexane (100 mL, 0.163 mol). The resulting solution was stirred for 1 h at 0 °C, cooled to -78 °C, treated with freshly distilled *n*-heptanal (25 mL, 179 mmol), stirred for 30 min at the same temperature, and finally quenched with saturated aqueous NH_4Cl. After extraction with ether, the organic phases were evaporated to dryness to give a crude product which was purified by silica gel (700 g) chromatography (*n*-hexane/AcOEt) to give pure **14** as an oil (54.1 g, 98%). Anal. Found: C, 70.9; H, 8.3. $C_{22}H_{30}OS_2$ requires: C, 70.59; H, 8.07. ν_{max} (neat) 3450 (OH), 1090 (C–O), 720, 700 cm^{-1} (C–S); ^1H NMR δ (80 MHz, $CDCl_3$) 0.85 (3 H, t, J = 6 Hz, CH_3CH_2), 1.05–1.70 (10 H, m, CH_2), 2.35 (6 H, s, CH_3–Ar), 2.75 (1 H, broad s, OH), 3.77 (1 H, q, J = 4 Hz, CHOH), 4.35 (1 H, d, J = 4 Hz, SCHS), 7.12 (4 H, d, J = 8.4 Hz, H ortho to CH_3Ar), 7.36 and 7.38 (2 × 2 H, 2d, J = 8.4 Hz, H meta to CH_3Ar); MS, m/z 374 (M^+, 3.7), 280 (6.1), 260 (12.2), 259 (5.8), 251 (57.8), 246 (5.0), 233 (7.3), 137 (100), 123 (29.7), 109 (28.1), 91 (34.4).

1,1-Bis(*p*-tolylthio)-2-[(benzyloxy)methoxy]octane (15). A solution of **14** (10 g, 26.7 mmol) and anhydrous NaI (16 g, 107 mmol) in anhydrous CH_2Cl_2 (100 mL) was treated with diisopropylethylamine (27.7 mL, 160 mmol) and with freshly distilled chloromethyl benzyl ether (15 mL, 107 mmol). The mixture was stirred for 2 days at room temperature, quenched with water, extracted with CH_2Cl_2, and evaporated to dryness to give a crude oil which is purified by "flash" chromatography[34] (*n*-hexane/AcOEt 96:4) (10.6 g, 80%). Anal. Found: C, 72.85; H, 7.7. $C_{30}H_{38}O_2S_2$ requires: C, 72.83; H, 7.74. ν_{max} (neat) 1100, 1040, and 905 (C–O), 735 and 700 cm^{-1} (C–S); ^1H NMR δ (80 MHz, $CDCl_3$) 0.88 (3 H, t, J = 6 Hz, CH_3CH_2), 1.05–1.70 (10 H, m, $(CH_2)_5$), 2.33 (6 H, s, CH_3Ar), 3.80–4.17 (1 H, m, CH–O), 4.58–4.77 (1 H, m, SCHS), 4.67 (2 H, s, CH_2Ph), 4.88 (2 H, s, OCH_2O), 6.33–7.60 (13 H, m, ArH); MS, m/z 494 (M^+, 6.4), 371 (1.7), 341 (100), 260 (91), 259 (64), 235 (13), 233 (27), 214 (59), 167 (11), 165 (10), 157 (82), 138 (91), 123 (73), 121 (25), 108 (14), 107 (77), 91 (92), 77 (50).

1,1-Bis(*p*-tolylthio)-2-(methoxymethoxy)octane (16). It was synthesized as described for **15** starting from **14** (5.4 g, 14.4 mmol) and freshly distilled chloromethyl methyl ether. Purification was performed by chromatography on silica gel (200 g) (*n*-hexane/AcOEt 9:1) (5.8 g, 97%). Anal. Found: C, 68.75; H, 8.25. $C_{24}H_{34}O_2S_2$ requires: C, 68.85; H, 8.19. ν_{max} (neat) 1150, 1100, and 915 (C–O), 720 cm^{-1} (C–S); ^1H NMR δ (80 MHz, $CDCl_3$) 0.90 (3 H, t, J = 6 Hz, CH_3CH_2), 1.10–1.67 (10 H, m, $(CH_2)_5$), 2.30 (6 H, s, CH_3Ar), 3.40 (3 H, s, OCH_3), 3.67–4.00 (1 H, m, CH–O), 4.57 (1 H, d, J = 2.0 Hz, SCHS), 4.70 (2 H, s, OCH_2O), 7.10 (4 H, d, J = 8.0 Hz, H ortho to CH_3Ar), 7.70 (4 H, d, J = 8.0 Hz, H meta to CH_3Ar); MS, m/z 418 (M^+, 2.5), 295 (23.5), 265 (24.7), 263 (23.4), 259 (18.5), 179 (45.7), 197 (100), 124 (24.7), 91 (23.5).

1,1-Bis(*p*-tolylthio)-2-methoxyoctane (17). NaH (55% dispersion in mineral oil) (1.855 g, 43 mmol) was washed three times, by decantation, with anhydrous *n*-hexane. A solution of **14** (10.6 g, 28 mmol) in anhydrous dimethylformamide (280 mL) was then added at 0 °C and the resulting mixture stirred for 30 min at room temperature, treated with methyl iodide (3.53 mL, 56.7 mmol), and stirred for 10 min more. After the reaction was quenched with water and extracted with ether, the crude product was purified by silica gel chromatography (*n*-hexane/ether) (10.7 g, 100%). Anal. Found: C, 70.8; H, 8.45. $C_{23}H_{32}OS_2$ requires: C, 71.08; H, 8.30. ν_{max} ($CHCl_3$) 1465, 1380, 1110, 720 cm^{-1}; ^1H NMR δ (80 MHz, $CDCl_3$) 0.83 (3 H, t, J = 6 Hz, CH_3CH_2), 0.99–1.49 (10 H, m, $(CH_2)_5$), 2.26 (3 H, s, CH_3Ar), 3.30 (3 H, s, CH_3O), 3.50–3.85 (1 H, m, CHOMe), 4.40 (1 H, d, J = 2 Hz, SCHS), 7.00–7.43 (8 H, m, ArH).

(35) Corey, E. J.; Seebach, D. *J. Org. Chem.* **1966**, *31*, 4097.

2-[(Benzyloxy)methoxy]octan-1-al (18). A suspension of yellow HgO (3.1 g, 14.3 mmol) in tetrahydrofuran/water 85:15 (187 mL) was treated with freshly distilled $BF_3{\cdot}Et_2O$ (1.8 mL, 14.6 mmol) and then with a solution of **15** (5.1 g, 10.3 mmol) in the minimum quantity of tetrahydrofuran. After 1 h the reaction was quenched with saturated aqueous $NaHCO_3$ to pH 8. After the reaction was extracted with CH_2Cl_2 and washed with water to neutrality, the organic phase was evaporated under reduced pressure to dryness, taken up with ether, and filtered or centrifugated to eliminate most of the mercuric salts. This crude product was then filtered through a column of Florisil eluted with ether and further purified by "flash" chromatography[34] (*n*-hexane/AcOEt 88:12) to give **18** (2.1 g, 77%). Anal. Found: C, 72.8; H, 8.95. $C_{16}H_{24}O_3$ requires: C, 72.69; H, 9.15. ν_{max} (neat) 2810 (O=C—H), 1730 (C=O), 1100, 1040, and 905 cm^{-1} (C–O); ^1H NMR δ (80 MHz, $CDCl_3$) 1.00 (3 H, t, J = 6 Hz, CH_3), 1.17–2.00 (10 H, m, $(CH_2)_5$), 4.02 (1 H, dt, J = 6, 2 Hz, CH–O), 4.73 (2 H, s, OCH_2Ph), 4.87 (2 H, s, OCH_2O), 7.43 (5 H, s, ArH), 9.75 (1 H, d, J = 2 Hz, O=C—H); MS, m/z 264 (M^+, 0.2), 246 (8.3), 180 (4.5), 165 (1.0), 157 (10.0), 138 (30.0), 127 (100), 121 (95.0), 91 (99.0), 85 (22.0), 77 (78.0).

2-(Methoxymethoxy)octan-1-al (19). It was prepared like **18** starting from **16** (2 g, 4.78 mmol). Pure **19** can be obtained either via the procedure above described (750 mg, 83%) or by bulb-to-bulb distillation (10 mmHg) (oven temperature 120 °C) (633 mg, 70%). The latter method gave purer samples. Anal. Found: C, 63.85; H, 10.6. $C_{10}H_{20}O_3$ requires: C, 63.78; H, 10.71. ν_{max} (neat) 2810 (O=C—H), 1730 (C=O), 1210, 1030, and 915 cm^{-1} (C–O); ^1H NMR δ (80 MHz, $CDCl_3$) 0.87 (3 H, t, J = 6 Hz, CH_3CH_2), 1.17–1.83 (10 H, m, $(CH_2)_5$), 3.47 (3 H, s, OCH_3), 3.85 (1 H, dt, J = 5.4, 2.0 Hz, CH–O), 4.77 (2 H, s, OCH_2O), 9.73 (1 H, d, J = 2.0 Hz, O=C—H); MS, m/z 159 (M^+ - 29, 10.6), 157 (1.7), 129 (15.2), 55 (8.6), 45 (100).

2-Methoxyoctan-1-al (20). A solution of **17** (9 g, 23 mmol) in THF/H_2O 85:15 (200 mL) was treated with iodine (11.8 g, 46 mmol) and $NaHCO_3$ (3.5 g, 42 mmol). The reaction was stirred for 30 min and then a second portion of iodine (11.8 g) and $NaHCO_3$ (3.5 g) was added. The treatment was repeated again after 30 min and the reaction stirred for 1 h more, diluted with water, and extracted with CH_2Cl_2. Evaporation to dryness under reduced pressure gave an oil which was purified by bulb-to-bulb distillation [40 °C (0.1 mmHg)] to give pure **20** (3.09 g, 85%). Anal. Found: C, 68.25; H, 11.4. $C_9H_{18}O_2$ requires: C, 68.31; H, 11.46. ν_{max} ($CHCl_3$) 1735, 1465, 1380, 1110 cm^{-1}; ^1H NMR δ (80 MHz, $CDCl_3$) 0.93 (3 H, t, J = 6 Hz, CH_3CH_2), 1.06–1.85 (10 H, m, $(CH_2)_5$), 3.48 (3 H, s, CH_3O), 3.48–3.63 (1 H, m, CH_3OCH), 9.63 (1 H, d, CH=O, J = 2.6 Hz).

Synthesis of α-Methylene-β-hydroxy-γ-alkoxy Esters 21–38. General Procedure. To a solution of a base (see Tables I and II) (1.5 mmol) in anhydrous tetrahydrofuran or ether (0.5 mL) were added the esters **3** or **4** at the proper temperature (see tables). The solution was stirred for the requested time and then cooled to -78 °C. A solution of the α-alkoxy aldehyde (1 mmol) in tetrahydrofuran or ether (0.2 mL) was added and, after 5 min, the solution was treated with a solution of CH_3COOH in the same solvent. The organic phase was extracted with ether and evaporated under reduced pressure to give an oil which was dissolved in anhydrous MeOH (0.42 mL), cooled to -15 °C, and treated with methyl iodide (5.8 mmol). The mixture was stirred overnight at -15 °C and 5 h at room temperature. The solvent was evaporated under reduced pressure (bath temperature 30 °C) to give a crude solid which was taken up in anhydrous acetone (1.5 mL) and treated with 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) (1.8 mmol). The mixture was stirred for 5 h at room temperature, quenched with saturated aqueous NH_4Cl, and extracted with CH_2Cl_2 after removal under reduced pressure of acetone. The organic extracts were evaporated to give a crude oil which was analyzed by GLC (see Tables I and II). Purification by "flash" chromatography[34] (*n*-hexane/AcOEt) furnished the pure diastereomeric mixtures. In the case of **21–22** and **23–24**, pure **21** and **23** were obtained by a second chromatographic separation. Full spectroscopic and analytical data for these compounds, including ^{13}C spectra, are reported in the supplementary material.

Methyl 2-Methylene-3-(mesyloxy)-4-(methoxymethoxy)-decanoates (39 and 43). A 73:27 mixture of **33** and **34** (685 mg, 2.5 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL), cooled

to 0 °C, and treated with freshly distilled mesyl chloride (0.39 mL, 5.0 mmol) and with anhydrous Et_3N (0.7 mL, 5.0 mmol). The resulting solution was stirred for 15 min and then quenched with saturated aqueous NH_4Cl. The phases were separated and the aqueous layer extracted twice with ether. The organic extracts, evaporated under reduced pressure, gave a crude product which was purified by "flash" chromatography[34] to give pure **39** (516 mg, 59%) and **43** (199 mg, 20%).

***tert*-Butyl 2-Methylene-3-(mesyloxy)-4-(methoxymethoxy)decanoates (40 and 44).** They were prepared as described above for **39** and **43**. If an 82:18 mixture of **35** and **36** (1.20 g, 3.79 mmol) was used, pure **40** (895 mg, 60%) and **44** (225 mg, 15%) were obtained.

Methyl 2-Methylene-3-(mesyloxy)-4-hydroxydecanoates (41 and 45). A solution of **39** or **43** (175 mg, 0.5 mmol) in tetrahydrofuran (10 cc) was treated with concentrated aqueous HCl (2 cc) and stirred for 1 h at room temperature. After neutralization with $NaHCO_3$ and extraction with ether, evaporation of the solvent under reduced pressure gave an oil which was purified by "flash" chromatography[34] (*n*-hexane/AcOEt) to afford pure **41** (97 mg, 63%) or **45** (108 mg, 70%).

***tert*-Butyl 2-Methylene-3-(mesyloxy)-4-hydroxydecanoates (42 and 46).** A solution of **40** or **44** (50 mg, 0.127 mmol) in tetrahydrofuran (2.5 mL) was treated with concentrated aqueous HCl (0.82 mL), stirred for 2 h at room temperature, and then neutralized with a pH 7 posphate buffer solution. Extraction with ether and evaporation of the solvent under reduced pressure gave an oil which was purified by "flash" chromatography[34] (*n*-hexane/AcOEt) to give pure **42** (33 mg, 75%) or **46** (32 mg, 73%).

***tert*-Butyl 2-Methylene-3,4-epoxydecanoates (47 and 48).** To a solution of NaOH (140 mg, 3.5 mmol) in water (1 mL), solid $(n\text{-}Bu_4N)HSO_4$ was added (92 mg, 0.27 mmol), and the solution was stirred for 30 min at room temperature. A solution of **42** or **46** (56 mg, 0.16 mmol) in CH_2Cl_2 (1 mL) was then added. After 7 min the mixture was diluted with CH_2Cl_2 and the organic phase was separated, washed with saturated aqueous NH_4Cl, and evaporated to dryness under reduced pressure to give a crude product which was purified by preparative TLC (*n*-hexane/AcOEt 9:1) to afford pure **47** (30 mg, 75%) or **48** (27 mg, 66%). Anal. Found **47**: C, 70.6; H, 10.4. **48**: C, 70.55; H, 10.4. $C_{15}H_{26}O_3$ requires: C, 70.83; H, 10.30. ^1H NMR δ (80 MHz, $CDCl_3$) **47** 0.88 (3 H, t, J = 5.8 Hz, CH_3CH_2), 1.20–1.80 (10 H, m, $(CH_2)_5$), 1.51 (9 H, s, $C(CH_3)_3$), 2.68 (1 H, dt, J = 2.2, 4.8 Hz, H_d), 3.44 (1 H, dd, J = 2.2, 1.2 Hz, H_c), 5.67 (1 H, t, J = 1.2 Hz, H_b), 6.12 (1 H, d, J = 1.2 Hz, H_a); **48** 0.88 (3 H, t, J = 5.8 Hz, CH_3CH_2), 1.20–1.80 (10 H, m, $(CH_2)_5$), 1.51 (9 H, s, $C(CH_3)_3$), 3.14 (1 H, dt, J = 4.6, 5.5 Hz, H_d), 3.77 (1 H, dd, J = 4.6, 1.2 Hz, H_c), 5.67 (1 H, t, J = 1.2 Hz, H_b), 6.30 (1 H, d, J = 1.2 Hz, H_a); ^{13}C NMR δ (100 MHz, $CDCl_3$) **47** 164.6 (C-1), 139.2 (C-2), 122.9 (C-2′), 81.2 ($C(CH_3)_3$), 62.8 (C-3), 55.2 (C-4), 32.2 (C-5), 31.8 (C-8), 29.1 (C-7), 28.1 ($C(CH_3)_3$), 26.0 (C-6), 22.6 (C-9), 14.0 (C-10); **48** 164.6 (C-1), 139.3 (C-2), 125.7 (C-2′), 81.2 ($C(CH_3)_3$), 59.0 (C-3), 55.4 (C-4), 31.8 (C-8), 29.1 (C-7), 28.1 ($C(CH_3)_3$), 26.4 (C-5), 25.8 (C-6), 22.6 (C-9), 14.0 (C-10).

Methyl 2-Methylene-3,4-epoxydecanoate (49). To a solution of NaOH (28 mg, 0.7 mmol) in water (1 mL), was added solid $(n\text{-}Bu_4N)HSO_4$ (48 mg, 0.14 mmol), and the solution was stirred for 30 min at room temperature. A solution of **41** (49 mg, 0.16 mmol) in CH_2Cl_2 (1 mL) was added. The resulting mixture was stirred for 1–2 min at room temperature, and after dilution with CH_2Cl_2, the organic phase was suddenly separated and washed with saturated aqueous NH_4Cl. Evaporation to dryness and purification through preparative TLC (*n*-hexane/AcOEt 9:1) gave pure **49** (17 mg, 50%). Anal. Found: C, 67.95; H, 9.55. $C_{12}H_{20}O_3$ requires: C, 67.89; H, 9.50. ^1H NMR δ (80 MHz, $CDCl_3$) 0.90 (3 H, t, J = 6.5 Hz, CH_3CH_2), 1.10–1.80 (10 H, m, $(CH_2)_5$), 2.68 (1 H, dt, J = 2.1, 5.3 Hz, H_d), 3.49 (1 H, dd, J = 1.2, 2.1 Hz, H_c), 3.79 (3 H, s, OCH_3), 5.75 (1 H, t, J = 1.2 Hz, H_b), 6.21 (1 H, d, J = 1.2 Hz, H_a).

NMR of 1-[(dimethyl-*tert*-butylsilyl)oxy]-1-*tert*-butoxy-3-(dimethylamino)propenes (53 and 54): ^1H NMR δ (80 MHz, $CDCl_3$) A (see Results and Discussion) 0.19 (6 H, s, CH_3Si), 0.91 (9 H, s, $(CH_3)_3CSi$), 1.32 (9 H, s, $(CH_3)_3CO$), 2.22 (6 H, s, $N(CH_3)_2$), 2.90 (2 H, d, J = 7 Hz, CH_2N), 3.96 (1 H, t, J = 7 Hz, CH); B 0.15 (6 H, s, CH_3Si), 0.91 (9 H, s, $(CH_3)_3CSi$), 1.34 (9 H, s, $(CH_3)_3CO$), 2.22 (6 H, s, $N(CH_3)_2$), 2.93 (2 H, d, J = 7 Hz, CH_2N), 3.94 (1 H, t, J = 7 Hz, CH).

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Registry No. **3**, 3853-06-3; **4**, 88722-74-1; **5**, 687-47-8; **6**, 63296-55-9; **7**, 91191-93-4; **8**, 86163-00-0; **9**, 91191-94-5; **10**, 91191-95-6; **11**, 63296-56-0; **12**, 88722-70-7; **13**, 86163-01-1; **14**, 91191-96-7; **15**, 91191-97-8; **16**, 91191-98-9; **17**, 91191-99-0; **18**, 88722-71-8; **19**, 88722-72-9; **20**, 88722-73-0; **21**, 90866-16-3; **22**, 90866-17-4; **23**, 90866-18-5; **24**, 90866-19-6; **25**, 90866-20-9; **26**, 90866-21-0; **27**, 91237-35-3; **28**, 91237-36-4; **29**, 90866-22-1; **30**, 90866-23-2; **31**, 90832-48-7; **32**, 90832-49-8; **33**, 90832-50-1; **34**, 90832-51-2; **35**, 90832-52-3; **36**, 90832-53-4; **37**, 91192-00-6; **38**, 91192-01-7; **39**, 91192-02-8; **40**, 91192-04-0; **41**, 91192-06-2; **42**, 91192-08-4; **43**, 91192-03-9; **44**, 91192-05-1; **45**, 91192-07-3; **46**, 91192-09-5; **47**, 91192-10-8; **48**, 91192-11-9; **49**, 91192-12-0; **53**, 91192-14-2; **54**, 91192-13-1; chloromethyl benzyl ether, 3587-60-8; chloromethyl methyl ether, 107-30-2; (methoxyethoxy)methyl chloromethyl ether, 89268-03-1; bis(*p*-tolylthio)methane, 17241-04-2; heptanal, 111-71-7.

Supplementary Material Available: Tables III–VII containing elemental analyses, ^1H and ^{13}C NMR spectra, and IR and mass spectra for compounds **21–46** (12 pages). Ordering information is given on any current masthead page.