($CDCl_3$) δ 3.76 (s, 3 H), 3.80 (s, 3 H), 3.85 (s, 3 H), 5.73 (s, 1 H), 6.84–6.98 (m, 5 H), 7.28–7.32 (m, 2 H); IR (KBr) 2239, 1593 cm^{-1}. Anal. Calcd for $C_{17}H_{17}O_3N$: C, 72.06, H, 6.04; N, 4.94. Found: C, 72.17; H, 6.09; N, 4.86.

α-(3′,4′-Dimethoxyphenyl)-2,5-dimethoxyphenylacetonitrile (10b): colorless thick oil; ^1H NMR ($CDCl_3$) δ 3.70 (s, 3 H), 3.77 (s, 3 H), 3.82 (s, 6 H), 5.46 (s, 1 H), 6.80–6.91 (m, 6 H); IR 2240, 1595 cm^{-1}.

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Synthesis of 1-(2-Hydroxyaryl)-1,2,3-propanetriol and 1-(2-Hydroxyaryl)-2-amino-1,3-propanediol Derivatives of either *threo* or *erythro* Configuration[1]

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The title arylglycerols **3A** and **4A** and arylaminopropanediols **3B** and **4B**, in either optical series (D or L) and with either configuration (*threo* or *erythro*), were prepared in optically pure form by direct arylation of 2,3-*O*-isopropylidene-D- or -L-glyceraldehyde (**2A**) and *N*-*t*-Boc-2,3-*N*,*O*-isopropylidene-D- or -L-serinal (**2B**) with Mg-based or Ti-based phenolates **1** in a highly diastereodivergent manner.

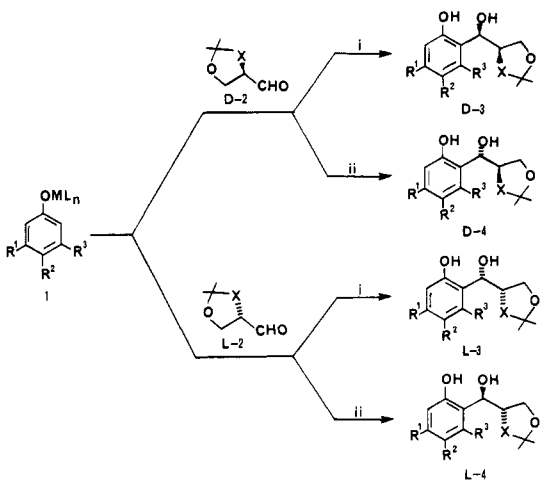
The regiospecific ortho-arylation of carbonyl compounds having chiral centers by means of metal phenolates, investigated recently in our laboratory, has proven to be a promising route to homochiral multifunctional aromatics.[1,3] Very high, often complete, stereodivergence has been achieved via metal tuning, thus allowing different stereochemical arrangements of the emerging molecules to be generated.

As an extension of this work, we now report a practical synthesis of all four possible stereoisomers of the ring-hydroxylated 1-aryl-1,2,3-propanetriols **3A** and **4A** and 1-aryl-2-amino-1,3-propanediol acetonides **3B** and **4B** via regio- and diastereoselective arylation of isopropylidene-blocked D- and L-glyceraldehyde (**2A**)[4] and D- and L-*N*-*t*-Boc-serinal (**2B**)[5] with bromomagnesium or triisopropoxytitanium phenolates [**1**; ML_n = $MgBr^+$ or $Ti(O\text{-}i\text{-}Pr)_3^+$] in apolar media.

Results and Discussion

Synthesis of Arylglycerols. We first investigated the reaction between the bromomagnesium salt of 4-*tert*-butylphenol (**1a**, ML_n = $MgBr^+$) and D-glyceraldehyde acetonide (D-**2A**) under the conditions we generally used for regiocontrolled arylation of carbonyl compounds.[3] In the event, by using anhydrous ethanol-free methylene dichloride as solvent at ambient temperature and magnetically stirring the resulting slurry, a mixture of D-*threo*- and D-*erythro*-arylglycerols D-**3Aa** and D-**4Aa** was obtained in 32% combined yield with a diastereoselectivity in favor of *threo* derivative D-**3Aa** as moderate as 85:15 (60% diastereoisomeric excess) (Scheme I).

Scheme I[a]



[a] **A**, X = O; **B**, X = *N*-*t*-Boc; (i) ML_n = $MgBr^+$, CH_2Cl_2; (ii) ML_n = $Ti(O\text{-}i\text{-}Pr)_3^+$, toluene.

To improve the reactant conversion and the selectivity, we turned toward ultrasound. The use of sonication in organic chemistry as a tool for improving reaction rates and modifying the physicochemical state of the reaction components is well-documented.[6] In the reaction above (homogeneous conditions at 0 °C), this simple expedient improved both the yield and diastereoselectivity significantly, so that D-**3Aa** was obtained in 70% isolated yield and 92% de.

The extension of this reaction and improved procedure (CH_2Cl_2; 0 °C) to a variety of ring-substituted phenols and both enantiomers of **2A** was successful. The complete

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Table I. Synthesis of *threo*- and *erythro*-1-Aryl-1,2,3-propanetriol Acetonides 3A and 4A

entry	phenol	R^1	R^2	R^3	counterion ML_n	aldehyde	product	yield,[a] %	mp, °C	$[\alpha]^{20}_D$,[b] deg	de,[c] %	config[d]
1	**1a**	H	t-C_4H_9	H	$MgBr^+$	D-**2a**	D-**3Aa**	70	157–158	−36.4	92	D-*threo*
2	**1a**	H	t-C_4H_9	H	$Ti(O\text{-}i\text{-}Pr)_3^+$	D-**2A**	D-**4Aa**	76	142–143	+43.9	90	D-*erythro*
3	**1a**	H	t-C_4H_9	H	$MgBr^+$	L-**2A**	L-**3Aa**	72	155–156	+35.6	92	L-*threo*
4	**1a**	H	t-C_4H_9	H	$Ti(O\text{-}i\text{-}Pr)_3^+$	L-**2A**	L-**4Aa**	75	140–141	−43.1	91	L-*erythro*
5	**1b**	H	H	H	$MgBr^+$	D-**2A**	D-**3Ab**	63	syrup	−17.8	91	D-*threo*
6	**1b**	H	H	H	$Ti(O\text{-}i\text{-}Pr)_3^+$	D-**2A**	D-**4Ab**	61	syrup	+15.4	90	D-*erythro*
7	**1c**	OMe	H	H	$MgBr^+$	D-**2A**	D-**3Ac**	76	103–105	−9.3	93	D-*threo*
8	**1c**	OMe	H	H	$Ti(O\text{-}i\text{-}Pr)_3^+$	D-**2A**	D-**4Ac**	67	107–110	+9.1	93	D-*erythro*

[a] Actual yield of pure isolated compounds, based on starting **1**. [b] *c* 1, benzene. [c] Diastereoisomeric excess (de) assayed on the crude reaction mixtures by reversed-phase HPLC. [d] Absolute configuration: D-*threo* = 1*R*,2*R*; L-*threo* = 1*S*,2*S*; D-*erythro* = 1*S*,2*R*; L-*erythro* = 1*R*,2*S*.

Table II. Synthesis of *threo*- and *erythro*-1-Aryl-2-amino-1,3-propanediol Acetonides 3B and 4B

entry	phenol	R^1	R^2	R^3	counterion ML_n	aldehyde	product	yield,[a] %	mp, °C	$[\alpha]^{20}_D$,[b] deg	de,[c] %	config[d]
1	**1a**	H	t-C_4H_9	H	$MgBr^+$	L-**2B**	L-**3Ba**	70	syrup	+21.0	96	L-*threo*
2	**1a**	H	t-C_4H_9	H	$Ti(O\text{-}i\text{-}Pr)_3^+$	L-**2B**	L-**4Ba**	61	syrup	+5.3	97	L-*erythro*
3	**1a**	H	t-C_4H_9	H	$MgBr^+$	D-**2B**	D-**3Ba**	72	syrup	−20.8	96	D-*threo*
4	**1a**	H	t-C_4H_9	H	$Ti(O\text{-}i\text{-}Pr)_3^+$	D-**2B**	D-**4Ba**	60	syrup	−5.6	96	D-*erythro*
5	**1d**	$-OCH_2O-$		H	$MgBr^+$	L-**2B**	L-**3Bd**	67	150–151	+13.2	94	L-*threo*
6	**1d**	$-OCH_2O-$		H	$Ti(O\text{-}i\text{-}Pr)_3^+$	L-**2B**	L-**4Bd**	64	145–147	+36.0	95	L-*erythro*
7	**1e**	$-(CH{=}CH)_2-$		H	$MgBr^+$	L-**2B**	L-**3Be**	74	syrup	+61.6	92	L-*threo*
8	**1e**	$-(CH{=}CH)_2-$		H	$Ti(O\text{-}i\text{-}Pr)_3^+$	L-**2B**	L-**4Be**	64	syrup	+88.9	91	L-*erythro*
9	**1f**	n-$C_{15}H_{31}$	H	H	$MgBr^+$	L-**2B**	L-**3Bf**	63	syrup	+3.2	94	L-*threo*
10	**1f**	n-$C_{15}H_{31}$	H	H	$Ti(O\text{-}i\text{-}Pr)_3^+$	L-**2B**	L-**4Bf**	60	syrup	−2.2	96	L-*erythro*
11	**1g**	n-$C_{15}H_{31}$	H	OH	$MgBr^+$	L-**2B**	L-**3Bg**	70	syrup	+31.2	95	L-*threo*
12	**1g**	n-$C_{15}H_{31}$	H	OH	$Ti(O\text{-}i\text{-}Pr)_3^+$	L-**2B**	L-**4Bg**	62	syrup	+18.3	>98	L-*erythro*
13	**1g**	n-$C_{15}H_{31}$	H	OH	$MgBr^+$	D-**2B**	D-**3Bg**	72	syrup	−32.3	96	D-*threo*
14	**1g**	n-$C_{15}H_{31}$	H	OH	$Ti(O\text{-}i\text{-}Pr)_3^+$	D-**2B**	D-**4Bg**	60	syrup	−19.1	>98	D-*erythro*

[a,c,d] See notes *a*, *c*, and *d* for Table I. [b] *c* 1, chloroform.

results are listed in the odd-numbered entries of Table I.

The use of bromomagnesium phenolates gave access to homochiral arylglycerol acetonides of the D- and L-*threo* series, but a convenient route to the corresponding *erythro* system was still lacking. We sought to take advantage of the recent findings of Reetz,[7] who has pointed out the ability of suitably ligated titanium(IV) derivatives to promote anti selectivity in the carbon–carbon bond-forming reactions involving chiral α-alkoxycarbonyl compounds.

Triisopropoxytitanium phenolates [**1**, ML_n = $Ti(O\text{-}i\text{-}Pr)_3^+$] ought to be favorable substrates in view of the reluctance of this metal cation to form chelates with potentially bidentate carbonyl reactants. Indeed, treatment of **1** [ML_n = $Ti(O\text{-}i\text{-}Pr)_3^+$] with D- or L-**2A** in anhydrous toluene did give nearly complete reversal of stereochemistry with the consequence that *erythro*-glycerols **4A** in either the D or L series were produced (Table I, even-numbered entries).

Thus, for a given reactant pair, *threo* or *erythro* epimers of the arylated glycerols **3A** or **4A** were synthesized in a complementary fashion by using the simple expedient of varying the phenolate metal counterion.

Synthesis of Arylaminopropanediols. The next task was to apply this divergent methodology to serine-derived aldehydes D- and L-**2B** en route to homochiral ring-hydroxylated 1-aryl-2-amino-1,3-propanediol derivatives, a structural feature present in important pharmaceuticals.[8]

Through the above simple protocol, the $MgBr^+$-promoted reactions furnished predominantly or exclusively *threo* compounds D- and L-**3B**, whereas access to the *erythro* compounds D- and L-**4B** was easily achieved by using $Ti(O\text{-}i\text{-}Pr)_3^+$ counterion. The overall results are collected in Table II, wherein odd-numbered entries refer to *threo*-selective reactions while even-numbered entries apply to *erythro*-preferred processes.

Unlike the glyceraldehyde-based reactions, the application of ultrasound did not affect the stereochemical outcome of the condensations with the protected serinal substrates, although the kinetic advantages of sonication remained. Once more, the desired products were obtained in excellent yield and with the same stereoselectivity. Thus diastereoface selection can be achieved by proper choice of the metal ion.

Structural Assignments. The *threo* and *erythro* diastereoisomers **3** and **4** are easily distinguished by ^1H NMR spectroscopy on the basis of vicinal coupling constants ($J_{1,2}$) between H-1 and H-2. The chemical shift value for the benzylic H-1 is also extremely diagnostic.[9]

As a general rule, the spectra of the *threo* compounds (**3**), possessing 1,2-syn arrangement, display $J_{1,2}$ of ca. 8 Hz, while a $J_{1,2}$ of 4 Hz or less is observed for the *erythro* derivatives (**4**) (1,2-anti). In addition, in the ^1H NMR spectra, the H-1 resonance in compounds **3** appears 0.3–0.4 ppm further upfield compared to the corresponding peak in the epimers (**4**). These assignments are supported by a single-crystal structure determination performed on D-**3Aa**.[1] Since the absolute configuration at C-2 corresponds to that of the unaltered C-2 atom of starting D-**2A**, D-**3Aa** and all its relatives D-**3** have the 1*R*,2*R* absolute configuration and their enantiomers (L-**3**) have the 1*S*,2*S* configuration.

Compounds **4** are C-1 epimers of **3**, and this was substantiated by ^1H NMR analysis. The assignments of *erythro* configuration to **4** follow from the key ^1H NMR parameters for H-1 as described above.

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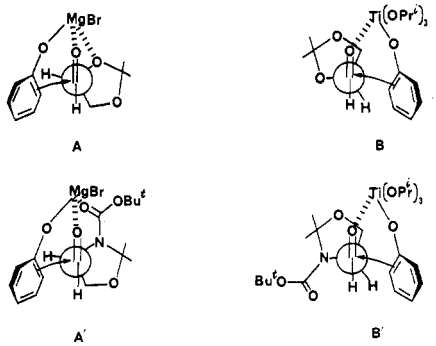
Scheme II



The structural assignments indicated in Tables I and II for a given epimeric pair appear to be general on the basis of the consistency of the ^{1}H NMR spectral data presented in this paper.

Enantiomeric Purity. The arylglycerols **3A** and **4A** and arylaminopropanediols **3B** and **4B** reported in this work are diastereoisomerically pure compounds as ascertained by ^{1}H NMR and HPLC analysis. However, ^{1}H NMR analysis in a chiral environment was necessary in order to determine the enantiomeric excesses accurately.

Four representative enantiomeric pairs were selected: D-**3Aa** and L-**3Aa**; D-**4Aa** and L-**4Aa**; D-**3Ba** and L-**3Ba**; D-**4Ba** and L-**4Ba**. Enantiomeric excesses of above 98% were ascertained for all eight compounds, by comparing the NMR spectra of the synthesized compounds with those of their racemates in the presence of the chiral shift reagent Eu(hfc)$_3$. In no case, could signals from the opposite enantiomer be detected. The other molecules, on which this analysis was not been performed, should have similar enantiomeric purity, since the reaction conditions and the enantiomeric purity of the starting chiral aldehydes were the same.

Conclusions. In summary, we have presented a complementary highly stereoselective synthesis of ring-hydroxylated 1-*C*-arylglycerols and 1-*C*-aryl-2-amino-1,3-propanediol acetonides. Either the *threo* isomers or their *erythro* epimers are available in a predictable manner and in a stereoisomerically pure state starting from readily available precursors. The method is general, and provides access to a variety of homochiral Ar-C(3) synthons of potential synthetic and pharmaceutical utility.

We attribute the striking difference in the sense of induction (Scheme II; L-**2** depicted) to Mg-chelated transition states A with both the aldehyde oxygen and α or Boc oxygen involved and, alternatively, to the Ti(O-*i*-Pr)$_3$-monocoordinated transition states B.[7,10] The marked shielding of the carbonyl *re* face in A or *si* face in B is consistent with the observed diastereoface discrimination. Thus, the ortho-regiospecific arylation of L-**2** governed by model A produces *threo* compounds preferentially, whereas model B accounts for *erythro* selection.

Reagents such as metal phenolates have the double advantage of being Lewis acids as well as providing a nucleophilic aromatic ring. This dual reactivity allows direct arylation of aldehyde reactants,[3b] thus giving access to a wide variety of arylated carbinols and their derivatives.

(10) For related examples of chelation vs nonchelation control in reactions of carbon nucleophiles with chiral carbonyl compounds, see: Hanson, G. J.; Lindberg, T. *J. Org. Chem.* **1985**, *50*, 5399. Danishefsky, S. J.; DeNinno, M. P.; Phillips, G. B.; Zelle, R. E.; Lartey, P. A. *Tetrahedron* **1986**, *42*, 2809. Kusakabe, M.; Sato, F. *Chem. Lett.* **1986**, 1473. Keck, G. E.; Castellino, S. *J. Am. Chem. Soc.* **1986**, *108*, 3847. Bernardi, A.; Cardani, S.; Colombo, L.; Poli, G.; Schimperna, G.; Scolastico, C. *J. Org. Chem.* **1987**, *52*, 888. Iida, H.; Yamazaki, N.; Kibayashi, C. *J. Org. Chem.* **1987**, *52*, 1956. Williams, D. R.; Klingler, F. D. *Tetrahedron Lett.* **1987**, *28*, 869. Reetz, M. T.; Drewes, M. W.; Schmitz, A. *Angew. Chem., Int. Ed. Engl.* **1987**, *26*, 1141.

Experimental Section

General directions and routine apparatus are reported in our previous papers on this and related subjects.[3] All sonicated reactions were performed by using a Branson Model B-3200E2 Model ultrasonic cleaner with the reaction vessel completely submerged.

Materials. All phenols were commercial products. Both the enantiomers of 2,3-*O*-isopropilydeneglyceraldehyde (D-**2A** and L-**2A**) were prepared by literature methods.[4] Their enantiomeric purity was shown to be ≥98% ee by ^{1}H NMR spectra in the presence of Eu(hfc)$_3$. D-**2A** had $[\alpha]^{20}_D$ +65.20° (*c* 1, benzene) [lit.[4a] +64.9° (*c* 6, benzene)]; L-**2A** had $[\alpha]^{20}_D$ −65.71° (*c* 1, benzene) [lit.[4d] −63.5° (*c* 8, benzene)]. *N*-*t*-Boc-2,3-*N*,*O*-isopropylidene-D- and -L-serinal (D-**2B** and L-**2B**) were prepared, as reported,[5] from *N*-*t*-Boc-L- and -D-serine via the sequence involving acetonide formation and DIBAH reduction of the corresponding methyl esters. D-**2B** had $[\alpha]^{20}_D$ +103.5° (*c* 1, $CHCl_3$) [lit.[5a] +103° (*c* 1, $CHCl_3$)]; L-**2B** had $[\alpha]^{20}_D$ −102.9° (*c* 1, $CHCl_3$). The enantiomeric purity of D- and L-**2B** was at least 98% ee as checked by ^{1}H NMR in the presence of Eu(hfc)$_3$. In accordance with the literature, no appreciable racemization occurred after storing these materials in a refrigerator (−20 °C) for 3 months.

General Procedure for Reaction of Bromomagnesium Phenolates with Aldehydes. Synthesis of *threo* Derivatives 3A and 3B. To a solution of EtMgBr (50 mmol) in diethyl ether was added the appropriate phenol (50 mmol). The ether was removed under vacuum and anhydrous ethanol-free CH_2Cl_2 (200 mL) added. The reaction vessel was placed into an ice-cooled sonication bath and the selected aldehyde **2A** or **2B** (75 mmol) was added dropwise as a solution in 50 mL of CH_2Cl_2. After 6 h at 0–5 °C, the reaction mixture was quenched by adding a saturated aqueous NH_4Cl solution and extracted with CH_2Cl_2. Drying ($MgSO_4$) and removal of the solvent furnished a crude product from which the major D- and L-*threo* derivatives **3** were obtained in a pure state by chromatography on silica gel using hexane/ethyl acetate solvent mixtures.

The following compounds were prepared by the above procedure.

D-***threo*-3Aa**: ^{1}H NMR δ 1.27 (s, 9 H, *t*-Bu), 1.39 (s, 3 H, Me), 1.52 (s, 3 H, Me), 3.34 (s, 1 H, OH), 3.83 (dd, 1 H, *J* = 8.8, 6.4 Hz, H-3a), 3.87 (dd, 1 H, *J* = 8.8, 5.1 Hz, H-3b), 4.37 (ddd, 1 H, *J* = 8.1, 6.4, 5.1 Hz, H-2), 4.64 (d, 1 H, *J* = 8.1 Hz, H-1), 6.83 (d, 1 H, *J* = 8.6 Hz, H-3′), 7.00 (d, 1 H, *J* = 2.4 Hz, H-6′), 7.23 (dd, 1 H, *J* = 8.6, 2.4 Hz, H-4′), 7.80 (s, 1 H, OH); IR 3280, 2880, 1430, 1370, 1255, 1220, 1060, 850, 820 cm^{-1}. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.68; H, 8.91.

L-***threo*-3Aa**: ^{1}H NMR and IR characteristics as for D-**3Aa**. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.64; H, 8.86.

D-***threo*-3Ab**: ^{1}H NMR δ 1.36 (s, 3 H, Me), 1.47 (s, 3 H, Me), 3.85 (s, 1 H, OH), 3.79 (m, 2 H, H-3), 4.36 (ddd, 1 H, *J* = 7.8, 7.8, 5.90 Hz, H-2), 4.68 (d, 1 H, *J* = 7.8 Hz, H-1), 6.7–7.2 (m, 4 H, Ar), 8.02 (s, 1 H, OH); IR 3220, 2920, 1590, 1455, 1375, 1260, 1050, 850, 740 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.36; H, 7.20.

D-***threo*-3Ac**: ^{1}H NMR δ 1.39 (s, 3 H, Me), 1.51 (s, 3 H, Me), 3.67 (s, 3 H, OMe), 3.79 (m, 3 H, H-3 and OH), 4.37 (ddd, 1 H, *J* = 7.8, 7.7, 5.9 Hz, H-2), 4.64 (d, 1 H, *J* = 7.8 Hz, H-1), 6.39 (dd, 1 H, *J* = 8.2, 2.2 Hz, H-5′), 6.43 (d, 1 H, *J* = 2.2, H-3′), 6.92 (d, 1 H, *J* = 8.2 Hz, H-6′), 8.08 (br s, 1 H, OH); IR 3300, 2950, 1600, 1430, 1370, 1200, 1160, 1030, 850, 740 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14. Found: C, 61.59; H, 7.09.

L-***threo*-3Ba**: ^{1}H NMR δ 1.28 (s, 9 H, *t*-Bu), 1.50 (s, 3 H, Me), 1.57 (s, 9 H, *t*-Bu), 1.62 (s, 3 H, Me), 3.66 (m, 2 H, H-3), 4.38 (ddd, 1 H, *J* = 8.2, 5.1, 3.6 Hz, H-2), 4.83 (d, 1 H, *J* = 8.2 Hz, H-1), 6.58 (br s, 1 H, OH), 6.78 (d, 1 H, *J* = 8.6, H-3′), 6.98 (d, 1 H, *J* = 2.5 Hz, H-6′), 7.23 (dd, 1 H, *J* = 8.60, 2.50 Hz, H-4′), 8.30 (br s, 1 H, OH); IR 3290, 2965, 1650, 1365, 1240, 1160, 1080, 830, 740 cm^{-1}. Anal. Calcd for $C_{21}H_{33}NO_5$: C, 66.46; H, 8.77; N, 3.69. Found: C, 66.70; H, 8.71; N, 3.54.

D-***threo*-3Ba**: ^{1}H NMR and IR characteristics as for L-**3Ba**. Anal. Calcd for $C_{21}H_{33}NO_5$: C, 66.46; H, 8.77; N, 3.69. Found: C, 66.74; H, 8.64; N, 3.47.

L-*threo*-**3Bd**: ^{1}H NMR δ 1.51 (s, 3 H, Me), 1.58 (s, 9 H, *t*-Bu), 1.60 (s, 3 H, Me), 3.71 (d, 2 H, *J* = 4.2, H-3), 4.35 (ddd, *J* = 8.5, 4.2, 4.2, Hz, H-2), 4.74 (d, 1 H, *J* = 8.5 Hz, H-1), 5.89 (s, 2 H, CH_2), 6.44 (s, 1 H, H-6′), 6.49 (s, 1 H, H-3′), 6.62 (br s, 1 H, OH), 8.33 (br s, 1 H, OH); IR 3361, 2978, 1662, 1403, 1172, 1039, 847, 767 cm^{-1}. Anal. Calcd for $C_{18}H_{25}NO_7$: C, 58.84; H, 6.86; N, 3.81. Found: C, 58.90; H, 6.94; N, 3.59.

L-*threo*-**3Be**: ^{1}H NMR δ 1.51 (s, 9 H, *t*-Bu), 1.45 (s, 3 H, Me), 1.66 (s, 3 H, Me), 3.53 (m, 2 H, H-3), 4.56 (ddd, 1 H, *J* = 8.0, 5.7, 2.3 Hz, H-2), 5.85 (d, 1 H, *J* = 8.0, H-1), 6.90 (s, 1 H, OH), 7.0–8.0 (m, 6 H, Ar), 9.70 (br s, 1 H, OH); IR 3300, 2980, 1640, 1400, 1265, 1160, 1060, 740 cm^{-1}. Anal. Calcd for $C_{21}H_{27}NO_5$: C, 67.54; H, 7.29; N, 3.75. Found: C, 67.61; H, 7.16; N, 3.61.

L-*threo*-**3Bf**: ^{1}H NMR δ 0.90 (t, 3 H, ω-Me), 1.1–2.0 (m, 41 H, 2 Me, *t*-Bu, 13 CH_2), 2.52 (t, 2 H, α-CH_2), 3.70 (m, 2 H, H-3), 4.37 (ddd, 1 H, *J* = 8.2, 6.3, 3.7 Hz, H-2), 4.84 (d, 1 H, *J* = 8.2 Hz, H-1), 6.41 (br s, 1 H, OH), 6.5–7.3 (m, 3 H, Ar), 8.48 (br s, 1 H, OH); IR 3300, 2910, 1660, 1390, 1250, 1170, 1100, 850, 760 cm^{-1}. Anal. Calcd for $C_{32}H_{55}NO_5$: C, 72.00; H, 10.38; N, 2.62. Found: C, 72.13; H, 10.19; N, 2.44.

L-*threo*-**3Bg**: ^{1}H NMR δ 0.90 (t, 3 H, ω-Me), 1.0–2.0 (m, 41 H, 2 Me, *t*-Bu, 13 CH_2), 2.45 (t, 2 H, α-CH_2), 3.78 (m, 2 H, H-3), 4.40 (ddd, 1 H, *J* = 8.5, 4.3, 4.2 Hz, H-2), 5.38 (d, 1 H, *J* = 8.5 Hz, H-1), 6.20 (s, 2 H, Ar), 6.65 (br s, 1 H, OH), 7.35 (br s, 1 H, OH); IR 3280, 2875, 1650, 1370, 1250, 1170, 1030, 850, 740 cm^{-1}. Anal. Calcd for $C_{32}H_{55}NO_6$: C, 69.91; H, 10.08; N, 2.55. Found: C, 69.89; H, 10.09; N, 2.46.

D-*threo*-**3Bg**: ^{1}H NMR and IR characteristics as for L-**3Bg**. Anal. Calcd for $C_{32}H_{55}NO_6$: C, 69.91; H, 10.08; N, 2.55. Found: C, 69.98; H, 10.17; N, 2.39.

General Procedure for Reaction of Isopropoxytitanium Phenolates with Aldehydes. Synthesis of *erythro* Derivatives 4A and 4B. To a solution of titanium tetraisopropoxide (50 mmol) in toluene (200 mL) was added the appropriate phenol (50 mmol); the mixture was distilled in order to remove the propan-2-ol formed and the volume was adjusted to 200 mL by adding toluene. The reaction vessel was placed in an ice-cooled sonication bath and the selected aldehyde **2A** or **2B** (75 mmol) was added dropwise as a solution in 50 mL of toluene. After 6 h at 0–5 °C, the reaction mixture was quenched (NH_4Cl/H_2O) and extracted with ether. Drying ($MgSO_4$) and removal of the solvent furnished a crude product from which the major *erythro* diastereoisomer **4** was separated in a pure state by chromatography on silica gel (hexane/ethyl acetate).

The following compounds were prepared by the above procedure.

D-*erythro*-**4Aa**: ^{1}H NMR δ 1.28 (s, 9 H, *t*-Bu), 1.38 (s, 3 H, Me), 1.49 (s, 3 H, Me), 3.02 (s, 1 H, OH), 3.96 (dd, 1 H, *J* = 7.9, 6.0 Hz, H-3a), 4.05 (dd, 1 H, *J* = 7.9, 5.3 Hz, H-3b), 4.40 (ddd, 1 H, *J* = 6.0, 5.3, 4.2 Hz, H-2), 5.04 (d, 1 H, *J* = 4.2 Hz, H-1), 6.80 (d, 1 H, *J* = 8.4 Hz, H-3′), 7.03 (d, 1 H, *J* = 2.0 Hz, H-6′), 7.20 (dd, 1 H, *J* = 8.4, 2.0 Hz, H-4′), 7.82 (s, 1 H, OH); IR 3250, 2920, 1370, 1260, 1220, 1060, 850, 820 cm^{-1}. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.61; H, 8.74.

L-*erythro*-**4Aa**: ^{1}H NMR and IR characteristics as for D-**4Aa**. Anal. Calcd for $C_{16}H_{24}O_4$: C, 68.54; H, 8.63. Found: C, 68.69; H, 8.69.

D-*erythro*-**4Ab**: ^{1}H NMR δ 1.31 (s, 3 H, Me), 1.41 (s, 3 H, Me), 3.59 (s, 1 H, OH), 3.92 (m, 2 H, H-3), 4.26 (ddd, 1 H, *J* = 6.0, 5.4, 4.2 Hz, H-2), 4.91 (d, 1 H, *J* = 4.2 Hz, H-1), 6.7–7.2 (m, 4 H, Ar), 8.05 (s, 1 H, OH); IR 3300, 2920, 1700, 1690, 1455, 1370, 1280, 1055, 850, 760 cm^{-1}. Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.40; H, 7.24.

D-*erythro*-**4Ac**: ^{1}H NMR δ 1.39 (s, 3 H, Me), 1.49 (s, 3 H, Me), 3.09 (br s, 1 H, OH), 3.78 (s, 3 H, OMe), 4.0 (m, 2 H, H-3), 4.39 (ddd, 1 H, *J* = 6.4, 5.2, 4.4 Hz, H-2), 4.98 (d, 1 H, *J* = 4.4 Hz, H-1), 6.40 (dd, 1 H, *J* = 8.4, 2.3 Hz, H-5′), 6.45 (d, 1 H, *J* = 2.3 Hz, H-3′), 6.92 (d, 1 H, *J* = 8.4 Hz, H-6′), 8.20 (br s, 1 H, OH); IR 3270, 2920, 1615, 1585, 1420, 1370, 1265, 1200, 1065, 850, 750 cm^{-1}. Anal. Calcd for $C_{13}H_{18}O_5$: C, 61.40; H, 7.14. Found: C, 61.64; H, 7.29.

L-*erythro*-**4Ba**: ^{1}H NMR δ 1.28 (s, 9 H, *t*-Bu), 1.47 (s, 9 H, *t*-Bu), 1.47 (s, 3 H, Me), 1.62 (s, 3 H, Me), 3.13 (br s, 1 H, OH), 3.6–4.3 (m, 3 H, H-2 and H-3), 5.19 (br s, 1 H, H-1), 6.75 (d, 1 H, *J* = 8.5 Hz, H-3′), 7.14 (dd, 1 H, *J* = 8.5, 2.4 Hz, H-4′), 7.21 (d, 1 H, *J* = 2.4 Hz, H-6′), 7.98 (br s, 1 H, OH); IR 3300, 2910, 1670, 1370, 1250, 1165, 1080, 830, 740 cm^{-1}. Anal. Calcd for $C_{21}H_{33}NO_5$: C, 66.46; H, 8.77; N, 3.69. Found: C, 66.51; H, 8.73; N, 3.46.

D-*erythro*-**4Ba**: ^{1}H NMR and IR characteristics as for L-**4Ba**. Anal. Calcd for $C_{21}H_{33}NO_5$: C, 66.46; H, 8.77; N, 3.69. Found: C, 66.62; H, 8.88; N, 3.51.

L-*erythro*-**4Bd**: ^{1}H NMR δ 1.52 (s, 3 H, Me), 1.53 (s, 9 H, *t*-Bu), 1.61 (s, 3 H, Me), 3.21 (s, 1 H, OH), 3.88 (dd, 1 H, *J* = 10.0, 6.7 Hz, H-3a), 4.20 (d, 1 H, *J* = 10.0 Hz, H-3b), 4.11 (m, 1 H, H-2), 5.14 (br s, 1 H, H-1), 5.85 (s, 2 H, CH_2), 6.42 (s, 1 H, H-6′), 6.70 (s, 1 H, H-3′), 8.10 (br s, 1 H, OH); IR 3433, 3339, 2932, 2875, 1618, 1419, 1159, 839, 776 cm^{-1}. Anal. Calcd for $C_{18}H_{25}NO_7$: C, 58.84; H, 6.86; N, 3.81. Found: C, 59.02; H, 6.91; N, 3.60.

L-*erythro*-**4Be**: ^{1}H NMR δ 1.52 (s, 3 H, Me), 1.62 (s, 9 H, *t*-Bu), 1.64 (s, 3 H, Me), 3.24 (s, 1 H, OH), 3.83 (dd, 1 H, *J* = 10.7, 7.7 Hz, H-3a), 4.30 (dd, 1 H, *J* = 10.7, 3.0 Hz, H-3b), 4.42 (m, 1 H, H-2), 6.18 (br s, 1 H, H-1), 7.1–7.9 (m, 6 H, Ar), 9.80 (s, 1 H, OH); IR 3300, 2980, 1660, 1370, 1230, 1170, 1090, 850, 745 cm^{-1}. Anal. Calcd for $C_{21}H_{27}NO_5$: C, 67.54; H, 7.29; N, 3.75. Found: C, 67.67; H, 7.33; N, 3.39.

L-*erythro*-**4Bf**: ^{1}H NMR δ 0.90 (t, 3 H, ω-Me), 1.1–2.0 (m, 41 H, 2 Me, *t*-Bu, 13 CH_2), 2.50 (t, 2 H, α-CH_2), 3.18 (br s, 1 H, OH), 3.87 (dd, 1 H, *J* = 9.3, 6.0 Hz, H-3a), 4.09 (dd, 1 H, *J* = 9.3, 3.0 Hz, H-3b), 4.20 (m, 1 H, H-2), 5.22 (br s, 1 H, H-1), 6.5–7.3 (m, 3 H, Ar), 8.18 (br s, 1 H, OH); IR 3280, 2920, 1685, 1370, 1250, 1165, 1100, 850, 745 cm^{-1}. Anal. Calcd for $C_{32}H_{55}NO_5$: C, 72.00; H, 10.38; N, 2.62. Found: C, 72.21; H, 10.54; N, 2.40.

L-*erythro*-**4Bg**: ^{1}H NMR δ 0.90 (t, 3 H, ω-Me), 1.0–2.1 (m, 41 H, 2 Me, *t*-Bu, 13 CH_2), 2.47 (t, 2 H, α-CH_2), 2.73 (br s, 1 H, OH), 3.5–4.5 (m, 3 H, H-2 and H-3), 5.45 (br s, 1 H, H-1), 6.25 (s, 2 H, Ar), 8.35 (br s, 1 H, OH); IR 3280, 2850, 1665, 1370, 1250, 1160, 1100, 850, 760 cm^{-1}. Anal. Calcd for $C_{32}H_{55}NO_6$: C, 69.91; H, 10.08; N, 2.55. Found: C, 70.14; H, 10.19; N, 2.37.

D-*erythro*-**4Bg**: ^{1}H NMR and IR characteristics as for L-**4Bg**. Anal. Calcd for $C_{32}H_{55}NO_6$: C, 69.91; H, 10.08; N, 2.55. Found: C, 70.11; H, 10.19; N, 2.32.

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Registry No. **1a**, 98-54-4; **1b**, 108-95-2; **1c**, 150-19-6; **1d**, 533-31-3; **1e**, 135-19-3; **1f**, 501-24-6; **1g**, 3158-56-3; D-**2A**, 15186-48-8; L-**2A**, 22323-80-4; D-**2B**, 95715-87-0; L-**2B**, 102308-32-7; D-**3Aa**, 112156-62-4; L-**3Aa**, 112156-68-0; D-**3Ab**, 112156-64-6; D-**3Ac**, 112156-66-8; D-**3Ba**, 116079-35-7; L-**3Ba**, 116079-33-5; L-**3Bd**, 116079-37-9; L-**3Be**, 116079-39-1; L-**3Bf**, 116079-41-5; D-**3Bg**, 116079-45-9; L-**3Bg**, 116079-43-7; D-**4Aa**, 112156-63-5; L-**4Aa**, 112156-69-1; D-**4Ab**, 112156-65-7; D-**4Ac**, 112156-67-9; D-**4Ba**, 116079-36-8; L-**4Ba**, 116079-34-6; L-**4Bd**, 116079-38-0; L-**4Be**, 116079-40-4; L-**4Bf**, 116079-42-6; D-**4Bg**, 116079-46-0; L-**4Bg**, 116079-44-8.