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Enantio- and Diastereoselective Titanium-TADDOLate Catalyzed Addition of Diethyl and bis(3-Buten-1-yl) Zinc to Aldehydes A Full Account with Preparative Details[1,2]

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Abstract: α,α,α',α'-Tetraaryl-2-mono- and -2,2-disubstituted-1,3-dioxolan-4,5-dimethanolates (TADDOLates) of titanium (IV) are used in substoichiometric amounts for the *Lewis* acid-mediated enantioselective addition of alkyl groups from organozinc reagents to aldehydes (19 examples). With 0.05 - 0.20 equiv. of the diisopropoxy-Ti-TADDOLate bearing four 2-naphthyl groups and 1.2 equiv. of $Ti(OCHMe_2)_4$ in toluene or ether solution the best results are obtained: ≥ 98 : 2 enantiomer ratios with all types of aldehydes tested (saturated, olefinic, and acetylenic aliphatic, aromatic, and heteroaromatic). The nucleophilic addition occurs from the (*Si*)-face of the aldehydes when the (*R,R*)-TADDOLate is employed. - With chiral aldehydes, diastereoselective additions of diethyl zinc were achieved (7 examples). In the absence of additional functional groups in the aldehyde the diastereoselectivities are independent of its chirality ("reagent control", two examples). - The TADDOLate method of adding dialkyl zinc reagents to aldehydes enantioselectively is compared with other *Lewis* acid or aminoalcohol mediated methods. Full experimental detail and correlations of the absolute configurations of some of the products obtained with literature assignments are given.

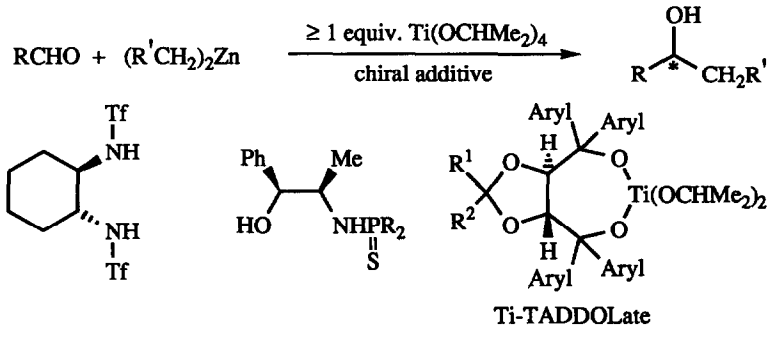
INTRODUCTION

Of the enantioselective catalytic transformations those involving C,C bond formation are especially attractive for the synthetic organic chemist. So far, this type of reaction is rather rare, as compared to functionalizing conversions of a given carbon skeleton.[5,6] Among the best studied reactions of this type are nucleophilic additions to carbonyl compounds,[7,8] particularly of diethyl zinc to aldehydes.[8,9] This latter reaction has become prototypal, and the number of papers from laboratories around the world is legion; for the most recent, excellent account and survey see the article by *Soai* and *Niwa*.[9] Originally, all investigations were carried out with the commercially available diethyl zinc which was activated to react with aldehydes by the addition of chiral 1,2-, 1,3-, and 1,4-diol, aminoalcohol and diamine derivatives. In these cases, mechanistic

studies indicate that dimeric zinc centers, in a complex with the chiral ligands, function both as *Lewis* acid for carbonyl activation, and as the origin from which the nucleophilic R group is transferred.[7]

Most recently, it was found that the Et_2Zn addition to aldehydes can also be mediated by typical *Lewis* acids such as the oxazaborolidines[10] and titanates.[1,2,11-13] The results available so far suggest that the titanate mediated version of enantioselective R_2Zn addition to aldehydes is superior to the "aminoalcohol version" for several reasons: (i) high enantioselectivities are obtained not only with aromatic but also with aliphatic (saturated, α,β-unsaturated and acetylenic) aldehydes, (ii) instead of toluene and hexane, ether solvents can be used with equal success, opening the possibility of employing *Grignard* reagents which are transmetallated to Zn compounds *in situ*,[13] (iii) certain functionalized $(FG\text{-}R)_2Zn$ reagents[13,14] and, as will also be shown herein, aldehydes may be used. The most intriguing facet of the titanate-mediated reactions is the fact that a small amount of chiral Ti derivative (0.02 - 0.2 equivalents) is applied, together with an excess (> 1.0 equivalent) of the achiral $Ti(OCHMe_2)_4$, see *Scheme 1*. For the tetraaryl-1,3-dioxolan-dimethanol derivatives, the Ti-TADDOLates, it was concluded[2] that the sterically hindered Ti center is subject to faster dynamic ligand

Scheme 1



Ti-TADDOLate

exchange than that of $Ti(OCHMe_2)_4$ (with a less congested ligand sphere), and thus becomes "the site where the action is";[15] one role of $Ti(OCHMe_2)_4$ is to prevent the product alkoxide from being attached to the Ti-TADDOLate, another one may be the transfer of the nucleophilic alkyl group to the aldehyde (Zn-free $R\text{-}Ti(OCHMe_2)_3$ can be used with equal success![16]).[17]

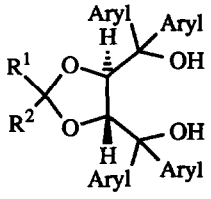
It is the purpose of the present paper to give full experimental detail, including scope and limitations, and to present the data which led to the conclusions in our preliminary publications[1] about the TADDOLate-mediated enantioselective and diastereoselective nucleophilic additions to aldehydes of diethyl zinc in toluene and of bis(3-buten-1-yl)Zn in diethylether. It should be kept in mind, that other alkyl groups can be transferred equally selectively, using R_2Zn and $R^1Ti(OR^2)_3$ derivatives generated *in situ* from the more common *Grignard*[13] and lithium[16] reagents.

PREPARATION OF THE Ti-TADDOLates 2a - 2f

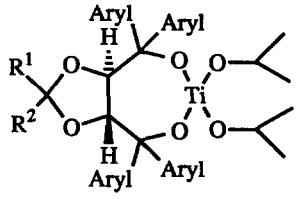
There are two practical ways of preparing Ti-TADDOLates **2**, the chiral *Lewis* acid catalysts for alkyl zinc additions to aldehydes, from $Ti(OCHMe_2)_4$ and the TADDOLs **1**, see *Scheme 2*. Originally,[1a,13] we used

the spirotitanate **3** as an intermediate; it is readily prepared by azeotropic removal of isopropanol from a 1 : 2 mixture of $Ti(OCHMe_2)_4$ and the TADDOL **1a** in toluene, and it is a crystalline solid which is stable enough to moisture to be handled in air without precautions. We use **3** as a storage form in multigram quantities. When dissolved, **3** is sensitive to moisture, and stock solutions should be kept under an inert atmosphere and manipulated by syringe techniques. Mixing the spirotitanate **3** with $Ti(OCHMe_2)_4$ in a 1 : 1 ratio gives the titanate **2a** quantitatively and instantaneously (Method B in *Scheme 2*), and NMR analysis indicates that excess tetraiso-

Scheme 2

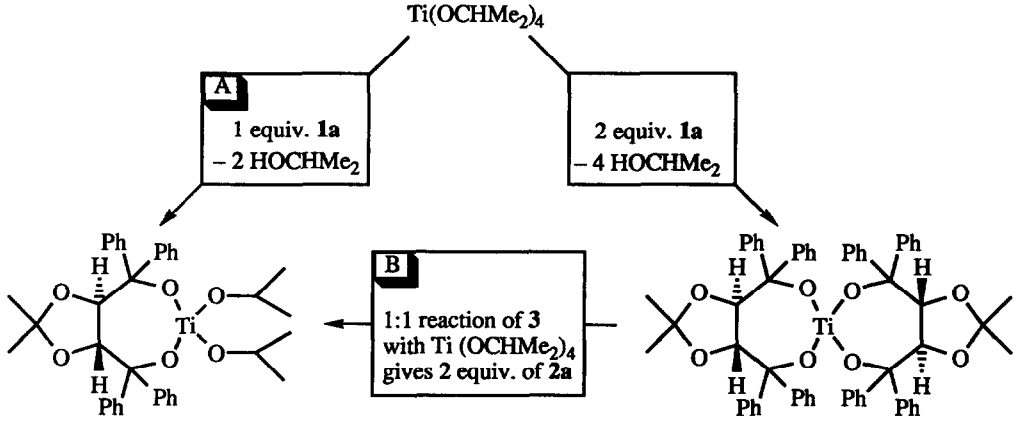


1



2

1, 2	a	b	c	d	e	f
R^1	Me	Me	Ph	Ph	t-Bu	$-(CH_2)_5-$
R^2	Me	Me	H	Ph	H	
Aryl	Ph	2-Nap	Ph	Ph	Ph	Ph



2a **3**

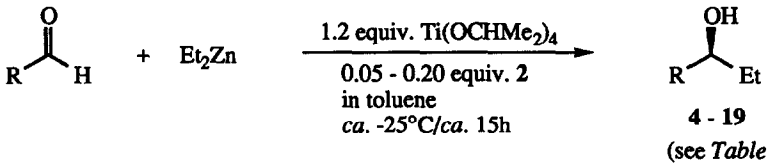
propyl titanate does not lead to new species such as doubly titanated TADDOLate.[2] The solutions of **2a** thus obtained are used directly for the subsequent reactions. An alternative procedure[1b,2] for preparing solutions of the Ti-TADDOLates **2** is the 1 : 1 reaction of $Ti(OCHMe_2)_4$ and a TADDOL **1**, again with azeotropic removal of two equivalents of isopropanol (Method A in *Scheme 2*). For the β-naphthyl derivative **2b** this is the only feasible route; the corresponding octanaphthyl-spirotitanate is so crowded that it does not form quantitatively

(see the crystal structure of the octaphenyl-spirotitanate **3** in ref.[2]). Of the numerous Ti-TADDOLates made so far,[2] only **2a** - **2f** were used for the present study. The preparation of the TADDOLs **1** themselves from tartrate acetals and aryl *Grignard* reagents has been described in a whole series of papers[18-23] since 1983. Since the enantiomeric tartrates and thus the TADDOLs are equally readily available[24] the enantiomers or epimers of all products described herein can of course also be prepared, with the same enantiomeric or diastereomeric purities.

ENANTIOSELECTIVE ADDITIONS OF Et_2Zn AND OF $(CH_2=CH-CH_2CH_2)_2Zn$ TO ALDEHYDES

Normally, the reactions of the commercial diethyl zinc in toluene solution are carried out at temperatures around -25°C, kept with a thermostat, and with overnight stirring (*Scheme 3*). A stoichiometric excess over the aldehyde of 20 - 80% Et_2Zn and of 20% tetraisopropoxy titanate is employed in all cases, and 0.2 equivalents of the chiral titanante **2** are added under the standard conditions. The results obtained with 16 different aldehydes are collected in the *Table*. With few exceptions, the products **4** - **19**, isolated from 5 - 10 mmol runs

Scheme 3



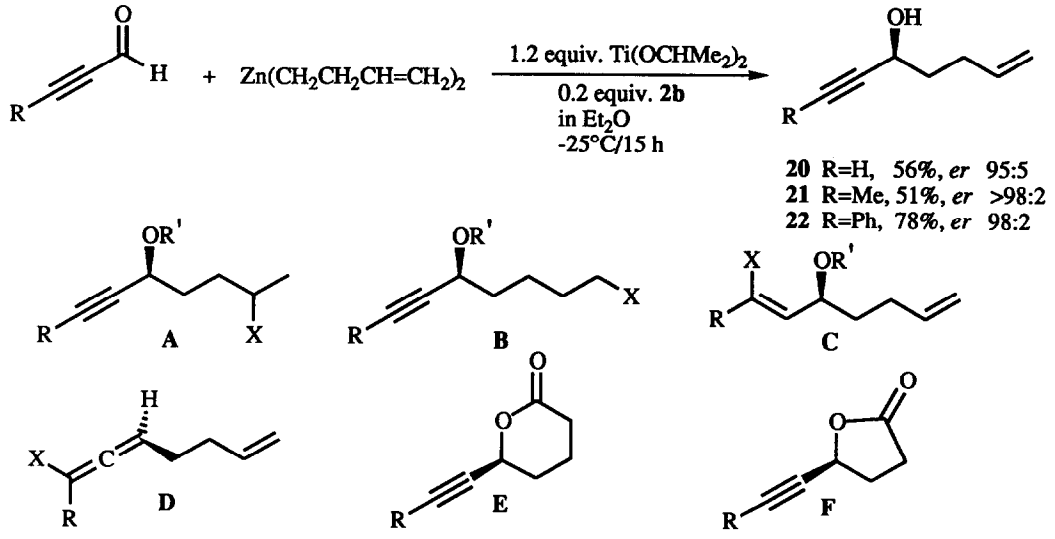
in high yields (after purification!), contain at least 98% of one enantiomer when the β-naphthyl-substituted TADDOLate **2b** is applied. Variations of the conditions lead to the following conclusions.

a) Especially with *aromatic aldehydes*, the most simple *TADDOL* **1a** can be used as a ligand for best results, but the reaction of *aliphatic aldehydes* is clearly more enantioselective with the naphthyl derivatives. b) As was shown previously for the addition of diethyl zinc to benzaldehyde[2], neither *variation of the aryl groups* nor of the *substituents in 2-position of the dioxolane ring* causes the enantiomer ratios to drop below 95 : 5 with the aldehydes tested[25,26]. c) Also, *the mode A or B of preparation of the titanates* **2** does not really influence the result, as long as the solutions of the chiral titanate are prepared with proper care.[27] d) *The amount of TADDOLate* was varied from 0.2 to 0.001 equivalents in the addition to cinnamaldehyde (→ **11**), it turns out that down to 5 mol % the selectivity decreases only minimally. e) It is worthwhile to determine *the best temperature* for a particular aldehyde substrate; with the aldehydo-ester leading to the hydroxyester **10** we have found that ice-bath temperature is best (*er* 95 : 5 at 0°C) while lower and higher reaction temperatures give rise to poorer selectivities (*er* 78 : 22 at -50 and 92 : 8 at +20°C).

Experience with enantioselective additions of nucleophilic organometallic reagents to aldehydes and ketones teaches us that functional groups in *both* components of the reaction normally lead to decreased selectivity[7,8], especially if heteroatoms of the functional group are in a position to form chelates with the metal center - intramolecularly within the organometallic reagent or intermolecularly with the substrate carbonyl

compound. One solution to this problem is to choose a geometry of the aldehyde which prevents chelation (*cf.* the precursor to **10** in the *Table*), or to choose a constitution of the aldehyde or of the nucleophilic reagent which renders chelation unfavorable (*cf.* ω-haloalkyl- or ω-alkoxy- and silyloxy-alkyl zinc compounds with a long chain between the metalated center and the donor substituent).[14] We can also avoid the problem by having "latent"[28] - or should we say innocent - functional groups (*cf.* C,C double and triple bonds,[1,8,13] possibly silyl or stannyl substituted,[14] or aryl groups[13]) which can be later transformed into "real" functional groups (see also the general discussion on functional group reactivity *umpolung*).[29] In *Scheme 4* we describe an example of enantioselective assembly of the highly unsaturated alcohols **20** - **22** from α,β-acetylenic aldehydes and homoallyl zinc reagent. An ether solution of dibutenyl zinc was prepared *in situ* from the corresponding magne-

Scheme 4



sium compound and $ZnCl_2$ following our previously published procedure.[13] Subsequent addition to propynal, butynal and phenyl-propynal in the presence of the naphthyl substituted Ti-TADDOLate gives the dextrorotatory alcohols **20** - **22** of high enantiopurity. Considering characteristic reactivities of C,C double and triple bonds we can envision simple transformations of these alcohols leading, for instance, to compounds of type **A** - **F**.

DETERMINATION OF ENANTIOMER RATIOS AND ASSIGNMENT OF THE SENSE OF CHIRALITY TO THE ALCOHOLS 4 - 22

All enantiomer ratios were determined by non-optical methods. A number of capillary gas chromatography (CGC) columns with chiral, cyclodextrin-derived[30] stationary phases, specified in the *experimental section*, were available to us for determining the enantiomer ratios of the alcohols **4** - **22**. In many cases this was possible without derivatization, often, however, better GC separation was observed with the

Table. *Ti-TADDOLate (2) Catalyzed Enantioselective Et_2Zn Addition to Aldehydes According to the Equation in Scheme 3.*
The product *formulae* **4** - **19** are presented with (*S*)-configuration, although the absolute configuration of some products is unknown (see references and $[a]_D$ values in the *experimental section*). The reactions were generally carried out on a 5 - 10 mmol scale in toluene. Method A and B refer to the way the TADDOLate **2** was prepared (see *Scheme 2*). All enantiomer ratios (*er*) were determinated either by ^{19}F-NMR spectroscopy of the *Mosher* esters or by gas chromatography (GC) on cyclodextrin columns of the free alcohols or of their trifluoro acetates (TFA), for details see *experimental section.*

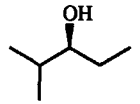
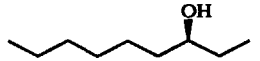
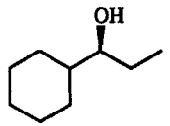
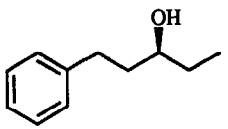
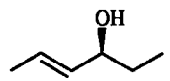
Product		Conditions						Yield	Enantiomer Ratio	
formula	No.	equiv. of Et_2Zn	equiv. of **2**		method of preparation	reaction time [h]	temperature [°C]	[%]	*er*	method of determination
	**4**	1.2	0.2	**2a**	B	17	-76 to -15	44	97 : 3	NMR
	5	1.2	0.2	**2a**	A	18	-27	82	96 : 4	NMR
	5	1.2	0.2	**2a**	B	24	-76 to -10	75	96 : 4	NMR
	**5**	1.2	0.2	**2b**	A	20	-28	70	**98.5** : **1.5**	NMR
	5	1.2	0.2	**2c**	A	18	-70 to -30	91	98 : 2	GC
	5	1.8	0.2	**2d**	A	30	-25	80	97 : 3	GC
	5	1.8	0.2	**2e**	A	24	-25	81	96 : 4	GC-TFA
	6	1.2	0.2	**2a**	B	20	-76 to +10	67	91 : 9	NMR
	**6**	1.2	0.2	**2b**	A	24	-27	77	**99.5** : **0.5**	GC
	6	1.2	0.2	**2c**	A	4	-27	64	96.5 : 3.5	GC-TFA
	6	1.8	0.2	**2d**	A	30	-25	88	89 : 11	GC-TFA
	6	1.8	0.2	**2e**	A	15	-25	84	90 : 10	GC
	**7**	1.2	0.2	**2a**	B	18	-76 to +20	85	90 : 10	[a]
	7	1.2	0.2	**2b**	A	13	-20	87	**> 99** : **1**	GC-TFA
	**8**	1.2	0.2	**2b**	A	24	-76 to -27	56	>99 : 1	GC

Table continued

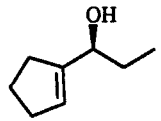
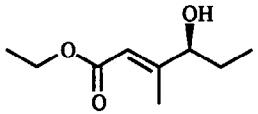
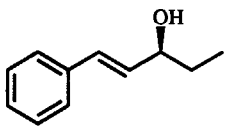
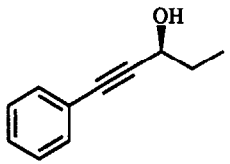
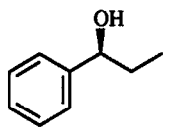
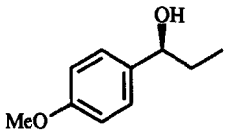
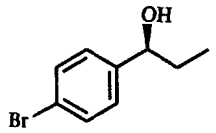
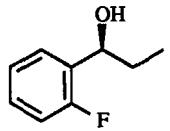
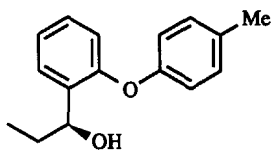
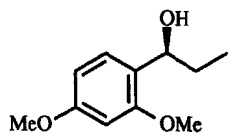
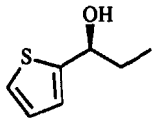
	**9**	1.2	0.2	**2b**	A	20	-29	79	99.5 : 0.5	GC
	10	1.8	0.2	**2a**	A	16	-26	83	92 : 8	GC
	10	1.8	1.0	**2a**	A	18	-25	92	94 : 6	GC
	10	1.8	0.2	**2b**	A	15	-90		72 : 28	GC
	**10**	1.8	0.2	**2b**	A	15	-70	81[a]	72 : 28	GC
	10	1.8	0.2	**2b**	A	15	-50	91[a]	78 : 22	GC
	10	1.8	0.2	**2b**	A	15	-60 to -25	97	94 : 6	GC
	10	1.8	0.2	**2b**	A	15	0	99[a]	**95** : **5**	GC
	10	1.8	0.2	**2b**	A	2	+20	99[a,b]	92 : 8	GC
	10	1.8	0.2	**2b**	A	1	+50	99[a,c]	86 : 14	GC
	10	1.8	0.2	**2c**	A	24	-25	77	95 : 5	GC
	11	1.2	0.2	**2a**	B	22	-75 to 0	89	**98** : **2**	NMR
	11	1.8	0.2	**2b**	A	23	-27	87	95.5 : 4.5	GC
	**11**	1.8	0.2	**2d**	A	14	-25	93	98 : 2	GC
	11	1.8	0.05	**2d**	A	18	-25	96	97 : 3	GC
	11	1.8	0.01	**2d**	A	18	-25	95	86 : 14	GC
	11	1.8	0.001	**2d**	A	18	-25	83	69 : 31	GC
	11	1.8	0.2	**2e**	A	21	-23	72	97 : 3	GC
	11	1.8	0.2	**2f**	A	21	-23	99	97 : 3	GC
	**12**	1.2	0.2	**2b**	A	22	-27	83	>99.5 : 0.5	GC
	**13**	1.8	0.2	**2a**	A	15	-25	99	99 : 1	GC

Table continued

	**14**	1.2	0.2	**2a**	B	20	-75 to +20	86	97 : 3	NMR
	14	1.8	0.2	**2a**	A	15	-25	95	**98** : **2**	GC
	**15**	1.2	0.2	**2a**	B	22	-75 to -30	88	95 : 5	NMR
	**16**	1.8	0.2	**2a**	A	14	-26	93	81 : 19	GC
	**17**	1.8	0.2	**2a**	A	14	-25	87	96 : 4	NMR
	**18**	1.8	0.2	**2a**	A	13	-25	95	85 : 15	GC
	18	1.8	0.2	**2b**	A	17	-25	98	81 : 19	GC
	**19**	1.2	0.2	**2a**	B	13	-75 to -30	75	97 : 3	NMR

a) Conversion of aldehyde to alcohol, detected by GC. b) Yield of isolated product 55%. c) Yield of isolated product 66%.

trifluoroacetates (TFA). Alternatively, or as an independent measurement, we determined the enantiomer ratios by preparing the *Mosher* esters[31] of the alcohols and analyzing the ratios of the resulting diastereoisomers by ^{19}F-NMR spectroscopy. The ratios are given in the *Table* and in the *experimental section*, together with the retention times in the case of GC analysis. The determination of enantiomer ratios in our products was always performed by comparison with independently prepared racemic samples. In those cases where we did not detect a second peak we give ratios >98 : 2, >99 : 1, or >99.5 : 0.5, depending upon the degree of our confidence in the detection limit of the particular column and compound (sometimes we added a small amount of racemic material to find out).

We should like to make a point in specifying the enantioselectivities of our reactions as ratios of enantiomers (*er*), values we actually determined, rather than as enantiomeric excesses (%ee), which result by substracting the smaller from the larger one of the measured numbers. We propose to drop the use of %ee which might have had some practical purpose in the times passed when we used "optical activities" and determined "optical purities" as a measure of enantiomer ratios.

In all *formulae* of this paper we draw the hydroxy substituted stereogenic centers generated with the aid of (*R*,*R*)-TADDOL in the (*S*)-configuration, corresponding to nucleophilic addition from the (*Si*)-face of the aldehyde groups (*relative topicity ul*[32]). This can be considered as established for the products **4** - **7** and **11**; references are given in the *experimental section*. For the 1-aryl-propanols **13** - **19**, **28** and **30** which are all laevorotatory, the absolute configuration (*S*) follows by comparison with literature data on known 1-aryl-1-alkanols.[33] In all other cases, the (*S*)-configuration of the newly formed stereogenic center is assigned by analogy.

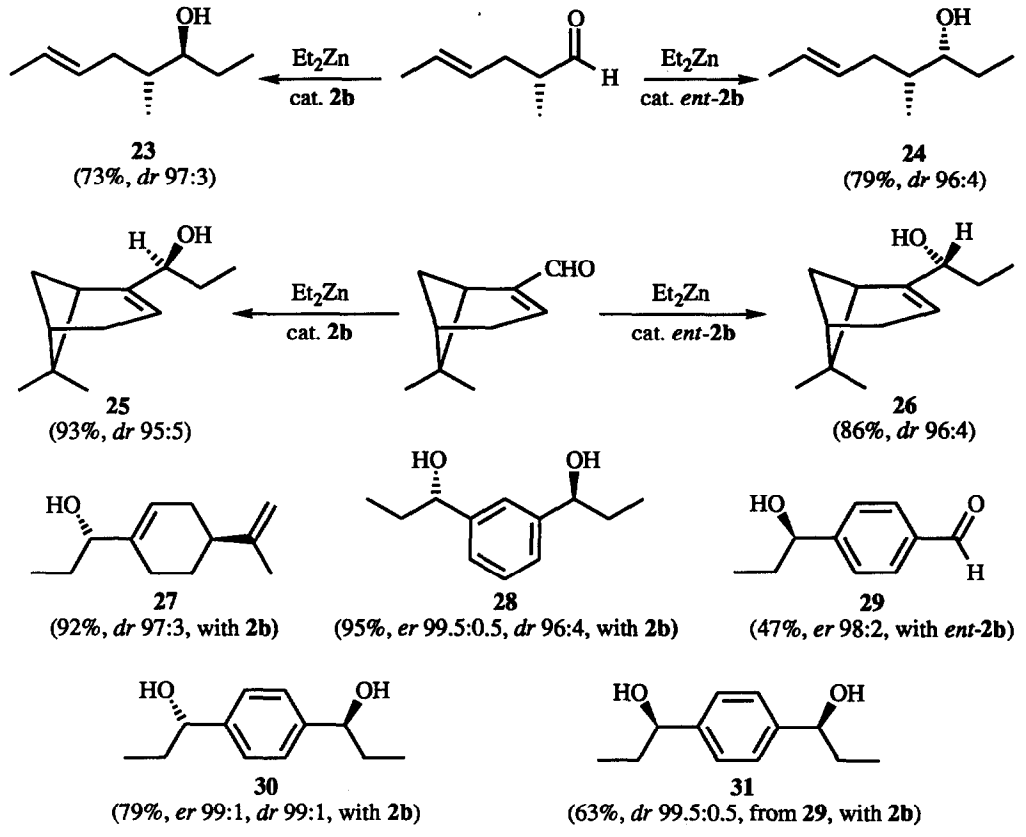
DIASTEREOSELECTIVE (*Re*)- AND (*Si*)-ADDITION OF Et_2Zn TO CHIRAL ALDEHYDES

As may have been expected, the Ti-TADDOLate mediated nucleophilic additions are highly *diastereoselective* with chiral aldehydes as substrates. Some examples are shown in *Scheme 5*.

Thus, (*R*)-2-methyl-4-hexanal, the aldehyde used for the synthesis of Me-Bmt, the unique aminoacid component of the cyclosporines,[34] is converted to the (3*S*,4*R*)-alcohol **23** by addition of Et_2Zn in the presence of the TADDOLate **2b**, while the (3*R*,4*R*)-epimer **24** is formed with *ent*-**2b**, with almost the same diastereoselectivities (97 : 3 *vs.* 96 : 4). Also, myrtenal gives the epimeric alcohols **25** and **26** by Et_2Zn addition, catalyzed with **2b** and *ent*-**2b**, respectively, and perillaldehyde is converted to the secondary alcohol **27** (*dr* 97 : 3). In all these cases we have not proved the absolute configuration of the newly formed stereogenic center; the configurational assignment solely rests upon the assumption that the TADDOLate mediated additions occur with relative topicities *ul*, i.e. that the (*R*,*R*)-titanate effects (*Si*) and its enantiomer (*Re*) addition.[35,36]

We have also added diethyl zinc to *meta*- and *para*-phthalaldehyde to prepare the diols **28**, **30**, and **31**, and the hydroxyaldehyde **29** in very high configurational purities. The configurations shown in *Scheme 5* are again not assigned by correlation but by analogy.[37]

Scheme 5



CONCLUSIONS

In summary, we have presented results delineating the scope and limitations of Ti-TADDOLate mediated enantioselective dialkyl zinc additions to aldehydes. Among the catalytic enantioselective C,C bond forming reactions this is one of the most general ones, considering the variety of aldehydes and alkyl nucleophiles to which it can be applied successfully (*er* ≥ 98 : 2, see the *Table*, *Scheme 4*, and ref.[13]). The solvent may not only be saturated hydrocarbons and toluene, but also ethers. The first systematic investigation of the chiral *Lewis* acid induced dialkyl zinc addition to chiral aldehydes indicates (*Scheme 5*) that the reaction is highly diastereoselective; there is essentially no influence of chirality centers in the aldehydes on the stereochemical outcome. The limitation of the method is its sensitivity to the presence of heteroatoms participating in chelations and of steric hindrance in the reactands.

As far as the mechanism of the reaction is concerned, our previous conclusions[2] are compatible with the findings reported herein: the aldehyde is complexing with the Ti-TADDOLate metal center in a trigonal bipyramidal or octahedral ligand sphere[38] in such a way that its (*Si*)-face is open to attack by the nucleophilic alkyl group. From the fact that saturated and unsaturated or aromatic aldehydes give the same results we conclude

that π-stacking or charge transfer interactions between the aldehyde substrates and the aryl groups on the TADDOL moiety are not important; *van der Waals* interactions appear to be the dominating factors controlling the stereochemical outcome of the reaction[39].

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EXPERIMENTAL SECTION

General. *Abbreviations*: GP (general procedure), HV (high vacuum), RV (evaporator), R_f (retention factor), R_t (retention time), r.t. (room temperature), TFA (trifluoroacetate).

Starting materials and reagents: A 2 M stock soln. of Et_2Zn was prepared from 10.25 ml of Et_2Zn (*Schering AG*, without purification) and 39.75 ml of toluene. A 1.0 M soln. of $ZnCl_2$ in diethylether (*Aldrich*) was used directly. $Ti(O^iPr)_4$ (*Hüls AG*) and aldehydes were distilled. Toluene and diethylether used in the reactions were dried immediately before use by refluxing and distillation over metallic potassium with benzophenone as indicator. All the reactions were carried out under Ar atmosphere. For the preparation of the TADDOLs **1a** - **f** see ref.[21,23], for the spirotitanate **3** see ref.[1a,13b] The commercially unavailable propargyl aldehyde and 2-butynal were prepared according to ref.[40]

Equipment: The addition reactions at constant low temperatures were performed using a cryostat *Frigomix* ® S (*B. Braun*) (*ca.* -25°C) or a special low temperature apparatus (-50°C, -70°C, -90°C) described in ref.[41]; for reactions with warming-up rates (*ca.* -76°C to 0°C, for exact temp. see *table*), a dry ice bath was used. Thin-layer chromatography (TLC): precoated silica gel 60 F_{254} plates (*Merck*); visualization by UV_{254} light, development using anisaldehyde soln. (9.2 ml anisaldehyde, 3.8 ml AcOH, 338 ml EtOH, 12.5 ml H_2SO_4) or phosphomolybdic acid soln. (25 g phosphomolybdic acid, 10 g $Ce(SO_4)_2 \cdot 4H_2O$, 60 ml H_2SO_4, 940 ml H_2O). Flash chromatography (FC): SiO_2 60 (0.040 - 0.063 mm, *Fluka*), pressure: 0.2 bar. Distillation for purification of the products: *Büchi GKR-50* bulb to bulb distillation apparatus. Boiling points (b.p.): correspond to uncorrected air bath temp. Melting points (m.p.): open glass capillaries, *Büchi 510* (*Tottoli* apparatus), 50°C range *Anschütz* thermometers, uncorrected. $[\alpha]_D^{RT}$ at r.t. (*ca.* 20°C) *Perkin-Elmer 241* polarimeter (*p.a.* solvents, *Fluka*). Capillary gas chromatography (CGC): *HRGC* or *MEGA HRGC 5160* (*Carlo Erba*); injector temp.: 230°C, detector temp.: 250°C, initial temp.: 50° - 80°C, heating rate: 0.5° - 1°C/min, pressure: 1.0 - 2.4 kPa (H_2). Columns: ß-CD: WCOT Fused Silica, Cyclodextrin-ß-2,3,6-M-19, 50 m x 0.25 mm (*Chrompack*); γ-CD: FS-Lipodex® E, 2,6-O-pentyl-3-O-butyryl-γ-CD, 50 m x 0.25 mm (*Macherey-Nagel AG*); CD-6: Heptakis(2,3,6-tri-O-methyl)-ß-cyclodextrin in OV 1701 Vi, 52 m x 0.27 mm (self-made)[42a,b] CD-17: Octakis(3-O-butanoyl-2,6-di-O-n-pentyl)-γ-cyclodextrin[42a,c] in OV 1701 Vi (1 : 2), 50 mm x 0.27 mm (self-made); CD-18: Hexakis(3-O-acetyl-2,6-O-dipentyl)-α-cyclodextrin[42a,d] in OV 1701 Vi (1 : 2), 52 m x 0.28

mm (self-made). IR: $CHCl_3$ soln. or film; *Perkin-Elmer 983* or *1600*; $\tilde{\upsilon}$ in cm^{-1}. ^1H and ^{13}C-NMR spectra: *Varian Gemini 200* (200 and 50 MHz, resp.) or *Bruker WM 300* (300 and 75 MHz, resp.), δ in ppm downfield of TMS ($\delta = 0$), J in Hz. ^{19}F-NMR spectra: *Varian Gemini 300* or *Bruker WM 300* (282 MHz), δ in ppm downfield of CCl_3F ($\delta = 0$). MS: VG-*Tribid* spectrometer, fragment ions in *m/z* with relative intensities (%) in parentheses. Elemental analyses were performed by the *Microanalytical Service Laboratory of the Laboratorium für Organische Chemie (ETH Zürich).*

Preparation of the trifluoroacetate (TFA)-derivatives [43]: To a soln. of 1 mg of alcohol in 200 µl of methylene chloride was added 50 µl of trifluoroacetic anhydride. The soln. was stirred for 10 - 30 min at r.t. and then nitrogen gas was passed through for several minutes. The obtained sample was used directly for GC.

Preparation of the Mosher-*derivatives*:[31] To a soln. of 25 µl of alcohol in 500 µl of pyridine was added 20 µl of (*S*)-(+)- or (*R*)-(-)-α-methoxy-α-(trifluoromethyl)phenyl acetyl chloride. The mixture was stirred over night (*ca.* 15 h) at r.t. and then poured into 15 ml of ether, washed with ice cold 2 N HCl soln. and sat. $NaHCO_3$ soln. The organic layer was dried over $MgSO_4$ and evaporated (RV). The residue was dried under HV and then used directly for ^{19}F-NMR.

Enantioselective Addition of dialkyl zinc to aldehydes

I. *Using chiral "monocyclic" titanates as catalysts prepared from TADDOLs and Ti(O^{i}Pr)$_4$ (Method A, see Scheme 2) (GPI):*

For a detailed procedure and NMR data of the titanates **2a-c, e, f** see ref.[2] NMR data of hexaphenyl TADDOL "monocyclic" titanate **2d**: ^1H-NMR (300 MHz): 7.80 - 6.70 (m, 30 H, arom.); 5.38 (s, 2 H, 2 OCH); 4.60 - 4.33 (br. s, 2 H, $CHMe_2$); 1.25 - 1.00 (m, 12 H, 4 CH_3). ^{13}C-NMR (75 MHz): 148.04, 144.24, 141.40, 128.79, 128.61, 128.42, 128.02, 127.83, 127.60, 127.47, 127.14, 127.00, 126.70, 126.58, 126.32, 125.92, 125.80, 125.55, 112.22, 93.61, 84.25, 77.86 (br.), 25.99.

To a stirred soln. of 0.001 - 1 equiv. (0.1 - 100 mol%) of the chiral "monocyclic" titanate **2a-f** and 1.2 equiv. of Ti(O^{i}Pr)$_4$ in toluene (20 ml/*ca.* 5 mmol aldehyde) was added 1 equiv. aldehyde (neat). The resulting slightly yellow soln. was cooled to *ca.* -25°C and 1.8 equiv. of Et_2Zn soln. were introduced at such a rate that the temperature was kept below -20°C. This yellow soln. was then stirred at *ca.* -25°C until no aldehyde could be detected by TLC (*ca.* 1 - 30 h). After hydrolysis with 15 ml of sat. NH_4Cl soln., the mixture was allowed to slowly warm up to r.t. and was then filtered through celite to remove the insoluble products of the hydrolysis. The organic phase was separated and the aqueous layer was extracted with 3 x 30 ml of ether. The combined organic phases were washed with sat. NaCl soln., dried over $MgSO_4$, evaporated (RV) and the product was isolated by bulb to bulb distillation or FC. The ratios of enantiomers or diastereoisomers were determined by CGC of the isolated alcohols or their trifluoroacetate derivatives on chiral columns or by ^{19}F-NMR of the *Mosher*-ester derivatives.

II. *Using chiral "monocyclic" titanates prepared from the spirotitanate 3 and Ti(O^{i}Pr)$_4$ (Method B, see Scheme 2) (GPII):*

To a stirred soln. of 0.1 equiv. of the spirotitanate **3** and 1.2 equiv. of Ti(O^{i}Pr)$_4$ in toluene (10 ml/*ca.* 7 mmol aldehyde) was added at *ca.* -25°C 1.2 equiv. of Et_2Zn soln. After 15 min, the solution was cooled to *ca.* -78°C and 1 equiv. of aldehyde (neat or dissolved in toluene) was added dropwise. The reaction mixture was then stirred for *ca.* 15 h with gradual warming to *ca.* 10°C (for exact reaction times and temperatures see *Table* and procedures below). Upon completion of the reaction (TLC detection), 10 ml of sat. NH_4Cl soln. and 30 - 50 ml of ether were added. The mixture was stirred for 30 min at r.t., then filtered through celite. The organic layer

was washed with sat. NaCl soln., then dried over Na_2SO_4 and evaporated (RV). The residue was then purified by FC through a short column (hexane/ether 3 : 1) to remove unreacted aldehyde and traces of a light yellow impurity. The pure alcohols were obtained by bulb to bulb distillation under reduced pressure (*ca.* 25 Torr).

Preparation of the dihomoallyl zinc reagent[13b]: *a) 3-Buten-1-yl-magnesium bromide*: To 5.0 g (206 mmol) of magnesium powder (*Fluka*, purity: 99.8%) in 50 ml ether was added *ca.* 1 ml of a total of 20.5 ml (200 mmol) of 1-bromo-3-butene. After the reaction had started, the rest of 1-bromo-3-butene, dissolved in 150 ml of ether, was added dropwise, so that the ether remained boiling. After the addition the mixture was stirred at r.t. for 2 h and then refluxed for another 2 h. The obtained *Grignard* reagent (*ca.* 1.4 - 1.8 M) was standardized by titration with *sec* - butanol using 1,10-phenantroline as indicator.[44] *b) Dihomoallyl zinc*: To a soln. of 20 ml (20 mmol) of 1.0 M zinc chloride soln. were added 10 ml of ether and 40 mmol of 3-buten-1-yl-magnesium bromide (*ca.* 30 ml soln. see *a)*, above). The resulting suspension was stirred at r.t. for 2 h, then 12 ml of 1,4-dioxane was added, at which time precipitation of the dioxane-magnesium complex occurred. After stirring for an additional 45 min and subsequent filtration through a *Schlenk* filter under Ar, a clear soln. of the dihomoallyl zinc reagent was obtained.

Enantioselective homoallylation using tetra(ß-naphthyl) "monocyclic" titanate **2b** *as catalyst* (GPIII): Aldehyde (5 or 10 mmol, 1 equiv.) was added to a soln. of 1 or 2 mmol (20 mol%) of tetra(ß-naphthyl) "monocyclic" titanate **2b** and 1.2 equiv. of $Ti(O^iPr)_4$ in 20 ml of ether. The yellow soln. was cooled to *ca.* -25°C and 2 or 3 equiv. of dihomoallyl zinc were added slowly, so that the temperature remained below -20°C. The reaction mixture was then stirred for *ca.* 15 h. After complete conversion of the aldehyde (TLC) the reaction was quenched at *ca.* -25°C with 15 ml of sat. NH_4Cl soln. The mixture was allowed to warm to r.t. and was then filtered through celite. The organic layer was washed with 30 ml of sat. NaCl soln., dried over $MgSO_4$ and evaporated (RV). The product was isolated by FC (hexane/ether 4 : 1) or by bulb to bulb distillation.

(S)-2-Methyl pentan-3-ol (**4**): Following GPII, 0.72 g (0.92 ml, 10 mmol) of isobutyraldehyde, 3.55 ml (12 mmol) of $Ti(O^iPr)_4$, 6 ml (12 mmol) of Et_2Zn soln. with 1 mmol (10 mol%) of spirotitanate **3** in 20 ml hexane gave after 17 h at -76° to -15°C 0.44 g (44%) of **4** as colorless oil [(*S*)/(*R*) = 97 : 3, ^{19}F-NMR]; b.p.: 100°C/500 Torr (ref.[45]: 126°C/760 Torr); $[\alpha]_D^{RT}$ = -12.97 (c = 2.2, $CHCl_3$) (ref.[45]: $[M]_D^{25}$ = -16.7 (neat) for the (*S*)-form). IR (film): 3380s, 2960s, 2940s, 2880s, 1465s, 1385m, 1370m, 1105m, 978s, 960s. ^{1}H-NMR (300 MHz): 3.27 (m, 1 H, C(3)-H); 1.59 (s, 1 H, OH); 1.72 - 1.32 (m, 3 H, C(2)-H, C(4)-H_2); 0.98 - 0.90 (m, 9 H, 3 CH_3); ^{13}C-NMR (75 MHz): 78.24, 33.11, 26.96, 18.94, 17.12, 10.32; MS: 101 (M^+-1), 84 (4), 73 (70), 59 (100), 58 (35), 57 (13), 55 (35), 45 (18), 43 (24), 41 (36), 39 (11), 31 (51), 29 (16), 27 (17).

(S)-3-Nonanol (**5**): Following GPI, 0.89 ml (6.35 mmol) of heptanal and 5.72 ml (11.43 mmol) of Et_2Zn soln. with 1.27 mmol (20 mol%) of titanate **2e** and 2.24 ml (7.62 mmol) of $Ti(O^iPr)_4$ gave after 24 h at *ca.* -25°C 0.74 g (81%) of **5** as colorless oil [(*S*)/(*R*) = 96 : 4, TFA, ß-CD, R_t: 41.02/41.71]; b.p.: 150°C/25 Torr (ref.[46]: 96° - 98°C/19 Torr); $[\alpha]_D^{RT}$ = +6.05 (c = 1.14, $CHCl_3$) (ref.[46]: $[\alpha]_D^{25}$ = +7.08 (neat) for the (*S*)-form). ^{1}H-NMR (200 MHz): 3.60 - 3.40 (m, 1 H, C(3)-H); 1.78 - 1.00 (m, 13 H, 6 CH_2, OH); 1.00 - 0.70 (m, 6 H, 2 CH_3); ^{13}C-NMR (75 MHz): 73.35, 27.03, 31.92, 30.20, 29.46, 25.70, 22.69, 14.11, 9.90; MS: 143 (M^+-1); 126 (5), 115 (29), 97 (60), 69 (16), 59 (100), 58 (12), 57 (11), 55 (82), 43 (22), 41 (27), 31 (20), 29 (16), 27 (10).

(S)-1-Cyclohexyl-1-propanol (**6**): Following GPI, 0.78 g (0.87 ml, 7 mmol) of cyclohexylcarbaldehyde and 4.0 ml (8.0 mmol) of Et_2Zn soln. with 1.4 mmol (20 mol%) of titanate **2b** and 2.47 ml (8.4 mmol) of $Ti(O^iPr)_4$ gave after 24 h at -27°C 0.77 g (77%) of **6** as colorless oil [(*S*)/(*R*) = 99.5 : 0.5, CD-6, R_t: 33.93/34.53]; b.p. 110° - 120°C/14 Torr (ref.[47]106°C/19Torr; $[\alpha]_D^{RT}$ = -7.35 (neat) (ref.[47]: $[\alpha]_D^{3.0}$ = -8.1 (neat) for the

(*S*)-form). ^{1}H-NMR (200 MHz): 3.34 - 3.20 (m, 1 H, C(1)-H); 1.90 - 1.00 (m, 14 H, 6 CH_2, CH, OH); 0.95 (t, J = 7.5, 3 H, CH_3).

(S)-1-Phenyl-pentan-3-ol (**7**): Following GPI, 0.93 g (0.93 ml, 7 mmol) of 3-phenylpropanal and 4.2 ml (8.4 mmol) of Et_2Zn soln. with 1.4 mmol of titante **2b** and 2.47 ml (8.4 mmol) of $Ti(O^iPr)_4$ gave after 13 h at -28°C 1.0 g (87%) of **7** as colorless oil [(*S*)/(*R*) = > 99 : 1, TFA, CD-17, R_t: 90.28]; b.p. 132° - 135°C/22 Torr (ref.[48]: 98° - 100°C/0.03 Torr); $[\alpha]_D^{RT}$ = +22.6 (c = 7, EtOH) (ref.[48]: $[\alpha]_D^{20}$ = +26.8 (c = 5, EtOH) for the (*S*)-form).

(S)-2-Hexen-4-ol (**8**): Following GPI, 0.49 g (0.58 ml, 7 mmol) of crotonaldehyde and 4.2 ml (8.4 mmol) of Et_2Zn with 1.4 mmol (20 mol%) of titanate **2b** and 2.47 ml (8.4 mmol) of $Ti(O^iPr)_4$ gave after 24 h at -76° to -27°C 0.39 g (56%) of **8** as colorless oil [(*S*)/(*R*) = > 99 : 1, CD-6, R_t: 23.71]; $[\alpha]_D^{RT}$ = -2.8 (c = 1.3, $CHCl_3$). ^{1}H-NMR (200 MHz): 5.55 (ddd, $J_1 = J_2 = 6$, $J_3 = 1$, 1 H, C(3)-H); 5.50 (qd, $J_1 = J_2 = 6$, 1 H, C(2)-H); 3.95 (ddd, $J_1 = J_2 = J_3 = 6$, 1 H, C(4)-H); 1.70 (dd, $J_1 = 6$, $J_2 = 1$, 3 H, C(1)-H_3); 1.6 - 1.3 (m, 3 H, OH, CH_2); 0.89 (t, J = 7, 3 H, C(6)-H_3); ^{13}C-NMR (50 MHz): 134.40, 127.26, 74.76, 30.30, 17.83, 9.91; MS: 100 (M^+, 11), 85 (28), 72 (12), 71 (100), 69 (15), 67 (11), 57 (31), 55 (15), 53 (35), 43 (90), 42 (10), 41(65), 39 (32), 31 (17), 29 (37), 28 (21), 27 (39).

(S)-1-(1'-Cyclopentenyl)-propanol (**9**): Following GPI, 0.67 g (0.74 ml, 7 mmol) of 1-cyclopentenylcarbaldehyde and 4.2 ml (8.4 mmol) of Et_2Zn soln. with 1.4 mmol (20 mol%) of titanate **2b** and 2.5 ml (8.4 mmol, 20 mol%) of $Ti(O^iPr)_4$ gave after 20 h at -29°C 0.70 g (79%) of **9** as colorless oil [(*S*)/(*R*) = 99.5 : 0.5, ß-CD, R_t: 35.95]; b.p.: 110° - 120°C/14 Torr; $[\alpha]_D^{RT}$ = -15.9 (c = 3, $CHCl_3$). IR (film): 3354s, 2959s, 2847s, 1651w, 1462w, 1154w, 1093w, 1035w, 1004w, 948m, 897w, 821w; ^{1}H-NMR (200 MHz): 5.58 - 5.57 (m, 1 H, C(2')-H); 4.17 (dd, $J_1 = J_2 = 6$, 1 H, C(1)-H); 2.40 - 2.20 (m, 4 H, C(3')-H_2, C(5')-H_2); 1.95 - 1.98 (m, 2 H, C(4')-H_2); 1.70 - 1.50 (m, 3 H, C(2)-H_2, OH); 0.92 (t, J = 7.5, 3 H, CH_3); ^{13}C-NMR (50 MHz): 146.60, 125.38, 72.43, 31.85, 30.71, 28.07, 23.08, 9.81; MS: 127 (8), 126 (M^+, 64), 109 (9), 98 (38), 97 (100), 95 (28), 93 (17), 91 (9), 85 (15), 83 (8), 79 (69), 77 (30), 69 (88), 67 (73), 65 (18), 59 (12), 57 (44), 55 (47), 53 (19), 51 (11), 43 (43), 41 (77), 39 (55), 31 (25), 29 (47), 28 (56), 27 (37).

Ethyl (E,S)-4-Hydroxy-3-methyl-2-hexenoate (**10**): Following GPI, 0.76 ml (5.56 mmol) ethyl 3-methyl-4-oxocrotonate and 5 ml (10.0 mmol) of Et_2Zn soln. with 1.11 mmol (20 mol%) of titanate **2b** and 1.97 ml (6.67 mmol) of $Ti(O^iPr)_4$ gave after 17 h at -60° to -25°C 0.93 g (97%) of **10** as colorless oil [(*S*)/(*R*) = 94 : 6, γ-CD, R_t: 52.00/51.51]; R_f (hexane/ether 1 : 1): 0.41; $[\alpha]_D^{RT}$ = -10.20 (c = 1.47, $CHCl_3$). IR (film): 3456m(br.), 2977m, 2937m, 2877s, 1715s, 1695s, 1652m, 1456w, 1368m, 1281w, 1220s, 1257s, 1114m, 1095m, 1040m, 984w, 870w, 833w, 652w; ^{1}H-NMR (300 MHz): 5.92 - 5.90 (m, 1 H, C(2)-H); 4.16 (q, J = 7, 2 H, OCH_2); 4.04 - 4.00 (m, 1 H, C*H*OH); 2.10 (d, J = 1, 3 H, 3-CH_3); 2.01 (d, J = 4, 1 H, OH); 1.77 - 1.47 (m, 2 H, C(5)-H2); 1.26 (t, J = 7, 3 H, OCH_2CH_3); 0.93 (t, J = 7, 3 H, C(6)-H_3); ^{13}C-NMR (75 MHz): 166.90, 159.92, 115.34, 77.88, 59,79, 27.90, 74.73, 14.31, 9.68. Anal. calcd. for $C_7H_{16}O_3$ (172.22): C 62.77, H 9.36; Found: C 63.07, H 9.34.

(E,S)-1-Phenyl-1-penten-3-ol (**11**): Following GPI, 0.63 ml (0.66 g, 5 mmol) of *trans*-cinnamaldehyde and 4.5 ml (9 mmol) of Et_2Zn soln. with 1 mmol (20 mol%) of titanate **2d** and 1.77 ml (6 mmol) of $Ti(O^iPr)_4$ gave after 14 h at *ca.* -25°C 0.75 g (93%) **11** as colorless oil [(*S*)/(*R*) = 98 : 2, CD-18, R_t: 95.57/94.29]; $[\alpha]_D^{RT}$ = -6.18 (c = 1.65, $CHCl_3$) (ref.[49a]: $[\alpha]_D^{21}$ = -6.7 (neat), ref.[49b]: $[\alpha]_D^{21}$ = -6.23 (2.6, $CHCl_3$) for the (*S*)-form).

(S)-1-Phenyl-1-pentyn-3-ol (**12**): Following GPI, 0.91 g (0.86 ml, 7 mmol) of phenylpropargyl aldehyde and 4.5 ml (9.0 mmol) of Et_2Zn soln. with 1.4 mmol (20 mol%) of titanate **2b** and 2.5 ml (8.4 mmol) $Ti(O^iPr)_4$ gave after 22 h at -27°C 0.93 g (83%) of **12** as colorless oil [(*S*)/(*R*) = > 99.5 : 0.5, CD-18, R_t: 39.94];

b.p.: 120°C/0.35 Torr (ref.[50]: 105° - 106°C/0.5 Torr); $[\alpha]_D^{RT}$ = -59.32 (neat). IR (film): 3343s, 2967s, 2934m, 2876m, 2220w, 1598w, 1489s, 1443m, 1339m, 1098m, 1070w, 1048m, 1014m, 963m, 915w, 865w, 756s, 691s; ^{1}H-NMR (200 MHz): 7.46 - 7.40 (m, 2 H, arom.); 7.34 - 7.26 (m, 3 H, arom.); 4.55 (ddd, $J_1 = J_2 = J_3 = 6$, 1 H, C(3)-H); 2.10 (d, J = 6, 1 H, OH); 1.83 (ddt, $J_1 = J_2 = 8$, $J_3 = 7.5$, 2 H, C(4)-H_2); 1.10 (t, J = 7.5, 3 H, CH_3); ^{13}C-NMR (50 MHz): 132.06, 128.72, 128.64, 123.03, 90.27, 85.22, 64.48, 31.19, 9.70; MS: 161 (4), 160 (31), 159 (14), 132 (20), 131 (100), 129 (8), 115 (7), 103 (40), 102 (9), 77 (22).

(S)-1-Phenyl-1-propanol (**13**) *and (S)-1-(4'-Methoxyphenyl)-1-propanol* (**14**): For experimental details and characterization see ref.[2]

(S)-1-(4'-Bromophenyl)-1-propanol (**15**): Following GPII, 1.32 g (7 mmol) of 4-bromobenzaldehyde (in 5 ml toluene), 2.6 ml (9 mmol) of Ti(O^{i}Pr)$_4$, 0.7 g (10 mol%) of spirotitanate **3** and 4.5 ml (9 mmol) of Et_2Zn soln. gave after 22 h at -76° to -30°C 1.33 g (88%) **15** as colorless oil [(*S*)/(*R*) = 95 : 5, ^{19}F-NMR]; b.p.: 125°C/0.3 Torr (ref.[51]: 140° - 142°C/13 Torr); $[\alpha]_D^{RT}$ = -17.9° (c = 3.8, C_6D_6). IR (film): 3365s(br.), 3080w, 3060w, 3042w, 3020w, 2970s, 2935s, 2880s, 1592m, 1488s, 1465s, 1405s, 1095s, 1085s, 1072s, 1047m, 1012s, 978s, 840s, 823s; ^{1}H-NMR (300 MHz): 7.47 (d, J = 8, 2 H, arom. 3', 5'-H); 7.18 (d, J = 8, arom. 2', 6'-H); 4.52 (t, J = 6.5, 1 H, C*H*OH); 2.24 (s, 1 H, OH); 1.74 (m, 2 H, CH_2); 0.88 (t, J = 7.5, 3 H, CH_3); ^{13}C-NMR (75 MHz): 143.56, 131.46, 127.74, 121.16, 75.26, 31.88, 9.97; MS: 216 (42), 214 (42), 199 (44), 197 (44), 188 (18), 187 (98), 185 (100), 159 (31), 157 (39), 105 (10), 78 (56), 77 (80), 75 (19), 59 (8), 57 (8), 51 (18), 50 (10), 29 (9).

(S)-1-(2'-Fluorophenyl)-1-propanol (**16**): Following GPI, 0.82 g (6.61 mmol) of 2-fluorobenzaldehyde and 5.95 ml (11.90 mmol) of Et_2Zn soln. with 1.32 mmol (20 mol%) of titanate **2a** and 2.34 ml (7.93 mmol) of Ti(O^{i}Pr)$_4$ gave after 14 h at *ca.* -25°C 0.94 g (93%) **16** as colorless oil [(*S*)/(*R*) = 81 : 19, ß-CD, R_t: 35.07/34.21]; R_f (hexane/ether 4 : 1): 0.13; $[\alpha]_D^{RT}$ = -20.06 (c = 1.77, $CHCl_3$); b.p.: 105°/0.2 Torr. IR (film): 3360s(br.), 3065w, 3040w, 2960s, 2940s, 2889m, 1615m, 1585m, 1490s, 1455s, 1380w, 1360w, 1330w, 1270m, 1220s, 1180m, 1150w, 1120w, 1085m, 1050m, 1030w, 1015m, 980m, 940w, 905w, 830w, 815w, 800w; ^{1}H-NMR (300 MHz): 7.46 - 6.96 (m, 4 H, arom.), 4.92 (t, J = 6, 1 H, C*H*OH); 2.05 (s, 1 H, OH); 1.85 - 1.74 (m, 2 H, CH_2); 0.93 (t, J = 7, CH_3); ^{13}C-NMR (75 MHz): 161.60, 158.35, 131.62, 131.46, 128.80, 128.70, 127.41, 127.34, 124.21, 115.40, 115.11, 69.76, 30.98, 9.94; MS: 154 (M^+, 19), 137 (56), 125 (100), 115 (5), 109 (25), 97 (86), 77 (70), 70 (11), 63 (11), 57 (23), 51 (57), 43 (16), 39 (20), 31 (15), 29 (43), 18 (19). Anal. calcd. for $C_9H_{14}OF$ (154.18): C 70.01, H 7.19; Found: C 70.03, H 7.21.

(S)-1-[2-(4'-methylphenoxy)phenyl]-1-propanol (**17**): Following GPI, 1.28 g (6.01 mmol) of 2-(4'-methylphenoxy)benzaldehyde and 5.41 ml (10.82 mmol) Et_2Zn soln. with 1.2 mmol (20 mol%) of titanate **2a** and 2.12 ml (7.21 mmol) of Ti(O^{i}Pr)$_4$ gave after 14 h at *ca.* -25°C 1.27 g (87%) of **17** as colorless oil [(*S*)/(*R*) = 96 : 4, ^{19}F-NMR]; R_f (hexane/ether 4 : 1): 0.18; b.p.: 150°C/10^{-3} Torr; $[\alpha]_D^{RT}$ = -18.02 (c = 1.77, $CHCl_3$). IR (film): 3380m(br.), 3030w, 2960m, 2930m, 2880m, 1605m, 1585s, 1505s, 1485s, 1445s, 1380w, 1350w, 1310w, 1250s, 1215s, 1170m, 1140w, 1105w, 1045w, 1020w, 980w, 950w, 880w, 825m, 790m, 700m; ^{1}H-NMR (300 MHz): 7.29 - 6.84 (m, 8 H, arom.); 4.53 (t, J = 7, 1 H, C*H*OH); 2.33 (s, 3 H, CH_3Ph); 2.03 (s, br., 1 H, OH); 1.82 = 1.65 (m, 2 H, CH_2); 0.94 (t, J = 7, 3 H, CH_3CH_2); ^{13}C-NMR (75 MHz): 157.92, 154.64, 146.71, 132.92, 130.24, 129.58, 120.36, 119.25, 119.95, 118.96, 117.24, 115.89, 75.65, 31.85, 20,69; MS: 242 (M^+, 62), 225 (13), 213 (67), 185 (76), 167 (28), 152 (13), 141 (7), 128 (5), 115 (18), 197 (76), 91 (82), 77 (82), 65 (100), 51 (58), 39 (44), 29 (37). Anal. calcd. for $C_{16}H_{18}O_2$ (242.32): C 79.31, H 7.49; Found: C 79.34, H 7.57.

(S)-1-(2',4'-Dimethoxyphenyl)-1-propanol (**18**): Following GPI, 1.06 g (6.4 mmol) of 2,4-dimethoxybenzaldehyde and 5.76 ml (11.52 mmol) of Et_2Zn soln. with 1.28 mmol (20 mol%) titanate **2a** and 2.26 ml (7.68 mmol) of $Ti(O^iPr)_4$ gave after 14 h at *ca.* -25°C 1.19 g (95%) of **18** as colorless oil [(*S*)/(*R*) = 85 : 15, ß-CD, R_t: 78.20/78.94]; R_f (hexane/ether 4 : 1): 0.23; $[\alpha]_D^{RT}$ = -17.05 (c = 1.12, $CHCl_3$). IR (film): 3420m(br.), 3000m, 2960s, 2935s, 2865m, 2835m, 1610s, 1585s, 1505s, 1460s, 1435m, 1415m, 1285s, 1260s, 1205s, 1180m, 1155s, 1130s, 1095m, 1040s, 970m, 935m, 920m, 895w, 830m, 800m, 635w; ^{1}H-NMR (300 MHz): 7.20 - 7.17 (m, 1 H, arom.); 6.48 - 6.44 (m, 2 H, arom.); 4.75 - 4.69 (m, 1 H, C*H*OH); 3.80 (s, 3 H, OCH_3); 3.79 (s, 3 H, OCH_3); 2.53 (d, J = 5, OH); 1.86 - 1.73 (m, 2 H, CH_2); 0.92 (t, J = 7, 3 H, CH_3); ^{13}C-NMR (75 MHz): 159.98, 157.74, 127.63, 125.07, 110.13, 104.09, 98.67, 71.83, 59.26, 30.17, 10.49; MS: 196 (M^+, 3), 178 (100), 167 (54), 165 (6), 134 (17), 121 (23), 103 (18), 91 (13), 77 (13), 65 (5), 28 (6).

(S)-1-(2'-Thienyl)-1-propanol (**19**): Following GPII, 0.97 g (0.80 ml, 8.6 mmol) of thiophen-2-carbaldehyde and 5.2 ml (10.4 mmol) of Et_2Zn soln. with 0.86 mmol (10 mol%) of spirotitanate **3** and 3.0 ml (10.3 mmol) of $Ti(O^iPr)_4$ gave after 13 h at -76° to -30°C 0.92 g (75%) of **19** as colorless oil [(*S*)/(*R*) = 97 : 3, ^{19}F-NMR]; b.p.: 125°C/14 Torr; $[\alpha]_D^{RT}$ = -26.8 (c = 10.24, $CHCl_3$). IR (film): 3389s, 3110w, 3075w, 2970s, 2935s, 2880s, 1625m, 1610m, 1462s, 1455m, 1440m, 1429m, 1175m, 1095m, 1072m, 1045m, 1035m, 1020m, 1005s, 972s, 700s; ^{1}H-NMR (300 MHz): 7.25 (m, 1 H, CHS); 6.95 (m, 2 H, arom.); 4.80 (m, 1 H, C*H*OH); 2.30 (d, J = 3.5, 1 H, OH); 1.86 (m, 2 H, CH_2); 0.95 (t, J = 7, 3 H, CH_3); ^{13}C-NMR (75 MHz): 148.68, 126.57, 124.44, 123.76, 71.73, 32.23, 10.15; MS: 143 (9), 142 (M^+, 69), 126 (18), 125 (91), 115 (15), 114 (20), 113 (100), 112 (16), 111 (26), 97 (15), 85 (90), 69 (7), 59 (13), 58 (10), 57 (12), 45 (55), 41 (16), 39 (34), 29 (20), 27 (18), 18 (8).

(S)-6-Hepten-1-yn-3-ol (**20**): Following GPIII, 0.27 g (5 mmol) of propiolaldehyde and 15 mmol of homoallyl zinc reagent with 1 mmol (20 mol%) of titanate **2b** and 1.77 ml (6 mmol) of $Ti(O^iPr)_4$ gave after 14 h at *ca.* -25°C 0.31 g (56%) **20** as colorless oil [(*S*)/(*R*) = 95 : 5, ^{19}F-NMR]; R_f (hexane/ether 4 : 1): 0.25; b.p.: 90°C/25 Torr; $[\alpha]_D^{RT}$ = +1.00 (c = 1.10, $CHCl_3$). IR (film): 3298s(br.), 3079m, 2089m, 2047s, 2862m, 2115w, 1840w, 1641s, 1441m, 1416m, 1328m, 1305m, 1118m, 1067s, 1024s, 916s, 856w, 658s; ^{1}H-NMR (300 MHz): 5.84 (ddt, J_1 = 7, J_2 = 10, J_3 = 17, 1 H, C(6)-H); 5.08 (dq, J_1 = 17, J_2 = 2, 1 H, C(7)-H); 5.01 (dq, J_1 = 10, J_2 = 2, 1 H, C(7)-H); 4.40 (t, J = 6, 1 H, C(3)-H); 2.49 (d, J = 2, 1 H, C(1)-H); 2.09 - 2.21 (m, 2 H, CH_2); 2.21 (s, br., 1 H, OH); 1.91 - 1.74 (m, 2 H, CH_2); ^{13}C-NMR (75 MHz): 137.51, 115.40, 84.75, 73.13, 61.77, 36.71, 29.26; MS: 109 (M^+-1, 11), 95 (18), 91 (100), 81 (18), 79 (16), 68 (28), 63 (3), 55 (93), 53 (17), 51 (7), 43 (5), 41 (17), 39 (20), 29 (8), 27 (10).

(S)-7-Octen-2-yn-4-ol (**21**): Following GPIII, 0.34 g (5 mmol) of 2-butynal and 10 mmol of homoallyl zinc reagent with 1 mmol (20 mol%) of titanate **2b** and 1.77 ml (6 mmol) of $Ti(O^iPr)_4$ gave after 14 h at *ca.* -25°C 0.32 g (51%) of **21** as colorless oil [(*S*)/(*R*) = > 98 : 2, ß-CD, R_t: 38.53, and ^{19}F-NMR]; R_f (hexane/ether 7 : 3): 0.34; $[\alpha]_D^{RT}$ = +8.71 (c = 1.24, $CHCl_3$). IR (film): 3373m(br.), 3078s, 2974w, 2921m, 2862w, 2236w, 1641m, 1441m, 1339w, 1149w, 1103w, 1060m, 1018m, 905m, 800w, 646w; ^{1}H-NMR (300 MHz): 5.84 (ddt, J_1 = 7, J_2 = 10, J_3 = 17, 1 H, C(7)-H); 5.06 (dq, J_1 = 17, J_2 = 2, 1 H, C(8)-H); 4.99 (dq, J_1 = 10, J_2 = 1 H, C*H*OH); 2.28 - 2.18 (m, 2 H, CH_2); 1.85 (d, J = 2, 3 H, CH_3); 1.83 - 1.72 (m, 3 H, OH, CH_2); ^{13}C-NMR (75 MHz): 137.87, 115.13, 81.28, 80.22, 62.28, 37.19, 29.46, 3.53; MS: 123 (M^+-1, 3), 109 (16), 105 (10), 95 (19), 91 (55), 82 (44), 79 (16), 69 (100), 55 (17), 43 (12), 39 (33), 32 (4), 28 (23), 18 (14).

(S)-1-Phenyl-6-hepten-1-yn-3-ol (**22**): Following GPIII, 1.27 ml (10 mmol) of phenylpropargyl aldehyde and 20 mmol of homoallyl zinc reagent with 2 mmol (20 mol%) of titanate **2b** and 3.53 ml (12 mmol) of $Ti(O^iPr)_4$

gave after 14 h at *ca.* -25°C 1.45 g (78%) of **22** as colorless crystals [(*S*)/(*R*) = 98 : 2, ^{19}F-NMR]; R_f (hexane/ether 4 : 1): 0.19; b.p.: 200°C/0.1 Torr; m.p.: 53.8° - 54.4°C; $[\alpha]_D^{RT}$ = +23.8 (c = 1.0, $CHCl_3$). IR ($CHCl_3$): 3601m, 3412w(br.), 3081m, 3008m, 2947m, 2862w, 2228w, 1954w, 1882w, 1831w, 1754w, 1641m, 1600w, 1569s, 1450s, 1443m, 1380m, 1114w, 1056m, 1007w, 918s, 646w; ^{1}H-NMR (300 MHz): 7.46 - 7.39 (m, 2 H, arom.); 7.35 - 7.27 (m, 3 H, arom.); 5.87 (ddt, J_1 = 7, J_2 =10, J_3 = 17, 1 H, C(6)-H); 5.10 (dq, J_1 = 17, J_2 = 2, 1 H, C(7)-H); 5.02 (dq, J_1 = 10, J_2 = 2, 1 H, C(7)-H); 4.67 - 4.60 (m, 1 H, C*H*OH); 2.35 - 2.27 (m, 2 H, CH_2); 2.01 (d, J = 5, 1 H, OH); 1.94 - 1.87 (m, 2 H, CH_2); ^{13}C-NMR (75 MHz): 137.68, 131.69, 128.42, 128.29, 122.62, 115.34, 89.86, 85.17, 62.48, 36.94, 29.49; MS: 186 (M^+, 4), 185 (M^+-1, 21), 168 (58), 167 (75), 157 (22), 153 (26), 142 (44), 131 (100), 129 (47), 115 (28), 103 (55), 91 (11), 89 (3), 83 (10), 77 (31), 63 (4), 51 (5), 39 (3), 28 (9), 18 (4). Anal. calcd. for $C_{13}H_{14}O$ (186.25): C 83.83, H 7.58, Found: C 83.78, H 7.29.

(E,3S,4R)-4-Methyl-6-octen-3-ol (**23**): Following GPI, 0.78 g (0.88 ml, 7 mmol) of *(E,R)*-2-methyl-4-hexenal[52] and 5 ml (10 mmol) of Et_2Zn soln. with 1.4 mmol (20 mol%) of titanate **2b** and 2.5 ml (8.4 mmol) $Ti(O^iPr)_4$ gave after 20 h at -25°C (73%) of **23** as colorless oil [(3*S*,4*R*)/(3*R*,4*R*) = 97 : 3, CD-6 R_t: 17.70/17.25]. ^{13}C-NMR (50 MHz, the main diastereoisomer): 129.57, 126.09, 76.90, 38.41, 35.31, 26.23, 17.68, 15.28, 9.9.

(E,3R,4R)-4-Methyl-6-octen-3-ol (**24**): Following GPI, 0.78 g (0.88 ml, 7 mmol) of *(E,R)*-2-methyl-4-hexenal[52] and 5 ml (10 mmol) of Et_2Zn soln. with 1.4 mmol (20 mol%) of titanate *ent*-**2b** and 2.5 ml (8.4 mmol) $Ti(O^iPr)_4$ gave after 21 h at -23°C 0.79 g (79%) of **24** as colorless oil [(3*R*,4*R*)/(3*S*,4*R*) = >96 : 4, CD-6, R_t: 49.59]; b.p.: 100°C/14 Torr; $[\alpha]_D^{RT}$ = +1.8 (c = 2, $CHCl_3$). ^{1}H-NMR (200 MHz, the main diastereoisomer): 5.47 (m, 2 H, C(6, 7)-H); 3.41 (m, 1 H, C*H*OH); 2.12 (m, 1 H, C(5)-H); 1.90 (m, 1 H, C(5)-H); 1.65 (s, 1 H, OH); 1.64 (d, J = 4.5, 4-CH_3); 1.65 - 1.32 (m, 3 H, C(2)-H_2, C*H*CH_3); 0.93 (t, J = 7, 3 H, C(1)-H_3); 0.84 (d, J = 6.5, 3 H, C(8)-H_3); ^{13}C-NMR (50 MHz, the main diastereoisomer): 130.21, 126.71, 65.34, 38.20, 37.09, 27.49, 18.10, 13.38, 10.72.

(1S,1'R)-1-(6,6-Dimethyl-bicyclo[3.1.1.]hept-2-en-2-yl)-1-propanol (**25**): Following GPI, 0.52 g (9.53 ml, 3.47 mmol) of (1*R*)-(-)-myrtenal and 3.12 ml (6.25 mmol) of Et_2Zn soln. with 0.69 mmol (20 mol%) of titanate **2b** and 1.23 ml (4.16 mmol) of $Ti(O^iPr)_4$ gave after 15 h at -25°C 0.58 g (93%) of **25** as colorless oil [(1*S*,1'*R*)/(1*R*,1'*R*) = 95 : 5, CD-17, R_t: 20.57/21.66]; R_f (hexane/ether 1 : 1): 0.54; $[\alpha]_D^{RT}$ = -55.50° (c = 1.96, $CHCl_3$). IR (film): 3375m(br.), 2915s, 2977m, 2832m, 1465w, 1381w, 1365w, 1310w, 1265w, 1204w, 1165w, 1132w, 1091w, 1047w, 1003w, 962w, 913w, 886w, 803w; ^{1}H-NMR (300 MHz, the main diastereoisomer): 5.45 - 5.42 (m, 1 H, C(3)-H); 3.91 (t, J = 7, 1 H, C*H*OH); 2.44 - 2.38 (m, 1 H, C(7)-H); 2.29 - 2.25 (m, 2 H, C(4)-H_2); 2.26 - 2.18 (m, 1 H, C(5)-H); 2.15 - 2.06 (m, 1 H, C(1)-H); 1.54 - 1.46 (m, 2 H, C$H_2$$CH_3$); 1.37 (s, 1 H, OH); 1.30 (s, 1 H, 6-CH_3); 1.13 (d, J = 8.5, 1 H, C(7)-H); 0.89 (t, J = 7, 3 H, CH_2CH_3); 0.85 (s, 1 H, 6-CH_3); ^{13}C-NMR (75 MHz, the main diastereoisomer): 149.94, 118.22, 76.49, 41.82, 41.11, 37.78, 31.85, 31.21, 27.39, 26.16, 21.43, 10.24; MS: 180 (8), 162 (40), 147 (46), 133 (23), 119 (58), 107 (61), 91 (100), 85 (11), 79 (42), 67 (13), 59 (94), 41 (29), 29 (9), 18 (5). Anal. calcd. for $C_{12}H_{20}O$ (180.29): C 79.94, H 11.18; Found: C 79.68, H 11.12.

(1R,1'R)-1-(6,6-Dimethyl-bicyclo[3.1.1.]hept-2-en-2-yl)-1-propanol (**26**): Following GPI, 0.59 g (3.95 mmol) of (1*R*)-(-)-myrtenal and 3.56 ml (7.12 mmol) of Et_2Zn soln. with 0.79 mmol (20 mol%) of titanate *ent*-**2b** and 1.40 ml (4.74 mmol) of $Ti(O^iPr)_4$ gave 0.61 g (86%) of **26** as colorless oil [(1*R*,1'*R*)/(1*S*,1'*R*) = 95 : 5, CD-17, R_t: 21.70/20.50]; $[\alpha]_D^{RT}$ = -27.20 (c = 1.5, $CHCl_3$). ^{1}H-NMR (300 MHz): 5.45 - 5.35 (m, br., 1 H, C(3)-H); 3.89 (t, J = 6, 1 H, C*H*OH); 2.48 - 2.35 (m, 1 H, C(7)-H); 2.30 - 2.13 (m, 3 H, C(4)-H2, C(5)-H); 2.13 - 2.00

(m, 1 H, C(1)-H); 1.90 - 1.70 (s, br., 1 H, OH); 1.55 - 1.40 (m, 2 H, CH_2CH_3); 1.27 (s, 3 H, 6-CH_3); 1.16 (d, J = 9, C(7)-H); 0.90 (t, J = 7, 3 H, CH_2CH_3); 0.80 (s, 3 H, 6 CH_3); ^{13}C-NMR (75 MHz): 150.50, 117.56, 76.44, 42.07, 40.99, 37.74, 31.84, 31.12, 27.53, 26.22, 21.42, 9.97.

(1S,4'S)-1-(4'-Isopropenyl-cyclohex-1-enyl)-1-propanol (**27**): Following GPI, 0.75 g (5 mmol) of (*S*)-(-)-perillaldehyde and 4.5 ml (9 mmol) of Et_2Zn soln. with 1 mmol of titanate **2a** and 1.77 ml (6 mmol) of $Ti(O^iPr)_4$ gave after 18 h at -26°C 0.83 g (92%) of **27** as colorless oil [(1*S*,4'*S*)/(1*R*,4'*S*) = 97 : 3, γ-CD, R_t: 44.28/43.72]; R_f (hexane/ether 4 : 1): 0.28; $[\alpha]_D^{RT}$ = -86.28 (c = 1.39, $CHCl_3$). IR (film): 3364m(br.), 3077w, 2960s, 2923s, 2872s, 1667w, 1641m, 1451m, 1436m, 1374m, 1328s, 1236w, 1154w, 1092w, 1041w, 1005w, 964m, 887s, 820w, 718w; ^{1}H-NMR (300 MHz, the main diastereoisomer): 5.67 - 5.65 (m, 1 H, C(2)-H); 4.74 - 4.70 (m, 2 H, C(1')-H_2); 3.91 (t, J = 7, 1 H, C*H*OH); 2.22 - 1.78 (m, 7 H, C(3)-H_2, C(4)-H, C(5)-H_2, C(6)-H_2); 1.74 (s, 3 H, C(3')-H_3); 1.62 - 1.40 (m, 3 H, CH_3CH_2, OH); 0.86 (t, J = 7, 3 H, CH_3CH_2); ^{13}C-NMR (75 MHz, the main diastereoisomer): 149.72, 139.33, 122.16, 108.64, 77.63, 41.21, 30.40, 27.87, 27.48, 24.01, 20.81, 9.91; MS: 181 (M^++1, 2), 180 (M^+, 15), 162 (70), 151 (42), 147 (52), 133 (71), 119 (37), 105 (56), 91 (67), 79 (100), 67 (28), 57 (36), 41 (35), 29 (16). Anal. calcd. for $C_{12}H_{20}O$ (180.29): C 79.94, H 11.18; Found: C 80.14, H 11.85.

(1S,1'S)-m-*Phenylenebis(1-propanol)* (**28**): Analogous to GPI, 0.94 g (7 mmol) of isophthaldialdehyde and 19 ml (19 mmol, 1 M in hexane) of Et_2Zn soln. with 2.8 mmol (40 mol%) of titanate **2b** and 5.0 ml (17 mmol, 2.4 equiv.) $Ti(O^iPr)_4$ gave after 24 h at -76° to -25°C 1.31 g (96%) of **28** as colorless crystals (after two recrystallizations from hexane: (*S,S*)/(*meso*) = 96 : 3.5, *er* 99.5 : 0.5, TFA, CD-17, R_t: 22.19/23.09); m.p.: 58° - 59°C (hexane); $[\alpha]_D^{RT}$ = -59.65 (c = 3, $CHCl_3$). IR (KBr): 3270s, 3055w, 3020w, 2960s, 2930s, 2900m, 2870s, 1605w, 1489m, 1460s, 1445s, 1435s, 1400m, 1350m, 1339m, 1220s, 1205s, 1050s, 1025s, 980s, 790s, 702m, 670m; ^{1}H-NMR (200 MHz): 7.28 - 7.14 (m, 4 H, arom.); 4.56 (ddd, $J_1 = J_2 = 3.5$, $J_3 = 3$, 2 H, 2 C*H*OH); 1.98 (d, J = 3, 2 H, 2 OH); 1.75 (m, 4 H, 2 CH_2); 0.90 (t, J = 7, 6 H, 2 CH_3); ^{13}C-NMR (50 MHz): 145.14, 128.64, 125.40, 123.96, 76.11, 32.00, 10.33; MS: 194 (3), 166 (15), 165 (100), 119 (20), 107 (21), 91 (27), 79 (30), 77 (22), 59 (51), 57 (12), 41 (12), 31 (15). Anal. calcd. for $C_{12}H_{18}O_2$ (194.27): C 74.19, H 9.34; Found: C 74.37, H 9.47.

(S)-4-(1-Hydroxy-propyl)-benzaldehyde (**29**): Following GPI, 0.94 g (7 mmol) of phthaldialdehyde and 3.6 ml (7.2 mmol) of Et_2Zn soln. with 1.4 mmol (20 mol%) of titanate *ent*-**2b** and 2.5 ml of (8.4 mmol) $Ti(O^iPr)_4$ gave after 20 h at -29°C 0.54 g (47%) of **29** as colorless oil [(*R*)/(*S*) = 98 : 2, ß-CD, R_t: 51.55/52.08]; $[\alpha]_D^{RT}$ = +35.74 (c = 1, $CHCl_3$) (ref.[37b]: $[\alpha]_D^{25}$ = +37 (c = 1.18, $CHCl_3$) with (*R*)/(*S*) = 97 : 3). IR (film): 3430m, 2966m, 1698s, 1608s, 1577m, 1305m, 1211s, 1167m, 1097m, 1046w, 979m, 830s; ^{1}H-NMR (200 MHz): 9.98 (s, 1 H, CHO); 7.85 (d, J = 8, 2 H, arom.); 7.50 (d, J = 8, 2 H, arom.); 4.35 (dd, $J_1 = J_2 = 6$, 1 H, C*H*OH); 2.1 (s, br. 1 H, OH); 1.92 - 1.88 (m, 2 H, CH_2); 0.93 (t, J = 7, 3 H, CH_3); ^{13}C-NMR (50 MHz): 191.72, 151.24, 135.36, 129.63, 126.20, 75.07, 31.76, 9.60; MS: 164 (6), 163 (16), 152 (15), 151 (80), 149 (50), 136 (33), 135 (100), 134 (11), 133 (28), 123 (24), 107 (58), 106 (24), 105 (39), 91 (18), 80 (17), 79 (99), 78 (26), 77 (82), 65 (21), 57 (24), 51 (50), 50 (22), 39 (24), 29 (53), 28 (29), 27 (31), 18 (67), 17 (21).

(1S,1'S)-p-*Phenylenebis(1-propanol)* (**30**): Following GPI, 0.94 g (7 mmol) of phthaldialdehyde and 17 ml (17 mmol, 1 M in hexane) of Et_2Zn soln. with 2.8 mmol (40 mol%) of titanate **2b** and 5.0 ml (17 mmol, 2.4 equiv.) of $Ti(O^iPr)_4$ gave after 26 h at -76° to -23°C 1.97 g (79%) **30** as colorless crystals (after recrystallization (*S,S*)/(*meso*) = 99 : 1, CD-6, R_t: 50.83/50.11; on an achiral column OV 1701 Vi, only one diastereoisomer detectable, R_t: 53.78); m.p.: 50° - 51°C (hexane); $[\alpha]_D^{RT}$ = -59.43 (c = 5, $CHCl_3$). ^{1}H-NMR (200 MHz):

7.28 (s, 4 H, arom.); 4.52 (ddd, $J_1 = J_2 = 6$, $J_3 = 2$, 2 H, 2 C*H*OH); 2.2 (d, J = 2, 2 H, 2 OH); 1.75 - 1.72 (m, 4 H, 2 CH_2); 0.89 (t, J = 7, 6 H, 2 CH_3); ^{13}C-NMR (50 MHz): 144.20, 126.37, 76.00, 32.94, 10.31; MS: 194 (13), 166 (56), 165 (100), 147 (11), 136 (59), 134 (19), 119 (19), 107 (48), 91 (55), 79 (59), 77 (45), 59 (60), 57 (77), 51 (15), 43 (15), 41 (19), 28 (50), 18 (87), 17 (53). Anal. calcd. for C_{12} $H_{18}O_2$ (194.27): C 74.19, H 9.34; Found: C 74.10, H 9.55.

*(1*R,*1'*S*)- or* meso-p-*Phenylenebis(1-propanol)* (**31**): Analogous to GPI, 0.458 g (2.8 mmol) of (*R*)-1-(4'-formylphenyl)-1-propanol and 3.36 ml (6.72 mmol, 2.4 equiv.) of Et_2Zn soln. with 0.56 mmol (20 mol%) of titanate **2b** and 1.8 ml (6.8 mmol, 2.4 equiv.) of $Ti(O^iPr)_4$ gave after 20 h at -30°C 0.34 g (63%) of **31** as colorless crystals [(*meso*)/(*R*,*R*) = 99.5 : 0.5, ß-CD, R_t: 49.21]; m.p.: 112° - 113°C. IR (KBr): 3250s, 3170s, 3020m, 2970s, 2955s, 2925s, 2890s, 2865s, 1460s, 1425m, 1328m, 1203m, 1118m, 1097s, 1045s, 900m, 828m, 560m; ^{1}H-NMR (200 MHz): 7.3 (s, 4 H, arom.); 4.58 (dd, $J_1 = J_2 = 7.5$, 2 H; s C*H*OH); 1.93 (s, 2 H, 2 OH); 1.75 (m, 4 H, 2 CH_2); 0.91 (t, J = 7.5, 6 H, 2 CH_3); ^{13}C-NMR (75 MHz): 143.89, 126.08, 75.84, 31.89, 10,16; MS: 194 (7), 166 (24), 165 (100), 147 (10), 136 (29), 119 (10), 107 (29), 91 (41), 79 (47), 77 (28), 69 (20), 59 (44), 57 (61), 55 (20), 43 (27), 41 (28), 32 (22), 29 (33), 28 (82), 18 (89), 17 (38).

REFERENCES AND NOTES

1. Preliminary communications: a) Schmidt, B.; Seebach, D. *Angew. Chem.* **1991**, *103*, 100 - 101; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 99 - 100; b) *iidem Angew. Chem.* **1991**, *103*, 1383 - 1385; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1321 - 1325.
2. Full paper on the mechanism: Seebach, D.; Plattner, D. A.; Beck, A. K.; Wang, Y. M.; Hunziker, D.; Petter, W. *Helv. Chim. Acta* **1992**, *75*, 2171 - 2209.
3. Part of the Ph. D. thesis of B. S., Diss. No. 9698, ETH Zürich, **1992**.
4. Part of the projected Ph. D. thesis of Y. M. W., ETH Zürich.
5. For a discussion see: Seebach, D.; Hayakawa, M.; Sakaki, J.; Schweizer, W. B. *Tetrahedron*, **1993**, *49*, 1711 - 1724 [Tetrahedron-Symposia-in-Print **49** on *"Synthesis of Optically Active Compounds - Prospects for the 21st Century"*].
6. A review article describing our view of the future of organic synthesis see: Seebach, D. *Angew. Chem.* **1990**, *102*, 1363 - 1409; *Angew. Chem. Int. Ed. Engl.* **1990**, *29*, 1320 - 1367.
7. Review: Noyori, R.; Kitamura, M. *Angew. Chem.* **1991**, *103*, 34 - 55; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 49 - 69.
8. For a general discussion see the introduction in: Weber, B.; Seebach, D. *Tetrahedron* **1993**, *49*, in print [Tetrahedron-Symposia-in-Print on *"Mechanistic Aspects of Polar Organometallic Chemistry"*].
9. Review: Soai, K.; Niwa S. *Chem. Rev.* **1992**, *92*, 833 - 856.
10. Joshi, N. N.; Srebnik, M.; Brown, H. C. *Tetrahedron Lett.* **1989**, *30*, 5551 - 5554.
11. Yoshioka, M.; Kawakita, T.; Ohno, M. *Tetrahedron Lett.* **1989**, *30*, 1657 - 1660; Takahashi, H.; Kawakita, T.; Yoshioka, M.; Kobayashi, S.; Ohno, M. *Tetrahedron Lett.* **1989**, *30*, 7095 - 7098; Takahashi, H.; Kawakita, T.; Ohno, M.; Yoshioka, M.; Kobayashi, S. *Tetrahedron Lett.* **1992**, *48*, 5691 - 5700.

12. Soai, K.; Hirose, Y.; Ohno, Y. *Tetrahedron: Asymmetry* **1993**, *4*, 1473 - 1474.
13. a) Seebach, D.; Behrendt (-von dem Bussche-Hünnefeld), L.; Felix, D. *Angew. Chem.* **1991**, *103*, 991 - 992; *Angew. Chem. Int. Ed. Engl.* **1991**, *30*, 1008 - 1009; b) von dem Bussche-Hünnefeld, J. L.; Seebach, D. *Tetrahedron* **1992**, *48*, 5719 - 5730 [Tetrahedron-Symposia-in-Print **47** on *"Organotitanium Reagents in Organic Chemistry"*].
14. Rozema, M. J.; Sidduri, A. R.; Knochel, P. *J. Org. Chem.* **1992**, *57*, 1956 - 1958; Rozema, M. J.; Rajagopal, D.; Tucker, C. E.; Knochel, P. *J. Organomet. Chem.* **1992**, *438*, 11 - 27; Knochel, P.; Brieden, W.; Rozema, M. J.; Eisenberg, C. *Tetrahedron Lett.* **1993**, *34*, 5881 - 5884.
15. 1.2 Equivalents of $Ti(OCHMe_2)_4$ cause a 70% conversion after 6h at -25°C of the 1 : 1 reaction between PhCHO and Et_2Zn;[2] for a contrasting result see page 843, bottom left column in ref.[9]
16. Weber, B.; hithero unpublished results, ETH Zürich, **1993**; see also Scheme 3 in ref.[2]
17. In the case of the *trans*-cyclohexane bis-triflamide[11] electronic rather than steric reasons must be responsible for the extraordinary activity of the Ti centers bearing such triflamide ligands; the ratio of Ti-triflamide over $Ti(OCHMe_2)_4$ may be as small as 1 : 200 for high enantioselectivity to be observed!
18. For a complete list of all TADDOLs as of July 1992 see *Table 2* in ref.[2]
19. Seebach, D.; Weidmann, B.; Widler, L. *Modern Synthetic Methods 1983*, Scheffold, R., Ed.; Salle + Sauerländer, Aarau and J. Wiley and Sons, New York, 1983, vol. 3, pp. 217 - 353; Weidmann, B.; Seebach, D. *Angew. Chem.* **1983**, *95*, 12 - 26; *Angew. Chem. Int. Ed. Engl.* **1983**, *22*, 31 - 45; Seebach, D.; Beck, A. K.; Schiess, M.; Widler, L.; Wonnacott, A. *Pure & Appl. Chem.* **1983**, *55*, 1807 - 1822.
20. Seebach, D.; Beck, A. K.; Imwinkelried, R.; Roggo, S.; Wonnacott, A. *Helv. Chim. Acta* **1987**, *70*, 954 - 974.
21. Beck, A. K.; Bastani, B.; Plattner, D. A.; Petter, W.; Seebach, D.; Braunschweiger, H.; Gysi, P.; La Vecchia, L. *Chimia*, **1991**, *45*, 238 - 244.
22. von dem Bussche-Hünnefeld, C.; Beck, A. K.; Lengweiler, U.; Seebach, D. *Helv. Chim. Acta* **1992**, *75*, 438 - 441.
23. The hexaphenyl derivative **1d** will be described in a forthcoming paper on the mechanism of Ti-TADDOLate catalyzed *Diels-Alder* reactions (Marti, R.; Dahinden, R.; Beck, A. K.; Kühnle, F., ETH Zürich), see also Irurre, J.; Alonso-Alija, C.; Piniella, J. F.; Alvarez-Larena, A. *Tetrahedron: Asymmetry* **1992**, *3*, 1591 - 1596; Weber, E.; Dörpinghaus, N.; Goldberg, I. *J. Chem. Soc., Chem. Commun.* **1988**, 1566 - 1568. For a full paper on Ti-TADDOLate (R^1 = Me, R^2 = Aryl = Ph) catalyzed *Diels-Alder* additions see: Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340 - 5345.
24. The preparation and characterization of several (*S*, *S*)-TADDOLs has been described in ref.[21].
25. So far, the α-naphthyl-TADDOL was the poorest ligand for the nucleophilic addition to aldehydes described here. *ortho*-Tolyl- and *ortho*-methoxyphenyl-TADDOLs have not been tested as yet.
26. For other reactions, such as the *Diels-Alder* addition, the situation is quite different; rather dramatic effects can be found with different TADDOLs, see also footnote[23] above.
27. Traces of alcohols (isopropanol or TADDOL) are probably removed by reaction with the excess Et_2Zn and the resulting alkoxides react with the "pool" of $Ti(OCHMe_2)_4$.[2]
28. Lednicer, D. *Adv. Org. Chem.* **1972**, *8*, 179 - 293; Lever, Jr., O. W. *Tetrahedron* **1976**, *32*, 1943 - 1971; Call, I. *Chem. Unserer Zeit* **1978**, *12*, 123 - 133.

29. Seebach, D. *Angew. Chem.* **1979**, *91*, 259 - 178; *Angew. Chem. Int. Ed. Engl.* **1979**, *18*, 239 - 258.
30. For a very recent review article see Hinshaw, J.V. *LC ·GC Int.* **1993**, *6*, 606 - 610, and references cited therein.
31. Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543 - 2549.
32. Seebach, D.; Prelog, V. *Angew. Chem.* ,**1982**, *94*, 696 - 702; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 654 - 660; Prelog, V.; Helmchen, G. *Angew. Chem.* **1982**, *94*, 614 - 631; *Angew. Chem. Int. Ed. Engl.* **1982**, *21*, 567 - 583.
33. Jacques, J.; Gros, C.; Bourcier, S. *Stereochemistry. Fundamentals and Methods*, Kagan, H. B., Ed.; G. Thieme Publishers, Stuttgart 1977, vol. 4 (Absolute Configurations of 6000 Selected Compounds with One Asymmetric Carbon Atom), pp. 229 - 233.
34. Wenger, R. M. *Angew. Chem.* **1985**, *97*, 88 - 96; *Angew. Chem. Int. Ed. Engl.* **1985**, *24*, 77 - 85; Seebach, D.; Beck, A. K.; Bossler, H. G.; Gerber, C.; Ko, S. Y.; Murtiashaw, C. W.; Naef, R.; Shoda, S.-i., Thaler, A.; Krieger, M.; Wenger, R. *Helv. Chim. Acta* **1993**, *76*, 1564 - 1590.
35. We should like to point out that we follow the CIP convention[32] and use capital spelling *Re* and *Si* rather than small *re* and *si* (the *Hanson* convention).[36] In the revised CIP rules, *re* and *si* are used to specify reflection-invariant heterotopic half-spaces.[32]
36. According to the old-fashioned but widely used *Hanson* convention *re* and *si* are used irrespective of whether the face topicities are reflection-variant or reflection-invariant: Hanson, K. R. *J. Am. Chem. Soc.* **1966**, *88*, 2731 - 2742.
37. *Cf. Soai's* related work with terephthaldehyde: a) Soai, K.; Hori, H.; Kawahara, M. *J. Chem. Soc., Chem. Commun.* **1992**, 106 - 108; b) *iidem Tetrahedron: Asymmetry* **1990**, *1*, 769 - 770. The assignment of configurations was done by analogy as in our case.
38. In ref.[2] we have discussed tetragonal, trigonal bipyramidal and octahedral geometries; the tetragonal one (bearing no OR group on Ti) is not in agreement with the role we have shown $Ti(OCHMe_2)_4$ to play in the mechanism.
39. We have just had the opportunity to test the cyclohexyl derivative **1** (Aryl = cyclohexyl) as a ligand. It was converted to a titanate of type **2** and used for the standard reaction Et_2Zn + PhCHO. The result was a 70 : 30 enantioselectivity for the (*S*)-enantiomer **13**. This means either that the cyclohexyl group (like CH_3 and CH_2Ph) is effectively smaller than phenyl or that it acts as a much larger substituent (like α-naphthyl). In both cases we would expect a decrease of selectivity[2]. The cyclohexyl derivative is now being tested in other types of reactions, and we hope to obtain the crystal structure of this compound. The results will be reported elsewhere. We gratefully acknowledge receipt of a generous sample of the cyclohexyl analog of **1a** from *Dr. R. O. Duthaler* of the *Ciba Company* (Basel); the compound was prepared by hydrogenation of the TADDOL **1a**: Rothe-Streit, P.; Duthaler, R. O.; Hafner, A. unpublished results.
40. Veliev, M. G.; Guseinov, M. M. *Synthesis* **1980**, 461.
41. Seebach, D.; Hidber A. *Chimia* **1983**, *37*, 449 - 462.
42. a) Grob, K. *Making and Manipulating Capillary Columns for Gas Chromatography*, Dr. Alfred Hüthig Verlag, Heidelberg 1986; b) Schurig, V.; Nowotny, H.-P. *J. Chromatography* **1988**, *441*, 155 - 163; c) König, W. A.; Krebber, R.; Mischnick, P. *J. High Resol. Chromatography* **1989**, *12*, 732 - 738;

d) König, W. A.; Lutz, S.; Colberg, C.; Schmidt, N.; Wenz, G.; von der Bey, E.; Mosandl, A.; Günther, C.; Kustermann, A. *J. High Resol. Chromatography* **1988**, *11*, 621 - 625.

43. König, W. A.; Lutz, S.; Wenz, G.; von der Bey, E. *J. High Resol. Chromatography* & Chromatography Commun. **1988**, *11*, 506 - 509.
44. Furniss, B. S.; Hannaford, A. J.; Smith, P. W. G.; Tatchell, A. R. *Vogel's Textbook of Practical Organic Chemistry*, Fifth Edition, Longman Scientific & Technical, 1989, 443 - 444.
45. Beilsteins Handbuch der Organischen Chemie, **1**, E I, 203, E III, 1668.
46. Beilsteins Handbuch der Organischen Chemie, **1**, E III, 1746.
47. Beilsteins Handbuch der Organischen Chemie, **6**, E III, 108.
48. Beilsteins Handbuch der Organischen Chemie, **6**, E II, 504; E III, 1953.
49. a) Beilsteins Handbuch der Organischen Chemie, **6**, E III, 2465; b) Soai, K.; Ookawa, A.; Kaba, T.; Ogawa, K. *J. Am. Chem. Soc.* **1987**, *109*, 7111 - 7115.
50. Beilsteins Handbuch der Organischen Chemie, **6**, E III, 2741.
51. Beilsteins Handbuch der Organischen Chemie, **6**, E II, 472.
52. Blaser, D.; Ko, S. Y.; Seebach, D. *J. Org. Chem.* **1991**, *56*, 6230 - 6233, and references cited therein.

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