161. On the Mechanisms of Enantioselective Reactions Using α,α,α′,α′-Tetraaryl-1,3-dioxolane-4,5-dimethanol(TADDOL)-Derived Titanates: Differences between C_2- and C_1-Symmetrical TADDOLs – Facts, Implications and Generalizations[1])

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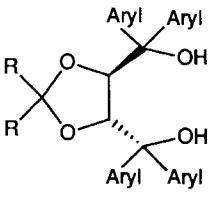
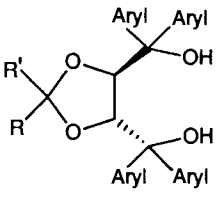
The titanates derived from α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLs, prepared from tartrate) act as catalysts for enantioselective additions of dialkylzinc compounds to aldehydes. For the standard reaction chosen for this investigation of the mechanism, the addition of diethylzinc to benzaldehyde, there is very little change of selectivity with different aryl substituents on the TADDOLate ligands (*Tables 2–4*, examples). With 0.02 to 0.2 equiv. of the chiral titanates, selectivities above 90% are observed only in the presence of excess tetraisopropyl titanate! According to NMR measurements (*Fig. 2*), the chiral bicyclic titanate and the achiral titanate do not react to give new species under these conditions. From experiments with different stoichiometries of the components, and with different achiral or chiral OR groups on the Ti-atom of the seven-membered ring titanate, it is concluded *i*) that a single chiral titanate is involved in the product-forming step, *ii*) that the bulky TADDOLate ligand renders the Ti-center catalytically more active than that of $(i\text{-PrO})_4Ti$, due to fast dynamics of ligand exchange on the sterically hindered Ti-center (*Table 5*, *Fig. 3*), and *iii*) that the role of excess $(i\text{-PrO})_4Ti$ is to remove – by ligand exchange – the product alkoxides (R*O) from the catalytically active Ti-center (*Scheme 4*, *Table 6*). Three new crystal structures of TADDOL derivatives (two clathrates with secondary amines, and a dimethyl ether) have been determined by X-ray diffraction (*Figs. 5–7*), and are compared with those previously reported. The distances between the $C(aryl)_2O$ oxygen atoms in the C_2- and C_1-symmetrical structures vary from 2.58 to 2.94 Å, depending upon the conformation of their dioxolane rings and the presence or absence of an intramolecular H-bond (*Fig. 8*). A single-crystal X-ray structure of a spiro-titanate, with two TADDOLate ligands on the Ti-atom, is described (*Fig. 9*); it contains six different seven-membered titanate-ring conformations in the asymmetric unit (*Fig. 10*), which suggests a highly flexible solution structure. The structures of Ti TADDOLate complexes are compared with those of C_2-symmetrical Ru, Rh, and Pd disphosphine chelates (*Table 7*). A common topological model is presented for all nucleophilic additions to aldehydes involving Ti TADDOLates (*Si* attack with (*R,R*)-derivatives, relative topicity *unlike*; *Fig. 11*). Possible structures of complexes containing bidentate substrates for Ti TADDOLate-mediated ene reactions and cycloadditions are proposed (*Fig. 12*). A simple six-membered ring chair-type arrangement of the atoms involved can be used to describe the result of TADDOLate-mediated nucleophilic additions to aldehydes and ketones, with Ti, Zr, Mg, or Al bearing the chiral ligand (*Scheme 6*). A proposal is also made for the geometry of the intermediate responsible for enantioselective hydrogenation of *N*-(acetylamino)cinnamate catalyzed by Rh complexes containing C_2-symmetrical diphosphines (*Fig. 13*).

[1]) Parts of the projected Ph. D. Theses of *D. A. P.* and *Y. W.*, and of the Master's Thesis of *D. H.* (ETH-Zürich, 1992).



1 (C_2-symmetrical)



2 (C_1-symmetrical)

Titanates derived from the chiral diols **1** and **2** [1–5] prove to be useful in stoichiometric and catalytic enantioselective reactions; TADDOL was proposed [4] as a generic abbreviation of their systematic name – α,α,α′,α′-tetraaryl-1,3-dioxolane-4,5-dimethanols – and will be used herein. Last year, we have described TADDOL-titanate-catalyzed additions of dialkylzinc reagents to aliphatic and aromatic aldehydes with enantioselectivities generally > 98% [6–8]. In addition to the preparative aspects reported so far, we also embarked on mechanistic investigations, hoping to eventually understand – or at least interpret – some of the unusual features of this reaction, and it is the purpose of the present paper to describe the results, to propose a mechanistic model, and to extend the conclusions drawn to other TADDOL-mediated conversions, such as [2 + 2] and [4 + 2] cycloadditions, ene reactions, LAH reductions, cyanohydrin formation, aldol additions, and allylic transfer (see the review articles in [9–11]). A comparison with transition-metal-catalyzed reactions involving other C_2-symmetrical ligands is also made.

A) Preparation of TADDOLs and of TADDOL-Titanates. – The diols **1** and **2** are readily prepared from the corresponding tartrate ester acetals and aryl *Grignard* reagents. Depending upon the aldehyde or ketone from which the tartrate acetal precursors are formed, the molecules have C_2 or C_1 symmetry (see *Table 1*). The yields from the *Grignard* reactions are usually in the range of 50–75%, calculated for pure diols. Most TADDOLs have a tendency to form clathrates with various guest molecules, *e.g.* CCl_4 [3] [4] and other solvents [4] [13], carbonyl compounds [12] [21], alcohols [22], and amines [18]. This property must be borne in mind not only when preparing and purifying them, but also when isolating products from TADDOL-mediated reactions[2]). In *Table 1*, the TADDOLs prepared to date are listed, together with the corresponding references. The compounds **2a**, **i**, and **j** are described herein for the first time (see *Exper. Part*).

The diols **1** and **2**, formally 2,3-acetals of 1,1,4,4-tetraaryl-threitols, are remarkably stable compounds: we have observed neither acetal hydrolysis nor transacetalization[3]) during acidic aqueous workup, or in the presence of *Lewis* acids[4]). The formaldehyde-derived 2-unsubstituted dioxolanes **1w** and **1x** are expected to be the most stable, followed by the other acetals derived from aliphatic and aromatic aldehydes. The hydrolytically most unstable TADDOLs should be the 2-methyl-2-phenyl- (**2l**), the 2,2-diphenyl- (**1y**), and the fluorenyliden derivative (**1z**). With the exception of **1w** (a glass) and **2l** (an

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[2]) The interactions between certain TADDOLs and alcohols or amines lead to anisochrony of enantiotopic nuclei in the NMR spectra [5].

[3]) ... with formation of the isomeric threitol 1,2-acetals.

[4]) Cyclization of the 1,4-diols **1** and **2** with dehydration, leading to formation of a tetrahydrofuran ring, is not favorable due to the strain arising in the resulting *trans*-fused bicyclo[3.3.0]skeleton!

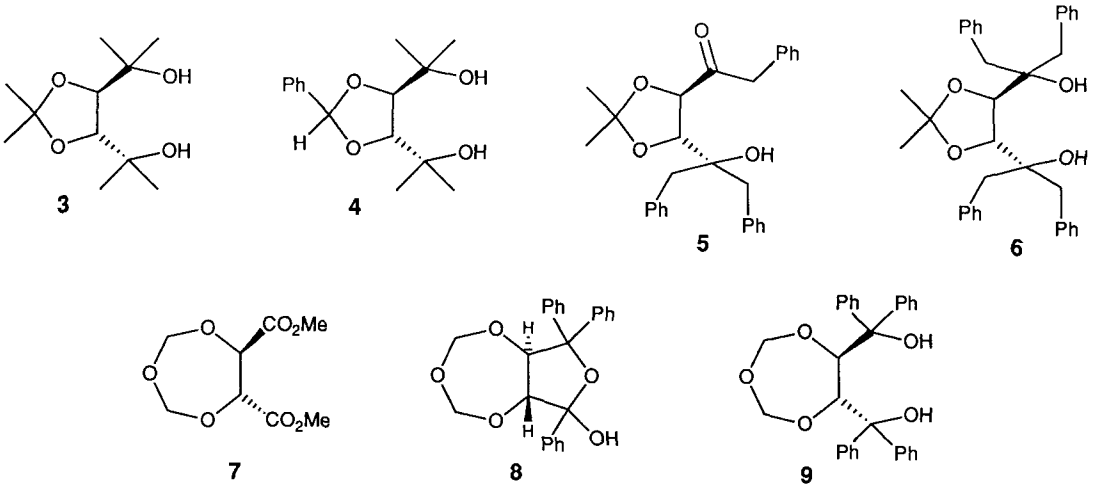
Table 1. *2,2-Disubstituted and 2-Monosubstituted* C_2- *and* C_1-*Symmetrical α,α,α',α'-Tetraaryl-1,3-dioxolane-4,5-dimethanols (TADDOLs)* **1** and **2**. In many cases, the enantiomers have been also prepared [4]. For analogous compounds bearing heteroaryl, alkenyl, and alkyl substituents on the dimethanol unit or containing a heterocycle other than dioxolane, see [14] and **3** [3], **4**, **6**, and **9** below.

Compound	R	R'	Aryl	Ref.
1a	Me		Ph	[1–4]
b	Me		2-Me-Ph	[12]
c	Me		4-Me-Ph	[12]
d	Me		4-CF_3-Ph	[13]
e	Me		4-F-Ph	[13]
f	Me		3,5-F_2-Ph	[13]
g	Me		F_5-Ph	[14]
h	Me		4-Cl-Ph	[13]
i	Me		4-MeO-Ph	[4]
j	Me		4-Ph-Ph	[4]
k	Me		Naphth-1-yl	[4]
l	Me		Naphth-2-yl	[4]
m	Et		Ph	[15]
n	Et		Naphth-2-yl	[15]
o	Et		6-MeO-Naphth-2-yl	[15]
p	Et		3,5-Me_2-Ph	[15]
q	Et		3,5-$(CF_3)_2$-Ph	[15]
r	Et		3,5-Cl_2-Ph	[15]
s	Bu		Ph	[16]
t	$-(CH_2)_4-$		Ph	[17]
u	$-(CH_2)_5-$		Ph	[3] [4]
v	$-(CH_2)_5-$		Naphth-1-yl	[4]
w	H		Ph	[3] [4]
x	H		4-Me_2N-Ph	[5]
y	Ph		Ph	[18]
z	Fluoren-9-yliden		Ph	[18]
2a	Me	H	Ph	This paper
b	*t*-Bu	H	Ph	[3] [4]
c	*t*-Bu	H	Naphth-1-yl	[4]
d	*t*-Bu	H	Naphth-2-yl	[4]
e	C_6H_{11}	H	Ph	[3]
f	Ph	H	Ph	[3] [5]
g	4-MeO-Ph	H	Ph	[19]
h	2,4,6-Me_3-Ph	H	Ph	[3]
i	Naphth-1-yl	H	Ph	This paper
j	Naphth-2-yl	H	Ph	This Paper
k	Hexyl	Me	Ph	[16]
l	Ph	Me	Ph	[16] [20]

amorphous powder)[5]), the TADDOLs we have dealt with so far possess a good-to-excellent crystallization tendency, and thus are easy to isolate, purify, or recover after workup: It is, therefore, normally not necessary to resort to chromatographic techniques. The discussion in this paper is restricted to the (4*R*,5*R*)-dioxolanes obtained from (*R*,*R*)-tartaric acid, but it is obvious that the enantiomeric TADDOLs are equally well accessible.

[5]) We have found that the 2-aryl-2-methyldioxolanes of type **2**, which we have tried to prepare so far (**2l** [16] [20] and the α-naphthyl analogue), are very difficult to purify as they do not crystallize. Chromatographic purification of the 2-methyl-2-(naphth-1-yl)dioxolane was hampered by the presence of an unidentified impurity. The precipitation of **2l** as an propan-2-ol clathrate [16] could not be reproduced in our laboratory.

Alkyl *Grignard* reagents[6]) can be employed to prepare the corresponding dioxolanes **3**, **4**, and **6**. In the latter case, the hydroxy ketone **5** and the diol **6** were formed in comparable amounts[7]). The cyclic hemiacetal **8** of a hydroxy ketone was the major



product obtained with the 2,4,6-trioxacycloheptane-1,2-dicarboxylate **7** under standard conditions (4 equiv. PhMgBr), the desired diol **9** being formed in *ca.* 10% yield only when a large excess of *Grignard* reagent was used[8]). The structure of **8** was determined by X-ray crystal structure analysis (*Fig. 1*).

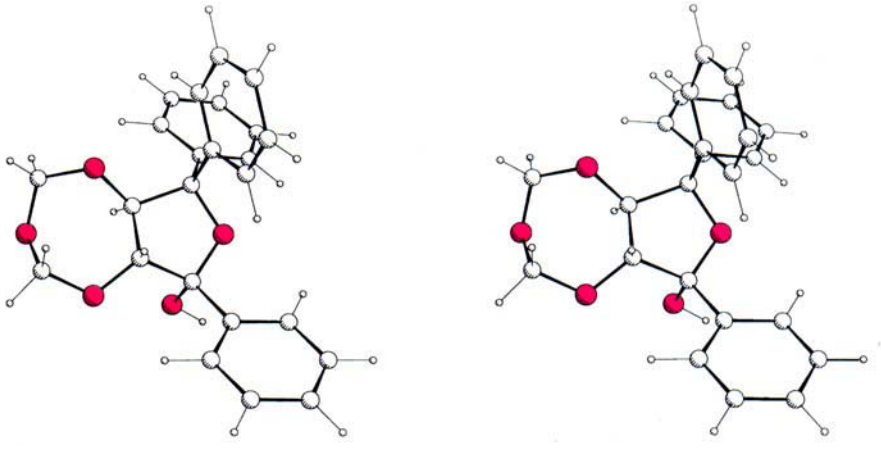


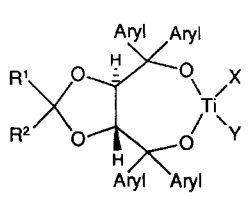
Fig. 1. *Stereo PLUTO presentation of* **8** *in the solid state.* Only one of the two H-bridged molecules in the asymmetric unit is depicted.

[6]) MeLi cannot be used to prepare **3** in good yields, see Footnote 10 in [3].
[7]) This is possibly due to formation of the enolate from **5** in the reaction mixture.
[8]) The restriction alluded to in *Footnote 4* does not hold in this case: **8** contains a bicyclo[5.3.0]skeleton.

There are several procedures by which the TADDOLs can be converted to cyclic titanates, all involving ligand exchange at the Ti-atom. It is possible to remove volatile components *in vacuo* or by azeotropic distillation[9]). Alternatively, alkoxy groups on the Ti-atom may be replaced by Cl substituents *via* metathesis (*cf.* $(RO)_4Ti + TiCl_4 \rightarrow 2\ (RO)_2TiCl_2$), or by treatment with $SiCl_4$ [15]. In many cases, formation of supposed TADDOL complexes is achieved by mixing a diol **1** or **2** with $TiCl_4$ in a solvent, and the resulting solution is used without isolation or identification of the species formed, occasionally in the presence of molecular sieves [16] [23] [24][10]).

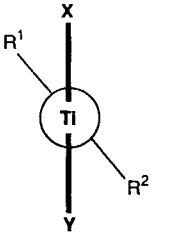
In our own work, we have, in most cases, isolated the complexes by evaporation of their solutions to dryness before use in a reaction. Often, we have characterized the complexes by ^1H- and ^{13}C-NMR spectroscopy, or even obtained correct elemental analyses and molecular weights by osmometry [8], and, in one case, we were able to determine the solid-state structure (*vide infra*). The solid obtained from TADDOL **1a** and $(i\text{-PrO})_4Ti$ in a 2:1 reaction (*Scheme 1*) could be recrystallized and identified as the spiro-titanate **10**.

Scheme 1. *Preparation of TADDOL Complexes* **11** *and Diastereoisomerism* (**A**, **B**) *in the* C_1*-Symmetrical Derivatives*

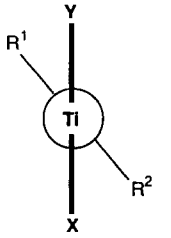


11

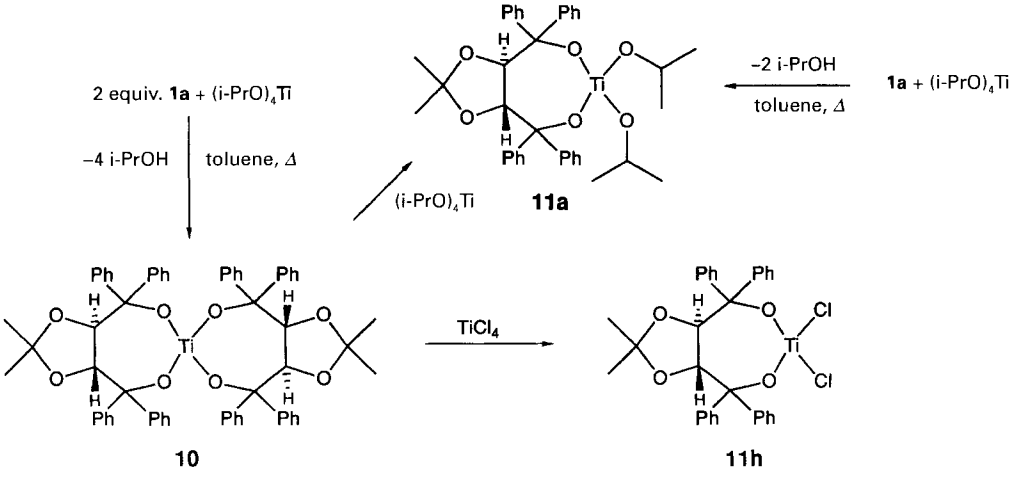
(Specification of R^1 and R^2, Aryl, X and Y see *Table 2*)



A



B



10 **11h**

[9]) See Footnote a in Table 7 of [3].

[10]) An NMR investigation of the mixture formed from **2l** and $(i\text{-PrO})_2TiCl_2$ was published by *Narasaka* and coworkers [24a]; the interpretation of the spectra and the conclusions regarding the *Lewis*-acid catalysis by this mixture are somewhat confusing to us.

Crystallization from Et_2O gave samples containing **10** and Et_2O in a ratio of 6:1. The solid spiro-titanate is stable in air for several hours and is used by us as a convenient storage form for *in situ* generation of other Ti-complexes. Thus, when mixed with equimolar amounts of $(i\text{-PrO})_4Ti$ or $TiCl_4$, the TADDOL derivatives **11a** and **11h**, with only one Ti-containing ring, are formed, the former crystallizing from pentane to give solvent-free samples [7b] [8], the latter crystallizing from Et_2O/pentane as a monosolvate [8]. The conversion of the spiro-titanate **10** to **11a**, containing only one TADDOLate, by addition of 1 equiv. of $(i\text{-PrO})_4Ti$ can be observed by NMR spectroscopy (*Fig. 2*). For the following discussions, it is important to note that excess $(i\text{-PrO})_4Ti$ (up to 9 equiv.) does not

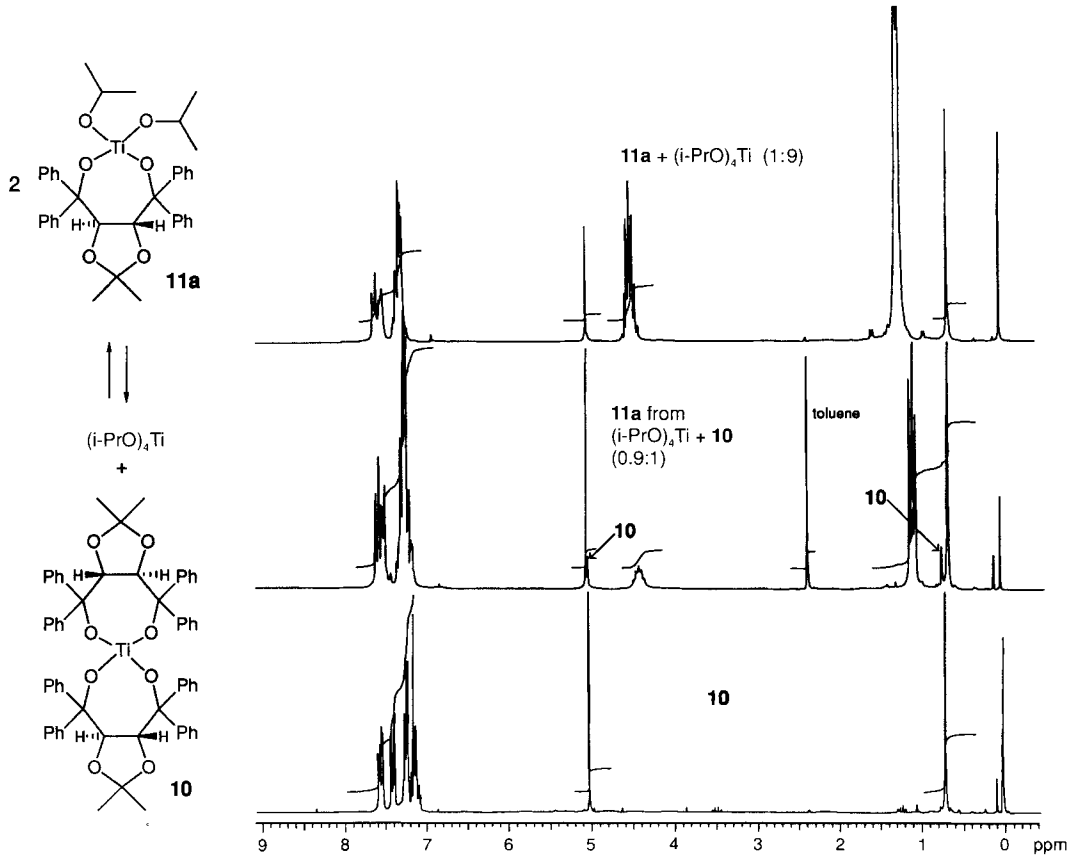


Fig. 2. *^{1}H-NMR Spectra of the spiro-titanate* **10**, *of the seven-membered-ring titanate* **11a**, *and of a 1:9 mixture of* **11a** *with $(i\text{-PrO})_4Ti$.* In **10** (*bottom*), the signals of the Me groups at C(2) of the dioxolane ring appear at slighthly lower field than those in the **11a** 'monocycle' (*middle*) ($\Delta\delta$ = 0.04 ppm), while the opposite is true for the H-atoms at C(4) and C(5) ($\Delta\delta$ = 0.03 ppm). Besides the necessary appearance of signals from the i-PrO group, the most pronounced changes in the NMR spectra upon going from **10** to **11a** occur in the aromatic region. The minimal changes observed on addition of excess $(i\text{-PrO})_4Ti$ (*top*) are taken as proof that no further structural changes, such as formation of a TADDOL-derived bis-titanate, occur. Both **10** and **11a** have been fully characterized by molecular-weight determination, spectroscopy, and elemental analysis [7b] [8]. A list of other TADDOL derivatives of type **11** is given in *Table 2*.

Table 2. *TADDOL-Derived Bicyclo[5.3.0]titanates* **11** *Which Have Been Isolated and Characterized by NMR Spectroscopy to Date* (see *Exper. Part* and [8] [9] [14] [15]). The titanates **11b–d** and **v** have been prepared for the mechanistic studies described below (see *Table 6*). The ^{1}H-NMR spectrum of **11a** is shown in *Fig. 2*.

	R^1	R^2	Aryl	X	Y
11a	Me	Me	Ph	$OCHMe_2$	$OCHMe_2$
b	Me	Me	Ph	$OCHMe_2$	OCH(Ph)Et (*S*)
c	Me	Me	Ph	OCH(Ph)Et (*R*)	OCH(Ph)Et (*R*)
d	Me	Me	Ph	OCH(Ph)Et (*S*)	OCH(Ph)Et (*S*)
e	Me	Me	Ph	Cp	CH_2CHCH_2
f	Me	Me	Ph	Cp	$CH_2CHCHCH_3$
g	Me	Me	Ph	Cp	Cl
h	Me	Me	Ph	Cl	Cl
i	Me	Me	4-MeO-Ph	$OCHMe_2$	$OCHMe_2$
j	Me	Me	4-Ph-Ph	$OCHMe_2$	$OCHMe_2$
k	Me	Me	Naphth-1-yl	$OCHMe_2$	$OCHMe_2$
l	Me	Me	Naphth-2-yl	$OCHMe_2$	$OCHMe_2$
m	Et	Et	3,5-Me_2-Ph	Cl	Cl
n	$-(CH_2)_5-$		Ph	$OCHMe_2$	$OCHMe_2$
o	H	H	Ph	$OCHMe_2$	$OCHMe_2$
p	H	H	4-Me_2N-Ph	$OCHMe_2$	$OCHMe_2$
q	Me	H	Ph	$OCHMe_2$	$OCHMe_2$
r	*t*-Bu	H	Ph	$OCHMe_2$	$OCHMe_2$
s[a])	*t*-Bu	H	Ph	Cp	Cl
t	*t*-Bu	H	Naphth-2-yl	$OCHMe_2$	$OCHMe_2$
u	Ph	H	Ph	$OCHMe_2$	$OCHMe_2$
v[b])	Ph	H	Ph	$OCHMe_2$	OCH(Ph)Et (*S*)
w	Naphth-1-yl	H	Ph	$OCHMe_2$	$OCHMe_2$
x	Naphth-2-yl	H	Ph	$OCHMe_2$	$OCHMe_2$
y	Ph	Me	Ph	$OCHMe_2$	$OCHMe_2$

[a]) See *Footnote 12*.

[b]) The location of $OCHMe_2$ and OCH(Ph)Et in positions X and Y, respectively, is chosen arbitrarily.

seem to lead to the formation of other Ti-TADDOL complexes[11]) (top of *Fig. 2*). The NMR spectra of many other TADDOL complexes of type **11** (examples listed in *Table 2*), look very similar to those of **11a** shown in the middle of *Fig. 2* and are described in detail in the *Exper. Part*. We have prepared most titanates of type **11** by removing i-PrOH, in an azeotropic distillation with toluene, from a 1:1 mixture of the corresponding diol **1** or **2** and $(i\text{-PrO})_4Ti$ (see *Scheme 1* for two routes to **11a**).

Of the complexes with $R^1 \neq R^2$ and $X \neq Y$, two diastereoisomers **A** and **B** (see *Scheme 1*) exist. In addition, two different groups R^1/R^2 render two identical substituents X/Y diastereotopic, and *vice versa*. In our NMR measurements, we have not detected non-equivalence of nuclei in the groups R^1, R^2, X, or Y due to such diastereotopicities[12]).

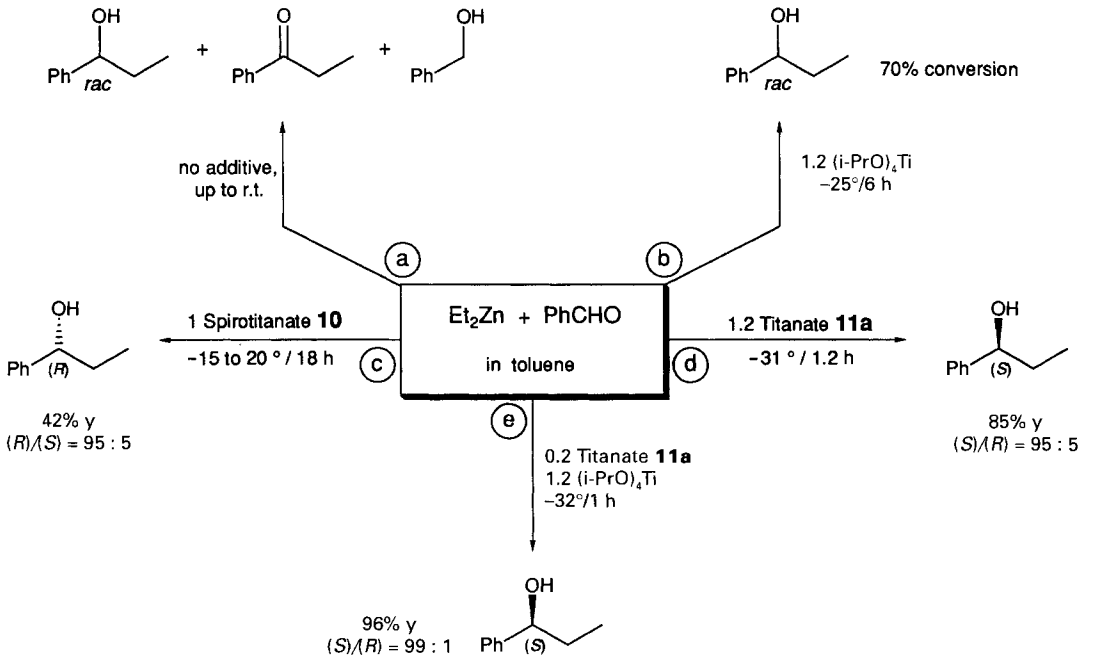
B) Addition of Et_2Zn to Aldehydes in the Presence of TADDOL-Titanates. – The results from our previous studies[13]) [6–8] are shown in *Scheme 2*. *a*) Et_2Zn does not react

[11]) Although we have not identified other species in the NMR spectra of titanates **11**, we cannot definitely exclude their occurrence in small amounts.

[12]) In contrast to our observations, the diastereoisomers **A** and **B** could be detected with the Cp derivative **11s**, by ^{1}H- and ^{13}C-NMR spectroscopy, in a 4:1 ratio [14].

[13]) In the *Exper. Part*, we describe only those experiments which have not already appeared in our previous publications [6–8].

Scheme 2. *Reactions of Et_2Zn with PhCHO under Various Conditions.* The conversions (*c*), (*d*), and (*e*) are taken from [6] [8].



with benzaldehyde to any appreciable extent in toluene at temperatures around −30°, whereas at room temperature, benzyl alcohol, 1-phenylpropan-1-ol, and propiophenone are produced[14]). *b*) In contrast, the nucleophilic transfer of an Et group to benzaldehyde from Et_2Zn occurs at *ca.* −25° in the presence of 1.2 equiv. of $(i\text{-PrO})_4Ti$. *c*) The corresponding experiment with the chiral spiro-titanate **10** leads to a 95:5 mixture of (*R*)- and (*S*)-alcohols in a slow reaction requiring temperatures above 0°. *d*) On the other hand, the titanate **11a** leads to the formation of a 95:5 mixture, with the (*S*)-enantiomer predominant under identical conditions. *e*) Finally, an improvement of the enantioselectivity, from 95:5 to 99:1 for the formation of the (*S*)-enantiomer, is achieved by applying 0.2 equiv. of **11a** and 1.2 equiv. of $(i\text{-PrO})_4Ti$. Thus, reducing the amount of the chiral titanate by a factor of six and adding a sixfold excess of the achiral titanate gives the best result[15])!

To test the relationship between the structure of the chiral titanate and the selectivity in this catalytic enantioselective reaction, we employed other C_2- and C_1-symmetrical complexes **11**–**15**, other aldehydes [6–8] and other zinc alkyls [7]; some of the results are listed in *Tables 3–5*.

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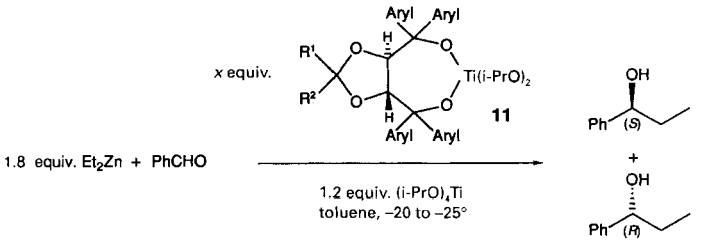
[14]) The *Meerwein-Ponndorf-Verley-Oppenauer*-type reaction of the zinc alkoxide formed with benzaldehyde is found to be faster than the addition of Et_2Zn to PhCHO. $PhCH_2OH$ has previously been identified as a side product from the reaction of Et_2Zn with PhCHO in the presence of $(i\text{-PrO})_4Ti$ [25].

[15]) At −20 to −25° the reaction proceeds to 90% conversion in 1.5 h with the *β*-naphthyl ligand; see also *Table 3*.

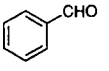
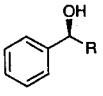
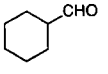
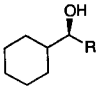
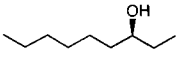
Table 3. *Addition of Et_2Zn to PhCHO in the Presence of TADDOL-Titanates* **11** *and of Excess (i-PrO)$_4$Ti.* These experiments were carried out only once, usually on a 5-mmol scale. In most cases, the reactions were run overnight, or until no more benzaldehyde could be detected by TLC. With the β-naphthyl derivative **11l**, there is a 90% conversion of the aldehyde after 1.5 h (sampling and NMR analysis). To separate the alcohols from the TADDOL, the crude products were distilled after workup. The ratios of the enantiomers formed were determined by GC on a β-cyclodextrin column (see *Exper. Part*).



		x [equiv.]	Time [h]	1-Phenylpropan-1-ol	
				Yield [%]	(S)/(R)
C_2-symmetrical	**11a**	0.02	24	quant.	84:16
		0.05	16	quant.	95:5
		0.20	21	99	99:1
	i	0.20	48	95	97:3
	j	0.05	18	90	96:4
	k	0.20	20	90	64:36
	l	0.05	30	97	96:4
		0.20	16	quant.	98:2
		0.20	1.5	90	98:2
	n	0.05	18	quant.	97:3
		0.20	30	98	97:3
	o	0.20	17	quant.	97:3
	p	0.20	17	90	97:3
C_1-symmetrical	**11q**	0.20	14	97	98:2
	r	0.05	17	96	95:5
		0.20	19	quant.	98:2
	t	0.05	30	90	97:3
		0.20	22	81	98:2
	u	0.05	15	quant.	94:6
		0.20	18	87	99:1
	w	0.20	14	94	97:3
	x	0.20	16	97	98:2
	y	0.20	14	98	97:3

Inspection of *Table 3* reveals that all complexes bearing substituted Ph rings, or having differing substituents at the acetal center (C(2) of the dioxolane ring), give very similar results in the standard reaction. Much higher selectivity is observed with the β-naphthyl-substituted complex **11l** than with the α-naphthyl analogue **11k**. With the transfer of alkyl groups other than Et, and especially with aliphatic aldehydes as receptors, the C_1-symmetrical pentaphenyl-TADDOL **2f** gives a complex **11u** almost as effective as that of the β-naphthyl-derivative (see *Table 4*). Finally, the data in *Table 5* show

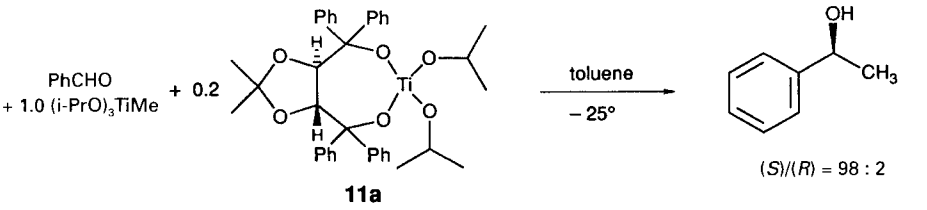
Table 4. *Comparison of C_2- and C_1-Symmetrical TADDOL Complexes in the Addition of Dialkylzinc to Aldehydes.* The results with **11a**, **11l**, and **11u** (except for the reaction of PhCHO with Et_2Zn) are taken from [6–8]. Me_2Zn and Bu_2Zn were prepared from the *Grignard* reagents and used in Et_2O instead of toluene [7]. All reactions with **11r**, and the reaction of Et_2Zn with PhCHO using **11u**, were performed following the general procedure (GPa) in the *Exper. Part.*

Aldehyde	(*S*)/(*R*) Ratios obtained with titanates of type **11**				Product (Alcohol)
	C_2-symmetrical		C_1-symmetrical		
	11a ('tetra-phenyl')	**11l** ('tetra-naphthyl')	**11r** ('*t*-Bu-tetra-phenyl')	**11u** ('penta-phenyl')	
	97:3 99:1	99 :1 99.5:0.5	– 98:2	98.5:1.5 98.5:1.5	 R = Me R = Et
	91:9 95:5	99.5:0.5 96 :4	90:10 –	96.5:3.5 95.5:4.5	 R = Et R = Bu
	96:4	98.5:1.5	98:2	98 :2	

that there is a fundamental difference between the gem.-diaryl- and gem.-dialkyl-substituted complexes: In the absence of achiral titanate the tetramethyl and tetrabenzyl derivatives **12**–**14** give rise to small selectivities, which disappear altogether on addition of $(i\text{-PrO})_4Ti$[16]), while the complex **15** from the seven-membered-ring dimethanol **9** behaves like the TADDOL derivatives.

Information about the role of Zn in the reaction mixture was obtained by the experiment outlined in *Scheme 3*. PhCHO was allowed to react with 1.0 equiv. $(i\text{-PrO})_3TiMe$, which had been prepared independently and purified by distillation [2], in the presence of 0.2 equiv. of the chiral complex **11a**. The resulting alcohol consisted of mainly the (*S*)-enantiomer. The preferred addition of the nucleophile from the *Si*-face of the aldehyde – as in the case of all the other reactions carried out with dialkylzinc and **11a** –

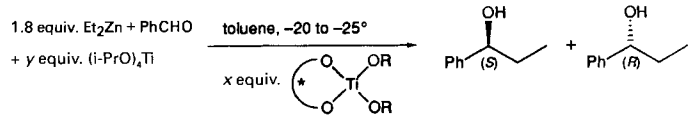
Scheme 3. Si-*Selective*, **11a**-*Catalyzed Addition of $(i\text{-PrO})_3TiMe$ to PhCHO in the Absence of Zn or Li Salts.* In [2], we have shown that the $(i\text{-PrO})_3TiMe$ used here adds to PhCHO in THF at −50° within 1 h.

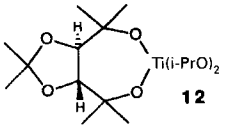
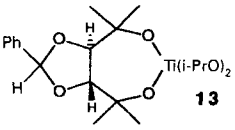
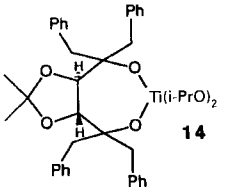
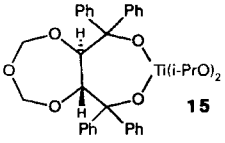


11a

[16]) In the case of the tetrabenzyl derivative **14**, the lack of selectivity could possibly have two causes: *a*) the Ti-center of **14** is – as with **12** – not hindered enough to be more reactive than that of $(i\text{-PrO})_4Ti$ (see *Fig. 3* and accompanying text.). *b*) The Ti-center of **14** is too highly hindered – as with the α-naphthyl analogue **11k** (see *Table 3*), and, therefore, is not involved in the catalysis (see *Sect. C*).

Table 5. *Addition of Et_2Zn to PhCHO in the Presence of Chiral Titanates* **12–15** *Prepared from the Diols* **3**, **4**, **6**, *and* **9**. For determination of the (*R*)/(*S*) ratios, see *Table 3*.



	Chiral Titanate x [equiv.]	$(i\text{-PrO})_4Ti$ y [equiv.]	Time [h]	Yield [%]	1-Phenylpropan-1-ol (*S*)/(*R*)
 **12**	0.20	–	45	49[a])	68:32
	1.00	–	20	80[b])	53:47
	0.05	1.2	22	97	50:50
 **13**	0.20	1.2	15	99	58:42
 **14**	1.00	–	20	98	75:25
	0.20	1.2	15	98	54:46
 **15**	0.20	1.2	20	96	95:5

[a]) Determined by CGC. The other components could be identified as PhCHO (38%), $PhCH_2OH$ (6%), and propiophenone (6%; see also *Footnote 14*).

[b]) An additional 8% of PhCHO could be detected by ^{1}H-NMR.

might be interpreted as indicating that Zn is actually not involved at all in the product-forming step of the other reactions[17]).

C) Catalysis with TADDOLate Complexes: – a Clearly Defined Case of Ligand-Accelerated Catalysis. – The results described in the previous section can be summarized as follows: *i*) the more highly hindered chiral titanates are more active catalysts than is $(i\text{-PrO})_4Ti$. *ii*) With increasing bulkyness of the α-substituents in the dioxolane-dimethanols, the efficiency of the chiral catalyst increases in the order hydrogen[18]) < alkyl < Ph < β-naphthyl. *iii*) When the steric hindrance becomes too large, as in the α-naphthyl derivative **11k**, the rate and the enantioselectivity of the reaction decreases.

[17]) However, for a discussion of the importance of bimetallic transition states see the review article 'Stereoselective Organic Reactions: Catalysts for Carbonyl Addition Processes' [26], and *Scheme 6* in *Sect. E*.

[18]) The diol without substituents at the dimethanol unit (**1a**, H instead of Ph) [27] [28] seems to form polynuclear, rather than cyclic complexes with $(i\text{-PrO})_3TiCl$, as indicated by NMR studies [29].

iv) The Ti-complexes with less hindering dioxolane-dimethanol groups, such as **12**, do not successfully compete as catalysts with $(i\text{-PrO})_4Ti$. *v*) The enantioselectivity is higher with substoichiometric amounts of the TADDOLate-Ti complex in the presence of excess $(i\text{-PrO})_4Ti$ than it is with equimolar amounts of the chiral complex alone.

These findings are compatible with the following mechanistic considerations, illustrated for the β-naphthyl-substituted complex **11l** in *Fig. 3*. Due to steric hindrance to coordination, there exists fast dynamics of ligand exchange at the Ti-site in the bulky TADDOLate complex. The Ti-center bearing four i-PrO groups achieves the preferred, stable hexacoordination by aggregation (*cf.* the section of the crystal structure of $(EtO)_4Ti$ [33] in *Fig. 3*) or by attachment of some donor atoms, and it undergoes ligand exchange more slowly than the TADDOL titanate. Thus, the chiral titanate is the catalytically active species in the presence of excess $(i\text{-PrO})_4Ti$.

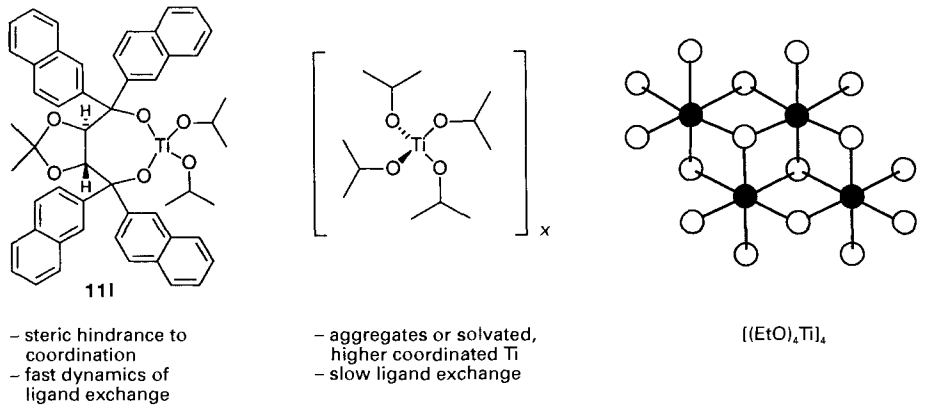
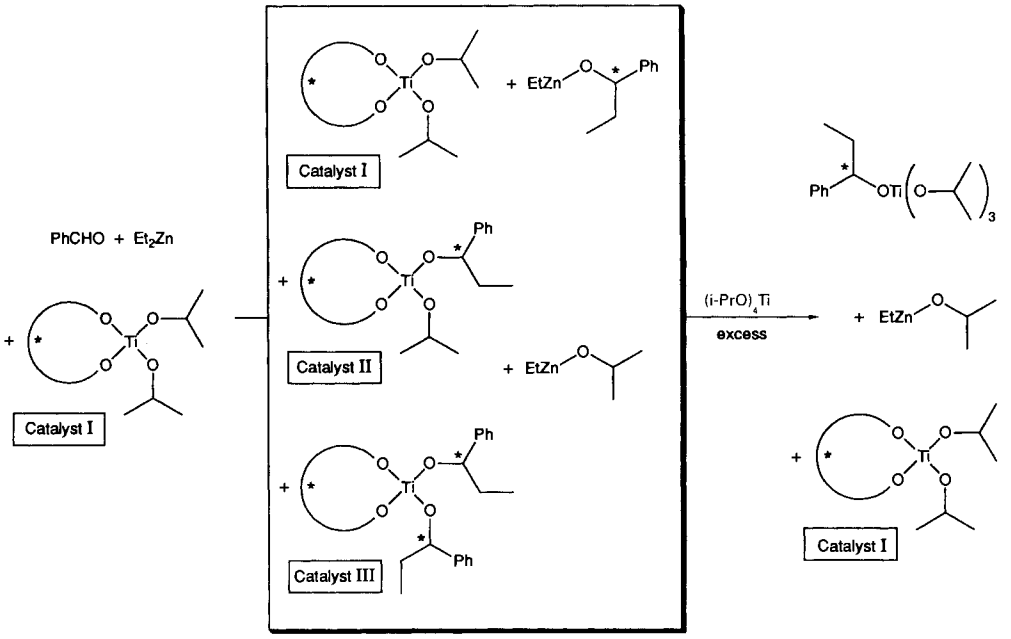


Fig. 3. *Ligand-accelerated catalysis with TADDOL-derived titanates. Left*: the ligand sphere of the Ti in **11l** is sterically hindered; binding of additional ligands causes congestion; therefore, the Ti-center bearing the TADDOLate ligand is subject to fast dynamics of ligand exchange (*cf.* the dicussion of steric effects in the chemistry of transition-metal phosphine complexes [30]). *Middle*: $(i\text{-PrO})_4Ti$ is usually aggregated [31] [32] and is expected to undergo ligand exchange more slowly than complexes of type **11**. *Right*: schematic presentation of the crystal structure of the tetrameric tetraethyl titanate showing hexacoordinated Ti; note that this hexacoordination is achieved by binding up to three Ti on a single oxygen [33] (*cf.* also the tetramers of Li enolates [34]).

Why is the selectivity obtained with the TADDOLate-Ti complex alone almost an order of magnitude smaller than with the combination of the chiral complex and achiral $(i\text{-PrO})_4Ti$ (19:1 *vs.* 99:1 with **11a**, see *Scheme 2*)? We assume that this may be due to the fact that new chiral titanate catalysts are formed as the reaction proceeds (see *Scheme 4*): The original titanate (catalyst I) is in equilibrium with titanates containing the product alkoxy ligands (catalysts II and III, see box in *Scheme 4*), and these newly formed titanates give rise to altered selectivities[19]). This assumption was tested by preparing

[19]) See the discussion of *non-stoichiometric effects* in the chemistry of Li compounds [34], observations concerning product metal alkoxides catalyzing their own formation (referred to as 'the principle of enantioselective autoinduction') [35], and the iso-inversion principle [36]. It is interesting to note at this point that with $(EtO)_4Ti$ and $(t\text{-BuO})_4Ti$, instead of $(i\text{-PrO})_4Ti$, the enantioselectivity of Et_2Zn addition to PhCHO is much lower; we also found that $(i\text{-PrO})_4Ti$ cannot successfully be replaced by $(i\text{-PrO})_4Si$ in our reaction.

Scheme 4. *(i-PrO)$_4$Ti as a 'Cleansing Agent' for the Chiral Catalyst I*



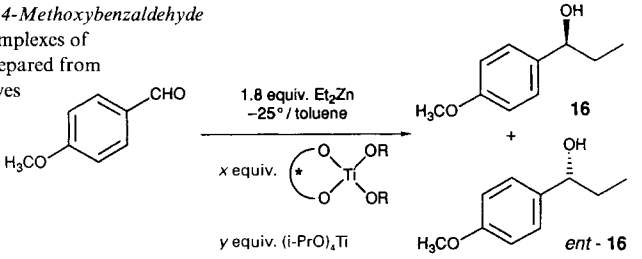
titanates **11** with one or two chiral RO groups (derived from PhCHO + Et_2Zn) and by using them for mediating the addition of Et_2Zn to 4-methoxybenzaldehyde (*Table 6*). Indeed, the attachment of (*R*)- or (*S*)-1-phenylpropoxy ligands to the seven-membered Ti-containing ring of the titanates **11** leads to *Lewis* acids which are much less effective at inducing enantioselectivity in the reaction. Addition of $(i\text{-PrO})_4Ti$, on the other hand, restores the high degrees of selectivity. Thus, the role of excess $(i\text{-PrO})_4Ti$ can be viewed as a pool for the product alkoxides, a means to reconstitute the original catalyst; the catalysts II and III shown in *Scheme 4* are converted back to catalyst I.

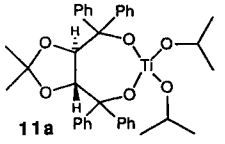
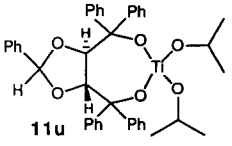
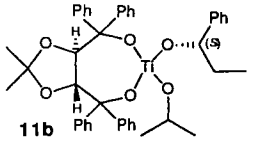
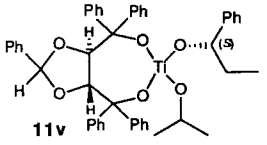
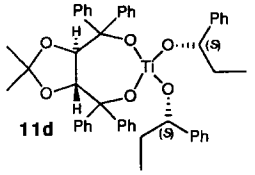
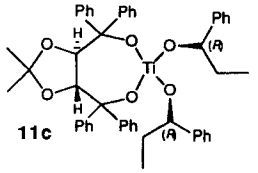
The high activity of TADDOLate-complexed metal centers is also evident from two observations with different reactions. The Zr complex corresponding to **11a**, when dissolved in i-PrOH (0.06M), catalyzes a moderately enantioselective *Meerwein-Ponndorf-Verley* reduction of acetophenone (*Scheme 5*) [37]. If one assumes that there is achiral zirconate $(i\text{-PrO})_4Zr$ in equilibrium with the chiral species under these conditions, the conclusion would be that the Zr-center with the bulky chiral ligand is much more active[20]). We have also tested the titanates **11a** and **11l** as catalysts for epoxidation of geraniol[21]) by *t*-BuOOH in CH_2Cl_2 at −75° [8]. With a 1:1:0.1 molar ratio of the allylic alcohol, $(i\text{-PrO})_4Ti$, and the naphth-2-yl derivative **11l**, a 15% ee in the resulting epoxide

[20]) When the reaction mixture is kept for longer periods of time and/or at higher temperatures, the enantiomeric excess of 1-phenylethanol decreases – due to equilibration (eventually, when thermodynamic equilibrium has been reached, there should be no enantiomeric excess observed under these conditions!).

[21]) For discussions of synthetic and mechanistic aspects of the *Sharpless* reaction, see the review articles [38] and the recent contributions by *Sharpless* and coworkers [32] [39] and by *Corey* [40].

Table 6. *Nucleophilic Ethyl Addition of 4-Methoxybenzaldehyde with Et_2Zn/Chiral Titanates.* The Ti complexes of type **11** with chiral RO ligands were prepared from the corresponding isopropoxy derivatives (see also *Table 2* and *Exper. Part*). The alcohols were isolated by column chromatography of the crude product, except for the case of 0.04 equiv. of **11a**, where the products were obtained by distillation.

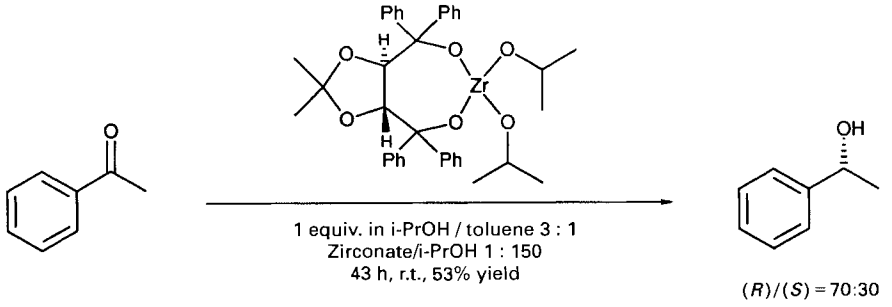


	x [equiv.]	*y* [equiv.]	Time [h]	Yield [%]	**16**/*ent*-**16**
 **11a**	1.4	–	40	69[a])	71:29
	0.2	1.2	15	95	98:2
	0.04	1.2	40	98	93:7
 **11u**	1.4	–	40	76[a])	71:29
	0.2	1.2	15	98	97:3
 **11b**	1.4	–	40	63[a])	83:17
	0.2	–	40	27[b])	62:38
	0.2	1.2	15	98	98:2
 **11v**	1.4	–	40	73[a])	71:29
	0.2	–	40	23[a])[b])	51:49
	0.2	1.2	15	98	96:4
 **11d**	1.4	–	40	52[a])[b])	67:33
	0.2	–	40	19[a])[b])	54:46
	0.2	1.2	15	96	97:3
 **11c**	1.4	–	40	45[a])[b])	50:50
	0.2	–	40	46[a])	58:42
	0.2	1.2	15	98	97:3

[a]) By ^{1}H-NMR analysis of the crude product. 1-(4′-Methoxyphenyl)propan-1-one, formed by a *Meerwein-Ponndorf-Verley-Oppenauer*-type reaction (see also *Footnote 14*), was identified as a by-product. The corresponding amount of 4-methoxybenzyl alcohol could not be detected ; it is probably lost during workup.

[b]) Unreacted 4-methoxybenzaldehyde was detected by ^{1}H-NMR analysis of the crude product.

Scheme 5. *Enantioselective Hydride Transfer from i-PrOH to Acetophenone by a TADDOL-Zirconate Complex* [37]



was observed. Again, the Ti-centers which bear the bulky TADDOLate ligand must be somewhat more active catalytic sites than those which do not[22]).

These results are a demonstration of what has been called the *ligand acceleration effect* by *Sharpless* and coworkers [42]. In the case described here, the nature of the acceleration can be clearly related to a structural feature, namely the steric hindrance to coordination of the metal center involved in the reaction (see *Fig. 3*)[23]).

D) Structural Investigation: Conformers of the Dioxolane Ring and of the Seven-Membered-Ring Titanate in TADDOL Derivatives 1, 2, and 10. – We have previously reported the crystal structure of TADDOL **1a**·2 CCl_4, and compared it with a number of other solid-state structures containing **1a** and **1u** [4]. In all cases, the two OH groups of these TADDOLs form intramolecular H-bonds in an O–H···O containing seven-membered ring; the dioxolane rings are present in approximate envelope forms; the Ph groups occupy *quasi*axial and *quasi*equatorial positions, and there are various conformations around the C–Ph bonds (see *Fig. 4*)[24]). The diol structure can be taken as a model for the Ti complexes, *cf.* the O–O distances in O–H···O (*ca.* 2.6 Å [4]) and in O–Ti–O (*ca.* 2.8 Å, see structure of **10** below). Thus, little distortion is necessary to substitute the bridging H-atom of the diol by a Ti-atom. The question arises as to whether a bridging or complexing atom is necessary at all to hold the diphenyldimethanol groups in their respective positions, *i.e.* whether there are actually any other stable conformations around the $Ph_2(HO)C$–CH bonds of the TADDOLs; inspection of a model would indicate that there are none (see *Fig. 4*). To test this hypothesis, we obtained[25]) crystals of

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[22]) There is a report [41] according to which the titanate $(i\text{-PrO})_3TiOCMePh_2$ forms a complex with PhCOMe while $(i\text{-PrO})_4Ti$ does not. This was concluded from degrees of conversion in the addition of $(i\text{-PrO})_3TiPh$ to PhCOMe and from NMR measurements. The rate effect may arise for different reasons, and the observed NMR shifts seem too small to be convincing.

[23]) The bis(trifluoromethylsulfonyl amide) of (*R,R*)- or (*S,S*)-cyclohexane-1,2-diamine used as a chiral ligand in the presence of huge amounts of $(i\text{-PrO})_4Ti$ for enantioselective catalysis of the addition of Et_2Zn to aldehydes by *Ohno* and coworkers [25] also induces a strong acceleration of ligand exchange. This must be different in nature from the one we observed, because there is no excessive hindrance introduced by their ligand. Moreover, it is not clear, whether a cyclic Ti derivative is formed with the bis-triflamide, because five-membered ring Ti-containing systems are known to be unfavorable (see the discussions in [9]).

[24]) The barrier to rotation around the C–Ph bond is probably very small. On the other hand, the naphthyl groups of the α-naphthyl derivatives **1k**, **1v**, **2c** rotate slowly on the NMR time scale at room temperature, but fast at 120° [4].

[25]) We thank Dr. *Jun-ichi Sakaki* for preparing a sample of **17**.

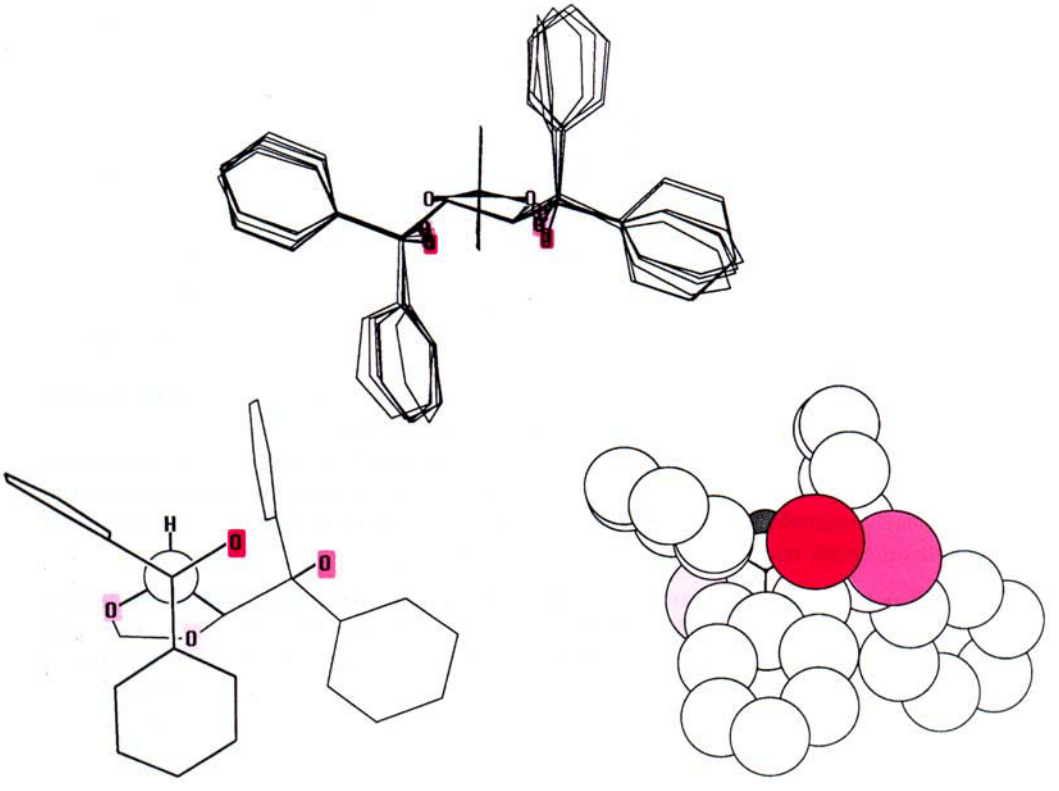


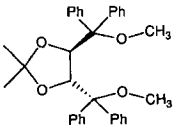
Fig. 4. *TADDOL* **1a** *in various crystal structures* [4]. *Top*: superposition of six different **1a**-containing structures viewed from the face of the molecules bearing the OH groups. *Bottom left*: *Newman* projection along the $Ph_2(HO)C-CH$ bond as present in the crystal structure of **1a**·2 CCl_4. *Bottom right*: space-filling model of the *Newman* projection.

17, the known [13] [19] dimethyl ether of diol **1a** and determined the solid-state structure (*Fig. 5*). Indeed, the geometry of the ether is quite similar to that of the diol, with the two *O*–Me groups occupying an antiperiplanar position with respect to the neighboring *quasi* axial Ph group. The dioxolane ring is less puckered than in the diols themselves (see the comparison below), and the $CH_3O\cdots OCH_3$ distance is 2.9 Å. Thus, the juxtaposition of the two O-atoms in the diols **1** and **2** is apparently a consequence of conformational stability and is enforced by the size and bulkyness of the aryl groups; the TADDOLs would seem to be ideal ligands, ready to form seven-membered rings[26]), a situation reminiscent of the gem.-dimethyl or *Thorpe-Ingold* effect on cyclization rates [44a]. This same conformational effect is likely to be important in other applications of diarylmethanol containing chiral auxiliaries, too [44b]; *cf.* [44c] for other types of conformational control of diastereoselectivity published in recent years.

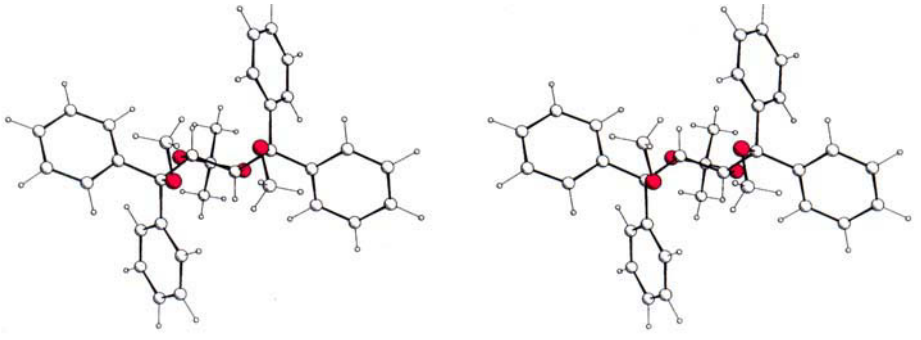
The tendency of TADDOLs to form cyclic titanates, and the stability of these titanates even in the presence of excess $(i\text{-PrO})_4Ti$ are compatible with the stability of

[26]) The preparation and a crystal structure of seven-membered-ring O,S-acetals formed from a monothiol analog of **1a** have been described recently [43].

Fig. 5. *Stereo PLUTO presentation of* **17**, *the dimethyl ether of* **1a** *in the crystal structure of the clathrate with* CCl_4 *(1:1)*



17



these ligands in a conformationally fixed arrangement putting the donor O-atoms next to each other[27]).

We then turned out attention to a structural comparison of C_2- and C_1-symmetrical diols **1** and **2**, respectively. We were able to prepare suitable crystals of the C_1-TADDOLs **2b** and **2f** with a *t*-Bu and a Ph substituent, respectively, at the acetal C-atom of the dioxolane moiety. Both were crystallized from hexane in the presence of 1 equiv. of a secondary amine ($Me_2CHNHMe$ and piperidine, respectively) with which they formed clathrates [18]. It is our experience that the TADDOLs alone form dimers in the solid state which leads to huge unit cells; guest molecules break up these dimers by forming H-bonds with the diols, and this results in asymmetric units containing fewer atoms, facilitating the solution of the structures. *Fig. 6* shows the crystal structure of the *t*-

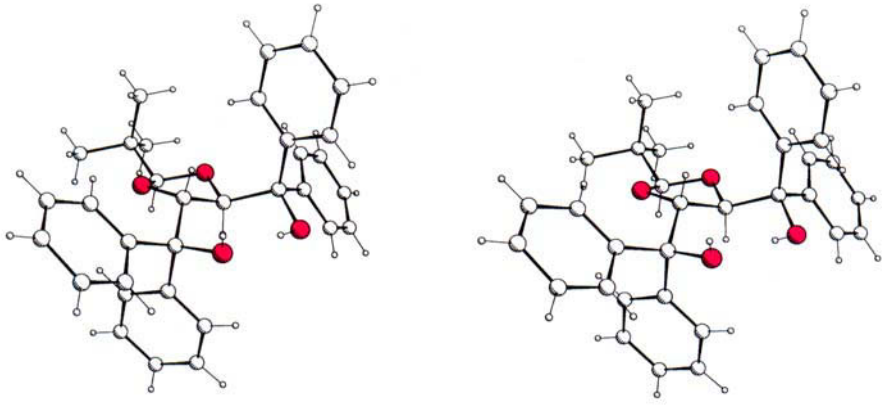


Fig. 6. *Stereo PLUTO presentation of the diol* **2b** *in the crystal structure of the clathrate formed with* $Me_2CHNHMe$

[27]) Also, from this point of view, it seems not surprising that the dioxolane-dimethanols bearing no or small substituents on the OH-substituted C-atom behave quite differently (see *Table 5* and *Footnote 18*).

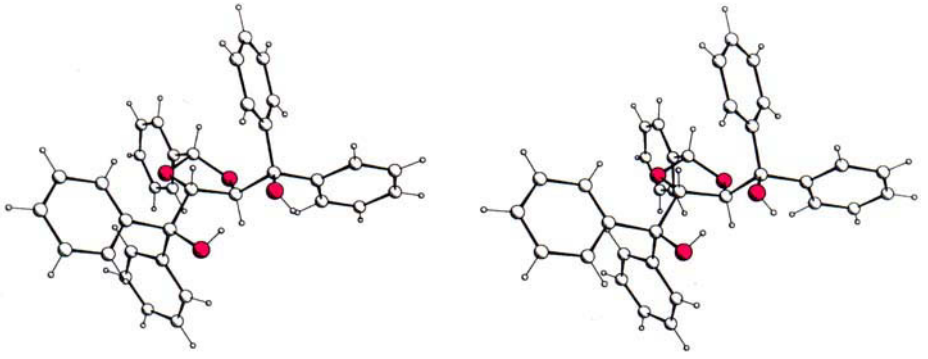


Fig. 7. *Stereo PLUTO presentation of the diol* **2f** *in the crystal structure of the clathrate formed with piperidine*

butyltetraphenyl, *Fig. 7* of the pentaphenyl derivative. In both structures there is the expected [18] H-bond between one of the diol protons and the guest molecule's amino N-atom. As can be seen from the comparison made in *Fig. 8*, the dioxolane rings of the

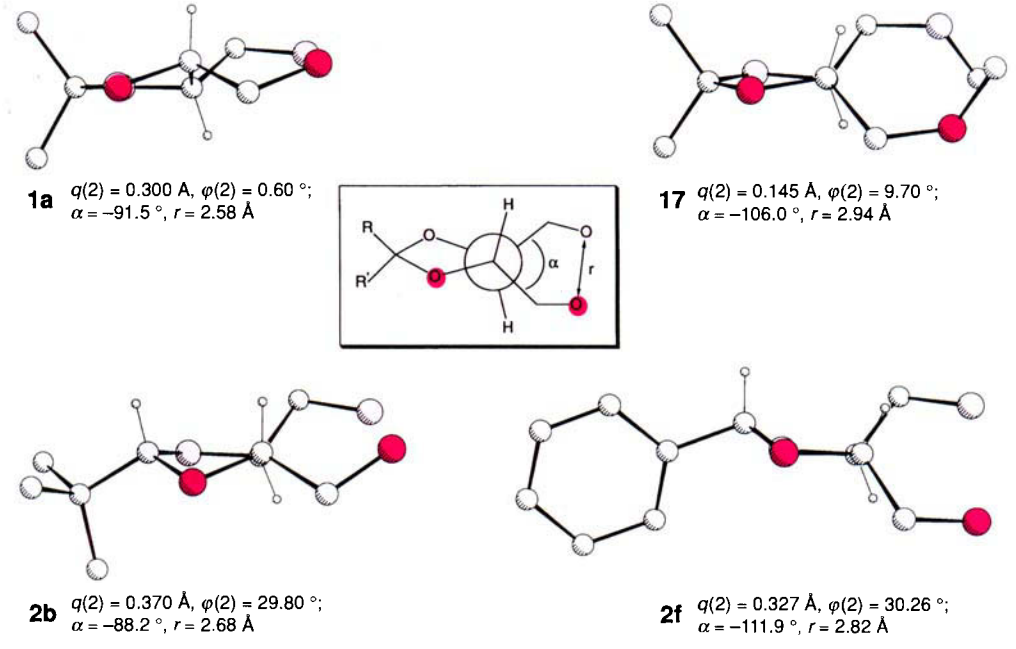


Fig. 8. *Structural comparison of the diols* **1a**, **2b**, **2f**, *and the dimethyl ether* **17** *of* **1a** (the four α,α,α′,α′ -Ph groups have been omitted for clarity). The diols have envelope-type dioxolane conformations. In the dimethyl acetal **1a**, there is a conformation with one of the *tertiary* C-atoms out of plane, in the pivalaldehyde acetal **2b** an envelope with one O-atom out of plane, and, in the pentaphenyl derivative **2f**, with the acetal C-atom out of plane. In contrast, the dioxolane ring of the diether can neither be classified as twist- nor as envelope-type. The conformer classification was made according to the ring puckering coordinates as defined by *Cremer* and *Pople* [45]. The values for the puckering amplitude (q) and the phase angle (φ) are shown for each case. The corresponding values for the torsion angle (α) between the diphenylmethanol substituents and the O···O distance (r) between the excocylic O-atoms are also given. In the diols, there are intramolecular H-bonds between the OH groups. See also the comparison with the spiro-titanate **10** in *Fig. 10*.

diols are present in the crystal in a type of envelope conformation, while the dioxolane ring of the dimethyl ether **17** shows a conformation somewhere between the ideal twist and envelope-type conformations, with a concomitant alteration of the dihedral angles around the dioxolane C(4)–C(5) bond: the CPh_2O groups on the dioxolane rings form synclinal angles ranging from 88 to 112°. Thus, these structures demonstrate that changes of the substituents at the acetal center of the dioxolane ring not only lead to different conformations of this ring, but will eventually also effect the disposition of groups in the neighborhood of the metal center – five bonds remote! – in the corresponding complexes[28]).

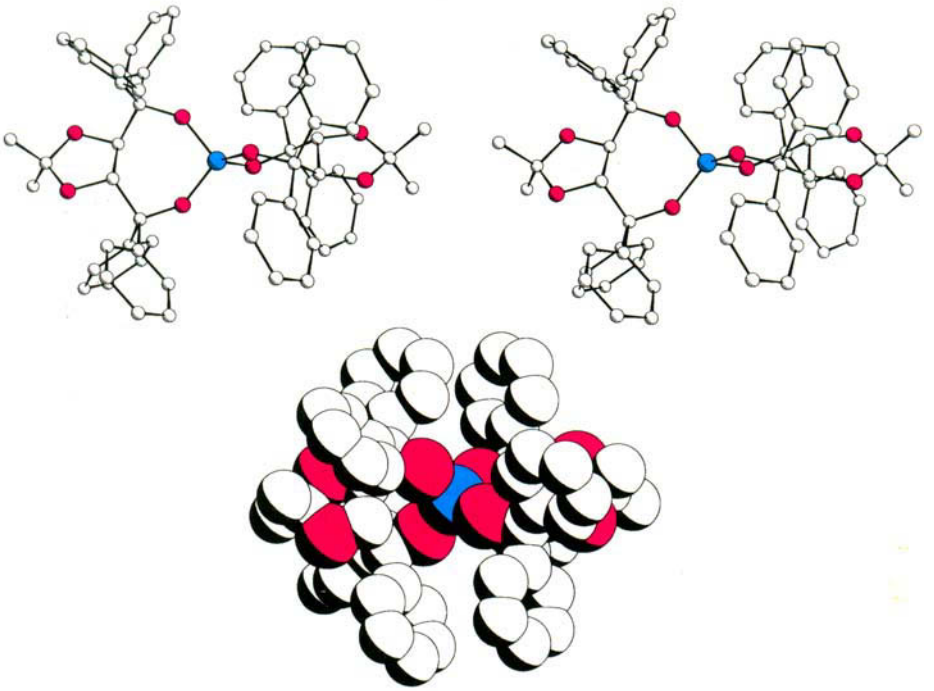


Fig. 9. *Stereo PLUTO presentation and a space-filling presentation of one of the three spiro-titanate molecules in the crystal structure of* [3·**10**·0.5 Et_2O]. The H-atoms have been omitted for clarity.

We succeeded in preparing single crystals, suitable for X-ray structure analysis [48] of the rather air-stable spiro-titanate **10**, which had been recrystallized from Et_2O. The asymmetric unit of the crystal contained three molecules of **10** and *ca.* 1/2 Et_2O molecule, *i.e.* more than 200 non-H-atoms. Together with partial disorder, this made the solution and refinement of the structure very difficult, and, accordingly, the resolution was rather poor. In *Fig. 9*, one of the three independent spiro-titanate molecules is depicted; the

[28]) Compare the 'remote' effects of stereogenic centers found in some recent investigations of reactions of heterocyclic acetals [46] and in chiral (ferrocenyl)phosphines [47].

space-filling presentation shows the shielding of the Ti-atom by the Ph groups. For additional ligands, access to the metal center is sterically hindered, and conversion to a pentacoordinated ligand sphere would create additional strain, since tetrahedral angles would have to be changed to 90°. It is, thus, not surprizing that the spiro-titanate **10** is a very inactive catalyst in the addition of Et_2Zn to PhCHO (*Scheme 2*). It appears likely that the reaction is actually not catalyzed by **10** but by some less hindered species formed in the early stages of the process[29]). In view of this suspicion, the reversal of the steric course (addition from the *Re*-face of the aldehyde with **10**, and from the *Si*-face with all the non-spiro derivatives of type **11**) is much less discomforting to us (since we know the crystal structure of **10**), than it was when we first observed it [6a]. Experiments aimed at the elucidation of the mechanism in the spirotitanate-mediated process are in progress[30]).

It is remarkable that all six titanate-containing seven-membered rings in the asymmetric unit of [3·**10**·0.5 Et_2O] are in a different conformation (see upper part of *Fig. 10*). They range from more or less strongly twisted C_2-symmetrical forms to sofa-type shapes, with two atoms out of a plane occupied by the other five. A reversal of the 'local chirality' may result among the conformers, with *quasi*axial Ph groups on either side of the Ti-center[31]). The crystal structure must be taken as evidence for a highly flexible, fluctuating seven-membered titanate ring conformation in solution. Such flexibility is probably an ideal feature for a catalytically active center to adapt to different substrates.

Inspection of the structure of **10** led us to recognize another noteworthy feature: on average, there is a twist of the Ph_2C group upon incorporation of Ti into the diolate unit. Compare the superposition of the *side views* of the titanate rings of **10** with the corresponding projection of the diol **1a** in *Fig. 10*: on each side one of the Ph groups moves *towards*, the other geminal one *away* from the Ti-center due to this twist. It is intriguing that the C_1-symmetrical pentaphenyl-substituted free diol **2f**, the Ti complex of which often gives better results than those of the tetraphenyl TADDOL **1a**, shows the same kind of shift of the relative position of the Ph_2C groups, and the less effective *t*-Bu analogue **2b** does not (see bottom part of *Fig. 10*).

As has been pointed out before [4], the propeller-type arrangement of the Ph groups in the TADDOLs, and now in the spiro-titanate as well, is similar to that in phenylphosphine complexes of transition metals [49]. A comparison between the crystal structures of various complexes with C_2-symmetrical ligands can be made by considering a plane through the metal center and the two atoms bearing a pair of Ph groups each, and determining the angles which the C–Ph or P–Ph bonds form with this plane (see the

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[29]) See the effect of product alkoxides outlined in *Scheme 4* and demonstrated in *Table 6*.

[30]) It is important to note at this point that (*R*)-products are also formed when stoichiometric amounts of Li or XMg derivatives and the spiro-titanate **10** are first mixed and then combined with 1 equiv. of an aldehyde, conditions under which an ate-complex might be the actual reagent. On the other hand, (*S*)-products result with the reagent prepared from MeLi and the (chloro)(isopropoxy)-Ti complex of type **11** (see *Scheme 3*).

[31]) Such a reversal of 'local chirality' imposed upon a metal center by a change of diphenylphosphine 'propellers' (δ or λ chirality, see the discussion in [49]), without changing the sense of chirality of the stereogenic centers, was recently postulated to explain the reversal of the stereochemical course of hydrogenation with a DIOP complex by attaching $Me_3N^{\oplus}$ substituents in the *para*-position of the P–Ph groups, and at the same time switching from organic solvents to H_2O [49b] [50].

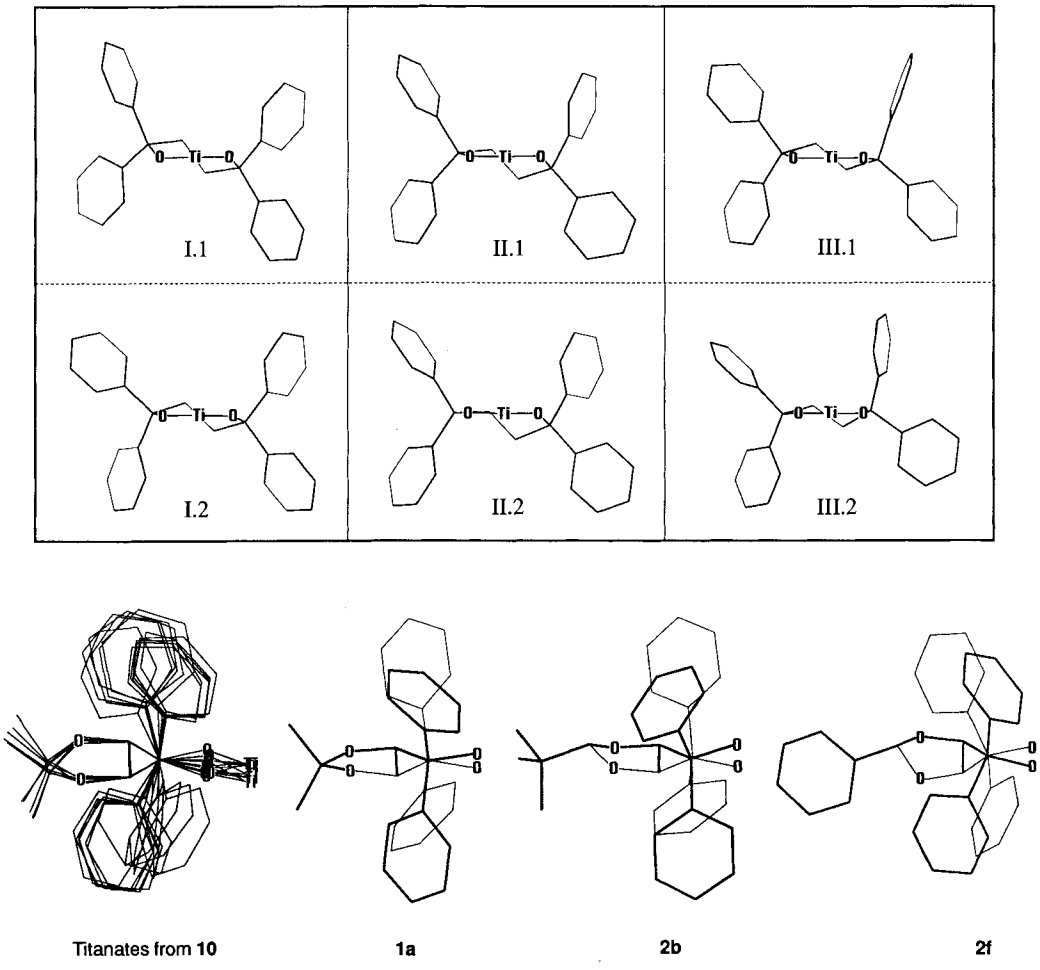
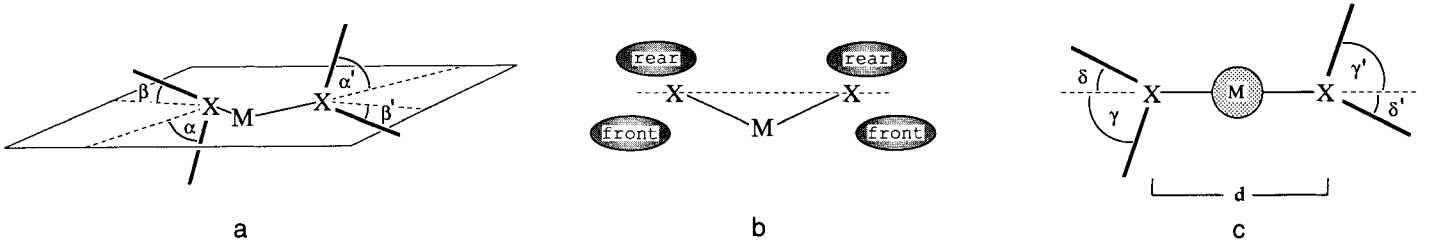


Fig. 10. *The six different seven-membered-ring titanate moieties* (I.1–III.2) *in the asymmetric unit of* [3·**10**·0.5 Et_2O] (top), *and a side-view comparison of the structures of the diols* **1a**, **2b**, *and* **2f** *with the six superimposed titanates* (bottom). The Latin numbers I, II, and III refer to the three independent spiro-titanate molecules in the asymmetric unit, the additional numbers 1 and 2 to the two seven-membered ring titanates in each spiro-titanate. The average of the endocyclic six O–Ti–O bond angles is 102.5°, and the average of the six corresponding O–O distances is 2.78 Å.

general presentation and some examples in *Table 7*). As can be see from the values in *Table 7*, there is a strong bias, at least on one side of the metal center, for the *quasi* axial Ph substituent to form a larger angle with the defined plane than that of the geminal, *quasi* equatorial Ph group. In addition, the Ph groups may lean towards the metal center (Ph front), or away from it (Ph rear in *Table 7*, *cf.* side views in *Fig. 10*). The difference between the angles is particularly large in those complexes which give high degrees of enantioselectivity in the reactions they catalyze. It is useful, therefore, to look for this

Table 7. *Comparison of the Spiro-titanate* **10** *with Some Chiral Diphosphine Complexes. a*) Plane formed by the metal center and the two C- or the two P-atoms (X) bearing two Ph groups each. The angles α and β represent those between the plane and the C–Ph or P–Ph bond. *b*) View perpendicular to the plane defined in *a*, with the areas representing the Ph groups specified as *front* (f) and *rear* (r). *c*) Definition of angles γ and δ formed between the line connecting the above mentioned C- or P-atoms and the C–Ph or P–Ph bond direction. In this projection, the metal is located in front of the line connecting the two X-atoms at a position within the circle drawn. The data for five of the phosphine complexes [51–53] [55] [56] shown below the table are taken from the *Cambridge Crystallographic Data Base* (see the REFCodes in parentheses). The hitherto unpublished coordinates of the CHIRAPHOS complex [54] were given to us by Prof. *J. Halpern* (University of Chicago). A similar treatment of chiral semicorrin (*cf.* KAFSEP [57]) and bipyridyl complexes [58], with groups of different sizes on stereogenic centers, leads to comparable angle biases. The presentation chosen here and in our previous paper [4] was used before by other authors [49] [56] in their discussions of the structures of C_2-symmetrical diphosphine complexes. For better comparison with the (*R,R*)-TADDOL derivatives, all the crystal structures of the phosphine complexes are presented such that the *quasi*axial substituents are located on the upper right and lower left side. For this purpose, the actually determined crystal structures of (*S,S*)-DIOP, (*P*)-BINAP, and (*R,R*)-CHIRAPHOS have been inverted to the (*R,R*)-, (*M*)-, and (*S,S*)-enantiomers, respectively. For clarity, only the basic skeleton is shown in each case.

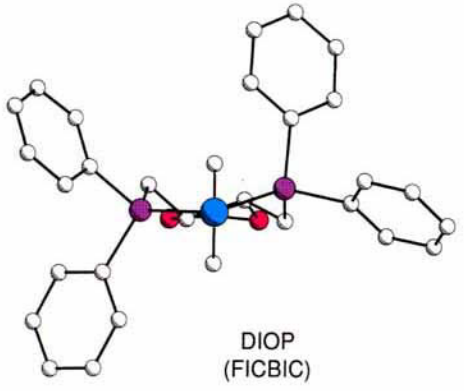


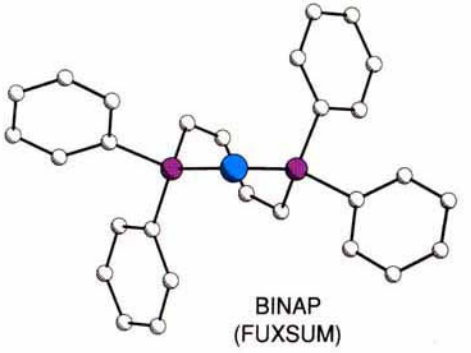
Complex	α [°]	β [°]	α' [°]	β' [°]	γ [°]	δ [°]	γ' [°]	δ' [°]	d [Å]
Spiro-titanate I.1	51 (r)	53 (f)	54 (r)	44 (f)	62	53	65	45	3.68
Spiro-titanate I.2	66 (r)	39 (f)	61 (r)	44 (f)	74	39	66	44	3.71
Spiro-titanate II.1	56 (r)	50 (–)[a])	62 (r)	40 (f)	61	50	74	41	3.67
Spiro-titanate II.2	60 (r)	51 (r)	60 (r)	38 (f)	63	52	73	39	3.72
Spiro-titanate III.1	58 (r)	50 (f)	69 (r)	36 (r)	63	51	73	40	3.76
Spiro-titanate III.2	64 (r)	47 (–)[a])	67 (r)	37 (–)[a])	66	47	76	37	3.70
Pd-(*R,R*)-DIOP (CSD:FICBIC) [51][b])	49 (f)	51 (–)[a])	58 (r)	14 (f)	51	52	77	29	3.67
Ru-(*P*)-BINAP (CSD:FUXSUM) [52][b])	57 (r)	25 (f)	55 (r)	21 (f)	71	34	75	30	3.18
Ru-(*P*)-BINAP (CSD:JAPXAZ) [53][b])	54 (–)[a])	47 (f)	52 (r)	5 (f)	54	50	84	26	3.37
Rh-(*S,S*)-CHIRAPHOS (CSD:CHPSRH) [54][b])	64 (r)	42 (f)	68 (r)	37 (–)[a])	65	43	69	37	3.00
Rh-(*R,R*)-DIPAMP (CSD:VERYAS) [55]	63 (r)	41 (r)	63 (r)	41 (f)	64	41	65	42	2.99
Pd-(*R,R*)-BMPPP (CSD:SACHOT) [56a][c])	60 (r)	47 (f)	62 (r)	43 (f)	62	47	64	43	3.16

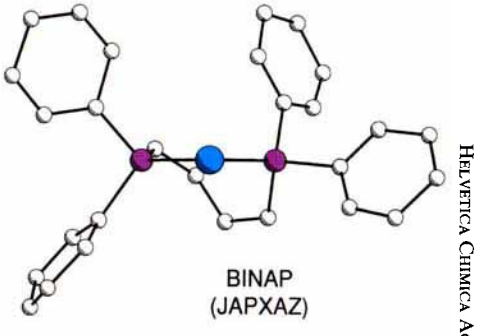
Table 7 (cont.)

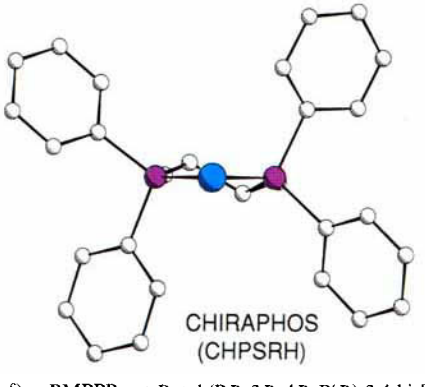
[a]) No differentiation between *rear* and *front* can be made.

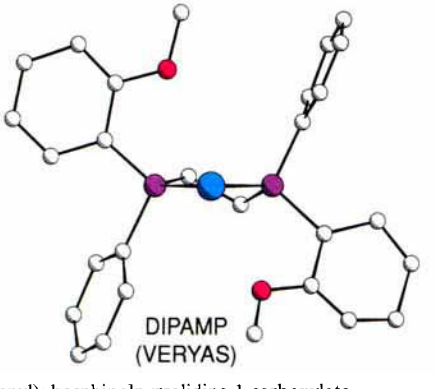
[b]) Inverted structure depicted below.

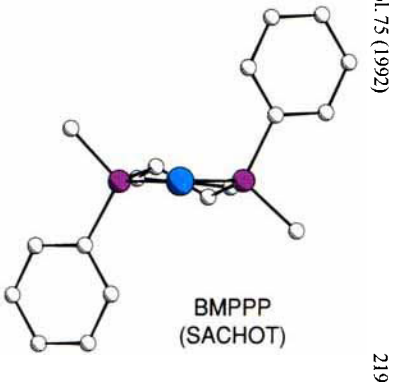










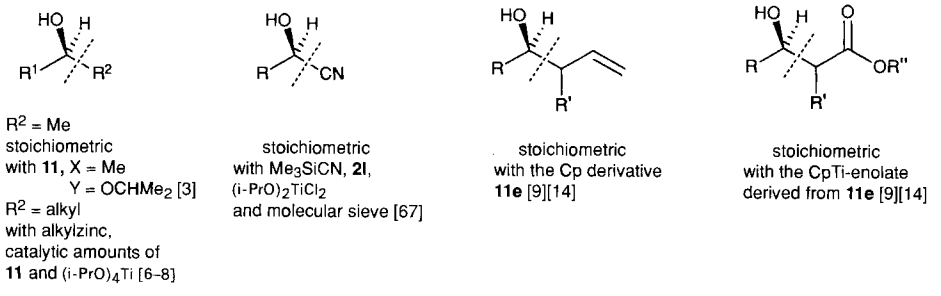


[c]) BMPPP = *t*-Butyl (P*R*, 3*R*, 4*R*, P′*R*)-3,4-bis[(methyl)(phenyl)phosphino]pyrrolidine-1-carboxylate.

feature of angle bias in the search for new ligands and their complexes for enantioselective catalysis[32]).

The C_2-type arrangement of the Ph groups around the metal center creates steric constraints for complexation of substrate molecules and for trajectories in subsequent combinations with reaction partners. It appears to be now generally agreed [59] that the *quasi*axial/equatorial disposition of the substituents on the P-atom and not their edge-on *vs.* face-on conformation [61] [62], creates steric hindrance to coordination of substrate and/or reagents in certain front octants around the metal.

E) Models for the Stereochemical Course of Reactions Mediated by TADDOL-Titanates – and Possible Extensions. – Inspite of all the information presented in the



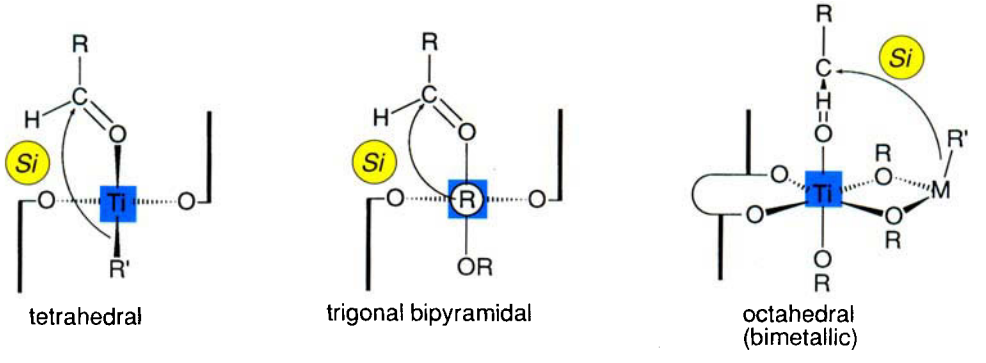


Fig. 11. *Products obtained by* Si*-addition of nucleophiles to aldehydes using (*R,R*)-TADDOL-titanates. Top*: invariably, with very different nucleophiles and various additional ligands on Ti the same relative topicity [66] of nucleophilic addition results (*Si* with the (*R,R*)-ligand). *Bottom*: the aldehyde, a monodentate ligand, is shown complexed to the metal center in such a way that a *trans*-configuration around the C=O bond results, with the aldehyde H-atom pointing away from the *quasi*axial Ph group (indicated by a bold-face bar). The TADDOLate is in the rear octands around the Ti-center. The observed nucleophilic addition from the *Si*-face of the aldehyde carbonyl C-atom could be realized in a tetragonal, pentagonal, or hexagonal Ti-ligand sphere. A search for Ti-alkoxide structures in the *Cambridge Crystallographic Data Base* (as of July 1991) revealed that with the Ti complexes found tetragonal coordination occurs more frequently than hexagonal, followed by the pentagonal one. A representative selection of these structures (*e.g.* exclusion of Cp derivatives) gave average O···O distances in the O–Ti–O substructures of 3.03, 2.90, and 3.20 Å, respectively. These numbers should be compared with the O···O distances given in *Fig. 8* and in the caption of *Fig. 10*.

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[32]) Compare the treatment of *Achiwa* and coworkers [59], who use the dihedral angle S–M–P–Ph (S = solvent or ligand, M = metal atom, P = phosphorus atom, Ph = C_6H_5 or other substituent on P) as a measure for the 'local chirality' in chiral bis-phosphine complexes. Rather confusingly, they use M and P (the CIP descriptors for the sense of chirality axes [60]) to indicate a negative or positive sign of this dihedral angle! Yet, another

previous section, and although we know [6b] that a single chiral TADDOL ligand is involved in the Et_2Zn addition studied by us[33]), there are too many uncertainties remaining which make it impossible to propose a mechanism for the reactions mediated by titanates of the chiral diols **1** and **2**. Especially in transition metal reactions, such as the one studied here, the coordination and the actual geometry of the metal center responsible for the rate-determining and the product-forming steps can often not be elucidated by structural studies; the most reactive intermediate may be present in only very small amounts (the *Curtin-Hammett* principle! [63]), and what is seen in the crystal or by NMR spectroscopy may be unreactive components of an equilibrium, a kind of stable storage stage [54] [55] [64][34]). What can be done is to fit the results of the reactions into as simple as possible a model, compatible with the structural studies, and to see whether a rule will arise which might stand the test of future experiments.

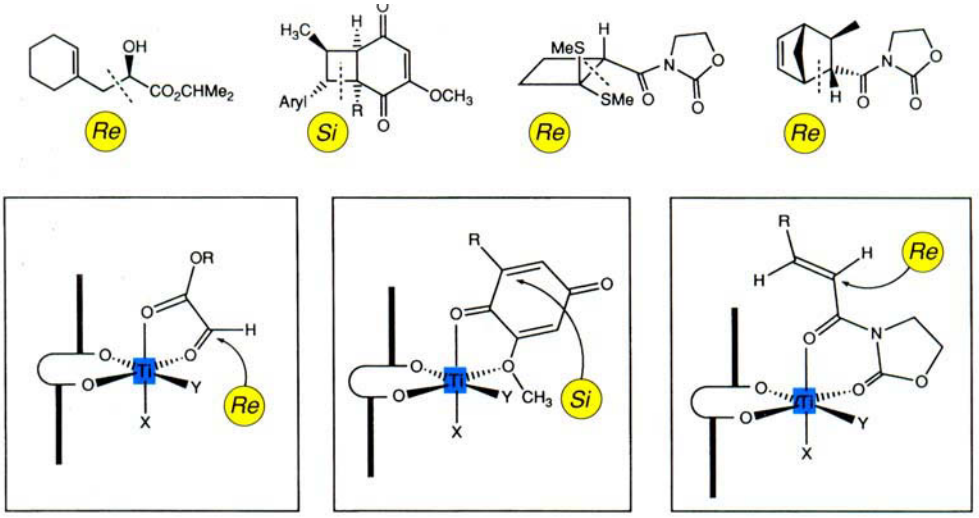

Fig. 12. *Products of an ene reaction and of [2 + 2] and [4 + 2] cycloadditions mediated or catalyzed by a complex of type* **11** *and the corresponding models for the Ti complexes of the bidentate electrophiles used. Top, left to right*: major product (72:28) from methylidenecyclohexane and isopropyl glyoxylate [23], cyclobutane derivative (*ca.* 95:5) from methylstyrene and methoxy-quinones [68], thioacetal of a cyclobutanonecarboxylic-acid derivative (94:6) from 3-acryloyl-1,3-oxazolidin-2-one and a ketene dithioketal [69], and a norbornenecarboxylic-acid derivative (> 95.5) obtained by *Diels-Alder* reactions with the corresponding *N*-crotonoylheterocycle [15] [16] [20]. *Bottom*: binding of the bidentate electrophiles, used for the above reactions, on a Ti with octahedral ligand sphere (X, Y represent additional ligands) such that the observed products would result by approach of nucleophiles in an octand not facing a *quasi*axial Ph group. The picture would be similar with a trigonal bipyramidal ligand sphere around Ti, see comments in the caption of *Fig. 11*. For discussions and mechanistic proposals concerning the *Diels-Alder* addition, see also [15] [24b].

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geometrical analysis was chosen by *Pavlov et al.* [49b] in their investigation on the relationship between the structure of Rh-phosphine complexes and the stereochemical course of dehydroacylamino-acid hydrogenation.

[33]) There is a perfect linear correlation between the enantiomeric purities of the TADDOL **11** and the product of Et_2Zn addition to PhCHO [6b] which proves that no more than one chiral ligand is involved in the step determining the enantioselectivity of the process.

[34]) For these reasons, *Halpern*, in a recent lecture, called the elucidation of the mechanism of transition-metal-catalyzed enantioselective hydrogenations a 'formidable task' [65].

Facts: All additions to aldehydes, stoichiometric or catalytic, involving cyclic titanates of type **11** (from (*R,R*)-tartrate), occur from the *Si*-face (*Fig. 11*, top). *Assumptions*: *i*) The aldehyde is activated by complexation to the Ti-center. *ii*) Reactions occur in and from the front octants around the metal center. *iii*) The cyclic titanate is in a conformation with *quasi*axial Ph groups on the upper right and lower left side, as viewed from the front octants. *Conclusion* (see *Fig. 11*, bottom): The observed *Si* nucleophilic addition would result in an intra- or intermolecular mono- or bimetallic transfer to the aldehyde complexed by titanium, as depicted.

For other types of reactions mediated by titanates **11**, we show in *Fig. 12* possible complexation geometries of the bidentate electrophiles, which would lead to the actually isolated products.

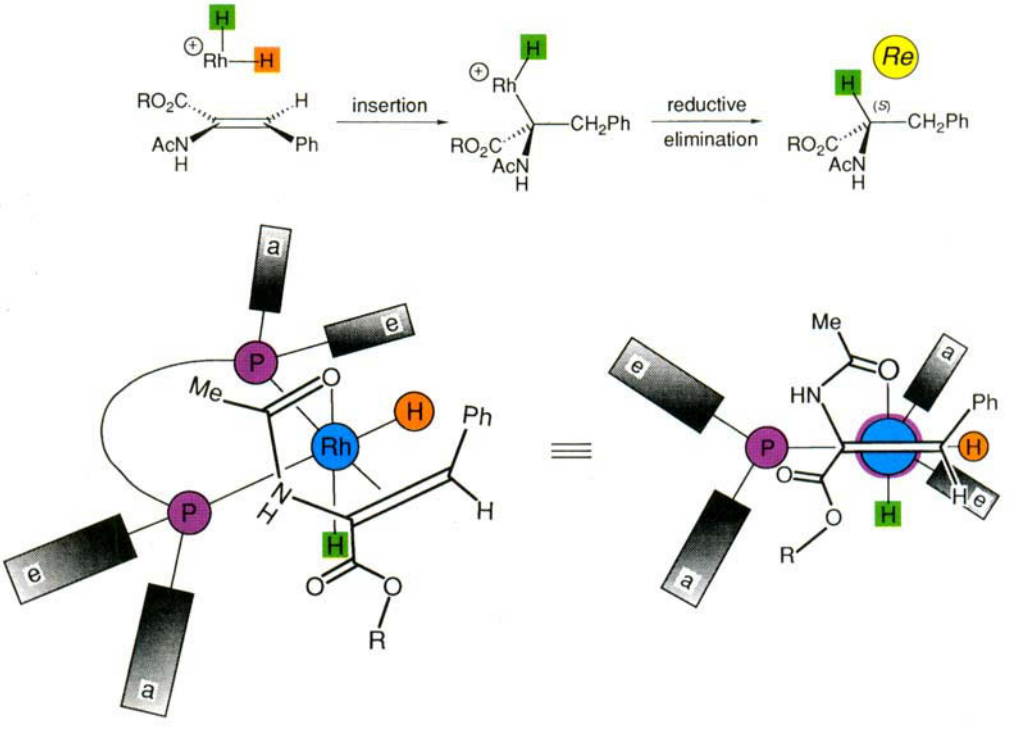
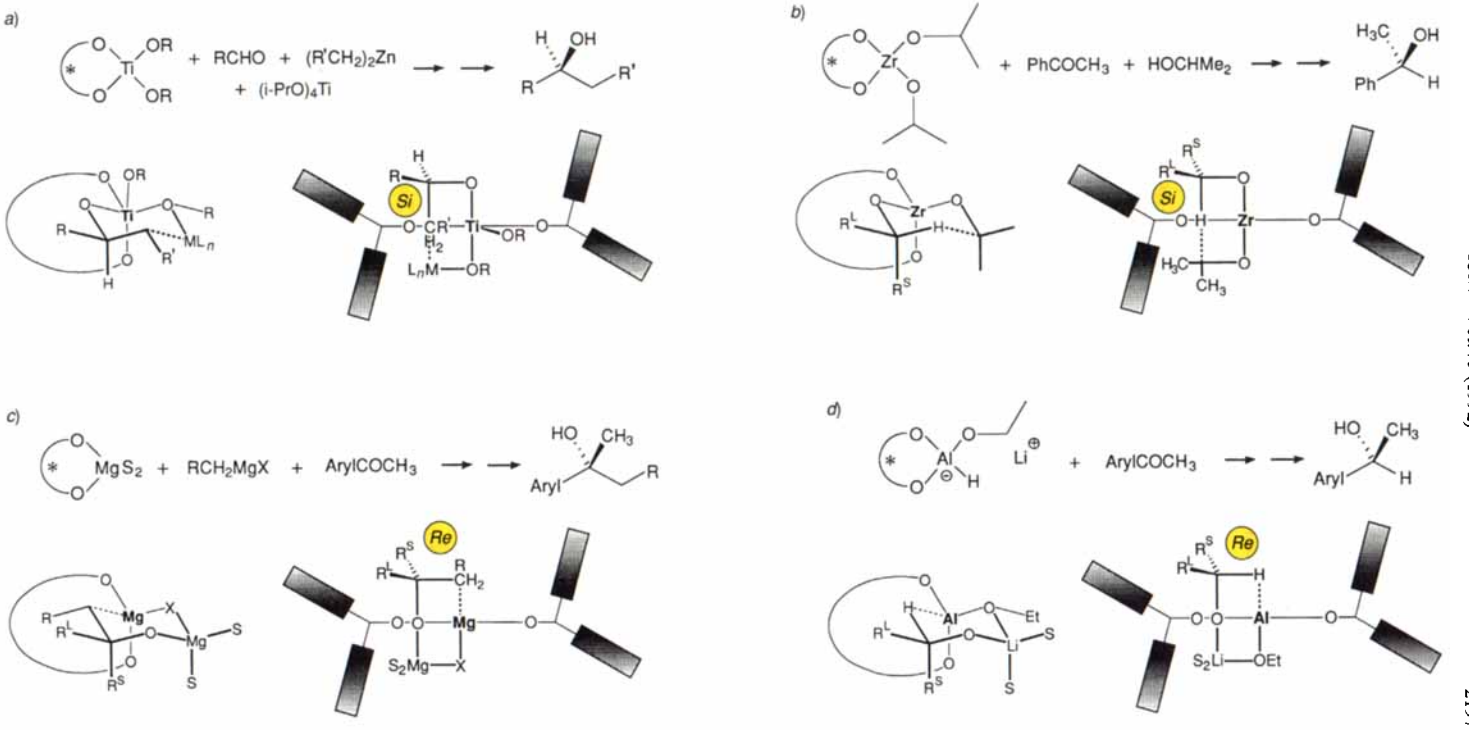


Fig. 13. *Hydrogen transfer to C(2) of aminocinnamates from the* Re*-face in catalytic hydrogenations by Rh complexes of C_2-symmetrical diphosphines.* The Rh complexes of (*S,S*)-DIOP, (*M*)-BINAP, (*R,R*)-CHIRAPHOS, (*R,R*)-DIPAMP, and (*R,R*)-BMPPP all lead to (*S*)-phenylalanine derivatives. For the structures of corresponding phosphine complexes, see bottom part of *Table 7*. The substrate is complexed in such a way that *a*) the *N*-acetyl ligand is located near the *quasi*equatorial substituent on the P-atom, *b*) the Ph group of the cinnamate resides in an unhindered position, *c*) the C=C bond inserts into the Rh–H bond which is '*trans*' to one of the P-atoms, and *d*) insertion occurs with a coplanar arrangement of the two double-bond C-atoms, the Rh- and the H-atoms. Except for the sense of chirality and the specification of the position of the substituents on the P-atoms, the general complex shown here is identical to the intermediate proposed by *Halpern et al.* (3^{min} in Fig. 2 and 9 of [64]). Unfortunately, in the same paper and in many other related publications, there are alternative presentations (with the H-atoms *trans* to the NCOMe ligand being transferred first, or with a perpendicular arrangement of the C=C bond with respect to the Rh–H bond prior to insertion!).

Scheme 6. *Common Picture of Four Different Complexes Resulting from Metal-TADDOLate-Mediated Reactions. a*) A bimetallic model for the reaction discussed in the present paper, also applicable to the other reactions shown in *Fig. 11. b*) The zirconate *Meerwein-Ponndorf-Verley* reduction outlined in *Scheme 5. c*) The addition of a *Grignard* reagent to a ketone in the presence of Mg alkoxide [70]. *d*) The reduction of a ketone by an aluminium hydride [71a]. The *quasi*axial and *quasi*equatorial Ph groups are indicated by the shaded bars. The former carbonyl C-atoms are located near the *quasi*equatorial Ph groups in all four cases. L (ligand) and S (solvent) represent neutral, and X anionic ligands. R^L and R^S are the larger and the smaller substituent on the carbonyl C-atom of the substrate, and the curve represents the TADDOLate ligand. For simplicity, tetrahedrally coordinated metal centers are drawn except in the case of the Ti derivative. The dotted lines indicate from which atom the nucleophilic transfer to the carbonyl C-atoms has occurred.



In *Scheme 6*, the bimetallic addition at a pentacoordinated Ti-center is sketched in 'the organic chemist's way' (*a*) and compared with the hydride transfer on an isopropoxy-Zr center (*b*; *cf. Scheme 5*), the addition of a *Grignard* reagent to an aryl ketone involving a Mg-TADDOLate [70] (*c*), and the TADDOLate aluminium hydride reduction of aryl ketones [71a] (*d*)[35] – the similarity may not be accidental or arbitrary!?

For the hydrogenation of *N*-acyldehydroamino acids an empirical *rule* connecting the λ- and δ-conformations of Rh-diphosphine complexes with the (*R*)- and (*S*)-configuration, respectively, of the products was proposed by *Pavlov et al.* [49b]. Using this relationship, the model pictured in *Fig. 13* results for hydrogenations with complexes of so-called λ sense of chirality; as with the TADDOL derivatives (*Scheme 6*), the space near a *quasi*equatorial Ph group is used for binding part of the substrate molecule.

Note Added in Proof. – After completion and submission of this paper, we obtained the coordinates of the crystal structures of two (*R,R*)-TADDOLateCpTi complexes by courtesy of Dr. *R. O. Duthaler* of *Ciba-Geigy AG*, Basel [9a] [14] [72]. The ClCpTi complexes with the **1a**- (= **11g**) and with the **1w**-derived TADDOLate ligands contain seven-ring titanate substructures very similar to those in our spiro-titanate, with *quasi*-axial Ph groups in the upper right and lower left positions of the projections chosen in *Fig. 10* (top) and in *Table 7*. Thus, the structures support the validity of inclusion of the *Si*-selective reactions observed with TADDOLateCpTi derivatives in *Fig. 11* and in the accompanying text.

For the preparation of several TADDOLs and other compounds we thank *T. Aeschbach*, *R. Dahinden*, *M. Jud*, *U. Lengweiler*, *S. Hintermann*, *U. Neidlein*, and *F. Schuler*. The experiments shown in *Scheme 2a/b* were carried out by *B. Schmidt* and *B. Weber*. For some help with the X-ray measurements, we wish to thank Dr. *V. Gramlich* and *P. Seiler*. *B. Lamatsch* assisted us in preparing illustrations for this paper. We are grateful to Dr. *M. Bailey* for the careful proof-reading of the final version of the manuscript. For the generous supply of tetrahydrofuran (*BASF AG*, D-Ludwigshafen), dimethyltartrate (*Chemische Fabrik Uetikon*, CH-Uetikon), tetraisopropyl titanate (*Hüls AG*, D-Troisdorf), and diethylzinc (*Schering AG*, D-Bergkamen), we thank the companies mentioned.

Experimental Part

General. Abbreviations: GP (general procedure); HV (high vacuum, 0.01–0.001 Torr).

Starting Materials and Reagents: Dimethyl tartrate (*Chemische Fabrik*, Uetikon) and Et_2Zn (*Schering AG*) were used as received without prior purification. A 2M stock soln. of Et_2Zn was prepared from 0.25 ml of Et_2Zn and 39.75 ml of toluene. $(i\text{-PrO})_4Ti$ (*Hüls AG*) and PhCHO were distilled. The TADDOLs **1a**, **i**[36])–**l**, **u**, **w**, **x**, **2b**, **d**, **f**, and **3** were prepared following reported procedures [4] [5]. The acetophenone-derived ligand **2l** was prepared in analogy to [16] and purified by flash chromatography (FC) [73], see also *Footnote 5*. All other commercially available chemicals used were of *p.a.* quality, or purified and dried according to standard methods.

Equipment: The alkyl addition reactions at low temp. were performed using a cryostat *Frigomix*® S (*B. Braun*). TLC: precoated silica gel *60* F_{254} plates (*Merck*); visualization by UV_{254} light, development using anisaldehdyde soln. (anisaldehyde (9.2 ml), AcOH (3.8 ml), EtOH (338 ml), H_2SO_4 (12.5 ml)) for aldehyde detection, or phosphomolybdic-acid soln. (phosphomolybdic acid (25 g), $Ce(SO_4)_2 \cdot 4\,H_2O$ (10 g), H_2SO_4 (60 ml), H_2O (940 ml)). Column chromatography: at normal pressure SiO_2 *60* (0.063–0.200 mm, *Fluka*). FC: SiO_2 *60* (0.040–0.063 mm, *Fluka*). Medium-pressure liquid chromatography (MPLC): *Büchi* system *B-680*. Distillation (of

[35]) See the analogous reaction using a binaphtholate Al hydride [71b].

[36]) The previously reported m.p. of **1i**·MeOH [4] has been revised: 171.5–172.5° (the compound undergoes a 'phase' change at *ca.* 110° due to loss of MeOH).

the isolated products): *Büchi GKR-50* or – for larger amounts (> 5 g) – an ETH-construction (bulb-to-bulb apparatuses). B.p. correspond to uncorrected air bath temp. M.p.: open glass capillaries, *Büchi 510* (*Tottoli* apparatus), 50° range *Anschütz* thermometer, uncorrected. n_D: *Abbe* refractometer (*Carl Zeiss*). $[\alpha]_D$: at r.t. (*ca.* 20°), *Perkin-Elmer 241* polarimeter (*p.a.* solvents, *Fluka*). Capillary gas chromatography (CGC): *HRGC* or *MEGA HRGC 5160* (*Carlo Erba*); column: *WCOT* Fused Silica, *CP-Cyclodextrin-β-2,3,6-M-19*, 50 m × 0.25 mm (*Chrompack*); injector temp. 230°, detector temp. 250°, heating rate: 80°/1° per min; pressure: 1.3 kPa H_2. IR: $CHCl_3$ solns. or KBr discs; *Perkin-Elmer 983* or *1600*; $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR spectra: *Varian Gemini 2000* (200 or 50 MHz, resp.) or *Bruker WM 300* (300 or 75 MHz, resp.); δ in ppm downfield of TMS ($\delta = 0$), J in Hz; unless stated otherwise, $CDCl_3$ solns. 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).

Preparation of TADDOLs **2a**, **i**, **j**, *and of* **4–6**, **8**, **9**. *Preparation of* **2a** *from (*R,R*)-Dimethyl Tartrate. (*R,R*)-Dimethyl* O,O*-Ethylidenetartrate*: In analogy to [74] 1.78 g (10 mmol) of (*R,R*)-dimethyl tartrate was suspended in 10 ml of Et_2O, and 10 mg (0.05 mmol) of red HgO, 0.2 ml (1.6 mmol) of $BF_3 \cdot Et_2O$, and 1.11 ml (12 mmol) of vinyl acetate were added at r.t. This mixture was heated, until a clear soln. was obtained and then stirred for 12 h at r.t. The mixture was poured into 10 ml of 10% $NaHCO_3$ soln. After phase separation, the aq. layer was extracted twice with Et_2O. The combined org. phases were washed with brine, dried ($MgSO_4$), and evaporated. The residue was distilled (b.p. 110–120°/0.05 Torr ([75]: 137°/16 Torr)): 1.85 g (90%) colorless oil. $[\alpha]_D^{r.t.} = -62.5$ ($c = 2.345$, $CHCl_3$). $n_D^{20} = 1.4418$ ([75]: $n_D^{27} = 1.4426$). IR ($CHCl_3$): 3032*m*, 3002*m*, 2957*m*, 1754*s*, 1439*s*, 1416*w*, 1352*w*, 1248*s*, 1151*s*, 1122*m*, 1091*m*, 1020*w*, 1010*w*, 988*w*, 869*m*. ^1H-NMR (300 MHz): 5.38 (*q*, $J = 4.9$, H–C(2)); 4.8 (*d*, $J = 4.0$, H–C(4) or H–C(5)); 4.71 (*d*, $J = 4.0$, H–C(4) or H–C(5)); 3.829 (*s*, CH_3O); 3.826 (*s*, CH_3O); 1.51 (*d*, $J = 4.9$, CH_3–C(2)). ^{13}C-NMR (75 MHz): 170.28, 169.62 ($COOCH_3$); 104.85 (C(2)); 77.30, 77.17 (C(4), C(5)); 52.86, 52.76 (CH_3O); 19.62 (CH_3–C(2)). MS (DEI): 205 (8), 203 (17), 190 (5), 189 (66), 162 (9), 161 (18), 160 (5), 146 (7), 145 (100), 129 (12), 117 (80), 116 (5), 113 (22), 103 (14), 101 (33), 99 (5), 89 (8), 86 (6), 85 (11), 73 (29), 71 (24), 69 (9), 59 (77), 45 (7), 43 (11), 29 (6), 28 (9). Anal. calc. for $C_8H_{12}O_6$ (204.18): C 47.06, H 5.92; found: C 46.79, H 6.18.

*(4*R*,5*R*)-2-Methyl-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol* (**2a**). Following the procedure described in [4], 5.00 g (24.5 mmol) of (*R,R*)-dimethyl *O,O*-ethylidenetartrate in 60 ml of THF were added to 105 mmol of PhMgBr (prepared from 2.56 g of Mg and 16.53 g of PhBr) in 60 ml of THF. The resulting yellow oil was dissolved in 5 ml Et_2O at r.t., and *ca.* 150 ml of pentane were added, giving a colorless precipitate. After filtration and drying under high vacuum, 10.2 g (92%) of **2a** was obtained. An anal. pure sample of **2a** was prepared by repeated recrystallization from Et_2O/pentane. M.p. 162–163°. $[\alpha]_D^{r.t.} = -47.4$ ($c = 1.87$, $CHCl_3$). IR (KBr): 3395*s*, 3091*w*, 3057*m*, 3012*m*, 2984*w*, 2915*w*, 2908*m*, 1952*w*, 1896*w*, 1811*w*, 1771*w*, 1621*w*, 1599*w*, 1582*w*, 1492*s*, 1447*s*, 1406*s*, 1353*m*, 1318*w*, 1299*w*, 1189*w*, 1150*s*, 1121*s*, 1103*s*, 1079*w*, 1040*s*, 1029*s*, 1008*s*, 913*w*, 892*m*, 884*m*, 848*w*, 788*m*, 758*s*, 728*w*, 698*s*, 647*m*, 624*m*, 586*w*, 570*m*. ^1H-NMR (300 MHz): 7.58–7.54 (*m*, 2 arom. H); 7.42–7.11 (*m*, 18 arom. H); 5.41 (*d*, $J = 4.9$, H–C(4) or H–C(5)); 4.92 (*d*, $J = 4.9$, H–C(4) or H–C(5)); 4.50 (*q*, $J = 4.8$, H–C(2)); 3.24 (*s*, OH); 1.92 (*s*, OH); 1.15 (*d*, $J = 4.8$, CH_3–C(2)). ^{13}C-NMR (75 MHz): 146.12, 144.48, 144.30, 143.24, 128.10, 127.78, 127.41, 127.28, 127.13, 127.00 (arom. C); 103.00 (C(2)); 81.46, 80.67, 78.70, 78.31 (2 Ph_2COH, C(4), C(5)); 20.14 (CH_3–C(2)). MS (DEI): 452 (0.02, M^+), 451 (0.01), 434 (0.01), 416 (0.03), 373 (0.08), 372 (0.09), 365 (0.02), 359 (0.03), 358 (0.12), 356 (0.04), 345 (0.05), 344 (0.08), 270 (0.13), 269 (0.53), 268 (0.13), 267 (0.15), 253 (0.15), 252 (0.56), 251 (0.18), 223 (5), 209 (8), 208 (51), 207 (60), 197 (4), 184 (14), 183 (100), 182 (6), 180 (5), 179 (10), 178 (5), 167 (4), 165 (4), 106 (6), 105 (68), 86 (8), 77 (27), 71 (6), 51 (4), 28 (8). Anal. calc. (1:1 clathrate with *N*-methylisopropylamine) for $C_{34}H_{39}O_4N$ (525.69): C 77.68, H 7.48, N 2.66; found: C 77.54, H 7.68, N 2.58.

A simple method to remove impurities was found in the formation of a 1:1 clathrate of **2a** with an amine: in a 25-ml round-bottomed flask 200 mg of the TADDOL was dissolved in a small amount of *N*-methylisopropylamine (*ca.* 2 ml). This soln. was saturated, by warming with a heat gun, to remove excess amine. After addition of 15 ml of hexane and filtration, the soln. was stored in a small flask stoppered with a perforated cap to allow slow evaporation. After several days, crystals of the clathrate were isolated as colorless prisms.

Preparation of **2i** *from (*R,R*)-Dimethyl Tartrate. (*R,R*)-Dimethyl* O,O*-(Naphth-1-yl)methylenetartrate.* Following the procedure described in [4], 145 ml (580 mmol) of $BF_3 \cdot Et_2O$ was added to 103.3 g (580 mmol) of (*R,R*)-dimethyl tartrate and 95 ml (690 mmol) of 1-naphthaldehyde in 1.1 l of AcOEt at 0°. After stirring for 20 h at r.t. and workup, 202 g of crude product, containing excess naphthalene-1-carbaldehyde and traces of solvent, were obtained. This material was used without further purification in the following reaction. For anal. purposes a sample was recrystallized twice from hexane. M.p. 64–65°. $[\alpha]_D^{r.t.} = -9.2$ ($c = 1.02$, CH_2Cl_2). IR (KBr): 3450*m* (br.), 3040*w*, 3000*w*, 2950*m*, 2900*w*, 2850*w*, 1760*s*, 1735*s*, 1465*m*, 1440*m*, 1430*m*, 1420*w*, 1395*w*, 1375*w*, 1350*m*, 1340*m*, 1320*m*, 1290*s*, 1240*s*, 1215*s*, 1175*m*, 1110*s*, 1080*s*, 1020*w*, 1000*s*, 980*w*, 965*s*, 930*w*, 915*w*, 885*w*, 870*w*, 860*w*, 810*w*,

785*s*, 770*m*, 560*m*. ^{1}H-NMR (300 MHz): 8.22 (*d*, *J* = 8.9, 1 arom. H); 7.96 (*d*, *J* = 7.1, 1 arom. H); 7.90–7.86 (*m*, 2 arom. H); 7.59–7.47 (*m*, 3 arom. H); 6.83 (*s*, H–C(2)); 5.08 (*d*, *J* = 4.0, H–C(4) or H–C(5)); 4.97 (*d*, *J* = 4.0, H–C(5) or H–C(4)); 3.92 (*s*, CH_3); 3.79 (*s*, CH_3). ^{13}C-NMR (75 MHz): 170.27, 169.33 ($COOCH_3$); 133.63, 130.94, 130.61, 130.23, 128.58, 126.64, 125.89, 125.08, 124.37, 123.62 (arom. C); 104.66 (C(2)); 77.40, 77.27 (C(4), C(5)); 52.86 (CH_3). MS: 316 (23, M^+), 315 (7), 257 (25), 172 (73), 169 (7), 156 (24), 155 (70), 141 (36), 139 (12), 128 (100), 127 (32), 59 (7), 32 (8), 28 (40), 18 (15), 15 (11). Anal. calc. for $C_{17}H_{16}O_6$ (316.31): C 64.55, H 5.10; found: C 64.49, H 5.13.

*(4*R*,5*R*)-2-(Naphth-1-yl)-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol* (**2i**). According to [4], 23.75 g (78 mmol) of (*R*,*R*)-dimethyl *O*,*O*-(naphth-1-yl)methylenetartrate in 200 ml of THF was added to 330 mmol of PhMgBr (prepared from 8.26 g of Mg an 51.9 g of PhBr) in 300 ml of THF. After workup, the crude product (45.4 g) was dissolved in 130 ml of toluene by heating at reflux. To the clear soln. was added 130 ml of hexane. A colorless solid precipitated on cooling and stirring. After further stirring for 12 h at r.t., filtration, washing twice with 50-ml portions of toluene/hexane 1:1, and drying under high vacuum, 26 g (61%) of **2i** were obtained. M.p. 229.4–231.5°. $[\alpha]_D^{r.t.} = +25.2$ (*c* = 1.00, $CHCl_3$). IR (KBr): 3650*s*, 3420*m* (br.), 3060*m*, 3020*m*, 2960*w*, 2895*w*, 1950*w*, 1890*w*, 1800*w*, 1750*w*, 1595*w*, 1510*w*, 1490*m*, 1445*s*, 1390*w*, 1370*w*, 1340*m*, 1320*m*, 1230*m*, 1170*s*, 1115*s*, 1070*m*, 1045*m*, 1030*m*, 1020*m*, 1000*m*, 990*m*, 940*m*, 890*m*, 870*w*, 810*m*, 790*m*, 770*m*, 760*m*, 750*s*, 695*s*, 670*m*, 635*m*, 615*m*, 550*w*, 500*w*, 450*w*. ^{1}H-NMR (300 MHz): 7.85–7.76 (*m*, 3 arom. H); 7.58–7.10 (*m*, 24 arom. H); 5.96 (*s*, H–C(2)); 5.5 (*d*, *J* = 4.6, H–C(5) or H–C(4)); 5.24 (*d*, *J* = 4.6, H–C(4) or H–C(5)); 3.24 (*s*, OH); 2.06 (*s*, OH). ^{13}C-NMR: 145.86, 144.76, 143.92, 143.33, 133.59, 132.79, 130.81, 129.61, 128.40, 128.29, 128.19, 128.06, 127.80, 127.71, 127.59, 127.38, 127.14, 127.00, 126.72, 126.10, 125.66, 125.08, 124.01, 123.37 (arom. C); 103.07 (C(2)); 81.74 (C(4) or C(5)); 81.15 (C(5) or C(4)); 79.02 (Ph_2COH); 78.82 (Ph_2COH). MS: 564 (0.5), 382 (1), 269 (1), 225 (4), 208 (39), 207 (36), 183 (73), 157 (62), 141 (10), 128 (14), 105 (100), 77 (29). Anal. calc. for $C_{39}H_{32}O_4$ (564.68): C 82.95, H 5.71; found: C 82.68, H 6.01.

Preparation of **2j** *from (*R,R*)-Dimethyl Tartrate. (*R,R*)-Dimethyl O,O-(Naphth-2-yl)methylenetartrate.* Following the procedure described in [4], to 4.75 g (27 mmol) of (*R*,*R*)-dimethyl tartrate and 5.00 g (32 mmol) of naphthalene-2-carbaldehyde in 30 ml of AcOEt at 0° was added 3.4 ml (27 mmol) of $BF_3 \cdot Et_2O$. After stirring for 3 h at r.t. and workup, a ruddy solid was isolated. This crude product was stirred with 100 ml of pentane for 3 h at r.t. to afford 4.82 g (57%) of colorless crystals. For anal. purposes, a small portion was distilled (200–210°/0.05 Torr) to furnish a highly viscous, colorless oil, which began to crystallize after a short period. M.p. 48.5–49.0°. $[\alpha]_D^{r.t.} = +1.4$ (*c* = 1.59, $CHCl_3$). IR (KBr): 3056*w*, 3010*w*, 2955*m*, 2906*w*, 2843*w*, 1760*s*, 1726*s*, 1634*w*, 1600*w*, 1508*w*, 1473*w*, 1449*m*, 1434*s*, 1410*m*, 1379*w*, 1341*m*, 1309*m*, 1290*s*, 1242*s*, 1217*s*, 1179*s*, 1138*s*, 1107*s*, 1018*m*, 989*m*, 976*m*, 901*m*, 866*m*, 838*m*, 798*w*, 751*m*, 704*w*, 482*m*, 385*w*, 351*w*. ^{1}H-NMR (300 MHz): 8.03 (*s*, 1 arom. H); 7.90–7.83 (*m*, 3 arom. H); 7.69 (*dd*, *J* = 8.4, 1.8, 1 arom. H); 7.54–7.47 (*m*, 2 arom. H); 6.31 (*s*, H–C(2)); 5.04 (*d*, *J* = 4.2, H–C(4) or H–C(5)); 4.92 (*d*, *J* = 4.0, H–C(4) or H–C(5)); 3.89 (*s*, CH_3O); 3.83 (*s*, CH_3O). ^{13}C-NMR (75 MHz): 170.11, 169.46 ($COOCH_3$); 134.24, 132.82, 132.75, 128.48, 128.42, 127.80, 127.38, 126.80, 126.30, 123.96 (arom. C); 106.99 (C(2)); 77.56, 77.33 (C(4), C(5)); 52.68 (CH_3O). MS (DEI): 316 (21, M^+), 315 (9), 257 (27), 197 (1), 173 (11), 172 (88), 171 (14), 169 (6), 157 (5), 156 (38), 155 (100), 142 (7), 141 (60), 140 (8), 139 (19), 129 (14), 128 (89), 127 (64), 126 (10), 115 (9), 113 (6), 102 (4), 101 (8), 77 (8), 75 (5), 59 (20), 45 (8), 29 (10), 18 (24), 17 (7), 15 (29). Anal. calc. for $C_{17}H_{16}O_6$ (316.31): C 64.55, H 5.10; found: C 64.25, H 5.26.

*(4*R*,5*R*)-2-(Naphth-2-yl)-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol* (**2j**). According to [4], 4.00 g (12.6 mmol) of (*R*,*R*)-dimethyl *O*,*O*-(naphth-2-yl)methylenetartrate in 25 ml of THF was added to 54 mmol of PhMgBr (prepared from 1.31 g of Mg and 8.44 g of PhBr) in 30 ml of THF. After workup, the crude product was dissolved in *ca.* 3 ml of piperidine at r.t. Hexane was added to the clear yellow soln. while stirring, until it became slightly cloudy (*ca.* 100 ml). After a few min, crystals of the 1:1 amine clathrate precipitated: 4.49 g (55%) of **2j**·piperidine. After evaporation of the mother liquor, the residue was treated again as described above to afford another 1.62 g (20%) of the clathrate.

To obtain amine-free TADDOL **2j** a sample was dissolved in Et_2O, the soln. extracted 3 times with 0.6N H_2SO_4, washed with brine, and dried ($MgSO_4$). After evaporation of the solvent, a colorless foam was isolated. Drying for several d (50°/0.05 Torr) was necessary to give solvent free **2j**. M.p. 109.0–110.0°. $[\alpha]_D^{r.t.} = +70.9$ (*c* = 0.85, $CHCl_3$). IR (KBr): 3555*m*, 3410*m* (br.), 3084*w*, 3059*m*, 3026*m*, 2898*w*, 1951*w*, 1896*w*, 1807*w*, 1771*w*, 1627*w*, 1600*w*, 1581*w*, 1509*w*, 1493*s*, 1474*w*, 1448*s*, 1407*m*, 1376*w*, 1340*m*, 1299*w*, 1271*w*, 1209*w*, 1178*s*, 1128*s*, 1090*s*, 1051*m*, 1033*m*, 1003*s*, 951*w*, 920*w*, 895*m*, 860*m*, 821*m*, 788*w*, 751*s*, 730*w*, 700*s*, 671*w*, 647*w*, 612*w*, 568*w*, 479*m*. ^{1}H-NMR (300 MHz): 7.80–7.70 (*m*, 3 arom. H); 7.60–7.50 (*m*, 4 arom. H); 7.48–7.15 (*m*, 20 arom. H); 5.35 (*s*, H–C(2)); 5.36 (*d*, *J* = 4.9, H–C(4) or H–C(5)); 5.20 (*d*, *J* = 5.0, H–C(4) or H–C(5)); 3.6–1.8 (br., 2 OH). ^{13}C-NMR (75 MHz): 146.09, 144.31, 144.25, 143.08, 134.40, 133.89, 132.75, 128.20, 127.94, 127.74, 127.57, 127.40, 127.28, 127.07, 126.89, 126.51, 126.44, 126.15, 124.04 (arom. C); 105.24 (C(2)); 81.65, 80.96, 78.73, 78.56

(2 Ph_2COH, C(4), C(5)). MS (1:1 clathrate with piperidine; DEI): 564 (0.05, M^+), 383 (0.05), 382 (0.16), 381 (0.06), 358 (0.10), 335 (0.05), 269 (0.16), 226 (0.10), 225 (0.20), 209 (0.40), 208 (1.82), 207 (1.80), 184 (0.53), 183 (3.70), 182 (1.14), 157 (3.96), 156 (1.14), 155 (1.25), 141 (0.68), 129 (0.56), 128 (0.50), 127 (1.21), 106 (0.65), 105 (7.94), 86 (4.05, piperidine), 85 (55, piperidine), 84 (100, piperidine), 70 (11, piperidine), 57 (35, piperidine), 56 (40, piperidine), 55 (10, piperidine), 44 (30, piperidine), 43 (22, piperidine), 42 (24, piperidine), 41 (15, piperidine), 30 (26, piperidine), 29 (30, piperidine), 28 (39, piperidine), 27 (14, piperidine), 18 (7), 15 (4). Anal. calc. for $C_{44}H_{43}O_4N$ (649.83) (1:1 clathrate with piperidine): C 81.33, H 6.67, N 2.16; found: C 81.10, H 6.95, N 2.17.

*Preparation of (4*R*,5*R*)-α,α,α′,α′-Tetramethyl-2-phenyl-1,3-dioxolane-4,5-dimethanol* (**4**). Following the procedure in [4], 131.3 g (0.49 mol) of (*R,R*)-dimethyl *O,O*-benzylidenetartrate (prepared according to the procedure in [4]) in 2.5 l of Et_2O were added to 2.45 mol of MeMgI (prepared from 60 g of Mg and 348 g of MeI) in 0.25 l of Et_2O. After workup, the crude product was recrystallized from 1.85 l of hexane and 0.085 l of AcOEt to yield 104 g (79%) of slightly yellow **4**. To obtain anal. pure **4**, a small portion was recrystallized from hexane and dried for 20 h (40°/0.05 Torr). M.p. 106°. $[\alpha]_D^{r.t.} = -13.2$ ($c = 1.09$, CH_2Cl_2). IR (KBr): 3280*s* (br.), 2980*s*, 2930*m*, 2880*m*, 1480*m*, 1460*m*, 1415*m*, 1400*m*, 1385*m*, 1370*m*, 1310*m*, 1295*w*, 1225*m*, 1190*m*, 1180*m*, 1160*m*, 1145*m*, 1090*s*, 1070*s*, 1050*s*, 1035*s*, 1025*m*, 1010*m*, 1000*m*, 980*m*, 970*m*, 930*m*, 910*m*, 865*w*, 795*w*, 770*m*, 725*m*, 700*s*, 650*m*, 640*m*, 570*m*, 445*m*. ^{1}H-NMR (300 MHz): 7.51–7.47 (*m*, 2 arom. H); 7.41–7.37 (*m*, 3 arom. H); 6.05 (*s*, H–C(2)); 4.12 (*d*, $J = 5.5$, H–C(4) or H–C(5)); 4.03 (*d*, $J = 5.4$, H–C(5) or H–C(**4**)); 2.57 (br. *s*, OH); 2.44 (br. *s*, OH); 1.37 (*s*, CH_3); 1.34 (*s*, CH_3); 1.30 (*s*, 2 CH_3). ^{13}C-NMR (75 MHz): 137.80, 129.48, 128.51, 126.64 (arom. C); 104.56 (C(2)); 83.93, 83.65 (C(4), C(5)); 72.54, 71.08 (Me_2COH); 28.06, 27.23, 25.71, 25.44 (CH_3). MS: 267 (7, $[M + 1]^+$), 266 (2, M^+), 265 (7, $[M - 1]^+$), 208 (5), 190 (8), 161 (29), 150 (13), 149 (9), 145 (10), 143 (43), 121 (7), 107 (100), 105 (27), 102 (39), 91 (22), 87 (40), 85 (17), 84 (52), 83 (40), 79 (25), 77 (19), 71 (33), 59 (78), 55 (10), 43 (53), 41 (12), 31 (15), 29 (11). Anal. calc. for $C_{15}H_{22}O$ (266.34): C 67.65, H 8.33; found: C 67.69, H 8.39.

*Preparation and Separation of (4′*R*,5′*R*)-1-[5′-(1″-Benzyl-1″-hydroxy-2″-phenylethyl)-2,2′-dimethyl-1,3-dioxolan-4′-yl]-2-phenylethanone* (**5**) *and (4*R*,5*R*)-α,α,α′,α′-Tetrabenzyl-2,2-dimethyl-1,3-dioxolane-4,5-dimethanol* (**6**). According to [4], 5.5 g (25 mmol) of (*R,R*)-dimethyl *O,O*-(2-propylidene)tartrate (for preparation, see [4]) in 50 ml of THF were added to 304 mmol of $PhCH_2MgBr$ (prepared from 10 g of Mg and 36 ml of $PhCH_2Br$) in 600 ml of THF. After workup, 19.4 g of a yellow oil was isolated. This crude product was chromatographed (50 × 3 cm, 120 g SiO_2), first with 1.5 l of pentane (5.7 g of by-products, rejected), then with 2.6 l of toluene. The first 90 ml (3 portions, each of 30 ml) contained 1.75 g, consisting mainly of **6**, the next 120 ml (4 portions, each of 30 ml) 1.87 g of a *ca.* 1:1 mixture **5**/**6**. The following 900 ml (10 portions, each of 30 ml, 3 portions, each of 200 ml) contained 4.81 g of enriched **5**. The last 2 fractions (2 × 750 ml) furnished 2.12 g of almost pure **5**.

To obtain pure **6**, the isolated 1.75 g and 1.87 g were purified separately by FC (50 × 5.5 cm, 200 g SiO_2, 0.2 bar, toluene) to afford 1.25 g and 0.98 g, respectively, of yellow oils. These portions were combined and heated *in vacuo* (180°/0.02 Torr) to remove low boiling components: 1.74 g (13%) of **6** resulted, as a yellow glass. $[\alpha]_D^{r.t.} = +70.7$ ($c = 1.00$, $CHCl_3$). IR ($CHCl_3$): 3530*w*, 3400*m*, 3080*w*, 3060*m*, 3030*m*, 3010*m*, 2980*m*, 2930*m*, 1600*m*, 1495*s*, 1455*s*, 1380*m*, 1370*m*, 1235*s*, 1175*m*, 1090*m*, 1070*s*, 1030*m*, 925*m*, 930*m*. ^{1}H-NMR (300 MHz): 7.27–7.10 (*m*, 20 arom. H); 3.67 (*s*, H–C(4), H–C(5)); 3.13 (*s*, 2 OH); 2.84 (*d*, $J = 13.7$, 2 H, *H*–CHPh); 2.75 (*d*, $J = 13.8$, 2 H, *H*–CHPh)[37]); 2.70 (*d*, $J = 13.9$, 2 H, *H*–CHPh)[37]); 2.46 (*d*, $J = 13.7$, 2 H, *H*–CHPh); 1.43 (*s*, 2 CH_3). ^{13}C-NMR (75 MHz): 136.99, 136.31, 130.88, 127.93, 126.54, 126.34 (arom. C); 106.85 (C(2)); 77.22 (C–OH); 72.96 (C(4), C(5)); 43.51, 40.98 ($PhCH_2$); 23.50 (CH_3). Anal. calc. for $C_{35}H_{38}O_4$ (522.68): C 80.43, H 7.33; found: C 80.14, H 7.47.

To obtain anal. pure **5**, the 2.12 g isolated after chromatography were also heated under vacuum (180°/0.01 Torr). This procedure gave 1.74 g (17%) of **5** as a yellow glass. $[\alpha]_D^{r.t.} = +51.8$ ($c = 1.00$, $CHCl_3$). IR ($CHCl_3$): 3560*w*, 3440*w*, 3080*m*, 3060*m*, 3010*s*, 2970*m*, 1720*s*, 1600*m*, 1495*s*, 1455*s*, 1385*s*, 1375*m*, 1160*m*, 1080*s*, 1040*m*, 840*m*. ^{1}H-NMR (300 MHz): 7.30–7.07 (*m*, 15 arom. H); 4.47 (*d*, $J = 6.5$, OC*H*CO); 4.11 (*d*, $J = 6.4$, OC*H*COH); 3.87 (*s*, CCOCH_2Ph); 2.93 (*s*, HOCCH_2Ph)[38]); 2.74 (*d*, $J = 13.9$, HOCC*H*HPh); 2.64 (*d*, $J = 13.9$, HOCCH*H*Ph); 2.35 (*s*, OH); 1.59 (*s*, CH_3); 1.30 (*s*, CH_3). ^{13}C-NMR (75 MHz): 209.02 (C=O); 136.83, 136.28, 133.17, 131.00, 130.92, 129.68, 128.55, 128.11, 127.93, 127.02, 126.57, 126.50 (arom. C); 110.47 (O*C*Me_2O); 80.25, 79.19 (O*C*H–*C*HO); 73.58 (Bn_2C); 45.90, 42.18, 41.85 (CH_2); 26.79, 25.54 (CH_3). Anal. calc. for $C_{28}H_{30}O_4$ (430.54): C 78.11, H 7.02; found: C 78.26, H 7.09.

*Preparation of (1*R*,7*R*,8*S*)-8-Hydroxy-8,10,10-triphenyl-2,4,6,9-tetraoxabicyclo[5.3.0]decane* (**8**). As described in [4], 11.0 g (50 mmol) of *(*R*,*R*)-dimethyl 1,3,6-trioxepane-4,5-dicarboxylate* (**7**) (for preparation, see [4])

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[37]) Extremely strong *roof effect*! [76].

[38]) A set of 2*d* would be expected. It seems that they collapse due to an extremely strong *roof effect* [76], and only an *s*-type signal can be observed.

in 110 ml of THF was added to 220 mmol of PhMgBr (prepared from 5.4 g of Mg and 31.4 g of PhBr) in 55 ml of THF. After workup, 24.4 g of a yellow oil was isolated. The product was purified by chromatography (50 × 5 cm, 450 g SiO_2), first with 7.5 l toluene to remove the non-polar by-products, followed by 0.5 l Et_2O to elute **8**. After removal of the solvent, 16.8 g of a viscous yellow oil remained. This material was dissolved in 35 ml of pentane/Et_2O 1:1. When the soln. was heated under reflux, a colorless precipitate formed: 9.97 g (51%) of **8**. M.p. 129.5–131.0°. $[\alpha]_D^{r.t.} = -76.4$ ($c = 1.00$, $CHCl_3$). IR ($CHCl_3$): 3579*m*, 3063*w*, 3007*w*, 2900*w*, 1683*w*, 1601*w*, 1494*s*, 1448*s*, 1381*m*, 1266*m*, 1149*s*, 1041*s*, 981*s*, 952*s*, 838*w*, 614*m*. ^{1}H-NMR (300 MHz): 7.81–7.77 (*m*, 2 arom. H); 7.58–7.54 (*m*, 2 arom. H); 7.46–7.16 (*m*, 11 arom. H); 5.25 (*d*, $J = 9.1$, OCH); 5.19 (*d*, $J = 5.9$, 1 H, CH_2); 5.12 (*d*, $J = 6.2$, 1 H, CH_2); 5.03 (*d*, $J = 6.3$, 1 H, CH_2); 4.92 (*d*, $J = 5.9$, 1 H, CH_2); 4.46 (*dd*, $J = 9.1$, 0.7, OCH); 3.04 (*s*, OH). ^{13}C-NMR (75 MHz): 146.69, 141.82, 141.20, 128.87, 128.55, 128.16, 127.67, 127.54, 127.32, 127.19, 125.86, 125.50 (arom. C); 99.54 (Ph*C*OH); 93.98 (CH_2); 86.37 (CH); 84.48 (Ph_2CO); 84.39 (CH). MS (DEI): 373 (1), 343 (1), 330 (10), 312 (2), 283 (1), 265 (3), 238 (6), 207 (81), 183 (98), 165 (25), 147 (55), 131 (11), 105 (100), 91 (32), 77 (83), 51 (39), 29 (17). Anal. calc. for $C_{24}H_{22}O_5$ (390.44): C 73.83, H 5.68; found: C 73.68, H 5.67.

*Preparation of (6*R,*7*R*)-α,α,α′,α′-Tetraphenyl-1,3,5-trioxepane-6,7-dimethanol* (**9**). By analogy with [4], 11.0 g (50 mmol) of **7** in 110 ml of THF was added to 400 mmol of PhMgBr (prepared from 10.7 g of Mg and 62.8 g of PhBr) in 250 ml of THF. After workup, 35.9 g of an orange oil was isolated. This crude product was adsorbed on 50 g of SiO_2 and loaded onto 240 g of SiO_2 in a 50 × 5.5 cm column. Elution with 4 l of pentane, followed by 0.5 l of CH_2Cl_2, led to 3.3 g of unidentified material, which was immediately rejected. Further elution with 1.8 l of CH_2Cl_2, followed by 100 ml of Et_2O, yielded 25.8 g of a mixture containing **9**, which was rechromatographed (50 × 5.5 cm, 300 g SiO_2) with 2.5 l of toluene. The first litre was rejected, and the remaining 1.5 l were evaporated to afford 6.4 g of enriched **9**, which was purified by FC (55 × 9 cm, 700 g SiO_2, 0.2 bar, CH_2Cl_2). From the 187 portions collected (25 ml each), fractions *74–109* were combined and evaporated to give 2.3 g (9%) of a brownish solid. To obtain anal. pure **9**, this sample was recrystallized from 30 ml of hexane/2 ml of AcOEt, affording 0.85 g (3.5%) of colorless crystals. M.p. 134.2–135.0°. $[\alpha]_D^{r.t.} = +106.9$ ($c = 1.00$, $CHCl_3$). IR ($CHCl_3$): 3480*s*, 3090*w*, 3060*m*, 3010*m*, 2910*m*, 1600*w*, 1440*m*, 1400*s*, 1390*m*, 1360*m*, 1265*m*, 1190*m*, 1170*s*, 1150*s*, 1130*s*, 1060*m*, 1030*m*, 1020*m*, 1000*m*, 990*m*, 960*m*, 910*m*. ^{1}H-NMR (300 MHz): 7.58–7.54 (*m*, 4 arom. H); 7.33–7.04 (*m*, 16 arom. H); 5.08 (*d*, $J = 6.2$, 2 H, OC*H*HO); 4.89 (*s*, H–C(6), H–C(7)); 4.78 (*d*, $J = 6.2$, 2 H, OCH*H*O); 4.76 (*s*, 2 OH). ^{13}C-NMR (75 MHz): 145.18, 143.90, 128.38, 128.06, 126.93, 126.36, 125.99 (arom. C); 91.24 (CH_2); 81.15 (Ph_2COH); 80.97 (C(6), C(7)). Anal. calc. for $C_{30}H_{28}O_5$ (468.55): C 76.90, H 6.02, O 17.07; found: C 76.85, H 6.04, O 17.11.

An alternative method for isolation and purification has been employed. From the isolated crude product, 10 g were purified by MPLC (46 × 7 cm, SiO_2 *Li-Chromprep Si 60*, 25–40 μm, 37 bar, gradient elution with hexane/0–30% Et_2O during 3.5 h, followed by isocratic elution with hexane/30% Et_2O for 1 h). The product containing fractions (R_f 0.55, hexane/Et_2O 1:1) were combined and evaporated, giving 685 mg (7%) of **9** as a yellow foam. Recrystallization from hexane/toluene 10:1 yielded 386 mg (3.8%) of pure **9** as colorless needles. The anal. data from this sample were identical to those given above.

Crystal Growth of Clathrates with **2b**, **2f**, *and* **17** *as Host Compounds.* **2b**·N-*Methylisopropylamine*. To obtain the clathrate of **2b** and *N*-methylisopropylamine, 200 mg of **2b** (for preparation see [3] [4]) were treated in the same way as described for the purification of **2a** to give colorless, transparent, square-faced prisms of 1:1 stoichiometry. ^{1}H-NMR (300 MHz): 7.57–7.53 (*m*, 2 arom. H); 7.46–7.38 (*m*, 6 arom. H); 7.32–7.12 (*m*, 12 arom. H); 4.91 (*d*, $J = 6.1$, H–C(4) or H–C(5)); 4.75 (*d*, $J = 6.1$, H–C(4) or H–C(5)); 3.69 (*s*, H–C(2)); 2.95–2.30 (*s*, 2 OH, NH); 2.60 (*sept.*, $J = 6.3$, 1 H, $(CH_3)_2CHN$); 2.25 (*s*, CH_3N); 1.00 (*d*, $J = 6.38$, $(CH_3)_2CHN$); 0.73 (*s*, *t*-Bu). ^{13}C-NMR (75 MHz): 147.26, 145.28, 144.25, 143.05, 128.55, 128.25, 127.90, 127.54, 127.46, 127.35, 127.17, 127.09, 126.96 (arom. C); 109.46 (C(2)); 81.62, 79.96, 77.82, 76.60 (2 Ph_2COH, C(4), C(5)); 50.01 (CH–N); 33.71 (C, *t*-Bu); 33.31 (CH_3–N); 24.34 (3 CH_3, *t*-Bu); 22.17 ($(CH_3)_2CHN$). Anal. calc. for $C_{37}H_{45}O_4N$ (567.77) (1:1 clathrate with (i-Pr)MeNH): C 78.27, H 7.99, N 2.47; found: C 78.24, H 7.85, N 2.55.

2f·*Piperidine*. In a round bottomed flask, 200 mg of **2f** (for preparation, see [3] [4]) was heated under reflux in *ca.* 15 ml of hexane. To this suspension was added piperidine, dropwise, until a clear soln. resulted (*ca.* 0.5 ml). After cooling to r.t. and maintaining this temp. for several h, bunches of colorless, rod-shaped, crystals formed. ^{1}H-NMR (300 MHz): 7.60–7.50 (*m*, 4 arom. H); 7.48–7.12 (*m*, 21 arom. H); 5.18 (*d*, $J = 5.5$, H–C(4) or H–C(5)); 5.14 (*s*, H–C(2)); 5.04 (*d*, $J = 5.5$, H–C(4) or H–C(5)); 3.25–2.40 (br., 2 OH, NH); 2.65–2.61 (*m*, 2 CH_2N); 1.55–1.41 (*m*, 3 CH_2, piperidine). ^{13}C-NMR (75 MHz): 146.65, 145.18, 143.86, 143.40, 136.99, 129.31, 128.48, 128.28, 128.12, 127.98, 127.74, 127.48, 127.32, 127.14, 127.02 (arom. C); 104.40 (C(2)); 82.38, 81.02, 77.92, 77.57 (2 Ph_2COH, C(4), C(5)); 46.54 (CH_2N); 26.74, 24.73 (CH_2, piperidine). Anal. calc. for $C_{40}H_{41}O_4N$ (599.77) (1:1 clathrate with piperidine): C 80.10, H 6.89, N 2.34; found: C 79.83, H 7.02, N 2.25.

17·CCl_4. In a round-bottomed flask, 200 mg of **17** (which was prepared according to the procedure in [13]) was dissolved by heating in a small amount of CCl_4 (*ca.* 20 ml). The solvent was partially removed, until striation could be observed. The flask was stoppered with a perforated cap, allowing slow evaporation. After 2 d, colorless prisms of the 1:1 clathrate were isolated. Anal. calc. for $C_{44}H_{34}O_4Cl_4$ (648.54) (1:1 clathrate with CCl_4): C 62.98, H 5.28; found: C 62.98, H 5.41.

Preparation of the Chiral Titanates **11–15** *and Their Use as Catalysts in the Addition of* Et_2Zn *to Aldehydes. Preparation of* **11–15**. *General Procedure Yielding Di(isopropyl)titanates (GP I).* To 0.25–6 mmol of diol **1–4**, **6** or **9**, under Ar in a 50 ml two-necked, round-bottomed flask equipped with a three-way stopcock and a serum cap, were added 15 ml of toluene and 0.25–6 mmol of (i-PrO)$_4$Ti. The resulting yellow soln. was stirred for 3 h at r.t. The i-PrOH liberated by ligand exchange was removed completely, with the solvent, under high vacuum at r.t. The residue thus obtained was dried under these conditions for 1–2 h.

General Procedure Yielding Mono- or Bis(1-Phenylpropyl)titanates (**11b–d, v**; *GP II*): To 6 mmol of diol **1a** or **2f** (apparatus, see *GP I*), under Ar, were added 15 ml of toluene and 1.0 equiv. (6 mmol) of (i-PrO)$_4$Ti and the mixture stirred for 3 h at r.t. The volatile components were removed under high vacuum at r.t., and the residue was dried for *ca.* 1 h under these conditions (checked occasionally by ^{1}H-NMR). The titanate **11a** or **11u** formed was dissolved in 30 ml toluene, and then 1 or 2 equiv. of (*S*)- or (*R*)-1-phenylpropan-1-ol was added (for **11b–d** 1-phenylpropan-1-ol of 95% ee, and for **11v** of 99% ee was used). This soln. was stirred for 3 h at r.t. Treatment as described in *GP I* furnished titanates bearing 1 or 2 chiral alkoxides, respectively.

NMR Data of the Chiral Titanates. **11a**: ^{1}H-NMR (200 MHz): 7.61–7.42 (*m*, 8 arom. H); 7.32–7.18 (*m*, 12 arom. H); 5.05 (*s*, H–C(4), H–C(5)); 4.50–4.25 (*m*, 2 $(CH_3)_2CH$); 1.11 (*d*, *J* = 6, $(CH_3)_2CH$); 1.07 (*d*, *J* = 6, $(CH_3)_2CH$); 0.66 (*s*, 2 CH_3–C(2)). ^{1}H-NMR (200 MHz, C_6D_6): 7.85–7.75 (*m*, 8 arom. H); 7.19–6.99 (*m*, 12 arom. H); 5.50 (*s*, H–C(4), H–C(5)); 4.50–4.35 (*m*, 2 $(CH_3)_2CH$); 1.10 (*d*, *J* = 4, $(CH_3)_2CH$); 1.07 (*d*, *J* = 4, $(CH_3)_2CH$); 0.76 (*s*, 2 CH_3–C(2)). ^{13}C-NMR (50 MHz): 148.74, 143.32, 129.67, 128.07, 127.66, 127.38, 127.24, 127.17 (arom. C); 111.52; 93.39; 82.24; 77.93; 27.57; 26.41.

11b: ^{1}H-NMR (200 MHz): 7.63–7.02 (*m*, 25 arom. H); 5.11 (*s*, H–C(4), H–C(5)); 5.06–4.91 (*m*, OC*H*(Ph)Et); 4.34–4.12 (*m*, $(CH_3)_2CH$); 1.70–1.48 (*m*, CH_2); 1.16–0.91 (*m*, CH_3CH_2); 0.90–0.70 (*m*, $(CH_3)_2CH$); 0.65 (*s*, 2 CH_3–C(2)). ^{13}C-NMR (50 MHz): 148.26, 147.46, 144.76, 142.69, 142.63, 129.29, 129.13, 129.03, 128.53, 128.19, 127.84, 127.32, 127.17, 127.10, 126.86, 125.79, 125.33 (arom. C); 111.36; 93.53; 88.50 (br.); 82.13; 81.82; 33.26; 27.30; 25.92; 10.14.

11c: ^{1}H-NMR (200 MHz): 7.67–7.51 (*m*, 4 arom. H); 7.41–6.94 (*m*, 26 arom. H); 5.03 (*s*, H–C(4), H–C(5)); 5.03–4.86 (*m*, 2 OC*H*(Ph)Et); 1.76–1.38 (*m*, 2 CH_2); 0.78 (*t*, *J* = 7, 2 CH_3CH_2); 0.60 (*s*, 2 CH_3–C(2)). ^{13}C-NMR (50 MHz): 148.00, 144.74, 142.44, 129.14, 128.97, 128.15, 127.79, 127.52, 127.21, 126.98, 126.77, 125.77 (arom. C); 111.22; 93.81; 88.84 (br.); 88.07; 81.82; 33.49; 27.35; 10.20.

11d: ^{1}H-NMR (200 MHz): 7.65–7.49 (*m*, 4 arom. H); 7.49–6.90 (*m*, 26 arom. H); 5.00 (*s*, H–C(4), H–C(5)); 4.90–4.66 (*m*, 2 OC*H*(Ph)Et); 1.75–1.38 (*m*, 2 CH_2); 0.78 (*t*, *J* = 7, 2 CH_3CH_2); 0.60 (*s*, 2 CH_3–C(2)). ^{13}C-NMR (50 MHz): 148.19, 144.70, 142.56, 129.26, 129.05, 128.24, 127.89, 127.52, 127.32, 127.22, 127.14, 126.88, 125.84 (arom. C); 111.42; 93.68; 81.75; 32.89; 27.28; 10.08.

11j: ^{1}H-NMR (300 MHz): 7.90–7.00 (*m*, 36 arom. H); 5.02 (*s*, H–C(4), H–C(5)); 4.72–4.19 (*m*, 2 $(CH_3)_2CH$); 1.33–0.45 (*m*, 6 CH_3).

11k: ^{1}H-NMR (200 MHz)[39]: 8.76 (*d*, *J* = 7.5, 1 arom. H); 8.33 (*d*, *J* = 7.5, 1 arom. H); 8.02 (*d*, *J* = 9, 1 arom. H); 7.97–7.35 (*m*, 15 arom. H); 7.35–6.81 (*m*, 8 arom. H); 6.81–6.63 (*m*, 2 arom. H); 4.62–4.31 (*m*, H–C(4), H–C(5)); 4.10–3.70 (*m*, 2 $(CH_3)_2CH$); 1.43–1.00 (*m*, 2 $(CH_3)_2CH$); 0.81–0.30 (*m*, 2 CH_3–C(2)).

11l: ^{1}H-NMR (200 MHz): 8.24 (*d*, *J* = 9, 4 arom. H); 7.95–7.18 (*m*, 24 arom. H); 5.36 (*s*, H–C(4), H–C(5)); 4.50–4.32 (*m*, 2 $(CH_3)_2CH$); 1.10 (*d*, *J* = 6, $(CH_3)_2CH$); 1.06 (*d*, *J* = 6, $(CH_3)_2CH$); 0.70 (*s*, 2 CH_3–C(2)). ^{13}C-NMR (50 MHz): 145.23, 140.56, 132.82, 132.50, 132.38, 128.68, 128.54, 128.38, 127.60, 127.48, 127.34, 126.65, 126.03, 125.81, 125.66, 125.08 (arom. C); 111.41; 93.46; 82.21; 77.61; 27.66; 26.18.

11n: ^{1}H-NMR (200 MHz): 7.60–7.03 (*m*, 20 arom. H); 4.93 (*s*, H–C(4), H–C(5)); 4.33–4.13 (*m*, 2 $(CH_3)_2CH$); 1.33–1.03 (*m*, 3 CH_2); 1.01 (*d*, *J* = 6, $(CH_3)_2CH$); 0.93 (*d*, *J* = 6, $(CH_3)_2CH$); 0.63–0.43 (*m*, 2 CH_2).

11o: ^{1}H-NMR (200 MHz): 7.91–6.77 (*m*, 20 arom. H); 4.90 (*s*, H–C(4), H–C(5)); 4.58–4.28 (*m*, 2 $(CH_3)_2CH$); 4.37 (*s*, CH_2); 1.27–0.98 (*m*, 4 CH_3). ^{13}C-NMR (50 MHz): 147.85, 143.06, 129.51, 128.71, 128.57, 128.47, 128.27, 128.11, 127.93, 127.65 (arom. C); 95.00; 91.80; 81.80; 76.00; 25.80.

11q: ^{1}H-NMR (200 MHz): 7.71–7.17 (*m*, 20 arom. H); 5.02 (*d*, *J* = 5, H–C(4) or H–C(5)); 4.89 (*d*, *J* = 5, H–C(5) or H–C(4)); 4.56–4.29 (*m*, 2 $(CH_3)_2CH$); 4.16–4.00 (*m*, H–C(2)); 1.37–0.97 (*m*, 4 CH_3). ^{13}C-NMR (50

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[39]) Broadened signals arise due to hindered rotation of the naphth-1-yl groups (see also [4]).

MHz): 148.11, 147.09, 142.79, 142.53, 129.04, 128.76, 128.66, 128.34, 128.25, 127.80, 127.72, 127.47, 127.28, 127.09 (arom. C); 101.92; 92.32; 91.93; 82.96; 82.03; 77.63; 26.03; 19.22.

11r: ^{1}H-NMR (200 MHz): 7.68–7.40 (*m*, 8 arom. H); 7.40–7.15 (*m*, 12 arom. H); 4.91 (*d*, *J* = 6, H–C(4) or H–C(5)); 4.86 (*d*, *J* = 6, H–C(5) or H–C(4)); 4.42–4.25 (*m*, 2 $(CH_3)_2CH$); 3.40 (*s*, H–C(2)); 1.16–0.98 (*m*, 2 $(CH_3)_2CH$); 0.63 (*s*, $(CH_3)_3C$).

11t: ^{1}H-NMR (200 MHz): 8.36–8.15 (*m*, 4 arom. H); 7.93–7.12 (*m*, 24 arom. H); 5.20 (*d*, *J* = 6, H–C(4) or H–C(5)); 5.15 (*d*, *J* = 6, H–C(5) or H–C(4)); 4.49–4.25 (*m*, 2 $(CH_3)_2CH$); 3.64 (*s*, H–C(2)); 1.16–0.90 (*m*, 2 $(CH_3)_2CH$); 0.65 (*s*, $(CH_3)_3C$).

11u: ^{1}H-NMR (200 MHz): 7.73–7.52 (*m*, 8 arom. H); 7.39–7.05 (*m*, 17 arom. H); 5.21 (*d*, *J* = 6, H–C(4) or H–C(5)); 5.13 (*d*, *J* = 6, H–C(5) or H–C(4)); 4.70 (*s*, H–C(2)); 4.54–4.29 (*m*, 2 $(CH_3)_2CH$); 1.14 (*d*, *J* = 5, 2 $(CH_3)_2CH$); 1.11 (*d*, *J* = 5, $(CH_3)_2CH$).

11v: ^{1}H-NMR (200 MHz): 7.50–6.84 (*m*, 30 arom. H); 5.10 (*d*, *J* = 6, H–C(4) or H–C(5)); 5.00 (*d*, *J* = 6, H–C(5) or H–C(4)); 5.05–4.72 (*m*, OCH(Ph)Et); 4.57 (*s*, H–C(2)); 4.31–4.11 (*m*, $(CH_3)_2CH$); 1.62–1.31 (*m*, CH_2); 1.03–0.53 (*m*, 3 CH_3). ^{13}C-NMR (50 MHz): 147.98, 147.24, 144.85, 142.50, 142.32, 136.21, 129.48, 129.36, 128.98, 128.63, 127.98, 127.85, 127.65, 127.56, 127.30, 127.19, 127.10, 125.88 (arom. C); 104.20, 92.40 (br.), 89.24 (br.), 82.59; 81.73; 33.41; 26.02; 10.18.

11w: ^{1}H-NMR (200 MHz): 7.82–7.51 (*m*, 10 arom. H); 7.51–7.00 (*m*, 17 arom. H); 5.47 (*s*, H–C(2)); 5.38 (*d*, *J* = 6, H–C(4) or H–C(5)); 5.30 (*d*, *J* = 6, H–C(5) or H–C(4)); 4.56–4.30 (*m*, 2 $(CH_3)_2CH$); 1.14 (*d*, *J* = 6, $(CH_3)_2CH$); 1.11 (*d*, *J* = 6, $(CH_3)_2CH$). ^{13}C-NMR (50 MHz): 147.49, 146.77, 142.28, 141.94, 132.72, 131.10, 130.30, 128.87, 128.64, 128.07, 127.98, 127.64, 127.22, 127.05, 126.60, 126.47, 125.28, 124.74, 124.28, 123.24 (arom. C); 100.80; 91.91; 91.65; 82.35; 81.22; 77.17 (br.); 25.41.

11x: ^{1}H-NMR (200 MHz): 7.81–7.53 (*m*, 10 arom. H); 7.53–6.97 (*m*, 17 arom. H); 5.48 (*d*, *J* = 6, H–C(4) or H–C(5)); 5.40 (*d*, *J* = 6, H–C(5) or H–C(4)); 4.90 (*s*, H–C(2)); 4.51–4.30 (*m*, 2 $(CH_3)_2CH$); 1.12 (*d*, *J* = 6, $(CH_3)_2CH$); 1.09 (*d*, *J* = 6, $(CH_3)_2CH$). ^{13}C-NMR (50 MHz): 148.16, 147.37, 142.82, 142.45, 134.05, 133.88, 132.84, 129.06, 128.92, 128.62, 128.26, 127.91, 127.80, 127.66, 127.41, 127.23, 127.17, 126.84, 126.48, 126.03, 125.34, 124.85 (arom. C); 104.37; 92.12; 82.73; 81.77; 77.93 (br.); 26.00.

11y: ^{1}H-NMR (200 MHz): 7.71–7.46 (*m*, 8 arom. H); 7.38–6.69 (*m*, 17 arom. H); 5.21 (*d*, *J* = 7, H–C(5) or H–C(4)); 4.57–4.34 (*m*, 2 $(CH_3)_2CH$); 1.13 (*d*, *J* = 6, $(CH_3)_2CH$); 1.10 (*d*, *J* = 6, $(CH_3)_2CH$); 0.77 (*s*, CH_3–C(2)). ^{13}C-NMR (50 MHz): 148.53, 147.97, 144.08, 143.28, 141.86, 129.73, 129.06, 128.26, 127.85, 127.61, 127.50, 127.20, 127.06, 126.95, 126.68, 126.52, 126.32, 124.83 (arom. C); 110.92; 93.86; 93.16; 82.71; 82.50; 77.44; 28.08; 26.01.

12: ^{1}H-NMR (200 MHz): 4.70–4.50 (*m*, 2 $(CH_3)_2CH$); 3.93 (*s*, H–C(4), H–C(5)); 1.39, 1.33 (2*s*, 2 CH_3–C(2), 2 CH_3–C(α), 2 CH_3–C(α′)); 1.26 (*d*, *J* = 6, 2 $(CH_3)_2CH$).

13: ^{1}H-NMR (200 MHz): 7.57–7.44 (*m*, 2 arom. H); 7.44–7.31 (*m*, 3 arom. H); 5.85 (*s*, H–C(2)); 4.72–4.50 (*m*, 2 $(CH_3)_2CH$); 4.23 (*d*, *J* = 7, H–C(4) or H–C(5)); 4.10 (*d*, *J* = 7, H–C(5) or H–C(4)); 1.44, 1.37 (2*s*, 2 CH_3–C(α), 2 CH_3–C(α′)); 1.28 (*d*, *J* = 6, 2 $(CH_3)_2CH$). ^{13}C-NMR (50 MHz): 137.60, 129.54, 128.41, 127.07 (arom. C); 103.65, 86.64, 85.75; 84.75; 84.41; 76.60; 30.51; 30.20; 25.76; 23.58; 22.92.

14: ^{1}H-NMR (200 MHz): 7.46–7.02 (*m*, 20 arom. H); 4.61 (*sept.*, *J* = 6, 2 $(CH_3)_2CH$); 3.94 (*s*, H–C(4), H–C(5)); 2.93 (*d*, *J* = 13, 2 H, *H*–CHPh); 2.76 (*d*, *J* = 13, 2 H, *H*–CHPh); 2.64 (*d*, *J* = 13, 2 H, *H*–CHPh); 2.32 (*d*, *J* = 13, 2 H, *H*–CHPh); 1.45 (*s*, 2 CH_3–C(2)); 1.30 (*d*, *J* = 6, $(CH_3)_2CH$); 1.23 (*d*, *J* = 6, $(CH_3)_2CH$).

15: ^{1}H-NMR (200 MHz): 7.65–6.91 (*m*, 20 arom. H); 5.10 (*d*, *J* = 6, 2 OCHHO); 4.90 (*s*, H–C(4), H–C5)); 4.79 (*d*, *J* = 6, 2 OCHHO); 4.15–3.92 (*m*, 2 $(CH_3)_2CH$); 1.20 (*d*, *J* = 6, 4 CH_3).

Procedure for the Reactions Described in Tables 3–5. *Addition of Et_2Zn to PhCHO in the Presence of Excess (i-PrO)$_4$Ti. (GPa)*: Benzaldehyde (0.51 ml, 5 mmol) was added to a stirred soln. of 0.05 or 0.20 equiv. of the chiral titanate **11** (for preparation and apparatus, see *GP I*) and 1.2 equiv. of (i-PrO)$_4$Ti in 20 ml of toluene, at r.t. under Ar. This soln. was cooled to *ca.* –25°, and 4.5 ml of a 2M Et_2Zn soln. (9 mmol) were introduced. The resulting yellow soln. was then stirred at this temp., until no more aldehyde could be detected by TLC. After hydrolysis with 15 ml of sat. NH_4Cl soln., the mixture was allowed to warm to r.t. within 30 min and filtered through *Celite*. The phases were separated, the aq. layer was extracted 3 times using Et_2O (30 ml each), and the combined org. phases were washed with brine (twice with 30 ml), dried ($MgSO_4$), and evaporated. The crude mixture was distilled (150°/0.2 Torr) in order to separate the products from the TADDOL. The ratio of enantiomers was determined by CGC. In one experiment, 0.02 equiv. of **11a** was employed. In this case, 1 mmol of **11a** was dissolved in 20 ml of toluene, and 2 ml of this soln. was used.

Addition of Et_2Zn to PhCHO Mediated by **12** *in the Absence of (i-PrO)$_4$Ti.* Benzaldehyde (0.51 or 0.61 ml, 5 or 6 mmol) was added to a stirred soln. of 0.2 or 1.00 equiv. of the chiral titanate **12** in 20 ml of toluene at r.t. under Ar (for apparatus, see *GP I*). The resulting soln. was further treated as described in *GPa*. Reaction time, yield, and ratio of enantiomers for each case are given in *Tables 3–5*.

Procedures for the Reactions Described in Table 6. Since several reactions were carried out using the same catalyst, 0.2M stock solns. were prepared by dissolving 6 mmol of the titanate **11a–d, u**, or **v** in 30 ml of toluene.

Titanate-Mediated Addition of Et_2Zn to 4-Methoxybenzaldehyde in the Absence *of (i-PrO)$_4$Ti.* a) *1.4 Equiv. of Catalyst* **11a–d, u, v**. From the stock soln. described above, 15 ml (3 mmol) was taken and diluted using 5 ml of toluene (for apparatus, see *GP I*), then 0.26 ml (2.14 mmol) of 4-methoxybenzaldehyde was introduced while stirring at r.t. This soln. was cooled to *ca.* −25° before the addition of 1.9 ml of a 2M Et_2Zn soln. (3.85 mmol). The resulting yellow soln. was stirred for 40 h at this temp. For workup and isolation, see *GPb* below.

b) *0.2 Equiv. of Catalyst* **11a–d, u, v**. From the stock soln. described above, 5 ml (1 mmol) was taken and diluted with 15 ml of toluene (for apparatus, see *GP I*), then 0.61 ml (5.0 mmol) of 4-methoxybenzaldehyde was added while stirring at r.t. This soln. was cooled to *ca.* −25° before the addition of 4.5 ml of a 2M Et_2Zn soln. (9.0 mmol). The resulting yellow soln. was stirred for 40 h at this temp. For workup and isolation, see *GPb* below.

Titanate-Mediated Addition of Et_2Zn to 4-Methoxybenzaldehyde in the Presence *of Excess (i-PrO)$_4$Ti.* From the stock soln. described above, 5 ml (1 mmol) were taken and diluted with 15 ml of toluene (for apparatus, see *GP I*, in the reaction using 0.04 equiv. of **11a**, 1 ml of the stock soln. was diluted using 20 ml of toluene), then 0.61 ml (5 mmol) 4-methoxybenzaldehyde and 1.77 ml (6 mmol) of (i-PrO)$_4$Ti were added while stirring at r.t. After cooling to *ca.* −25°, 4.5 ml of 2M Et_2Zn soln. (9 mmol) was introduced. The yellow soln. obtained was stirred for 15 h (in the case of 0.04 equiv. of **11a** for 40 h) at this temp. For workup and isolation, see *GPb* below.

General Procedure for Workup and Isolation of 1-(4-Methoxyphenyl)propan-1-ol (**16** and *ent-***16**; *GPb*). Hydrolysis was achieved by addition of 15 ml of sat. NH_4Cl soln. at −25°; then the mixture was allowed to warm to r.t. within 30 min and filtered through *Celite*. The phases were separated, the aq. layer was extracted 3 times using Et_2O (30 ml each), and the combined org. phases were washed with brine (twice with 30 ml), dried ($MgSO_4$), and evaporated. The resulting mixture was chromatographed (FC, 18 × 3 cm, 60 g SiO_2, 0.2 bar, hexane/Et_2O 7:3) separating **16** and *ent-***16** from the TADDOL and – when necessary – from unreacted aldehyde or by-products. For the yield and ratio of enantiomers (determined by CGC) in each case see *Table 6*.

In the reaction using 0.04 equiv. of **11a** as catalyst the isolation of the products was carried out by distillation, as in *GPa*.

*Preparation of (*S*)-1-Phenylpropan-1-ol.* Following *GPa*, 0.489 g (0.78 mmol) of **11a**, 1.37 ml (4.66 mmol) of (i-PrO)$_4$Ti, 3.92 ml (3.88 mmol) of PhCHO, and 0.72 ml (6.98 mmol) of Et_2Zn in 3 ml of toluene were combined and stirred at −20° for 21 h. After workup and distillation (100°/0.2 Torr), 0.52 g (99%) of 1-phenylpropan-1-ol ((*S*)/(*R*) = 98:2) was obtained. ^{1}H-NMR (200 MHz): 7.42–7.24 (*m*, 5 arom. H); 4.61 (*t*, *J* = 6, C*H*OH); 1.92–1.69 (*m*, CH_2, OH); 0.92 (*t*, *J* = 6, CH_3).

*Preparation of (*R*)-1-Phenylpropan-1-ol.* By analogy to *GP I*, 2.3 g (5.0 mmol) of *ent-***1a** (for preparation, see [4]) was mixed with 1.47 ml (5.0 mmol) of (i-PrO)$_4$Ti in 15 ml of toluene. After removal of the volatiles, the residue was redissolved in 20 ml of toluene and – following *GPa* – 8.84 ml (30 mmol) of (i-PrO)$_4$Ti, 2.53 ml (25 mmol) of PhCHO, and 4.61 ml (45 mmol) of Et_2Zn in 18 ml of toluene were added at −22°. The mixture was stirred for 15 h. After workup and distillation (100°/0.2 Torr), 2.82 g (83%) of 1-phenylpropan-1-ol ((*R*)/(*S*) = 96:4) was isolated.

*Preparation of (*S*)-1-Phenylethanol.* Following *GP I*, 0.47 g (1.0 mmol) of **1a** and 0.29 ml (1.0 mmol) of (i-PrO)$_4$Ti were dissolved in 50 ml of toluene. The product **11a** thus obtained was redissolved in 20 ml of toluene and 0.51 ml (5.0 mmol) of PhCHO was added at r.t. The soln. was cooled to *ca.* −25° and 1.20 g (5.0 mmol) of (i-PrO)$_3$TiMe (for preparation, see [2]) was introduced. After stirring for 2 h at this temp. the workup was performed according to *GPb*. In this case, the separation of the product and **1a** could not be achieved by FC. The resulting mixture (0.93 g) was distilled (150°/0.2 Torr) to give 0.50 g (82%) of 1-phenylethanol ((*S*)/(*R*) = 98:2).

Preparation of rac*-1-Phenylpropan-1-ol.* To 20 ml of cooled toluene (−45°) were added, consecutively, 2.48 ml (8.4 mmol) of (i-PrO)$_4$Ti, 0.83 ml (8 mmol) of Et_2Zn in 3 ml of toluene, and 0.71 ml (7 mmol) of PhCHO. The soln. was then stirred at −25°. The course of the reaction was followed – after hydrolysis (using sat. NH_4Cl soln.) of small samples withdrawn from the reaction mixture – by CGC analysis. After 6 h, a mixture of 30% unreacted benzaldehyde and 70% 1-phenylpropan-1-ol was detected.

Reaction of PhCHO and Et_2Zn without *Any Additives.* In 4 ml of ice-cold toluene were combined 1 ml of a 2M Et_2Zn soln. (2 mmol) and 0.1 ml (1 mmol) of PhCHO. The mixture was stirred for 20 h at r.t. After workup, the ^{1}H-NMR of the isolated oil (0.114 g) showed a 1:1:1.5 mixture of $PhCH_2OH$, propiophenone, and 1-phenylpropan-1-ol.

*Crystal Structure Analyses. (4*R*,5*R*)-2-(*tert*-Butyl)-α,α,α′,α′-tetraphenyl-1,3-dioxolane-4,5-dimethanol* (**2b**)·N-*Methylisopropylamine* ($C_{33}H_{34}O_4 \cdot C_4H_{11}N$). Determination of the cell parameters and collection of the reflection intensities were performed on a *Enraf-Nonius CAD4* four-circle diffractometer (graphite monochroma-

tized MoK_α radiation, $\lambda = 0.7107$ Å); monoclinic, space group $P2_1$, $a = 10.177(5)$, $b = 10.833(6)$, $c = 15.199(7)$ Å, $\beta = 98.05(4)°$, $V = 1659$ Å^3, $Z = 2$, $\rho_{calc.} = 1.14$ gcm^{-3}, $\mu = 0.40$ mm^{-1}, $F(000) = 612$. Number of reflections measured 3207 (ω scan, $2 < 2\vartheta < 50°$); 2983 unique reflections, of which 2630 with $I > 2\sigma(I)$ were used for the determination (Direct Methods, SHELXS-86 [77]) and the refinement (SHELX-76 [78]) of the structure. The non-H-atoms were refined anisotropically. The C–H H-atoms were added to the TADDOL molecule with constant isotropic temp. factors on calculated idealized positions and refined according to the riding model. The H-atoms bonded to O-atoms could be located from differential *Fourier* syntheses and were refined with constant isotropic temp. factors. Due to distortions in the skeleton of the amine, the H-atoms in this molecule were omitted. After elimination of 001-reflection, the refinement converged at $R = 0.054$ ($R_w = 0.063$, number of variables 384).

*(4*R,*5*R*)-2-Phenyl-α,α,α',α'-tetraphenyl-1,3-dioxolane-4,5-dimethanol* (**2f**)·*Piperidine* ($C_{35}H_{30}O_4 \cdot C_5H_{11}N$). Determination of the cell parameters and collection of the reflection intensities were performed on a *Enraf-Nonius CAD4* four-circle diffractometer (graphite monochromatized MoK_α radiation, $\lambda = 0.7107$ Å); orthorhombic, space group $P2_12_12_1$, $a = 9.593(2)$, $b = 18.394(6)$, $c = 18.819(6)$ Å, $V = 3321$ Å^3, $Z = 4$, $\rho_{calc.} = 1.20$ gcm^{-3}, $\mu = 0.42$ mm^{-1}, $F(000) = 1280$. Number of reflections measured: 3317 (ω scan, $2 < 2\vartheta < 50°$); 3014 unique reflections, of which 2091 with $I > 2\sigma(I)$ were used for the determination (Direct Methods, SHELXS-86) and the refinement (SHELX-76) of the structure. The non-H-atoms were refined anisotropically. A riding model with idealized geometry was employed for the C–H H-atom refinement. The H-atoms bonded to O- or N-atoms could be located from differential *Fourier* syntheses and were refined according to the riding model with fixed idealized lengths. The refinement finally converged at $R = 0.060$ ($R_w = 0.060$, number of variables 406).

*(1*R,*7*R,*8*S*)-8-Hydroxy-8,10,10-triphenyl-2,4,6,9-tetraoxabicyclo[5.3.0]decane* (**8**; $C_{24}H_{22}O_5$). Determination of the cell parameters and collection of the reflection intensities were performed on a *Picker-Stoe* single crystal diffractometer (graphite monochromatized MoK_α radiation, $\lambda = 0.7107$ Å); monoclinic, space group $P2_1$, $a = 8.397(4)$, $b = 13.275(7)$, $c = 18.042(9)$ Å, $\beta = 90.16(2)°$, $V = 2011$ Å^3, $Z = 4$, $\rho_{calc.} = 1.29$ gcm^{-3}, $\mu = 0.53$ mm^{-1}, $F(000) = 824$. Number of reflections measured: 3708 (ω-2ϑ scan, $2.5 < 2\vartheta < 50°$); 'learnt-profile' method; 3566 unique reflections, of which 3198 with $I > 2\sigma(I)$ were used for the determination (Direct Methods, SHELXS-86) and the refinement (SHELX-76) of the structure. The non-H-atoms were refined anisotropically. All C–H H-atoms were added to this structure model with constant isotropic temp. factors on calculated idealized positions and refined according to the riding model. The H-atoms bonded to O-atom could be located from differential *Fourier* syntheses and were refined with constant isotropic temp. factors. The refinement finally converged at $R = 0.044$ ($R_w = 0.058$, number of variables 528).

*[T-4-(4*R-trans*),(4*R-trans*)]-Bis[2,2-dimethyl-α,α,α',α'-tetraphenyl-1,3-dioxolane-4,5-dimethanolato(2 −)-*$O^\alpha, O^{\alpha'}$*]titanium* (**10**)·*1/6 Et$_2$O* ($C_{62}H_{56}O_8Ti \cdot 1/6\ Et_2O$). Determination of the cell parameters and collection of the reflection intensities were performed on a *Picker-Stoe* single crystal diffractometer (graphite monochromatized MoK_α radiation, $\lambda = 0.7107$ Å); monoclinic, space group $P2_1$, $a = 13.81(1)$, $b = 18.88(1)$, $c = 32.38(3)$ Å, $\beta = 102.00(7)°$, $V = 8260$ Å^3, $Z = 6$, $\rho_{calc.} = 1.19$ gcm^{-3}, $\mu = 0.20$ mm^{-1}, $F(000) = 3096$. Number of reflections measured: 21353 (ω-2ϑ scan, $3 < 2\vartheta < 40°$); 'learnt-profile' method; 8033 unique reflections, of which 4911 with $I > 4\sigma(I)$ were used for the determination (*Patterson* method) and the refinement (SHELXTL PLUS [79]) of the structure. The C- and O-atoms were refined isotropically, the Ti-atoms anisotropically. All Ph rings were treated as rigid groups. H-Atoms were added to this structure model with constant isotropic temp. factors on calculated idealized positions and refined according to the riding model. One of the three molecules showed unexpectedly high temp. factors of the C-atoms in the Ph groups of one TADDOLate moiety. Therefore, no H-atoms were added to these C-atoms. Additional hexagonal difference-peak arrangements in the neighborhood of these Ph rings suggest their disordering. Thus, these temp. factors should be interpreted in terms of the modulation amplitude rather than thermal motion. Additional peaks in the differential synthesis could be attributed to '1/2' an Et_2O molecule, the existence of which was proved independently by ^{1}H-NMR of crystals selected from the same sample. The resulting coordinates give only a rough estimate of the atom positions, and the observed deviations of some distances and angles from the expected values are probably due to disorder and, therefore, are not significant. The refinement finally converged at $R = 0.104$ ($R_w = 0.107$, number of variables 587).

*(4*R,*5*R*)-4,5-Bis[(methoxy)(diphenyl)methyl]-2,2-dimethyl-1,3-dioxolane* (**17**)·*CCl$_4$* ($C_{33}H_{34}O_4 \cdot CCl_4$). Determination of the cell parameters and collection of the reflection intensities were performed on a *Enraf-Nonius CAD4* four-circle diffractometer (graphite monochromatized MoK_α radiation, $\lambda = 0.7107$ Å); orthorhombic, space group $P2_12_12_1$, $a = 9.439(5)$, $b = 10.050(2)$, $c = 34.51(2)$ Å, $V = 3274$ Å^3, $Z = 4$, $\rho_{calc.} = 1.32$ gcm^{-3}, $\mu = 0.40$ mm^{-1}, $F(000) = 1352$. Number of reflections measured: 3322 (ω scan, $2 < 2\vartheta < 50°$); 3043 unique reflections, of which 1989 with $I > 4\sigma(I)$ were used for the determination (Direct Methods, SHELXS-86) and the refinement (SHELX-76) of the structure. The C-atoms of the Ph rings were refined isotropically, all other C- and

O-atoms anisotropically. All H-atoms were added to this structure model with constant isotropic temp. factors on calculated idealized positions and refined according to the riding model. The CCl_4 molecule 'rotates' around one C–Cl bond, and three maxima of sojourn probability could be refined isotropically with occupation numbers of 0.40, 0.35, and 0.25, respectively. The refinement finally converged at $R = 0.091$ ($R_w = 0.101$, number of variables 258).

All crystal-structure representations were prepared using the programs PLUTO [80] and MacMoMo [81].

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