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Enantioselective Preparation of *sec.* Alcohols from Aldehydes and Dialkyl Zinc Compounds, Generated *in situ* from Grignard Reagents, Using Substoichiometric Amounts of TADDOL-Titanates[1]

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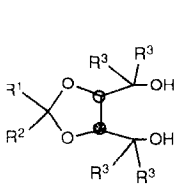
Abstract: Using the *Schlenk* trick (precipitation of MgX_2 from ethereal solutions by the addition of 1,4-dioxane) mixtures of a Grignard reagent RMgX (X = Cl, Br, I) and 0.5 equiv. $ZnCl_2$ in Et_2O can be converted to zinc alkyls R_2Zn which in turn are added with enantioselectivities of up to 99 : 1 to aliphatic and aromatic aldehydes in the presence of $Ti(OCHMe_2)_4$ and a chiral titanate derived from an α,α,α',α'-tetraaryl-1,3-dioxolane-4,5-dimethanol (TADDOL). Grignard reagents containing *remote* double bonds, benzene rings, or acetal groups can also be employed. Different TADDOLs are compared with respect to their usefulness in this kind of enantioselective reaction.

A) Introduction. - The diols **1** (TADDOLs = α,α,α',α'-tetraaryl-1,3-dioxolane-4,5-dimethanols), prepared from tartrate acetals or ketals and aryl Grignard reagents[3-5] turned out to form chiral titanates, useful for stoichiometric[3,4,6-9] and catalytic[10-12] enantioselective reactions. We found that a combination of 0.02 - 0.15 equiv. of the spirotitanate **2** and 1.2 equiv. $Ti(OCHMe_2)_4$ causes diethyl zinc to add highly selectively to aromatic and aliphatic aldehydes[13,14], see *Scheme 1*.



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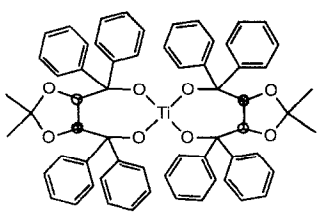
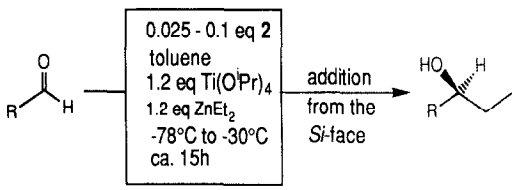


2
[derived from (*R,R*)-tartaric-acid]

This type of nucleophilic addition is normally catalyzed by chiral amino alcohols and it is mostly studied using the commercially available diethyl zinc[15,16], although there are notable exceptions[16f-o].



Scheme 1. Titanate-mediated enantioselective addition of diethyl zinc to aldehydes

It is also generally accepted that the reaction catalyzed by amino alcohols can be carried out successfully only with aromatic aldheydes and only in hydrocarbon solvents, preferably in hexane or toluene. Since the titanate-mediated reaction is rather insensitive to ether solvents, see *Table 1*, we figured that zinc reagents prepared in such solvents could be used to broaden the scope of this enantioselective addition even further.

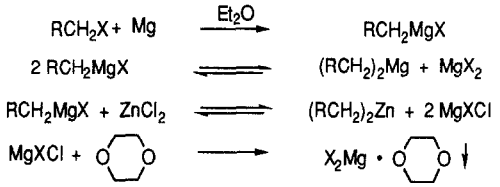
Alkyl, alkenyl, alkynyl and aryl zinc reagents have been described as isolable, liquid or solid, highly air-sensitive compounds[18], and they have been the first organometallic derivatives prepared (Frankland, 1849)[19]. We decided to test whether the dialkyl zinc reagents prepared *in situ* from Grignard

compounds in diethyl ether could be used for the titanate-mediated reaction.

Table 1. Influence of Different Solvents on the Selectivity of the Addition Reaction of Diethylzinc to Aldehydes Using Catalyst **1**. The data shown here are taken from the Ph. D. Thesis of B. Schmidt[17], see also ref[13].

aldehyde	solvent	T [°C]	t [h]	% y	*S/R*
PhCHO	toluene	-76 to -20	15	75	99.5:0.5
PhCHO	Et_2O	-76 to -20	20	62	99.5:0.5
PhCHO	THF	-76 to -20	20	63	91:9
PhCHO	dioxane	-15 to 0	20	69	90:10
^{i}PrCHO	hexane	-76 to -20	17	44	97:3

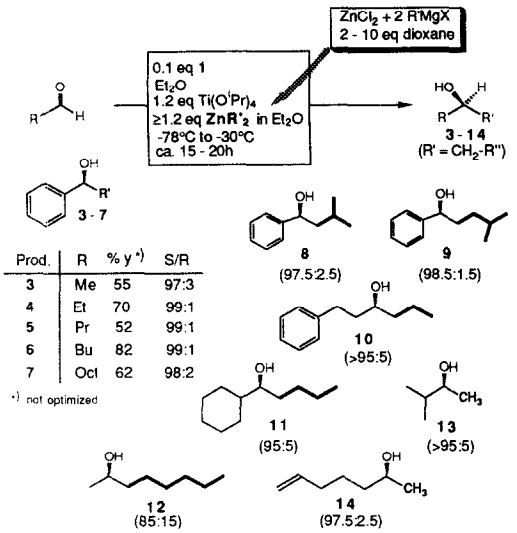
Initial experiments, in which we added 0.5 equiv. of anhydrous $ZnCl_2$ to a Grignard reagent, followed by the spirotitanate **2** and an aldehyde (at -15°C) yielded racemic product, just like RMgX alone does. We then followed a procedure described for aryl derivatives[20], exploiting the low solubility of magnesium halide dioxane complexes (used to prove the so-called *Schlenck* equilibrium)[21], to remove them from the ethereal solution. Thus, we prepared salt-free solutions of dialkyl zinc reagents in ether as outlined in *Scheme 2*. A freshly prepared solution of a Grignard compound (X in RCH_2MgX may be Cl, Br or I) was combined with a solution of 0.5 equiv. $ZnCl_2$, both in Et_2O, and with dry 1,4-dioxane (ca. 4 equiv.) at room temperature. The precipitate was removed by filtration under argon, and the resulting clear solution containing the dialkyl zinc compound used as described for the commercially available Et_2Zn solutions in toluene or hexane[13-17].



Scheme 2. Generation of salt-free dialkyl zinc solutions in Et_2O from Grignard reagents

B) Enantioselective Additions of Simple Zinc Alkyls to Aldehydes. - The solution of the zinc derivative was used in the titanate-mediated reaction by addition to an ethereal solution obtained from tetraisopropoxy titanium (1 equiv.) and the spirotitanate **2** (0.08 equiv.). At dry-ice temperature an aldehyde was added, the solution was kept at -30°C for up to 1 day, and worked up. As evident from the data given in *Scheme 3*, this procedure led to *sec.* alcohols of high enantiomeric excesses, especially with aromatic aldehydes[22]. Primary alkyl groups, straight-chain and α- or β-branched, can be transferred to benzaldehyde with generally ≥ 98 : 2 selectivity (determined by GC analysis on chiral columns), see products **3** - **9**. With aliphatic aldehydes (→ **10** - **14**) the selectivity drops, but usually stays above 95 : 5. The addition took place preferentially from the *Si*-face of the aldehyde groups, as proved by determination of the sense of chirality of the isolated products, mostly through optical comparison.

The limitation of the method is that only primary and non-hindered R_2Zn compounds can be added with high enantioselectivities. Steric hindrance either prevents the reaction from taking place at all (dineopentyl zinc does not add to benzaldehyde even at Et_2O reflux temperature) or renders it non-selective (diisopropyl zinc adds at -15°C with an enantioselectivity of *ca.* 7 : 3). Also, Zn derivatives with π-conjugation (allyl and benzyl) do not add selectively[23].

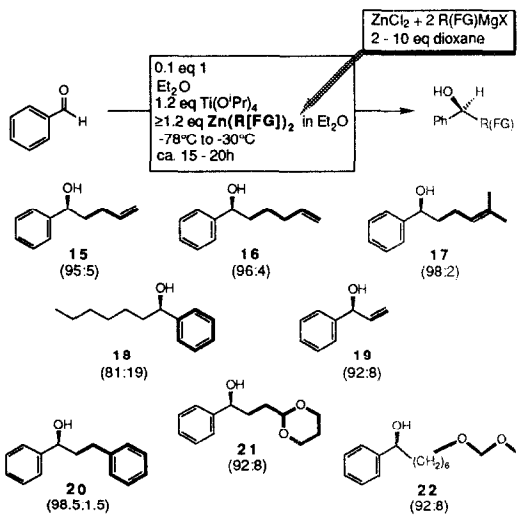


Scheme 3. Products from the addition of non-functionalized dialkylzinc compounds

As may be concluded from an experiment with butyllithium, a Li/Zn transmetalation is also feasible, at least in hydrocarbon solution, with removal of insoluble Li halide, for the *in situ* preparation and titanate catalyzed addition of zinc alkyls to aldehydes, see experimental section.

C) Additions of Functionalized R_2Zn Reagents. - So far, the enantioselective addition of R_2Zn to aldehydes is restricted to non-functionalized R groups. Apparently, heteroatoms in the Zn reagent are involved in complexations with the metal, see for instance the crystal structure of the Reformatzky reagent[24] in which the Zn is coordinated to a halogen, to a carbon, and to an oxygen atom. We find that the titanate-mediated enantioselective additions are no exception: neither $Zn(CH_2CO_2Et)_2$ nor the homologous $Zn(CH_2CH_2CO_2Et)_2$ add in good selectivities to benzaldehyde[25]. Thus, we checked the possibility of adding alkyl groups with double bonds separated from the reactive center by at least one CH_2 group.

In the corresponding products, hydroboration and other electrophilic additions would allow for introduction of functional groups. Indeed, homoallyl and pentenyl zinc reagents can be added with high enantioselectivities, see the products **15** - **17** in *Scheme 4*. Also, while phenyl (→ **18**) and benzyl zinc[23] add with poor or no selectivity, the usual enantiomeric excess is observed with the product **20** from benzaldehyde and bis(2-phenyl-ethyl) zinc. Vinylic zinc reagents, which lead to highly enantiomerically enriched adducts with aromatic aldehydes in the amino alcohol mediated version of the reaction[16f], give disappointing results in the Ti-TADDOLate catalyzed conversion[26], see **19** in *Scheme 4*. Finally, a decent 92 : 8 selectivity is obtained with acetal substituted zinc reagents furnishing the 4-hydroxy-aldehyde and the 1,7-diol derivatives **21** and **22**.



Scheme 4. Products from the addition of functionalized dialkylzinc compounds

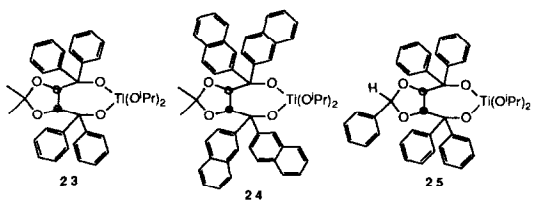
D) Modification of the Chiral Ligand in the Titanate. - In an attempt to find ways of improving the selectivities beyond the values given in *Schemes 3* and *4*, we also tested other TADDOL ligands. A whole collection of these diols with different substituents in the 2-position of the dioxolane ring, *i.e.* on the acetal center, as well as with different aryl groups on the dimethanol groups has been prepared[3-5, 27].

Table 2. Comparison of Catalysts **23**, **24** and **25** Concerning the Selectivity Obtained in a Number of Nucleophilic Additions of Dialkyl Zinc to Aldehydes in Et_2O[a)]

	S/R ratio obtained with catalyst			product
aldehyde	**23**	**24**	**25**	(*S* configuration)
benzaldehyde	99:1	99.5:0.5	98.5:1.5	**3**
benzaldehyde	97:3	99:1	98.5:1.5	**4**
benzaldehyde	95:5	96:4	95.5:4.5	**15**
cyclohexane carboxaldehyde	91:9	99.5:0.5	96.5:3.5	1-cyclohexyl-1-propanol[a)]
cyclohexane carboxaldehyde	95:5	96:4	95.5:4.5	**11**
heptanal	94:4	98.5:1.5	98:2	3-nonanol[a)]

a) These reactions were done in toluene with the commercial Et_2Zn. Experimental details are given in ref. [14,17]

Since we know[14,28] that the actual catalyst formed from the spirotitanate **2** and $Ti(OCHMe_2)_4$ is the simple titanate **23** we prepared this latter compound, the analogous β-naphthyl derivative **24**, and the pentaphenyl substituted titanate **25**, and used them for the preparation of *sec.* alcohols from aldehydes and zinc alkyls as described in the previous section C. The results are summarized in *Table 2*. All three ligands derived from *R,R*-tartrate give rise to addition from the *Si* face of the aldehyde. The β-naphthyl substituted titanate **24** is clearly the most effective one[14,17,28], followed by the pentaphenyl titanate **25** and the tetraphenyl titanate **23**.



23 **24** **25**

The differences are especially pronounced with aliphatic aldehydes. As can be seen in the experimental section, the originally used diol **1**, $R^1 = R^2 = CH_3$, $R^3 = C_6H_5$, has by far the best crystallization properties and can be removed from crude product mixtures and recovered most conveniently. It must also be realized that 2-bromo-naphthalene required for the preparation[5] of **24** is *very* expensive. The C_1-symmetrical pentaphenyl-diol **1**, $R^1 = H$, $R^2 = R^3 = C_6H_5$, is easily prepared from cheap starting materials (tartrate, benzaldehyde, bromo-benzene) and it can be crystallized and isolated in pure form without chromatographic purification[27], in sharp contrast to the C_1-symmetrical TADDOL **1**, $R^1 = CH_3$, $R^2 = R^3 = C_6H_5$ used by *Narasaka* et al.[11,12] to generate titanate Lewis acids for enantioselective cycloadditions and ene reactions.

Experimental Part

We thank Dr. B. Schmidt, S. Kaufmann, and H. Schriber for carrying out some of the experiments described herein. For preliminay communications of the preparations of **2**, **23**, and **24** see ref.[13,14,17].

We gratefully acknowledge the invaluable help of Dr. D. Felix in determining the ratios of enantiomeric alcohols by GC and of Stefan Blank in preparing this manuscript.

Preparation of Titanium-Catalysts:

Synthesis of "Spirotitanate" **2** (Bis-[(4R,5R)-2,2-dimethyl-α,α,α',α'-tetraphenyl-1,3-dioxolane-4,5-dimethoxy]titanate)

- Reaction extremely sensitive to moisture! -

Under an inert gas atmosphere 9.33g (20 mmol) of (*4R,5R*)-2-Dimethyl-α,α,α',α'-tetraphenyl-1,3-dioxolane-4,5-dimethanol ("diol-ligand") is treated with 2.3 ml of distilled tetraethoxy

titanate (11 mmol) [compound has to be stored and handled under inert gas atmosphere] and 20 ml of toluene [freshly distilled from potassium metal], giving rise to a slightly yellow suspension. This suspension is stirred at 40°C for approx. 12 h, the resulting clear solution is heated to reflux temperature for an additional 5 h. The solvent is then slowly evaporated in vacuo, the speed of distillation is controlled by the vacuum and the cooling-rate of the condensor. After about 30 min of evaporation the spirotitanate **2** is isolated as a yellow, waxy solid in quantitative yield and may be stored under argon.

Mp. (after further purification by stirring the solid with a small amount of ether and removal of the supernatant): >235°C (decomp.). - ^{1}H-NMR (300 MHz): δ = 7.60-7.54 (m, 8H, arom. H), 7.45-7.38 (m, 8H, arom. H), 7.30-7.11 (m, 24H, arom. H), 5.02 (s, 4H, O-C<u>H</u>R$_2$), 0.70 (s, 12H, 4xC<u>H</u>$_3$). - ^{1}H-NMR(C$_6$D$_6$, 300 MHz): δ = 7.85-7.82 (m, 8H, arom. H), 7.75-7.70 (m, 8H, arom. H), 7.15 (s, 4H, arom. H), 7.05 (s, 4H, arom. H), 7.00-6.90 (m, 16H, arom. H), 5.55 (s, 4H, O-C<u>H</u>R$_2$), 0.75 (s, 12H, 4xC<u>H</u>$_3$). - ^{13}C-NMR(50 MHz): δ = 146.89, 142.08, 128.70, 127.62, 127.00, 126.91, 126.40, 110.50, 94.13, 82.51, 26.66. - IR: (KBr) ν = 3400*br,w*, 3090*w*, 3060*m*, 3035*w*, 3022*w*, 2995*m*, 2938*w*, 2900*w*, 1600*w*, 1492*s*, 1445*s*, 1380*m*, 1370*m*, 1243*s*, 1215*s*, 1165*s*, 1065*s*, 1050*s*, 1015*s*, 890*s*, 845*s*, 805*m*, 735*s*, 700*s*, 640*m*, 505*m*. MS(FAB): m/z (%) = 934.34 (2), 933 (2), 449 (2), 431 (4), 391 (8), 268 (9), 267 (40), 265 (5), 238 (16), 237 (71), 225 (12), 209 (7), 207 (9), 197 (14), 195 (20), 184 (16), 183 (77), 180 (13), 179 (62), 178 (19), 168 (14), 167 (76), 165 (15), 154 (15), 137 (11), 136 (15), 106 (13), 105 (100), 91 (13), 77 (30), 54 (11). $C_{62}H_{56}O_8Ti$ (977.02) calculated: C 76.22, H 5.78; found: C 75.98, H 5.77.

<u>"Phenyl-monocycle" **23** ((4*R*,5*R*)-2,2-dimethyl-α,α,α´,α´-tetraphenyl-1,3-dioxolan-4,5-dimethoxydiisopropoxy titanate)</u>

In a round bottomed flask equipped with a condensor, argon inlet, and rubber septum are introduced 0.933 g (0.002 mol) of the dimethyl-tetraphenyl ligand **1** (R^1, R^2=CH$_3$, R^3=Ph) and the apparatus is flushed with argon. To the flask is then added 0.65 ml (0.0022 mol) of Ti(O^{i}Pr)$_4$ and 15-20 ml of toluene and the mixture is stirred at 40°C for 5 h. The solvent is then evaporated in vacuo and the resulting light yellow foam used without further purification in the alkylation reaction as described in the general procedure.

Mp. (of an analytical sample (recrystallized from pentane): 79-83°. - ^{1}H-NMR: δ = 7.61-7.42 (*m*, 8H, arom. H), 7.32-7.18 (*m*, 12H, arom. H), 5.05 (*s*, 2H, benzylic H), 4.50-4.25 (m, 2H, C<u>H</u>(CH$_3$)$_2$), 1.11 (d, J = 6, 6H, CH(C<u>H</u>$_3$)$_2$), 1.07 (d, J = 6, 6H, CH(C<u>H</u>$_3$)$_2$), 0.66 (s, 6H, C(C<u>H</u>$_3$)$_2$). - ^{1}H-NMR(C$_6$H$_6$): δ = 7.85-7.75 (m, 8H, arom. H), 7.19-6.99 (m, 12H, arom. H), 5.50 (*s*, 2H, O-C<u>H</u>R$_2$), 4.50-4.35 (m, 2H, C<u>H</u>(CH$_3$)$_2$), 1.10 (d, J = 3.5, 6H, CH(C<u>H</u>$_3$)$_2$), 1.07 (d, J = 3.5, 6H, CH(C<u>H</u>$_3$)$_2$), 0.76 (*s*, 6H, C(CH$_3$)$_2$). - ^{13}C-NMR(50MHz): δ = 148.74, 143.32, 129.67, 128.07, 127.66, 127.38, 127.24, 127.17, 111.52, 93.39, 82.24, 77.93, 27.57, 26.41. - IR: (KBr) ν = 3400*s,br*, 3090*m*, 3060*m*, 3030*m*, 2980*m*, 2930*m*, 2870*m*, 1490*m*, 1448*s*, 1380*m*, 1370*m*, 1240*m*, 1218*m*, 1165*s*, 1130*m*, 1080*s*, 1050*s*, 1020*s*, 888*m*, 743*s*, 700*s*. MS (FAB): m/z (%) = 633.2 (M$^+$, <1), 606 (1), 584 (1), 551 (1), 451 (1), 431 (2), 391 (2), 267 (15), 237 (40), 195 (13), 183 (49), 179 (63), 167 (63), 165 (15), 105 (100), 91 (15), 77 (28), 59 (8). $C_{37}H_{42}O_6Ti$ (630.63) calculated: C 70.47, H 6.71; found: C 70.58, H 7.41.

<u>(4*R*,5*R*)-2,2-Dimethyl-α,α,α´,α´-tetra(naphth-2-yl)-1,3-dioxolan-4,5-dimethoxydiisopropoxy titanate **24**</u>

Under an inert gas atmosphere 1.46 g (2.2 mmol) of (4*R*,5*R*)-2,2-Dimethyl-α,α,α´,α´-tetra(naphth-2-yl)-1,3-dioxolan-4,5-dimethanol (**1**, R^1, R^2= CH$_3$, R^3=β-naphtyl) are treated with 0.65 ml (2.2 mmol) of Ti(O^{i}Pr)$_4$ and 20 ml of toluene as described for the preparation of catalyst **23**. The mixture is stirred for 5 h at 40°C and the solvent evaporated in vacuo to give the title compound, in quantitative yield, as a pale yellow substance which is used directly in the alkylation reaction.

^{1}H-NMR (200 MHz): δ = 8.4-7.2 (m, 28H, arom. H), 5.43 (s, 2H, C-<u>H</u>), 4.5 (m, 2H, O-C<u>H</u>(CH$_3$)$_2$), 1.18 (2xd, br., 12H, CH(C<u>H</u>$_3$)$_2$), 0.74 (s, 6H, C(C<u>H</u>$_3$)$_2$).

<u>(4*R*,5*R*)-2,α,α,α´,α´-Pentaphenyl-1,3-dioxolan-4,5-dimethoxydiisopropoxy titanate **25**</u>

Following the same procedure as described for catalyst **23**, the title compound is prepared from 1.03 g of **1** (R^1=H, R^2, R^3=Ph, 0.002 mol) and 0.65 ml (2.2 mmol) of Ti(O^{i}Pr)$_4$ in

20 ml of toluene. It is isolated as described above, and can be used without further purification.

^{1}H-NMR (200 MHz): δ = 7.64-7.59 (m, 8H, arom. H), 7.37-7.19 (m, 15H, arom H), 7.06-7.01 (m, 2H, arom H), 5.21 (d, J= 5.9Hz, 1H, O-CH$_A$CH$_B$-O), 5.11 (d, J= 5.9Hz, 1H, O-CH$_A$CH$_B$-O), 4.71 (s, 1H, PhCH(OR)$_2$), 4.55-4.33 (br.m, 2H, 2x O-CH(CH$_3$)$_2$), 1.14 (br.m, 12H, O-CH(CH$_3$)$_2$).

General procedure for enantioselective alkylations with dialkylzinc compounds.

A 1.0 M zinc chloride solution in Et_2O (Aldrich) [20 ml, 0.02 mol] was diluted with 10 ml of Et_2O and 0.04 mol alkyl magnesium halide (in ether, 2.2 M, prepared as usual from the alkylhalide and magnesium turnings and titrated shortly before use) was added. The resulting suspension was stirred at r.t. for 2h, then treated with 12 ml of 1,4-dioxane (freshly distilled from sodium metal) and stirred for an additional 45 min. Subsequent filtration under an inert gas atmosphere (making use of a Schlenk filter) yielded a clear solution of the zinc reagent. This was directly added at -78 °C to a previously prepared solution of 1.38 g of compound **2** (1.4 mmol) (or 2.0 mmol catalyst **23**, **24** or **25** respectively) and 3.57 ml of $Ti(OCHMe_2)_4$ (12 mmol) in 20 ml of Et_2O. The mixture was stirred at -78 °C for 1h, 10 mmols of aldehyde were then added, and the reaction temperature raised to -30 °C, with a cryostat or a CCl_4/dry ice cooling bath. After complete conversion (TLC assay) the reaction was quenched at -30 °C with a saturated NH_4Cl solution (20 ml), ether was then added (50 ml), the mixture filtered through Celite, and the organic layer is washed with water and brine, dried over Na_2SO_4, filtered, and evaporated in vacuo. Pentane was added to the resulting oil to crystallize the diol ligand, originating from spirocompound **2**. (As the ligands in catalysts **24** and **25** do not show a similar cristallizing behavior, they have to be separated from the product either by bulb to bulb distillation or by flash-chromatography.) The supernatant was again concentrated in vacuo and the product alcohol was isolated by bulb to bulb distillation in 60-85% yield and in the enantiomeric purities stated in tables 1 and 2, and in schemes 3 and 4. The varying yields reflect the differing ease of filtrating the zinc reagent in different experiments. If there is some unreacted aldehyde still present after the procedure described herein, the product may additionally be purified by flash chromatography through a short silica gel column.

The specific rotations ($[\alpha]_D^{RT}$) were measured on a *Perkin-Elmer-241 Polarimeter* in 1 dm cuvettes at RT (20-25°).

Determination of enantiomeric purities by GC on chiral columns:

- Heptakis(2,3,6-tri-*O*-methyl)-β-cyclodextrin [29,30] in OV 1701 Vi, 52m x 0.27mm (inner diameter) ("S1").
- *Chrompack*: WCOT Fused Silica, CP-Cyclodextrin-β-2,3,6-*M*-19, 50m.x 0.25 mm (inner diameter) ("S2").
- Octakis(3-*O*-butanoyl-2,6-di-*O*-n-pentyl)-γ-cyclodextrin[30,31] in OV 1701 Vi (1:2), 50m x 0.27mm (inner diameter) ("S3").
- Heptakis(2,3,6-tri-*O*-ethyl)-β-cyclodextrin[29,30] in OV 1701 Vi (1:4), 17.5m x 0.27mm (inner diameter).("S4").

All alcohols obtained by the method described above have been compared with racemic samples, which were prepared via Grignard reaction, and with literature values where available.

If no literature reference concerning the absolute configuration could be found, the stated *S*/*R*-ratio is based on the assumption that the alkyl group is transferred to the *Si* face of the aldehyde, as always observed in this type of reaction.

S-(-)-1-Phenylethanol (**3**)

According to the general procedure, 1.02 ml benzaldehyde (0.01 mol) was allowed to react with a dimethylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 29.4 ml of methylmagnesium iodide (1.36 M, Et_2O), in the presence of 1.459 g of **2** (15 mol%) and 3.57 ml $Ti(O^iPr)_4$ (0.012 mol, 1.2 eq) in ether. Y: 55%, *S*/*R* = 97:3 (ee: 94%, GC, "S1"). Bp.: 98°C (20 mm). - $[\alpha]_D^{RT}$ = -39.1 (neat) (Lit: $[\alpha]_D^{RT}$ = +42.9 (neat)[32]). - ^{1}H-NMR (200MHz): δ = 7.45-7.30 (m, 5H, arom H), 4.89 (q, J=6.5Hz, 1H, CH(OH)), 2.00 (s, 1H, OH), 1.00 (d, J=6.5Hz, 3H, CH$_3$).

Results obtained under the same conditions in the presence of: catalyst **24**: *S*/*R* = 99:1 (98% ee); catalyst **25**: *S*/*R* = 98.5:1.5 (97% ee).

S-(-)-1-Phenylpropan-1-ol (**4**)

As described in the general procedure, 0.9 ml of benzaldehyde (0.009 mol) with a diethylzinc reagent, prepared from 15 ml of an 1.0 M $ZnCl_2$ solution and 12.3 ml of ethylmagnesium

bromide (2.45 M, Et_2O), in the presence of 1.342 g of **2** (10 mol%) and 3.57 ml $Ti(O^iPr)_4$ (0.012 mol, 1.3 eq) in ether afforded **4** in 40% y. *S/R* = 99:1 (ee: 98%, GC, "S1").

Bp.: 103°C (14 mm). - $[\alpha]_D^{RT}$ = -48.3 (c=5.38, $CHCl_3$) (Lit: $[\alpha]_D^{RT}$ = +45.5 (c=5.15, $CHCl_3$)[33]). - ^{1}H-NMR (200 MHz): δ = 7.35 (m, 5H, arom H), 4.60 (t, J=6.5Hz, 1H, C<u>H</u>(OH)), 1.93 (s, 1H, O<u>H</u>), 1.70 (d·q, J_1=6.5, J_2=7.2, 2H, $C\underline{H}_2CH_3$), 0.92 (t, J=7.4Hz, 3H, CH_3).

Results obtained under the same conditions in the presence of: catalyst **24**: *S/R* = 99.5:0.5 (99% ee); catalyst **25**: *S/R* = 98.5:1.5 (97% ee).

<u>S-(-)-1-Phenylbutan-1-ol (5)</u>

Following the general procedure, 1.15 ml of benzaldehyde (0.0113 mol) was converted to the title compound by a dipropylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 15.9 ml of propylmagnesium bromide (2.52 M, Et_2O), in the presence of 1.69 g of **2** (15 mol%) and 3.87 ml of $Ti(O^iPr)_4$ (0.013 mol, 1.2 eq) in ether. y: 52%, *S/R* = 99:1 (ee: 98%, GC, "S4").

Bp.: 116°C (16 mm). - $[\alpha]_D^{RT}$ = -92.0 (c=5.32, Bzl) (Lit: $[\alpha]_D^{RT}$ = -90.0 (c=5.0, Bzl)[34]). - ^{1}H-NMR (200 MHz): δ = 7.37-7.27 (m, 5H, arom H), 4.68 (t, J=7.0Hz, 1H, C<u>H</u>(OH)), 1.90 (s, 1H, O<u>H</u>), 1.85-1.58 (m, 2H, -$C\underline{H}_2$-), 1.55-1.21 (m, 2H, -$C\underline{H}_2$-), 0.95 (t, J=7.2Hz, 3H, -$C\underline{H}_3$).

<u>S-(-)-1-Phenylpentan-1-ol (6)</u>

According to the general procedure, 1.02 ml of benzaldehyde (0.01 mol) was allowed to react with a dibutylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 15 ml butylmagnesium bromide (2.66 M, Et_2O), in the presence of 1.383 g of 2 (14 mol%) and 3.57 ml of $Ti(O^iPr)_4$ (0.012 mol, 1.2 eq) in ether. y: 82%, *S/R* = 98:2 (ee: 96%, GC, "S1").

Bp.: 130°C (15 mm). - $[\alpha]_D^{RT}$ = -17.7 (neat) (Lit: $[\alpha]_D^{RT}$ = +17.2 (neat)[35]). - ^{1}H-NMR (200 MHz): δ = 7.42-7.20 (m, 5H, arom H), 4.65 (t, J=5.2Hz, 1H, C<u>H</u>(OH)), 1.90 (s, 1H, O<u>H</u>), 1.86-1.62 (m, 2H, -$C\underline{H}_2$-), 1.49-1.16 (m, 4H, 2x -$C\underline{H}_2$-), 0.88 (t, J=6.2Hz, 3H, $C\underline{H}_3$).

In a similar reaction, the zinc-reagent to be used was prepared by addition of 0.04 mol of butyllithium (25.5 ml of a 1.57M BuLi solution in hexane, Metallgesellschaft) to a solution of 0.02 mol $ZnCl_2$ (1.0M in ether, Aldrich) in an additional 20 ml of toluene. The precipitating LiCl was filtered and the reaction carried out as described above. y: 89%, *S/R* = 99:1 (ee: 98%, GC, "S1").

<u>S-(-)-1-Phenylnonan-1-ol (7)</u>

Following the general procedure, 1.02 ml of benzaldehyde (0.01 mol) with a dioctylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 22.5 ml octylmagnesium bromide (1.79 M, Et_2O), in the presence of 1.385 g of compound **2** (14 mol%) and 3.57 ml of $Ti(O^iPr)_4$ (0.012 mol, 1.2 eq) in ether gave **7**. Y: 31% (poor yield due to severe problems in filtrating off the magnesiumsalts in this special case, reaction has not been optimized), *S/R* = 98:2 (ee: 96%, GC, "S1").

Bp.: 124-129°C (3 mm). - $[\alpha]_D^{RT}$ = -25.6 (c=3.12, $CHCl_3$) (Lit: $[\alpha]_D^{RT}$ = not found ($[\alpha]_D$-values given in[36a] are not correlated to an optical purity, *R/S* correlation[36b]). - ^{1}H-NMR (200 MHz): δ = 7.38-7.22 (m, 5H, arom H), 4.65 (d·t, J_1=2.1Hz, J_2=3.0Hz, 1H, C<u>H</u>(OH)), 1.92 (d, J=2.1Hz, 1H, O<u>H</u>), 1.89-1.58 (br.m, 2H, CH(OH)$C\underline{H}_2$-), 1.50-1.18 (br.m, 12H, 6x -$C\underline{H}_2$-), 0.89 (t, J=5.5Hz, 3H, $C\underline{H}_3$).

<u>S-(-)-1-Phenyl-3-methylbutan-1-ol (8)</u>

As described in the general procedure, 1.02 ml of benzaldehyde (0.01 mol) was converted to the title compound by a diisobutylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 17.2 ml of isobutylmagnesium bromide (2.32 M, Et_2O), in the presence of 1.573 g of **2** (16 mol%) and 3.57 ml of $Ti(O^iPr)_4$ (0.012 mol, 1.2 eq) in ether. Y: 30% (very slow reaction), *S/R* = 97.5:2.5 (ee: 95%, GC, "S1").

Bp.: 112°C (9 mm). - $[\alpha]_D^{RT}$ = -28.7 (c=16.6, n-heptane) (Lit: $[\alpha]_D^{RT}$ = -32.3 (c=16.7, n-heptane)[33d,37]). - ^{1}H-NMR (200 MHz): δ = 7.36-7.26 (m, 5H, arom H), 4.75 (m, 1H, C<u>H</u>(OH)), 1.77 (d, J=3.5Hz, 1H, O<u>H</u>), 1.83-1.61 (m, 2H, -$C\underline{H}_2$-), 1.59-1.42 (m, 1H, $C\underline{H}(CH_3)_2$), 0.95 (d, J=5.0Hz, 6H, $CH(C\underline{H}_3)_2$).

<u>(-)-1-Phenyl-4-methylpentan-1-ol (9)</u>

As described in the general procedure, 1.02 ml of benzaldehyde (0.01 mol) was allowed to react with a diisopentylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 18.5 ml of isopentylmagnesium bromide (2.16 M, Et_2O), in the presence of 1.384 g of **2** (14 mol%) and 3.57 ml $Ti(O^iPr)_4$ (0.012 mol, 1.2 eq) in ether. Y: 82%, *S/R* = 98.5:1.5 (ee: 97%, GC, "S1").

Bp.: 132°C (8 mm). - $[\alpha]_D^{RT}$ = -36.5 (c=1.97, $CHCl_3$) (Lit: $[\alpha]_D^{RT}$ = not found). - ^{1}H-NMR (200 MHz): δ = 7.43-7.11 (br.m, 5H, arom H), 4.63 (d·t, J_1=2.0Hz, J_2=3.0Hz, 1H, C<u>H</u>(OH)), 1.87 (d, J=2.0Hz, 1H, O<u>H</u>), 1.83-1.68 (m, 2H, CH(OH)C<u>H</u>$_2$), 1.67-1.46 (m, 1H, C<u>H</u>$(CH_3)_2$), 1.45-1.06 (m, 2H, C<u>H</u>$_2$), 0.87 (d, J=14.0Hz, 6H, CH(C<u>H</u>$_3$)$_2$).

(+)-1-Phenyl-hexan-3-ol (**10**)

Following the general procedure, 1.34 ml of phenylpropionaldehyde (0.01 mol) with a dipropylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 15.9 ml of propylmagnesium bromide (2.51 M, Et_2O), in the presence of 1.20 g of **2** (12 mol%) and 3.57 ml of Ti(O^{i}Pr)$_4$ (0.012 mol, 1.2 eq) in ether yielded **10**. Y: 60%, op: »90% (GC-separation was not successful).

Bp.: 146°C (16 mm). - $[\alpha]_D^{RT}$ = +14.9 (c=5.0, C_6H_6) (Lit: $[\alpha]_D^{RT}$ = +14.9, c=5.0, C_6H_6[38]). - ^{1}H-NMR (200 MHz): δ = 7.38-7.12 (m, 5H, arom H), 3.67 (m, 1H, C<u>H</u>(OH)), 2.90-2.60 (br.m, 2H, benzylic H), 1.92-1.68 (br.m, 2H, CH(OH)-C<u>H</u>$_2$-$(CH_2)_2$-CH_3), 1.58-1.27 (br.m, 5H, O<u>H</u> & 2x C<u>H</u>$_2$), 0.92 (t, J=8.0Hz, 3H, CH_3).

S-(-)-1-Cyclohexylpentanol (**11**)

According to the general procedure, 1.20 ml of cyclohexylcarbaldehyde (0.01 mol) with a dibutylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 15.1 ml of butylmagnesium bromide (2.66 M, Et_2O), in the presence of 1.517 g of **2** (15 mol%) and 3.57 ml Ti(O^{i}Pr)$_4$ (0.012 mol, 1.2 eq) in ether afforded **11**. Y: 35%, *S*/*R* = 95:5 (ee: 90%, GC, "S1").

Bp.: 135°C (760 mm). - $[\alpha]_D^{RT}$ = -13.7 (neat) (Lit: $[\alpha]_D^{RT}$ = -12.9 (neat)[39]). - ^{1}H-NMR (200 MHz): δ = 3.85 (d, J=6.2Hz, 1H, O<u>H</u>), 3.31 (m, 1H, C<u>H</u>(OH)), 2.32-2.16 (br.m, 1H, CR$_2$<u>H</u>-CH(OH)), 1.98-1.00 (br.m, 16H, 8x -C<u>H</u>$_2$-), 1.90 (t, J=4.1Hz, 3H, C<u>H</u>$_3$).

Results obtained under the same conditions in the presence of: catalyst **24**: *S*/*R* = 96:4 (92% ee); catalyst **25**: *S*/*R* = 95.5:4.5 (91% ee).

R-(-)-Octan-2-ol (**12**)

According to the general procedure, 0.62 ml of acetaldehyde (0.011 mol) was allowed to react with a dihexylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 51.8 ml of hexylmagnesium iodide (0.85 M, Et_2O), in the presence of 1.448 g of compound **2** (15 mol%) and 3.57 ml of Ti(O^{i}Pr)$_4$ (0.012 mol, 1.2 eq) in ether. Y: 95%, op: 70% (GC-separation was not successful).

Bp.: 179°C (760 mm). - $[\alpha]_D^{RT}$ = -6.7 (neat) (Lit: $[\alpha]_D^{RT}$ = -9.7 (neat)[40]). - ^{1}H-NMR (200 MHz): δ = 3.76 (m, 1H, C<u>H</u>(OH)), 1.54 (br.s, 1H, O<u>H</u>), 1.50-1.21 (br.m, 10H, 5x -C<u>H</u>$_2$-), 1.17 (d, J=6.1, 3H, C<u>H</u>$_3$CH(OH), 0.88 (t, J=5.8Hz, 3H, CH_2C<u>H</u>$_3$).

S-(+)-3-Methylbutan-2-ol (**13**)

Following the general procedure, 0.91 ml of isobutyraldehyde (0.01 mol) was converted to the title compound by a dimethylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 29.4 ml of methylmagnesium bromide (1.36 M, Et_2O), in the presence of 1.365 g of **2** (14 mol%) and 3.57 ml of Ti(O^{i}Pr)$_4$ (0.012 mol, 1.2 eq) in ether. Y: 40%, *S*/*R* = >95:5 (ee: >90%, (GC-separation difficult, "S1").

Bp.: 113°C (760 mm). - $[\alpha]_D^{RT}$ = not measured (Lit: $[\alpha]_D^{RT}$ = +5.0 (neat) [40c]). - ^{1}H-NMR (200 MHz): δ = 3.64-3.40 (m, 1H, C<u>H</u>(OH)), 1.90 (s, 1H, O<u>H</u>), 1.72-1.52 (m, 2H), 1.22-1.16 (m, 4H), 0.94-0.84 (m, 3H).

(+)-Hept-6-en-2-ol (**14**)

As described in the general procedure, 0.7 g of 1-hexenal (0.007 mol) with a dimethylzinc reagent, prepared from 14.2 ml of an 1.0 M $ZnCl_2$ solution and 21.0 ml of methylmagnesium iodide (1.35 M, Et_2O), in the presence of 0.959 g of compound **2** (14 mol%) and 2.54 ml of Ti(O^{i}Pr)$_4$ (0.0085 mol, 1.2 eq) in ether afforded **14**. Y: 69%, *S*/*R* = 97.5:2.5 (ee: 95%, GC, "S3").

Bp.: 65°C (13 mm). - $[\alpha]_D^{RT}$ = +9.4 (c=5.0, EtOH) (Lit: $[\alpha]_D^{RT}$ = not found). - ^{1}H-NMR (200 MHz): δ = 5.85-5.72 (m, 1H, C<u>H</u>=CH$_2$), 5.03-4.89 (m, 2H, CH=C<u>H</u>$_2$), 3.82-3.70 (m, 1H, C<u>H</u>(OH)), 2.06-1.95 (br.m, 2H, C<u>H</u>$_2$-CH(OH)), 1.82-1.62 (br.s, 1H, O<u>H</u>).

(-)-1-Phenylpent-4-en-1-ol (**15**)

Following the general procedure, 1.02 ml of benzaldehyde (0.01 mol) were allowed to react with a dibutenylzinc reagent, prepared from 20 ml of an 1.0 M $ZnCl_2$ solution and 25.5 ml of butenylmagnesium bromide (1.57 M, Et_2O), in the presence of 1.264 g of **2** (13 mol%) and 3.57 ml of Ti(O^{i}Pr)$_4$ (0.012 mol, 1.2 eq) in ether. Y: 83%, *S*/*R* = 95:5 (ee: 90%, GC, "S3", as TFA-derivative).

$[\alpha]_D^{RT}$ = -31.9 (c=3.17, $CHCl_3$) (Lit: $[\alpha]_D^{RT}$ = not found). - ^{1}H-NMR (200 MHz): δ = 7.36-7.26 (m, 5H, arom H), 5.92-5.75 (m, 1H, C<u>H</u>=CH_2), 5.11-4.96 (m, 2H, CH=C<u>H</u>$_2$), 4.68 (t, J=6.7Hz, 1H, C<u>H</u>(OH)), 2.17-2.08 (m, 3H, O<u>H</u> & CH(OH)C<u>H</u>$_2$), 1.93-1.77 (m, 2H, C<u>H</u>$_2$).

Results obtained under the same conditions in the presence of: catalyst **24**: *S*/*R* = 96:4 (92% ee); catalyst **25**: *S*/*R* = 95.5:4.5 (91% ee).

<u>(-)-1-Phenylhex-5-en-1-ol (16)</u>

According to the general procedure, 0.51 ml of benzaldehyde (0.005 mol) with a dipentenylzinc reagent, prepared from 10 ml of an 1.0 M $ZnCl_2$ solution and 15.8 ml of pentenylmagnesium bromide (1.27 M, Et_2O), in the presence of 0.587 g of **2** (12 mol%) and 1.80 ml of Ti(O^iPr)$_4$ (0.006 mol, 1.2 eq) in ether gave **16**. Y: 64%, *S*/*R* = 96:4 (ee: 92%, GC, "S2").

$[\alpha]_D^{RT}$ = -35.1 (c=1.74, $CHCl_3$) (Lit: $[\alpha]_D^{RT}$ = not found). - ^{1}H-NMR (200 MHz): δ = 7.40-7.27 (m, 5H, arom H), 5.87-5.73 (m, 1H, C<u>H</u>=CH_2), 5.05-4.93 (m, 2H, CH=C<u>H</u>$_2$), 4.70-4.61 (d·t, J_1=3.8Hz, J_2=3.1Hz, 1H, C<u>H</u>(OH)), 2.17 (d, J=3.1Hz, 1H, O<u>H</u>), 2.16-2.03 (m, 2H, CH(OH)C<u>H</u>$_2$), 1.85-1.66 (m, 2H, C<u>H</u>$_2$), 1.57-1.22 (br.m, 2H, C<u>H</u>$_2$). - ^{13}C-NMR (75MHz): δ = 144.8, 138.6, 128.4, 127.5, 125.9, 114.7, 74.5, 38.5, 33.6, 25.1 - IR: (film) ν = 3383.2, 3063.1, 2934.1, 2859.8, 1639.9, 1493.2, 1453.7, 1062.8, 1027.8, 994.4, 911.1, - MS (FAB): m/z (%) = 176(M^+, 4), 158(1), 133(19), 120(11), 107(100), 105(11), 79(54), 77(26), 39(10), 27(7).

<u>(-)-1-Phenyl-5-methylhex-4-en-1-ol (17)</u>

Following the general procedure, 0.51 ml of benzaldehyde (0.005 mol) was allowed to react with a di(2-methylpent-2-enyl)zinc reagent, prepared from 10 ml of an 1.0 M $ZnCl_2$ solution and 19.0 ml of the corresponding Grignard reagent (1.05 M, Et_2O), in the presence of 0.856 g of **2** (17 mol%) and 1.80 ml of Ti(O^iPr)$_4$ (0.006 mol, 1.2 eq) in ether. Y: 89%, *S*/*R* = 98:2 (ee: 96%, GC, "S4")

$[\alpha]_D^n$ = -10.7 (c=1.60, $CHCl_3$) (Lit: $[\alpha]_D^n$ = not found) - ^{1}H-NMR (200 MHz): δ = 7.36-7.26 (m, 5H, arom H), 5.16-5.12 (m, 1H, C<u>H</u>=CR_2), 4.66 (t, J=5.7Hz, 1H, C<u>H</u>(OH)), 2.18-1.96 (m, 2H, C<u>H</u>$_2$), 2.05 (s, 1H, O<u>H</u>), 1.87-1.74 (br.m, 2H, C<u>H</u>$_2$), 1.71 (s, 3H, -C<u>H</u>$_3$), 1.56 (s, 3H, -C<u>H</u>$_3$) - ^{13}C-NMR (75MHz): δ = 144.8, 132.3, 128.4, 127.5, 125.9, 123.8, 74.2, 39.0, 25.9, 24.5, 17.7. - IR: (film) ν = 3374.3, 3028.9, 2965.6, 2925.9, 2855.9, 1947.1, 1704.8, 1601.9, 1493.3, 1452.8, 1376.4, 1202.9, 1061.3, 1022.2, 873.2, 830.2, 761.3 - MS: m/z (%) = 190(M^+, 24), 172(32), 157(38), 147(20), 133(64), 129(49), 119(47), 108(15), 107(100), 105(40), 104(49), 91(25), 83(16), 79(84), 78(17), 77(55), 69(34), 67(11), 55(44), 41(61), 27(34).

<u>(+)-1-Phenylheptan-1-ol (18)</u>

According to the general procedure, 0.98 ml of heptanal (0.007 mol) was converted to the title compound by a diphenylzinc reagent, prepared from 14 ml of an 1.0 M $ZnCl_2$ solution and 13.2 ml of phenylmagnesium bromide (2.12 M, Et_2O), in the presence of 1.045 g of **2** (15 mol%) and 2.50 ml of Ti(O^iPr)$_4$ (0.0084 mol, 1.2 eq) in ether. Y: 21% (very slow reaction), *R*/*S* = 81:19 (ee: 62%, GC, "S2")

Bp.: 135-137°C (7 mm). - $[\alpha]_D^{RT}$ = +7.8 (c=5.0, EtOH) (Lit: $[\alpha]_D^{RT}$ = not found). - ^{1}H-NMR (200 MHz): δ = 7.40-7.22 (br.m, 5H, arom H), 4.65 (t, J=5.9Hz, 1H, C<u>H</u>(OH)), 2.00 (s, 1H, O<u>H</u>), 1.90-1.62 (br.m, 2H, CH(OH)C<u>H</u>$_2$-), 1.42-1.20 (br.m, 8H, 4x -C<u>H</u>$_2$-), 0.87 (t, J=4.1Hz, 3H, C<u>H</u>$_3$).

<u>*S*-(+)-1-Phenylprop-2-en-1-ol (19)</u>

According to the general procedure, 0.51 ml of benzaldehyde (0.005 mol) with a divinylzinc reagent, prepared from 10 ml of an 1.0 M $ZnCl_2$ solution and 11.8 ml vinylmagnesium chloride (1.7 M, THF, Aldrich), in the presence of 0.660 g of **2** (13 mol%) and 1.80 ml of Ti(O^iPr)$_4$ (0.006 mol, 1.2 eq) in ether afforded **19** in 36% y. *S*/*R* = 92:8 (ee: 84%, GC, "S2").

Bp.: 111°C (18 mm). - $[\alpha]_D^{RT}$ = not taken, too little substance (Lit: $[\alpha]_D^{RT}$ = -5.19 (neat)[41]). - ^{1}H-NMR (200 MHz): δ = 7.38-7.26 (m, 5H, arom H), 6.13-5.97 (m, 1H, C<u>H</u>=CH_2), 5.37 (d, J=17.2Hz, 1H, C<u>H</u>(OH)), 5.21-5.16 (m, 2H, CH=C<u>H</u>$_2$), 2.62 (br.s, 1H, O<u>H</u>).

<u>(-)-1,3-Diphenylpropan-1-ol (20)</u>

As described in the general procedure, 0.61 ml of benzaldehyde (0.006 mol) was allowed to react with a zinc reagent, prepared from 12 ml of an 1.0 M $ZnCl_2$ solution and 31.2 ml of phenylethylmagnesium bromide (0.77 M, Et_2O), in the presence of 0.7063 g of **2** (12 mol%) and 2.14 ml of Ti(O^iPr)$_4$ (0.0072 mol, 1.2 eq) in ether. Y: 75%, op: 97% (GC-separation was not successful).

Bp.: 195°C (15 mm). - $[\alpha]_D^{RT}$ = -15.2 (c=5.56, EtOH) (Lit: $[\alpha]_D^{RT}$ = -15.6 (c=5.0, EtOH)[42]). - ^{1}H-NMR (200 MHz): δ = 7.40-7.21 (m, 10H, arom H), 4.70 (t, J=5.0Hz, 1H, C<u>H</u>(OH)), 2.90-2.62 (br.m, 2H, -C<u>H</u>$_2$-), 2.28-1.95 (br.m, 2H, -C<u>H</u>$_2$-), 2.10 (s, 1H, O<u>H</u>).

<u>1-Phenyl-3-(2',6'-dioxa-cyclohexyl)-propan-1-ol (21)</u>

Following the general procedure, 0.51 ml of benzaldehyde (0.005 mol) with a di(2(2',6'dioxa-cyclohexyl)ethyl)zinc reagent, prepared from 10 ml of an 1.0 M $ZnCl_2$ solution and 13.1 ml of the corresponding Grignard reagent (1.53 M, THF), in the presence of 0.614 g of **2** (13 mol%) and 1.80 ml of Ti(O^{i}Pr)$_4$ (0.006 mol, 1.2 eq) in ether yielded **21**. Y: 10% (very slow reaction, incomplete conversion), *S/R* = 92:8 (ee: 84%, GC, "S4").

$[\alpha]_D^{RT}$ = not measured (too little substance). - ^{1}H-NMR (200 MHz): δ = 7.34-7.23 (m, 5H, arom H), 4.84 (d·t, J_1=3.6Hz, J_2=3.3Hz, 1H, C<u>H</u>(OH)), 4.56 (t, J=4.8Hz, 1H, $CH_2C\underline{H}$=Cycl), 4.13-4.05 (m, 2H, O-C<u>H$_A$H$_B$</u>-CH$_2$-C<u>H$_A$H$_B$</u>-O), 3.81-3.68 (m, 2H, O-CH$_A$<u>H$_B$</u>-CH$_2$-CH$_A$<u>H$_B$</u>-O), 2.78 (d, J=3.6Hz, 1H, O<u>H</u>), 2.10-2.03 (br.m, 1H, O-CH$_2$-C<u>H$_A$H$_B$</u>-CH$_2$-O), 1.89-1.68 (br.m, 4H, -CH(OH)-(C<u>H</u>$_2$)$_2$-), 1.36-1.34 (m, 1H, O-CH$_2$-CH$_A$<u>H$_B$</u>-CH$_2$-O). - ^{13}C-NMR (75MHz): δ = 144.8, 128.3, 127.3, 125.8, 102.0, 74.0, 66.9, 33.4, 31.5, 25.7. - IR: (film) ν = 3431.0, 2960.6, 2854.3, 2731.8, 2659.7, 1725.9, 1603.2, 1452.5, 1404.5, 1378.7, 1286.0, 1244.8, 1146.0, 1083.2, 999.3, 720.2. - MS : m/z (%) = 221 (M^+-1, 3), 147(23), 146(100), 120(66), 117(33), 116(29), 107(42), 100(27), 87(89), 79(43), 78(13), 77(39), 59(42), 58(71).

<u>(-)-1-Phenyl-8,10-dioxa-undecan-1-ol (22)</u>

Following the general procedure, 0.51 ml of benzaldehyde (0.005 mol) was allowed to react with a di(2,4-dioxa-decyl)zinc reagent, prepared from 10 ml of an 1.0 M $ZnCl_2$ solution and 21.5 ml of the corresponding Grignard reagent (0.93 M, THF), in the presence of 0.910 g of **2** (18 mol%) and 1.80 ml of Ti(O^{i}Pr)$_4$ (0.006 mol, 1.2 eq) in ether. Y: 68%, *S/R* = 92:8 (ee: 84%, GC, "S4").

$[\alpha]_D^{RT}$ = -10.3 (c=3.05, EtOH) (Lit: $[\alpha]_D^{RT}$ = not found). - ^{1}H-NMR (200 MHz): δ = 7.34-7.26 (m, 5H, arom H), 4.72-4.69 (m, 1H, C<u>H</u>(OH)), 4.58 (s, 2H, O-C<u>H</u>$_2$-O), 3.50 (t, J=6.4Hz, 2H, C<u>H</u>$_2$-OCH$_2$O-), 3.33 (s, 3H, OC<u>H</u>$_3$), 2.23-2.05 (br.s, 1H, O<u>H</u>). - ^{13}C-NMR (75MHz): δ = 145.0, 128.4, 127.4, 125.9, 96.4, 74.5, 67.8, 55.0, 39.1, 29.6, 29.3, 26.1, 25.8 - IR: (film) ν = 3458.1, 2933.7, 2861.5, 1704.7, 1602.3, 1453.9, 1386.2, 1204.6, 1145.4, 1112.9, 1045.0, 919.4 - MS : m/z (%) = 251(M^+-1, <1), 220(3), 207(5), 151(11), 114(10), 113(28), 107(72), 105(18), 91(10), 85(16), 79(25), 77(15), 71(11), 68(12), 56(14), 55(13), 45(100), 43(18), 41(15), 29(10), 28(18).

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