# The Regioisomeric Triphenylaminoethanols – Comparison of their Efficiency in Enantioselective Catalysis

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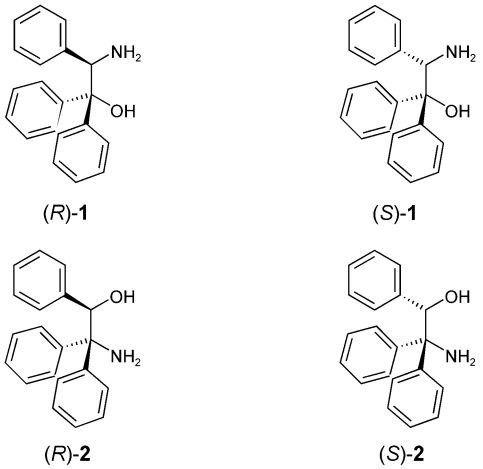
**Abstract:** Both enantiomers of the novel amino alcohol (*R*)- and (*S*)-**2** are prepared from the corresponding enantiomer of the mandelic acid-derived ethanediol **3**. The regioisomeric amino alcohols **1** and **2** are converted into the imines **7** and **8**, respectively. Titanium complexes **9** and **10** derived therefrom are used as catalysts for the addition of diethylzinc to benzaldehyde and yield the alcohol **11** in up to 92% ee. On the other hand, the chloro-substituted titanium complexes **14** and **15** are able to mediate the Torgov cyclization reaction of the diketone **16** to give the estrone derivative **17**. In both reactions titanium complexes **10** and **15** derived of the novel amino alcohol **2** give higher enantioselectivities than the complexes **9** and **14** that are based on the regioisomeric amino alcohol **1**.

**Keywords:** amino alcohols; asymmetric catalysis; cyclization; N,O ligands; nucleophilic addition; titanium

## Introduction

In various asymmetric syntheses, the diarylhydroxymethyl group has turned out to play a key role. Although not a stereogenic unit – at least not a permanent one – it proved itself to be crucial and led to an enhancement of stereoselectivity in many cases.[1] Among the chiral reagents containing the diarylhydroxymethyl group are fairly well known representatives like the TADDOLs,[2] triphenyl-glycol-derived carboxylic esters,[3] cyclic sulfides,[4] and the so-called CBS-catalysts.[5,6] In these and various other cases,[7] the diarylhydroxymethyl group, which may occur either in its free or deprotonated or protected from, is essential for sufficient stereoselectivity. The key role of this moiety has been studied intensively and the way its acts as a temporary stereogenic unit has been made plausible by transition state models based on crystal structure parameters of intermediates[8] and calculations.[9]

The diphenylhydroxymethyl group was introduced in chiral amino alcohols as early as in the first part of the last century, when McKenzie and Wills were able to obtain 2-amino-1,1,2-triphenylethanol (**1**) from phenylglycinate.[10] This readily available chiral compound has been used in recent years for enantioselective reductions of ketones[11] and allylic oxidations.[12] On the other hand, 2-amino-1,2,2-triphenylethanol (**2**), a regioisomer of McKenzie's amino alcohol, has neither been prepared in enantiomerically pure form nor used as a chiral auxiliary reagent (Scheme 1). Wondering whether the new amino alcohols (*R*)- and (*S*)-**2**, which contain as a structural unit the diphenyl*amino*methyl moiety,[13] might be suitable reagents for stereoselective conversions,[14] an efficient synthesis of (*R*)- and (*S*)-**2** had to be developed first.[15] Subsequently, alkoxy-imine-titanium complexes derived of the regioisomeric amino alcohols **1** and **2** were generated and tested in two cases of enantioselective catalysis.




**Scheme 1.** The regioisomeric triphenylaminoethanols **1** and **2**.

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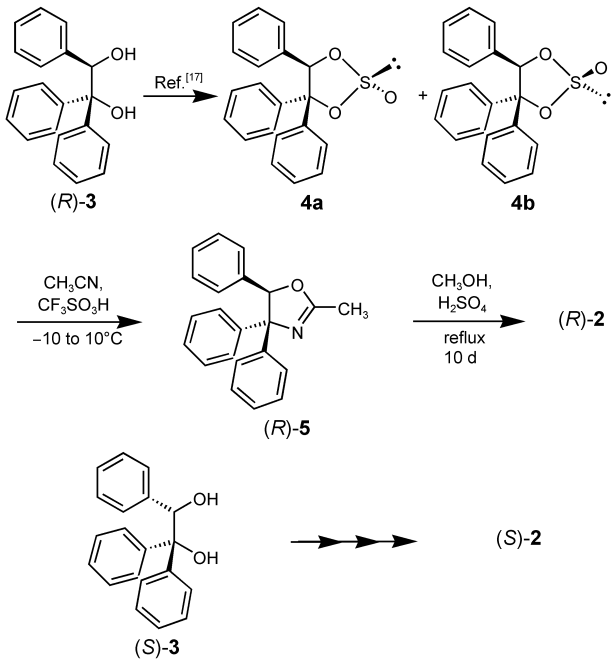
## Results and Discussion

The readily accessible mandelic-acid derived reagents (*R*)- and (*S*)-triphenylglycol **3**,[16] both commercially available, were chosen as starting materials for the synthesis of the corresponding enantiomer of the amino alcohol **2**. Thus, (*R*)-diol **3** was first treated with thionyl chloride in the presence of triethylamine to afford the diastereomeric sulfites **4a** and **4b** that were formed in a ratio of 90 : 10.[17] The diastereomeric mixture of **4a**/**b** was used in the following step without separation. Treatment with triflic acid in acetonitrile furnished the oxazoline (*R*)-**5**, a conversion that is obviously a hitherto unknown variant of the Ritter reaction.[18] Finally, the amino alcohol (*R*)-**2** was prepared from the oxazoline (*R*)-**5** by sulfuric acid-mediated methanolysis. Following the same protocol, (*S*)-**2** was prepared from (*S*)-**3** (Scheme 2). Racemic amino alcohol **2** is accessible by 1,3-dipolar cycloadditions of various benzhydrylisonitrile ylides and benzaldehyde.[19] After the synthesis of (*R*)- and (*S*)-**2** starting from the corresponding enantiomer of triphenylglycol **3** had been communicated,[15] an alternative access to non-racemic **2** based on an asymmetric epoxidation was reported.[20]



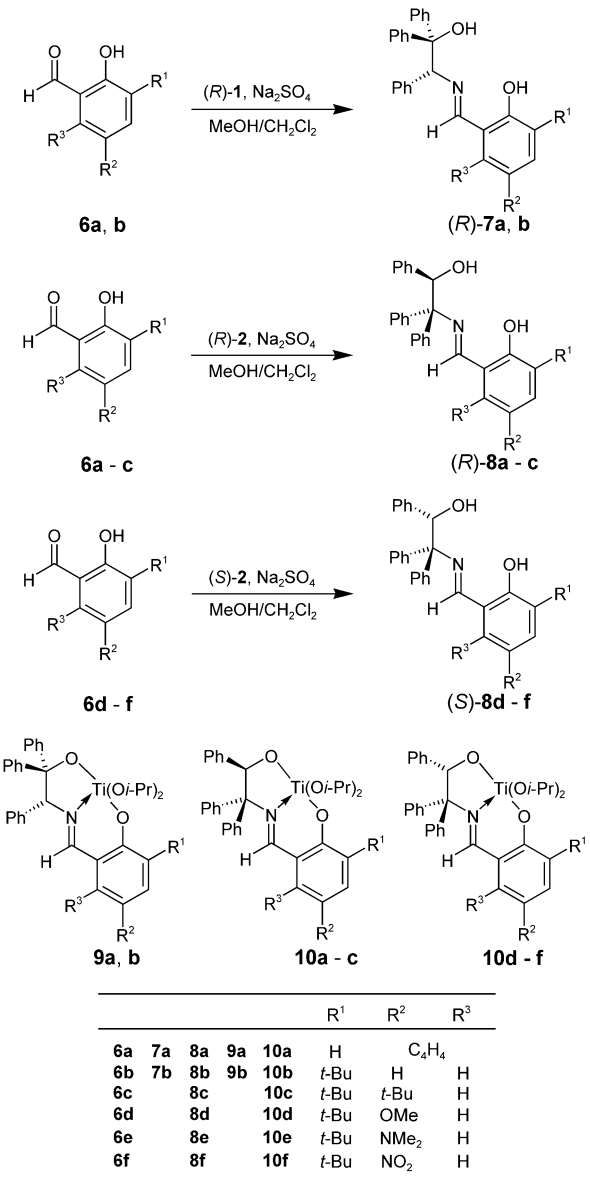

**Scheme 2.** Synthesis of (*R*)- and (*S*)-2-amino-1,2,2-tripheny-lethanol **2**.

The major compound of the sulfites **4a** and **4b** could be isolated, and its configuration, [$R_c$,$S_s$]-**4a**, was determined by chemical correlation[17] as well as by a crystal structure analysis.[21] It turned out that in the diastereomer **4a** the phenyl residue at the stereogenic carbon atom and the exocyclic oxygen atom are oriented in a *trans* configuration. Diastereomerically pure sulfite **4a** has been used as starting material for syntheses of enantiomerically pure sulfoxides.[17]

The imines **7a**,**b** were prepared from the amino alcohol (*R*)-**1** by condensation with *ortho*-formylphenols **6a**,**b** as described previously.[22] In an analogous way, the reaction of (*R*)-**2** with the aldehydes **6a – c** led to the imines **8a – c**, whereas the aldehydes **6d – f**[23] were condensed with the enantiomeric amino alcohol (*S*)-**2** to give the imines (*S*)-**8d – f**. Both regioisomeric structures **7** and **8** served us as tridentate ligands in mono- and bis-chelated titanium(IV) complexes. The mono-chelated titanium complexes **9** and **10** were usually not isolated but generated *in situ* by treatment of the imines **7** or **8** with titanium tetraisopropoxide and subsequent evaporation of 2-propanol (Scheme 3). Nevertheless, several examples of the titanium complexes **9** and **10** were isolated and characterized by their NMR spectra.[22]

First, they were used as catalysts in enantioselecitve additions of diethylzinc to benzaldehyde[24] (Scheme 4). As shown in Table 1, efficient conversions were feasible with all of the titanium complexes as far as the chemical yield was concerned. In all cases, an *lk* topicity was observed in that sense that *R* configurated imine ligands directed the addition of diethylzinc predominantly to the *Re* face of the aldehyde and, accordingly the enantiomeric ligands to the *Si* face. This result was obtained with both regioisomeric reagents. However, only moderate enantioselectivities were provided by the imines **7** that are derived from the amino alcohol **1** (entries 1 and 2). When, on the other hand, regioisomeric imines **8** were incorporated in the corresponding titanium complexes, distinctly higher enantioselectivities could be obtained (entries 3 – 6). A *t*-butyl substituent in the *ortho* position to the phenol residue turned out to be crucial for stereoselectivity (entries 1 *vs.* 2, 3 *vs.* 4). Being aware of the fact that, in asymmetric syntheses, enantioselectivity is not only determined by the sterical hindrance of substituents but might also by influenced by their electronic properties,[25] electron-donating and -withdrawing substituents were introduced into the *para* position to the phenolic moiety. Thus the performance of the titanium complexes **10d – f**, which were generated *in situ* from the corresponding imines **8d – f**, in the diethylzinc addition protocol was studied. It turned out that the presence of electron-donating substituents ($NMe_2$ and OMe) enhanced the enantioselectivity (entries 6 and 7), the optimum result being obtained with the titanium complex having methoxy-substituted imine **8d** as a chelating ligand (entry 6). The introduction of the electron-withdrawing nitro group, on the other hand, leads to a slightly reduced enantioselectivity (entry 8). As a result of the comparison between the regioisomeric imines **7** and **8**, it is more efficient to have a stereogenic center bearing the hydroxy than the amino group. In all cases, (*R*)-1-phenylpropanol **11** was obtained from the (*R*) enantiomers of the imines (*R*)-**7a, b** and (*R*)-**8a – c**. Accord-

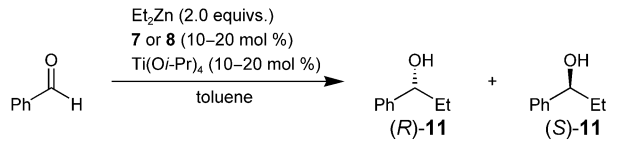



| | | | | | $R^1$ | $R^2$ | $R^3$ |
|---|---|---|---|---|---|---|---|
| **6a** | **7a** | **8a** | **9a** | **10a** | H | $C_4H_4$ | |
| **6b** | **7b** | **8b** | **9b** | **10b** | *t*-Bu | H | H |
| **6c** | | **8c** | | **10c** | *t*-Bu | *t*-Bu | H |
| **6d** | | **8d** | | **10d** | *t*-Bu | OMe | H |
| **6e** | | **8e** | | **10e** | *t*-Bu | $NMe_2$ | H |
| **6f** | | **8f** | | **10f** | *t*-Bu | $NO_2$ | H |

**Scheme 3.** Imines **7**, **8** and monochelated titanium complexes **9**, **10** derived from the regioisomeric amino alcohols **1** and **2**, respectively.

ingly, (*S*)-**11** was formed when the ligands (*S*)-**8d – f** were used.

Titanium complexes like **9** and **10** carrying alkoxy ligands are relatively weak Lewis acids compared to the corresponding halides. Thus, in order to obtain imine-




**Scheme 4.** Enantioselective addition of diethylzinc to benzaldehyde mediated by the imines **7** or **8** and titanium tetraisopropoxide.

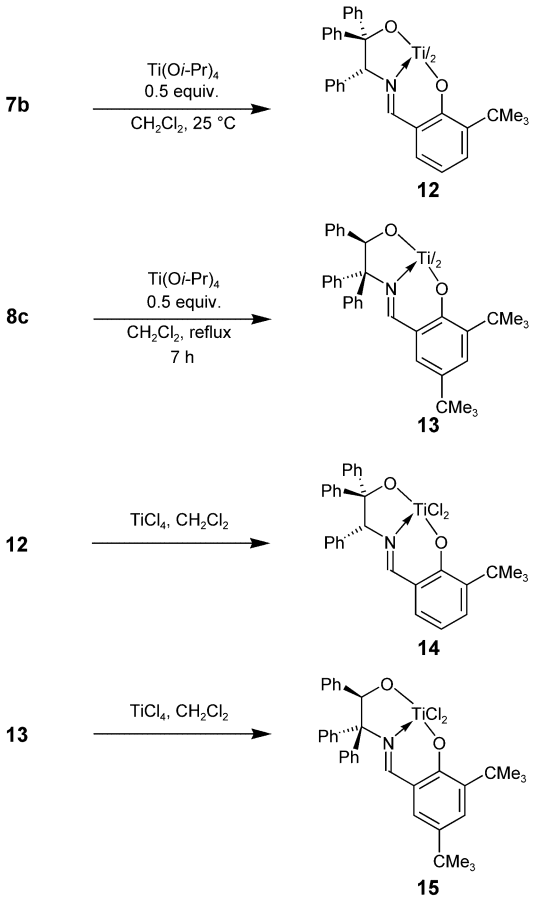
**Table 1.** Addition of diethylzinc to benzaldehyde, catalyzed by imines **7**/**8** and $Ti(Oi\text{-}Pr)_4$.

| Entry | Imine | **11** | | |
|---|---|---|---|---|
| | | Yield [%] | ee [%] | Configuration |
| 1 | (*R*)-**7a**[a] | 87 | 21 | *R* |
| 2 | (*R*)-**7b**[a] | 73 | 58 | *R* |
| 3 | (*R*)-**8a**[a] | 96 | 42 | *R* |
| 4 | (*R*)-**8b**[a] | 100 | 82 | *R* |
| 5 | (*R*)-**8c**[b] | 100 | 79 | *R* |
| 6 | (*S*)-**8d**[b] | 100 | 92 | *S* |
| 7 | (*S*)-**8e**[b] | 100 | 87 | *S* |
| 8 | (*S*)-**8f**[a] | 95 | 84 | *S* |

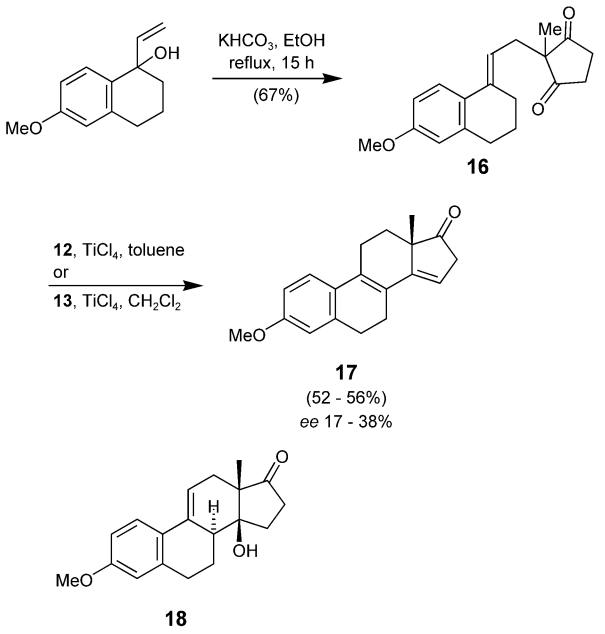
[a] 20 mol % imine/$Ti(Oi\text{-}Pr)_4$, 0 °C, 16 – 24 h.
[b] 10 mol % imine/$Ti(Oi\text{-}Pr)_4$, $-20\,^{\circ}C \rightarrow -10\,^{\circ}C$, 12 – 15 h.

derived titanium complexes as potential catalysts with higher Lewis acidity, the chloro complexes were generated. It turned out that the optimal access to these Lewis acids was provided by the bis-chelated complexes **12** and **13**, which were easily obtained when imines **7b** and **8c** were reacted with titanium tetraisopropoxide in a molar ratio of 2:1. They proved themselves to be compounds that are stable towards air, moisture, and protic solvents, could be purified by column chromatography, and their structures were elucidated.[22] Although a series of diastereomers could form from a combination of the tridentate ligands **7** or **8** with titanium in an octahedral arrangement, usually one diastereomer arose in excess or even exclusively, depending on the substitution pattern. Either the diastereomerically pure bis-chelated complexes **12** and **13** or the mixture of diastereomers were converted into the chloro complexes **14** and **15** by treatment with titanium tetrachloride (Scheme 5).

Looking for an application of the novel halo complexes as Lewis-acidic chiral catalysts, we turned to the cyclization of methyl secone **16**, the key step of the well-known Torgov synthesis,[26] which, undoubtedly, "belongs to the simplest conceivable strategies for the synthesis of steroids with estrane ... skeleton."[27] The conversion of methyl secone **16** into the tetracyclic product **17**, a valuable precursor of estrone, is the chirogenic step of the reaction sequence. Among the attempts for the enantioselective syntheses of estrone, the dissymetrization of the diketone **16** has turned out to be very efficient.[28] Nevertheless, the additional reduction step can be avoided if the secone **16** is converted *directly* into the tetracyclic product **17** by means of an enantioselectively catalyzed cyclization (Scheme 6). So far, only one attempt has been made in order to realize this concept, and the Torgov diene product **17** was obtained in a maximum of 70% ee. For this purpose, an estrane-based titanium complex had to be used as a chiral Lewis acid.[29] Another problem this protocol




**Scheme 5.** Synthesis of bis-chelated titanium complexes **12**, **13** and generation of dichloro complexes **14**, **15**.




**Scheme 6.** Cyclization of *meso*-diene **16** to Torgov diene **17**, mediated by Lewis acids generated from titanium complexes **12** or **13**.

encounters is the formation of a carbinol **18** as a by-product that arises with lower enantiomeric purity (30–36% ee).

In order to bring about enantioselective Torgov cyclizations of the secone **16**, the bis-chelated complexes **12** and **13** were first converted into the dichloro complexes **14** and **15** by treatment with equimolar amounts of titanium tetrachloride in dichloromethane or toluene in the presence of molecular sieves 4 Å. The Lewis acids **14** and **15**, thus generated *in situ* and used in a ratio of 0.2 molar equivalents, were able to mediate the cyclization of the diketone **16**. Remarkably, the carbinol **18** did not form at all and the diene **17**, a useful intermediate in estrone synthesis,[28,30] was the only product. It turned out that this compound was obtained in the desired (*S*)-configuration, when those titanium complexes **14** and **15** were used that are based on the (*S*)-enantiomer of the amino alcohols **1** and **2**. However, the enantiomeric excesses obtained were moderate: The enantioselectivity was only 17% ee when the reaction was mediated by chlorotitanate **14** (toluene) and 38% ee in the case of **15** (dichloromethane). Nevertheless, there is a substantial influence on the enantioselectivity exhibited by the tridentate ligand of the corresponding titanium complex (**14** *vs.* **15**). Remarkably, here again, the ligands that are based on the amino alcohol (*S*)-**2** are superior to those generated from phenylglycine-derived (*S*)-**1**. Thus, compared to the low enantioselectivity obtained by means of the titanium complex **14**, the catalyst **15** provided an enhancement of the enantiomeric excess.

## Conclusions

In two cases of enantioselective catalysis, titanium complexes that are generated from the novel amino alcohol **2** proved themselves to be superior to those derived of the regioisomeric amino alcohol **1**. As both enantiomers of **2** are accessible from the corresponding mandelic acid derivative **3**, a novel amino alcohol has become available, which could serve as a chiral building block or reagent in various other transformations. Aside from the two cases of asymmetric catalysis outlined above, triphenylaminoethanols (*R*)- and (*S*)-**2** also provided an access to new chiral dopants, which here again were more efficient than those derived of the amino alcohol **1**. This new application of the regioisomeric triphenylethanol that will be published elsewhere seems to meet some commercial interest.[31]

# Experimental Section

## General Remarks

Melting points (uncorrected) were determined with a Büchi melting point apparatus 540. Specific rotations were determined with a Perkin-Elmer 341 polarimeter. IR spectra: Bruker Vector 22. Mass spectra: Varian MAT 311 A. NMR spectra: Varian VXR 200 and VXR 300 and DRX 500. The spectra were recorded in $CDCl_3$ with TMS as internal standard. TLC: Silica gel 60 $F_{254}$ (Merck). Column chromatography: Macherey-Nagel-Kieselgel 60 and Merck Kieselgel 60, mesh size 0.04–0.063. All titanium-mediated reactions were performed under an atmosphere of dry nitrogen or argon. Reactions at temperatures below $-20\,^{\circ}C$ were monitored by a thermocouple connected to a resistance thermometer (Ebro). General remarks concerning the handling of moisture-sensitive compounds are given in Ref.[32]

## (2*S*,5*R*)- and (2*R*,5*R*)-4,4,5-Triphenyl-1,3,2-dioxathiolane-2-oxide (4a and 4b)

Prepared according to Ref.[17] as a mixture of diastereomers in 88% yield. The crude product, obtained from (*R*)-diol **3** (22.3 g, 76.9 mmol) as an oil was purified by chromatography on a short column (approximately 15 cm), which was protected against light. The yellowish eluate was concentrated, the oily residue was treated with 50 mL of *n*-hexane and stirred vigorously. The white precipitate thus formed was filtered through a sinter, washed with *n*-hexane and dried in an oil-pump vacuum (0.05 mbar, 40 °C, light protection). The diastereomeric mixture of **4a** and **4b** thus obtained in 88% yield (22.8 g) was kept at $-18\,^{\circ}C$. For analytical and spectroscopic data, see Ref.[17]

In an analogous way, a mixture of (2*R*,5*S*)-*ent*-**4a** and (2*S*,5*S*)-*ent*-**4b** was prepared from (*S*)-diol **3**.

## (*R*)-2-Methyl-4,4,5-triphenyl-4,5-dihydrooxazole (5)

Under argon, a solution of **4a**, **b** (19 g, 56.5 mmol) in 90 mL of absolute acetonitrile was stirred in a 250-mL three-necked flask equipped with a magnetic stirrer, a pressure-equalizing dropping funnel, a septum and a connection to the combined argon/vacuum line. The solution was cooled to $-10\,^{\circ}C$ the temperature being monitored by an electronic resistance thermometer the thermocouple of which was introduced through the septum. The dropping funnel was charged with trifluoromethanesulfonic acid (10 mL, 113 mmol) while a stream of argon was maintained. The acid was added dropwise within 1 h, and the temperature was not allowed to exceed $-5\,^{\circ}C$. The thermocouple was removed (to avoid corrosion) and the mixture was stirred at $-10\,^{\circ}C$ for 16 h.

A slight precipitate consisting of benzhydryl phenyl ketone was filtered and washed with *n*-hexane (50 mL). The combined filtrates were diluted with $H_2O$ (100 mL) and brought to pH = 8 by the addition of 2.5 M NaOH under vigorous stirring and cooling. The mixture was concentrated in a rotary evaporator in order to remove *n*-hexane and acetonitrile. The residue was treated with $CH_2Cl_2$ (150 mL) and stirred vigorously for 10 min. The phases were separated and the aqueous layer was extracted with $CH_2Cl_2$ (2 × 50 mL). The combined organic layers were dried with $MgSO_4$ and concentrated under vacuum to give light yellow, viscous crude **5**, which contained about 5% of benzhydryl phenyl ketone, but was sufficiently pure to be used in the following reaction.

Analytically pure samples of **5** were obtained by column chromatography to give white, crystalline material; yield: 11.3 g (64%); mp 58.5–60.0 °C; $R_f = 0.5$ (*n*-hexane/ethyl acetate, 3.5:1). IR (KBr): $\nu = 3070, 3060, 3030, 2360, 1660, 1600, 1495, 1445, 1385, 1250, 1210, 975\ cm^{-1}$; $^1H$ NMR (300 MHz): $\delta = 2.25$ (s, 3H, $CH_3$), 6.24 (s, 1H, 5-H), 6.91–7.07 (m, 10H, aromatic H); $^{13}C$ NMR (75 MHz): $\delta = 14.2$ ($CH_3$), 83.5 (C-4), 89.8 (C-5), 126.2–128.4 (aromatic C), 137.5, 141.9, 146.6 (aromatic ipso-C), 163.7 (C-2); MS (EI): $m/z = 314$ ($M^+ + 1$, 1%), 313 ($M^+$, 4%), 260 (10%), 208 (46%), 207 (100%), 167 (21%), 166 (75%), 165 (69%); anal. calcd. for $C_{22}H_{19}NO$: C 84.31, H 6.11, N 4.47; found: C 84.35, H 5.94, N 4.23; (*R*)-**5**: $[\alpha]_D^{20}$: +231 (*c* 1, $CHCl_3$).

(*S*)-**5** was prepared analogously from *ent*-**4a/b**: $[\alpha]_D^{20}$: −233 (*c* 1, $CHCl_3$).

## (*R*)-2-Amino-1,2,2-triphenylethanol (2)

A solution of (*R*)-**5** (10.9 g, 34.8 mmol) in absolute methanol (300 mL) was stirred in a 1-L two-necked flask equipped with a magnetic stirrer, a pressure-equalizing dropping funnel, which was closed with a stopper and reflux condenser with a drying tube. The mixture was cooled under stirring to 0 °C and concentrated $H_2SO_4$ (37 mL) was added within 30 min. The cooling bath was removed, the dropping funnel was replaced by a stopper, and the mixture was refluxed for 10 d. After cooling to 25 °C, the mixture was diluted with water (250 mL), methanol was removed in a rotary evaporator and the remaining aqueous mixture was further concentrated to about half of its volume. The precipitate (benzhydryl phenyl ketone) formed thereby was removed by filtration and the filtrate was washed twice with $Et_2O$. The aqueous layer (containing the hydrogen sulfate of **2**) was cooled to 0 °C and treated with 2.5 M NaOH (300 mL), which was added slowly. Thereby, a white suspension formed. After the addition of $CH_2Cl_2$ (150 mL) and stirring for 10 min, the precipitate had dissolved completely. The organic layer was separated, and the aqueous phase was extracted with $CH_2Cl_2$ (2 × 100 mL). The combined organic layers were washed with brine, dried with $MgSO_4$ and concentrated in a rotary evaporator to give a colorless solid. Recrystallization from toluene gave white crystalline **2**; yield: 8.87 g (88%); mp 152.0–153.5 °C [Ref.[19a]: 141–142° (*rac*-**2**); Ref.[19b]: 143–144 °C (*rac*-**2**)]. IR (KBr): $\nu = 3380, 3100, 3080, 3040, 2900, 1600, 1500, 1450, 1195, 1060, 1040, 1030, 960, 890, 835\ cm^{-1}$; $^1H$ NMR (500 MHz): $\delta = 1.90$ (broad s, 2H, $NH_2$), 3.25 (broad s, 1H, OH), 5.58 (s, 1H, 1-H), 6.86–6.88 (m, 1H, aromatic H), 7.02–7.32 (m, 11H, aromatic H), 7.55–7.57 (m, 2H, aromatic H); $^{13}C$ NMR (75 MHz): $\delta = 65.6$ (C-2), 77.4 (C-1), 126.4–128.2 (aromatic C), 139.7, 145.3, 145.8 (aromatic ipso-C); MS (FAB; NAB): $m/z = 290$ ($M^+ + 1$, 9%), 289 ($M^+$, 2%), 274 (22%), 273 (44%), 195 (20%), 183 (17%), 182 (100%), 167 (25%), 165 (18%), 1107 (17%), 105 (24%), 104 (26%); anal. calcd. for $C_{20}H_{19}NO$: C 83.01, H 6.62, N 4.84; found: C 83.16, H 6.7, N 4.69.

### 2-Hydroxy-3-(1,1-dimethylethyl)-5-nitrobenzaldehyde (6f)

A solution of **6b** (5.0 g, 2.80 mmol) in acetic acid (8 mL) was stirred in an ice bath at 5 °C. Fuming nitric acid (2.8 mL, 68 mmol) was added slowly by means of a dropping funnel at such a rate that the temperature did not exceed 10 °C. The cooling bath was removed and the mixture was stirred at 25 °C for 1 h. Then, the solution was poured into ice/water (250 mL) under vigorous stirring. The orange precipitate formed thereby was filtered through a sinter, washed with water (50 mL), recrystallized twice from ethanol and dried in oil-pump vacuum to give **6f**; yield: 4.3 g (68%), mp 90.4–91.0 °C. $^1$H NMR (500 MHz): δ = 1.47 [s, 9H, C(CH$_3$)$_3$], 8.41 (d, *J* = 2.9 Hz, 1H, 4-H or 6-H), 8.42 (d, *J* = 2.9 Hz, 1H, 6-H or 4-H), 9.98 (s, 1H, CHO), 12.44 (s, 1H, OH).

### 2-Hydroxy-5-(dimethylamino)-3-(1,1-dimethylethyl)benzaldehyde (6e)

In a hydrogenation apparatus, a mixture of **6f** (1.50 g, 6.72 mmol), ethanol (40 mL), aqueous formaldehyde solution (37%, 4.5 mL) and palladium on charcoal (10%, 0.17 g) was hydrogenated at normal pressure for 12 h under stirring. The red-brownish mixture was filtered through celite in a sinter and the residue was washed three times with ethanol (10 mL). The combined filtrates were concentrated in a rotary evaporator, the residue was dissolved in the minimum amount of $CH_2Cl_2$ and submitted to column chromatography (*n*-hexane/ethyl acetate, 5:1) to give crystalline **6e**; yield: 0.50 g (34%); mp 133.7–134 °C; $R_f$ = 0.4 (*n*-hexane/ethyl acetate, 5:1). IR (KBr): ν = 3450, 3000, 2950, 1715, 1650, 1610, 1490, 1460, 1435, 1355, 1265, 1180, 995, 880, 830, 710 cm$^{-1}$; $^1$H NMR (500 MHz): δ = 1.43 [s, 9H, C(CH$_3$)$_3$], 2.89 [s, 6H, N(CH$_3$)$_2$], 6.72 (d, *J* = 3.2 Hz, 1H, 4-H or 6-H), 7.15 (d, *J* = 3.2 Hz, 1H, 6-H or 4-H), 9.85 (s, 1H, CHO), 11.28 (s, 1H, OH); $^{13}$C NMR (125 MHz): δ = 29.2 [C(*C*H$_3$)$_3$], 35.1 [*C*(CH$_3$)$_3$], 41.9 [N(CH$_3$)$_2$], 114.7 (C-4 or C-6), 120.3 (C-1), 122.8 (C-6 or C-4), 138.9 (C-5), 144.3 (C-3), 154.2 (C-2), 197.3 (CHO); MS (CI; NH$_3$): *m/z* = 238 (M$^+$ + NH$_3$, 32%), 222 (M$^+$ + 1, 15%), 221 (M$^+$, 100%); anal. calcd. for $C_{13}H_{19}NO_2$: C 70.56, H 8.65, N 6.33; found: C 70.48, H 8.48, N 6.60.

**Imines 7a, b** were prepared as described in Ref.[22]

### Preparation of Imines 8a–f; General Procedure

A 100-mL two-necked flask was equipped with a magnetic stirrer, a reflux condenser, a septum, and a connection to the combined argon/vacuum line and charged with (*R*)- or (*S*)-**2** (1.15 g, 4.0 mmol) and dry $Na_2SO_4$ (1.2 g, 8.5 mmol). In the case of the preparation of the imine **8d**, molecular sieve 3 Å, which had been crushed with a pistil and mortar, was used instead of $Na_2SO_4$. The air in the flask was replaced with argon, and absolute $CH_3OH$ (10 mL) and $CH_2Cl_2$ (10 mL) were injected by syringe. In case of the imine **8d**, methanol was used exclusively. A solution of the corresponding 2-formylphenol **6** in absolute $CH_3OH$ (15 mL) was added dropwise to the stirred suspension at 25 °C. Stirring was continued under the conditions given below. The drying agent was removed by suction filtration, the filtrate was concentrated in a rotary evaporator and the residue was purified by column chromatography to give the yellow to orange products. According to this procedure, the following compounds were obtained:

**(*R*)-1-{[(2-Hydroxy-1,1,2-triphenylethyl)imino]methyl}-2-naphthol (8a)**: Prepared from (*R*)-**2** (4.0 mmol) and **6a** (4.0 mmol); reaction conditions: 20 h, 60 °C. $R_f$ = 0.6 ($CHCl_3$/ethyl acetate, 10:1); yield: 0.97 g (55%); mp 110–112 °C (decomp.), $[\alpha]_D^{20}$: +109 (*c* 1, $CHCl_3$). IR (KBr): ν = 3415, 3060, 3030, 1620, 1580, 1545, 1495, 1445, 1350, 1180, 835 cm$^{-1}$; $^1$H NMR (500 MHz): δ = 2.88 [d, *J* = 2.1 Hz, 1H, PhCH(O*H*)], 5.71 [d, *J* = 2.1 Hz, 1H, PhC*H*(OH)], 6.74–6.75 (m, 1H, phenyl H), 6.92 (d, *J* = 9.3 Hz, 1H, 3-H), 7.05–7.20 (m, 9H, aromatic H), 7.26 (dt, $J_d$ = 1.4 Hz, $J_t$ = 8.2 Hz, 1H, 7-H), 7.35–7.39 (m, 3H, aromatic H), 7.47 (d, *J* = 8.2 Hz, 1H, 8-H), 7.53–7.58 (m, 3H, aromatic H), 7.67 (d, *J* = 9.3 Hz, 1H, 4-H), 8.71 (d, *J* = 8.5 Hz, 1H, $Ph_2CN{=}CHC{=}C{-}OH$, $^3J$ = due to chelation with ArOH), 15.37 (d, *J* = 8.5 Hz, 1H, ArOH); $^{13}$C NMR (125 MHz): δ = 75.0 [$Ph_2C$(N)], 78.3 [PhCH(OH)], 107.1 (C-1), 118.1 (C-8), 122.8 (C-6), 124.8 (C-3), 126 (C-10), 127.4–130 (aromatic C), 134.1 (C-9), 137.5 (C-4), 138.8, 141.6, 142.1 (aromatic ipso-C), 159.3 (NCHAr), 176.1 (C-2); MS (FAB; NBA, NaI): *m/z* = 467 (M$^+$ + 1 + Na, 28%), 466 (M$^+$ + Na, 68%), 337 (43%), 336 (100%), 167 (66%), 165 (93%), 152 (39%), 139 (21%).

**(*R*)-2-(1,1-Dimethylethyl)-6-{[(2-hydroxy-1,1,2-triphenylethyl)imino]methyl}phenol (8b)**: Prepared from (*R*)-**2** (4.0 mmol) and **6b** (4.0 mmol); reaction conditions: 8 h, 60 °C. $R_f$ = 0.5 (*n*-hexane/ethyl acetate, 5:1); yield: 0.96 g (54%); $[\alpha]_D^{20}$: +58 (*c* 1, $CHCl_3$). IR (KBr): ν = 3440, 3070, 3030, 3000, 2960, 2910, 1620, 1495, 1435, 1270, 1200, 1145, 1090, 855 cm$^{-1}$; $^1$H NMR (500 MHz): δ = 1.48 [s, 9H, C(CH$_3$)$_3$], 2.26 [d, *J* = 3.8 Hz, 1H, PhCH(O*H*)], 5.60 [d, *J* = 3.8 Hz, 1H, PhC*H*(OH)], 6.73–6.75 (m, 2H, aromatic H), 6.77 (t, *J* = 7.7 Hz, 1H, 4-H), 6.98 (dd, *J* = 7.7 Hz, *J* = 1.6 Hz, 1H, 3-H or 5-H), 7.03–7.41 (m, 14H, aromatic H), 8.05 (s, 1H, NCHAr), 14.08 (s, 1H, ArOH); $^{13}$C NMR (125 MHz): δ = 29.3 [C(*C*H$_3$)$_3$], 34.9 [*C*(CH$_3$)$_3$], 77.8 [$Ph_2$C(N)], 78.5 [PhCH(OH)], 117.7 (C-4), 118.8 (C-6), 127.0–130.3 (aromatic C), 130.9 (C-3 or C-5), 137.5, 139.6, 142.7, 143.5 (aromatic ipso-C), 160.5 (C-1),167.8 (NCHAr); MS (FAB; NBA): *m/z* = 450 (M$^+$ + 1, 5%), 343 (36%), 342 (100%), 326 (12%), 178 (14%), 167 (20%), 165 (30%); anal. calcd. for $C_{31}H_{31}NO_2$: C 82.82, H 6.95, N 3.12; found: C 82.63, H 7.09, N,3.25.

**(*R*)-2,4-Bis(1,1-dimethylethyl)-6-{[(2-hydroxy-1,1,2-triphenylethyl)imino]methyl}phenol (8c)**: Prepared from (*R*)-**2** (4.0 mmol) and **6c** (4.0 mmol); reaction conditions: 12 h reflux; $R_f$ = 0.4 (*n*-hexane/EtOAc, 7:1); yield: 1.07 g (53%); $[\alpha]_D^{20}$: +92 (*c* 1, $CHCl_3$). IR (KBr): ν = 3595, 3445, 3060, 3030, 2955, 2855, 2890, 2860, 1625, 1495, 1470, 1440, 1360, 1275, 1275, 1250, 1170, 1025, 840 cm$^{-1}$; $^1$H NMR (500 MHz): δ = 1.27 [s, 9H, C(CH$_3$)$_3$], 1.49 [s, 9H, C(CH$_3$)$_3$], 2.28 [d, *J* = 3.8 Hz, 1H, PhC*H*(OH)], 6.76–6.77 (m, 2H, aromatic H), 6.97 (d, *J* = 2.5 Hz, 1H, 3-H or 5-H), 7.04–7.43 (m, 14H, aromatic H), 8.08 (s, 1H, NCHAr), 13.92 (s, 1H, ArOH); $^{13}$C NMR (125 MHz): δ = 29.4 and 31.5 [C(*C*H$_3$)$_3$], 34.2 and 35.1 [*C*(CH$_3$)$_3$], 77.7 [$Ph_2$C(N)], 78.5 [PhCH(OH)], 118.0 (C-6), 126.9–130.3 (aromatic C), 136.8, 139.6, 140.0, 142.9, 143.6 (aromatic ipso-C), 158.2 (C-1), 168.2 (NCHAr); MS (FAB; NBA): *m/z* = 506 (M$^+$ + 1, 10%), 505 (M$^+$, 3%), 400 (24%), 399 (100%), 398 (30%), 382 (19%), 342 (17%), 234 (20%); anal. calcd. for $C_{35}H_{39}NO_2$: C 82.72, H 7.96, N 2.84; found: C 82.97, H 8.08, N 2.64.

**(*S*)-2-(1,1-Dimethylethyl)-6-[(2-hydroxy-1,1,2-triphenylethyl)imino]methyl-4-methoxyphenol** (**8d**): Prepared from (*S*)-**2** (3.5 mmol) and **6d** (3.33 mmol); reaction conditions: 48 h, −20 °C to +25 °C. The product **8d** could not be obtained completely free of aldehyde **6d** by column chromatography. Therefore, the eluate was concentrated and the residue was treated with *n*-pentane (3 mL), stirred vigorously and cooled to −18 °C. The solvent was removed by decantation. The procedure was repeated twice. The remaining solvent was removed in an oil pump vacuum to give solid **8d**, which is recommended to be kept at −18 °C. $R_f = 0.6$ ($CHCl_3$); yield: 0.31 g (19%); $[\alpha]_D^{20}$: +74 (*c* 0.75, $CHCl_3$). IR (KBr): ν = 3450, 3060, 3030, 3000, 2955, 1630, 1590, 1450, 1430, 1335, 1150, 1060 $cm^{-1}$; $^1H$ NMR (500 MHz): δ = 1.47 [s, 9H, $C(CH_3)_3$], 2.28 [d, $J$ = 3.8 Hz, 1H, PhCH(O*H*)], 3.72 (s, 3H, $OCH_3$), 5.64 [d, $J$ = 3.8 Hz, 1H, PhC*H*(OH)], 6.50 (d, $J$ = 3.1 Hz, 1 H, 3-H or 5-H), 6.73–6.75 (m, 2H, aromatic H), 7.01 (d, $J$ = 3.1 Hz, 1H, 5-H or 3-H), 7.04–7.45 (m, 13H, aromatic H), 8.05 (s, 1H, NCHAr), 13.68 (s, 1H, ArOH); $^{13}C$ NMR (75 MHz): δ = 29.2 [$C(CH_3)_3$], 35.1 [$C(CH_3)_3$], 55.8 ($OCH_3$), 77.8 [PhC(N)], 78.5 [PhCH(OH)], 112.1 (C-3 or C-5), 118.0 (C-6), 119.0 (C-5 or C-3), 127.0–127.3 (aromatic C), 139.2, 139.6, 142.9, 143.5 (aromatic ipso-C), 151.1 (C-4), 155.1 (C-1), 167.7 (NCHAr); MS (FAB; NBA): $m/z$ = 480 ($M^+ + 1$, 6%), 479 ($M^+$, 3%), 374 (11%), 373 (48%), 372 (100%), 167 (21%), 165 (14%), 105 (26%).

**(*S*)-4-(Dimethylamino)-2-(1,1-dimethylethyl)-6-{[(2-hydroxy-1,1,2-triphenylethyl)imino]methyl}phenol** (**8e**): Prepared from (*S*)-**2** (1.8 mmol) and **6e** (1.8 mmol); reaction conditions: 72 h, 60 °C. $R_f = 0.2$ (*n*-hexane/ethyl acetate, 3.5:1); yield: 0.25 g (28%). The product could not be obtained in analytically pure form. $^1H$ NMR (500 MHz): δ = 1.49 [s, 1H, $C(CH_3)_3$], 2.41 [s, 1H, PhCH(O*H*)], 2.78 [s, 6H, $N(CH_3)_2$], 5.60 [s, 1H, PhC*H*(OH)], 6.42 (d, $J$ = 2.9 Hz, 1H, 3-H or 5-H), 6.73–6.75 (m, 3H, aromatic H), 7.42–7.43 (m, 2H, aromatic H), 8.06 (s, 1H, NCHAr), 13.50 (s, 1H, ArOH).

**(*S*)-2-(1,1-Dimethylethyl)-6-{[(2-hydroxy-1,1,2-triphenylethyl)imino]methyl}-4-nitrophenol** (**8f**): Prepared from (*S*)-**2** (1.8 mmol) and **6f** (1.8 mmol); reaction conditions: 8 h reflux. $R_f = 0.3$ ($CHCl_3$), yield: 0.65 g (73%); $[\alpha]_D^{20}$: −55 (*c* ,1 $CHCl_3$). $^1H$ NMR (300 MHz): δ = 1.48 [s, 9H, $C(CH_3)_3$], 2.30 [d, $J$ = 2.8 Hz, 1H, PhCH(O*H*)], 5.66 [d, $J$ = 2.8 Hz, 1H, PhC*H*(OH)], 6.69 (d, $J$ = 7.3 Hz, 2H, aromatic H), 7.13–7.43 (m, 13H, aromatic H), 8.01 (d, $J$ = 2.8 Hz, 1H, 3-H or 5-H), 8.09 (d, $J$ = 2.2 Hz, 1H, NCHAr), 8.23 (d, $J$ = 2.5 Hz, 1H, 5-H or 3-H), 15.70 (d, $J$ = 2.2 Hz, 1H, ArOH); $^{13}C$ NMR (125 MHz): δ = 28.9 [$C(CH_3)_3$], 35.9 [$C(CH_3)_3$], 77.8 [$Ph_2CN$], 78.1 [PhCH(OH)], 116.9 (C-6), 125.2–130.1 (aromatic C), 138.3–142.3 (aromatic ipso-C), 166.8 (C-1), 168.5 (NCHAr); MS (FAB; NBA): $m/z$ = 495 ($M^+ + 1$, 1%), 388 (100%), 387 (81%), 371 (22%), 182 (17%), 167 (28%), 165 (12%).

## Addition of Diethyl Zinc to Benzaldehyde; General Procedure

A 25-mL-two-necked flask was equipped with a magnetic stirrer and a connection to the combined argon/vacuum line, charged with the imine **7** or **8** (0.358 mmol) and closed with a septum. The air in the flask was carefully replaced by argon and absolute toluene (4.5 mL) was injected by syringe. Under stirring at 25 °C, Ti(O*i*-Pr)$_4$ (0.1 mL, 0.342 mmol) was injected, and stirring of the yellow solution was continued for 3 h. By means of the combined argon/vacuum line, the solvent was removed, the remaining bright yellow solid was exposed to high vacuum for 3 h and dissolved in toluene (3 mL). Benzaldehyde (0.17 mL, 1.7 mmol) was injected and the solution was cooled to −78 °C. A 1.1 M solution of $Et_2Zn$ in toluene (3.1 mL, 3.4 mmol) was added slowly drop by drop by means of a syringe. Stirring was continued for 15 h at −20 to 0 °C. A saturated aqueous solution of $NH_4Cl$ (10 mL) was added, the mixture was stirred for 30 min at 25 °C, and filtered through celite, which was subsequently washed with toluene (10 mL). The layers of the combined filtrates were separated, and the aqueous phase was extracted with $Et_2O$ (3 × 10 mL). The combined organic layers were washed with brine, dried with $MgSO_4$ and evaporated. The viscous residue was purified by a short-path distillation; bp 62 °C/0.2 mbar; $R_f = 0.6$ ($CHCl_3$/ethyl acetate, 5:1). The $^1H$ NMR spectrum corresponds to that of a commercial sample; ee values given in Table 1 were determined: a) based on the optical rotation:[33] (*S*)-**11**: $[\alpha]_D^{20}$: −47.6 (*c* 6.11, $CHCl_3$); 98% ee; b) from the $^1H$ NMR spectra of the corresponding MTPA ester (Mosher's ester): 1′-phenylpropyl-2-methoxy-2-trifluoromethyl-2-phenylacetate.[34] (1′*R*,2*S*): δ = 0.93 (t, $J$ = 7.6 Hz, 3H, 3′-H), 1.84–2.07 (m, 2H, 2′-H), 3.54 (m, 3H, $OCH_3$), 5.82 (dd, $J$ = 5.7 Hz, $J$ = 7.6 Hz, 1H, 1′-H), 7.28–7.42 (m, 10H, aromatic H). (1′*S*, 2*S*): $^1H$ NMR differs in: δ = 0.84 (t, $J$ = 7.6 Hz), 5.89 (dd, $J$ = 5.7 Hz, $J$ = 7.6 Hz).

## Bis-Chelated Titanium Complex 12

Obtained according to Ref.[22]

## [*OC*-6-22′-(*C*),(*S*),(*S*)]-Bis-{2,4-Bis-(1,1-dimethylethyl)-6-{[(2-hydroxy-1,2,2-triphenylethyl)imino]methyl}phenolato (2-)-*N,O,O′*]titanium (13)

A solution of the imine **8c** (1.21 g, 2.39 mmol) in dry $CH_2Cl_2$ (6 mL) was stirred under argon in a 50-mL two-necked flask equipped with a magnetic stirrer, a reflux condenser, a connection to the combined argon/vacuum line, and a septum. Ti(O*i*-Pr)$_4$ (0.35 mL, 1.19 mmol) was injected by syringe, and the solution was refluxed for 7 h. The solvent was removed in a rotary evaporator, and the orange residue was purified by column chromatography to give the main diastereomer in 23% yield (0.45 g); $R_f = 0.4$ ($CHCl_3$/*n*-hexane, 3:2); $[\alpha]_D^{20}$: −94.3 (*c* 1, $CHCl_3$). $^1H$ NMR (300 MHz): δ = 1.18 [s, 18H, $C(CH_3)_3$], 1.25 [s, 18H, $C(CH_3)_3$], 6.65–6.68 (m, 4H, aromatic H), 6.78 [s, 2H, PhCH(O)], 6.92–7.19 (m, 18H, aromatic H), 7.22–7.25 (m, 6H, aromatic H), 7.47 (d, $J$ = 2.5 Hz, 3-H or 5-H), 7.61–7.64 (m, 4H, aromatic H), 8.25 (s, 2H, N=CH); $^{13}C$ NMR (75 MHz): δ = 29.1, 31.6 [$C(CH_3)_3$], 34.5, 34.8 [$C(CH_3)_3$], 88.4 [PhCH(N)], 90.4 [$Ph_2C(OH)$], 120.6 (C-6), 125.5–126.9 (aromatic C), 127.8 (C-3 or C-5), 128.0–128.4 (aromatic C), 130.7 (C-5 or C-3), 131.0 (aromatic C), 136.5, 139.6, 141.4, 144.2, 148.2 (aromatic ipso-C, C-2, C-4), 161.8 (C-1), 162.0 [(N)CHAr]; MS (FAB; NBA): $m/z$ = 1056($M^+ + 1$, 9%), 1055 ($M^+$, 14%), 950 (76%), 949 (100%), 842 (70%), 398 (56%), 279 (53%), 253 (46%); anal. calcd. for $C_{70}H_{74}N_2O_4Ti$: C 79.68, H 7.14, N 2.64; found: C 79.54, H 7.27, N 2.52.

Two minor diastereomers separated by column chromatography differ in: δ =1.19 (s) and 1.33 (s); 1.20 (s) and 1.25 (s); 1.31 and 1.42 (s).

### Torgov-Cyclization of Secone 16; General Procedure

Under argon, a mixture of the corresponding bis-chelated titanium complex **13** (0.106 g, 0.10 mmol), molecular sieves 4 Å (0.50 g) and dry $CH_2Cl_2$ (2 mL) was stirred at $-78\,^{\circ}C$. A 0.25 M solution of $TiCl_4$ in $CH_2Cl_2$ (0.4 mL, 0.10 mmol), generated under argon as well, was added dropwise by a syringe below $-75\,^{\circ}C$. The mixture was allowed to reach $-22\,^{\circ}C$ within 3 h, and a solution of **16** (0.298 g, 1.0 mmol) in dry $CH_2Cl_2$ (3 mL) was added. Subsequently, the mixture was stirred for 3 d at $-22\,^{\circ}C$ under argon. A 20% solution of $Na_2CO_3$ was added, the layers were separated, and the aqueous layer was extracted with $CH_2Cl_2$ or toluene ($3 \times 20$ mL). The combined organic layers were dried with $Na_2SO_4$, concentrated in a rotary evaporator, and the residue was submitted to column chromatography to give **17** as a colorless solid compound; $R_f = 0.55$ (*n*-hexane/ethyl acetate, 3:1). The enantiomeric excess was determined by comparison of the optical rotation: $[\alpha]_D^{20}$: −39 (c 0.1, tetrahydrofuran); Ref.[29]: $[\alpha]_D^{20}$: −102 (c 0.1, tetrahydrofuran) and by HPLC (Chiracel OJ; Diacel Chemical Industries; *n*-hexane/2-propanol, 96:4): (*S*)-**17**: $t_R = 29.3$ min; (*R*)-**19**: $t_R = 52.4$ min The spectroscopic data correspond to these described in the literature[28] for **17**. Anal. calcd. for $C_{19}H_{22}O_3$: C 81.42, H 7.17; found: C 81.37, H 7.11.

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## References and Notes

[1] M. Braun, *Angew. Chem*. **1996**, *108*, 565; *Angew. Chem. Int. Ed. Engl*. **1996**, *35*, 519.
[2] D. Seebach, A. K. Beck, A. Heckel, *Angew. Chem.* **2001**, *113*, 96; *Angew. Chem. Int. Ed. Engl*. **2001**, *40*, 92 and references given therein.
[3] M. Braun, R. Devant, *Tetrahedron Lett*. **1984**, *25*, 5031; M. Braun, *Angew. Chem.* **1987**, *99*, 24; *Angew. Chem. Int. Ed. Engl*. **1987**, *26*, 24; M. Braun, in: *Houben-Weyl*, 4th edn., Vol. E 21b (Eds.: G. Helmchen, R. W. Hoffmann, J. Mulzer, E. Schaumann), Thieme: Stuttgart, **1995**, pp. 1603; 1713 and references given therein.
[4] H. B. Kagan, F. Rebiere, *Synlett* **1990**, 643.
[5] S. Itsuno, M. Nakano, K. Miyazaki, H. Masuda, K. Ito, A. Hirado, S. Nakahama, *J. Chem. Soc. Perkin Trans. 1* **1985**, 2039.
[6] E. J. Corey, C. J. Helal, *Angew. Chem*. **1998**, *110*, 2092; *Angew. Chem. Int. Ed. Engl*. **1998**, *37*, 1986 and references given therein.
[7] D. Enders, V. Bhushan, *Tetrahedron Lett*. **1988**, *29*, 2437; K. Soai, A. Ookawa, T. Kaba, K. Ogawa, *J. Am. Chem. Soc.* **1987**, *109*, 7111; S. Wassmann, J. Wilken, J. Martens, *Tetrahedron: Asymmetry* **1999**, *10*, 4437; K. R. K. Prasad, N. N. Joshi, *J. Org. Chem*. **1997**, *62*, 3770; H. Brunner, C. Henrichs, *Tetrahedron: Asymmetry* **1995**, *6*, 653; M. Watanabe, M. Komota, M. Nishimura, S. Araki, Y. Butsugan, *J. Chem. Soc. Perkin Trans. 1* **1993**, 2193; C. Bolm, K. Muñiz Fernández, A. Seger G. Raabe, *Synlett* **1997**, 1051; P. I. Dosa, J. C. Ruble, G. C. Fu, *J. Org. Chem*. **1997**, *62*, 444; R. Annunziata, M. Benaglia, M. Cinquini, F. Cozzi, P. Giaroni, *J. Org. Chem*. **1992**, *57*, 782; T. Hintermann, D. Seebach, *Helv. Chim. Acta* **1998**, *81*, 2093; M. Brenner, D. Seebach, *Helv. Chim. Acta* **1999**, *82*, 2365; C. Gaul, K. Schärer, D. Seebach, *J. Org. Chem*. **2001**, *66*, 3059.
[8] Y. N. Ito, X. Ariza, A. K. Beck, A. Bohác, C. Ganter, R. E. Gawley,. F. N. M. Kühnle, J. Tuleja, Y. M. Wang, D. Seebach, *Helv. Chim. Acta* **1994**, *77*, 2071; see also Ref.[2]
[9] D. K. Jones, D. C. Liotta, I. Shinkai, D. J. Mathre, *J. Org. Chem*. **1993**, *58*, 799; V. Nevalainen, R. Uggla, M. R. Sundberg, *Tetrahedron: Asymmetry* **1995**, *6*, 1431.
[10] A. McKenzie, G. O. Wills, *J. Chem. Soc*. **1925**, *127*, 283.
[11] R. Berenguer, J. Garcia, J. Vilarrasa, *Tetrahedron: Asymmetry* **1994**, *5*, 165; K. R. K. Prasad, N. N. Joshi, *Tetrahedron: Asymmetry* **1996**, *7*, 3147.
[12] G. Sekar, A. DattaGupta, V. K. Singh, *J. Org. Chem*. **1998**, *63*, 2961.
[13] The diarylaminomethyl moiety is also present in several chiral 1,2-diamines, recently used as co-ligands in hydrogenation catalysts, cf: T. Ohkuma, M. Koizumi, H. Doucet, T. Pham, M. Kozawa, K. Murata, E. Katayama, T. Yokozawa, T. Ikariya, R. Noyori, *J. Am. Chem. Soc*. **1998**, *120*, 13529; R. Noyori, T. Ohkuma, *Angew. Chem*. **2001**, *113*, 40; *Angew. Chem. Int. Ed*. **2001**, *40*, 40.
[14] For a review on the application of β-amino alcohols and heterocyclic compounds derived therefrom in asymmetric syntheses, see: D. J. Ager, I. Prakash, D. R. Schaad, *Chem. Rev.* **1996**, *96*, 835.
[15] Preliminary communication: R. Fleischer, M. Braun, *Synlett* **1998**, 1441.
[16] M. Braun, S. Gräf, S. Herzog, *Org. Synth*. **1993**, *72*, 32.
[17] R. Fleischer, D. Galle, M. Braun, *Liebigs Ann./Recueil* **1997**, 1189.
[18] J. J. Ritter, P. P. Minieri, *J. Am. Chem. Soc*. **1948**, *70*, 4045; L. I. Krimen, D. J. Cota, *Org. React*. **1969**, *17*, 213; for a Ritter reaction mediated by triflic acid, see: C. H. Senanayake, R. D. Larsen, L. M. DiMichele, J. Liu, P. H. Toma, R. G. Ball, T. R. Verhoeven, P. J. Reider, *Tetrahedron: Asymmetry* **1996**, *7*, 1501.
[19] a) G. Bittner, H. Witte, G. Hesse, *Justus Liebigs Ann. Chem*. **1968**, *713*, 1; b) M. Uminski, M. Jawdosiuk, *Pol. J. Chem*. **1983**, *57*, 67.
[20] K. S. Reddy, L. Sola, A. Moyano, M. A. Pericas, A. Riera, *J. Org. Chem.* **1999**, *64*, 3969.
[21] R. Fleischer, H. Wunderlich, unpublished results.
[22] R. Fleischer, H. Wunderlich, M. Braun, *Eur. J. Org. Chem*. **1998**, 1063.

  

[23] The aldehydes **6a** and **6c** are commercially available. The compounds **6b** and **6d** were prepared according to the following references: **6b**: M. Hayashi, H. Kaneda, N. Oguni, *Tetrahedron: Asymmetry* **1995**, *6*, 2511; **6d**: J. F. Larrow, E. N. Jacobsen, *J. Org. Chem*. **1994**, *59*, 1939; for the syntheses of **6e** and **6f**, see: experimental section.
[24] For reviews on enantioselective additions of diethylzinc to aldehydes, see: a) R. Noyori, *Asymmetric Catalysis in Organic Synthesis*, John Wiley and Sons, New York **1994**, pp. 255–297; b) K. Soai, S. Niwa, *Chem. Rev*. **1992**, *92*, 833; c) L. Pu, H. B. Yu, *Chem. Rev*. **2001**, *101*, 757.
[25] E. N. Jacobson, W. Zhang, M. L. Güler, *J. Am. Chem. Soc*. **1991**, *113*, 6703; M. Braun, K. Opdenbusch, *Liebigs Ann./ Recueil* **1997**, 141.
[26] S. N. Ananchenko, I. V. Torgov, *Tetrahedron Lett*. **1963**, 1553; **1966**, 3585.
[27] G. Quinkert, M. Del Grosso, A. Döring, R. I. Schenkel, M. Bauch, G. T. Dambacher, J. W. Bats, G. Zimmermann, G. Dürner, *Helv. Chim. Acta* **1995**, *78*, 1345.
[28] H. Kosmol, K. Kieslich, R. Vössing, H.-J. Koch, K. Petzoldt, H. Gibian, *Liebigs Ann. Chem*. **1967**, *701*, 199; C. Rufer, E. Schröder, H. Gibian, *Liebigs Ann. Chem.* **1967**, *701*, 206.
[29] V. S.Enev, J. Mohr, M. Harre, K. Nickisch, *Tetrahedron: Asymmetry* **1998**, *9*, 2693.
[30] For recent syntheses of non-racemic Torgov diene **17**, see: T. Sugahara, K. Ogasawara, *Tetrahedron Lett*. **1996**, *37*, 7403; K. Tanaka, H. Nakashima, T. Taniguchi, K. Ogasawara, *Org. Lett*. **2000**, *2*, 1915.
[31] F. Prechtl, S. Haremza, R. Parker, K. Kuerschner, M. Braun, A. Hahn, R. Fleischer, *Eur. Patent* 1213293, **2002**; *Chem. Abstr*. **2002**, *137*, 26396.
[32] R. Devant, U. Mahler, M. Braun, *Chem. Ber*. **1988**, *121*, 397.
[33] M. Kitamura, S. Suga, K. Kawai, R. Noyori, *J. Am. Chem. Soc*. **1986**, *108*, 6071.
[34] J. A. Dale, D. L. Dull, H. S. Mosher, *J. Org. Chem*. **1969**, *34*, 2543.

  