Catalyzed Enantioselective Alkylation of Aldehydes

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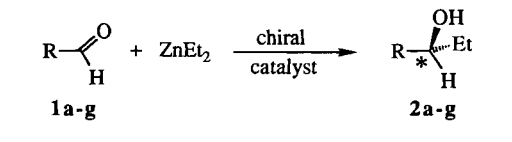
Enantioselective alkylation of a variety of aldehydes with diethylzinc was achieved by using catalytic amounts of optically active pyridines and C_2-symmetric 2-2'-bipyridines. The products were obtained in good yields with high enantioselectivities. Steric factors of the catalyst structure which govern the stereoselectivity were revealed, and important reaction intermediates were identified by spectroscopic means and single-crystal X-ray diffraction. The effect of additives on the optical purity of the product was studied. A strong asymmetric amplification was found with catalysts of low ee's.

Despite the increasing interest in enantioselective transformations catalyzed by organometallic reagents, significant progress has mainly been limited to asymmetric oxidations and reductions[2]. High enantioselectivities in catalyzed C–C bond-forming reactions still remain a major challenge. Considerable attention in this area has focused on the nucleophilic additions of organometallics to carbonyl compounds. Early studies were concerned with the use of chiral modifiers for organomagnesium or organolithium reagents[3]. However, in most cases stoichiometric or even excess amounts of the chiral auxiliary were required to achieve a high degree of enantioselection. In 1983, Oguni et al. reported an asymmetric ethyl transfer from diethylzinc to aryl aldehydes using cobalt and palladium complexes of camphorquinone dioxime as catalyst[4]. Rapid progress has followed the observation by Oguni[5] and Noyori et al.[6] that this alkylation is also efficiently catalyzed by β-amino alcohols giving the addition products in up to 99% ee. In a number of laboratories[7–9] the use of other chiral reagents[10] has been explored, and detailed mechanistic investigations have appeared[11]. During our studies on metal complexes containing chiral nitrogen chelators[12], we found that catalytic amounts of C_2-symmetric 2,2'-bipyridine **3** accelerated ethyl transfer from diethylzinc to aldehydes affording optically active alcohols with high enantiomeric excess[13]. In this full account, we describe the details for our preliminary reports[13,14], the use of chiral pyridine derivatives as catalysts, and additional experiments aimed at elucidating mechanistic features of this enantioselective catalytic alkylation.

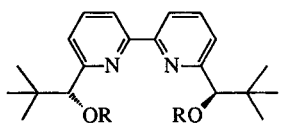
Substrate and Catalyst Variation

Asymmetric ethyl transfer from diethylzinc to aldehydes **1a–g** was efficiently catalyzed by C_2-symmetric 2,2'-bipyridine (*R,R*)-**3**[15]. Thus, the presence of catalytic amounts of **3** resulted in the rapid alkylation of aldehydes to give the corresponding secondary alcohols in good yields and with high enantioselectivities[13].

In general, the monomeric dialkylzinc compounds do not react with carbonyl compounds unless they are specifically activated. Alkyl transfer may occur upon addition of coordinating ligands which enhance reactivity by σ or π coordination[16]. This accelerating effect is believed to be caused mainly by the change of the linear geometry of the dialkylzinc compounds to more bent and coordinatively unsaturated structures. Initially, we tested to see if *achiral* 2,2'-bipyridine could be used for this activation of zinc reagents[17]. In the presence of catalytic amounts of the donor ligand ethyl transfer from diethylzinc to benzaldehyde (**1a**) occurred under mild reaction conditions. However, when an excess of 2,2'-bipyridine was used an orange precipitate (presumably 2,2'-bipy · $ZnEt_2$[18]) was formed which was inert to the carbonyl compound. With 5 mol-% of optically active C_2-symmetric 2,2'-bipyridine (*R,R*)-**4**, the desired secondary alcohol (*R*)-1-phenylpropanol (**2a**) was obtained in high yield, but the enantiomeric excess was disappointingly low though significant (28% ee). Although the expected activation was observed, long reaction times were still required for high conversion of **1a**. Blocking of the pyridine nitrogen atoms with a metal salt ($CoCl_2$) resulted in reduced activity, and **2a** was obtained in very low chemical yield and even further reduced enantioselectivity [7% chemical yield, 19% ee for (*R,R*)-**4** · $CoCl_2$]. Since the reactivity of organozinc compounds can also be influenced by changing the zinc–carbon bond polarity, we turned our attention to C_2-sym-



1a-g **2a-g**



	R
(*R,R*)-3	H
(*R,R*)-4	CH_3

1/2	R
a	C_6H_5-
b	*p*-ClC_6H_4-
c	*p*-$CH_3OC_6H_4$-
d	*n*-C_6H_{13}-
e	$H_2C{=}CH(CH_2)_2$-
f	*E*-$C_6H_5CH{=}CH$-
g	$C_6H_5C{\equiv}C$-

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metric 2,2'-bipyridine (*R,R*)-**3** bearing two unprotected hydroxy groups. Protonolysis led to a zinc species with markedly altered reactivity towards electrophilic reagents. The use of only 5 mol-% of (*R,R*)-**3** led to rapid alkylation of **1a**, and the desired secondary alcohol **2a** was obtained in good yield (92%) and with high optical purity (>90% ee). Increasing the amount of catalyst from 5 to 10 mol-% did not significantly effect the enantioselectivity. The same reaction with only 1 mol-% of (*R,R*)-**3** gave **2a** with only 56% ee presumably due to the competing uncatalyzed reaction of benzaldehyde and diethylzinc. Under these modified reaction conditions, a prolonged reaction time was required. Now, the zinc alkoxides produced during the reaction could also have a stereochemical effect by acting as a catalyst for further alkylation[19,20].

Under standard reaction conditions, a 1.5- or 2-fold excess of a commercially available 1 M solution of diethylzinc in hexane (or toluene) was added to a precooled mixture of substrate and catalyst in the appropriate solvent. Reactions were usually run at 0°C in hexane or toluene/hexane mixtures. In more polar solvents such as acetonitrile, reactivity as well as asymmetric induction were substantially decreased (Table 1). This solvent dependence is in marked contrast to that observed in the enantioselective conjugate addition of dialkylzinc compounds to chalcones catalyzed by nickel complexes of (*R,R*)-**3**[21]. In the latter catalysis the presence of aceto- or propionitrile as a coordinating solvent was essential for achieving high enantioselectivity.

Table 1. Enantioselective addition of diethylzinc to aldehydes using 5 mol-% of **3**

Entry	Aldehyde	Solvent[a]	Reaction temp. [°C]	Reaction time [h]	ee (%) of product[b]	Yield (%) of product[c]
1	**1a**	tol	0	3	93 (86)	83
2	**1a**	hex	0	3	94 (88)	92
3	**1a**	ace	[d]	[d]	79 (70)	71
4	**1a**	tol	22	0.5	91 (84)	90
5	**1a**	tol	−25	48	97 (92)	94
6	**1b**	tol	0	3	93 (90)	65
7	**1c**	tol	0	9.5	90 (80)	96
8	**1d**	tol	0	3	ca. 54 (70)[e]	ca. 75[e]
9	**1e**	hex	0	3	(70)	83
10	**1e**	hex	−30	33	(70)	49
11	**1e**	hex	−40	120	(68)	44
12	**1e**	hex	−78	33		–
13	**1f**	tol	0	3	28 (36)	76
14	**1g**	tol	0	3	25 (24)	88
15[f]	**1h**	tol	0	1	(16)	42

[a] Diethylzinc added as a solution in hexane; tol = toluene, hex = hexane, ace = acetonitrile. – [b] Based on optical rotation and (MTPA esters). – [c] After column chromatography. – [d] 0°C/ 9.5 h, then room temp./ 37 h. – [e] Slightly impure. – [f] Use of 6.5 mol-% of **6** instead of **3**.

Ethyl transfer from diethylzinc to benzaldehyde (**1a**) showed a slight temperature dependence (Table 1, entries 1, 4, 5). The asymmetric induction was increased from 93 to 97% ee by lowering the reaction temperature from 0°C to −25°C (in toluene). However, under these conditions longer reaction times were required to obtain the product in high yield. At room temperature, rapid alkylation occurred, and after 30 min **2a** was isolated in 90% yield with 91% ee. In the reaction with 4-pentenal (**1e**) no difference in optical yield was observed at lower temperature (Table 1, entries 9–12; in hexane). In the latter case, the reduced solubility of the resulting catalyst in hexane at lower temperatures was believed to be the major cause for this unexpected behavior[22]. At −78°C ethyl transfer was not observed.

Complete conversion of aldehydes was indicated by the disappearance of the initial yellow color. Acidic workup followed by column chromatography gave the pure products. The catalyst was recovered without loss of optical purity by eluting the column with a polar solvent followed by recrystallization of the isolated solid from hexane. The enantiomeric excess and the absolute configuration of the product were determined by optical rotation, NMR spectroscopy of the corresponding α-methoxy-α-(trifluoromethyl)phenylacetates (MTPA esters)[23] or HPLC using a chiral stationary phase (Chiralcel OD)[24].

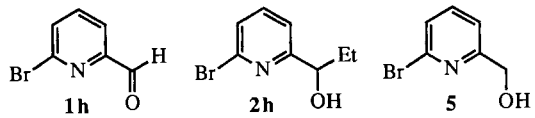
Table 1 shows that a variety of aldehydes could be alkylated by using 5 mol-% of (*R,R*)-**3** as the catalyst. In each case, we obtained predominantly secondary alcohols with (*R*) configuration. Benzaldehyde (**1a**) was chosen as substrate for most investigations to allow a comparison with previous work. However, other aromatic aldehydes were also alkylated with high enantioselectivities by using (*R,R*)-**3**. Whereas the reactions of benzaldehyde (**1a**) and *p*-chlorobenzaldehyde (**1b**) were complete within 3 h at 0°C and gave products with ee's >90%, ethylation of *p*-methoxybenzaldehyde (**1c**) required 9.5 h at 0°C for high conversion, and the optical purity was substantially lower (Table 1, entries 1, 6, 7). In this case, the competing uncatalyzed alkylation, as well as a structural alternation of the zinc reagent by coordination of the aldehyde methoxy group, might be responsible for the lower enantioselectivity[25].

Aliphatic aldehydes such as heptanal (**1d**) and 4-pentenal (**1e**) were alkylated with lower enantioselectivities (70% ee for **2d** and **2e**). Although the reasons for this behavior are not fully understood, it may be assumed that the structure of the catalyst/aldehyde complex plays a dominant role in the stereochemical course of the reaction. A recent ab initio MO calculation by Gung[26] revealed a significant bond-length difference between Lewis acid complexes of aliphatic and aromatic aldehydes. In addition, the relative energy differences between stable complex conformations were found to be substantially larger for aromatic than for aliphatic aldehydes. As a consequence, a tighter and more stereospecific coordination of the former to a chiral catalyst should be expected resulting in a higher enantioselectivity for the alkylation of aromatic aldehydes.

Unsaturated aldehydes **1f** and **1g** reacted rapidly with diethylzinc in the presence of (*R,R*)-**3** to give the corresponding products **2f** and **2g** in good chemical yield but only with moderate enantiomeric excess. As pointed out by Corey et al.[11b], the low enantioselectivity in the reaction of cinnamaldehyde with diethylzinc might be due to the unusually rapid competing uncatalyzed reaction or, as described

above, be a consequence of a less stereospecific complexation.

We also briefly investigated the question of autocatalysis[27,28]. Considering the fact that the product of the asymmetric alkylation is a zinc alkoxide which in itself could act as a catalyst, we attempted the alkylation of bromopyridinylcarbaldehyde **1h**. After a short induction period, rapid reaction occurred, and within a few minutes the conversion of **1h** was complete. However, besides the desired alkylated product **2h**, the formation of substantial amounts of achiral pyridyl alcohol **5** was observed. Both compounds should give catalytically active zinc alkoxides which could catalyze further product formation. The alkylated product **2h** was separated from **5** by column chromatography, and its optical purity was determined with the corresponding MTPA esters. A comparison with a sample obtained from *rac*-**2h** revealed an enantiomeric excess of only 16% for **2h**, indicating the competition between the catalytic pathways leading to optically active and racemic products[29].



Next, we turned our attention to the structure of the catalyst (Table 2). Ethyl transfer from diethylzinc to benzaldehyde (**1a**) was chosen as test reaction to allow a comparison with previous results. Optically active pyridines **6**–**15** were synthesized enantioselectively by asymmetric ketone reduction followed by either palladium-catalyzed cross couplings or radical dehalogenation[15].

Although C_2 symmetry has often been advantageous in asymmetric catalysis[30], it was not essential for achieving high enantioselectivity in the alkylation of aldehydes. Catalysts derived from optically active pyridines with aromatic substituents in the 6-position of the heterocycle were equally efficient in enhancing the reactivity of the zinc reagent. The highest optical yields were obtained when aryl-substituted pyridines **6** and **8** were used. These two compounds were also the most active catalysts, and complete conversion of **1a** was usually achieved within 2–3 h. With pyridines bearing non-aromatic substituents in the 6-position, ethylation was slower, and longer reaction times were required to obtain high yields of the desired product. Even after doubling the reaction time, less of the product was obtained due to reduced conversion of the aldehyde. Compounds with substituents that allowed further chelation or complexation (**7** and **9**) gave catalysts which produced the secondary alcohol **2a** in good yield, but with a slightly lower enantiomeric excess. The necessity of the sterically demanding group at the chiral center was illustrated by the low enantioselectivity with catalysts derived from compounds **13** and **14** having a methyl instead of *tert*-butyl substituent (5 and 21% ee, respectively). Changing the substitution pattern at the pyridine ring was deleterious for both the chemical and optical yield of **2a**. Thus, use of (*R*)-**15** gave only 3% of **2a** with very low enantiomeric excess. In all cases, (*R*)-**2a** was the major enantiomer obtained when pyridines with (*R*) configuration were used as catalysts.

Due to the ease of accessibility of pyridine (*R*)-**6**[15], we decided to study its catalytic properties in greater detail. With regard to the temperature dependence of the asymmetric induction in the formation of **2a**, no difference was found compared to 2,2′-bipyridine (*R*,*R*)-**3**. When 5 mol-% of (*R*)-**6** (with 96% ee) was used as catalyst in hexane at 0°C, **2a** was obtained in 82% yield with an ee of 90%. Raising the temperature to 22°C gave 91% of (*R*)-**2a** with 84% ee. Under these conditions, the initial yellow color of the reaction mixture faded within 20 min indicating the rapid conversion of reactants. No ethyl transfer was observed at −78°C presumably due to the low solubility of the catalyst. In contrast to earlier work[31], the enantioselectivity was essentially independent of the aldehyde-to-$ZnEt_2$ ratio. Increasing the amount of diethylzinc from 1.5 to 4 equivalents did not lead to any marked improvement in enantioselection. (*R*)-**2a** was obtained in 88% chemical yield with an optical purity of 91%.

Identification of Intermediates

Organozinc complexes derived from chiral sterically congested β-amino alcohols and dimethylzinc have been carefully studied by Noyori et al.[6]. Enantiopure and racemic amino alcohols led to the formation of dimeric zinc alkoxides which differed substantially in both stability and reactivity. A similar behavior was expected when diethylzinc was added to pyridines containing acidic hydroxy protons. This reaction has also been used by van Koten et al. in the synthesis of alkoxyaluminum compounds derived from pyridyl alcohols and trialkylaluminum derivatives[32]. Indeed, treatment of **6** with diethylzinc led to the protonolysis of the organozinc reagent and to a cleavage of one zinc–carbon bond. The resulting zinc alkoxide **16** was ultimately iden-

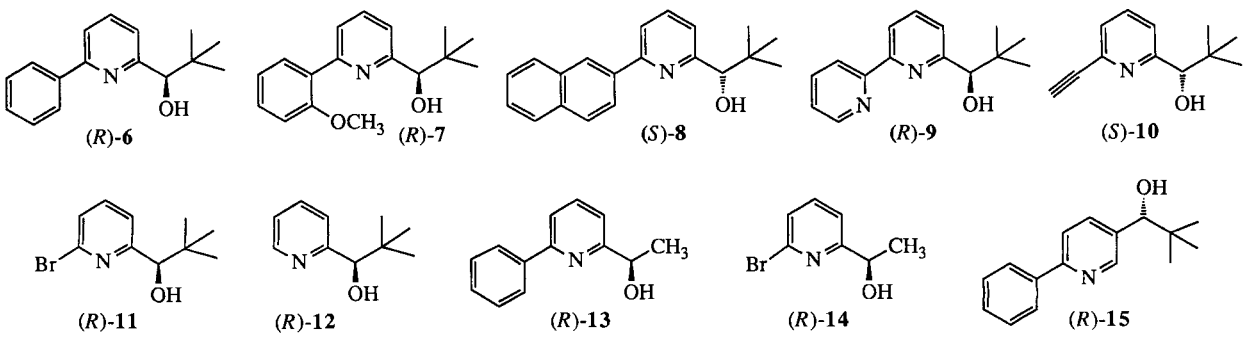


Table 2. Catalyst variation in the alkylation of benzaldehyde (**1a**) with diethylzinc

Entry	Catalyst	ee (%) of cat.	mol-% of cat.	Reaction time [h]	Yield (%)	Opt. rot. $[\alpha]_D^{RT}$ (*c*)[a]	ee (%) of **2a**[b]	Config. of **2a**
1	(*R*,*R*)-**3**	>98	5	3	83	+42.3 (9.63)	93 (86)	(*R*)
2	(*R*,*R*)-**4**	>98	10	52	93	+12.7 (3.63)	28	(*R*)
3	(*R*)-**6**	90	8	3	73	+42.3 (3.29)	93 (88)	(*R*)
4	(*R*)-**7**	96	5	3	51	+37.8 (3.21)	83 [78]	(*R*)
5	(*S*)-**8**	98	5	3	77	−43.0 (2.92)	95 (88)	(*S*)
6	(*R*)-**9**	90	11	3	80	+39.2 (4.65)	86 (78)	(*R*)
7	(*S*)-**10**	92	5	6	58	−37.2 (2.26)	82 (74)	(*S*)
8	(*R*)-**11**[c]	90	10	6	65	n.d.[d]	(81)	(*R*)
9	(*R*)-**12**	90	11	6	61	+35.4 (4.32)	78 (74)	(*R*)
10	(*R*)-**13**	70	10	6	64	+2.1 (2.63)	5 (5)	(*R*)
11	(*R*)-**14**	84	10	6	24	+9.5 (2.28)	21 (15)	(*R*)
12	(*R*)-**15**	87	5	3	3	n.d.	[7]	(*R*)

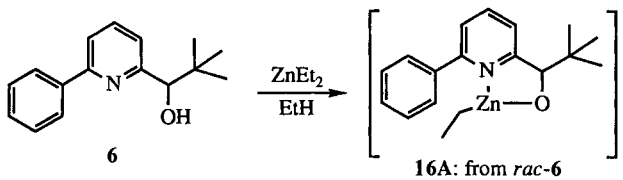
[a] In chloroform; RT: room temp. — [b] Determined by optical rotation, (NMR measurements of MTPA esters), or [HPLC using a chiral stationary phase]. — [c] Contained traces of the corresponding chloride. — [d] n.d. = not determined.

Table 3. ^{1}H-NMR data (400 MHz, C_6D_6) for compounds **6**, **16A**, and **16B**[a]

Assignment	**6**[b]		**16A**		**16B**	
CH_2	—		0.24–0.36	(m, 2H)	0.65–0.74	(m, 1H)
					0.77–0.89	(m, 1H)
$C(CH_3)_3$	1.00	(s, 9H)	0.99	(s, 9H)	0.89	(s, 9H)
CH_3	—		1.14	(t, J = 8, 3H)	1.77	(t, J = 8 Hz, 3H)
OH	4.37	(d, J = 6, 1H)	—		—	
C*H*(OH)	4.58	(d, J = 6, 1H)	5.01	(s, 1H)	3.86	(s, 1H)
aromatic H	6.71	(d, J = 8, 1H)	6.86–6.92	(m, 2H)	6.26–6.29	(m, 1H)
aromatic H	7.05	(dd, J = 8, 8, 1H)	6.96–7.00	(m, 1H)	6.69–6.70	(m, 2H)
aromatic H	7.15–7.25	(m, 4H)	7.24–7.32	(m, 1H)	7.18–7.22	(m, 1H)
aromatic H	7.92–7.95	(m, 2H)	7.39–7.42	(m, 2H)	7.30–7.34	(m, 2H)
aromatic H			8.00–8.02	(m, 2H)	7.62–7.64	(m, 2H)

[a] δ values relative to C_6D_5H (δ = 7.15); J in Hz. — [b] 300-MHz spectrum.

tified by mass spectrometry, NMR spectroscopy, and single-crystal X-ray diffraction.



6 **16A**: from *rac*-**6**
16B: from (*R*)-**6**

A white precipitate developed when an excess of diethylzinc was added to a hexane solution of *rac*-**6** at room temperature. Recrystallization from cyclohexane afforded colorless crystals which were analyzed by mass spectrometry. In the EI mass spectrum, signals corresponding to fragments containing two zinc atoms, two deprotonated pyridines and one ethyl group were identified [2 **16A**$^+$ − ethyl]. Calculated isotope distributions confirmed these peak assignments. Further fragmentation gave signals for ions of [**16**$^+$ + H] and [**16**$^+$ − ethyl]. These species were also detected by FAB MS using an NBA matrix. In the Cl mass spectrum, the ion series of an *unfragmented dimeric* associate was detected. Treatment of a hexane solution of enantiopure (*R*)-**6** with an excess of diethylzinc also gave a white precipitate. However, in this case, attempts to recrystallize the crude solid, which was isolated by removal of the supernatent, only led to decomposition. The mass spectra of the white air-sensitive solid were acquired and compared to the ones obtained from the sample of **16** which was prepared from *rac*-**6**/$ZnEt_2$. Whereas an almost identical EI mass spectrum was obtained, the Cl spectrum differed substantially. The dimeric associate of **16B** was only detected with a very weak intensity (< 1%). Due to rapid decomposition in the NBA matrix, no FAB mass spectrum could be obtained.

Next, we focused our attention on solution studies of **16**. ^{1}H- and ^{13}C-NMR spectra of **16A** (prepared from *rac*-**6** and $ZnEt_2$ followed by recrystallization) and of **16B** [from (*R*)-**6** and $ZnEt_2$ followed by evaporation of the solvent] were recorded in [D_6]benzene. The chemical shifts of the proton signals of **16A** and **16B** were significantly different. A comparison of the NMR spectra showed that most proton signals of the optically active complex **16B** were shifted upfield with respect to the ones of both the free ligand and the corresponding complex **16A** (Table 3). In the optically active complex **16B**, the protons of the methylene group gave two very distinct multiplets indicating their magnetic inequivalency. In **16A** only one multiplet was observed for these two protons.

The signal for the *tert*-butyl group of **16B** appeared only 0.1 ppm upfield from that of **16A**. A more significant shift difference was observed for the benzylic protons. Compared

to **6**, **16A** gave a signal which was shifted downfield by 0.43 ppm; the corresponding signal for **16B** was observed 0.72 ppm upfield from that of **6**. The difference in chemical shift for the aromatic protons of **16A** and **6** was markedly small. In comparison, most aromatic signals of **16B** were strongly shifted upfield. The observed upfield shift for most proton signals of the optically active complex could be a result of severe steric compression of the zinc-bound ligands by assuming the presence of a dimeric assembly of both complexes in solution. This effect must be stronger in the associate of the optically active complex due to the closer proximity of the attached chelates (vide infra). The complex multiplets of the methylene protons at the ethylzinc groups suggest a relatively strong coordination of the pyridine nitrogen atoms to the zinc atom and a slow dynamic decomplexation process with respect to the NMR time scale.

The ^{13}C-NMR spectra of **16A** and **16B** were almost identical with the exception of the signals for the methylene carbon atoms. Their absorptions differed by 3.1 ppm (**16A**: $\delta = -0.5$; **16B**: $\delta = 2.5$).

Recrystallization of **16A** (from *rac*-**6**/$ZnEt_2$) from cyclohexane gave crystals suitable for X-ray diffraction analysis (Figure 1). The compound crystallized in the monoclinic system with space group $C2/c$.

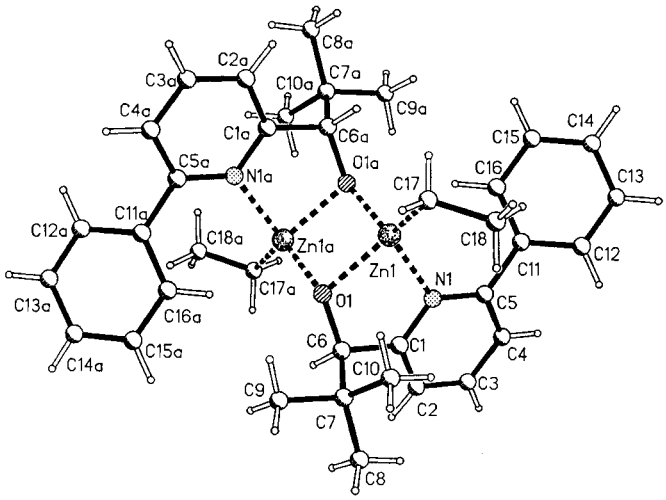


Figure 1. Molecular structure and labeling scheme for the dimer of **16A**; interatomic distances [Å]: Zn(1)–N(1) 2.185(2), Zn(1)–O(1) 2.009(2), Zn(1)–C(17) 1.973(3), Zn(1)–O(1A) 2.037(2); angles [°]: N(1)–Zn(1)–O(1) 79.4(1), Zn(1)–O(1)–Zn(1A) 95.2(1), O(1)–Zn(1)–C(17) 133.8(2), N(1)–Zn(1)–C(17) 122.7(1), N(1)–Zn(1)–O(1A) 103.2(1), O(1)–Zn(1)–O(1A) 84.8(1), C(17)–Zn(1)–O(1A) 121.6(1); torsion angles [°]: N(1)–Zn(1)–O(1)–Zn(1A) –104.5(9), C(17)–Zn(1)–O(1)–Zn(1A) 130.0(2), O(1A)–Zn(1)–O(1)–Zn(1A) 0.0(4), C(7)–C(6)–O(1)–Zn(1) 94.2(2)

A *dinuclear* zinc complex was formed in which two *heterochiral* zinc alkoxides were bridged by their zinc and oxygen atoms to form a central four-membered Zn_2O_2 heterocycle. In the two adjacent ethylzinc/pyridine subunits (**16**) the *tert*-butyl and ethyl substituents are *cis* to each other. The zinc atoms have distorted tetrahedral coordination geometries, and their bond distances to the carbon (1.973 Å), oxygen (2.009 and 2.037 Å), and nitrogen atoms (2.185 Å) do not differ substantially from other comparable complexes[6a,11b]. Since the two zinc alkoxides have opposite chirality, the resulting achiral associate possesses C_i symmetry (Figure 2, schematic representation a). Inspection of a three-dimensional space-filling model reveals that both zinc atoms are severely shielded by the sterically encumbered ligand system. All substituents are pointing away from each other, and they are as distant as possible from the rest of the molecule.

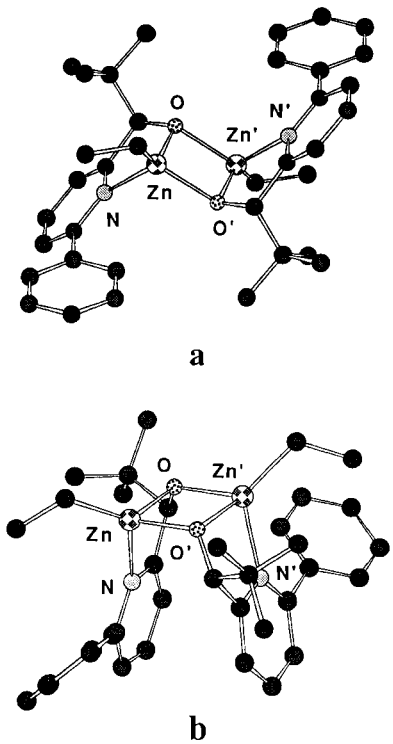


Figure 2. a: Molecular structure of the dimeric zinc alkoxide derived from *rac*-**6**; b: schematic representation of the suggested molecular structure of the dimeric zinc alkoxide derived from (*R*)-**6**

Figure 2 also shows a schematic drawing of a suggested dimeric complex derived from two zinc alkoxides with identical chirality (schematic representation b). Both chiral centers have the (*R*) configuration and the resulting complex has C_2 symmetry. A structure of this type was expected when enantiopure (*R*)-**6** was treated with diethylzinc. However, in this case, no crystals were obtained, and the resulting solid was highly air- and moisture-sensitive. Attempts to recrystallize **16B** from a variety of solvents led only to its decomposition. A comparison between the structures of the *meso* complex derived from *rac*-**6** (Figure 2, a) and this suggested associate (Figure 2, b) reveals that the latter should be less stable due to the steric congestion of the ligand system. In addition, the zinc–carbon bonds of the optically active associate are more exposed to the outside of the complex being located on its convex surface. This might well explain the enhanced reactivity of this zinc alkoxide towards air and moisture. The pronounced structural differences between the zinc alkoxides derived from *rac*-**6** and that of (*R*)-**6** were also

indicated by the differences of their mass and NMR spectra (vide supra).

The observed dimeric nature of the zinc alkoxides is in accord with the results described by Noyori et al. for complexes derived from β-amino alcohols[6b]. Structurally related pyridyl-containing dinuclear alkoxyaluminum compounds have extensively been studied by van Koten et al.[32]. A different molecular structure of an ethyl-containing zinc alkoxide was reported by Corey and co-workers[11b]. An additional internal dimethylamino ligand forms a coordinative bond to the zinc atom leading to an arrangement with a lower degree of association. In the light of this result, the lower enantioselectivities in the catalyzed alkylation of aldehydes using pyridines containing additional moieties allowing chelating or complexation (**7** and **9**) might either be due to a variation of the three-dimensional arrangement or to the presence of several competing catalytically active complexes.

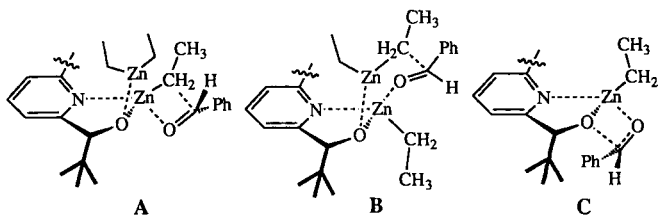
In general, the steric bulk of the oxygen-bound group in a zinc alkoxide determines the degree of intermolecular association and thereby controls the presence of coordinatively unsaturated zinc atoms[16,33]. All catalytically active complexes described in this work were obtained from compounds having the pyridine nitrogen atom in a suitable position for chelate-ring formation. Those derivatives which contained an aromatic substituent in the 6-position of the heterocycle, the sterically demanding *tert*-butyl group at the chiral center, and which allowed the formation of a five-membered chelate gave the most active catalysts.

The degree of association and the formation of complex aggregates are also significantly influenced by the polarity of the solvent, the concentration and relative ratio of reactants, and the presence of additives such as metal halides or other organometallic reagents. The highest enantioselectivity in this alkylation reaction was observed in hydrocarbons like hexane or toluene. In coordinating solvents like acetonitrile different types of associates are more likely to be involved in catalysis, and zinc species in the solvated form with a higher degree of saturation may be present. A considerable decrease in enantioselectivity was observed in acetonitrile. Salts and additives have a marked effect on the molecular structure of metal-containing compounds, and also on the distribution reactions of molecular associates[34]. In addition, they can serve as Lewis-acidic activators for the carbonyl compounds and can enhance their reactivity towards organometallic species. In the present case, trimethylsilyl chloride led to an enhanced activation, and **1a** was rapidly alkylated at substantially lower temperatures (−78°C to −40°C) than usual. By using 1.5 equivalents of trimethylsilyl chloride and 5 mol-% of (*R*)-**6** (of 96% ee) as catalyst, **2a** was isolated in 91% yield after acidic workup[35]. However, the addition product was racemic. This behavior parallels the observations of conjugate addition of cuprates to enones[36] and nickel-catalyzed alkylations of chalcones with diorganozinc reagents[21b,35]. In both cases, enhanced reactivity towards the carbonyl compounds was observed, and the stereochemical outcome was considerably influenced[37,38]. Activation with 3 equivalents of titanium tetraisopropoxide resulted in a markedly increased enantioselectivity (95% ee; yield of **2a**: 18% due to incomplete conversion at −78°C for 4 h)[39]. Other titanium reagents such as dichlorotitanium diisopropoxide or bis(cyclopentadienyl)titanium dichloride did not substantially enhance catalytic activity and led to the formation of **2a** of very low optical purity. Chiral titanium complexes prepared in situ or derived from stable well-defined spirotitanates have previously been used as catalysts by Yoshioka[8] and Seebach et al.[9], respectively. In these systems chiral ethyltitanium reagents are assumed to be involved.

Briefly, we investigated the ability of other diorganozinc reagents bearing functionalized alkyl chains to transfer these groups[40]. The use of bis[(trimethylsilyl)methyl]zinc[41] did not give any detectable addition product, and large quantities of benzaldehyde were recovered even after stirring at room temperature for a prolonged reaction time. The zinc homoenolate of ethyl propionate[42,43] already reacted in the absence of a catalyst to give a complex mixture of products that was not analyzed any further. Other organometallic compounds including modified alkylmagnesium and diorganozinc reagents afforded addition products with very low optical purity, presumably due to the competing uncatalyzed alkylation of the aldehyde.

In principle, the presence of only a *single* reactant in the reaction mixture can also influence the degree of association, thereby leading to a change in the catalyst structure. Upon addition of benzaldehyde (1 − 5 equivalents) to a solution of the zinc alkoxides in benzene, the ^{1}H-NMR signals attributed to the dimeric zinc complexes remained unaffected, regardless of whether the samples were prepared from *rac*-**6** or enantiopure (*R*)-**6**[44]. In addition, no appreciable change in the chemical shift for the aldehyde proton was observed. Apparently, the presence of the aldehyde scarcely changes the degree of association. However, several species may form when a dialkylzinc compound is added. In the light of the results described by van Koten et al.[32] and Noyori et al.[6b], the dimeric zinc alkoxides are believed to dissociate generating *mononuclear* unsaturated zinc species. Some of the possible intermediates that might be present in solution after the addition of the aldehyde and the dialkylzinc compound are schematically shown in Scheme 1[45].

Scheme 1



*Intra*molecular ethyl transfer could occur via a 5/4-bridged intermediate **A** or, more likely, as a result of a six-membered cyclic transition state (schematic representation **B**) involving the second alkylzinc equivalent attached to the alkoxide oxygen atom. Alternatively, an acetal-like inter-

mediate **C**[46] could be formed which is alkylated by an external zinc species[47]. In all three arrangements the aldehyde is activated by the formerly coordinatively unsaturated zinc alkoxide.

Steric interactions between the aldehyde substituents (Ph versus H for **1a**) determine the stereochemical outcome of the alkylation. The degree of enantioselectivity must be a delicate balance of steric factors. The preferred three-dimensional arrangement exposes the *re* face of the aldehyde to the incoming ethylzinc reagent leading to the predominant formation of the (*R*) enantiomer. Finally, liberation of the catalyst is facilitated by the strong tendency to form stable tetramers of the product zinc alkoxide[16].

Asymmetric Amplification

According to the mechanism described above, the concentration and relative stability of the intermediate dimeric zinc alkoxides, as well as their tendency to change the degree of association should have a marked influence on both reactivity and enantioselectivity. Mutual enantiomer recognition[48] and differential chemical behavior of the diastereomeric dinuclear metal complexes have been proposed to be the origin of a phenomenon described as *asymmetric amplification.* Nonlinear relationships between the optical purities of chiral auxiliaries and the products were found for an asymmetric oxidation and an aldol reaction by Kagan and Agami et al.[49]. Intensive studies by Oguni[50] and Noyori et al.[6b,11a] revealed the asymmetric amplification in the enantioselective alkylation of aldehydes catalyzed by chiral β-amino alcohols. Positive nonlinear effects were also found in asymmetric ene reactions[51a] and trimethylsilylcyanations[51b] catalyzed by titanium complexes, and stoichiometric enantioselective cuprate additions to enones[51c]. In previous investigations we found a strong amplification of chirality in the nickel-catalyzed conjugate addition of diorganozinc reagents to chalcone when (*R*)-**6** was used as the optically active ligand[21b,52]. We therefore decided to extend these studies and examine the correlation between the enantiomeric excess of the catalyst derived from scalemic **6** and the ee of product **2a** in the enantioselective alkylation of benzaldehyde (**1a**). A remarkable positive nonlinear relationship between the optical purities of the catalyst and alkylation products was observed with pyridines of low ee's. Scalemic[53] mixtures of **6** were prepared by mixing (*R*)-**6** with racemic **6**. The enantiomeric excess of each sample was calculated from the ratio of (*R*)-**6**/*rac*-**6** and confirmed by HPLC analysis using a chiral stationary phase[15]. The reactions were performed in hexane at 0°C by using 5 mol-% of scalemic **6** and 1.5 equivalents of diethylzinc. After 2.5 h, 1-phenylpropanol (**2a**) was isolated upon acidic workup followed by column chromatography and kugelrohr distillation. The enantiomeric excess of **2a** was determined by optical rotation and HPLC analysis using a chiral stationary phase. A strong *positive nonlinear relationship* between the ee of pyridine **6** and the ee of **2a** was found (Figure 3).

Figure 3 shows the dependence of the enantiomeric excess of **2a** on the optical purity of catalyst (*R*)-**6**. When samples of **6** with low enantiomeric excess were used as catalysts, a strong *amplification of chirality* was observed. Thus, (*R*)-**6** with an ee of 14% gave **2a** with 87% ee! Raising the optical purity of the catalyst did not lead to any further significant improvement of the product ee[54]. The strongest amplification was observed with a catalyst having only 2% ee. In this case, **2a** was isolated with an enantiomeric excess which was almost 20-fold (39% ee) that of the catalyst.

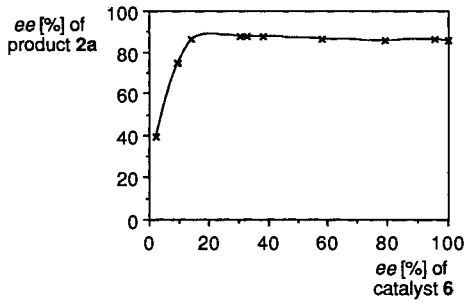


Figure 3. Dependence of the ee of **2a** on the optical purity of **6** (all data obtained by HPLC using a chiral stationary phase)

In order to gain an understanding of catalytic activity, all reactions were run under identical conditions and quenched after 2.5 h. Complete conversion of **1a** was only observed when catalysts with ee's > 30% were used, and **2a** was then isolated in 69–88% yield. The use of catalysts with very low optical purity resulted in reduced conversion of **1a**, and the yield of **2a** dropped significantly. In the latter cases, the initial yellow color of the reaction mixture was retained even after stirring at 0°C for 3 h. Reduction of the amount of catalyst from 5 to 3 mol-% had no major influence on the asymmetric amplification. (*R*)-**2a** was still isolated in 51% yield with 91% ee. Very similar results were obtained when a hexane/toluene solvent mixture was used instead of pure hexane. With 5 mol-% of (*R*)-**6** (42% ee), **2a** was formed in 81% yield with an optical purity of 94% ee.

We attribute this behavior to the difference in the chemical properties of the diastereomeric zinc complexes formed in a scalemic mixture of **6** upon addition of $ZnEt_2$. As described above, heterochiral dimerization led to the formation of a thermodynamically stable *meso* complex which was characterized by MS and NMR studies as well as single-crystal X-ray diffraction (Figure 2, schematic representation a). Thus, the minor enantiomer was trapped in a catalytically less active from, whereas the major enantiomer was enriched in solution. These results were also supported by solution studies which clearly showed the significant enrichment of the major enantiomer in the reaction mixture. Treatment of a solution of (*R*)-**6** of 50% ee [(*R*):(*S*) = 75:25] in hexane with 5 equivalents of diethylzinc resulted in the formation of the expected white precipitate. The remaining solution was decanted, and the precipitate and the solution were hydrolyzed separately. After acidic workup, 26% of isolated **6** was obtained from the solution and 74% of isolated **6** from the precipitate. Interestingly, both samples had *different* optical purities. From the solution, **6** was obtained with 84% ee [(*R*):(*S*) = 92:8], whereas **6** from the precipitate had

only 44% ee [(*R*):(*S*) = 72:28]. This difference indicates the predominant precipitation of the optically inactive *meso* complex containing two heterochiral ethylzinc/pyridine subunits. The zinc complex of the major enantiomer of **6** was thereby significantly enriched in the remaining solution.

Further investigations of the catalyzed alkyl transfer to carbonyl compounds should eventually extend the scope of enantioselective transformations and lead to a better understanding of the underlying features of asymmetric catalysis. Attractive opportunities are emerging in fundamental science as well as applied technologies[55,56].

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Experimental

^{1}H and ^{13}C NMR: Varian Gemini 300, Varian VXR 400; multiplicities determined with the APT pulse sequence; solvent $CDCl_3$, unless noted otherwise; chemical shifts in values relative to TMS (δ = 0) for protons or $CDCl_3$ (δ = 77) for carbon atoms. – Melting points: Kofler melting point apparatus (corrected values) and Büchi 530 (uncorrected values). – IR: Perkin-Elmer 781. – MS: VG 70-250 and Finnigan MAT 8430. – Optical rotations: Perkin-Elmer 141 (RT: room temp.). – Elemental analyses: Leco CHN 900. – HPLC: Kontron Instruments (pump: Kontron 420, detector: Kontron 432); column: Chiralcel OD (Daicel), 25 cm × 0.46 cm i.d. – X-ray: Enraf-Nonius CAD4. – All reactions were carried out in flame-dried glassware under argon by using anhydrous solvents; products were isolated by CC or flash chromatography on SiO_2 (Chemische Fabrik Uetikon, size: C 560, 35–70 micron) or Al_2O_3 (Fluka, type 507C neutral, activity I, 100–125 mesh) and detected by UV or revealed by coloration with phosphomolybdic acid (PMA). – The following compounds were commercially available and were used without further purification: diethylzinc (1 M in hexane; Fluka); (*R*)-(–)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride [(*R*)-(–)-MTPA chloride: JPS Chimie], 2,6-dibromopyridine (Aldrich), and 2,2′-biypridine (Fluka). Aldehydes were distilled prior to use.

Preparation of Compounds: Optically active bipyridines **3**, **4**, and pyridines **6**–**15**[15], 4-pentenal (**1e**)[57], phenylpropynal (**1g**)[58], and (2- bromopyridin-6-yl)carbaldehyde (**1h**)[59] were prepared according to published procedures.

(R)-1-Phenylpropanol [(*R*)-**2a**][60]. – *Representative Procedure for the Alkylation of Aldehydes*: A 10-ml Schlenk flask equipped with a magnetic stirrer was charged with 33 mg (0.1 mmol) of (*R,R*)-**3** and 4 ml of dry toluene. After cooling to 0°C, benzaldehyde (212 mg, 2 mmol) was added. To this stirred clear solution 4 ml of a 1 M solution of diethylzinc in hexane (4 mmol) was added dropwise over a 5-min period. The initial yellow solution became colorless after ca. 2 h. After stirring for 1 additional h at 0°C, the reaction was quenched by the addition of 10 ml of 1 N hydrogen chloride. The layers were separated, and the aqueous layer was extracted three times with 20 ml of dichloromethane. The combined organic layers were washed with 10 ml of brine and dried with Na_2SO_4. The solvent was removed in a rotary evaporator to give 419 mg of a yellowish viscous oil. CC [20 g of SiO_2, petroleum ether/ethyl acctate (15:1)] gave 226 mg (83%) of (*R*)-**2a** as a colorless oil. – ^{1}H NMR: δ = 0.93 (t, J = 7.4 Hz, 3H, CH_3), 1.71–1.88 (m, 3H, CH_2, OH), 4.61 (td, J = 6.5, 3.2 Hz, 1H, CH), 7.26–7.36 (m, 5H, aromatic H). – ee of **2a** determined by rotation ($[\alpha]_{589}^{RT}$ = +42.3 (c = 9.63, $CHCl_3$), 93% ee {ref.[60] $[\alpha]_{589}^{RT}$ = +45.45 (c = 5.15, $CHCl_3$) for (*R*)-**2a**}) and ^{1}H-NMR measurement of esters derived from (*R*)-(–)-MTPA chloride: (*R*)-**2a**:(*S*)-**2a** = 93:7. – HPLC: Daicel (Chiralcel OD), flow 1 ml/min, UV detector (254 nm), 1.5% 2-propanol in hexane; retention times: 15.7 min (k' = 4.2) for (*R*)-**2a**, 19.6 min (k' = 5.5) for (*S*)-**2a**. *rac*-**2a** gave two well-separated signals with equal peak areas. MTPA esters derived from (*R*)-(–)-MTPA chloride (characteristic signals only):

Diastereomer A [from (*R*)-**2a**]: ^{1}H NMR: δ =0.93 (t, J = 7.3 Hz, 3H, CH_3), 5.83 (dd, J = 7.6, 6.3 Hz, 1H, CH). – ^{13}C NMR: δ = 10.0, 29.2, 80.4

Diastereomer B [from (*S*)-**2a**]: ^{1}H NMR: δ = 0.83 (t, J = 7.7 Hz, 3H, CH_3), 5.90 (dd, J = 7.7, 6.0 Hz, 1H, CH). – ^{13}C NMR (mixture of diastereomers A and B): δ = 9.65/9.92, 28.92/29.14, 80.08/80.36.

(R)-1-(4-Chlorophenyl)propanol [(*R*)-**2b**][7a,61]: According to the representative procedure using 281 mg (2 mmol) of 4-chlorobenzaldehyde (**1b**), 33 mg (0.1 mmol) of (*R,R*)-**3**, 4 ml of diethylzinc (1 M in hexane, 4 mmol), and 4 ml of toluene; 434 mg of crude product. Yield 221 mg (65%) of (*R*)-**2b**. – ^{1}H NMR: δ = 0.90 (t, J = 7.5 Hz, 3H, CH_3), 1.68–1.83 (m, 2H, CH_2), 1.91 (br. s, 1H, OH), 4.58 (t, J = 6.4 Hz, 1H, CH), 7.25–7.33 (m, 4H, aromatic H). – ee of **2b** determined by rotation ($[\alpha]_{589}^{RT}$ = +26.7 (c = 6.77, C_6H_6), 93% ee {ref.[7a,61] $[\alpha]_{589}^{*}$ = +28.59 (c = 5.1, C_6H_6) for (*R*)-**2b**}) and ^{1}H-NMR measurement of esters derived from (*R*)-(–)-MTPA chloride: (*R*)-**2b**:(*S*)-**2b** = 95:5. MTPA esters derived from (*R*)-(–)-MTPA chloride (characteristic signals only):

Diastereomer A [from (*R*)-**2b**]: ^{1}H NMR: δ = 0.91 (t, J = 7.4 Hz, 3H, CH_3), 5.78 (dd, J = 7.5, 6.4 Hz, 1H, CH). – ^{13}C NMR: δ = 9.81, 29.05, 79.53.

Diastereomer B [from (*S*)-**2b**]: ^{1}H NMR: δ = 0.82 (t, J = 7.4 Hz, 3H, CH_3), 5.86 (dd, J = 7.6, 6.0 Hz, 1H, CH). – ^{13}C NMR: δ = 9.53, 28.87, 79.28.

(R)-1-(4-Methoxyphenyl)propanol [(*R*)-**2c**][7a,61]: According to the representative procedure using 272 mg (2 mmol) of 4-methoxybenzaldehyde (**1c**), 33 mg (0.1 mmol) of (*R,R*)-**3**, 4 ml of diethylzinc (1 M in hexane, 4 mmol), and 4 ml of toluene for 9.5 h; 413 mg of crude product. Yield 318 mg (96%) of (*R*)-**2c**. – ^{1}H NMR: δ = 0.89 (t, J = 7.5 Hz, 3H, CH_3), 1.68–1.86 (m, 3H, CH_2, OH), 3.80 (s, 3H, OCH_3), 4.54 (t, J = 6.6 Hz, 1H, CH), 6.86–6.90 (m, 2H, aromatic H), 7.24–7.28 (m, 2H, aromatic H). – ee of **2c** determined by rotation ($[\alpha]_{589}^{RT}$ = +30.4 (c = 5.95, C_6H_6), 90% ee {ref.[7a,61] $[\alpha]_{589}^{RT}$ = –33.73 (c = 5.0, C_6H_6) for (*S*)-**2c**}) and ^{1}H-NMR measurement of esters derived from (*R*)-(–)-MTPA chloride: (*R*)-**2c**:(*S*)-**2c** = 90:10. MTPA esters derived from (*R*)-(–)-MTPA chloride (characteristic signals only):

Diastereomer A [from (*R*)-**2c**]: ^{1}H NMR: δ = 5.78 (dd, J = 7.4, 6.7 Hz, 1H, CH). – ^{13}C NMR: δ = 80.22.

Diastereomer B [from (*S*)-**2c**]: ^{1}H NMR: δ = 5.85 (dd, J = 7.9, 6.2 Hz, 1H, CH). – ^{13}C NMR: δ = 79.92.

(R)-3-Nonanol [(*R*)-**2d**][62]: According to the representative procedure using 228 mg (2 mmol) of 1-heptanal (**1d**), 33 mg (0.1 mmol) of (*R,R*)-**3**, 4 ml of diethylzinc (1 M in hexane, 4 mmol), and 4 ml of toluene; 320 mg of crude product. Yield 217 mg (75%) of (*R*)-**2d**. – ^{1}H NMR: δ = 0.87–0.96 (m, 6H, 2 × CH_3), 1.29–1.54 (m, 13H, 6 × CH_2, OH), 3.51–3.53 (m, 1H, CH). – ee of **2d** determined by rotation ($[\alpha]_{589}^{RT}$ = –5.2 (c = 2.87, $CHCl_3$), 54% ee {ref.[62]

$[\alpha]_{589}^{24} = +9.6$ (c = 8.3, $CHCl_3$) for (*S*)-**2d**}) and ^{13}C-NMR measurements of esters derived from (*R*)-(−)-MTPA chloride: (*R*)-**2d**:(*S*)-**2d** = 85:15. MTPA esters derived from (*R*)-(−)-MTPA chloride (characteristic signals only):

Diastereomer A [from (*R*)-**2d**]: ^{13}C NMR: δ = 9.51, 22.46, 24.80, 26.65, 28.98, 31.61, 32.96.

Diastereomer B [from (*S*)-**2d**]: ^{13}C NMR: δ = 9.17, 22.50, 25.15, 26.39, 29.06, 31.66, 33.20.

(±)-6-Hepten-3-ol (*rac*-**2e**): A 250-ml round-bottomed flask equipped with a magnetic stirrer, addition funnel, reflux condenser, and argon inlet was charged with 4.38 g (180 mmol) of magnesium turnings and a few crystals of iodine. The mixture was heated until iodine sublimation was observed. After cooling, a mixture of 19.6 g (180 mmol) of ethyl bromide in 40 ml of dry diethyl ether was added dropwise over a 25-min period. After the addition was complete, the stirred mixture was refluxed for 45 min and then cooled to room temp. A solution of 10 g (ca. 113 mmol; contained ca. 5% butyl vinyl ether) of 4-pentenal (**1e**) in 45 ml of dry diethyl ether was added dropwise (slight reflux). Upon completion of the addition, the mixture was refluxed for 2 h, then allowed to cool to room temp., and the reaction was quenched by the addition of 70 ml of a satd. ammonium chloride solution. The layers were separated, and the aqueous layer was washed three times with 50 ml each of diethyl ether. The combined organic layers were extracted with 50 ml of brine and dried with Na_2SO_4. The solvent was removed (rotary evaporator, 200 mbar) to give the crude product. Distillation gave 2 fractions. Fraction 1: 52−94°C/194 mbar, 2.3 g (**2e** containing diethyl ether, water, and butyl vinyl ether). Fraction 2: 99−108°C/194 mbar, 9.1 g of **2e**. Fraction 1 was purified by CC [65 g of SiO_2, petroleum ether/diethyl ether (3:1)] to give 1.7 g of **2e**. Yield 10.8 g (84%) of **2e** as a colorless oil. − IR (film): $\tilde{\nu}$ = 3345 cm^{-1}, 2962, 2932, 1640, 1450, 992, 908. − ^1H NMR: δ = 0.95 (t, J = 7.6 Hz, 3H, CH_3), 1.37−1.65 (m, 5H, 2 × CH_2, OH), 2.10−2.27 (m, 2H, CH_2), 3.53−3.60 (m, 1H, C*H*OH), 4.96−5.10 (m, 2H, CH_2CH), 5.79−5.93 (m, 1H, CH_2C*H*). − ^{13}C NMR: δ = 9.6, 29.9, 30.0, 35.8, 72.8, 114.8, 138.9. − MS (EI, 70 eV): m/z (%) = 97 (15), 96 (24), 85 (32), 81 (31), 67 (59), 59 (100), 41 (93). − MS (CI, NH_3): m/z (%) = 132 (100) [$M^+ + NH_4$], 114 (9) [M^+], 96 (15), 85 (19), 81 (16), 59 (24); (CI, CH_4): m/z (%) = 115 (14) [$M^+ + 1$], 97 (100), 95 (13), 81 (13), 55 (26). − ee analysis by ^1H-NMR measurements of esters derived from (*R*)-(−)-MTPA chloride. CHN analysis of the corresponding 3,5-dinitrobenzoyl ester (m.p. 37−39°C).

$C_{14}H_{16}N_2O_6$ (308.3)	Calcd.	C 54.54	H 5.23 N 9.09
	Found	C 54.48	H 5.22 N 8.93

MTPA ester derived from (*R*)-(−)-MTPA chloride (characteristic signals only);

Diastereomer A [from (*R*)-**2e**]: ^1H NMR: δ = 0.93 (t, J = 7.5 Hz, 3H, CH_3).

Diastereomer B [from (*S*)-**2e**]: ^1H NMR: δ = 0.82 (t, J = 7.5 Hz, 3H, CH_3).

(S)-6-Hepten-3-ol [(*S*)-**2e**)]: A 100-ml Schlenk flask equipped with a magnetic stirrer was charged with 166 mg (0.5 mmol) of (*S,S*)-**3** and 20 ml of dry hexane. The mixture was rapidly stirred for 15 min to give a fine suspension of (*S,S*)-**3**. After cooling to 0°C, 4-pentenal (0.84 g, 10 mmol, **1e**) was added. To this stirred mixture 20 ml of a 1 M solution of diethylzinc in hexane (20 mmol) was added dropwise over a 7-min period. A clear yellow solution resulted, and after ca. 5 min a white precipitate developed. Stirring was continued at 0°C for 3 h. The reaction was quenched by the addition of 50 ml of 1 N hydrogen chloride. The layers were separated, and the aqueous layer was extracted three times with 50 ml each of dichloromethane. The combined organic layers were washed with 40 ml of brine and dried with Na_2SO_4. The solvent was removed in a rotary evaporator (35°C/200 mbar) to give 1.49 g of a yellowish viscous oil. ^1H-NMR measurements of the crude product mixture showed the expected signals for **2e** and (*S,S*)-**3**, exclusively. Kugelrohr distillation (110°C/18 mbar) gave 0.945 g (83%) of (*S*)-**2e**. (*S,S*)-**3** was recovered by CC followed by recrystallization of the remaining white solid. The spectral data of (*S*)-**2e** were identical to those of *rac*-**2e**. − $[\alpha]_{589}^{RT} = +9.9$ (c = 1.7, EtOH); the absolute configuration was determined after hydrogenation to give (*S*)-3-heptanol[63]. − ee analysis by ^1H-NMR measurements of esters derived from (*R*)-(−)-MTPA chloride: (*S*)-**2e**:(*R*)-**2e** = 85:15.

(S)-(+)-3-Heptanol[63] *by Hydrogenation of (S)-6-hepten-3-ol* [(*S*)-**2e**]: A 25-ml, two-necked, round-bottomed flask was charged with 67 mg (0.59 mmol) of (*S*)-**2e** and 2.5 ml of methanol. To this solution, 10 mg of platinum oxide (80%) was added, and the flask was flushed with hydrogen. After shaking at room temp. in an atmosphere of hydrogen for 6 h, the solvent was decanted from the catalyst (under a stream of argon). Remaining traces of the catalyst were removed by filtration through a short pad of silica gel and the solvent was removed in a rotary evaporator (40°C/200 mbar) to give 72 mg of a clear oil. (*S*)-3-heptanol and traces of methanol were identified by ^1H- and ^{13}C-NMR spectra[63b]. − ^1H NMR: δ = 0.91 (t, J = 7.6 Hz, 3H, CH_3), 0.94 (t, J = 7.5 Hz, 3H, CH_3), 1.22−1.60 (m, 8H, 4 × CH_2), 1.64 (br. s, 1H, OH), 3.50−3.56 (m, 1H, CH). − ^{13}C NMR: δ = 9.6, 13.8, 22.6, 27.6, 29.9, 36.5, 73.3. $-[\alpha]_{589}^{RT} = +5.4$ (c = 2.76, EtOH) {ref.[63b] $[\alpha]_D^{20} = +8.5$ (c = 0.8, EtOH) for (*S*)-3-heptanol}.

(S)-1-Phenyl-1-penten-3-ol [(*S*)-**2f**][6a,64]: According to the representative procedure using 264 mg (2 mmol) of (*E*)-3-phenyl-2-propenal (**1f**), 33 mg (0.1 mmol) of (*S,S*)-**3**, 4 ml of diethylzinc (1 M in hexane, 4 mmol), and 4 ml of toluene; 410 mg of crude product. Yield 246 mg (76%) of (*S*)-**2f**. − ^1H NMR: δ = 0.98 (t, J = 7.5 Hz, 3H, CH_3), 1.58 (d, J = 3.8 Hz, 1H, OH), 1.62−1.72 (m, 2H, CH_2), 4.21−4.24 (m, 1H, C*H*OH), 6.23 (dd, J = 15.9, 5.8 Hz, 1H, C*H*CH), 6.59 (d, J = 15.9 Hz, 1H, C*H*Ph), 7.22−7.41 (m, 5H, aromatic H). − ee of **2f** determined by rotation ($[\alpha]_{589}^{RT} = -1.6$ (c = 4.71, $CHCl_3$), 28% ee {ref.[6a,64] $[\alpha]_{589}^{22} = -5.7$ (c = 100, $CHCl_3$) for (*S*)-**2f**, 96%}) and ^1H-NMR measurement of esters derived from (*R*)-(−)-MTPA chloride: (*S*)-**2f**:(*R*)-**2f** = 68:32. MTPA esters derived from (*R*)-(−)-MTPA chloride (characteristic signals only):

Diastereomer A [from (*R*)-**2f**]: ^1H NMR: δ = 0.99 (t, J = 7.4 Hz, 3H, CH_3), 6.04 (dd, J = 15.9, 7.4 Hz, 1H, C*H*CH), 6.61 (d, J = 15.9 Hz, 1H, C*H*Ph).

Diastereomer B [from (*S*)-**2f**]: ^1H NMR: δ = 0.89 (t, J = 7.5 Hz, 3H, CH_3), 6.17 (dd, J = 15.9, 7.9 Hz, 1H, C*H*CH), 6.71 (d, J = 15.9 Hz, 1H, C*H*Ph).

(S)-1-Phenyl-1-pentyn-3-ol [(*S*)-**2g**][65]: According to the representative procedure using 260 mg (2 mmol) of phenylpropynal (**1g**), 33 mg (0.1 mmol) of (*S,S*)-**3**, 4 ml of diethylzinc (1 M in hexane, 4 mmol), and 4 ml of toluene; 456 mg of crude product. Yield 280 mg (88%) of (*S*)-**2g**. − ^1H NMR: δ = 1.08 (t, J = 7.4 Hz, 3H, CH_3), 1.80−1.87 (m, 2H, CH_2), 2.07−2.11 (m, 1H, OH), 4.56 (dt, J = 6.0, 6.4 Hz, 1H, C*H*OH), 7.29−7.32 (m, 3H, aromatic H), 7.42−7.46 (m, 2H, aromatic H). − ^{13}C NMR: δ = 9.2, 30.8, 64.1, 84.9, 90.0, 122.8, 128.4, 128.5, 131.9. − MS (EI, 70 eV): m/z (%) = 160 (11) [M^+], 131 (100), 103 (27), 77 (24). − ee of **2g** determined by rotation ($[\alpha]_{589}^{RT} = -4.8$ (c = 1.97, diethyl ether), 25% ee {ref.[65] $[\alpha]_{589}^{25} = -13.7$ (c = 2, diethyl ether) for (*S*)-**2g**, 70% ee}) and ^1H-NMR measurement of esters derived from (*R*)-(−)-MTPA chloride:

(*S*)-**2g**:(*R*)-**2g** = 62:38. MTPA ester derived from (*R*)-(−)-MTPA chloride (characteristic signals only):

Diastereomer A [from (*R*)-**2g**]: ^{1}H NMR: δ = 1.10 (t, *J* = 7.4 Hz, 3H, CH_3).

Diastereomer B [from (*S*)-**2g**]: ^{1}H NMR: δ = 1.01 (t, *J* = 7.4 Hz, 3H, CH_3).

(±)-1-(2-Bromopyridin-6-yl)propanol (**2h**): A 100-ml Schlenk flask equipped with a magnetic stirrer was charged with 1.78 g (7.5 mmol) of 2,6-dibromopyridine and 40 ml of dry diethyl ether. After cooling to −78°C, 4.7 ml of a 1.6 M solution of *n*-butyllithium in hexane (7.5 mmol) was added dropwise. The resulting yellow solution was stirred for 30 min at this temperature and then treated with 0.48 g (8.25 mmol) of propanal. Stirring was continued for 1.25 h at −78°C, and the reaction was quenched by the addition of 10 ml of dilute hydrogen chloride. The layers were separated, and the aqueous layer was extracted eight times with 5 ml each of diethyl ether. The combined organic layers were washed with 10 ml of a satd. aqueous $NaHCO_3$ solution followed by extraction with 10 ml of brine and dried with Na_2SO_4. The solvent was removed in a rotary evaporator to give 1.72 g of a yellowish, viscous oil. Kugelrohr distillation afforded 1.2 g (74%, ca. 95% chemical purity) of *rac*-**2h** as a colorless oil. – TLC: R_f = 0.28 [petroleum ether/ethyl acetate (2:1)]. – IR (film): $\tilde{\nu}$ = 3395 cm^{-1}, 2965, 1582, 1552, 1432, 1405, 1125, 982, 788, 730. – ^{1}H NMR: δ = 0.95 (t, *J* = 7.4 Hz, 3H, CH_3), 1.68–1.77 (m, 1H, CH_2), 1.80–1.91 (m, 1H, CH_2), 3.54 (d, *J* = 6.0 Hz, 1H, OH), 4.66 (dt, *J* = 5.6, 12.6 Hz, 1H, CH), 7.28 (d, *J* = 7.6 Hz, 1H, aromatic H), 7.38 (d, *J* = 7.7 Hz, 1H, aromatic H), 7.55 (dd, *J* = 7.6, 7.7 Hz, 1H, aromatic H). – ^{13}C NMR: δ = 9.2, 30.9, 74.1, 119.3, 126.7, 139.1, 141.3, 164.6. – MS (EI, 70 eV): *m/z* (%) = 189 (56), 188 (99), 187 (58), 186 (100), 106 (32), 78 (98), 51 (50). – MS (Cl, NH_3): *m/z* (%) = 218 (98) [M^+], 216 (100) [M^+], 138 (29). – ee analysis by ^{1}H-NMR measurements of esters derived from (*R*)-(−)-MTPA chloride. Elemental analyis of the corresponding 3,5-dinitrobenzoyl ester.

$C_{15}H_{12}BrN_3O_6$ (410.1) Calcd. C 43.93 H 2.95 N 10.24
Found C 43.69 H 2.89 N 10.06

MTPA esters derived from (*R*)-(−)-MTPA chloride (characteristic signals only):

Diastereomer A: ^{1}H NMR: δ = 0.95 (t, *J* = 7.4 Hz, 3H, CH_3).

Diastereomer B: ^{1}H NMR: δ = 0.86 (t, *J* = 7.4 Hz, 3H, CH_3).

1-(2-Bromopyridin-6-yl)-propanol (**2h**). – *Autocatalysis:* According to the representative procedure using 372 mg (2 mmol) of **1h**, 32 mg (0.13 mmol) of (*S*)-**6**, 4 ml of diethylzinc (1 M in hexane, 4 mmol), and 4 ml of dry toluene. Addition of diethylzinc at 0°C gave a red solution which rapidly turned yellow. Product analysis by TLC after 10 min indicated complete conversion of **1h**. Workup after 1 h at 0°C; 451 mg of a crude, yellowish, viscous oil. Ratio of **2h**:**5** ≈ 1:1 (^{1}H-NMR measurement). Separation by CC [20 g of SiO_2, petroleum ether/ethyl acetate (3:1 then 1:1)] gave 180 mg (42%) of **2h** and 160 mg (43%) of **5** as colorless oils.

2h: Spectral data identical to those of *rac*-**2h**. – $[\alpha]_{589}^{RT}$ = −0.6 (*c* = 2.57, CH_2Cl_2) (absolute configuration not determined). – Ratio of enantiomers A:B (determined by ^{1}H-NMR measurements of esters derived from (*R*)-(−)-MTPA chloride): 42:58.

(2-Bromopyridin-6-yl)methanol (**5**): M.p. 33–36°C. – TLC: R_f = 0.15 [petroleum ether/ethyl acetate (2:1)]. – IR (film): $\tilde{\nu}$ = 3340 cm^{-1}, 2910, 1586, 1556, 1432, 1156, 1128, 993, 985, 672. – ^{1}H NMR: δ = 3.50–3.80 (br. s, 1H, OH), 4.75 (d, *J* = 5.5 Hz, 2H, CH_2), 7.33 (d, *J* = 7.6 Hz, 1H, aromatic H), 7.37–7.41 (m, 1H, aromatic H), 7.54–7.60 (m, 1H, aromatic H). – ^{13}C NMR: δ = 64.1, 119.5, 126.7, 139.3, 141.4, 161.6. – MS (EI, 70 eV): *m/z* (%) = 189 (33) [M^+], 188 (50), 187 (35) [M^+], 186 (49), 160 (31), 158 (39), 78 (100), 51 (50). – MS (Cl, NH_3): *m/z* (%) = 190 (96) [M^+ + 1], 188 (100) [M^+ + 1], 110 (42), 94 (16).

C_6H_6BrNO (188.0) Calcd. C 38.32 H 3.22 N 7.45
Found C 38.49 H 3.06 N 7.36

Reaction Modifications: (i) No addition of (*S*)-**6**: Ratio of **2h**:**5** = 46:54. – (ii) Use of (*S,S*)-**3** (0.1 mmol) instead of (*S*)-**6** gave **2h**:**5** in a ratio of ca. 1:1. – (iii) Addition of 1.5 equiv. of 3-hexyne: Ratio of **2h**:**5** = 55:45. – (iv) Addition of *p*-benzoquinone: Only traces of **2h** and **5** were formed.

Effect of 2,2′-Bipyridine on the Alkylation of Benzaldehyde (**1a**): According to the representative procedure using 212 mg (2 mmol) of benzaldehyde (**1a**), 4 ml of diethylzinc (1 M in hexane, 4 mmol), and the amount of 2,2′-bipyridine indicated in Table 4 in 4 ml of toluene. The results are summarized in Table 4.

Table 4. Effect of 2,2′-bipyridine (2,2′-bipy) on the conversion of **1a**[a]

Entry	2,2′-bipy (mol-%)[b]	2,2′-bipy (mol-%)[c]	Reaction time [h]	Ratio of **1a**:**2a**[d]
1	–	–	24	92: 8
2	50	33	24	24:76
3	15	10	3	82:18
4	25	17	3	74:26
5	38	25	3	70:30
6[e]	52	26	3	67:33
7	75	50	3	76:24
8	100	67	3	72:18
9	150	100	3	100:0
10	250	167	3	100:0

[a] A **1a**:$ZnEt_2$ ratio of 1:1.5 was used. – [b] With respect to **1a**. – [c] With respect to $ZnEt_2$. – [d] Determined by ^{1}H-NMR analysis of the crude mixture. – [e] A **1a**:$ZnEt_2$ ratio of 1:2 was used.

Temperature Dependence of the Enantiomeric Excess. – a) *Alkylation of Benzaldehyde* (**1a**): According to the representative procedure using 212 mg (2 mmol) of benzaldehyde (**1a**), 33 mg (0.1 mmol) of (*R,R*)-**3**, 4 ml of diethylzinc (1 M in hexane, 4 mmol), and 4 ml of toluene. The ee of **2a** was determined by rotation ({ref.[60]} $[\alpha]_{589}^{RT}$ = −45.45 (*c* = 5.15, $CHCl_3$) for (*S*)-**2a**}) and ^{1}H-NMR measurements of MTPA esters (Table 1).

(i) 22°C, 0.5 h: Yield 246 mg (90%) of **2a**. – $[\alpha]_{589}^{RT}$ = +41.6 (*c* = 5.59, $CHCl_3$), 91% ee. – (*R*)-**2a**:(*S*)-**2a** = 92:8 (MTPA ester).

(ii) 0°C, 3 h: Yield 226 mg (83%) of **2a**. – $[\alpha]_{589}^{RT}$ = +42.3 (*c* = 9.63, $CHCl_3$), 93% ee. – (*R*)-**2a**:(*S*)-**2a** = 93:7 (MTPA ester).

(iii) −25°C, 48 h: Yield 255 mg (94%) of **2a**. – $[\alpha]_{589}^{RT}$ = +44.1 (*c* = 5.74, $CHCl_3$), 97% ee. – (*R*)-**2a**:(*S*)-**2a** = 96:4 (MTPA ester).

b) *Alkylation of 4-Pentenal* (**1e**): According to the representative procedure using 168 mg (2 mmol) of 4-pentenal (**1e**), 33 mg (0.1 mmol) of (*S,S*)-**3**, 4 ml of diethylzinc (1 M in hexane, 4 mmol), and 4 ml of hexane. Conversion of **1e** was determined by ^{1}H-NMR measurements of the crude product; the ee of **2e** was determined by ^{1}H-NMR measurements of MTPA esters (Table 1).

(i) 0°C, 3 h: Complete conversion. Yield 140 mg (61%) of **2e**. – (*S*)-**2e**:(*R*)-**2e** = 85:15.

(ii) −30°C, 33 h: Crude product; **1e**:**2e** = 8:92. Yield 112 mg (49%) of **2e**. – (*S*)-**2e**:(*R*)-**2e** = 85:15.

(iii) −40 °C, 5 d: **1e**:**2e** = 7:93, Yield 100 mg (44%) of **2e**. − (*S*)-**2e**:(*R*)-**2e** = 84:16.

(iv) −78 °C, 33 h: No **2e** formed.

(v) Addition of 341 mg (1.2 mmol) of $Ti(OiPr)_4$, −30 °C, 18 h: **1e**:**2e** = 15:85. Yield 120 mg (53%) of **2e**. − (*S*)-**2e**:(*R*)-**2e** = 51:49.

(vi) Use of 39 mg (0.16 mmol) of (*S*)-**6** instead of (*S,S*)-**3**, −40 °C, 5 d: **1e**:**2e** = 15:85. Yield 116 mg (51%) of **2e**. − (*S*)-**2e**:(*R*)-**2e** = 82:18.

Asymmetric Amplification Studies: The optical purity of (*R*)-**6** was adjusted by mixing appropriate amounts of (*R*)-**6** and *rac*-**6** to give 24 mg (0.1 mmol) of a scalemic mixture. Pyridine **6** was dissolved in 2 ml of hexane, and 20 µl of the resulting solution was withdrawn. From this sample the solvent was removed, and the optical purity of **6** was determined by HPLC[15]. The remaining solution of **6** was cooled to 0 °C, and 212 mg (2.0 mmol) of benzaldehyde (**1a**) followed by a solution of diethylzinc (1 M in hexane, 3 ml, 3 mmol) was added. After stirring for 2.5 h at this temperature, the reaction was quenched with hydrochlorid acid. Workup followed the representative procedure. **2a** was isolated by CC [16 g SiO_2, petroleum ether/ethyl acetate (15:1)] followed by kugelrohr distillation (50–75 °C/0.02 mbar). The optical purity of **2a** was determined by optical rotation[60] and HPLC using a chiral stationary phase (Chiralcel OD). Chemical and optical yields are given in Table 5.

Table 5. Asymmetric amplification in the formation of **2a** using scalemic **6**

Entry	ee of **6** (%) calcd.[a]	ee of **6** (%) HPLC	ee of **2a** (%) HPLC	ee of **2a** (%) opt. rot.	Yield of **2a** (%)
1	1.6	2.1	39.0	41	15
2	9.2	9.6	74.7	83	28
3	14.8	14.0	86.6	92	49
4	29.8	30.8	87.8	93	84
5	37.2	33.1	87.4	93	69
6	39.1	38.5	87.7	94	81
7	56.7	57.8	86.5	92	88
8	78.1	78.9	85.7	91	74
9	–	95.6	86.5	90	82
10	–	>99	85.7	89	83

[a] Calculated from known amounts of *rac*-**6** and (*R*)-**6**.

Preparation, NMR Spectroscopy, and MS Analysis of **16A**: In a flame-dried Schlenk flask under argon, 100 mg (0.41 mmol) of *rac*-**6** was dissolved in 3.5 ml of hexane. The clear solution was cooled to 0 °C, and 2.2 ml (2.2 mmol) of a 1 M solution of diethylzinc in hexane was added dropwise over a period of 5 min. During the addition, mixing of the reactants was ensured by occasional careful shaking of the reaction flask. The mixture was allowed to stand for 10 min at 0 °C. The supernatent was then removed with a syringe from the white precipitate, and the remaining solid was washed twice with 2 ml each of hexanc. Drying in vacuo (15 h, 35 °C/0.04 mbar) gave 166 mg (121%) of **16A** as a white solid, which was recrystallized from cyclohexane (0.6 ml/100 mg, heating to 80 °C). Standing at room temp. for 15 h afforded 71 mg (52%) of **16A** as colorless crystals. The crystal structure of **16A** was determined by X-ray diffraction analysis[66]. For the NMR measurements, 22.9 mg (0.069 mmol) of recrystallized **16A** was placed into a dry NMR tube in an argon-filled dry bag. 10 min before the measurement 0.7 ml of carefully dried [D_6]benzene (reflux over Na for 2 d) was added to give a saturated solution of the complex (undissolved crystals were allowed to precipitate). All spectra were recorded at room temp. ^{1}H-NMR data are listed in Table 3. − ^{13}C NMR ([D_6]benzene): δ = −0.5 (CH_2), 13.2 (CH_3), 26.9 (CH_3), 37.6 (C), 85.7 (CH), 122.2 (CH), 122.5 (CH), 128.9 (2 CH), 128.9 (2 CH), 129.3 (CH), 137.0 (CH), 140.2 (C), 158.5 (C), 165.8 (C). − MS (EI, 70 eV): *m/z* (%) = [2 **16A**$^+$ − ethyl]: 645 (1), 644 (1), 643 (4), 642 (3), 641 (9), 640 (4), 639 (9), 638 (2), 637 (7); [**16A**$^+$ + H]: 338 (1), 336 (2), 334 (5); [**16A**$^+$ − ethyl]: 306 (2), 304 (3); [**16A**$^+$ − *tert*-butyl]: 282 (1), 281 (5), 280 (40), 279 (17), 278 (58), 277 (15), 276 (100); other signals: 491 (13), 489 (20), 488 (10), 487 (32), 430 (13), 184 (40), 155 (40), 127 (12). − MS (Cl, NH_3): *m/z* (%) = [2 **16A**$^+$ + H]: 673 (17), 672 (15), 671 (35), 670 (18), 669 (36), 668 (12), 667 (29); [2 **16A**$^+$ − ethyl]: 645 (14), 644 (17), 643 (38), 642 (35), 641 (82), 640 (41), 639 (81), 638 (26), 637 (68); [**16A**$^+$ + H]: 338 (39), 337 (12), 336 (59), 335 (20), 334 (100); other signals: 976 (12), 974 (15), 972 (11), 767 (15), 766 (13), 765 (23), 764 (15), 763 (31), 762 (13), 761 (23), 759 (12), 549 (27), 548 (17), 547 (39), 546 (22), 545 (62), 243 (14), 242 (75); (FAB, NBA): *m/z* (%) = [2 **16A**$^+$ − ethyl]: 643 (0.1), 641 (0.3), 639 (0.3), 637 (0.3); [**16A**$^+$ + H]: 338 (1), 336 (2), 334 (3); [**16A**$^+$ − ethyl]: 306 (1), 304 (1); other signals: 243 (20), 242 (100), 224 (28), 185 (24), 184 (43). Calculated intensity distribution for [2 **16A**$^+$ − ethyl]: 647 (2), 646 (6), 645 (18), 644 (22), 643 (48), 642 (44), 641 (100), 640 (50), 639 (97), 638 (31), 637 (79).

Preparation, NMR Spectroscopy, and MS Analysis of **16B**: The synthesis followed the procedure described for the preparation of **16A**. 50 mg (0.21 mmol) of (*R*)-**6** in 1.7 ml of hexane and 1.1 ml of a 1 M solution of diethylzinc (1.1 mmol) were used. The colorless, air- and moisture-sensitive solid (45 mg) was isolated as described above. Attempts to recrystallize from hexane, cyclohexane, toluene,

Table 6. Crystal-structure determination data for **16A**

Formula $C_{18}H_{23}NOZn$; M_r = 334.7
a = 25.436(5), b = 10.255(2), c = 14.294(3) Å; β = 113.78(3)°, V = 3412.0(12) Å^3, Z = 8; monoclinic system; space group $C2/c$ (No. 15); μ(Cu-K_α) = 1.981 mm^{-1} (λ = 1.54178 Å); graphite monochromator; T = 293 K; 2Θ range: 6.8–110.0°, index range: $0 \le h \le 26$, $0 \le k \le 10$, $-15 \le l \le 13$; scan range (ω) = (1.40 + 0.35 tg Θ)°; max. scan time: 45.00 s; mode: ω 2141 independent reflections; 1814 reflections with $F > 4.0\sigma(F)$; 193 refined parameters; R = 0.0307; R_w = 0.028; $w^{-1} = \sigma^2(F) + 0.0000F^2$

Table 7. Fractional atomic coordinates (× 10^4) and equivalent isotropic displacement coefficients (× 10^3) [Å^2] for **16A**

	x	y	z	U(eq)[a]
Zn(1)	3034(1)	3309(1)	391(1)	38(1)
N(1)	3575(1)	1588(2)	969(2)	35(1)
O(1)	2563(1)	2301(2)	984(1)	36(1)
C(1)	3380(1)	863(3)	1543(2)	37(1)
C(2)	3639(1)	-332(3)	1946(2)	48(2)
C(3)	4117(2)	-723(3)	1802(3)	53(2)
C(4)	4323(1)	43(3)	1248(3)	51(2)
C(5)	4043(1)	1202(3)	815(2)	38(1)
C(6)	2877(1)	1397(3)	1744(2)	37(1)
C(7)	3069(1)	2009(3)	2829(2)	40(1)
C(8)	3370(2)	1035(3)	3682(2)	67(2)
C(9)	2531(1)	2476(4)	2945(3)	63(2)
C(10)	3465(1)	3173(3)	2955(3)	60(2)
C(11)	4245(1)	2021(3)	181(2)	40(1)
C(12)	4829(1)	2213(4)	449(3)	61(2)
C(13)	5022(2)	2961(4)	-143(3)	74(2)
C(14)	4637(2)	3528(4)	-1020(3)	62(2)
C(15)	4056(1)	3340(3)	-1311(3)	50(2)
C(16)	3860(1)	2591(3)	-711(2)	41(1)
C(17)	3347(2)	5097(3)	590(3)	64(2)
C(18)	3991(2)	5229(4)	1142(3)	84(2)

[a] Equivalent isotropic U defined as one third of the trace of the orthogonalized U_{ij} tensor.

and benzene mixtures, as well as from the pure solvents led to rapid decomposition. The NMR samples were prepared as described for **16A**; this complex was completely soluble. All spectra were recorded at room temp. ^{1}H-NMR data are listed in Table 3. – ^{13}C NMR ([D$_6$]benzene): δ = 2.5 (CH_2), 13.7 (CH_3), 26.5 (CH_3), 37.7 (C), 85.1 (CH), 121.0 (CH), 121.7 (CH), 128.7 (2 CH), 129.0 (2 CH), 129.8 (CH), 136.2 (CH), 139.2 (C), 157.9 (C), 166.5 (C). – MS (EI, 70 eV): *m/z* (%) = [2**16B**$^+$ – ethyl]: 645 (1), 644 (1), 643 (2), 642 (2), 641 (5), 640 (2), 639 (5), 638 (2), 637 (4); [**16B**$^+$ – *tert*-butyl]: 281 (3), 280 (24), 279 (10), 278 (36), 277 (9), 276 (63); other signals: 491 (15), 489 (22), 488 (11), 487 (36), 430 (10), 247 (21), 184 (100), 155 (54), 127 (20), 57 (25), 41 (21); (Cl, NH_3): *m/z* (%) = [2**16B**$^+$ + H]: (<1), higher associates not observed. Attempted analysis of **16B** by FAB MS (NBA) led to foaming indicating the decomposition of **16B**.

Crystal-Structure Determination[66]: Suitable crystals of **16A** were obtained after recrystallization from cyclohexane. A summary of the data collection and structure refinement parameters is given in Table 6. Table 7 contains the fractional atomic coordinates for **16A**.

CAS Registry Numbers

1a: 100-52-7 / **1b**: 104-88-1 / **1c**: 123-11-5 / **1d**: 111-71-7 / **1e**: 2100-17-6 / **1f**: 14371-10-9 / **1g**: 2579-22-8 / **1h**: 34160-40-2 / (*R*)-**2a**: 1565-74-8 / (*S*)-**2a**: 613-87-6 / (*R*)-**2a** (MPTA ester): 139342-08-8 / (*S*)-**2a** (MPTA ester): 139342-09-9 / (*R*)-**2b**: 110611-21-7 / (*R*)-**2b** (MPTA ester): 139199-67-0 / (*S*)-**2b** (MPTA ester): 139199-68-1 / (*R*)-**2c**: 105836-14-4 / (*S*)-**2c**: 73854-04-3 / (*R*)-**2c** (MPTA ester): 139199-69-2 / (*S*)-**2c** (MPTA ester): 139199-70-5 / (*R*)-**2d**: 61925-50-6 / (*S*)-**2d**: 61925-49-3 / (*R*)-**2d** (MPTA ester): 139199-71-6 / (*S*)-**2d** (MPTA ester): 139199-72-7 / (*S*)-**2e**: 139342-10-2 / *rac*-**2e**: 113579-78-5 / *rac*-**2e** (3,5-dinitrobenzoyl ester): 139199-73-8 / (*R*)-**2e** (MPTA ester): 139199-74-9 / (*S*)-**2e** (MPTA ester): 139199-75-0 / (*S*)-**2f**: 103729-97-1 / (*R*)-**2f** (MPTA ester): 139199-76-1 / (*S*)-**2f** (MPTA ester): 139199-77-2 / (*S*)-**2g**: 123762-09-4 / (*R*)-**2g** (MPTA ester): 123762-15-2 / (*S*)-**2g** (MPTA ester): 123762-16-3 / (*R*)-**2h**: 139199-78-3 / (*S*)-**2h**: 139199-79-4 / *rac*-**2h**: 139342-11-3 / *rac*-**2h** (3,5-dinitrobenzoyl ester): 139199-80-7 / (*R*)-**2h** (MPTA ester): 139242-27-6 / (*S*)-**2h** (MPTA ester): 139199-81-8 / (*R,R*)-**3**: 127049-50-7 / (*R,R*)-**4**: 127049-51-8 / **5**: 33674-96-3 / (*R*)-**6**: 138982-99-7 / (*S*)-**6**: 136859-86-4 / *rac*-**6**: 139163-57-8 / (*R*)-7: 138983-02-5 / (*S*)-**8**: 136859-87-5 / (*R*)-**9**: 139042-71-0 / (*S*)-**10**: 137569-58-5 / (*R*)-**11**: 127912-58-7 / (*R*)-**12**: 80459-03-6 / (*R*)-**13**: 138983-03-6 / (*R*)-**14**: 139199-82-9 / (*R*)-**15**: 138983-05-8 / **16A**: 139344-57-3 / **16B**: 139199-83-0 / Et_2Zn: 557-20-0 / EtBr: 74-96-4 / 2,6-dibromopyridine: 626-05-1 / propanal: 123-38-6 / 2,2′-bipyridine: 366-18-7

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