Pergamon

Tetrahedron: *Asymmetry* 9 (1998) 667–679

TETRAHEDRON: *ASYMMETRY*

Enantioselective addition of diethylzinc to aldehydes using novel axially chiral 2-aminomethyl-1-(2′-hydroxyphenyl)naphthalene catalysts[1]

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Received 22 December 1997; accepted 15 January 1998

Abstract

The synthesis of atropo-enantiomerically pure aminomethyl and hydroxymethyl substituted biaryls derivatives *M*-**2** and *M*-**3** (and, optionally, their enantiomers), by dynamic kinetic resolution of a racemic lactone precursor, is described. Their application as chiral catalysts in the asymmetric addition of diethylzinc to aldehydes leads to excellent enantiomeric ratios of up to 99:1 and high chemical yields.

1. Introduction

The discovery of asymmetric additions of diorganozinc reagents to aldehydes in the presence of catalytic amounts of chiral auxiliaries,[2] has initiated a search for other efficient chiral ligands for this type of reaction.[3] Besides β-amino thiols,[4] β-amino thiocarboxylates,[5] piperazines,[6] oxazaborolidines,[7] diols,[8,9] and titanium complexes,[10–12] especially *N*,*N*-dialkylated β-amino alcohols[3] like DBNE **1**[13,14] or DAIB **4**[15–17] have been used as chiral catalysts, often affording virtually enantiopure secondary alcohols. C_2-Symmetric axially chiral biaryl alcohols, however, often utilized as excellent chiral auxiliaries in asymmetric synthesis,[18] were found to give good ee's as alkylation catalysts only in polymeric forms,[19] in titanium complexes[12] or as biscarboxamides **6b**,[20] while with the cheap BINOL **6a** itself, no addition of diethylzinc to benzaldehyde was observed.[9]

With this background in mind we have started to develop a new class of catalysts, which combine the successfully used *N*,*O*- (or *O*,*O*-) functionalities with the biaryl axis as a stereogenic element. First efforts in this field by Chan et al. with the axially chiral pyridylphenol **5**, however, gave only moderate to good enantioselectivities.[21] In this paper we describe the directed synthesis of enantiopure 2-aminomethyl and

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0957-4166/98/$19.00
PII: S0957-4166(98)00020-2

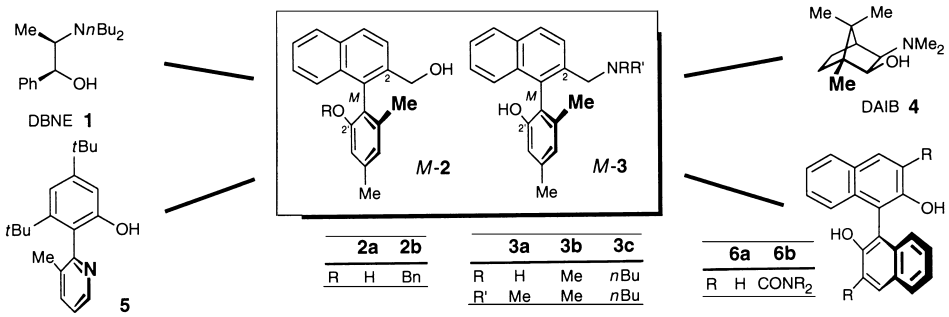


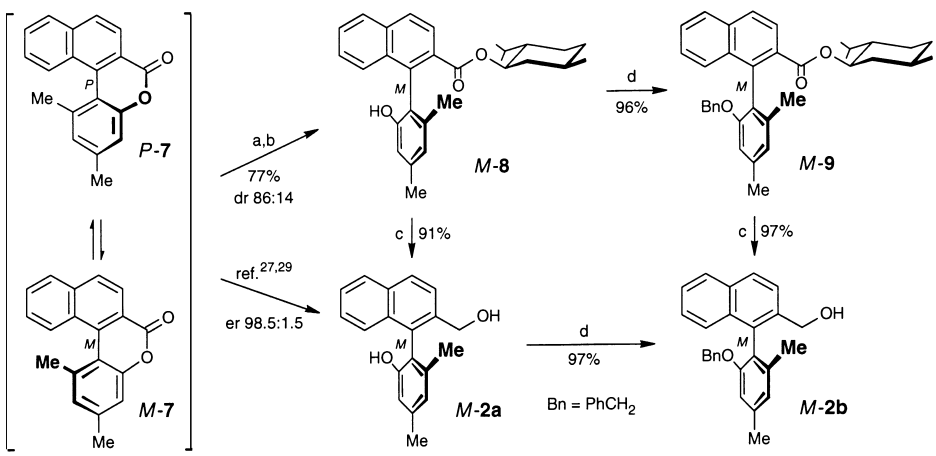
Fig. 1. The novel biaryls **2** and **3** as a combination of structural elements of known chiral ligands in asymmetric synthesis

2-hydroxymethyl substituted 1-(2′-hydroxy- or 2′-alkoxyphenyl)naphthalene derivatives *M*-**2** and *M*-**3**, and their use as chiral catalysts in the asymmetric addition of diethylzinc to aldehydes (Fig. 1).

2. Results and discussion

2.1. Synthesis of the catalysts

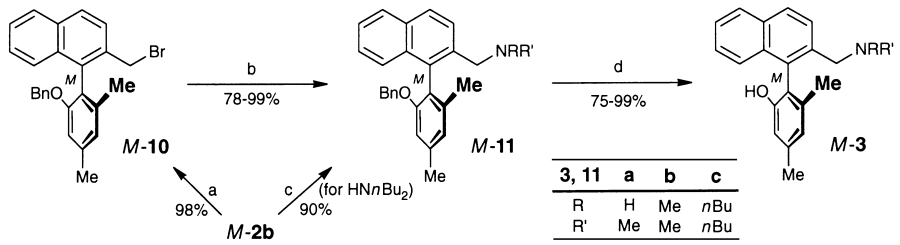
As an efficient access to enantiopure, *non* C_2-symmetric biaryl ligands, we chose the 'lactone methodology', previously developed in our group.[22,23] Key intermediates in this procedure are helically distorted, but configuratively unstable biaryl lactones like **7** (Scheme 1).[22,24] Easily prepared by intramolecular coupling,[25] they can be cleaved such that one of the (now configuratively stable) atropisomeric ring opened biaryl products is formed in high enantio- or diastereoselectivities — by dynamic kinetic resolution of the atropo-enantiomeric mixture, *P*-**7**⇌*M*-**7**.[22,26–30]



Scheme 1. Alternative pathways to *M*-**2b**, by atropo-diastereo- or -enantioselective cleavage of **7**. Reaction conditions: (a) NaH, 1*R*-menthol, diethyl ether, rt; (b) separation of diastereomers by column chromatography; (c) $LiAlH_4$, THF, rt; (d) BnBr, Cs_2CO_3, acetone, rt

An important intermediate in the synthesis of the envisaged catalysts is the biaryl alcohol *M*-**2a**. Instead of its preparation by highly atropo-enantioselective oxazaborolidine·BH_3 assisted reduction of **7** as described previously,[27,29] we preferred a two-step procedure by atropo-diastereoselective cleavage (dr 84:16) using 1*R*-menthol as a cheap reagent, allowing a facile separation from its (undesired) diastereomer. Subsequent reduction of stereochemically pure *M*-**8** gave enantiomerically homogeneous

M-**2a**. The minor *P*-configured diastereomer of *M*-**8** is not lost, but can be recycled into the process by cyclization back to **7**[22,23] — or can of course be used for the preparation of the enantiomeric reagents (likewise synthesized, but not shown in Schemes 1 and 2). Mono-*O*-benzylation of *M*-**2a** gave *M*-**2b**. Alternatively, *M*-**8** can first be benzylated to afford *M*-**9** and then be reduced. Despite the excellent yields thus obtained, the former route from *M*-**8** to *M*-**2b** via *M*-**2a** is preferable, due to the good crystallization properties of this diol, which allow an additional enantiomeric enrichment.[27,29]

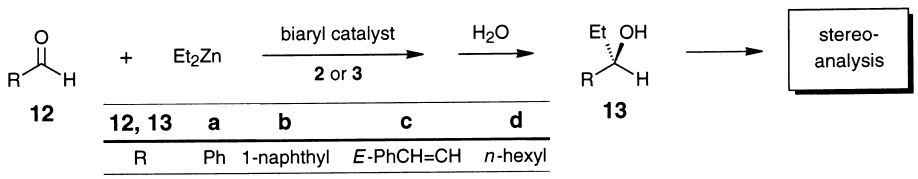


Scheme 2. Synthesis of the axially chiral amino alcohols *M*-**3a**, **b**, and **c**. Reaction conditions: (a) $(CCl_2Br)_2$, PPh_3, CH_2Cl_2, rt; (b) H_2NMe, $HNMe_2$, or $HNnBu_2$; (c) 1. NaH, $Ph(Me)NPPh_3^+I^-$, DMF, rt; 2. $HNnBu_2$, 80°C; (d) BCl_3, CH_2Cl_2, 0°C

The transformation of *M*-**2b** into the target biaryls, *M*-**3a**, **b**, and **c**, was straightforward, as shown in Scheme 2: Hydroxy–halogen exchange with $(CCl_2Br)_2/PPh_3$[31] gave *M*-**10**,[32,33] which was converted into *M*-**11a**, **b**, and **c**, respectively, by reaction in the amines as the solvents. Compound *M*-**11c** was also prepared directly from *M*-**2b**, after activation of the OH group with $Ph(Me)NPPh_3^+I^-$ (Murahashi's reagent),[34] but this route was practical only for the high-boiling $HNnBu_2$, because of the reaction temperatures needed. The resulting oils of *M*-**11a**, **b**, and **c** were converted into white powders by precipitation as hydrochlorides from diethyl ether:petroleum ether. Debenzylation gave the unprotected amino alcohols *M*-**3a**, **b**, and **c**. These enantiopure biaryls are thus accessible from the racemic lactone precursor **7** in five or six simple tranformations and good yields.

2.2. Application of the catalysts to the asymmetric addition of diethylzinc to aldehydes

In order to study the efficiency of the chiral biaryls as catalysts, we selected the asymmetric addition of diethylzinc to benzaldehyde **12a** in *n*-hexane at 20°C as a test reaction, using a 1:3:0.2 molar ratio for **12a**:diethylzinc:catalyst.[3] The enantiomeric ratio of the product, 1-phenyl-1-propanol **13a**, was determined by HPLC analysis on a Chiracel OD-H column (for conditions, see Experimental Section).



Scheme 3. The asymmetric addition of diethylzinc to the aldehydes **12**

In initial investigations, the biaryl alcohols *M*-**2** and the amino alcohols *M*-**3a** and *P*-**3b**, **c** were tested for their potentials as chiral catalysts. In contrast to the C_2-symmetric BINOL **6a**,[9] the dialcohol *M*-**2a** and its monobenzyl ether *M*-**2b** did catalyze the addition of diethylzinc to **12a** (see Table 1, entries 1–3 and Scheme 3). The er's of the product **13a**, however, were only moderate. 'Preheating' of the alcohol catalyst *M*-**2a** with 1.0 equivalents of diethylzinc according to Joshi et al.,[9] which should lead to a more rigid eight-membered cyclic monozinc dialkoxide structure and thus to more differentiated

diastereomeric transition states, gave slightly decreased asymmetric inductions, instead (entry 1 versus 2).

Table 1
Asymmetric addition of diethylzinc to benzaldehyde **12a** catalyzed by **2** and **3**

entry[a] No.	biaryl catalyst (20 mol%)	reaction time [h]	conversion[b]	configuration[c]	er[d] [%]
1	*M*-**2a**	48	*quant.*	*R*	79 : 21
2	*M*-**2a**[e]	16	*quant.*	*R*	76 : 24
3	*M*-**2b**	16	ca 50%	*R*	85 : 15
4	*M*-**3a**	16	ca 50%	*R*	86 : 14
5	*P*-**3b**	16	*quant.*	*S*	2 : 98
6	*P*-**3c**	16	*quant.*	*S*	1 : 99

[a]All reactions were performed in *n*-hexane at 20°C using a 1:3:0.2 molar ratio for **12a**:diethylzinc:catalyst. [b]Conversions were estimated by TLC. [c]Based on the sign of specific rotation for the known[35] compound **13a**. [d]Determined by HPLC analysis (Chiracel OD-H). [e]Equimolar amounts of *M*-**2a** and diethylzinc were 'preheated' for 1 h at 70-80°C, prior to the alkylation reaction.[9]

For the secondary amine *M*-**3a**, again a moderate enantiomeric ratio was obtained (entry 4). By contrast, the tertiary amines *P*-**3b** and *P*-**3c** gave excellent er's of up to 99:1 (entries 5 and 6). Earlier investigations by Soai et al. with *N*,*N*-dialkylnorephedrines[14] and by Noyori et al. with *N*,*N*-dialkylaminoisoborneols[17] as catalysts in the ethylation of **12a** had shown a strong dependence of the enantiomeric ratio on the substituents of the amino function. The optical purity of the product increased with the length of the *N*-alkyl chains, with an optimum chain length of four carbon atoms.[14] In accordance with that report the catalytic properties of the di-*n*-butyl amine *P*-**3c** were even better than those of the *N*,*N*-dimethyl compound *P*-**3b** (entry 5 versus 6).

Based on this promising first result with *P*-**3c**, the enantioselective addition of diethylzinc to **12a** catalyzed by *P*-**3c** was further optimized. Thus, reduction of the quantity of the catalyst *P*-**3c** showed that even with 2 mol% no major loss of selectivity occurred (Table 2, entries 1–4). Disadvantages like the required longer reaction times and the slightly diminished enantiomeric ratios were not observed when upscaling the reaction (see Table 3, entry 1). Both a change of the solvent from *n*-hexane to toluene (entry 5) and a variation of the temperature (entries 6 and 7) caused a decrease in enantiomeric excesses. In previous reactions with DPMPM [diphenyl(1′-methylpyrrolidin-2′-yl)methanol] as the catalyst, an increase in enantioselectivity had been observed if the lithium alkoxide was taken instead of the β-amino alcohol itself.[35] Deprotonation of *P*-**3c** with *n*-butyllithium, however, resulted in a strong decrease of the er (entry 8 versus 2). The addition of 0.50 equivalents of lithium chloride to the reaction mixture did not give rise to a significant salt effect on the asymmetric induction as found recently for some β-amino alcohols.[36,37]

In further investigations, the more easily available enantiomeric catalyst *M*-**3c** was used instead of *P*-**3c**, now resulting in *R*-**13a** as the main product in the asymmetric ethylation of benzaldehyde **12a**. In contrast to the remarkable nonlinear relationship in the addition of diethylzinc to **12a** catalyzed by DAIB **4**, which, in the presence of, *e.g.*, 8 mol% **4** of only 15% optical purity, led to **13a** in 95% ee,[3,16] a fully linear relationship was observed for the use of *M*-**3c** as the catalyst (Fig. 2). Apparently, *M*-**3c** does not form chemically stable, catalytically inactive *meso* zinc clusters as **4** does.

Finally, the use of *M*-**3c** as a catalyst in the addition of diethylzinc was extended to some other aldehydes (Table 3). All reactions were carried out under optimized conditions with 1.0 mmol aldehyde, 2 mol% catalyst, *M*-**3c**, and 2.0 equivalents of diethylzinc in *n*-hexane at 20°C. The crude products were

Table 2
Optimization of the ethylation of benzaldehyde **12a** with *P*-**3c** as the chiral catalyst, to give *S*-**13a**

entry[a] No.	*P*-**3c** [mol-%]	solvent	temperature [°C]	reaction time [h]	er[b] [%]
1[c]	20	*n*-hexane	20	16	1 : 99
2	10	*n*-hexane	20	16	1 : 99
3	5	*n*-hexane	20	48	3 : 97
4	2	*n*-hexane	20	72	3 : 97
5	10	toluene	20	16	4 : 96
6	10	*n*-hexane	0	16	4 : 96
7	10	*n*-hexane	40	16	9 : 91
8[d]	10	*n*-hexane	20	16	11 : 89
9[e]	10	*n*-hexane	20	16	2 : 98

[a]All reactions were performed using a 1:2 molar ratio for **12a**:diethylzinc. Conversions were estimated to be quantitative by TLC. [b]Determined by HPLC analysis (Chiracel OD-H). [c]3.0 equivalents of diethylzinc were used. [d]An equimolar amount of *n*-butyllithium was added to the catalyst. [e]0.50 equivalents of lithium chloride were added to the catalyst.

Table 3
Enantioselective addition of diethylzinc to aldehydes **12** catalyzed by 2.0 mol% of *M*-**3c**

entry[a] No.	aldehyde	yield[b] [%]	configuration[c]	er[d] [%]
1	**12a**	95	*R*	99 : 1
2	**12b**	98	*R*	98 : 2
3	**12c**	94	*R*	92 : 8
4	**12d**	88	*R*	96 : 4[f]

[a]All reactions were performed in *n*-hexane at 20°C for 16h using a 1:2:0.02 molar ratio for **12**:diethylzinc:catalyst *M*-**3c**. [b]Isolated yield after bulb-to-bulb distillation (conversion estimated by TLC: quantitative in all cases). [c]Based on the sign of optical rotation for the known[6b,35] compounds **13**. [d]Determined by HPLC analysis (Chiracel OD-H). [f]Determined by ^{19}F NMR spectroscopy after derivatization with *S*-Mosher acid chloride.[38]

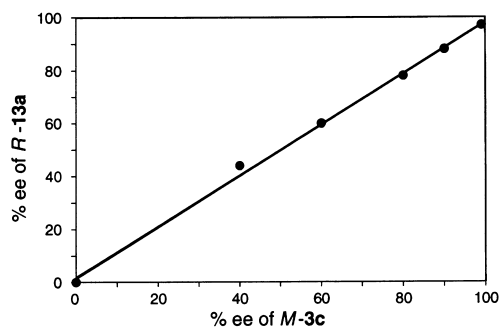


Fig. 2. Linear correlation between the ee's of the chiral auxiliary, *M*-**3c**, and the product, *R*-**13a**

purified by bulb-to-bulb distillation and the er's were analyzed by HPLC on a Chiracel OD-H phase or, for 3-nonanol **13d**, by ^{19}F NMR spectroscopy after esterification with *S*-Mosher acid chloride[38] (for conditions, see Experimental Section).

As illustrated in Table 3, *M*-**3c** catalyzed the asymmetric ethylation of various aldehydes **12**, giving the ethyl carbinols in more than 88% isolated yield, with high to excellent enantiomeric ratios of more than 92:8, even for the sometimes problematic[3] long-chain aliphatic aldehyde **12d**.

In conclusion, the novel axially chiral biaryl amino alcohols *M*-**3** prepared have been found to be efficient catalysts in the asymmetric addition of diethylzinc to aldehydes **12**. Especially *M*-**3c** catalyzes the ethylation of various aldehydes in high yields with excellent enantiomeric ratios of up to 99:1. Thus, *M*-**3c** represents the first *non* C_2-symmetric, *N*,*O*-functionalized chiral biaryl catalyst to give comparably good enantioselectivities as the well examined aliphatic β-amino alcohols. The preparation of further *non* C_2-symmetric axially chiral biaryls and the investigation of their use as catalysts in the addition of various other organozinc reagents to aldehydes, are in progress.

3. Experimental

Melting points were determined with an Kofler hot plate apparatus and are uncorrected. IR spectra were recorded on a Perkin–Elmer 1420 infrared spectrophotometer and are reported in wave numbers (cm^{-1}). ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectra were taken on a Bruker AC 200 (200 MHz), AC 250 (250 MHz) or AMX 400 (400 MHz). Chemical shifts are given in parts per million (ppm) with the deuterated solvent as an internal reference. Coupling constants, *J*, are given in hertz. In ^{13}C NMR spectra, sometimes not all quaternary Ar–C signals were detected due to their similar shifts and to their long T_1 relaxation times. Mass spectra were recorded on a Finnigan MTA 8200 spectrometer at 70 eV in the EI mode. Optical rotations were measured on a Perkin–Elmer 241 MC polarimeter. HPLC analyses were carried out with a combination of a Waters M 510 pump, a Chiracel OD-H column (Daicel Chem. Ind. Ltd, 4.6 mm×250 mm) and an ERC-7215 UV-detector.

Diethylzinc and *S*-Mosher acid chloride were purchased from Aldrich, 1*R*-menthol (>99% ee) from Fluka. All aldehydes were distilled before use and stored under argon. NaH was washed with pentane before use, gaseous methylamine and dimethylamine were prepared from the corresponding hydrochlorides with KOH in a small amount of water. THF was freshly distilled from potassium. Diethyl ether, toluene and *n*-hexane were distilled from sodium wire and stored over molecular sieves 4Å. All reactions were carried out with dry glassware under an argon atmosphere. The Schlenk tube technique was used for the asymmetric addition of diethylzinc to aldehydes.

*3.1. Atropo-diastereoselective ring opening of lactone **7** with sodium 1*R*-mentholate*

To 1*R*-menthol (5.06 g, 32.4 mmol) in diethyl ether (200 ml) NaH (778 mg, 32.4 mmol) was added cautiously at room temperature. After gas evolution had ended and a further 30 min of stirring, the lactone **7** (4.45 g, 16.2 mmol) was added to the cloudy reaction mixture, which was stirred until complete conversion was detected by TLC (petroleum ether:diethyl ether 1:1). Water (200 ml) was added carefully, the solution was acidified with 2 N HCl and extracted with diethyl ether (3×200 ml). The organic phase was dried over $MgSO_4$ and the solvent was removed *in vacuo*. Chromatographic separation of the residue on silica gel (petroleum ether:diethyl ether 30:1→3:1) yielded the diastereomeric menthyl esters *P*-**8** (1.08 g, 2.51 mmol, 15%, chromatographically more rapid) and *M*-**8** (5.39 g, 12.5 mmol, 77%,

chromatographically less rapid) as slightly yellow oils, which gave colorless crystals from petroleum ether:diethyl ether.

1′′*R*-Menthyl *P*-1-(2′-hydroxy-4′,6′-dimethylphenyl)-2-naphthoate *P*-**8**: mp 147–149°C; $[\alpha]_D^{20}$ −43.2 (*c* 0.31, EtOH); IR (KBr): ν 3300, 2940, 1650, 1600, 1310, 1130, 770; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.53–1.83 (m, 8H, menthyl H), 0.67 (d, *J*=6.7 Hz, 3H, menthyl CH_3), 0.81 (d, *J*=7.0 Hz, 3H, menthyl CH_3), 0.84 (d, *J*=6.7 Hz, 3H, menthyl CH_3), 1.76 (s, 3H, 6′-CH_3), 2.38 (s, 3H, 4′-CH_3), 4.45 (s, 1H, OH), 4.74 (dt, *J*=10.7 Hz, *J*=4.3 Hz, 1H, 1′′-H), 6.72 (s, 2H, 3′-H and 5′-H), 7.40–7.52 (m, 2H, Ar–H), 7.57 (m_c, 1H, Ar–H), 7.90–8.00 (m, 3H, Ar–H); ^{13}C NMR (63 MHz, $CDCl_3$): δ 16.04, 19.68, 20.83, 21.30, 22.00 (CH and CH_3), 23.14 (CH_2), 25.99, 31.22 (CH and CH_3), 34.19, 39.94 (CH_2), 46.70 (CH or CH_3), 75.21 (C-1′′), 113.8, 122.2, 123.0, 125.6, 126.5, 127.4, 127.8, 128.2, 128.7, 131.2, 132.5, 133.8, 134.9, 137.6, 138.8, 153.3 (Ar–C), 167.9 (C=O); MS: *m/z* (%) 430 (12) [M^+], 292 (35) [$M^+ - C_{10}H_{18}$ (menthene)], 274 (100) [$C_{19}H_{14}O_2^+$], 231 (6), 202 (5). Anal. calcd for $C_{29}H_{34}O_3$ (430.6): C, 80.83; H, 7.96. Found: C, 80.84; H, 7.74.

1′′*R*-Menthyl *M*-1-(2′-hydroxy-4′,6′-dimethylphenyl)-2-naphthoate *M*-**8**: mp 108°C; $[\alpha]_D^{20}$ −84.5 (*c* 0.30, EtOH); IR (KBr): ν 3400, 2940, 1690, 1560, 1450, 1270, 1130, 760; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.60–1.70 (m, 8H, menthyl H), 0.70 (d, *J*=7.0 Hz, 3H, menthyl CH_3), 0.81, 0.85 (d, d, *J*=7.0 Hz each, 3H each, menthyl CH_3), 1.80 (s, 3H, 6′-CH_3), 2.38 (s, 3H, 4′-CH_3), 4.45 (s, 1H, OH), 4.78 (dt, *J*=10.7 Hz, *J*=4.4 Hz, 1H, 1′′-H), 6.71, 6.74 (s, s, 1H each, 3′-H and 5′-H), 7.37–7.52 (m, 2H, Ar–H), 7.57 (m_c, 1H, Ar–H), 7.93 (d, *J*=7.9 Hz, 1H, Ar–H), 7.97 (m_c, 2H, Ar–H); ^{13}C NMR (63 MHz, $CDCl_3$): δ 15.88, 19.74, 20.94, 21.32, 21.97 (CH and CH_3), 22.93 (CH_2), 25.78, 31.25 (CH and CH_3), 34.16, 40.07 (CH_2), 46.75 (CH or CH_3), 75.10 (C-1′′), 113.6, 122.1, 122.9, 125.8, 126.6, 127.3, 127.8, 128.1, 128.6, 130.8, 132.5, 134.1, 135.0, 137.8, 138.7, 153.1 (Ar–C), 167.7 (C=O); MS: *m/z* (%) 430 (13) [M^+], 292 (36) [$M^+ - C_{10}H_{18}$ (menthene)], 274 (100) [$C_{19}H_{14}O_2^+$], 231 (6), 202 (5). Anal. calcd for $C_{29}H_{34}O_3$ (430.6): C, 80.83; H, 7.96. Found: C, 81.08; H, 8.25.

3.2. M-*1-(2′-Hydroxy-4′,6′-dimethylphenyl)-2-hydroxymethylnaphthalene* M-***2a***

$LiAlH_4$ (3.57 mg, 94.1 mmol) was added at room temperature cautiously to a solution of *M*-**8** (4.05 g, 9.41 mmol) in THF (100 ml). After 1 h of stirring the reaction mixture was hydrolyzed carefully with water (100 ml), acidified with 2 N HCl and extracted with diethyl ether (4×100 ml). The organic phase was dried over $MgSO_4$, the solvent was removed *in vacuo* and the remaining menthol was distilled off *in vacuo*. Chromatography of the residue on silica gel (petroleum ether:diethyl ether 4:1→1:2) afforded the alcohol *M*-**2a** (2.51 g, 9.02 mmol, 96%) as a slightly yellow oil, which gave colorless crystals from petroleum ether:diethyl ether (2.38 g, 8.55 mmol, 91%). HPLC analysis on a chiral phase [Chiracel OD-H, solvent: *n*-hexane:*i*-PrOH 95:5, detection at 280 nm, flow rate 1.0 ml/min: t_R=15 min (*M*), t_R=23 min (*P*)] gave >99.8:0.2 er. The spectroscopic data were identical to those of material previously obtained.[27,29]

Remark: Larger quantities of residual menthol, as remaining from the preparation of *M*-**8**, did not disturb the reduction, if $LiAlH_4$ was used in excess. Crystallization was found to be an excellent device for the conversion of enantiomerically enriched *M*-**2a** (er>95:5) into virtually enantiopure material (er>99.8:0.2).

*3.3. 1′′*R-*Menthyl* M-*1-(2′-benzyloxy-4′,6′-dimethylphenyl)-2-naphthoate* M-***9***

The menthyl ester *M*-**8** (1.01 g, 2.35 mmol), benzyl bromide (558 ml, 804 mg, 4.70 mmol) and Cs_2CO_3 (1.53 g, 4.70 mmol) were dissolved in acetone (50 ml) and stirred for 12 h at room temperature. The solvent was removed *in vacuo* and the residual benzyl bromide was distilled off *in vacuo*. Chromatography

on silica gel (petroleum ether:diethyl ether 10:1) resulted in *M*-**9** (1.17 g, 2.25 mmol, 96%) as a slightly yellow oil: $[\alpha]_D^{22}$ −58.6 (*c* 0.19, $CHCl_3$); IR (film): ν 3040, 2930, 2910, 2850, 1690, 1600, 1560, 1270, 1125, 1095, 765; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.55 (q, *J*=11.0 Hz, 1H, menthyl H), 0.64 (d, *J*=7.0 Hz, 3H, menthyl CH_3), 0.70–1.83 (m, 7H, menthyl H), 0.76 (d, *J*=6.7 Hz, 3H, menthyl CH_3), 0.80 (d, *J*=7.0 Hz, 3H, menthyl CH_3), 1.86 (s, 3H, 6′-CH_3), 2.40 (s, 3H, 4′-CH_3), 4.72 (dt, *J*=10.7 Hz, *J*=4.3 Hz, 1H, 1′′-H), 4.83, 4.89 (d, d, *J*=12.8 Hz each, 1H each, OCH_2Ph), 6.68, 6.79 (s, s, 1H each, 3′-H and 5′-H), 6.89 (m_c, 2H, Ar–H), 7.11 (m_c, 3H, Ar–H), 7.36 (m_c, 1H, Ar–H), 7.46–7.55 (m, 2H, Ar–H), 7.90 (d, *J*=8.5 Hz, 2H, Ar–H), 8.05 (d, *J*=8.5 Hz, 1H, Ar–H); ^{13}C NMR (63 MHz, $CDCl_3$): δ 15.95, 19.79, 20.85, 21.71, 22.05 (CH and CH_3), 23.02 (CH_2), 25.81, 31.19 (CH and CH_3), 34.27, 40.21 (CH_2), 46.81 (CH or CH_3), 69.69 (OCH_2Ph), 74.31 (C-1′′), 110.8, 123.2, 125.4, 126.0, 126.3, 126.4, 127.0, 127.2, 127.9, 128.0, 129.1, 132.5, 134.9, 137.5, 137.7, 137.9, 138.1, 156.0 (Ar–C), 167.7 (C=O); MS: *m/z* (%) 520 (4) [M^+], 382 (10) [$M^+-C_{10}H_{18}$ (menthene)], 275 (13) [$C_{19}H_{15}O_2^+$], 274 (35) [$C_{19}H_{14}O_2^+$], 107 (26) [$C_7H_7O^+$], 91 (100) [$C_7H_7^+$], 79 (21) [$C_6H_7^+$]; HR-MS: *m/z* calcd for $C_{36}H_{40}O_3$: 520.298. Found: 520.299.

3.4. M-*1-(2′-Benzyloxy-4′,6′-dimethylphenyl)-2-hydroxymethylnaphthalene* M-***2b***

From *M*-**2a**: In analogy to the benzylation of *M*-**8**, *M*-**2a** (2.00 g, 7.19 mmol) was stirred with benzyl bromide (1.70 ml, 2.46 g, 14.4 mmol) and Cs_2CO_3 (4.68 g, 14.4 mmol) in acetone (100 ml) for 12 h at room temperature. After removal of excessive benzyl bromide *in vacuo*, the residue was chromatographed on silica gel (petroleum ether:diethyl ether 10:1→1:1) to yield *M*-**2b** (2.57 g, 6.97 mmol, 97%) as a slightly yellow oil, the spectroscopic data of which were identical to material previously obtained.[28]

From *M*-**9**: *M*-**9** (1.17 g, 2.25 mmol) was reduced in THF (30 ml) at room temperature with $LiAlH_4$ (853 mg, 22.5 mmol) as described in the preparation of *M*-**2a**. After removal of the menthol *in vacuo*, chromatography of the residue on silica gel (petroleum ether:diethyl ether 4:1→1:1) afforded *M*-**2b** (805 mg, 2.19 mmol, 97%) as a slightly yellow oil.

3.5. M-*1-(2′-Benzyloxy-4′,6′-dimethylphenyl)-2-bromomethylnaphthalene* M-***10***

M-**2b** (600 mg, 1.63 mmol), PPh_3 (854 mg, 3.26 mmol) and $(CCl_2Br)_2$ (1.06 g, 3.26 mmol) were dissolved in dichloromethane (10 ml) and stirred for 30 min at room temperature. The solvent was removed *in vacuo* and the residue was chromatographed on silica gel (petroleum ether:diethyl ether 10:1) to yield in *M*-**10** (689 mg, 1.60 mmol, 98%) as a yellow oil: $[\alpha]_D^{23}$ −83.0 (*c* 0.1, EtOH); CD: $\Delta\varepsilon_{213}$ −135.5, $\Delta\varepsilon_{217}$ −117.7, $\Delta\varepsilon_{224}$ −157.3, $\Delta\varepsilon_{239}$ +194.0, $\Delta\varepsilon_{273}$ −0.5, $\Delta\varepsilon_{295}$ −64.1; IR (KBr): ν 3040, 3020, 2940, 2900, 2840, 1600, 1560, 1090, 815, 750; ^{1}H NMR (200 MHz, $CDCl_3$): δ 1.96 (s, 3H, 6′-CH_3), 2.46 (s, 3H, 4′-CH_3), 4.46, 4.50 (d, d, *J*=11.2 Hz each, 1H each, CH_2Br), 4.92, 4.99 (d, d, *J*=16.2 Hz each, 1H each, OCH_2), 6.78–7.00 (m, 4H, Ar–H), 7.14–7.20 (m, 3H, Ar–H), 7.32–7.56 (m, 3H, Ar–H), 7.71 (d, *J*=8.5 Hz, 1H, 3-H or 4-H), 7.90 (m, 1H, 8-H), 7.92 (d, *J*=8.5 Hz, 1H, 3-H or 4-H); ^{13}C NMR (50 MHz, CD_3OD): δ 19.98, 21.70 (CH_3 at C-4′ and CH_3 at C-6′), 33.14 (CH_2Br), 69.86 (OCH_2), 111.2, 123.4, 123.8, 126.1, 126.2, 127.2, 127.5, 128.0, 128.1, 132.5, 133.2, 133.4, 135.2, 137.4, 138.8, 156.2 (Ar–C); MS: *m/z* (%) 432/430 (6/6) [M^+], 351 (4) [M^+-Br], 260 (100) [$M^+-C_7H_7Br$], 245 (17). Anal. calcd for $C_{26}H_{23}BrO$ (431.4): C, 72.39; H, 5.37. Found: C, 71.99; H, 5.53.

Compound *P*-**10** was prepared analogously from *P*-**8** via *P*-**2b**.

3.6. General procedure A for the preparation of the benzylated amines M-**11** from M-**10**

A solution of *M*-**10** in dichloromethane (2–4 ml/mmol *M*-**10**) was added to the amine (for the primary amine H_2NMe, also 2.00 equivalents of the amine hydrochloride were added) and stirred until complete conversion was detected by TLC (deactivated silica gel, petroleum ether:acetone 6:1). The amine was removed (for $HNnBu_2$ *in vacuo*), the resulting oil was dissolved in diethyl ether and water (20 ml/mmol *M*-**10** each), alkalized with K_2CO_3 and exhaustively extracted with diethyl ether. The combined organic layers were dried over $MgSO_4$ and the solvent was removed *in vacuo*. For characterization, the resulting oily *M*-**11** was precipitated as a white solid from a solution in a little diethyl ether:petroleum ether 1:1, by passing HCl gas over the solution, and collected by filtration. A second crop was obtained by concentration of the mother liquor.

3.7. M-*1-(2′-Benzyloxy-4′,6′-dimethylphenyl)-2-(*N-*methylaminomethyl)naphthalene* M-**11a**

According to the general procedure A, *M*-**10** (2.12 g, 4.91 mmol) and $H_3NMe^+Cl^-$ (644 mg, 9.82 mmol) were added to H_2NMe (ca. 200 ml) in a three-necked flask with a dry ice condenser. After 1 h of stirring at room temperature, the solution was worked up, yielding *M*-**11a** (1.85 g, 4.85 mmol, 99%). For characterization a small amount *M*-**11a**·HCl was precipitated as a white solid: mp 82–87°C; $[\alpha]_D^{20}$ +20.4 (*c* 0.35, EtOH); IR (KBr): ν 3380, 3200–2200, 2920, 1595, 1555, 1440, 1085, 1065, 810, 740, 690; ^{1}H NMR (250 MHz, CD_3OD): δ 1.81 (s, 3H, 6′-CH_3), 2.44 (s, 6H, 4′-CH_3 and NCH_3), 3.92, 4.19 (d, d, *J*=13.5 Hz each, 1H each, CH_2N), 4.88, 5.00 (d, d, *J*=11.8 Hz each, 1H each, OCH_2), 6.75–6.79 (m, 2H, 3′-H and 5′-H), 6.93–7.14 (m, 5H, Ar–H), 7.30 (br. d, *J*=7.9 Hz, 1H, Ar–H), 7.43, 7.57 (m_c, 1H each, Ar–H), 7.64 (d, *J*=8.6 Hz, 1H, 3-H or 4-H), 7.99 (d, *J*=8.2 Hz, 1H, 8-H), 8.04 (d, *J*=8.6 Hz, 1H, 3-H or 4-H); ^{13}C NMR (63 MHz, CD_3OD): δ 19.86, 21.72 (CH_3 at C-4′ and CH_3 at C-6′), 33.03, 51.55, 71.47 (CH_2N, NCH_3 and OCH_2), 113.2, 124.1, 125.4, 126.2, 127.2, 128.0, 128.1, 128.8, 129.3, 129.4, 129.9, 133.8, 135.3, 138.1, 139.6, 141.3, 157.4 (Ar–C); MS: *m/z* (%) 381 (37) [M^+-HCl], 366 (14) [M^+-CH_4Cl], 350 (60) [M^+-CH_6ClN], 290 (100) [$M^+-C_7H_8Cl$], 259 (69) [$C_{19}H_{15}O^+$], 91 (30) [$C_7H_7^+$]; HR-MS: *m/z* calcd for $C_{27}H_{27}NO$: 381.209. Found: 381.210.

3.8. P-*1-(2′-Benzyloxy-4′,6′-dimethylphenyl)-2-(*N,N-*dimethylaminomethyl)naphthalene* P-**11b**

According to the general procedure A, *P*-**10** (800 mg, 1.85 mmol) was added to $HNMe_2$ (ca. 50 ml) in a three-necked flask with a dry ice condenser. After 30 min of stirring at room temperature, the solution was worked up and *P*-**11b**·HCl (621 mg, 1.44 mmol, 78%) was precipitated as a white solid: mp 89–91°C; $[\alpha]_D^{20}$ −23.7 (*c* 1.0, $CHCl_3$); IR (KBr): ν 3600–3100, 2920, 2880, 2750–2100, 1590, 1555, 1435, 1300, 1080, 1065, 805, 745, 690; ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.80 (s, 3H, 6′-CH_3), 2.41, 243 (s, s, 9H, 4′-CH_3 and $N(CH_3)_2$), 3.68, 3.96 (d, d, *J*=11.4 Hz each, 1H each, CH_2N), 4.83, 4.88 (d, d, *J*=13.4 Hz each, 1H each, OCH_2), 6.70–6.77 (m, 2H, Ar–H), 6.79, 6.85 (s, s, 1H each, 3′-H and 5′-H), 7.04–7.16 (m, 3H, Ar–H), 7.26–7.39 (m, 2H, Ar–H), 7.49 (m_c, 1H, Ar–H), 7.90 (d, *J*=8.2 Hz, 1H, 8-H), 7.96, 8.15 (d, d, *J*=8.5 Hz each, 1H each, 3-H and 4-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ 19.79, 21.71 (CH_3 at C-4′ and CH_3 at C-6′), 43.58 ($N(CH_3)_2$), 59.41, 70.08 (NCH_2 and OCH_2), 111.4, 123.5, 124.1, 126.1, 126.3, 126.4, 126.5, 127.6, 128.2, 128.2, 128.6, 132.3, 133.5, 136.6, 138.5, 139.2, 156.1 (Ar–C); MS: *m/z* (%) 395 (44) [M^+-HCl], 380 (14) [M^+-CH_4Cl], 350 (82) [$M^+-C_2H_8ClN$], 304 (24) [$M^+-C_7H_8Cl$], 259 (100) [$C_{19}H_{15}O^+$], 91 (22) [$C_7H_7^+$], 58 (11) [$C_3H_8N^+$]; HR-MS: *m/z* calcd for $C_{28}H_{29}NO$: 395.225. Found: 395.226.

3.9. P-*1-(2′-Benzyloxy-4′,6′-dimethylphenyl)-2-(*N,N-*di*-n-*butylaminomethyl)naphthalene* P-***11c***

According to the general procedure A, *P*-**10** (784 mg, 1.82 mmol) was dissolved in HN*n*Bu$_2$ (10 ml) and heated for 1 h at 120°C. Work up and precipitation gave *P*-**11c**·HCl (883 mg, 1.71 mmol, 94%) as a white solid: mp 65–68°C; $[\alpha]_D^{20}$ −29.0 (*c* 0.78, $CHCl_3$); IR (KBr): ν 3600–3100, 2940, 2700–2100, 1595, 1555, 1440, 1085, 730, 690; ^{1}H NMR (200 MHz, $CDCl_3$): δ 0.61–0.93 (m, 8H, 2 CH_2CH_3, CH_2CH_3), 1.14–1.63 (m, 6H, 3CH_2CH_2), 1.81 (s, 3H, 6′-CH_3), 2.44 (s, 3H, 4′-CH_3), 2.44–2.56 (m, 1H, NC*H*HCH_2), 2.75–2.93 (m, 3H, NC*H*HCH_2 and NCH_2CH_2), 3.90 (dd, *J*=13.2 Hz, *J*=7.1 Hz, 1H, C*H*HN), 4.28 (dd, *J*=13.0 Hz, *J*=4.8 Hz, 1H, CH*H*N), 4.81, 4.87 (d, d, *J*=11.9 Hz, 1H each, OCH_2), 6.62 (m_c, 2H, Ar–H), 6.82 (s, 2H, 3′-H and 5′-H), 6.99–7.23 (m, 3H, Ar–H), 7.31–7.40 (m, 2H, Ar–H), 7.52 (m_c, 1H, Ar–H), 7.93 (d, *J*=8.1 Hz, 1H, 8-H), 8.00 (d, *J*=8.7 Hz, 1H, 3-H or 4-H), 8.51 (d, *J*=8.6 Hz, 1H, 3-H or 4-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ 13.42 (2 CH_2CH_3), 19.79 (CH_3 at C-4′ or CH_3 at C-6′), 20.06 (2 CH_2CH_2), 21.64 (CH_3 at C-4′ or CH_3 at C-6′), 24.56, 25.50 (2 CH_2CH_2), 51.14, 52.64, 54.71 (2 NCH_2CH_2 and CH_2N), 70.29 (OCH_2), 111.6, 123.2, 124.2, 126.2, 126.4, 126.6, 127.1, 127.6, 128.2, 128.2, 128.9, 132.2, 133.6, 136.3, 138.5, 139.5, 156.0 (Ar–C); MS: *m/z* (%) 479 (28) [M^+−HCl], 436 (91) [$M^+-C_3H_8Cl$], 351 (34) [$M^+-C_8H_{19}ClN$], 260 (57) [$C_{19}H_{16}O^+$], 259 (100) [$C_{19}H_{15}O^+$], 91 (54) [$C_7H_7^+$]; HR-MS: *m/z* calcd for $C_{34}H_{41}NO$: 479.319. Found: 479.319.

3.10. M-***11c*** *From* M-***2b***

To *M*-**2b** (888 mg, 2.41 mmol) in DMF (20 ml), NaH (63.6 mg, 2.65 mmol) was added cautiously. After 30 min of stirring at room temperature, Ph(Me)N$PPh_3^+I^-$ (1.31 g, 2.65 mmol) was given to the solution, which was stirred again for 30 min. HN*n*Bu$_2$ (963 μl, 739 mg, 4.82 mmol) was dropped in via a syringe and the reaction mixture was heated for 2 h at 80°C. Water (50 ml) was added, the solution was extracted with diethyl ether (5×50 ml) and the organic phase was dried over $MgSO_4$. After removal of the solvent *in vacuo*, the residue was chromatographed on deactivated silica gel (7.5% NH_3, petroleum ether:diethyl ether 6:1) to yield *M*-**11b** (1.04 g, 2.17 mmol, 90%) as a yellow oil, along with unreacted starting material *M*-**2b** (44.5 mg, 121 μmol, 5%). For comparison of the NMR spectroscopic data of those with *P*-**11b**·HCl, a small amount of *M*-**11b** was converted into *M*-**11b**·HCl as described above.

3.11. *General procedure B for the debenzylation of the amines* ***11***

To a solution of the amine **11** in dichloromethane (10 ml/mmol **11**), 2.0 equivalents (3.0 equivalents for the amine hydrochlorides **11**·HCl) of a 1.0 M solution of BCl_3 in hexane were added at 0°C. After 40 min of stirring, the reaction mixture was hydrolyzed cautiously with water (15 ml/mmol **11**), made alkaline with K_2CO_3 and exhaustively extracted with dichloromethane. The combined organic layers were dried over $MgSO_4$ and the solvent was removed *in vacuo*. The resulting oily **3** was purified by chromatography.

3.12. M-*1-(2′-Hydroxy-4′,6′-dimethylphenyl)-2-(*N-*methylaminomethyl)naphthalene* M-***3a***

According to the general procedure B, *M*-**11a** (1.85 g, 4.85 mmol) in dichloromethane (50 ml) was debenzylated with 9.70 ml (9.70 mmol) of a 1.0 M BCl_3 solution. Chromatography on deactivated silica gel (7.5% NH_3, diethyl ether:methanol 100:0→5:1) and subsequent precipitation from dichloromethane:diethyl ether:pentane gave *M*-**3a** (1.40 g, 4.80 mmol, 99%) as a white solid: mp 199–203°C; $[\alpha]_D^{20}$ −13.8 (*c* 0.37, EtOH); IR (KBr): ν 3220, 2930, 2750, 2700, 1595, 1575, 1560, 1440, 1295, 810, 745; ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.67 (s, 3H, 6′-CH_3), 2.24 (s, 3H, 4′-CH_3), 2.33

(s, 3H, NCH_3), 3.68, 3.84 (d, d, J=12.2 Hz each, 1H each, CH_2N), 6.73, 6.91 (s, s, 1H each, 3′-H and 5′-H), 6.97 (br. s, 2H, NH and OH), 7.32 (m_c, 2H, Ar–H), 7.40–7.48 (m, 1H, Ar–H), 7.60, 7.78 (d, d, J=8.5 Hz each, 1H each, 3-H and 4-H), 7.79 (d, J=8.2 Hz, 1H, 8-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ 19.91, 21.24 (CH_3 at C-4′ and CH_3 at C-6′), 33.77 (NCH_3), 53.39 (CH_2N), 116.3, 122.2, 123.2, 126.3, 126.5, 126.7, 127.5, 128.0, 128.2, 129.4, 132.7, 133.8, 136.5, 138.0, 139.4, 154.4 (Ar–C); MS: *m/z* (%) 291 (58) [M^+], 276 (30) [M^+-CH_3], 260 (85) [$C_{19}H_{16}O^+$], 259 (100) [$C_{19}H_{15}O^+$], 245 (38), 215 (24); HR-MS: *m/z* calcd for $C_{20}H_{21}NO$: 291.162. Found: 291.163.

3.13. P-*1-(4′,6′-Dimethyl-2′-hydroxyphenyl)-2-(*N,N-*dimethylaminomethyl)naphthalene* P-***3b***

According to the general procedure B, *P*-**11b**·HCl (491 mg, 1.14 mmol) in dichloromethane (12 ml) was debenzylated with 3.41 ml (3.41 mmol) of a 1.0 M BCl_3 solution. Chromatography on deactivated silica gel (7.5% NH_3, petroleum ether:diethyl ether 2:1) afforded *P*-**3b** (261 mg, 1.86 mmol, 75%) as a slighty yellow oil: $[\alpha]_D^{20}$ +90.4 (*c* 0.82, $CHCl_3$); IR (KBr): ν 3500–2000, 3010, 2920, 2800, 1595, 1440, 1300, 1035, 835, 800; ^{1}H NMR (250 MHz, $CDCl_3$): δ 1.65 (s, 3H, 6′-CH_3), 2.25, 2.38 (s, s, 9H, 4′-CH_3 and $N(CH_3)_2$), 3.13, 3.74 (d, d, J=11.8 Hz each, 1H each, CH_2N), 5.30 (s, 1H, OH), 6.75, 6.86 (s, s, 1H each, 3′-H and 5′-H), 7.27–7.33 (m, 2H, Ar–H), 7.39–7.47 (m, 1H, Ar–H), 7.41 (d, J=8.2 Hz, 1H, 3-H or 4-H), 7.83 (d, J=8.5 Hz, 1H, 8-H), 7.85 (d, J=8.2 Hz, 1H, 3-H or 4-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ 20.14, 21.27 (CH_3 at C-4′ and CH_3 at C-6′), 44.34 ($N(CH_3)_2$), 63.29 (CH_2N), 118.7, 123.2, 125.7, 125.8, 126.3, 126.4, 127.2, 127.9, 128.2, 133.3, 133.3, 133.5, 136.5, 137.8, 138.7, 156.0 (Ar–C); MS: *m/z* (%) 305 (99) [M^+], 304 (17) [M^+-H], 290 (50) [M^+-CH_3], 260 (100) [$C_{19}H_{17}O^+$], 259 (88) [$C_{19}H_{16}O^+$], 245 (45), 58 (19) [$C_3H_8N^+$]. Anal. calcd for $C_{21}H_{23}NO$ (305.4): C, 82.58; H, 7.59; N, 4.58. Found: C, 82.19; H, 7.70; N, 4.29.

3.14. M-*1-(4′,6′-Dimethyl-2′-hydroxyphenyl)-2-(*N,N-*di-*n*-butylaminomethyl)naphthalene* M-***3c***

According to the general procedure B, *M*-**11c** (988 mg, 2.08 mmol) in dichloromethane (40 ml) was debenzylated with 5.20 ml (5.20 mmol) of a 1.0 M BCl_3 solution. Chromatography on deactivated silica gel (7.5% NH_3, petroleum ether:diethyl ether 8:1) gave *M*-**3c** (794 mg, 2.04 mmol, 99%) as a slighty yellow oil: $[\alpha]_D^{20}$ +15.8 (*c* 1.2, $CHCl_3$); IR (KBr): ν 3600–2100, 3010, 2930, 2840, 1595, 1440, 1300, 830, 805; ^{1}H NMR (250 MHz, $CDCl_3$): δ 0.61–0.93 (m, 6H, 2 CH_2CH_3), 1.10–1.50 (m, 8H, 4 CH_2CH_2), 1.65 (s, 3H, 6′-CH_3), 2.28–2.38 (m, 2H, NCH_2CH_2), 2.38 (s, 3H, 4′-CH_3), 2.55–2.68 (m, 2H, NCH_2CH_2), 3.31, 3.75 (d, d, J=11.9 Hz each, 1H each, CH_2N), 6.75, 6.83 (s, s, 1H each, 3′-H and 5′-H), 7.29–7.46 (m, 2H, Ar–H), 7.35–7.46 (m, 1H, Ar–H), 7.42 (d, J=8.2 Hz, 1H, 3-H or 4-H), 7.81 (d, J=8.5 Hz, 1H, 8-H), 7.85 (d, J=8.2 Hz, 1H, 3-H or 4-H); ^{13}C NMR (63 MHz, $CDCl_3$): δ 13.96 (2 CH_2CH_3), 20.11 (CH_3 at C-4′ or CH_3 at C-6′), 20.74 (2 CH_2CH_2), 21.24 (CH_3 at C-4′ or CH_3 at C-6′), 27.26 (2 CH_2CH_2), 52.39 (2 NCH_2CH_2), 58.82 (CH_2N), 119.1, 123.2, 125.7, 125.9, 126.3, 126.4, 126.9, 127.8, 128.8, 133.3, 133.4, 133.7, 136.5, 137.6, 138.5, 155.7 (Ar–C); MS: *m/z* (%) 389 (20) [M^+], 346 (50) [$M^+-C_3H_7$], 261 (100) [$C_{19}H_{17}O^+$], 246 (19). Anal. calcd for $C_{27}H_{35}NO$ (389.6): C, 83.24; H, 9.06; N, 3.60. Found: C, 82.59; H, 8.81; N, 3.61.

The analogous debenzylation of *P*-**11c**·HCl with 3.0 equivalents of a BCl_3 solution afforded the enantiomer *P*-**3c** in 86% yield: $[\alpha]_D^{20}$ −13.2 (*c* 1.0, $CHCl_3$).

*3.15. General procedure for enantioselective addition of diethylzinc to aldehydes **12** catalyzed by chiral biaryls*

According to the reaction conditions (see Tables 1–3), 2.00–20.0 mol% of the biaryl catalyst (0.050 M in the used solvent) were treated with 2.00–3.00 equivalents of diethylzinc (1.00 M in *n*-hexane) at room temperature. After 10 min of stirring the reaction mixture was adjusted to the given temperature and 1.00 equivalent of the aldehyde **12** (100 μmol for optimation reactions, 1.00 mmol for alkylation of various aldehydes) were added. Stirring was continued for 16–72 h, the reaction mixture was diluted with diethyl ether (5 ml), hydrolyzed carefully with 3 ml 2 N HCl, and extracted with diethyl ether (3×5 ml). After drying over $MgSO_4$, the solvent was removed *in vacuo*. For reactions described in Tables 1 and 2, the resulting secondary alcohol **13a** was only purified by TLC. In the other cases, the crude product was bulb-to-bulb distilled. Er's were determined by HPLC on chiral phase for aryl compounds [Chiracel OD-H, detection at 254 nm, flow rate 1.0 ml/min]: **13a** (solvent: *n*-hexane:*i*-PrOH 98:2): t_R=15 min (*S*), t_R=17 min (*R*); **13b** (solvent: *n*-hexane:*i*-PrOH 95:5): t_R=14 min (*S*), t_R=26 min (*R*); **13c** (solvent: *n*-hexane:*i*-PrOH 95:5): t_R=14 min (*R*), t_R=23 min (*S*). The absolute configurations were based on the sign of their known optical rotations[6b,35] or by ^{19}F NMR after derivatization[38] with *S*-Mosher acid chloride for **13d**.

Acknowledgements

This work has been supported by the Deutsche Forschungsgemeinschaft (SFB 347 'Selektive Reaktionen Metall-aktivierter Moleküle') and by the Fonds der Chemischen Industrie (research funds and a graduate research fellowship for M. B.). We gratefully acknowledge the help of Stephan Link for experimental assistance.

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